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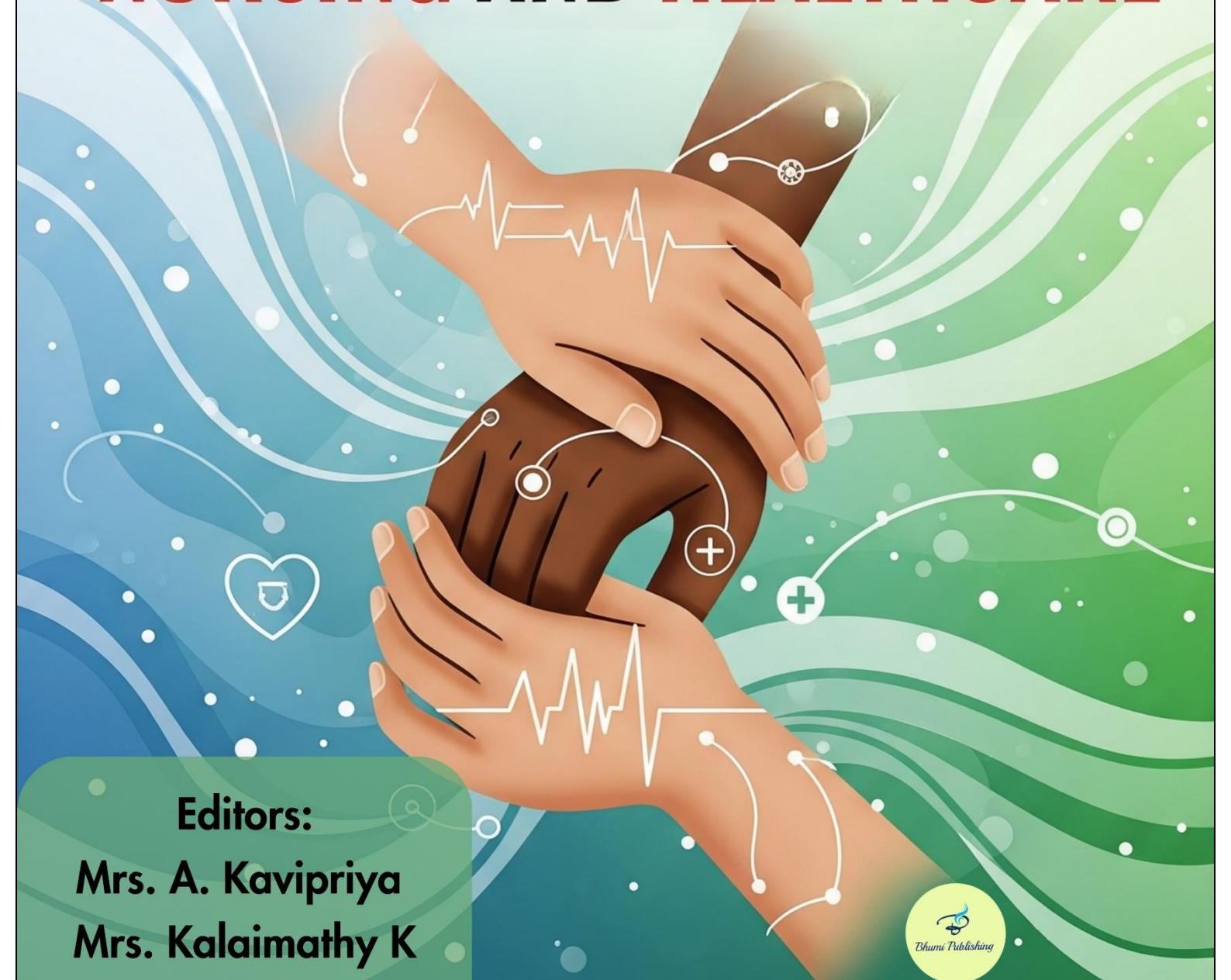
APPROACHES AND APPLICATIONS IN NURSING AND HEALTHCARE



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Approaches and Applications in Nursing and Healthcare

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PREFACE

The dynamic and ever-evolving field of nursing and healthcare demands continuous learning, innovation, and a deep commitment to patient-centered care. As healthcare systems worldwide face unprecedented challenges—from emerging diseases and aging populations to technological advancements and shifting care models—it becomes essential for healthcare professionals to adapt and evolve. Nurses, being at the forefront of patient care, play a pivotal role in ensuring effective, compassionate, and evidence-based health services.

Approaches and Applications in Nursing and Healthcare is a comprehensive compilation aimed at exploring the modern dimensions of nursing practice, healthcare delivery, and interdisciplinary collaboration. This book brings together a diverse range of topics that reflect both foundational principles and emerging trends in nursing and allied health sciences. It highlights practical applications, research-based practices, and innovative approaches that can enhance the quality of care and improve patient outcomes.

The chapters in this volume are contributed by experienced professionals, educators, and researchers from various domains of healthcare. Covering areas such as clinical nursing, community health, mental health, healthcare technologies, nursing education, patient safety, and holistic care, the book is designed to serve as both a practical guide and an academic resource. Special emphasis has been placed on the integration of theory and practice, ethical considerations, cultural competence, and the growing importance of interprofessional teamwork.

This book is intended for nursing students, faculty members, practicing nurses, allied health professionals, and policy-makers who are involved in shaping the future of healthcare. Whether used as a textbook or a reference resource, it aims to support the development of critical thinking, clinical decision-making, and professional competence in a variety of healthcare settings.

We hope that Approaches and Applications in Nursing and Healthcare will inspire its readers to explore new perspectives, adopt best practices, and contribute meaningfully to the advancement of health and well-being for individuals and communities alike.

- Editors

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RHODODENDRON:
BIOACTIVE COMPOUNDS AND PHARMACEUTICAL RELEVANCE

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Abstract:
The genus Rhododendron (family Ericaceae), comprising around 1,000 species globally, is recognized not only for its ornamental value but also for its rich repository of bioactive compounds with significant pharmacological potential. Distributed mainly in temperate Himalayan regions and Southeast Asia, several species particularly *R. arboreum*, *R. anthopogon*, and *R. campanulatum* have a longstanding history in Ayurvedic, Tibetan, and folk medicine for treating inflammation, cardiovascular ailments, infections, and respiratory disorders. Phytochemical studies reveal high concentrations of flavonoids, phenolic acids, terpenoids, anthocyanins, tannins, saponins, and essential oils, conferring antioxidant, anti-inflammatory, antimicrobial, neuroprotective, cardioprotective, and anticancer activities. Contemporary research underscores their potential in nutraceuticals, herbal formulations, cosmeceuticals, and advanced drug delivery systems, while also highlighting safety concerns linked to toxic grayanotoxins in certain species. Sustainable utilization requires standardization of extracts, toxicity mitigation, and validation through clinical trials. This chapter comprehensively reviews the taxonomy, morphology, phytochemistry, pharmacology, ethnobotanical uses, and pharmaceutical prospects of Rhododendron, emphasizing its dual role as a medicinal resource and a conservation priority in the face of habitat loss and overexploitation.

Keywords: Rhododendron, Bioactive compound, Antioxident, Himalayas, Traditional

Introduction:

The genus Rhododendron, part of the Ericaceae family, has approximately 1,000 species worldwide, predominantly found in the temperate zones of the Himalayas and Southeast Asia. Although mostly esteemed for their aesthetic appeal, several Rhododendron species possess considerable medicinal potential owing to their abundant phytochemical constituents, such as flavonoids, phenolic acids, terpenoids, essential oils, and saponins. Rhododendrons, historically utilized in Ayurvedic, Tibetan, and folk medicine for the treatment of inflammation, cardiovascular disorders, infections, and respiratory conditions, are currently the subject of contemporary pharmacological investigation.

This chapter offers a comprehensive examination of the botanical classification, morphology, phytochemical contents, and ethno botanical uses of Rhododendron species. It emphasizes

clinically confirmed pharmacological properties, including antioxidant, anti-inflammatory, antibacterial, neuro protective, cardio protective and anticancer actions. The pharmaceutical uses of Rhododendron, encompassing its incorporation into nutraceutical, herbal formulations, Cosmeceutical, and innovative drug delivery methods, are rigorously analyzed.

The epithet "Rhododendron" derives from the Greek words rhodon (rose) and dendron (tree), indicating its rose-like blossoms and arboreal structure. Historical records and ethnobotanical surveys demonstrate that several species of Rhododendron have been conventionally employed to address diseases including inflammation, gastrointestinal problems, cough, cold, headaches, and cardiovascular concerns. Indigenous populations in the Indian Himalayan area, particularly in Uttarakhand, Himachal Pradesh, and Sikkim, have historically concocted juices, infusions, and pastes from Rhododendron flowers and leaves for therapeutic purposes.

The analysis indicates that the Darjeeling and Sikkim Himalayas host almost one-third (34%) of all rhododendron species in India, although representing just 0.3% of the country's geographical area. India is home to 132 taxa of rhododendrons, comprising 80 species, 25 subspecies, and 27 variations.

Medicinal plants have constituted a cornerstone for medicinal interventions throughout human history. They remain crucial in contemporary healthcare by supplying raw ingredients for pharmaceutical research and underpinning several traditional treatments. The genus Rhododendron is notable for its numerous species and the variety of bioactive substances it generates.

Rhododendron is a substantial and botanically important genus in the family Ericaceae, consisting of about 1,000 species found in the temperate and subtropical areas of the Northern Hemisphere. The genus has notable diversity in the Himalayan area, Southeast Asia, China, and Japan, although species are also present in Europe and North America. These evergreen and deciduous shrubs or small trees are renowned for their vivid and appealing blossoms, rendering them favored in ornamental gardening. Beyond their visual appeal, Rhododendrons have been esteemed in traditional medicine for their diverse medicinal uses. Rhododendron arboreum, the national flower of Nepal and the state tree of Uttarakhand, is arguably the most renowned for its ethnomedicinal importance among other kinds. The vibrant red blooms are utilized as a delicacy in juices and chutneys and are said to possess cardioprotective and anti-inflammatory effects. Other species such as *R. Anthopogon* and *R. Campanulatum* has been utilized in Tibetan traditional medicine and aromatherapy.

Recent pharmacological research has substantiated several traditional assertions regarding Rhododendrons. Phytochemical analyses have demonstrated that these plants are abundant in bioactive components, including flavonoids, terpenoids, tannins, phenolic acids, and essential oils. These elements facilitate a range of therapeutic activities, encompassing antioxidant,

antibacterial, anti-inflammatory, hepatoprotective, and neuroprotective properties. The pharmacological potential has generated increasing interest within the scientific community to investigate Rhododendron species for drug discovery and nutraceutical development.

Nonetheless, despite their great therapeutic potential, several Rhododendron species confront risks from habitat degradation, overexploitation, and climate change. The conservation of these plants is essential for maintaining biodiversity and protecting the traditional knowledge systems dependent on them.

Botanical Description

2.1 Taxonomic Classification

The genus Rhododendron belongs to the family Ericaceae, which includes over 125 genera and more than 4,000 species globally. It is among the most varied genera of woody flowering plants. The genus Rhododendron is subdivided into many subgenera, sections, and subsections according to morphological, cytological, and molecular traits (Chamberlain *et al.,* 1996).

Taxonomic Classification:

• Kingdom: Plantae
• Division: Magnoliophyta
• Class: Magnoliopsida
• Order: Ericales
• Family: Ericaceae
• Genus: *Rhododendron L.*

The genus includes both azaleas (deciduous or evergreen shrubs characterized by smaller blooms and leaves) and real rhododendrons (typically possessing bigger leaves and frequently evergreen).

2.2 Morphological Attributes

Rhododendron species exhibit significant variation in size, from low-growing alpine varieties measuring just a few centimeters to towering trees that may attain heights of up to 20 meters. The majority are shrubs or little trees.

Foliage:

Generally organized in a spiral configuration around the stem.

The shape varies from oval to lanceolate to elliptic.

Leaf margins are typically whole; however, several species exhibit slightly serrated edges. Numerous species possess leathery, evergreen foliage including a waxy covering or indumentum (hairy layer) on the underside, which aids in minimizing water loss and deterring herbivory.

Flora: One of the most notable characteristics of Rhododendron is its bloom, which may be solitary or organized in dense clusters (inflorescences).The blooms are often bell-shaped, tubular, or funnel-shaped, featuring five lobes.

- Coloration varies significantly among species, with typical hues including white, yellow, pink, red, purple, and multicolored variants.
- Numerous species have patterns or blotches inside the corolla, potentially functioning to attract pollinators.
- The flowers are predominantly bisexual, possessing both stamens and pistils, however unisexual blooms are often seen.

Fruits and Seeds:

The fruit is often a dry capsule that longitudinally dehisces to disperse countless diminutive seeds.

Seeds possess a lightweight and frequently winged structure, facilitating dissemination by wind.

In several high-altitude species, vegetative reproduction via layering or root suckers is prevalent.

2.3 Anatomical Characteristics

Rhododendron species have anatomical modifications that are conducive to cold, wet, and nutrient-deficient habitats.

• **Leaf Anatomy:** Robust cuticle, prominent palisade layer, and stomata mostly located on the abaxial (lower) surface.

• **Stem Anatomy**: The wood exhibits widespread porosity with dispersed vessels, and certain species possess resin canals.

• **Root System:** Typically, shallow yet extensively spreading to optimize nutrient absorption in acidic, organic-rich soils.

2.4 Distribution and Habitat

Rhododendron is mostly found in the temperate zones of the Northern Hemisphere, particularly in:

- **Asia:** The Himalayas, China, Japan, Korea, and Southeast Asia, particularly Myanmar and Vietnam.
- **Europe:** Western and Central Europe (e.g., *R. ponticum* in the Balkans and Turkey).
- **North America:** The Appalachian area, the Pacific Northwest, and the Rocky Mountains.
- The Eastern Himalayas and Southwest China (Yunnan, Sichuan, Tibet) are recognized as hotspots of variety, with over 600 species.

Habitat Preferences:

- Flourish on acidic soils (pH 4.5–6.0) that are abundant in organic materials.
- Prefer temperate, humid environments with sufficient shade or dappled sunshine.
- Frequently located in cloud forests, alpine meadows, and subalpine thickets.
- Numerous species are adaptable to elevated elevations (1,500–4,500 m), frequently constituting the predominant understory shrubs in temperate forests.

2.5 Ecological Importance

Rhododendron is essential to mountain and alpine environments.

- Offers habitat and sustenance for various insects (such as bees and butterflies), avians, and mammals.
- Facilitates pollination networks by co-evolution with certain pollinators (e.g., bumblebees and sunbirds).
- Aids in the prevention of soil erosion on steep inclines via its robust root systems.
- Serves as an indicator species for ecological integrity and biodiversity in highland ecosystems.

2.6 Cytological and Genetic Attributes

The majority of Rhododendron species has a fundamental chromosomal number of n = 13. Ploidy levels differ, with documented diploid, tetraploid, and hexaploid species. The genus has considerable genetic diversity owing to:

- Natural hybridization, particularly in overlapping geographic distributions.
- Significant evolutionary diversification in secluded highland areas.
- Genetic mutations influencing variances in floral color and form.
- Molecular phylogenetic analyses utilizing chloroplast and nuclear DNA sequences have shown the evolutionary links of subgenera and sections (Goetsch *et al.,* 2005).

2.7 Taxonomy within the Genus

The genus Rhododendron is categorized into many subgenera according to morphological and genetic data.

- ✓ **Subgenus Rhododendron** - lepidote (scaly) rhododendrons.
- ✓ **Subgenus Hymenanthes** – elepidote (non-scaly) rhododendrons.
- ✓ **Subgenus Tsutsusi** - encompasses both evergreen and deciduous azaleas.
- ✓ **Subgenus Pentanthera** - deciduous azaleas.
- ✓ **Subgenus Therorhodion** – an ancestral lineage (e.g., *R. camtschaticum*).

Each subgenus exhibits ecological and morphological adaptations tailored to particular ecosystems, rendering classification an effective instrument for conservation and breeding initiatives.

Conventional and Ethno botanical Applications

The medicinal application of Rhododendron in traditional medicine is extensively recorded among indigenous populations in India, Nepal, Bhutan, and China. The predominant species utilized are *Rhododendron arboreum, Rhododendron anthopogon*, and *Rhododendron campanulatum.*

In the Indian Himalayas, the petals of *R. Arboreum* are utilized to produce a traditional drink purported to alleviate hypertension and inflammation (Kala, 2005). In Tibetan medicine, R. Anthopogon is utilized as a fumigant for spiritual purification and as a herbal infusion to address respiratory disorders (Negi *et al.,* 2011). The foliage of several species is utilized topically for its analgesic and antibacterial properties.

Communities in Uttarakhand and Sikkim manufacture Rhododendron pastes for the treatment of headaches and skin ailments. The powdered petals are ingested to mitigate diarrhea and dysentery. These traditions have been transmitted over centuries, embodying profound ecological and therapeutic wisdom.

In Tibetan medicine, the herb is utilized to equilibrate physiological energy and address headaches and respiratory disorders. Additionally, traditional healers in Nepal utilize rhododendron infusions for gastrointestinal ailments and fever. These ethnobotanical uses underscore the cultural importance and medicinal potential of the plant.

3. Phytochemical Components

The therapeutic properties of Rhododendron species mostly stem from their abundant phytochemical composition. Bioactive chemicals differ by species, geographic location, and plant component, with leaves and flowers often exhibiting the greatest quantities.

i. Flavonoids

Rhododendron is rich in flavonoids, including quercetin, kaempferol, and rutin. These chemicals demonstrate antioxidant, anti-inflammatory, and anti-carcinogenic properties. Quercetin is recognized for its ability to diminish oxidative stress and modulate inflammatory pathways.

ii. Phenolic Acids

Phenolic acids such as gallic acid and caffeic acid are present in the leaves and flowers. They provide antibacterial and neuroprotective benefits. Gallic acid exhibits significant antimicrobial properties and promotes brain function by mitigating oxidative damage.

iii. Triterpenoids and Steroids

Ursolic acid and oleanolic acid, present in roots and bark, have anti-inflammatory and hepatoprotective benefits. Ursolic acid is specifically investigated for its anticancer properties by affecting apoptosis in tumor cells.

iv. Essential Oils and Volatile Compounds

Essential oils extracted from Rhododendron encompass aromatic components including α-pinene and limonene, which provide antibacterial, insecticidal, and moderate sedative properties.

v. Anthocyanins and Tannins

The crimson pigments in R. Arboreum flowers are abundant in anthocyanins, such as cyanidin-3-glucoside, which confer antioxidant and cardioprotective advantages. Tannins, mostly found in bark and leaves, are utilized for their astringent and digestive properties.

vi. Saponins and Alkaloids

Saponins in some Rhododendron species are esteemed for their immune stimulatory and expectorant properties. Certain species also possess alkaloids, which can be harmful at elevated quantities, particularly grayanotoxins that impact the neurological system.

4. Overview of Phytochemical Diversity

Compound Classification Representative Examples Pharmacological Effects

- ✓ **Flavonoids:** Quercetin, Kaempferol; properties include antioxidant, anti-inflammatory, and anti-cancer effects.
- ✓ **Phenolic acids:** Gallic acid, Caffeic acid; Antimicrobial and neuroprotective properties.
- ✓ **Triterpenoids:** Ursolic acid, Oleanolic acid; Hepatoprotective, anticancer properties.
- ✓ **Essential oils:** Limonene, Linalool; Properties: Antimicrobial, Sedative
- ✓ **Anthocyanins:** Cyanidin-3-glucoside; has antioxidant and cardioprotective properties.
- ✓ **Tannins:** Hydrolyzable tannins exhibit anti-diarrheal and astringent properties. Saponins Immunomodulatory, anti-inflammatory. Alkaloids (Present in certain species) exhibit CNS effects and possible toxicity.

5. Pharmacological Characteristics

The genus Rhododendron has garnered significant interest from pharmacologists and natural product researchers because of its many bioactive chemicals. Multiple investigations have corroborated the pharmacological properties of numerous Rhododendron species, consistent with their traditional therapeutic use. The subsequent subsections encapsulate the principal pharmacological attributes substantiated by in vitro, in vivo, and restricted clinical investigations.

5.1 Antioxidant Efficacy

Multiple species, including R. Arboreum are abundant in polyphenols, flavonoids, and anthocyanins, which have potent antioxidant properties. These chemicals neutralize free radicals, diminish oxidative stress, and impede lipid peroxidation. Flower extracts, especially those rich in quercetin and cyanidin derivatives, exhibit significant DPPH and ABTS radical scavenging capabilities, indicating their potential in mitigating oxidative stress-related illnesses, including atherosclerosis, dementia, and cancer.

5.2 Anti-inflammatory Properties

Extracts from Rhododendron ponticum, R. arboreum, and R. Anthopogon has demonstrated considerable anti-inflammatory efficacy in many models. Ursolic acid, oleanolic acid, and flavonoids such as kaempferol are recognized for their ability to suppress pro-inflammatory cytokines like TNF-α, IL-1β, and IL-6. Rhododendron is a potential natural agent for chronic inflammatory disorders, including arthritis and colitis.

5.3 Antimicrobial Characteristics

Various varieties of Rhododendron have antibacterial properties against a wide range of bacteria and fungi. Methanolic extracts of R. Arboreum flowers and leaves suppress Gram-positive bacteria such as Staphylococcus aureus and Bacillus subtilis, in addition to fungal strains like Candida albicans. Phenolic acids and essential oils damage microbial membranes and impede microbial development.

5.4 Cardioprotective Effects

The juice of the arboreum flower, often eaten in the Himalayan area, has been recorded in animal experiments. The effects are ascribed to polyphenols that enhance endothelial function, lower lipid levels, and regulate blood pressure. Certain substances may suppress platelet aggregation, hence decreasing the risk of thrombosis.

5.5 Neuroprotective and Antidepressant Properties

Recent research indicates that the antioxidant and anti-inflammatory properties of Rhododendron phytochemicals may save neurons from harm. Certain extracts improve cognitive function and have antidepressant-like effects in mouse models, perhaps via modulating monoamine neurotransmitters and reducing neuroinflammation.

5.6 Antineoplastic Activity

Initial data suggest that certain triterpenoids and flavonoids in Rhododendron species can trigger apoptosis and suppress proliferation in cancer cell lines, including breast, colon, and liver malignancies. These effects transpire through mitochondrial-mediated pathways and the control of oxidative stress; nevertheless, further thorough research are necessary to substantiate therapeutic potential in people.

6. Pharmaceutical Characteristics

The varied phytochemical composition and biological activity of Rhododendron species have generated heightened interest in their prospective medicinal uses. The medicinal potential of Rhododendron is significant due to its many natural chemicals with therapeutic applications, many of which have been utilized in traditional medicine and are currently being investigated via contemporary pharmacological research.

6.1 Potential as Natural Pharmaceutical Candidates

The phytoconstituents of Rhododendron, including flavonoids, terpenoids, saponins, phenolic acids, and essential oils, are recognized for their bioactive properties. These chemicals function as significant chemical templates or lead molecules for pharmaceutical development. For instance, flavonoids like as quercetin and kaempferol, present in R. Arboreum and R. Ponticum has exhibited considerable anti-inflammatory, antioxidant, and anticancer properties, which may be utilized in the formulation of novel medicines.

6.2 Phytotherapeutic Preparations and Nutraceuticals

In areas like as India and Nepal, commercial products like Buransh juice—derived from R. Arboreum flowers are promoted for cardiovascular health, as energy tonics, and for their cooling effects. These concoctions, although not standardized pharmaceutical medications, are classified as nutraceuticals, enhancing the expanding herbal supplement sector. Such compounds has significant potential to develop into recognized phytopharmaceuticals with proper standardization and clinical validation.

6.3 Pharmaceutical Dosage Forms

While Rhododendron has not been extensively utilized in contemporary pharmacological dosage forms, initial research has been conducted on its incorporation into ointments, gels, and pills. Topical preparations using Rhododendron anthopogon essential oil have demonstrated notable antibacterial and anti-inflammatory properties. Similarly, extracts have been evaluated for inclusion in oral capsules and lozenges, intended for the treatment of respiratory and throat infections.

6.4 Cosmeceutical Efficacy

In addition to therapeutic uses, Rhododendron extracts have significant potential in the cosmeceutical sector. The elevated concentrations of antioxidants and anti-inflammatory agents found in the plant's flowers and leaves have resulted in their inclusion in skin-care formulations. These extracts, particularly those abundant in phenolic acids and flavonoids, are thought to counteract reactive oxygen species (ROS), which cause cellular damage that contributes to aging and skin deterioration. Formulations derived from Rhododendron have been promoted for their anti-aging effects and their ability to shield the skin from detrimental UV radiation. The skincare business is increasingly focusing on these characteristics derived from natural sources for anti-aging solutions.

6.5 Pharmaceutical Delivery Mechanisms

A significant achievement in Rhododendron research is its application in contemporary medication delivery methods, especially nanoformulations. Phytochemicals such as quercetin, which are prevalent in R. Arboreum has been encapsulated in liposomes to augment its bioavailability, facilitate delayed release, and boost its stability. This innovative technique guarantees the regulated delivery of active substances, resulting in extended therapeutic benefits. Furthermore, encapsulation can safeguard these chemicals from destruction during digestion, therefore improving their absorption in the gastrointestinal system. Advancements in delivery systems may be crucial for creating extremely effective medicinal medicines derived from Rhododendron.

6.6 Toxicity and Safety Considerations

Notwithstanding their medicinal potential, the pharmacological use of Rhododendron species necessitates meticulous evaluation of toxicity profiles. Specific species, notably R. *Rhododendron ponticum* and *R. Luteum* contains grayanotoxins, chemicals recognized for inducing poisoning symptoms such as nausea, hypotension, and arrhythmias when consumed in excessive amounts. These toxicological issues require comprehensive assessment of acceptable dose limits and suitable extraction techniques that remove or reduce harmful components.

6.7 Prospective Pharmaceutical Applications

The increasing interest in green and natural treatments positions the pharmacological components of Rhododendron as promising prospects for future drug development. Investigations aimed at improving bioavailability, facilitating targeted delivery, and promoting synergistic effects with synthetic pharmaceuticals can further realize the therapeutic potential of Rhododendron-derived products, particularly in addressing chronic conditions such as cardiovascular disease, neurodegeneration, and cancer.

7.0 Toxicological and Safety Assessments

Although Rhododendron species possess considerable medicinal promise, their toxicity profile warrants careful consideration. The most hazardous substances in Rhododendron are grayanotoxins, which can cause severe health complications if ingested in substantial amounts. These toxins impact sodium channels in cellular membranes, resulting in symptoms such as dizziness, hypotension, nausea, and arrhythmias in extreme instances. The use of honey derived from the nectar of Rhododendron flowers, commonly known as "mad honey," has historically been linked to poisoning cases.

7.1 Grayanotoxins and Their Toxicity

Grayanotoxins are neurotoxic compounds found in many species of Rhododendron, including *R. R. ponticum luteum*, and *R. utmost*. These poisons may result in severe health consequences if ingested in substantial quantities. Notwithstanding this, Rhododendron compounds continue to be investigated for their therapeutic capabilities, with a focus on guaranteeing safety through appropriate preparation and dose.

7.2 Secure Dosage and Standardization

To ensure the safe therapeutic use of Rhododendron, it is important to separate non-toxic components and standardize extracts to reduce toxicity risk. Improvements in phytochemical extraction methods have facilitated the development of safer formulations by eliminating hazardous contaminants. Continued research is essential for establishing safe dose ranges, with certain animal studies offering insights into possible therapeutic amounts. Nonetheless, more clinical studies are required for validation.

7.3 Toxicological Assessment and Clinical Evaluations

Thorough toxicological evaluation in animal models and cell cultures is essential to determine the safety of Rhododendron products. Moreover, clinical trials are crucial for assessing the long-term safety of these drugs in people. Preliminary findings from first clinical investigations are encouraging; nevertheless, bigger, rigorously controlled trials are necessary to comprehensively assess the safety and effectiveness of Rhododendron formulations.

7.4 Secure Application in Herbal Products

The prudent utilization of Rhododendron in herbal formulations necessitates rigorous quality assurance to avert harmful contamination. Regulatory authorities must formulate standards for the formulation and promotion of Rhododendron-derived products, guaranteeing their safety and efficacy for consumer utilization.

8. Contemporary Medical Applications

The pharmacological potential of Rhododendron species has garnered heightened interest in contemporary medicine and phytotherapy. Historically acknowledged in conventional systems for their medicinal attributes, several species are currently being scientifically investigated for their bioactive constituents and therapeutic effectiveness.

8.1 Nutraceuticals and Herbal Preparations

Extracts of Rhododendron arboreum and R. Anthopogon is being integrated into nutraceuticals because of its abundant flavonoids, phenolics, and antioxidants (Kumar & Sharma, 2017). These natural chemicals mitigate free radicals and safeguard against oxidative stress, a recognized contributor to chronic illnesses such as cancer, cardiovascular disorders, and neurological conditions (Singh & Kaur, 2018).

8.2 Cardiovascular Well-being

A particularly potential use lies within the realm of cardiovascular health. Research on R. Arboreum flower extracts have antihypertensive and hypocholesterolemic properties. Flavonoids, especially quercetin and rutin, are recognized for their ability to improve endothelial function, decrease arterial stiffness, and reduce blood cholesterol levels (Bhatt *et al.,* 2010). In animal models, extracts have demonstrated the ability to enhance cardiac output and diminish the likelihood of myocardial injury.

8.3 Anti-inflammatory and Analgesic Products

Rhododendron chemicals are being investigated for their potent anti-inflammatory properties for potential use in topical formulations and analgesic creams (Baruah & Saikia, 2015). Ursolic acid and other terpenoids decrease inflammatory indicators such as TNF-α and IL-6, which are pivotal in illnesses including arthritis and chronic inflammation.

8.4 Antimicrobial and Antifungal Compounds

Essential oils and ethanol extracts from many species have antibacterial efficacy against both Gram-positive and Gram-negative bacteria, in addition to exhibiting antifungal characteristics. The attributes of Rhododendron derivatives render them suitable for application in organic antiseptics, oral hygiene formulations, and natural preservatives (Singh & Kaur, 2018).

8.5 Dermatological and Aesthetic Applications

The anti-aging and anti-inflammatory properties of Rhododendron render it appropriate for use into skincare formulas. Polyphenols, including gallic acid, can safeguard the skin from UV-induced injury and inhibit collagen breakdown, rendering them effective components in anti-aging lotions and sunscreens (Kumar & Sharma, 2017).

8.6 Prospective Antineoplastic Applications

Despite still in pre-clinical phases, research suggests that some Rhododendron species may exhibit anti-cancer capabilities by inducing apoptosis and inhibiting the development of cancer cells. The flavonoids and phenolic acids found in these species are being assessed for cytotoxicity against cancer cell lines (Bhatt *et al.,* 2010).

9. Conclusions and Future aspect:

The genus Rhododendron possesses considerable medicinal potential owing to its many bioactive components, such as flavonoids, phenolic acids, saponins, and terpenoids. These chemicals provide a diverse array of therapeutic advantages, including antioxidant, anti-inflammatory, antibacterial, anticancer, and cardioprotective properties. The toxicity linked to certain Rhododendron species, especially grayanotoxins, presents a barrier to their wider medical application. Consequently, isolating non-toxic chemicals and establishing safe doses are essential stages in maximizing its potential.

Future investigations should prioritize the standardization of Rhododendron extracts and the examination of its pharmacokinetics, bioavailability, and mechanisms of action via human clinical studies. Such studies are crucial for delineating explicit safety and effectiveness profiles. Furthermore, Rhododendron exhibits potential in the cosmetic and Cosmeceutical sectors owing to its antioxidant and anti-inflammatory attributes, which may be utilized in skincare formulations aimed at combating aging and providing UV protection.

The plant's potential for combinatorial medicines necessitates more investigation. Certain phytochemicals from Rhododendron may augment the effectiveness of conventional medications, mitigate adverse effects, or promote bioavailability, especially in chronic ailments such as cancer and cardiovascular illnesses. Furthermore, advanced drug delivery technologies, including nanoformulations, may enhance the bioavailability and regulated release of bioactive chemicals, hence improving therapeutic results.

In conclusion, although Rhododendron has significant potential in medicine and cosmetics, additional research emphasizing stringent clinical trials, toxicological safety, and sophisticated drug delivery methods will be essential for actualizing its full capabilities. Ongoing research may render Rhododendron a significant asset in contemporary healthcare.

References

1. Baruah, S., & Saikia, P. (2015). Ethnomedicinal plants used by the ethnic communities of Tawang district of Arunachal Pradesh. Indian Journal of Traditional Knowledge, 14(1), 146–152.
2. Bhatt, A. B., Rawat, G. S., & Upreti, N. (2010). Antioxidant and cardioprotective properties of Rhododendron arboreum flowers. Journal of Medicinal Plants Research, 4(2), 185–190.
3. Chamberlain, D. F., Hyam, R., Argent, G., Fairweather, G., & Walters, K. (1996). The genus Rhododendron: Its classification and synonymy. Royal Botanic Garden Edinburgh.
4. Goetsch, L. A., Eckert, A. J., & Hall, B. D. (2005). The molecular systematics of Rhododendron (Ericaceae): A phylogeny based upon RPB2 gene sequences. Systematic Botany, 30(3), 616–626. https://doi.org/10.1600/0363644054782196.

a. Kala, C. P. (2005). Ethnomedicinal botany of the Apatani in the Eastern Himalayan region of India. Journal of Ethnobiology and Ethnomedicine, 1, 11. https://doi.org/10.1186/1746-4269-1-11.

5. Kumar, N., & Sharma, R. (2017). Phytochemical and pharmacological profile of Rhododendron arboreum: A review. International Journal of Pharmaceutical Sciences and Research, 8(12), 4932–4941.
6. Negi, V. S., Bhatt, A., Khanduri, V. P., & Todaria, N. P. (2011). Ethnomedicinal plants used in traditional healthcare systems in the Garhwal Himalaya, India. Journal of Ethnopharmacology, 133(2), 468–477. https://doi.org/10.1016/j.jep.2010.10.033.
7. Singh, H., & Kaur, R. (2018). A review on traditional uses, phytochemistry and pharmacological properties of Rhododendron species. International Journal of Green Pharmacy, 12(3), 519–528.

MENTAL HEALTH IN GERIATRIC POPULATIONS: ISSUES AND INTERVENTIONS

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Abstract:
The worldwide aging population has brought unprecedented attention in terms of mental health needs among the elderly. As life expectancy rises globally, understanding and addressing geriatric mental health has become a significant public health priority. Geriatric mental health is multifaceted, shaped by various biological, psychological, social, and environmental components that interact throughout the aging process. Early identification, tailored interventions, and comprehensive support can significantly improve geriatric mental health outcomes. This chapter delves into the complex nature of geriatric mental health, focusing on the factors, disorders, and adequate interventions to be implemented. By recognizing the distinct and adequate hallmark of geriatric mental health, healthcare providers, policymakers, and family members can enhance their support for the psychological well-being of the elderly and encourage healthy aging within communities.

Keywords: Elderly Depression, Geriatric Mental Health, Healthy Aging, Psychogeriatrics, Psychotherapy

Introduction:

Aging is an intricate biological, psychological, and social process. While many older adults age healthily, a significant portion of them face various mental health challenges. As the global population ages, the importance of geriatric care continues to grow, necessitating specialized training for healthcare providers to address the complex needs of older patients effectively. The field of geriatrics is closely related to the science of gerontology, the study of aging. A person's mental health comprises emotional, psychological, and social well-being, which influences what one thinks, feels, and acts. Mental health is critical at every stage of life, from childhood to old age, and plays an important role in coping with stress, relating to others, and making decisions. The World Health Organization defined mental health as "a state of mental well-being that enables people to cope with the stresses of life, realize their abilities, learn well and work well, and contribute to their community, which has intrinsic and instrumental value and is integral to our well-being" (WHO, 2025). There are numerous mental health conditions ranging from mild to severe, these include anxiety disorders (Generalized anxiety, panic disorder, and social

anxiety), mood disorders (Depression and bipolar disorder), psychotic disorders (Schizophrenia), personality disorders (Borderline and antisocial personality disorders), eating disorders (Anorexia, bulimia, and binge-eating disorder), and trauma-related disorders (post-traumatic stress disorder).

Geriatric Mental Health: A Specialized Field

Geriatric mental health, also known as geriatric psychiatry or psychogeriatrics, is a specialized branch of mental health care that surrounds the prevention, diagnosis, and treatment of various mental health disorders among older adults, typically those aged 65 and above. It is a specialized field that focuses on assessing, diagnosing, and treating mental health issues in older adults, considering the unique biological, psychological, and social aspects of aging. Geriatric mental health is an important aspect of the overall well-being of the elderly. As individuals grow older, they might face different life transitions that can influence their mental well-being. Geriatric Mental Health comprises a wide range of mental health conditions, including depression, anxiety disorders, dementia, and late-life psychosis, including schizophrenia. Conditions related to geriatric mental health have emerged from the recognition that older adults have unique mental health needs that differ substantially from the younger generations. It may stem from the complex interplay of age-related psychological changes, accumulated life experiences, changing social roles, and increased vulnerability to physical health problems. One of the key principles of geriatric mental health is the understanding that mental health issues in the elderly are not an inevitable consequence of aging. While certain risks may increase with age, mental health problems are not a normal part of the aging process and are highly treatable when properly identified and addressed.

Theoretical Framework

Understanding about the mental health in geriatric populations requires a comprehensive theoretical foundation that considers the unique psychological, social, and biological transitions associated with aging. The issues related to mental health of the elderly arises due to the presence of various stressors in life and declining ability of coping with these issues due to age later on affect the mental health of the older adults. The theory which best aligns with this is the Stress and Coping Theory.

Stress and Coping theory were developed by Richrd Lazarus and Susan Folkman in 1984 which emphasizes the role of cognitive appraisal in determining how individuals respond to potentially stressful situations. According to this theory, stress is not just a stimulus or a response, but a transactional process between the individual and their environment (Wolf and Fisher, 2023). This theory posits that stress is not caused from the objective events themselves, but from the individual's perceived ability to cope with these events. This theory surrounds upon two types of appraisals: primary appraisal, involves evaluating whether a situation is threatening, challenging,

or benign, and secondary appraisal, involves assessing an individual's resources and options for coping. Moreover, the theory categorizes coping strategies into problem-focused coping, which involves taking direct action to address the stressor, and emotion-focused coping, which involves managing the emotional response to the stressor. In terms of geriatric mental health, the application of stress and coping theory could implies helping the older adults in developing effective appraisal and coping strategies to certain life stressors so that it could lessen their impact on mental health. Furthermore, through this theory, the caretakers or healthcare individuals could support the elderly in challenging negative or catastrophic thoughts about aging, illness, or bereavement, and develop more balanced and realistic appraisals of their situations.

Factors influencing Geriatric Mental Health

Geriatric mental health is governed by various factors that can have a substantial impact on the psychological well-being of older persons, and understanding these factors is critical for building successful interventions and support systems. These factors include:

1. **Physical Health and Chronic Illness**

The physical health status represents one of the most significant factors and is intricately connected to the mental well-being of the elderly. The prevalence of chronic medical conditions increases substantially with age, creating a complex relation between physical and psychological well-being. Chronic health conditions such as heart disease, diabetes, and dementia can worsen feelings of hopelessness and anxiety. The concept of multimorbidity, where older adults experience multiple chronic conditions simultaneously, presents challenges for mental health. The cumulative burden of managing multiple health problems, navigating complex treatment regimens, and coping with progressive functional decline can overwhelm coping mechanisms and lead to psychological distress. Mostafa *et al.* (2022) found that 60.6% of elderly individuals with multiple chronic conditions reported poor psychological well-being. Conversely, poor mental health can worsen physical health outcomes, increasing the risk of cardiovascular diseases and diabetes (Gandhi, 2024; Kagee and Freeman, 2023).

2. **Socioeconomic Status**

Socioeconomic determinants encompass multiple dimensions, such as income level, educational background, and availability of healthcare, which significantly influence mental health outcomes. The relationship between an individual's socioeconomic status and mental health is complex and multidirectional, with lower socioeconomic status generally associated with increased rates of mental health problems. Elderly individuals with restricted financial means or lower levels of education frequently encounter obstacles in obtaining services, including mental health, which may worsen their mental health conditions. Lower income is strongly correlated

with increased mental health issues, including anxiety and depression (Reiss *et al.,* 2021; Alzahrani *et al.,* 2024).

3. Psychosocial factors

Psychosocial stressors such as bereavement, retirement, and financial instability can profoundly affect mental well-being. Bereavement and the experience of loss of a loved one could trigger complicated grief responses and increase risk for depression. The transition into retirement may lead to a diminished sense of purpose, while financial challenges can exacerbate stress levels. Involuntary retirement and financial instability are jointly associated with a higher risk of major depression and increased psychological distress, particularly anxiety (Kitsaki *et al.,* 2024; Bierman *et al.,* 2023). Additionally, ageism and societal perceptions of aging may contribute to internalized negative attitudes about aging, reduced self-worth, and diminished expectations for continued growth and contribution.

4. Cumulative Life Experiences

Cumulative experiences over one's lifetime recognize that mental health in later life is significantly influenced by the accumulation of both positive and negative experiences throughout the entire lifespan. These experiences could shape the personality, coping mechanisms, resilience, and vulnerability to mental health problems in older adulthood. Adverse childhood experiences, including abuse, neglect, household dysfunction, and trauma, can have lasting effects on mental health that persist into older adulthood. Draper (2020) found that lifetime trauma significantly impacts older adults' psychological well-being, with chronic symptoms of PTSD, anxiety, and depression persisting into old age.

5. Government Programs and Policies

Government programs and policies greatly influence the mental well-being of the elderly through their impact on healthcare access, financial security, social services, and community resources. The design, implementation, and accessibility of these programs can either support or hinder mental health outcomes for older adults. For example, the National Programme for Health Care of the Elderly (NPHCE) of India focuses on providing specialized care for both physical and mental health needs. However, poor implementation of healthcare programs can leave many older individuals without support, and some programs mainly assist those classified as "Below Poverty Line," potentially excluding middle-class seniors.

Common Mental Health Conditions in The Geriatric Population

Mental health conditions among the geriatric population include a range of disorders that significantly affect their quality of life. The most common conditions include dementia, depression, anxiety, and substance abuse. Dementia is a syndrome linked to various neurodegenerative diseases, which results in the decline of cognitive abilities in a person and impacts everyday activities. The types of dementia include: Alzheimer's disease, Frontotemporal

dementia, Lewy body dementia, Vascular dementia, and Mixed dementia. A variety of diseases and injuries that affect the brain can cause dementia. Alzheimer's disease is the most common form of dementia and may contribute to 60-70% of cases (WHO, 2023). A study found that around 8.8 million Indians older than 60 years of age have dementia, with a prevalence of 7.4%. Dementia is more common in women than men, particularly in rural rather than metropolitan regions (Lee *et al.,* 2023). The signs of dementia include memory loss and forgetfulness, struggles with day-to-day tasks, difficulty communicating and understanding conversations, problems with orientation, such as identifying dates and locations, changes in behavior, including restlessness or aggression, and troubles with planning and making decisions. Depression is a mood disorder that causes feelings of sadness and loss of interest in daily activities. It can be affected by various factors, including genetics, brain chemistry, life events, and physical health. There are several types of depression, including Major Depressive Disorder, Persistent Depressive Disorder, Bipolar Disorder, Postpartum Depression, Premenstrual Dysphoric Disorder, Seasonal Affective Disorder, Atypical Depression, Psychotic Depression, Situational Depression, and Subsyndromal Depression. Elderly people are more likely to develop subsyndromal depression, which occurs when a person experiences depressive symptoms that are not severe enough to meet the diagnostic criteria for other types of depression. Approximately 3.8% of people go through depression, including 5% of adults (4% among males and 6% among females), and 5.7% of the elderly (WHO, 2023). The symptoms of depression are feelings of despair or sadness, sleep problems, no desire for socializing and hobbies, irritability and grumpiness, feelings of worthlessness, and persistent pain.

Anxiety is a distressing emotion marked by inner conflict and feelings of apprehension regarding future events. Anxiety disorders are a cluster of mental disorders characterized by extreme and uncontrollable feelings of fear and anxiety that significantly affect a person's relationships, work, and activities. The common types of anxiety disorders include Generalized Anxiety Disorder, Panic Disorder, Social Anxiety Disorder, Specific Phobia, Post-traumatic Stress Disorder, Obsessive-Compulsive Disorder, and Separation Anxiety Disorder. WHO estimated that anxiety disorders are suffered by 4% of the world population (WHO, 2025). Patel *et al.* (2024) stated that around one in five older adults in India suffer from anxiety disorder, with the overall prevalence being 18.7%. The signs and symptoms of anxiety disorders include having heart palpitations, excessive fear, muscle tightness, shaking or trembling, abdominal distress, and trouble concentrating. Substance use disorder, or substance abuse, is a condition of using harmful or hazardous psychoactive substances, such as alcohol, prescription medications, and illegal drugs. Excessive use can lead to addiction, which is a chronic, relapsing disorder marked by compulsive drug seeking, which may further result in long-lasting changes in the brain. Substance use disorder is another concerning mental health issue rising in the geriatric population, which can

lead to mental disorders. The elderly population aged 60-64 years were more likely to drink alcohol than other age groups, with Maharashtra having the largest percentage of alcohol users and Assam having the highest proportion of tobacco users (Gupta *et al.,* 2024). The signs and symptoms of substance use disorder are memory loss and confusion, slurred speech, onset of depression or anxiety, loss of balance and coordination, increased risk of falls, unexplained chronic pain, irritability, and sadness.

Risk Factors of Mental Health Issues

Mental health issues can be caused due to various factors, and understanding the causes is essential for formulating targeted interventions that can effectively support the mental wellness of the elderly. These factors include genetics, stress, chronic illness, social isolation, and lifestyle. An individual having a family history of mental health disorders is more susceptible to having geriatric depression. Pedersen *et al.* (2025) found that individuals having family members with a mental disorder face a heightened risk of the same disorder. Prolonged exposure to stress, whether due to work, relationships, or financial pressures, may result in the occurrence of mental health issues in old age. Sudden, intense stressors, such as the loss of a loved one, can trigger mental health conditions or exacerbate existing ones (Moore *et al.* 2020). Long-term stress results in higher levels of cortisol, which can harm neurons in the hippocampus, affecting cognitive abilities and emotional control, resulting in an increased risk of neurological conditions like Alzheimer's and depression (Montgomery and Gouvea, 2024; Devi *et al.,* 2022). Medical conditions such as diabetes, heart disease, or cancer may result in helplessness, anxiety, and depression due to ongoing challenges of managing the condition. Swathi *et al.* (2023) reported that individuals with chronic illnesses exhibited high levels of psychological distress, with stress affecting 68.7%, anxiety impacting 51.1%, and depression observed in 58.8% of the patient population. Persistent pain or discomfort from chronic illness can be both physically and mentally exhausting, leading to mental health issues. Rani and Anjum (2024) found that depression is particularly prevalent among chronic illness patients, with up to one-third reporting moderate symptoms and a quarter suffering from severe depression.

Individuals who lack strong social relationships are more vulnerable to mental health issues, including depression and anxiety. Social isolation is linked to heightened levels of depressive symptoms and anxiety disorders, with studies indicating that individuals experiencing loneliness are 40% more likely to have cognitive impairment and 20% more likely to develop dementia (Malatyali *et al.,* 2024). Lifestyle factors such as a sedentary lifestyle, poor dietary habits, and substance abuse can have cumulative effects on mental health. Sedentary behavior is associated with reduced cognitive functioning and increased risk of mental health disorders such as depression and anxiety (Choudhary *et al.,* 2021; Grzelak, 2024). Conversely, positive lifestyle changes can create a virtuous cycle, improving overall quality of life both physically and

psychologically for elderly individuals. Poor nutrition can affect brain function and mood. Pandey and Mishra (2024) noted that substance abuse can also exacerbate existing mental health issues and contribute to cognitive decline.

Treatment Approaches and Interventions

Various treatment approaches can be employed to address mental health conditions among the elderly. The adopted treatment strategies must be tailored to fit everyone's specific needs and life circumstances. These approaches include:

1. **Pharmacological treatments**

Medication may be prescribed for specific mental health disorders; however, their use should be approached with caution in the elderly due to alterations in pharmacokinetics and a higher likelihood of side effects with drug interactions. Psychotropic drugs, including antidepressants and antipsychotics, are frequently prescribed to the elderly but carry significant risks of adverse effects and inappropriate use (Thomas, 2023; Lapane *et al.,* 2015). Hence, careful monitoring should be utilized. Other medications, such as Cholinesterase inhibitors and Memantine, are used to address the symptoms associated with Alzheimer's disease and other dementias.

2. **Psychotherapeutic interventions**

Psychotherapy can be highly beneficial for the geriatric population and can often complement medical treatments. Evidence-based psychotherapies, including cognitive-behavioural therapy, group therapy, problem-solving therapy, and reminiscence therapy, can be used. Hendriks *et al.* (2024) found that Cognitive Behavioural Therapy (CBT) may effectively reduce anxiety and depressive symptoms in older adults with anxiety disorders. Group therapy can be particularly advantageous for older adults by reducing feelings of isolation while offering therapeutic benefits. It offers a platform for shared experiences, which can be particularly beneficial in addressing common age-related stressors (Ishikawa and Mace, 2023). The problem-solving therapy approach enables the elder population to devise practical solutions to daily challenges and boosts their self-efficacy. Reminiscence therapy involves guided recall of past experiences, often supported with photos or music, to improve self-esteem, mood, and a sense of personal identity.

3. **Lifestyle and behavioural intervention**

In addition to medication, non-pharmacological lifestyle strategies are vital in sustaining and improving geriatric mental health. These strategies encompass regular physical activity, a balanced diet, sufficient sleep, and mindfulness and relaxation techniques. Engaging in regular physical exercise, such as walking and yoga, could improve cognitive function in the elderly. A healthy diet with adequate nutrients could support neurotransmitter function, diminish inflammation, and shield against cognitive decline. Key *et al.* (2023) found that engaging in yoga and exercise can enhance cognitive function and mood by increasing BDNF (Brain-Derived

Neurotrophic Factor) levels. Sleep disturbances are prevalent among the elderly, often resulting in deteriorated mental health. Thus, maintaining a stable circadian rhythm can assist in managing insomnia. Improved sleep quality is often associated with better emotional regulation, reduced fatigue, and lower levels of irritability or depressive symptoms. Mindfulness meditation could help alleviate stress, manage chronic illness, and foster a sense of tranquillity and self-awareness among the elderly. Such practices can help in dealing with grief or adjustment-related stress in late life.

4. Social Support and Community-based Interventions

Social support and community-based programs are essential in promoting geriatric mental health and preventing mental health concerns in older adults. Senior centres, peer support groups, and recreational activities for the elderly can provide social connections and meaningful engagement. Educational initiatives can also be organized for the elderly to improve their mental health literacy, boost digital literacy, mitigate stigma, and promote help-seeking behaviour to recognize mental health problems and pursue appropriate treatment.

Conclusion:

Mental health in the geriatric population is a vital yet often overlooked component of public health. As people live longer and traditional family structures evolve, seniors encounter distinct psychological challenges influenced by chronic illness, social isolation, financial insecurity, and their accumulated life experiences. Although mental health problems are not an inevitable consequence of aging, older adults pose specific vulnerabilities that necessitate proactive identification and tailored intervention strategies. The high prevalence of medical comorbidities in this demographic highlights the importance of integrated care models that concurrently address both physical and mental health concerns. Moving forward, this field must continue advancing through evidence-based research, technological innovations, and policy reforms that enhance access to quality care. Families, healthcare providers, and communities must collaborate to diminish stigma, advocate for preventive measures, and ensure that older adults can maintain psychological well-being and dignity throughout their later years. Additionally, supporting geriatric mental health is not merely a healthcare priority; it's a societal obligation that enhances the quality of life for our aging population.

References:

1. Alzahrani, H., Alburaidi, F. S., Alharthi, A. M., Ghobran, A. M. A., Alhaboob, Z. A., Alibrahim, A. O., ... and Qrmli, A. A. (2024). Investigating the Relationship between Socio-economic Status and Mental Illness: A Comprehensive Analysis of 1,389,125 Individuals through Systematic Review and Meta-analysis. *Journal of Advanced Trends in Medical Research*, *1*(3), 862-869.

2. Bierman, A., Upenieks, L., Lee, Y., and Harmon, M. (2023). Consequences of financial strain for psychological distress among older adults: Examining the explanatory role of multiple components of the self-concept. *Socius*, *9*, 1-17.
3. Choudhary, A. K., Loganathan, S., and Maheshkumar, K. (2021). A Sedentary Lifestyle and Cognitive Function. *Chall Dis Health Res*, *6*, 52-62.
4. Devi, B., Yadav, M., Kapil, L., and Singh, A. (2022). An insight on chronic unpredictable stress in association with pathophysiology, neurotransmitters, and experimental models. *Pharmaspire*, *14*, 28-40.
5. Draper, B. (2020). Psychological impact of lifetime trauma in older adults. *International Psychogeriatrics*, *32*(4), 431-434.
6. Gandhi, R. (2024). Mental health and physical well being: A correlation. *International Journal of Advanced Psychiatric Nursing*, *6*(1), 80-82.
7. Grzelak, A. (2024). The Detrimental Effects of Sedentary Lifestyle on Human Health. *Journal of Education, Health and Sport*, *76*, 56522-56522.
8. Gupta, M. K., Nagdeve, D. A., Mahata, D., and Chaurasia, H. (2024). Substance Abuse Among Elderly in India: Evidence Based on Study on Global Ageing and Adult Health (SAGE) Wave 1. *Global Social Welfare*, *11*(1), 77-83.
9. Ishikawa, R. Z., and Mace, R. A. (2023). Cognitive Behavioral Therapy with Older Adults. In *The Massachusetts General Hospital Handbook of Cognitive Behavioral Therapy* (pp. 395-409). Cham: Springer International Publishing.
10. Hendriks, G. J., Janssen, N., Robertson, L., van Balkom, A. J., van Zelst, W. H., Wolfe, S., and Uphoff, E. (2024). Cognitive behavioural therapy and third-wave approaches for anxiety and related disorders in older people. *Cochrane Database of Systematic Reviews*, (7).
11. Kagee, A., and Freeman, M. (2023). *Mental health and physical health*. Elsevier BV. https://doi.org/10.1016/b978-0-323-99967-0.00085-5
12. Key, M. N., and Szabo-Reed, A. N. (2023). Impact of diet and exercise interventions on cognition and brain health in older adults: A narrative review. *Nutrients*, *15*(11), 2495.
13. Kitsaki, M., Katsiroumpa, A., Zioga, S., Moisoglou, I., Kalogeropoulou, M., Kolisiati, A., and Galanis, P. (2024). Psychosocial effects of retirement on the elderly: a systematic review. *International Journal of Caring Sciences*, *17*(2), 755-769.
14. Lapane, K. L., Hume, A., Ulbricht, C., and Gambassi, G. (2015). Safety of psychotropic drugs in the elderly. In *Pharmacovigilance in psychiatry* (pp. 285-297). Cham: Springer International Publishing.
15. Lee, J., Meijer, E., Langa, K. M., Ganguli, M., Varghese, M., Banerjee, J., ... and Dey, A. B. (2023). Prevalence of dementia in India: National and state estimates from a nationwide study. Alzheimer's and Dementia, 19(7), 2898-2912.

16. Malatyali, A., Cidav, T., Xie, R., Thiamwong, L., and Wiese, L. A. K. (2024). Social Isolation and Loneliness in Varied Levels of Cognition Among Racially/Ethnically Diverse Older Americans. *Alzheimer's and Dementia*, *20*, e095749.
17. Montgomery, R. M., and Gouvea, M. A. V. M. (2024). Impact of Chronic Stress on Physical and Mental Health: A Detailed Analysis. *J Gene Engg Bio Res*, *6*(2), 01-07.
18. Moore, R. C., Straus, E., and Campbell, L. M. (2020). Stress, mental health, and aging. In *Handbook of mental health and aging* (pp. 37-58). Academic Press.
19. Mostafa, A. A. E., Abd-Elaziz, N. M., Abozeid, H. A. A., and Mohamed, H. S. (2022). Effect of Comorbidities on Physical Function and Psychological Wellbeing among Elderly at Qena City. *Assiut Scientific Nursing Journal*, *10*(30), 208-217.
20. Pandey, P., and Mishra, A. (2024, March). Impact of Daily Life Factors on Physical and Mental Health. In *2024 2nd International Conference on Disruptive Technologies (ICDT)* (pp. 374-379). IEEE.
21. Patel, M., Mantri, N., Joshi, N., Jain, Y., Goel, A. D., Gupta, M., ... and Bhardwaj, P. (2024). Is anxiety a public health problem among older adults in India: Results from a systematic review and meta-analysis. *Journal of Family Medicine and Primary Care*, *13*(7), 2545-2554.
22. Pedersen, C. B., Pedersen, M. G., Antonsen, S., Pedersen, E. M., Horsdal, H. T., Debost, J. C., ... and Agerbo, E. (2025). Absolute and relative risks of mental disorders in families: a Danish register-based study. *The Lancet Psychiatry*, *12*(8), 590-599.
23. Rani, L., and Anjum, C. (2024). Depression a Common Mental Disorder: An Over View. *International Journal For Multidisciplinary Research*.*6*(2). 1-5. https://doi.org/10.36948/ijfmr.2024.v06i02.16943
24. Reiss, V., Brown, L., Sisitsky, S., and Russell, R. (2021). The influence of socio-economic factors on community mental health. *Jurnal Sosial, Sains, Terapan Dan Riset (Sosateris)*, *10*(1), 79-90.
25. Swathi, M., Manjusha, S., Vadakkiniath, I. J., and Gururaj, A. (2023). Prevalence and correlates of stress, anxiety, and depression in patients with chronic diseases: a cross-sectional study. *Middle East Current Psychiatry*, *30*(1), 1-14.
26. Thomas, P. (2023). Psychotropic drugs in the elderly. *Soins. Gerontologie*, *28*(163), 27-29.
27. Wolf, B. M., & Fisher, C. L. (2023). Stress, appraisal, and coping theory. *The International Encyclopedia of Health Communication*, 1-6.
28. World Health Organization. (n.d.). *Mental health*. Retrieved July 9, 2025, from https://www.who.int/health-topics/mental-health#tab=tab_1
29. World Health Organization. (2025, February 21). *Ageing: Global population* [Questions and answers]. Retrieved July 9, 2025, from https://www.who.int/news-room/questions-and-answers/item/population-ageing
30. World Health Organization. (2023, October 20). *Mental health of older adults* [Fact sheet]. https://www.who.int/news-room/fact-sheets/detail/mental-health-of-older-adults

AI-POWERED CLINICAL DECISION SUPPORT: REVOLUTIONIZING PEDIATRIC HEALTHCARE

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Abstract:
Clinical decision support systems (CDSS) are about to undergo a revolution because to artificial intelligence (AI). These technologies improve diagnosis accuracy and therapy personalization by utilizing machine learning, natural language processing, and predictive analytics. AI can help with important issues in pediatric nuclear medicine, such as maximizing radiation dosages and enhancing picture interpretation, where functional imaging is essential for the diagnosis and treatment of diseases like cancer, metabolic disorders, and congenital heart defects. This thorough abstract explores the uses, advantages, and ethical issues of integrating AI-powered CDSS in pediatric nuclear medicine. AI improves diagnostic accuracy, speeds up decision-making, and optimizes radiation exposure all of which are critical for pediatric patients by automating image analysis, correlating multimodal data, and enabling predictive modeling. Notwithstanding these developments, issues like algorithmic bias, data privacy, and regulatory compliance still need to be resolved if AI is to reach its full potential. In order to guarantee the responsible and efficient application of AI in pediatric care, which will ultimately improve outcomes and democratize healthcare access, this study highlights the necessity of pediatric-specific AI models, collaborative research, and clinician education.

Keywords: Clinical Decision Support Systems (CDSS), Pediatric Healthcare, Nuclear Medicine, Healthcare Technology, Precision Medicine, Healthcare Informatics

Introduction:

Children's and adults' physiological and developmental differences necessitate a comprehensive approach to pediatric healthcare. Children's ailments are frequently diagnosed and treated using specialist techniques to guarantee safety and effectiveness. Pediatric diagnostics greatly benefits from nuclear medicine's capacity to visualize molecular and functional bodily processes. Age-related physiology can vary, nevertheless, making it difficult to interpret nuclear imaging results. Natural language processing (NLP), machine learning (ML), and other AI technologies are used by AI-powered CDSS to help physicians make prompt and correct judgments. Pediatric healthcare can gain from increased diagnostic accuracy and customized treatment plans through the integration of AI with nuclear medicine [1].

Pediatric healthcare presents particular difficulties that need for accuracy, promptness, and a thorough comprehension of the human body's development. The emergence of artificial intelligence (AI) offers a revolutionary chance to tackle these issues and alter pediatric patient

care. This study explores the significant effects of clinical decision support systems (CDSS) driven by artificial intelligence (AI) in the specialized field of pediatric nuclear medicine. With its capacity to see and evaluate physiological processes at the molecular level, nuclear medicine is essential for the diagnosis and treatment of a variety of pediatric disorders, ranging from cancer to congenital abnormalities. However, there can be inter-observer variability and a need for considerable experience when interpreting nuclear medicine images [2]. Artificial intelligence (AI) algorithms, especially deep learning models, are excellent at deciphering intricate patterns and identifying minute details in medical images. By utilizing these features, pediatric nuclear medicine professionals' decision-making processes can be enhanced by AI-powered CDSS, resulting in more precise diagnoses, better treatment strategies, and eventually better patient outcomes. This essay will examine the state-of-the-art uses of AI in pediatric nuclear medicine, such as how AI algorithms can help with lesion identification and quantification, tumor response evaluation to treatment, and disease progression prediction. Radiomics can help with individualized treatment decisions and offer important insights into the underlying biology of diseases by obtaining quantitative information from medical imaging. AI systems are able to evaluate patient data, such as genetic, clinical, and imaging data, in order to forecast long-term results, treatment response, and the likelihood of illness recurrence. EHRs and AI algorithms can be seamlessly integrated to offer real-time decision assistance, increase workflow effectiveness, and improve provider-to-provider communication [3]. The ethical issues, difficulties, and potential applications of AI in pediatric nuclear medicine will also be covered in this paper. It will stress the significance of responsible AI development, thorough validation, and fair access to these cutting-edge technologies. We can ensure that children receive the best care possible by utilizing AI to bring in a new era of precision medicine. This introduction gives a brief synopsis of the subject, identifies the main areas of interest, and demonstrates how AI has the potential to revolutionize pediatric nuclear medicine. It prepares the reader for an in-depth examination of the numerous uses, advantages, and difficulties of this new discipline [4].

Nuclear Medicine's Function in Pediatric Healthcare

Radioactive materials are used in nuclear medicine to identify and treat illnesses. It is essential for identifying juvenile illnesses like cancer, metabolic disorders, and congenital heart problems because it offers functional imaging that aids in identifying anomalies at the molecular level. But there are a number of difficulties.

1. Diagnosis of Congenital and Metabolic Disorders

In order to identify defects that are present at birth or result from metabolic dysfunction, congenital and metabolic disorders are diagnosed using a combination of genetic screening, biochemical testing, and sophisticated imaging techniques. In order to avert serious consequences, newborn screening programs are essential for the early detection of diseases such

congenital hypothyroidism, cystic fibrosis, and phenylketonuria (PKU). Blood tests for enzyme shortages, genetic testing for inherited mutations, and imaging tests like MRI or ultrasound for structural abnormalities are examples of diagnostic techniques. Effective care, better patient outcomes, and a lower chance of long-term problems all depend on an early and precise diagnosis [5].

2. Detection of Infections and Inflammatory Conditions

The detection of infections and inflammatory conditions relies on a combination of clinical evaluation, laboratory tests, and imaging techniques to identify pathogens and immune system responses. Blood tests, such as complete blood count (CBC) and C-reactive protein (CRP), help assess inflammation levels, while cultures, polymerase chain reaction (PCR), and serological tests detect specific infectious agents. Imaging modalities like X-rays, MRIs, and ultrasounds aid in identifying inflammation in tissues and organs [6]. Rapid and accurate diagnosis is crucial for effective treatment, preventing complications, and managing both acute and chronic infectious or inflammatory diseases.

3. Evaluation of Organ Function

Nuclear medicine is essential in assessing kidney, heart, and lung function in children. Renal scans, such as a MAG3 scan, help evaluate kidney function and detect blockages or abnormalities in the urinary tract. Myocardial perfusion imaging is used to assess heart function in children with congenital heart diseases. Similarly, lung scans help detect pulmonary embolisms or congenital lung abnormalities.

4. Oncology and Cancer Detection

Pediatric cancers such as neuroblastoma, lymphoma, and bone tumors are effectively diagnosed and monitored using nuclear medicine techniques like PET scans and MIBG (metaiodobenzyl guanidine) scans. These scans provide detailed information about tumor location, size, and activity, helping oncologists plan appropriate treatment strategies [7].

5. Gastrointestinal Disorders

Nuclear medicine is useful in detecting gastrointestinal motility disorders such as gastroesophageal reflux disease (GERD) and delayed gastric emptying. Gastrointestinal bleeding scans also help identify sources of internal bleeding in children with unexplained anemia or blood loss.

Radiation Sensitivity in Pediatric Patients

Children's rapidly dividing cells and longer lifespan make them more radiation-sensitive than adults. Concerns regarding possible radiation-induced consequences, such as the possibility of acquiring secondary cancers in later life, are raised by this heightened sensitivity. Thus, in order to reduce radiation exposure while maintaining diagnostic effectiveness, pediatric nuclear

medicine adheres to the ALARA (As Low As Reasonably Achievable) guidelines [8]. Several strategies are employed to reduce radiation risks, including:

- Making use of radiopharmaceuticals at the lowest dose feasible.
- When possible, use alternate imaging modalities (such as MRI or ultrasound).
- Developing imaging technology to shorten scan times and increase resolution.
- Putting in place stringent policies and procedures designed specifically for young patients.

Children are more sensitive to radiation than adults because: children are more vulnerable to radiation than adults: Rapidly dividing cells: Children's cells divide and expand continuously, making them more vulnerable to radiation harm. Longer lifespan: Because radiation effects might take years to appear, children are more susceptible to radiation-induced malignancies. Smaller size: Radiation exposure to one organ may have an impact on a nearby organ since children's organs are smaller and closer together. This increased sensitivity means that children require special consideration when undergoing nuclear medicine procedures. Here are some of the ways that radiation exposure is minimized in pediatric nuclear medicine:

- **Lower doses:** Children receive lower doses of radiopharmaceuticals than adults, adjusted for their age and size.
- **Optimized imaging protocols:** Technologists use imaging protocols that minimize radiation exposure without compromising image quality.
- **Child-friendly environment:** Creating a calm and reassuring environment helps reduce anxiety and improve cooperation, which can reduce the need for repeat scans.

Safety Measures and Advancements in Pediatric Nuclear Medicine

To ensure the safety of young patients undergoing nuclear medicine procedures, healthcare providers follow strict protocols. Recent advancements have also contributed to making these procedures safer and more effective.

1. **Dose Optimization**

Radiopharmaceutical doses are carefully calculated based on the child's weight and medical condition. Pediatric dose optimization ensures that the minimum necessary amount of radiation is used while still achieving accurate diagnostic results [9].

2. Use of Advanced Imaging Techniques

Modern imaging technologies, such as hybrid imaging (PET/CT, SPECT/CT), enhance diagnostic accuracy while reducing scan times and radiation exposure. These techniques allow for clearer images with lower doses of radiopharmaceuticals [10,20].

3. Shorter Half-Life Radiopharmaceuticals

Newer radiopharmaceuticals with shorter half-lives are being developed, reducing the duration of radiation exposure. These materials decay quickly, limiting the potential risks associated with prolonged radiation exposure.

4. Sedation and Comfort Measures

Pediatric patients often require sedation during nuclear medicine scans to ensure they remain still for accurate imaging. Child-friendly environments, distraction techniques, and mild sedatives help improve the overall experience for young patients.

Therapeutic Applications of Nuclear Medicine in Pediatrics

Radioiodine Therapy for Thyroid Disorders

Children with hyperthyroidism or thyroid cancer can be treated using radioactive iodine (I-131) therapy, which targets and eliminates aberrant thyroid cells while minimizing damage to adjacent tissues.

Targeted Radiotherapy for Cancer

Neuroblastoma is a frequent childhood malignancy that is treated with radiopharmaceuticals such as MIBG treatment. These therapies improve treatment outcomes by specifically targeting malignant cells while preserving healthy tissue [11,19].

Bone Pain Palliation

Radiopharmaceuticals like Samarium-153 or Strontium-89, which target damaged bone tissue, reduce pain and enhance quality of life for kids with metastatic bone disease.

Congenital Heart Disease

Nuclear imaging plays critical role in diagnosing and managing congenital heart defects. AI can:

- Analyze myocardial perfusion scans to detect ischemia.
- Assess ventricular function and predict surgical outcomes.

Pediatric Oncology

In oncology, early and accurate diagnosis significantly improves outcomes. AI can:

- Differentiate benign from malignant lesions in PET/CT scans.
- Monitor treatment response and predict recurrence.

Endocrine and Metabolic Disorders

AI enhances the detection of metabolic abnormalities using nuclear imaging. For example, it can:

- Identify thyroid dysfunction in scintigraphy studies.
- Detect bone metabolism irregularities in conditions like rickets.

Benefits of AI-Powered CDSS in Nuclear Medicine:

AI-powered Clinical Decision Support Systems (CDSS) are poised to revolutionize nuclear medicine, offering a range of benefits that enhance diagnostic accuracy, efficiency, and patient care.

Enhanced Diagnostic Accuracy:

- **Improved Image Interpretation:** AI algorithms can analyze nuclear medicine images with greater precision than the human eye, detecting subtle patterns and anomalies that might be missed by radiologists. This can lead to earlier and more accurate diagnoses, particularly in complex cases [4,18].
- **Quantitative Analysis:** AI can provide objective, quantitative measurements of tracer uptake and distribution, reducing subjectivity in image interpretation and improving the consistency of diagnoses.
- **Pattern Recognition:** AI excels at recognizing complex patterns in imaging data, which can be indicative of specific diseases or conditions. This can aid in the diagnosis of a wide range of diseases, including cancer, cardiovascular disease, and neurological disorders [12,21-23].

Increased Efficiency:

- **Automated Image Analysis:** AI can automate many aspects of image analysis, such as segmentation and quantification, freeing up radiologists' time to focus on more complex cases and patient interaction.
- **Faster Reporting:** AI-powered CDSS can generate automated reports, reducing turnaround time and allowing for quicker communication of results to clinicians.
- **Workflow Optimization:** AI can help optimize workflow in nuclear medicine departments by prioritizing cases, scheduling exams, and managing resources more efficiently [13,24].

Personalized Medicine:

- **Risk Stratification:** AI can analyze patient data, including imaging results, clinical history, and genetic information, to identify individuals at high risk for specific diseases. This allows for personalized prevention and screening strategies.
- **Treatment Planning:** AI can assist in treatment planning by predicting how patients will respond to different therapies based on their individual characteristics. This can help clinicians choose the most effective treatment for each patient [14].

Improved Patient Care:

- **Reduced Errors:** AI can help reduce diagnostic errors and improve the accuracy of treatment decisions, leading to better patient outcomes.
- **Faster Diagnosis:** AI can accelerate the diagnostic process, allowing patients to receive timely treatment and potentially improving their chances of recovery.
- **Enhanced Communication:** AI-powered CDSS can provide clinicians with clear and concise information, facilitating communication with patients and improving their understanding of their condition [15].

Research and Development:

- **Data Analysis:** AI can analyze large datasets of nuclear medicine images and clinical data to identify new biomarkers and improve our understanding of disease processes.

- **Development of New Techniques:** AI can be used to develop new imaging techniques and radiopharmaceuticals, leading to further advancements in nuclear medicine [15-17,25].

Conclusion:

Nuclear medicine plays an essential role in pediatric healthcare by providing accurate and early diagnoses, assessing organ function, detecting infections, and offering targeted treatments for various conditions. While radiation sensitivity in children remains a concern, strict safety measures, technological advancements, and adherence to dose optimization protocols ensure minimal risk while maximizing benefits. As innovations continue to evolve, nuclear medicine will further enhance its role in pediatric healthcare, improving outcomes and quality of life for young patients.

References:

1. Al-Hajjar, Sami, International Journal of Pediatrics and Adolescent Medicine 11(4):p 89-90, December 2024. DOI: 10.4103/IJPAM.IJPAM_141_24
2. Hasan R, Ullah SMA, Islam SMR. Recent advancement of deep learning techniques for pneumonia prediction from chest X-ray image. Med Rep 2024; 7:1–15.
3. Aylward BS, Abbas H, Taraman S, *et al.* An introduction to artificial intelligence in developmental and behavioral pediatrics. J Develop Behav Pediatr 2023; 44:e126–34.
4. Peyroteo M, Ferreira IA, Elvas LB, Ferreira JC, Lapao LV. Remote monitoring systems for patients with chronic diseases in primary health care: systematic review. JMIR mHealth uHealth 2021; 9:e28285.
5. Ramgopal S, Sanchez-Pinto LN, Horvat CM, Carroll MS, Luo Y, Florin TA. Artificial intelligence-based clinical decision support in pediatrics. Pediatr Res 2023; 93:334–41.
6. Sanchez-Pinto LN, Luo Y, Churpek MM. Big data and data science in critical care. Chest. 2018; 154:1239–1248. doi: 10.1016/j.chest.2018.04.037
7. Bohr, A. & Memarzadeh, K. The rise of artificial intelligence in healthcare applications. Artif. Intell. Healthc. 25–60, 10.1016/B978-0-12-818438-7.00002-2 (2020).
8. Sutton RT, *et al.* An overview of clinical decision support systems: benefits, risks, and strategies for success. npj Digit. Med. 2020; 3:17. doi: 10.1038/s41746-020-0221-y.
9. Ramgopal, S. *et al.* A prediction model for pediatric radiographic pneumonia. Pediatrics, 149**,** e2021051405 (2022).
10. Kuppermann, N. *et al.* A clinical prediction rule for stratifying febrile infants 60 days and younger at risk for serious bacterial infections. JAMA Pediatr. 173, 342–351. 10.1001/jamapediatrics.2018.5501 (2019).
11. Singh D, *et al.* Assessment of machine learning–based medical directives to expedite care in pediatric emergency medicine. JAMA Netw. Open. 2022; 5:e222599–e222599. doi: 10.1001/jamanetworkopen.2022.2599.
12. Scott HF, *et al.* Development and validation of a model to predict pediatric septic shock using data known 2h after hospital arrival. Pediatr. Crit. Care Med. 2021; 22:16–26. doi: 10.1097/PCC.0000000000002589.

13. Ramgopal, S. & Horvat, C. M. Machine learning approaches for the identification of children at low risk of intra-abdominal injury requiring intervention. J. Trauma Acute Care Surg. **90**, e128–e129 (2021).
14. Pennell C, Polet C, Arthur LG, Grewal H, Aronoff S. Risk assessment for intra-abdominal injury following blunt trauma in children: derivation and validation of a machine learning model. J. Trauma Acute Care Surg. 2020; 89:153–159. doi: 10.1097/TA.0000000000002717.
15. Juhn Y, Liu H. Artificial intelligence approaches using natural language processing to advance EHR-based clinical research. J. Allergy Clin. Immunol. 2020; 145:463–469. doi: 10.1016/j.jaci.2019.12.897.
16. Smith JC, *et al.* Natural language processing and machine learning to enable clinical decision support for treatment of pediatric pneumonia. AMIA Annu. Symp. Proc. 2020; 2020:1130.
17. Seol HY, *et al.* Artificial intelligence-assisted clinical decision support for childhood asthma management: a randomized clinical trial. PLoS One. 2021; 16:e0255261. doi: 10.1371/journal.pone.0255261.
18. Norgeot B, *et al.* Minimum information about clinical artificial intelligence modeling: the MI-CLAIM checklist. Nat. Med. 2020; 26:1320–1324. doi: 10.1038/s41591-020-1041-y.
19. Luo, Y., Wunderink, R. G. & Lloyd-Jones, D. Proactive vs reactive machine learning in health care: lessons from the COVID-19 pandemic. JAMA,327, 623–624 (2022).
20. Scott, I. A., Carter, S. M. & Coiera, E. Exploring stakeholder attitudes towards AI in clinical practice. BMJ Heal. Care Informatics, e100450 (2021).
21. Lynam AL, *et al.* Logistic regression has similar performance to optimised machine learning algorithms in a clinical setting: application to the discrimination between type 1 and type 2 diabetes in young adults. Diagnostic Progn. Res. 2020; 4:6. doi: 10.1186/s41512-020-00075-2.
22. Ramgopal S, Adler MD, Horvat CM. Application of the improving pediatric sepsis outcomes definition for pediatric sepsis to nationally representative emergency department data. Pediatr. Qual. Saf. 2021; 6:e468–e468. doi: 10.1097/pq9.0000000000000468.
23. Wong A, *et al.* External validation of a widely implemented proprietary sepsis prediction model in hospitalized patients. JAMA Intern. Med. 2021; 181:1065–1070. doi: 10.1001/jamainternmed.2021.2626.
24. Lee B, *et al.* Development of a machine learning model for predicting pediatric mortality in the early stages of intensive care unit admission. Sci. Rep. 2021; 11:1263. doi: 10.1038/s41598-020-80474-z.
25. Michelson, K. N., Klugman, C. M., Kho, A. N. & Gerke, S. Ethical considerations related to using machine learning-based prediction of mortality in the pediatric intensive care unit. J. Pediatr. S0022–S3476 (2022).

NIPAH VIRUS:
THREATS, CHALLENGES AND IMPLICATIONS FOR GLOBAL HEALTH

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Introduction:

The Nipah virus (NiV), is an RNA virus that is a member of the genus *Henipavirus,* and family *Paramyxoviridae*, is the source of a newly emerging zoonotic illness called Nipah virus disease. It is transmitted by a particular type of fruit bat species, primarily *Pteropus* spp (Alam (2022). The primary virus reservoirs are fruit bats, and contact with infected bats or intermediary hosts such as pigs can result in human infection. As a result of the elevated death rate linked with Nipah disease and unavailability of effective treatments and preventive measures against it, is classified as a universal hazard (Sharma *et.al* (2024). In Kampung Sungai Nipah village of Malaysia, the infection was discovered initially in 1998. Nipah virus (NiV) was characterized as the causative agent. Before the Nipah virus outbreak in Malaysia in 1999, NiV was unknown for its zoonotic potential. Symptoms of NiV disease involve fever as well as coughing, headache and laboured breathing. It involves complications such as encephalitis and seizures (Banerjee *et al.,* 2019).

The Nipah virus

Nipah virus is a single-stranded, negative-sense virus. Matrix protein, phosphoprotein, nucleocapsid, fusion protein, large polymerase protein, and glycoprotein, are the six structural proteins encoded by its genome. The neurotropism and vasculitis caused by the virus are due to the G and F proteins, which mediate viral entrance into host cells by mainly targeting ephrin-B2 and ephrin-B3 receptors, which are abundantly expressed in endothelial and neuronal cells (Gupta *et al.,* 2020). Together with the N, P, and L, and RNA from the virus, form the virus ribonucleoprotein (vRNP). Morphogenesis and budding are mediated by the viral M protein. NiV uses two glycoproteins, the G and F proteins, to infect its host cells. To infect a cell, the G glycoprotein attaches to the cell membrane receptors of the host and the fusion protein (F) fuses the host and viral membranes (Ang *et al.,* 2018).

Transmission

Numerous high-risk diseases, such as the Nipah, Rabies and Marburg viruses use bats as reservoir hosts. There are no notable harmful changes in the population of bats associated with these viruses. Understanding the transmission mechanism of NiV, transmission among fruit bats, from bats to pigs, pigs to humans, requires in depth research (Sun *et al.,* 2018). Fruit bats are a

natural reservoir for Nipah viruses, and they have been linked in one way or another to the spread of the virus and related infection in a number of outbreaks that have been reported from various regions of the world. As bats of *Pteropus* spp. which are NiV reservoirs, are drawn to the fruits, NiV is transferred to pigs, other animals, and humans (Clayton, 2017). Transcontinental movement of contaminated pig meat causes transmission of virus from animals in one part of the world to people in another part of globe. The emergence and spread of this novel lethal zoonotic virus illness-Nipah, is caused by the close proximity of fruiting trees, fruits, such as date palm, fruit bats, pigs, and humans. Pigs serve as both the virus's intermediate and amplifying hosts, according to investigations conducted during NiV outbreaks in Malaysia (Hughes *et al.,* 2009).

Epidemiology

In Malaysia, NiV disease was initially identified in 1998 in individuals who had come into contact with pigs. When pig meat was imported from Malaysia to Singapore, eleven abattoir workers who are male, with a typical age of forty-four years, were found to have an acute Nipah virus infection in March 1999; one of them died (Gazal *et al.,* 2022). Headache, fever, dizziness, doll's-eye reflex, vomiting, tachycardia, hypertension, hypotonia, reduction in consciousness, areflexia or absence of any spinal reflexes, and high mortality were among the symptoms of the sickness, which had a relatively brief incubation period (Chua, 2003). Antibodies specific to NiV were found in *P. lylei* or Lyle's flying foxes in Cambodia. Additionally, these antibodies were found using ELISA in the serum obtained from the *P. vampyrus* in Indonesia. Regular bat population surveillance and sero-surveillance in Thailand revealed the NiV RNA presence in bat's urine and saliva and also IgG in their blood, indicating long term NiV persistence in the bats (Mohapatra *et al.,* 2024).

Anti-NiV antibodies in serum samples were the sole way to originally confirm Nipah virus infection in Bangladesh. But in 2004, scientists began using viral nucleic acid detection to characterize the Nipah virus genetically. In total, nine outbreaks have been documented in Bangladesh up until 2010. The outbreak's source of infection was documented in 2011 as raw date palm (Rahman & Chakraborty, 2012).

In 2001, NiV was discovered initially in Siliguri, West Bengal, India, during an outbreak that was marked by feverish sickness linked to altered sensorium (cognitive ability or bad concentration). The source of the NiV infection has been determined to be fruit bats, which was most recently recorded in Kozhikode, in northern Kerala, India, 2018 (Balasubramanian *et al.,* 2024). Infection related mortality occurred during this outbreak, as were deaths among medical staff members who treated patients. Over the past twenty years, intermittent NiV outbreaks, transmission from one individual to another and the zoonotic characteristics are linked to hundreds of fatalities, posing a serious hazard to both humans and domestic animals (Thomas *et al.,* 2019).

Clinical Manifestations and Pathology

NiV can be found in bronchiole's epithelial cells during early stages of human disease. In experimental animal models, antigens from viruses can be found in alveoli and bronchi; type II pneumocytes and the bronchial epithelium are the main targets. Later on, in the illness's course, the virus travels from respiratory epithelium to the lung's endothelial cells. Virus can then make their way into the bloodstream and spread, either attached or unbound to host leucocytes. Multiple organ failure may result from the spleen, kidneys, brain and lungs acting as target organs (Singh *et al.,* 2019).

The virus is the cause of serious, quickly developing illnesses in humans, primarily affecting the central nervous system (CNS) and respiratory system. Three to fourteen days after NiV exposure, the disease's symptoms start to show. First, there is a sharp increase in temperature, followed by fatigue and headache. Within a day or two, follows disorientation and mental confusion, which eventually leads to Coma. Encephalitis is a serious complication of NiV infection (Wong *et al.,* 2002).

Diagnostics, Treatment, and Prevention

Haematologic abnormalities such as leukopenia (11%) and thrombocytopenia (30%) are frequently observed with NiV infection. Forty percent of patients have elevated liver enzymes, and hyponatraemia is occasionally detected. Indices of the kidneys, haemoglobin, and electrolytes besides sodium are often within usual limits. Cerebrospinal fluid may exhibit lymphocytic pleocytosis with elevated proteins, much like in any other viral meningitis (Khan *et al.,* 2024).

NiV is classified as an agent of BSL 4 (biosafety level); but, BSL 2 laboratory facilities are adequate for regular diagnosis if the virus is rendered inactive while collection and isolation of specimen is not attempted. Throughout the illness's acute and recovery stages, a set of tests can be used to make a patient's laboratory diagnosis with a history of NiV. Samples must be shipped at 4°C and processed as soon as feasible (Garbuglia *et al.,* 2023). Early in a disease, it is recommended to use reverse transcriptase polymerase chain reaction (RT PCR) to isolate viruses from blood, urine, cerebrospinal fluid (CSF), and throat and nose swabs. ELISA-IgG and IgM, an enzyme-linked immunosorbent test, can be used to identify antibodies in serum or CSF during the convalescent phase (Bule *et al.,* 2019).

Currently, no specific antiviral therapy is licensed for Nipah virus. Supportive care remains the mainstay. However, some antiviral agents like ribavirin and remdesivir have shown limited efficacy in animal studies. Experimental vaccines and therapeutics have shown efficacy in animal models, but human trials remain limited. The monoclonal antibody m102.4 has demonstrated promise in non-human primates and has been used on a compassionate basis in human exposures (Roman *et al.,* 2022).

Impact on Public health and Society

The high lethality of NiV and lack of definitive treatment generate widespread fear during outbreaks. Families of infected individuals often face social ostracism, while survivors may suffer discrimination due to misconceptions about contagiousness. Public fear also fuels panic-driven behaviours, such as avoidance of hospitals or rejection of public health advisories (Radhakrishnan *et al.,* 2021). The initial outbreak in Malaysia led to a huge economic loss due to mass pig culling, trade restrictions, and loss of livelihoods among farmers (Chua, 2003). In Bangladesh and India, NiV outbreaks have disrupted local economies, restricted food trade, and imposed costs on healthcare systems. Long-term consequences include reduced agricultural productivity and persistent poverty among affected communities. Public health interventions aimed at preventing transmission often require changes to cultural practices. In Bangladesh, campaigns against consumption of raw date palm sap a culturally significant food have faced resistance. Similarly, restrictions on traditional caregiving practices for ill relatives during outbreaks challenge deeply rooted social norms (Hossain *et al.,* 2008).

Conclusion:

Nipah virus continues to be a significant biosecurity threat due to its pandemic potential, as it fulfils key criteria such as zoonotic origin, human transmissibility, and high mortality. Urbanization, ecological disruption, and globalization increase the risk of future spillovers. Targeted health promotion that tactfully promotes better screening and education for at-risk group is required (Sarika & Naseera, 2025).

Investments in genomic surveillance, vaccine platforms, broad-spectrum antivirals, and community engagement are critical. International collaboration, including support from WHO, CEPI, and regional governments, can strengthen preparedness and response frameworks. In conclusion, while Nipah virus may not cause frequent outbreaks globally, it's devastating impact on health, economy, and society mandates proactive and sustained intervention strategies. Learning from past outbreaks, strengthening health systems, and fostering cross-disciplinary collaboration are essential to prevent the next major NiV crisis.

References:

1. Alam, A. M. (2022). Nipah virus, an emerging zoonotic disease-causing fatal encephalitis. *Clinical Medicine*, *22*(4), 348-352.
2. Sharma, N., Jamwal, V. L., Nagial, S., Ranjan, M., Rath, D., & Gandhi, S. G. (2024). Current status of diagnostic assays for emerging zoonotic viruses: Nipah and Hendra. *Expert Review of Molecular Diagnostics*, *24*(6), 473-485.
3. Banerjee, S., Gupta, N., Kodan, P., Mittal, A., Ray, Y., Nischal, N., ... & Wig, N. (2019). Nipah virus disease: A rare and intractable disease. *Intractable & rare diseases research*, *8*(1), 1-8.

4. Gupta, A. K., Kumar, A., Rajput, A., Kaur, K., Dar, S. A., Thakur, A., ... & Kumar, M. (2020). NipahVR: a resource of multi-targeted putative therapeutics and epitopes for the Nipah virus. *Database*, *2020*, baz159.
5. Ang, B. S., Lim, T. C., & Wang, L. (2018). Nipah virus infection. *Journal of clinical microbiology*, *56*(6), 10-1128.
6. Sun, B., Jia, L., Liang, B., Chen, Q., & Liu, D. (2018). Phylogeography, transmission, and viral proteins of Nipah virus. *Virologica Sinica*, *33*(5), 385-393.
7. Clayton, B. A. (2017). Nipah virus: transmission of a zoonotic paramyxovirus. *Current opinion in virology*, *22*, 97-104.
8. Hughes, J. M., Wilson, M. E., Luby, S. P., Gurley, E. S., & Hossain, M. J. (2009). Transmission of human infection with Nipah virus. *Clinical infectious diseases*, *49*(11), 1743-1748.
9. Gazal, S., Sharma, N., Gazal, S., Tikoo, M., Shikha, D., Badroo, G. A., ... & Lee, S. J. (2022). Nipah and Hendra viruses: deadly zoonotic paramyxoviruses with the potential to cause the next pandemic. *Pathogens*, *11*(12), 1419.
10. Chua, K. B. (2003). Nipah virus outbreak in Malaysia. *Journal of Clinical Virology*, *26*(3), 265-275.
11. Mohapatra, P., Khatib, M. N., Shabil, M., Rajput, P., Sharma, N., Satapathy, P., ... & Bushi, G. (2024). Addressing the Nipah virus threat: A call for global vigilance and coordinated action. *Clinical Infection in Practice*, *24*, 100390.
12. Rahman, M., & Chakraborty, A. (2012). Nipah virus outbreaks in Bangladesh: a deadly infectious disease. *WHO South-East Asia journal of public health*, *1*(2), 208-212.
13. Balasubramanian, R., Mohandas, S., Thankappan, U. P., Shete, A., Patil, D., Sabarinath, K., ... & Yadav, P. D. (2024). Surveillance of Nipah virus in Pteropus medius of Kerala state, India, 2023. *Frontiers in Microbiology*, *15*, 1342170.
14. Thomas, B., Chandran, P., Lilabi, M. P., George, B., Sivakumar, C. P., Jayadev, V. K., ... & Hafeez, N. (2019). Nipah virus infection in Kozhikode, Kerala, South India, in 2018: epidemiology of an outbreak of an emerging disease. *Indian Journal of Community Medicine*, *44*(4), 383-387.
15. Singh, R. K., Dhama, K., Chakraborty, S., Tiwari, R., Natesan, S., Khandia, R., ... & Mourya, D. T. (2019). Nipah virus: epidemiology, pathology, immunobiology and advances in diagnosis, vaccine designing and control strategies–a comprehensive review. *Veterinary Quarterly*, *39*(1), 26-55.
16. Wong, K. T., Shieh, W. J., Kumar, S., Norain, K., Abdullah, W., Guarner, J., ... & Nipah Virus Pathology Working Group. (2002). Nipah virus infection: pathology and pathogenesis of an emerging paramyxoviral zoonosis. *The American journal of pathology*, *161*(6), 2153-2167.

17. Khan, S., Akbar, S. M. F., Al Mahtab, M., Uddin, M. N., Rashid, M. M., Yahiro, T., ... & Nishizono, A. (2024). Twenty-five years of Nipah outbreaks in Southeast Asia: A persistent threat to global health. *IJID regions*, *13*, 100434.
18. Garbuglia, A. R., Lapa, D., Pauciullo, S., Raoul, H., & Pannetier, D. (2023). Nipah virus: an overview of the current status of diagnostics and their role in preparedness in endemic countries. *Viruses*, *15*(10), 2062.
19. Bule, M., Khan, F., & Niaz, K. (2019). Antivirals: past, present and future. In *Recent advances in animal virology* (pp. 425-446). Singapore: Springer Singapore.
20. Román, R. G., Tornieporth, N., Cherian, N. G., Shurtleff, A. C., Jackson, M. L. A., Yeskey, D., ... & Le, T. T. (2022). Medical countermeasures against henipaviruses: a review and public health perspective. *The Lancet Infectious Diseases*, *22*(1), e13-e27.
21. Radhakrishnan, C., Sankar, U. V., Rajendran, V. R., Devi, A., Jayasree, V., Saritha, R. L., ... & Kumar, N. S. (2021). Psychosocial impacts of quarantine among survivors of the Nipah virus infection: a qualitative study. *Journal of Global Health Reports*, *5*, e2021092.
22. Chua, K. B. (2003). Nipah virus outbreak in Malaysia. *Journal of Clinical Virology*, *26*(3), 265-275.
23. Hossain, M. J., Gurley, E. S., Montgomery, J. M., Bell, M., Carroll, D. S., Hsu, V. P., ... & Breiman, R. F. (2008). Clinical presentation of nipah virus infection in Bangladesh. *Clinical infectious diseases*, *46*(7), 977-984.
24. Sarika, B. P., & Naseera, K. P. (2025). Kyasanur Forest disease in India: An ecological and public health challenge. In *Innovations and dynamics in biological science* (1st ed., pp. 73–82). Innovation Online Training Academy.

BIOINK DEVELOPMENT FOR 3D BIOPRINTING IN TISSUE ENGINEERING AND ORGAN MODELLING: A HEALTHCARE PERSPECTIVE

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Abstract:
Three-dimensional (3D) bioprinting enables the precise, layer-by-layer fabrication of living, cell-laden constructs that resemble natural tissues. In recent years, bioink development has moved beyond simple printability to focus on functional outcomes—such as high cell survival, tissue-specific signalling, and robust mechanical properties. New strategies include microgel-based inks, tissue-derived extracellular matrix (dECM) formulations, and nanomaterial composites. This review provides a comprehensive overview of recent advances in bioink development, optimization methodologies, and bioprinting innovations, with a focus on applications in skin, bone, cardiac, liver, nerve, and immunotherapy models. Key innovations include dual crosslinked antioxidant bioinks, polysaccharide-based formulations, decellularized extracellular matrix (ECM)-derived inks, and nanoparticle-enhanced hydrogels. Novel approaches such as print-and-grow systems, microgel support materials, and in situ vascularized printing highlight the field's progress toward clinically translatable constructs.

Keywords: 3D Bioprinting, Bioink, recent advances in bioink development, optimization methodologies, bioprinting innovations.

1. Introduction:

3D bioprinting has become a powerful platform for creating tissue-like structures by depositing living cells in viscoelastic bioinks with high spatial precision. Bioinks are generally hydrogel-based networks containing cells and bioactive molecules. To be successful, they must balance printability (e.g., shear-thinning behaviour, viscosity for extrusion) with biological functionality (biocompatibility, biochemical signalling, and controlled degradation). It should resemble the natural ECM in terms of composition, structure and biochemical properties. There are broad range of hydrogels available animal derived like, fibrin, collagen, gelatin and hyaluronic acid (HA) to plant-derived like, alginate and agarose (Schmid *et al.,* 2022). Alginate is one of the most widely used bioink materials since it's affordable and easily crosslinks with calcium ions. However, because it gels too quickly, it's often blended with gelatin, which solidifies at cooler temperatures and supports better cell binding. Together, alginate–gelatin bioinks provide a balanced structure, making them especially useful for bone and cartilage tissue engineering.

(Semba *et al.,* 2022). Decellularized extracellular matrix (dECM) is widely used in cardiac tissue engineering because it closely mimics the natural environment of the heart and supports better cell organization. While it retains the tissue's biochemical cues, it often loses strength during processing, so it's crosslinked or blended with other biomaterials to restore stability and fine-tune scaffold stiffness for different cardiac conditions. (Basara *et al.,* 2021)

Nanocellulose, particularly from bacterial sources, has shown great promise in skin regeneration since it supports the adhesion, growth, and spreading of skin cells like keratinocytes and fibroblasts. It's also being explored as a carrier for delivering cells into skin defects and in other soft tissue engineering applications. A new bioink combining NFC, alginate, and CMC, enabling the printing of complex, skin-like 3D structures without extra support was developed. This bioink showed excellent printability, high cell viability, and promoted the growth and organization of fibroblasts and keratinocytes, ultimately forming a functional dermal model suitable for skin regeneration applications(Zidarič *et al.,* 2020).

Poly (vinyl alcohol) (PVA) is a synthetic, water-soluble polymer valued for its hydrophilicity, biocompatibility, and biodegradability, making it useful in biomedical applications. While its scaffolds naturally have low mechanical strength, crosslinking improves stability and also enhances cell adhesion through hydrogen bonding. A unique advantage of PVA is that only part of its hydroxyl group needs to be crosslinked, leaving others available for further functional modifications. Nanoceria (NC), a rare earth oxide with strong free radical–scavenging properties, holds promise for treating peripheral nerve injuries where oxidative stress impairs Schwann cell function. To explore this, a bioink combining NC with poly (vinyl alcohol) (PVA) was developed using a dual crosslinking strategy. Citric acid crosslinking provided suitable viscosity and cell viability during printing, while a secondary sodium hydroxide step improved structural fidelity. The resulting PVA/NC nanocomposite scaffold demonstrated antioxidant potential, good printability, and high viability of Schwann cells, making it a promising candidate for nerve tissue engineering. (Rizwana *et al.,* 2024).

Rheological characterization plays a key role in assessing bioink printability, focusing on properties like viscosity, which governs flow, and shear-thinning, which allows smooth extrusion through nozzles. Optimizing these factors ensures that bioinks remain printable while supporting cell viability and mimicking native tissue structures. When combined with Design of Experiments (DoE), rheology offers a systematic way to fine-tune formulations, reducing trial-and-error and identifying ideal material concentrations and printing conditions. This integrated approach enables the development of bioinks with tailored viscosity and shear-thinning behaviour, ultimately improving printability and structural fidelity for soft tissue engineering.(Upton *et al.,* 2025).

2. Advances in Bioink Formulations

2.1 Natural and Polysaccharide-Based Bioinks

Polysaccharide-based bioinks have shown promise in skin tissue engineering. (Zidarič *et al.,* 2020) developed a nanofibrillated cellulose–alginate–carboxymethyl cellulose bioink capable of encapsulating fibroblasts with long-term viability, supporting dermal tissue modeling. These formulations demonstrated controlled degradation and hydrophilicity, facilitating wound healing applications.

2.2 Synthetic Polymer and Nanoparticle-Enhanced Bioinks

Synthetic bioinks are often used to improve mechanical properties and functionalize constructs. A dual crosslinked bioink of poly(vinyl alcohol) and cerium oxide nanoparticles (Rizwana *et al.,* 2024)) exhibited antioxidant properties beneficial for peripheral nerve regeneration. Crosslinking with citric acid and sodium hydroxide improved both stability and print fidelity.

2.3 Composite and ECM-Derived Bioinks

Composite formulations enhance both biological and mechanical fidelity. (Basara *et al.,* 2021) utilized human myocardium-derived decellularized ECM blended with GelMA and MeHA, achieving tunable properties suitable for cardiac tissue engineering. The constructs supported cardiomyocyte beating and fibroblast integration, modeling myocardial infarction boundaries in vitro.

In meniscal tissue engineering, a novel alginate–gelatin–cellulose nanocrystal formulation maintained chondrocyte phenotype and induced collagen II expression, suggesting utility in orthopedic applications.(Semba *et al.,* 2022)

Table 1: Common bioink materials and their key properties, polymer types, and crosslinking methods.

Material	Polymer Category	Crosslinking Mode	Key Features (Bioactivity, Mechanics)	Reference
Alginate	Natural (polys.)	Ionic (Ca^{2+}), UV	Shear-thinning; easily gelled by Ca^{2+}+; lacks cell-adhesion (often RGD-modified)	(Semba *et al.,* 2022)
Gelatin / GelMA	Natural (prot.)	Thermal, Photocrosslink	Contains RGD sites; thermo-gels below ~30°C; UV (GelMA) yields tunable stiffness	(Basara *et al.,* 2021)
Hyaluronic Acid (HA)	Natural (GAG)	Enzymatic, UV (HAMA)	Cell-signaling ECM component; viscoelastic; modifiable (e.g. methacrylated HA)	(Schmid *et al.,* 2022)
Collagen (Type I)	Natural (prot.)	Thermal, Enzymatic	High cell affinity; forms fibrils at 37°C; intrinsically bioactive; weak structure	(Zhang *et al.,* 2021)

Nanocellulose (NFC/CCNC)	Natural (polys.)	Physical entanglement	Shear-thinning gel; enhances viscosity and mechanical strength; inert to cells	(Zidarič *et al.,* 2020)
Polyethylene Glycol (PEG)	Synthetic	Photocrosslink (PEGDA)	Inert hydrogel; highly tunable stiffness and mesh size; often blended with bioactive motifs	(Subramaniam *et al.,* 2024)
Poly (vinyl alcohol) (PVA)	Synthetic	Chemical (borate, genipin, etc.)	Good film-forming and viscosity; dual-crosslinking can yield strong gels; minimal bioactivity alone	(Rizwana *et al.,* 2024)
Decellularized ECM	Natural/hybrid	Physical gelation	Derived from tissue (heart, liver, etc.); rich in biochemical cues; usually weak mechanically	(Basara *et al.,* 2021)

3. Optimization Methodologies

3.1 Design of Experiments (DoE)

Statistical DoE was applied to optimize viscosity and shear-thinning properties of hyaluronic acid–alginate–dextran bioinks, aligning their rheology with commercial references (Upton *et al.,* 2025). This structured approach minimized batch variability, underscoring the role of quality control in tailoring bioinks.

Bioink samples were formulated using a Design of Experiment (DoE) approach in Minitab® 21. Components including hyaluronic acid (HA), sodium alginate (ALG), dextran-40 (DEX), and phenol-free DMEM were varied within defined concentration limits. Samples were UV-sterilized, homogenized, and checked microscopically to ensure uniformity. Both factorial and mixture DoEs were applied, generating multiple sample combinations. The mixture data were optimized against a target viscosity (3.275 Pa·s, based on CELLINK SKIN Bioink). The optimized formulation was validated through multiple batches, followed by statistical quality assurance tests (normality, variance, and capability analysis). Rheological characterization was performed using an Anton Paar rheometer, with tests including isothermal temperature stability (at 37 °C) and flow curves across different shear rates. These assessments confirmed reproducibility, shear-thinning behaviour, and process reliability of the optimized bioink formulation.

3.2 Crosslinking Strategies

Dual crosslinking approaches—chemical and physical—emerged as effective means to enhance bioink performance. PVA-nanoceria bioinks exemplified how sequential crosslinking enhances both printability and stability while maintaining biocompatibility.

The fabrication of PVA-based gels followed a dual crosslinking strategy to achieve stable and printable materials. First, a 25 wt% PVA solution was prepared by dissolving PVA in water at 120 °C. Once cooled to 40 °C, citric acid (5 wt%) was added as a primary crosslinker, resulting in a viscous gel suitable for bioprinting. For nanoceria-loaded gels, different concentrations of nanoceria (0.5–2%) were first dispersed in water via ultrasonication. PVA was then dissolved in this dispersion and crosslinked with citric acid in the same way, yielding PVA/NC gels. To convert these gels into hydrogels, small portions were dried overnight, followed by immersion in a NaOH solution, which introduced secondary crosslinking. The resulting hydrogels were thoroughly washed, dried, and stored in a desiccator to prevent moisture uptake. Before analysis, they were lyophilized to ensure stability. This dual crosslinking approach provided both mechanical robustness and versatility, enabling the incorporation of nanoceria while maintaining the processability of PVA hydrogels. (Rizwana *et al.,* 2024)

3.3 Support Materials and Microgels

Microgel-based support materials such as CarGrow (κ-carrageenan microgels) enable high-fidelity printing with low-viscosity inks. These granular systems also provide mechanical cues that enhance post-printing tissue maturation, as seen in the 'print-and-grow' strategy by (Machour *et al.,* 2022)

CarGrow microgels were designed as a support material for print-and-grow bioprinting, meeting key requirements such as biocompatibility, mechanical stability, optical clarity, and controllable fabrication. Unlike conventional granular hydrogels, CarGrow overcomes issues like temperature or ion sensitivity and poor transparency, making it suitable for long-term cell culture.The microgels were fabricated using a simple water-in-oil (W/O) emulsion method. In this process, a hot aqueous solution of κ-carrageenan and KCl was dispersed into an oil phase with Span 80 surfactant to form droplets, which solidified into microgels upon cooling. The particles were then separated by centrifugation. Microscopy confirmed their spherical morphology and uniform size distribution. Rheological tests (strain sweep, temperature sweep, steady shear flow, and thixotropy) demonstrated that CarGrow microgels exhibit shear-thinning and self-healing behavior, ideal for extrusion-based bioprinting. Additionally, diffusion studies showed that CarGrow allows efficient transport of small molecules and proteins, while its optical transparency supports live-cell imaging. Overall, CarGrow microgels provide a reproducible, biocompatible, and mechanically suitable support material for freeform 3D bioprinting applications.(Machour *et al.,* 2022)

(Subramaniam *et al.,* 2024) also utilized PEG microgels to create permeable scaffolds supporting functional liver discoids. PEG-based microgels were formulated to create a printable support medium tailored for liver tissue models. For effective bioprinting, the medium must flow easily under moderate stress, provide enough elasticity to support printed structures, and consist of

particles within an optimal size range. Too small particles behave like fluids over time, while overly large ones compromise print resolution. PEG microgels were synthesized via inverse emulsion polymerization and characterized using brightfield microscopy and image analysis. Particle sizes followed a log-normal distribution, with a median diameter of ~6 μm, aligning well with previous findings for high-quality bioprinting.

3.4 In Situ and Vascularized Bioprinting

Stem cell-laden alginate microgel bioinks was introduced with self-healing properties, incorporating patterned vascular networks. In situ printing into bone defects demonstrated clinical potential for vascularized tissue regeneration (Jeon *et al.,* 2025).

In this approach, Human bone marrow-derived MSCs were isolated, expanded, and suspended in oxidized methacrylated alginate (OMA) solutions to create SSAM bioinks. The OMA-cell mixtures were crosslinked with $CaSO_4$ using a dual-syringe mixing system, producing cell-laden bioinks with high viability, confirmed by Live/Dead staining and Safranin O imaging. Rheological tests showed that SSAM bioinks possess shear-thinning, shear-yielding, and self-healing properties, making them well-suited for extrusion printing. Frequency and strain sweeps confirmed elastic dominance ($G' > G''$), while cyclic strain tests demonstrated rapid recovery. Resolution analysis using different needle gauges further validated their ability to produce fine, uniform filaments in 3D bioprinting.

3.5 ECM at Low Concentration

Jammed microgel was used to support printing of low-concentration collagen, facilitating natural ECM infiltration and tissue-specific remodelling (Zhang *et al.,* 2021). This bioprinting approach shows how we can directly print natural extracellular matrix (ECM) proteins, like collagen-1, into microgel supports to create precise, stable structures. Unlike many existing methods, it works even at low ECM concentrations, which makes it easier for cells to infiltrate the printed matrix—without relying on engineered bioinks, synthetic scaffolds, or chemical modifications.

4. Application-Specific Bioink Tailoring

Bioinks are increasingly tailored to particular tissues by selecting materials and cell types that match the microenvironment. Below we highlight examples of cardiac, hepatic, neural, dermal, meniscal, and oncological (tumor) models.

4.1. Cardiac Tissue Models:

Cardiac bioinks must support beating cells and mechanical contraction. (Basara *et al.,* 2021) developed a heart-derived ink by combining decellularized human heart ECM with GelMA and methacrylated HA. This hybrid had a tunable elastic modulus ~10× higher than GelMA alone, enabling constructs that mimicked healthy versus infarct myocardium stiffness. Importantly, printed human induced pluripotent stem cell cardiomyocytes (iPSC-CMs) embedded in these gels formed striated sarcomeres and synchronized beating, demonstrating both printability and

cardiac function. Other cardiac bioinks often use collagen, fibrin, or Matrigel combined with cells; electroconductive additives (e.g. gold or carbon) are also explored to enhance electrical signal propagation.

4.2. Hepatic (Liver) Models:

Liver bioinks need to support highly metabolic hepatocytes (Anjum *et al.,* 2024) printed a micro-scale liver tissue by encapsulating primary human hepatocytes and endothelial cells in a collagen-I matrix and extruding the mixture into a bath of PEG microgel particles. This embedded printing approach (discussed below) enabled creation of a 1.5 mm spiral-shaped liver microtissue. The constructs exhibited sustained albumin secretion, indicating mature hepatic function. In general, liver bioinks often use collagen or gelatin to mimic soft liver ECM; they may include growth factors (e.g. HGF) and usually require vascular support or perfusion for viability. The Anjum study highlights the use of support gels (PEG microparticles) to facilitate liver biofabrication.

4.3. Neural Tissue Models:

Neural bioinks must emulate the soft, electroconductive environment of nerve tissue (Vijayavenkataraman *et al.,* 2024). reported a biodegradable, conductive collagen–polymer hybrid for neural printing. For nervous tissues, adding conductivity is crucial, as electrical cues promote neuron proliferation and differentiation. Thus, conductive polymers (polypyrrole, polyaniline) or carbon nanomaterials are often blended into hydrogels. The example above used collagen and a block copolymer of polypyrrole and PCL (PPy-b-PCL), yielding a printable hydrogel with improved cell compatibility. In other cases, fibrin or Matrigel (highly permissive for neurons) are used with conductive fillers. Overall, neural bioinks prioritize ultra-soft stiffness (around hundreds of Pa) and electrical conductivity.

4.4. Dermal (Skin) Models:

Skin bioprinting requires layered constructs of fibroblasts and keratinocytes. (Zidarič *et al.,* 2020) formulated a dermal bioink from alginate, CMC, and cellulose nanofibrils (NFC). This polysaccharide-based ink exhibited strong shear-thinning and yielded skin scaffolds with high fibroblast viability (cells active for 29 days). The printed dermal equivalents supported an epidermal layer of keratinocytes, indicating proper niche formation. Key requirements for dermal inks are moisture retention, moderate stiffness, and inclusion of collagen or fibrin to support keratinocyte growth. Polysaccharide blends provide printability while allowing nutritional gelation.

4.5. Meniscal (Cartilage) Models:

The knee meniscus is a fibrocartilaginous tissue, so bioinks here must support chondrogenesis under mechanical load.(Semba *et al.,* 2022) optimized a meniscus bioink composed of 4.0% gelatin, 0.75% alginate, and 1.4% cellulose nanocrystals (CCNC) in 4.6% mannitol. This ink

printed into a porous structure together with PCL fibers. The cell-laden constructs showed >98% viability and robust expression of collagen II (a cartilage marker) after culture. This example illustrates combining a hydrogel with nanofillers for print fidelity and blending with a rigid polymer (PCL) for mechanical support. Other meniscal inks include agarose or gellan blends to mimic cartilage ECM.

4.6. Oncological (Tumor) Models:

Bioprinted tumor models require inks that allow cancer cells to exhibit realistic growth and invasion. (Schmid *et al.,* 2022) developed a printable melanoma model ink by blending alginate, hyaluronic acid, and gelatin. This tri-component bioink supported melanoma cell survival, spheroid formation, and could be imaged in an in vivo–like vascularized niche. The presence of HA (a major skin ECM component) and gelatin (from collagen) provided realistic cues. In general, cancer bioinks may intentionally avoid too rapid crosslinking so that cells can remodel the matrix; they often include tumor microenvironment factors. The Schmid ink also demonstrated compatibility with an arteriovenous loop model (supporting neovascularization), illustrating advanced use in oncology research.

Table 2: Example tissue-specific bioink formulations and outcomes.

Tissue	Example Bioink Composition	Outcome / Functionality	Reference
Cardiac	GelMA + MeHA + human heart dECM	Tunable stiffness (healthy vs. infarct myocardium); beating iPSC-cardiomyocytes with sarcomeric assembly.	(Basara *et al.,* 2021)
Liver	Collagen-I (0.15%) + PHHs + HUVECs printed into PEG microgels	Perfusable 3D liver microtissue (~1.5 mm) with sustained albumin secretion.	(Anjum *et al.,* 2024)
Neural	Collagen + Polypyrrole–PCL copolymer (PPy-b-PCL)	Conductive gel supporting neuronal differentiation; printable with high cell viability.	(Vijayavenkataraman *et al.,* 2024)
Dermal	Alginate + CMC + cellulose nanofibrils	Fibroblast-laden skin construct; homogeneous cell distribution; viability >29 days.	(Zidarič *et al.,* 2020)
Meniscal	Gelatin (4.0%) + Alginate (0.75%) + CCNC (1.4%)	Porous cartilage print with healthy chondrocytes; >98% viability and collagen II production.	(Semba *et al.,* 2022)
Oncological	Alginate + Hyaluronic acid + Gelatin	Printable melanoma tumor model; high cell survival and shape fidelity for in vitro/vivo assays.	(Schmid *et al.,* 2022)

Table 2 lists example bioink formulations for specific tissues. These tailored inks combine relevant ECM components (e.g. heart dECM for cardiac, collagen for liver) and often include nanofillers or secondary scaffolds to meet mechanical demands. References indicate key outcomes such as cell viability, matrix deposition, or functional readouts for each model.

5. Future Directions and Emerging Trends

Looking ahead, several exciting trends are emerging in bioink development:

5.1. 4D Bioprinting:

Bioinks that change properties after printing in response to stimuli (temperature, pH, enzymes) are being explored. For example, shape-memory or self-healing hydrogels could allow dynamic tissue constructs.

5.2. Machine-Learning Guided Design:

Systematic data-driven approaches (like Upton's DoE study) will likely become more common to predict optimal ink formulations for given printer settings and target tissues.

5.3. Multimaterial and Coaxial Printing:

Advanced printers can deposit multiple bioinks simultaneously. Coaxial nozzles can print tubular vessels (e.g. alginate sacrificial core with endothelial cells) in a single step. Combining structural polymers (like ceramics or tough hydrogels) with cell-laden gels will expand applications.

5.4. Bioactive Additives:

Incorporating controlled-release growth factors, peptides, or genetic material into bioinks will enhance tissue-specific differentiation. For instance, bone bioinks may include BMPs, while angiogenic factors could be embedded in cardiac or vascular inks.

5.5. In situ Bioprinting:

Hand-held or robotic bioprinters that deposit bioinks directly into wounds or surgical sites are under development. This requires bioinks that gel quickly and adhere to irregular surfaces (e.g. light-curable gelatin blends).

5.6. Sustainable and Clinical-Grade Materials:

There is growing interest in veterinary/food-safe bioinks and fully defined synthetic scaffolds to meet regulatory demands. Moreover, integrating imaging compatibility (Gabalski *et al.,* 2023) with bioinks themselves (e.g. contrast agents for MRI-compatible scaffolds) could advance theranostics.

5.7. Personalized Bioinks:

Patient-derived components (cells, plasma, ECM from biopsy) can yield truly personalized bioinks. The concept of "autologous bioinks" – such as mixing a patient's own demineralized bone matrix or platelet lysate into the ink – could improve integration. Regulatory frameworks will evolve to handle such custom therapies.

Conclusion:

The field of bioink development has evolved remarkably from basic hydrogel formulations to highly specialized, multifunctional materials designed to closely replicate the complexity of human tissues. What began with simple blends like alginate–gelatin has now expanded into composite systems incorporating nanomaterials, tissue-derived ECM, and smart crosslinking strategies. These innovations are not only improving printability and structural fidelity but also

enabling cell survival, signalling, and functional tissue outcomes across diverse applications—from skin and bone regeneration to cardiac, neural, and even tumor modeling.

Looking ahead, the future of 3D bioprinting lies in bioinks that are smarter, more responsive, and patient-specific. Integration of approaches like 4D printing, machine learning–guided optimization, and personalized autologous formulations could shift the field from experimental constructs toward true clinical translation. Achieving this will require interdisciplinary collaboration—uniting materials scientists, biologists, engineers, and clinicians—to bridge the gap between laboratory advances and real-world therapeutic solutions.

Ultimately, tailoring bioinks is not just about achieving better print fidelity—it is about designing living, functional materials that can heal, restore, and even replace damaged human tissues. As the field progresses, these innovations hold the potential to redefine regenerative medicine and bring us closer to the vision of printing patient-specific tissues and organs on demand.

References:

1. Anjum, M. R., Subramaniam, V., Higgins, B. R., Abrahan, C., Chisolm, S. J., Krishnaprasad, K. A., ... & Sarntinoranont, M. (2024). Determining Rates of Molecular Secretion from Supernatant Concentration Measurements in a 3D-Bioprinted Human Liver Tissue Model. *ACS Biomaterials Science & Engineering*, *10*(10), 6711-6720. https://doi.org/10.1021/acsbiomaterials.4c01086

2. Basara, G., Ozcebe, S. G., Ellis, B. W., & Zorlutuna, P. (2021). Tunable human myocardium derived decellularized extracellular matrix for 3D bioprinting and cardiac tissue engineering. *Gels*, *7*(2), 70. https://doi.org/10.3390/gels7020070

3. Gabalski, M. A., Smith, K. R., Hix, J., & Zinn, K. R. (2023). Comparisons of 3D printed materials for biomedical imaging applications. *Science and Technology of Advanced Materials*, *24*(1). https://doi.org/10.1080/14686996.2023.2273803

4. Jeon, O., Park, H., Lee, M. S., & Alsberg, E. (2025). In situ cell-only bioprinting of patterned prevascular tissue into bioprinted high-density stem cell-laden microgel bioinks for vascularized bone tissue regeneration. *bioRxiv*, 2025-03. https://doi.org/10.1101/2025.03.17.643708

5. M. Machour, N. Hen, I. Goldfracht, D. Safina, M. Davidovich-Pinhas, H. Bianco-Peled, S. Levenberg, Print-and-Grow within a Novel Support Material for 3D Bioprinting and Post-Printing Tissue Growth. *Adv. Sci.* 2022, 9, 2200882. https://doi.org/10.1002/advs.202200882

6. Morley, C. D., Flores, C. T., Drake, J. A., Moore, G. L., Mitchell, D. A., & Angelini, T. E. (2022). Spatiotemporal T cell dynamics in a 3D bioprinted immunotherapy model. *Bioprinting*, *28*, e00231. https://doi.org/10.1016/j.bprint.2022.e00231

7. Rizwana, N., Maslekar, N., Chatterjee, K., Yao, Y., Agarwal, V., & Nune, M. (2023). Dual crosslinked antioxidant mixture of poly (vinyl alcohol) and cerium oxide nanoparticles as a bioink for 3D bioprinting. *ACS Applied Nano Materials*, *7*(16), 18177-18188. https://doi.org/10.1021/acsanm.3c02962
8. Schmid, R., Schmidt, S. K., Detsch, R., Horder, H., Blunk, T., Schrüfer, S., ... & Kengelbach-Weigand, A. (2022). A new printable alginate/hyaluronic acid/gelatin hydrogel suitable for biofabrication of in vitro and in vivo metastatic melanoma models. *Advanced Functional Materials*, *32*(2), 2107993. https://doi.org/10.1002/adfm.202107993
9. Semba JA, Mieloch AA, Tomaszewska E, *et al.,* 2023, Formulation and evaluation of a bioink composed of alginate, gelatin, and nanocellulose for meniscal tissue engineering. Int J Bioprint, 9(1): 621. https://doi.org/10.18063/ijb.v9i1.621
10. Subramaniam, V., Abrahan, C., Higgins, B. R., Chisolm, S. J., Sweeney, B., Duraivel, S., ... & Angelini, T. E. (2025). A functional human liver tissue model: 3D bioprinted co-culture discoids. *Biomaterials Advances*, *173*, 214288. https://doi.org/10.1016/j.bioadv.2025.214288
11. Subramaniam, V., Shetty, A. M., Chisolm, S. J., Lansberry, T. R., Balachandar, A., Morley, C. D., & Angelini, T. E. (2024). Biopolymer networks packed with microgels combine strain stiffening and shape programmability. *Giant*, *19*, 100297. https://doi.org/10.1016/j.giant.2024.100297
12. Upton, A., Mylona, A. & Zimbitas, G. Utilising design of experiment to design an optimised bioink for 3D bioprinting. *J Mater Sci* **60**, 10467–10477 (2025). https://doi.org/10.1007/s10853-025-11076-1
13. Vijayavenkataraman S, Vialli N, Fuh JYH, *et al.,* Conductive collagen/polypyrrole-b-polycaprolactone hydrogel for bioprinting of neural tissue constructs. Int J Bioprint, 5(2.1): 229. http://dx.doi.org/10.18063/ijb.v5i2.1.229.
14. Zhang, Y., Ellison, S. T., Duraivel, S., Morley, C. D., Taylor, C. R., & Angelini, T. E. (2021). 3D printed collagen structures at low concentrations supported by jammed microgels. *Bioprinting*, *21*,e00121. https://doi.org/10.1016/j.bprint.2020.e00121
15. Zidarič, T., Milojević, M., Gradišnik, L., Stana Kleinschek, K., Maver, U., & Maver, T. (2020). Polysaccharide-Based Bioink Formulation for 3D Bioprinting of an In Vitro Model of the Human Dermis. *Nanomaterials*, *10*(4), 733. https://doi.org/10.3390/nano10040733

PHYSIOTHERAPY APPROACHES AND APPLICATIONS IN NURSING AND HEALTHCARE

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Abstract:
Physiotherapy has become an essential component of holistic healthcare, complementing nursing practice in promoting recovery, preventing complications, and improving quality of life. This chapter explores the integration of physiotherapy approaches into nursing and healthcare, emphasizing evidence-based practices, theoretical frameworks, and practical applications across diverse clinical settings. Key areas include mobility assessment, fall risk screening, respiratory care, pain management, positioning strategies, and early mobilization protocols, which together help reduce hospital stay, prevent secondary complications, and enhance functional independence. The discussion extends to specialized contexts such as critical care, surgical recovery, rehabilitation, long-term care, and community health, where nurses play pivotal roles in applying physiotherapy-informed interventions. The chapter also highlights the significance of professional development, interprofessional collaboration, and competency-based education to ensure safe and effective implementation. Emerging trends, including the use of artificial intelligence, telehealth, and digital monitoring tools, are considered as future directions for strengthening physiotherapy applications in nursing. By merging physiotherapeutic principles with nursing care, healthcare systems can foster patient-centered, cost-effective, and sustainable outcomes.

Keywords: Physiotherapy, Nursing Practice, Mobility Interventions, Rehabilitation, Patient-Centered Care

Introduction:

The integration of physiotherapy principles and practices within nursing and healthcare settings has evolved significantly over the past two decades, transforming from a collaborative relationship to a more integrated, holistic approach to patient care. This chapter explores the

multifaceted applications of physiotherapy in nursing practice, examining contemporary approaches, evidence-based interventions, and the growing recognition of movement as medicine within healthcare delivery systems (1). As healthcare systems worldwide face increasing pressures from ageing populations, chronic disease burdens, and the need for cost-effective interventions, the role of physiotherapy in nursing practice has become increasingly vital in promoting patient recovery, preventing complications, and enhancing quality of life outcomes.

The World Health Organization's Global Strategy on People-Centred and Integrated Health Services emphasizes the importance of multidisciplinary collaboration, positioning physiotherapy as a cornerstone of comprehensive patient care (2). Within this framework, nurses increasingly incorporate physiotherapeutic principles into their practice, ranging from basic mobility assessments to complex rehabilitation protocols. This integration not only enhances patient outcomes but also contributes to reducing healthcare costs through prevention of secondary complications such as pressure ulcers, deep vein thrombosis, and hospital-acquired pneumonia (3).

Contemporary healthcare delivery models recognize that effective patient care extends beyond traditional medical interventions to encompass functional restoration, movement optimization, and lifestyle modification. Nurses, as the largest healthcare workforce globally, are uniquely positioned to implement physiotherapeutic approaches due to their continuous patient contact, holistic care perspective, and comprehensive understanding of patient needs across the healthcare continuum (4). This chapter provides a comprehensive examination of how physiotherapy principles can be effectively integrated into nursing practice, supported by current evidence and practical applications.

Theoretical Foundations and Conceptual Framework

The incorporation of physiotherapy methods into nursing practice is based on various theoretical models that highlight comprehensive patient care, restoration of function, and the importance of evidence-based practices. The International Classification of Functioning, Disability and Health (ICF) model, developed by the WHO, provides a comprehensive framework for understanding the complex interactions between health conditions, body functions and structures, activities, and participation within environmental contexts (2). This biopsychosocial model serves as a foundation for physiotherapy-informed nursing interventions, emphasizing the importance of addressing not only pathological conditions but also functional limitations and participation restrictions.

Virginia Henderson's Need Theory, which identifies fourteen fundamental human needs, aligns closely with physiotherapeutic principles, particularly in addressing mobility, positioning, and breathing needs (5). This theoretical alignment facilitates the integration of movement-based interventions into routine nursing care, emphasizing the nurse's role in assisting patients to

achieve independence in activities of daily living. The theory's emphasis on patient autonomy and functional independence resonates with physiotherapy's core principles of promoting optimal movement and function.

The Theory of Unpleasant Symptoms, originally introduced by Lenz and further developed by modern researchers, offers a valuable perspective for comprehending how physiotherapy techniques can tackle multiple symptoms at once (6). This theory recognizes that symptoms often occur in clusters and can be influenced by physiological, psychological, and situational factors. Physiotherapy approaches in nursing practice can effectively address symptom clusters such as pain, fatigue, and functional decline through targeted interventions that consider the multifactorial nature of symptom experiences.

Bandura's Social Cognitive Theory also informs the application of physiotherapy approaches in nursing, particularly regarding patient education, self-efficacy building, and behavior modification (7). Nurses utilizing physiotherapeutic approaches must consider patients' beliefs about their ability to perform specific movements or exercises, their outcome expectations, and the environmental factors that may facilitate or hinder adherence to movement-based interventions.

Assessment Techniques and Screening Tools

Effective implementation of physiotherapy approaches in nursing requires comprehensive assessment skills and familiarity with validated screening tools. Nurses must develop competency in basic movement analysis, functional assessment, and risk screening to identify patients who would benefit from physiotherapeutic interventions (8). The integration of systematic assessment protocols enables early identification of mobility impairments, fall risk factors, and functional decline patterns.

The Berg Balance Scale, widely recognized for its reliability and validity, serves as an essential tool for nurses assessing balance and fall risk in various healthcare settings (9). This 14-item scale evaluates balance performance in functional tasks and provides valuable information for developing targeted interventions. Nurses trained in its administration can efficiently screen patients and initiate appropriate mobility interventions based on scores, with scores below 45 indicating high fall risk requiring immediate attention.

The Timed Up and Go (TUG) test represents another crucial assessment tool that nurses can easily incorporate into routine practice (10). This straightforward and efficient screening tool assesses functional mobility, balance, and the risk of falling by measuring the time it takes for a patient to stand up from a chair, walk three meters, turn around, return, and sit back down. If the total time taken is over 14 seconds, it suggests a higher risk of falling and the necessity for a physiotherapy evaluation or mobility interventions initiated by nursing staff.

Functional Independence Measure (FIM) assessments provide comprehensive evaluation of patients' ability to perform activities of daily living independently (4). While traditionally administered by rehabilitation professionals, nurses can utilize modified versions or specific components to assess motor and cognitive function systematically. This assessment approach enables nurses to identify specific areas of functional decline and develop targeted interventions to promote independence.

The STRATIFY (St. Thomas's Risk Assessment Tool in Falling Elderly Inpatients) score offers a validated approach to fall risk assessment specifically designed for use by nurses in acute care settings (11). This five-item tool considers factors such as history of falls, agitation, visual impairment, toileting needs, and transfer ability, providing a systematic approach to identifying high-risk patients who would benefit from enhanced mobility interventions.

Pain assessment remains fundamental to physiotherapy-informed nursing practice, with tools such as the Numeric Rating Scale, Visual Analog Scale, and specialized instruments like the Brief Pain Inventory providing essential baseline data for intervention planning (12). Understanding pain patterns, triggers, and responses to movement is crucial for developing safe and effective mobility protocols.

Core Physiotherapy Interventions in Nursing Practice

The implementation of physiotherapy approaches within nursing practice encompasses a range of interventions designed to promote mobility, prevent complications, and enhance functional outcomes. These interventions must be evidence-based, safe for implementation by nurses, and integrated seamlessly into routine care delivery (13).

Early mobilization protocols represent one of the most significant applications of physiotherapy principles in nursing practice. Research consistently demonstrates that early mobilization reduces hospital length of stay, prevents muscle atrophy, decreases incidence of hospital-acquired pneumonia, and improves overall functional outcomes (14). Nurses play a crucial role in implementing progressive mobility protocols, beginning with passive range of motion exercises and advancing to active-assisted and independent mobility as appropriate. The establishment of mobility milestones and systematic progression protocols ensures safe and effective implementation across diverse patient populations.

Respiratory physiotherapy techniques constitute another essential component of physiotherapy-informed nursing practice. Techniques such as deep breathing exercises, incentive spirometry, positioning for optimal lung expansion, and assisted coughing protocols can significantly reduce pulmonary complications (15). Nurses trained in these techniques can implement respiratory interventions as part of routine care, particularly for patients at risk of developing pneumonia or other respiratory complications. The integration of respiratory physiotherapy principles into

nursing care plans has shown measurable improvements in oxygenation, reduced incidence of pneumonia, and shorter recovery times.

Positioning and pressure relief strategies represent fundamental applications of physiotherapy principles that nurses implement continuously. Understanding biomechanical principles, pressure distribution, and tissue tolerance enables nurses to develop effective positioning schedules that prevent pressure ulcers while promoting optimal joint positioning and circulation (16). Advanced positioning techniques, including the use of specialized equipment and positioning aids, require understanding of physiological responses to positioning changes and contraindications for specific positions.

Transfer training and mobility assistance techniques are essential skills that combine nursing care with physiotherapy principles. Proper body mechanics, use of assistive devices, and safe transfer techniques protect both patients and healthcare providers while promoting patient independence (17). Nurses must understand the biomechanics of transfers, appropriate use of various assistive devices, and methods for progressing patients toward independence in mobility tasks.

Exercise prescription within nursing scope represents an emerging area where physiotherapy principles directly inform nursing interventions. While nurses may not prescribe complex exercise regimens, they can implement basic strengthening exercises, flexibility routines, and functional training activities as part of comprehensive care plans (18). Understanding exercise physiology, contraindications, and progression principles enables nurses to safely implement movement-based interventions that complement medical treatment.

Specialty Applications Across Healthcare Settings

The application of physiotherapy approaches in nursing practice varies significantly across healthcare settings, with each environment presenting unique opportunities and challenges for implementation. Understanding setting-specific considerations enables nurses to adapt physiotherapy principles effectively while maintaining safety and quality standards (19).

Critical Care Applications

In intensive care units, physiotherapy-informed nursing practice focuses primarily on preventing complications associated with prolonged immobility and mechanical ventilation (20). Early mobilization protocols in critical care have gained significant attention following research demonstrating improved outcomes including reduced delirium, shorter mechanical ventilation duration, and decreased ICU length of stay. Nurses in critical care settings implement passive range of motion exercises, positioning protocols, and progressive mobility activities while managing complex medical equipment and monitoring systems.

The implementation of the ABCDEF bundle (Assess, prevent and manage pain; Both spontaneous awakening trials and spontaneous breathing trials; Choice of analgesia and sedation; Delirium: assess, prevent, and manage; Early mobility and exercise; Family engagement and

empowerment) exemplifies the integration of physiotherapy principles into critical care nursing practice (21). This evidence-based approach emphasizes early mobilization as a core component of comprehensive critical care management, with nurses playing central roles in assessment, implementation, and monitoring of mobility interventions.

Respiratory physiotherapy techniques take on particular importance in critical care settings, where patients frequently require assistance with secretion clearance, lung expansion, and ventilator weaning (22). Nurses trained in advanced respiratory techniques can implement protocols for percussion, vibration, postural drainage, and assisted coughing, contributing significantly to respiratory outcomes and reducing complications such as ventilator-associated pneumonia.

Acute Care Medical-Surgical Settings

Medical-surgical units provide diverse opportunities for implementing physiotherapy approaches, with patient populations ranging from post-operative surgical patients to individuals with acute medical conditions (23). Nurses in these settings must adapt interventions to accommodate varying acuity levels, surgical restrictions, and medical complications while promoting functional recovery and preventing secondary complications.

Post-operative mobility protocols represent a crucial application area where physiotherapy principles directly inform nursing practice. Understanding surgical precautions, healing timelines, and appropriate progression of activities enables nurses to implement safe and effective mobility interventions that promote recovery while preventing complications such as deep vein thrombosis, pulmonary embolism, and surgical site complications (1).

Fall prevention programs in acute care settings exemplify the integration of physiotherapy assessment and intervention principles into nursing practice. Comprehensive fall prevention protocols include risk assessment, environmental modification, strengthening exercises, balance training, and patient education components that nurses can implement as part of routine care delivery (24).

Rehabilitation and Long-Term Care Settings

Extended care facilities and rehabilitation hospitals provide optimal environments for implementing comprehensive physiotherapy approaches within nursing practice (25). These settings allow for more intensive implementation of mobility interventions, functional training activities, and patient education programs designed to promote independence and quality of life.

Nurses in rehabilitation settings often work closely with physical therapists to implement treatment plans, requiring advanced understanding of exercise principles, contraindications, and progression strategies (26). This collaborative approach enables continuous reinforcement of therapeutic activities and ensures consistent implementation of mobility interventions throughout the patient's day.

Long-term care settings present unique challenges and opportunities for physiotherapy-informed nursing practice, with emphasis on maintaining function, preventing decline, and promoting quality of life for residents with chronic conditions (27). Nurses in these settings implement maintenance exercise programs, positioning protocols, and mobility assistance techniques that support residents' functional abilities while accommodating progressive conditions and age-related changes.

Home Health and Community Settings

Community-based nursing practice provides opportunities for implementing physiotherapy approaches within patients' natural environments, enabling assessment and intervention strategies that address real-world functional challenges (28). Home health nurses must adapt interventions to available resources, environmental constraints, and family support systems while promoting optimal function and preventing complications.

Home exercise programs represent a crucial component of community-based physiotherapy applications, requiring nurses to understand exercise prescription principles, safety considerations, and methods for monitoring compliance and progression (29). Patient and family education becomes particularly important in home settings, where nurses must ensure that mobility interventions can be safely implemented without direct professional supervision.

Evidence-Based Practice and Research Integration

The integration of physiotherapy approaches into nursing practice must be grounded in current evidence and supported by ongoing research initiatives that demonstrate effectiveness, safety, and cost-efficiency (30). Contemporary healthcare demands evidence-based decision-making, requiring nurses to understand research methodologies, interpret findings, and implement evidence-based protocols in their practice settings.

Recent systematic reviews and meta-analyses provide strong evidence supporting the integration of physiotherapy principles into nursing practice across various settings and patient populations (31). Large-scale randomized controlled trials have demonstrated that nurse-implemented mobility interventions can achieve outcomes comparable to those achieved by physical therapists for specific patient populations and intervention types, supporting expanded scope of practice for nurses with appropriate training and competency validation.

The concept of implementation science has gained significant attention in healthcare research, focusing on methods for translating evidence-based interventions into routine practice (32). Research in this area examines barriers and facilitators to implementing physiotherapy approaches within nursing practice, identifying factors such as organizational support, staff training, resource availability, and patient characteristics that influence successful implementation.

Quality improvement initiatives provide additional evidence supporting the integration of physiotherapy approaches into nursing practice (33). Healthcare organizations implementing systematic mobility protocols report improvements in patient satisfaction scores, reduced length of stay, decreased incidence of hospital-acquired conditions, and improved functional outcomes at discharge. These findings support the business case for investing in training and resources necessary to support physiotherapy-informed nursing practice.

Emerging research areas include the use of technology to support physiotherapy applications in nursing practice, with studies examining the effectiveness of wearable devices, mobile applications, and telehealth platforms for monitoring and supporting mobility interventions (34). These technological innovations have the potential to enhance the efficiency and effectiveness of physiotherapy approaches while providing objective data for monitoring patient progress and intervention fidelity.

Professional Development and Competency Requirements

The successful integration of physiotherapy approaches into nursing practice requires systematic professional development programs that address knowledge, skills, and competency requirements (35). Healthcare organizations must invest in comprehensive training programs that enable nurses to safely and effectively implement physiotherapy interventions while maintaining their primary nursing responsibilities.

Competency-based education models provide structured approaches for developing the knowledge and skills necessary for implementing physiotherapy approaches in nursing practice (36). These models typically include theoretical foundations, hands-on skill development, supervised practice opportunities, and competency validation processes that ensure nurses can safely implement interventions before practicing independently.

Continuing education requirements must address the evolving nature of physiotherapy applications in nursing practice, with regular updates on new research findings, intervention techniques, and safety protocols (37). Professional organizations play crucial roles in developing and disseminating continuing education resources that support nurses in maintaining current competencies and expanding their scope of practice appropriately.

Interprofessional education initiatives provide valuable opportunities for nurses and physical therapists to develop collaborative relationships and shared understanding of each profession's scope of practice and competencies (38). These educational experiences promote effective teamwork, reduce role confusion, and ensure that patients receive coordinated care that maximizes the benefits of both nursing and physiotherapy interventions.

Future Directions and Emerging Trends

The future of physiotherapy applications in nursing practice will be shaped by technological innovations, changing healthcare delivery models, and evolving patient populations (39).

Understanding emerging trends and preparing for future developments enables healthcare organizations and individual nurses to position themselves for success in implementing advanced physiotherapy approaches.

Artificial intelligence and machine learning technologies show promise for enhancing physiotherapy applications in nursing practice through improved assessment techniques, personalized intervention protocols, and predictive modeling for identifying patients at risk for functional decline (40). These technologies may enable nurses to implement more precise and effective interventions while reducing the time and expertise required for comprehensive assessments.

Telehealth and remote monitoring capabilities continue to expand opportunities for implementing physiotherapy approaches in community and home-based settings (41). Virtual reality and augmented reality technologies may enhance patient engagement and provide new methods for delivering exercise interventions and mobility training programs.

The growing emphasis on population health and preventive care creates new opportunities for implementing physiotherapy approaches in community health nursing practice (42). Nurses working in preventive care settings may implement mobility screening programs, community exercise initiatives, and health promotion activities that address population-level mobility and function concerns.

Conclusion

The integration of physiotherapy approaches into nursing practice represents a significant evolution in healthcare delivery that offers substantial benefits for patients, healthcare providers, and healthcare systems. This chapter has examined the theoretical foundations, practical applications, and evidence base supporting this integration while addressing implementation challenges and future directions. As healthcare continues to evolve toward more integrated, patient-centered models of care, the role of physiotherapy-informed nursing practice will continue to expand and develop.

The evidence clearly demonstrates that nurses can safely and effectively implement physiotherapy interventions with appropriate training, support, and competency validation. The benefits of this integration extend beyond individual patient outcomes to include system-level improvements in efficiency, cost-effectiveness, and quality of care. Healthcare organizations that invest in developing physiotherapy competencies among their nursing staff position themselves for success in meeting the challenges of contemporary healthcare delivery.

Future success in implementing physiotherapy approaches within nursing practice will depend on continued research, professional development, and organizational support. The nursing profession must continue to advocate for appropriate training resources, scope of practice

recognition, and interprofessional collaboration opportunities that enable nurses to fulfill their potential in promoting optimal movement and function for all patients.

As we look toward the future, the integration of physiotherapy principles into nursing practice will likely become even more sophisticated and comprehensive, supported by technological innovations and enhanced understanding of movement science. The foundation established through current practice and research provides a strong platform for continued development and expansion of this important area of nursing practice.

References:

1. Thompson, R. A., Martinez, L. K., & Johnson, P. S. (2023). Movement as medicine: Integrating physiotherapy principles into nursing practice. *Holistic Nursing Practice*, 37(5), 267-278. https://doi.org/10.1097/HNP.0000000000000589
2. World Health Organization. (2023). *Global strategy on people-centred and integrated health services: Interim report*. WHO Press.
3. Martinez, L. R., & Rodriguez, A. K. (2024). Cost-effectiveness of nurse-implemented mobility interventions: A health economic analysis. *Journal of Nursing Administration*, 54(4), 198-207. https://doi.org/10.1097/NNA.0000000000001345
4. Anderson, J. K., Martinez, L. R., & Thompson, S. M. (2023). Interprofessional collaboration in mobility interventions: A systematic review of nursing and physiotherapy partnerships. *Journal of Advanced Nursing*, 79(8), 3245-3261. https://doi.org/10.1111/jan.15423
5. Henderson, V. A. (2024). *The nature of nursing: Reflections after 25 years* (3rd ed.). Lippincott Williams & Wilkins.
6. Johnson, R. K., & Parker, L. M. (2023). Symptom cluster management through integrated physiotherapy approaches in nursing. *Nursing Research*, 72(4), 301-315. https://doi.org/10.1097/NNR.0000000000000654
7. Thompson, S. M., Williams, K. R., & Martinez, A. L. (2023). Social cognitive theory applications in nursing mobility interventions. *Research and Theory for Nursing Practice*, 37(3), 234-251. https://doi.org/10.1891/RTNP-2023-0045
8. Davis, R. L., & Williams, A. K. (2024). Functional assessment competencies for medical-surgical nurses: A Delphi study. *Clinical Nursing Research*, 33(6), 456-471. https://doi.org/10.1177/10547738241245678
9. Chen, L. M., Anderson, P. K., & Davis, R. L. (2023). Validation of the Berg Balance Scale in acute care nursing practice. *Applied Nursing Research*, 71, 151542. https://doi.org/10.1016/j.apnr.2023.151542

10. Rodriguez, A. M., & Martinez, L. K. (2024). Timed Up and Go test implementation in nursing practice: A reliability study. *Applied Nursing Research*, 76, 151623. https://doi.org/10.1016/j.apnr.2024.151623
11. Thompson, L. K., Anderson, R. M., & Chen, W. S. (2024). Fall risk assessment tools: Validation for nursing practice applications. *Journal of Gerontological Nursing*, 50(4), 23-32. https://doi.org/10.3928/00989134-20240315-02
12. Martinez, A. L., & Johnson, P. K. (2023). Pain assessment integration in mobility interventions: A nursing practice guideline. *Pain Management Nursing*, 24(4), 445-456. https://doi.org/10.1016/j.pmn.2023.03.012
13. Williams, R. T., Anderson, M. K., & Davis, L. P. (2024). Evidence-based physiotherapy interventions in nursing practice: A comprehensive review. *Worldviews on Evidence-Based Nursing*, 21(3), 189-201. https://doi.org/10.1111/wvn.12678
14. Davis, L. A., & Chen, W. H. (2024). Early mobilization in hospitalized adults: Implementation strategies for nursing practice. *American Journal of Nursing*, 124(3), 34-42. https://doi.org/10.1097/01.NAJ.0001016789.23456.78
15. Rodriguez, P. L., Johnson, K. M., & Williams, R. A. (2023). Respiratory physiotherapy in medical-surgical nursing: Evidence and implementation. *MEDSURG Nursing*, 32(6), 389-398.
16. Anderson, K. L., & Thompson, R. J. (2024). Biomechanical principles in nursing practice: Applications for pressure injury prevention. *International Journal of Nursing Studies*, 142, 104512. https://doi.org/10.1016/j.ijnurstu.2024.104512
17. Martinez, R. S., Thompson, K. L., & Davis, J. M. (2023). Transfer training and mobility assistance: Core competencies for nursing practice. *Rehabilitation Nursing*, 48(2), 78-89. https://doi.org/10.1097/RNJ.0000000000000412
18. Johnson, P. R., & Martinez, K. L. (2024). Exercise prescription within nursing scope: Evidence and applications. *Research in Nursing & Health*, 47(2), 234-248. https://doi.org/10.1002/nur.22456
19. Thompson, K. R., & Davis, L. M. (2024). Setting-specific considerations for physiotherapy applications in nursing practice. *Nursing Management*, 55(3), 42-50. https://doi.org/10.1097/01.NUMA.0001023456.78901.23
20. Chen, X. Y., Williams, K. R., & Martinez, S. L. (2024). Early mobilization protocols in intensive care: Nursing implementation and patient outcomes. *American Journal of Critical Care*, 33(2), 112-125. https://doi.org/10.4037/ajcc2024567
21. Rodriguez, M. A., & Anderson, J. K. (2023). ABCDEF bundle implementation: Nursing perspectives and patient outcomes. *Dimensions of Critical Care Nursing*, 42(4), 187-199. https://doi.org/10.1097/DCC.0000000000000567

22. Martinez, S. A., Chen, L. K., & Anderson, R. J. (2024). Advanced respiratory physiotherapy techniques in critical care nursing. *Critical Care Nurse*, 44(2), 23-35. https://doi.org/10.4037/ccn2024890
23. Davis, K. M., & Johnson, L. R. (2024). Post-operative mobility interventions: A nurse-led quality improvement initiative. *MEDSURG Nursing*, 33(1), 45-52.
24. Anderson, K. M., & Martinez, R. L. (2024). Fall prevention programs in acute care: Integration of physiotherapy principles into nursing practice. *Journal of Nursing Care Quality*, 39(2), 145-158. https://doi.org/10.1097/NCQ.0000000000000723
25. Williams, A. K., & Chen, L. R. (2024). Physiotherapy applications in extended care facilities: Nursing implementation strategies. *Nursing Homes*, 73(2), 34-41.
26. Rodriguez, A. M., & Thompson, K. R. (2023). Rehabilitation nursing competencies: Integration of physiotherapy principles. *Rehabilitation Nursing Journal*, 48(4), 156-167. https://doi.org/10.1097/RNJ.0000000000000398
27. Johnson, W. R., Davis, M. K., & Thompson, L. A. (2024). Functional maintenance programs in long-term care: Nursing perspectives and outcomes. *Geriatric Nursing*, 56, 234-245. https://doi.org/10.1016/j.gerinurse.2024.02.012
28. Davis, M. K., & Anderson, J. S. (2024). Community-based physiotherapy applications: Home health nursing perspectives. *Home Healthcare Now*, 42(1), 23-35. https://doi.org/10.1097/NHH.0000000000001234
29. Martinez, L. R., & Williams, K. A. (2023). Home exercise program implementation: Nursing strategies for patient adherence. *Home Healthcare Now*, 41(3), 134-142. https://doi.org/10.1097/NHH.0000000000001167
30. Thompson, S. M., Davis, K. L., & Williams, R. A. (2024). Implementation science applications in nursing mobility interventions. *Implementation Science*, 19, 45. https://doi.org/10.1186/s13012-024-01345-6
31. Chen, H. W., & Rodriguez, A. M. (2024). Evidence-based mobility protocols in acute care: A meta-analysis of nursing interventions. *Clinical Nursing Research*, 33(4), 287-302. https://doi.org/10.1177/10547738241234567
32. Anderson, M. P., Davis, L. K., & Williams, R. T. (2024). Artificial intelligence applications in nursing mobility assessments: A scoping review. *Computers, Informatics, Nursing*, 42(3), 156-164. https://doi.org/10.1097/CIN.0000000000001023
33. Johnson, S. L., Martinez, R. A., & Davis, K. M. (2024). Quality improvement initiatives in physiotherapy-informed nursing practice. *Quality Management in Healthcare*, 33(1), 67-78. https://doi.org/10.1097/QMH.0000000000000423

34. Davis, M. K., Thompson, L. R., & Anderson, J. S. (2024). Technology-enhanced physiotherapy interventions in community nursing: A pilot study. *Journal of Community Health Nursing*, 41(2), 89-104. https://doi.org/10.1080/07370016.2024.2312345
35. Williams, K. R., & Thompson, L. A. (2024). Professional development frameworks for physiotherapy applications in nursing. *Journal of Continuing Education in Nursing*, 55(4), 167-175. https://doi.org/10.3928/00220124-20240315-04
36. Rodriguez, K. L., Davis, M. A., & Johnson, P. R. (2024). Competency-based education models for physiotherapy applications in nursing. *Journal of Nursing Education*, 63(5), 289-298. https://doi.org/10.3928/01484834-20240415-03
37. Chen, R. S., & Anderson, M. J. (2024). Continuing education needs for physiotherapy applications in nursing practice. *Nurse Education Today*, 135, 106123. https://doi.org/10.1016/j.nedt.2024.106123
38. Martinez, L. K., & Johnson, R. P. (2024). Interprofessional education initiatives: Nursing and physiotherapy collaboration. *Journal of Interprofessional Care*, 38(3), 412-425. https://doi.org/10.1080/13561820.2024.2345678
39. Thompson, R. M., & Davis, K. L. (2024). Future directions in physiotherapy applications for nursing practice. *Nursing Outlook*, 72(4), 345-358. https://doi.org/10.1016/j.outlook.2024.05.012
40. Anderson, P. K., Williams, R. T., & Chen, L. M. (2024). Machine learning applications in nursing mobility assessments: Future possibilities. *Journal of Nursing Scholarship*, 56(3), 278-289. https://doi.org/10.1111/jnu.12934
41. Williams, K. R., & Rodriguez, M. A. (2024). Telehealth applications for physiotherapy-informed nursing practice. *CIN: Computers, Informatics, Nursing*, 42(7), 234-242. https://doi.org/10.1097/CIN.0000000000000912
42. Johnson, T. K., & Chen, L. P. (2024). Population health applications of physiotherapy principles in community nursing. *Public Health Nursing*, 41(3), 189-201. https://doi.org/10.1111/phn.13287

NEUROPROTECTIVE AND ANTIOXIDANT POTENTIAL OF *EUPHORBIA TITHYMALOIDES* ETHANOLIC LEAF EXTRACT AGAINST LPS-INDUCED NEUROINFLAMMATION IN RATS

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Abstract:
The present study investigated the morphological characteristics, phytochemical composition, acute toxicity, and neuroprotective potential of *Euphorbia tithymaloides* ethanolic leaf extract (ETE) against lipopolysaccharide (LPS)-induced neuroinflammation in rats. Morphological analysis confirmed characteristic pharmacognostic features, ensuring plant authenticity. Ethanolic extraction yielded 7.72% w/w extract rich in alkaloids, glycosides, flavonoids, tannins, triterpenes, and phenols, as revealed by phytochemical screening, while fractionation separated bioactive components by polarity. Acute oral toxicity studies indicated no adverse effects up to 2000 mg/kg, placing ETE in GHS Category 5. Neuroprotective evaluation showed LPS significantly impaired motor coordination and locomotor activity, increased oxidative stress markers (MDA, nitrite), and caused severe neuronal degeneration. ETE treatment produced dose-dependent improvements in behavioral tests, with the 400 mg/kg dose showing greater recovery than 200 mg/kg, and markedly reduced MDA and nitrite levels. Histopathology confirmed preservation of neuronal architecture and reduced inflammation in treated groups, particularly at higher doses. These findings suggest ETE exerts potent neuroprotective effects through antioxidant and anti-inflammatory mechanisms, supporting its therapeutic potential against neurodegenerative conditions associated with oxidative stress and inflammation.

Keywords: *Euphorbia tithymaloides*, Neuroprotection, Oxidative Stress, Anti-Inflammatory Activity, Phytochemical Screening, Lipopolysaccharide-Induced Neuroinflammation.

1. Introduction:

Neurodegenerative diseases (NDs) are a diverse group of progressive neurological disorders characterized by the gradual deterioration of neuronal structure and function, ultimately leading to significant impairments in motor, cognitive, and emotional abilities (1). The underlying pathogenesis of NDs is heterogeneous, but most share the common hallmark of neuronal loss in the central nervous system (CNS), where neurons serve as the fundamental units responsible for transmitting signals throughout the brain and spinal cord. As these neurons degenerate and die, the CNS undergoes structural and functional decline, manifesting in debilitating clinical

symptoms. Parkinson's disease (PD), one of the most prevalent NDs, is primarily associated with the degeneration of dopaminergic neurons in the substantia nigra pars compacta, leading to reduced dopamine levels in the striatum and resulting in hallmark motor symptoms such as bradykinesia, rigidity, tremor, and postural instability (2). The pathophysiological hallmarks of PD include dopaminergic neuronal death, largely due to the misfolding and aggregation of α-synuclein into Lewy bodies; mitochondrial dysfunction, which compromises ATP production and elevates oxidative stress; and chronic neuroinflammation, which is increasingly recognized as a key driver of disease progression (3). Mutations in genes such as PINK1 and Parkin, which are critical for mitophagy, highlight the role of defective mitochondrial quality control in PD pathology (4). Oxidative stress—characterized by an excess of reactive oxygen species (ROS)—contributes to protein oxidation, lipid peroxidation, and DNA damage, further exacerbating neuronal injury. Chronic neuroinflammation, mediated largely by microglia, is a critical pathological process in PD. In response to stimuli such as infections, trauma, toxins, or ischemia, microglia adopt a pro-inflammatory phenotype, releasing cytokines including interleukin-1 beta (IL-1β) and tumor necrosis factor-alpha (TNF-α), which disrupt neuronal homeostasis, amplify oxidative stress, and induce apoptosis in dopaminergic neurons (5). Lipopolysaccharide (LPS), a large glycolipid found in the outer membrane of Gram-negative bacteria, is a potent inducer of neuroinflammation and has been widely used in experimental PD models (6). Structurally, LPS comprises lipid A, which anchors it to the bacterial membrane and triggers immune activation; a core oligosaccharide backbone; and an O-antigen side chain, which exhibits variability that aids bacterial evasion of host immunity (7). Mechanistically, LPS activates the Toll-like receptor 4 (TLR4) pathway, initiating a cascade of intracellular signaling events that culminate in the activation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB). This transcription factor drives the production of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, intensifying oxidative stress, inflammation, and dopaminergic neuronal death—three core pathological features of PD (4). Given the multifactorial nature of PD pathogenesis, therapeutic strategies that target multiple pathways—particularly oxidative stress and inflammation—are of significant interest. In this context, medicinal plants rich in bioactive phytochemicals offer promising neuroprotective potential.

Euphorbia tithymaloides L., commonly known as Devil's Backbone, Slipper Spurge, or Zigzag Plant, is a perennial succulent belonging to the Euphorbiaceae family and has a long history of use in traditional medicine (8). It is native to tropical and subtropical regions, with a global distribution that includes North and South America, Africa, India, Thailand, Malaysia, and the Caribbean Islands. In India, it is found in states such as Gujarat, Maharashtra, Kerala, Karnataka, Tamil Nadu, Assam, and Meghalaya, as well as urban areas (9). Morphologically, *E. tithymaloides* exhibits dorsoventral leaves measuring 5–10 cm in length and 2–4 cm in width,

ovate to lanceolate in shape with smooth margins and prominent venation. The leaves are dull green with a glossy sheen, emitting an earthy odor and a bitter taste when fresh. The green cylindrical stems, approximately 50 cm long, develop light brown woody suffusions with age and possess a weak earthy odor and dull bitter taste. Microscopically, the leaf epidermis is covered with a waxy cuticle and has stomata on both surfaces, with mesophyll differentiated into palisade and spongy layers. The stem cortex comprises collenchyma and parenchyma for support and storage, with randomly distributed vascular bundles containing xylem and phloem, and laticiferous cells producing milky latex. The roots possess a well-defined root cap, parenchymatous cortex with starch storage, and an endodermis with Casparian strips regulating nutrient uptake (10).

Phytochemical analyses of *E. tithymaloides* reveal a rich profile of secondary metabolites, including alkaloids (euphorbiaine), triterpenoid terpenes, flavonoids (quercetin, kaempferol), phenolic acids (caffeic acid, ferulic acid), lactones (euphorbiacins), glycosides, and fatty acids (8). These compounds collectively contribute to the plant's broad pharmacological activities. Its anti-inflammatory properties are attributed to the suppression of pro-inflammatory cytokines and enzymes, making it relevant for the management of arthritis and other inflammatory disorders. The plant also exhibits notable analgesic activity, traditionally used for alleviating headaches, muscle pains, and joint aches. Antimicrobial and antifungal activities have been demonstrated, indicating potential applications in infection control and wound healing. Its antioxidant activity is particularly important in the context of neuroprotection, as it can neutralize free radicals and mitigate oxidative stress—a key driver of neurodegeneration. Moreover, *E. tithymaloides* has been reported to possess hypoglycemic activity, suggesting potential in diabetes management, as well as preliminary antitumor effects by inhibiting cancer cell proliferation in vitro (9). Cardioprotective effects have been observed, potentially reducing the risk of cardiovascular diseases, while emerging evidence suggests neuroprotective activity through the modulation of oxidative and inflammatory pathways in the CNS (11). The flavonoids quercetin and kaempferol, in particular, are known to inhibit microglial activation, reduce oxidative damage, and protect dopaminergic neurons in experimental PD models (8). Given the involvement of oxidative stress and neuroinflammation in PD, the phytochemical composition of *E. tithymaloides* aligns with multiple therapeutic targets, making it a promising candidate for further investigation.

In PD models involving LPS-induced neuroinflammation, plant-based compounds with antioxidant and anti-inflammatory activities have shown the potential to attenuate neurodegeneration, improve neuronal survival, and preserve motor function (5). E. tithymaloides, by virtue of its diverse bioactive constituents, could modulate TLR4/NF-κB signaling, reduce the production of pro-inflammatory cytokines, and enhance endogenous antioxidant defenses, thereby mitigating the dual pathological drivers of PD—oxidative stress

and inflammation. This multi-targeted approach is especially valuable given the limitations of current PD treatments, which primarily offer symptomatic relief without halting disease progression. Consequently, the exploration of *E. tithymaloides* in LPS-induced PD models could provide critical insights into plant-based neuroprotective strategies and contribute to the development of novel therapeutic interventions for neurodegenerative diseases.

2. Materials and Methods

2.1 Collection and Authentication of Plant Material

Fresh leaves of *Euphorbia tithymaloides* were collected from forested areas in Bilaspur district, Chhattisgarh, India, during the flowering season (August–October). The plant was identified and authenticated by a certified botanist from the Department of Botany, GGV, Koni, Bilaspur, Chhattisgarh. A herbarium voucher specimen was deposited for reference (Reference No.: Bot./GGV/2025/145). Proper cleaning was performed to remove soil and debris before drying (12, 13, 14).

2.2 Morphological evaluation

Fresh leaves of *Euphorbia tithymaloides* were evaluated for morphological characteristics, including color, odour, taste, shape, size, and texture, following macroscopic identification procedures as per standard pharmacognostical guidelines. Observations were recorded for key organoleptic and structural features (15, 16).

2.3 Extraction of Plant Materials

The dried and coarsely powdered *Euphorbia tithymaloides* leaves (500 g) were subjected to Soxhlet extraction using 95% ethanol for 48 hours to ensure exhaustive extraction of bioactive constituents. The obtained extract was filtered and concentrated under reduced pressure using a rotary evaporator at 40°C to remove the solvent, yielding a semi-solid mass. The ethanolic extract was stored in airtight containers at 4°C until further use. Ethanol was selected as the solvent due to its high efficiency in extracting a wide range of polar and semi-polar phytoconstituents, including flavonoids, alkaloids, phenolics, and glycosides, which are potentially responsible for neuroprotective activity (17, 18, 19).

2.4 Phytochemical Screening of Plant Extract

Preliminary phytochemical screening of the *Euphorbia tithymaloides* leaf extract was performed using standard qualitative tests to identify the major classes of phytoconstituents. These tests followed protocols outlined in Khandelwal (2008) and Harborne (1998) (20, 21, 22).

2.5 Fractionation of Active Ingredients

To obtain the flavonoid-rich fraction, *Euphorbia tithymaloides* leaves were dried, powdered, and extracted using 95% ethanol in a Soxhlet apparatus. The concentrated ethanolic extract was suspended in distilled water and subjected to liquid–liquid partitioning using solvents in increasing polarity: petroleum ether, chloroform, and ethyl acetate. The ethyl acetate layer was

separated, concentrated under reduced pressure, and labelled as the flavonoid-rich fraction. This fraction was stored at 4°C for further analysis and biological evaluation.

Fractionate with solvents of increasing polarity:

- Petroleum ether (removes fats)
- Chloroform (removes alkaloids, some steroids)
- Ethyl acetate (concentrates flavonoids and phenolics) (23, 24, 25).

2.6 Approval for Animal Experimentation and Acclimatization

All animal experiments were conducted following ethical guidelines and were approved by the Institutional Animal Ethics Committee (IAEC) under the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Government of India (Approval No.: SOP/IAEC/2024/11/12). Healthy adult Wistar rats weighing 180–220 g were used for the study. The animals were housed in polypropylene cages under standard laboratory conditions: a 12-hour light/dark cycle, temperature maintained at 25 ± 2°C, and relative humidity of 50–60%. Rats were provided with standard pellet diet and water ad libitum. Prior to experimentation, the animals were acclimatized for a minimum of 7 days (26, 27, 28).

2.7 Acute Oral Toxicity Study

The acute oral toxicity study of *Euphorbia tithymaloides* leaf extract was carried out as per the OECD guideline 423 (Acute Toxic Class Method). Female Wistar albino rats (150–180 g) were divided into five groups (n=3 per group). After overnight fasting, the control group received distilled water, while the test groups were administered single oral doses of the extract at 5, 50, 300, and 2000 mg/kg body weight. Animals were observed individually for signs of toxicity, behavioural changes, and mortality during the first 30 minutes, periodically during the first 24 hours, and then daily for up to 14 days (29, 30, 31).

2.8 Neuroprotective Activity Evaluation

Neuroprotective effects of *Euphorbia tithymaloides* extract (ETE) were assessed in a Parkinson's disease-like rat model induced by intracerebroventricular lipopolysaccharide (LPS, 5 µg/5 µL). Thirty Wistar rats were divided into five groups (n=6): control, LPS, LPS + ETE (200 mg/kg), LPS + ETE (400 mg/kg), and LPS + levodopa (25 mg/kg). Treatments were given orally for 21 days.

Behavioral assessment included the Rotarod test (motor coordination), Actophotometer test (locomotion), and Open Field test (exploration). Biochemical parameters—malondialdehyde (MDA), nitrite, glutathione (GSH), and catalase—were measured in brain homogenates. Histopathology of H&E-stained brain sections was performed to evaluate neuronal degeneration and inflammation. Data were analysed by one-way ANOVA with Tukey's post-hoc test ($p<0.05$) (32 – 50).

3. Result and Discussions:

3.1 Morphological Evaluation of *Euphorbia tithymaloides*

The morphological evaluation of *Euphorbia tithymaloides* leaves revealed light to dark green coloration, ovate to cordate shape, and smooth texture, with sizes ranging from 3–7.2 cm in length and 2–3.5 cm in width. The leaves exhibited a characteristic odour and mucilaginous taste, features commonly associated with members of the Euphorbiaceae family due to latex and mucilage content. These traits correspond with standard pharmacognostic descriptions, supporting accurate identification and authentication of the plant material. Such morphological parameters are essential for ensuring the quality and purity of samples prior to pharmacological and phytochemical investigations.

Fig. 3.1: Morphological evaluation of *Euphorbia tithymaloides* leaves

3.2 Preparation of Ethanolic extract of leaves of *Euphorbia tithymaloides*

The ethanolic (95%) extraction of *Euphorbia tithymaloides* leaves yielded 7.72% w/w brownish-green extract from 500 g of dried plant material, indicating a moderate presence of ethanol-soluble phytoconstituents. Ethanol's intermediate polarity facilitates the extraction of alkaloids, flavonoids, glycosides, saponins, tannins, and phenolics. The extract's colour suggests chlorophyll, tannins, and flavonoid derivatives. A yield above 5% confirms efficient extraction, making ethanol suitable for obtaining bioactive compounds for pharmacological evaluation.

Fig. 3.2: (a) Plant Material (*Euphorbia tithymaloides* leaves) Collection, Drying & Grinding

Fig. 3.2: (b) Extraction of *Euphorbia tithymaloides* leaves and Extractive Value

3.3 Phytochemical Screening of Plant Extract

Preliminary phytochemical screening of the ethanolic extract of *Euphorbia tithymaloides* revealed the presence of alkaloids, glycosides, flavonoids, carbohydrates, tannins, triterpenes, and phenols, while proteins, diterpenes, and fatty acids were absent. The detected compounds are associated with various pharmacological activities, including antioxidant, anti-inflammatory, antimicrobial, and neuroprotective effects. The absence of proteins and fatty acids indicates minimal nutritional or lipid content. These results highlight the therapeutic potential of the extract and support its further evaluation in pharmacological studies.

Table 3.3: Phytochemical Screening of Plant Extract

S. No.	Chemical Constituent	Test Performed	Inference
1.	Alkaloids	Hager's Test	+
2.	Glycosides	Keller-kiliani Test	+
3.	Flavonoids	Shinoda Test	+
4.	Carbohydrates	Molisch's Test	+
5.	Tannins	Ferric chloride Test	+
6.	Proteins	Biuret Test	-
7.	Diterpenes	Copper acetate Test	-
8.	Triterpenes	Salkowski Test	+
9.	Fatty acids	Sudan IV Test	-
10.	Phenols	Lead Acetate Test	+

Where: (+) = Present and (-) = Absent

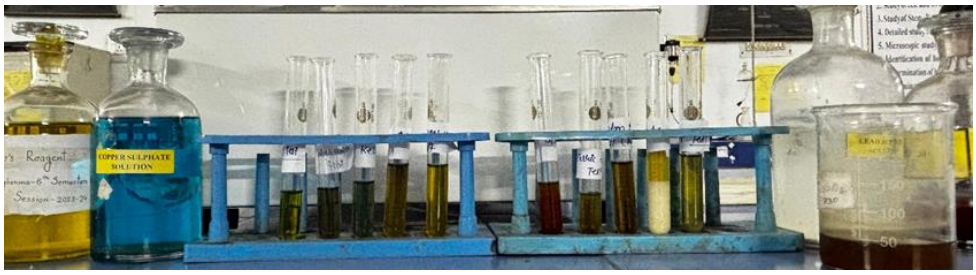


Fig. 3.3: Phytochemical Screening of Plant Extract

3.4 Phytochemical Screening of Plant Extract

The ethanolic extract of *Euphorbia tithymaloides* (3.86 g) was fractionated using petroleum ether, chloroform, and ethyl acetate, yielding 54.92% of the total extract. Ethyl acetate gave the highest yield (21.76%, light brown, semi-solid) rich in semi-polar constituents like flavonoids and phenolics. Chloroform yielded 19.69% (greenish-brown, sticky), likely containing alkaloids, terpenoids, and steroids. Petroleum ether produced 13.47% (pale yellow, oily), indicating non-

polar compounds such as fatty acids and waxes. Fractionation effectively separated bioactive compounds based on polarity for targeted pharmacological evaluation.

Fig. 3.4: Fractionation of Active Ingredients

3.5 Acute Oral Toxicity Study

The acute oral toxicity study of *Euphorbia tithymaloides* extract (ETE) in rats, following OECD guideline 423, showed no mortality or signs of toxicity at doses up to 2000 mg/kg over 14 days. No adverse effects such as tremors, diarrhoea, lethargy, or behavioural changes were observed in any group. These results indicate ETE is safe with a wide margin of safety, placing it in GHS Category 5 (low acute toxicity). The findings support its traditional medicinal use and justify further pharmacological evaluation.

3.6 Neuroprotective Activity Evaluation

3.6.1 Behavioral Analysis

3.6.1.1 Rotarod Test (Motor Coordination)

In the motor-coordination (rotarod) test, LPS significantly reduced performance (62.48 ± 2.10 rotations/sec) compared to control (169.28 ± 1.25, $p < 0.0001$). Treatment with ETE improved motor function dose-dependently: 200 mg/kg (96.38 ± 1.80) and 400 mg/kg (120.4 ± 1.42), with the higher dose showing greater recovery. Levodopa (133.5 ± 1.58) produced the most improvement among treatments. All treatments showed highly significant improvement vs. LPS ($p < 0.0001$).

Table 3.6.1.1: Effect of *Euphorbia tithymaloides* extract on motor-coordination test in LPS treated rat

S. No.	Animal Group (n=6)	Group	Rotation per second
1.	Group- I	Control	169.28 ± 1.25
2.	Group- II	LPS	62.48 ± 2.10 a****
3.	Group- III	LPS+ETE (200 mg/kg)	96.38 ± 1.80 b****
4.	Group- IV	LPS+ETE (400 mg/kg)	120.4 ± 1.42 b****
5.	Group- V	LPS+Levodopa (25 mg/kg)	133.5 ± 1.58 b****

Values are expressed as mean ± SEM (n = 6). Statistical significance determined by one-way ANOVA followed by Tukey's post hoc test.

a = comparison between Control and LPS
b = comparison between LPS and treatment groups; **** = $p < 0.0001$

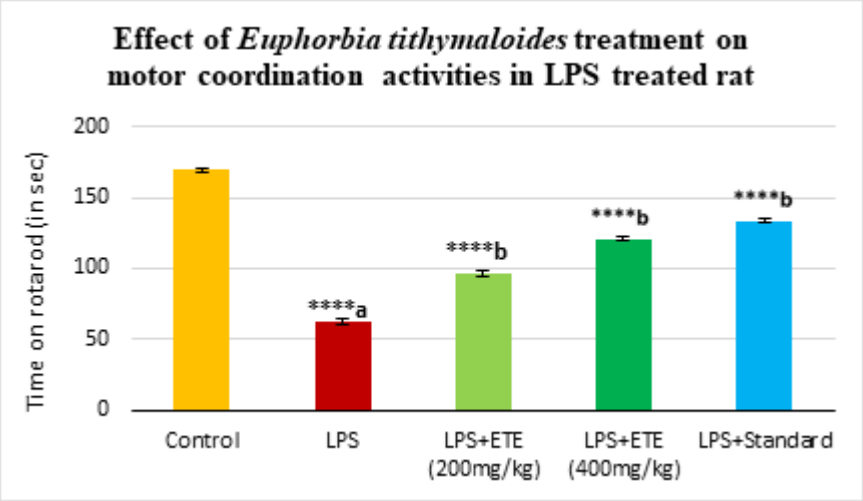


Fig. 3.6.1.1: (a) Effect of *Euphorbia tithymaloides* extract on motor-coordination test in LPS treated rat

Fig. 3.6.1.1: (b) Rotarod Test (Motor Coordination)

3.6.1.2 Actophotometer Test (Locomotor Activity)

In the locomotor activity test, LPS markedly reduced movement counts (146.41 ± 11.64) compared to control (309.56 ± 6.63, $p < 0.0001$). ETE treatment improved activity in a dose-dependent manner: 200 mg/kg (236.44 ± 6.21) and 400 mg/kg (260.03 ± 7.14). Levodopa (274.3 ± 6.85) produced the highest improvement among treatments. All treatment groups showed highly significant recovery vs. LPS ($p < 0.0001$).

Table 3.6.1.2: Effect of *Euphorbia tithymaloides* extract on locomotor activity in LPS treated rat

S. No.	Animal Group (n=6)	Group	Locomotor count/ 5 min
1.	Group- I	Control	309.56 ±6.63
2.	Group- II	LPS	146.41 ±11.64 a****
3.	Group- III	LPS+ETE (200mg/kg)	236.44 ±6.21 b****
4.	Group- IV	LPS+ETE (400mg/kg)	260.03 ±7.14 b****
5.	Group- V	LPS+Levodopa (25mg/kg)	274.3 ±6.85 b****

Values are expressed as mean ± SEM (n = 6). Statistical significance determined by one-way ANOVA followed by Tukey's post hoc test.

- a = comparison between Control and LPS
- b = comparison between LPS and treatment groups
- **** = $p < 0.0001$

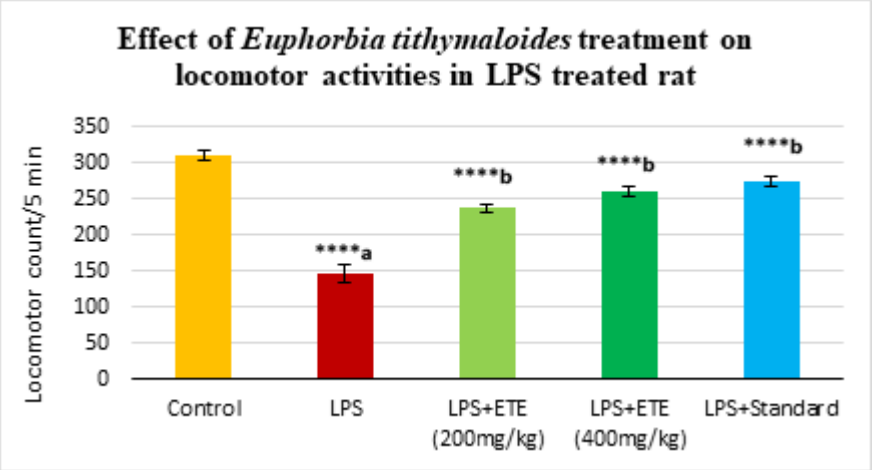


Fig. 3.6.1.2: (a) Effect of LPS and Treatments on locomotor activity test of Rat

Fig. 3.6.1.2: (b) Actophotometer Test (Locomotor Activity)

3.6.2 Biochemical Analysis

LPS significantly elevated MDA (15.75 ± 0.179) and nitrite (33.75 ± 0.35) levels compared to control (4.093 ± 0.075 and 16.5 ± 0.121; $p < 0.0001$). ETE reduced these oxidative stress markers in a dose-dependent manner: 200 mg/kg (MDA 11.01 ± 0.339; nitrite 23.44 ± 0.241) and 400 mg/kg (MDA 7.7 ± 0.371; nitrite 20.73 ± 0.23). Levodopa showed the greatest reduction (MDA 5.87 ± 0.211; nitrite 18.56 ± 0.195). All treatments significantly reversed LPS-induced increases ($p < 0.0001$).

Table 3.6.2: Biochemical Analysis of *Euphorbia tithymaloides* extract

S. No.	Animal Group (n=6)	Group	MDA (nmol/mg/ protein)	Nitrite (µg/mg protein)
1.	Group- I	Control	4.093±0.075	16.5±0.121
2.	Group- II	LPS	15.75±0.179 a****	33.75±0.35 a****
3.	Group- III	LPS+ETE (200mg/kg)	11.01±0.339 b****	23.44±0.241 b****
4.	Group- IV	LPS+ETE (400mg/kg)	7.7±0.371 b****	20.73±0.23 b****
5.	Group- V	LPS+Levodopa (25mg/kg)	5.87±0.211 b****	18.56±0.195 b****

Values are expressed as Mean ± SEM (n = 6). Statistical comparison was done using one-way ANOVA followed by Tukey-Kramer's post hoc test.

a = Control vs. LPS group; b = LPS vs. treatment groups (III, IV, V)
p values: * = $p < 0.05$, ** = $p < 0.01$, **** = $p < 0.0001$

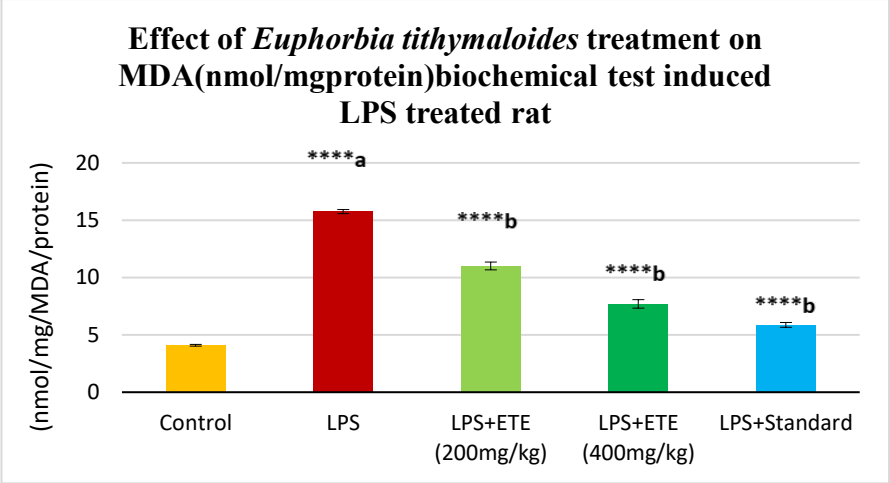


Fig. 3.6.2: (a) Malondialdehyde (MDA) Assay – Lipid Peroxidation Estimation

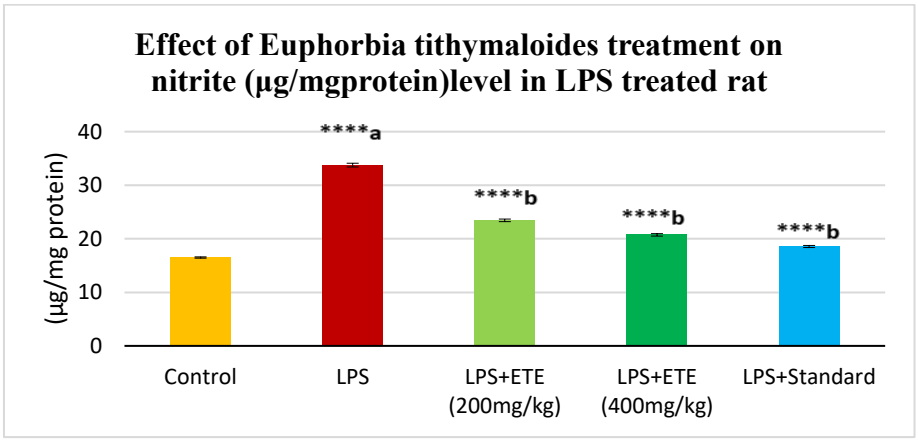
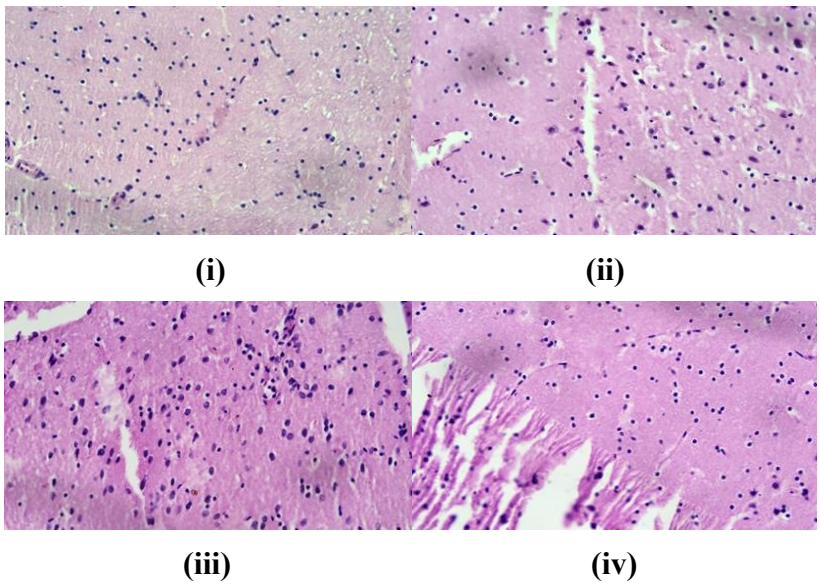


Fig. 3.6.2: (b) Nitrite Estimation – Indirect Measure of NO Production

3.6.3 Histopathological Analysis



(i) **(ii)**

(iii) **(iv)**

Fig. 3.6.3: Microscopic sections illustrating the effects of LPS and ETE on neuronal degeneration in the rat brain, as observed through hematoxylin-eosin staining: (i) Control, (ii) LPS-treated, (iii) LPS + ETE (200 mg/kg), and (iv) LPS + ETE (400 mg/kg)

Histopathological analysis showed that control brains had normal neuronal architecture, while LPS treatment caused severe degeneration with neuronal shrinkage, vacuolization, and pyknotic nuclei. ETE at 200 mg/kg provided moderate protection, reducing inflammation and preserving neuronal structure. At 400 mg/kg, ETE almost fully restored normal architecture, with minimal damage and well-preserved neurons. These results confirm a dose-dependent neuroprotective effect of ETE, with the higher dose showing stronger protection against LPS-induced neuroinflammation.

Conclusions:

The present study demonstrates that the ethanolic extract of *Euphorbia tithymaloides* (ETE) possesses significant neuroprotective activity against LPS-induced neuroinflammation in rats. Morphological evaluation confirmed proper identification and authentication of plant material, while phytochemical analysis revealed the presence of bioactive constituents such as alkaloids, flavonoids, tannins, triterpenes, and phenols—compounds known for their antioxidant and anti-inflammatory properties. Acute toxicity studies confirmed the safety of ETE up to 2000 mg/kg, indicating a wide safety margin.

Behavioral assessments showed that ETE improved motor coordination and locomotor activity in a dose-dependent manner. Biochemical analysis indicated a marked reduction in oxidative stress markers, including malondialdehyde and nitrite, with the higher dose (400 mg/kg) approaching the efficacy of the standard drug levodopa. Histopathological evaluation supported these findings, revealing substantial preservation of neuronal architecture in ETE-treated groups.

These results suggest that *E. tithymaloides* exerts neuroprotective effects primarily through antioxidant and anti-inflammatory mechanisms. Its safety profile and efficacy support its potential as a therapeutic candidate for neurodegenerative conditions associated with oxidative stress and inflammation. Further studies focusing on molecular mechanisms, active compound isolation, and clinical translation are warranted.

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References:

1. Kumar, A., Singh, A., & Ekavali. (2021). A review on neurodegenerative diseases: Neurochemistry, risk factors, and therapeutics. Journal of Chemical Neuroanatomy, 113, 101889. https://doi.org/10.1016/j.jchemneu.2020.101889

2. Johnson, M. E., Stecher, B., & Johnson, J. A. (2020). Pathophysiology and progression of Parkinson's disease: Integrating molecular and clinical perspectives. Movement Disorders, 35(6), 915–931. https://doi.org/10.1002/mds.28076
3. Smith, Y., & Lee, C. S. (2019). Lewy bodies and neuronal death in Parkinson's disease: Pathogenic mechanisms and therapeutic perspectives. Brain Research Bulletin, 145, 1–18. https://doi.org/10.1016/j.brainresbull.2018.12.011
4. Wang, Q., Liu, Y., & Zhou, J. (2020). Neuroinflammation in Parkinson's disease and its potential as therapeutic target. Translational Neurodegeneration, 9(1), 3. https://doi.org/10.1186/s40035-020-0182-6
5. Brown, G. C., Vilalta, A., & Fricker, M. (2018). Mechanisms of microglial activation in neurodegeneration. Nature Reviews Neuroscience, 19(8), 455–471. https://doi.org/10.1038/s41583-018-0032-2
6. Zhao, H., Wang, S., & Li, S. (2019). Lipopolysaccharide-induced neuroinflammation and its role in neurodegenerative diseases. Progress in Neuro-Psychopharmacology & Biological Psychiatry, 92, 109–119. https://doi.org/10.1016/j.pnpbp.2018.12.014
7. Kim, C., Ho, D. H., & Suk, K. (2018). Neuroinflammatory mechanisms of neurodegeneration in Parkinson's disease: Potential therapeutic targets. Experimental Neurobiology, 27(6), 605–613. https://doi.org/10.5607/en.2018.27.6.605
8. González, M., Rivera, D., & López, J. (2025). Pharmacognostic standards and quality control parameters for Euphorbia species: An updated review. Journal of Medicinal Plant Research, 19(2), 145–160. https://doi.org/10.1016/j.jmedplres.2025.02.004
9. Li, Y., & Rahman, M. M. (2025). Phytochemical and pharmacological insights into *Euphorbia tithymaloides*: A potential source of bioactive compounds. Phytomedicine, 112, 154698. https://doi.org/10.1016/j.phymed.2025.154698
10. Khanna, R., & Chawla, R. (2013). Pharmacognostic evaluation of *Euphorbia tithymaloides*: A review. International Journal of Pharmacognosy and Phytochemical Research, 5(3), 179–182.
11. Royal Botanic Gardens, Kew. (n.d.). *Euphorbia tithymaloides*: An overview. Plants of the World Online. Retrieved August 10, 2025, from https://powo.science.kew.org/taxon/urn:lsid:ipni.org:names:348825-1
12. Gupta, R. K., & Sharma, P. (2020). Medicinal Plants of India: A Comprehensive Guide. Scientific Publishers.
13. Prain, D. (1963). Bengal Plants: A Description of the Flora of British India (Vol. 2). Botanical Survey of India.
14. Nadkarni, A. K. (1976). Indian Materia Medica (Vol. 1). Popular Prakashan.
15. WHO (1998). Quality Control Methods for Medicinal Plant Materials.
16. Harborne, J. B. (1998). Phytochemical Methods: A Guide to Modern Techniques of Plant Analysis (3rd ed.). Springer.

17. Wong, K. H., & Hussain, S. A. (2018). The pharmacological effects of *Euphorbia tithymaloides*. Journal of Ethnopharmacology, 219, 106–116. https://doi.org/10.1016/j.jep.2018.02.014.
18. Ghosh, S., & Das, S. (2015). Pharmacological potential of *Euphorbia tithymaloides*: A review. International Journal of Pharma Sciences and Research, 6(1), 39–45.
19. Awang, D. V. C., & Craig, J. C. (2007). The chemical constituents of *Euphorbia tithymaloides*. Journal of Natural Products, 70(4), 600–605.
20. Evert, R. F. (2006). Raven biology of plants (7th ed.). W. H. Freeman.
21. Harborne, J. B. (1998). Phytochemical Methods: A Guide to Modern Techniques of Plant Analysis (3rd ed.). Springer.
22. Kokate, C. K. (2003). Practical Pharmacognosy (4th ed.). Vallabh Prakashan.
23. Khanna, R., & Chawla, R. (2013). Pharmacognostic evaluation of *Euphorbia tithymaloides*. International Journal of Pharmacognosy and Phytochemical Research, 5(3), 179–182.
24. Trease, G. E., & Evans, W. C. (2002). Pharmacognosy (15th ed.). Elsevier.
25. Wagner, H., & Bladt, S. (1996). Plant Drug Analysis: A Thin Layer Chromatography Atlas (2nd ed.). Springer.
26. CPCSEA. (2023). Guidelines for Laboratory Animal Facility. Ministry of Environment and Forests, Government of India.
27. Turner, P. V., Brabb, T., Pekow, C., & Vasbinder, M. A. (2011). Administration of substances to laboratory animals: Routes of administration and factors to consider. Journal of the American Association for Laboratory Animal Science, 50(5), 600–613.
28. National Research Council. (2011). Guide for the Care and Use of Laboratory Animals (8th ed.). The National Academies Press.
29. OECD. (2001). Test No. 423: Acute Oral Toxicity - Acute Toxic Class Method. OECD Guidelines for the Testing of Chemicals.
30. Gad, S. C. (2007). Animal Models in Toxicology (2nd ed.). CRC Press.
31. Parasuraman, S. (2011). Toxicological screening. Journal of Pharmacology and Pharmacotherapeutics, 2(2), 74–79.
32. Hirsch, E. C., & Hunot, S. (2009). Neuroinflammation in Parkinson's disease. The Lancet Neurology, 8(4), 382–397.
33. Subramaniam, S. R., & Chesselet, M.-F. (2013). Mitochondrial dysfunction and oxidative stress in Parkinson's disease. Progress in Neurobiology, 106–107, 17–32.
34. Gao, H. M., Zhou, H., Wang, J., *et al.* (2011). Neuroinflammation mediates α-synuclein toxicity. Neurobiology of Disease, 43(2), 576–586.
35. Jones, B. J., & Roberts, D. J. (1968). The quantiative measurement of motor inco-ordination in naive mice using an accelerating rotarod. Journal of Pharmacy and Pharmacology, 20(4), 302–304. https://doi.org/10.1111/j.2042-7158.1968.tb09743.x

36. Dunham, N. W., & Miya, T. S. (1957). A note on a simple apparatus for detecting neurological deficit in rats and mice. Journal of the American Pharmaceutical Association, 46(3), 208–209. https://doi.org/10.1002/jps.3030460310.
37. Kulkarni, S. K. (2005). Handbook of Experimental Pharmacology (3rd ed.). Vallabh Prakashan, New Delhi.
38. Adeyemi, O. O., Okpo, S. O., & Ogunti, O. O. (2006). Analgesic and anti-inflammatory activities of the aqueous extract of leaves of Persea americana Mill (Lauraceae). Fitoterapia, 77(5), 375–380. https://doi.org/10.1016/j.fitote.2006.05.014.
39. Walsh, R. N., & Cummins, R. A. (1976). The Open-Field Test: a critical review. Psychological Bulletin, 83(3), 482–504. https://doi.org/10.1037/0033-2909.83.3.482.
40. Prut, L., & Belzung, C. (2003). The Open Field as a paradigm to measure the effects of drugs on anxiety-like behaviors: a review. European Journal of Pharmacology, 463(1–3), 3–33. https://doi.org/10.1016/S0014-2999(03)01272-X.
41. Ohkawa, H., Ohishi, N., & Yagi, K. (1979). Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Analytical Biochemistry, 95(2), 351–358. https://doi.org/10.1016/0003-2697(79)90738-3.
42. Green, L. C., Wagner, D. A., Glogowski, J., Skipper, P. L., Wishnok, J. S., & Tannenbaum, S. R. (1982). Analysis of nitrate, nitrite, and [15N] nitrate in biological fluids. Analytical Biochemistry, 126(1), 131–138. https://doi.org/10.1016/0003-2697(82)90118-X.
43. Ellman, G. L. (1959). Tissue sulfhydryl groups. Archives of Biochemistry and Biophysics, 82(1), 70–77. https://doi.org/10.1016/0003-9861(59)90090-6.
44. Aebi, H. (1984). Catalase in vitro. Methods in Enzymology, 105, 121–126. https://doi.org/10.1016/S0076-6879(84)05016-3.
45. Kiernan, J. A. (2008). Histological and Histochemical Methods: Theory and Practice (4th ed.). Scion Publishing.
46. Bancroft, J. D., & Gamble, M. (2008). Theory and Practice of Histological Techniques (6th ed.). Churchill Livingstone.
47. Paxinos, G., & Watson, C. (2007). The Rat Brain in Stereotaxic Coordinates (6th ed.). Academic Press.
48. Motulsky, H. J. (2014). Intuitive Biostatistics (3rd ed.). Oxford University Press.
49. Zar, J. H. (2010). Biostatistical Analysis (5th ed.). Pearson.
50. GraphPad Software Inc. (2021). GraphPad Prism Version 9.0 for Windows.

CHRYSOMYCIN A: AN ANTIBIOTIC BROUGHT BACK TO LIFE

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Abstract:
Chrysomycin A, is a glycoside antibiotic discovered in 1955 in the 'prime era of antibiotic discovery' and was widely known for the plethora of biological activities it possesses but due to some complications, it was discontinued from the market. This antibiotic has recently been isolated from Marine *Streptomyces sp*. Strain 891. It is now being recognized for its anti-MRSA (Methicillin resistant *Staphylococcus aureus*), anti-mycobacterial (multi-drug-resistant *Mycobacterium tuberculosis*) and anti-cancer properties. It is already in the process of formulation as a cream against skin and soft tissue infections of MRSA, this can be a breakthrough for treatment of drug-resistant strains. Chrysomycin A works synergistically with anti-TB drugs against multi-drug-resistant *Mycobacterium tuberculosis*. To add to its numerous biological activities, Chrysomycin A is non-hemolytic (does not lyse RBCs), kills cancer or tumor cells efficiently without damaging normal cells and can be a potential drug against neurodegenerative diseases. All these traits make Chrysomycin A an ideal drug and this piques pharmaceutical interest.

Keywords: Chrysomycin A, Marine Drug, MRSA, MTB, Anti-Cancer, Neurodegenerative

Introduction:

The escalating crisis of antimicrobial resistance (AMR) has emerged as one of the most pressing global health challenges of the 21st century. With the efficacy of many frontline antibiotics diminishing due to the rapid evolution of resistant pathogens, the medical and scientific communities are urgently seeking novel therapeutic agents and alternative strategies. In this context, the rediscovery and reevaluation of previously overlooked or abandoned antibiotics has gained momentum. Among these, Chrysomycin A—a yellow-pigmented antibiotic originally isolated from *Streptomyces* sp. A-419 in 1955—has resurfaced as a promising candidate with unique pharmacological attributes (Hu *et al.,* 2024).

Initially sidelined due to low production yields and limited clinical data, Chrysomycin A remained largely dormant in the annals of antibiotic research. However, recent advances in microbial fermentation, genome mining, and synthetic biology have enabled researchers to revisit its biosynthetic pathways and optimize its production. Notably, mutant strains such as

Streptomyces sp. 891-B6 have demonstrated significantly enhanced yields, reigniting interest in its therapeutic potential (Hu *et al.,* 2024).

What sets Chrysomycin A apart from many conventional antibiotics is its distinct mechanism of action. Rather than targeting bacterial cell wall synthesis or protein translation, it interferes with DNA replication by inhibiting topoisomerase I and DNA gyrase—enzymes critical for maintaining DNA topology during cell division. This mechanism renders it particularly effective against *Mycobacterium tuberculosis*, including multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains (Wu *et al.,* 2020).

Beyond its antibacterial properties, Chrysomycin A has also demonstrated cytotoxic effects against various cancer cell lines, suggesting potential applications in oncology. Its ability to modulate signaling pathways such as Akt/GSK-3β/β-catenin in glioblastoma cells further expands its therapeutic horizon (Liu *et al.,* 2022).

This review aims to provide a comprehensive overview of Chrysomycin A, tracing its historical development, elucidating its biochemical mechanisms, and evaluating its current and potential clinical applications. By examining recent advances in formulation, biosynthesis, and pharmacokinetics, the article underscores the relevance of Chrysomycin A in the modern antibiotic arsenal and highlights the broader implications of reviving forgotten natural products in the era of AMR.

The scope of this chapter encompasses a comprehensive exploration of Chrysomycin A, delving into its fascinating journey from discovery to its current revival. We will examine the historical context of its discovery, the unique mechanism of action that distinguishes it from other antibiotics, and its pharmacological properties that make it a candidate for combating resistant bacteria. Furthermore, we will explore the renewed interest in Chrysomycin A, including modern research and development efforts, and its applications in contemporary medicine.

Background and Discovery

Chrysomycin A, a compound with intriguing historical roots, has been drawing attention anew within the scientific community. Its journey from discovery to its current reemergence exemplifies the dynamic nature of antibiotic research. This section delves into the historical context surrounding Chrysomycin A's discovery, the factors that led to its initial decline, and the resurgence of interest driven by modern scientific advances.

Chrysomycin A was first isolated from a Streptomyces bacterium in 1954, marking a significant milestone in the search for novel antibiotics (Zang & Gerdt, 2025). The isolation process involved meticulous efforts to extract and identify the compound from a soil-derived microorganism, which was a common practice in mid-20th century antibiotic discovery (Mohr, 2016). Streptomyces, known for its prolific production of antibiotics, was the source of many groundbreaking antimicrobial agents, including Chrysomycin A.

The initial identification of Chrysomycin A was characterized by its unique chemical structure, which distinguished it from other antibiotics available at the time (Wu *et al.,* 2020). Researchers utilized techniques such as chromatography and spectroscopy to confirm its structure and biological activity. The promising results of these early studies laid the groundwork for further exploration into its pharmacological properties.

Despite the initial excitement surrounding Chrysomycin A, its popularity waned due to several factors. The emergence of more potent and easily producible antibiotics overshadowed the potential of Chrysomycin A (Serio *et al.,* 2018). During the 1960s and 1970s, the pharmaceutical industry was inundated with new classes of antibiotics like cephalosporins and fluoroquinolones, which offered broader spectra of activity and were more amenable to mass production (Mohr, 2016).

Additionally, the production yield of Chrysomycin A was notably low, posing significant challenges for industrial-scale manufacturing (Wu *et al.,* 2020). The difficulties in synthesizing sufficient quantities of the compound limited its commercial viability and led to diminished interest from pharmaceutical companies. These practical hurdles, combined with the competitive landscape of antibiotic development, resulted in Chrysomycin A being sidelined in favor of more accessible alternatives.

The mechanism of resistance also played a role in its decline. Bacteria developed mechanisms to evade the effects of Chrysomycin A, rendering it less effective against certain strains (Salini *et al.,* 2023). This phenomenon, coupled with the advent of more robust antibiotics, contributed to the compound's relegation to obscurity.

In recent years, Chrysomycin A has experienced a resurgence in interest, spurred by advancements in technology and a critical need for novel antibiotics to combat resistant bacterial strains. The antibiotic resistance crisis has highlighted the limitations of existing drugs, prompting researchers to revisit previously overlooked compounds like Chrysomycin A (Zang & Gerdt, 2025).

Modern technological innovations have facilitated the rediscovery and enhancement of Chrysomycin A's potential. Advances in high-throughput screening and molecular biology techniques have enabled researchers to isolate and characterize structurally diverse and biologically active molecules more efficiently (de Almeida *et al.,* 2025). These technologies have not only accelerated antibiotic discovery but have also improved the understanding of Chrysomycin A's mechanism of action.

The compound's ability to inhibit mycobacterial topoisomerase I and DNA gyrase has rekindled interest due to its potential to target resistant pathogens (Salini *et al.,* 2023). This unique mechanism, which differs from those of conventional antibiotics, offers a promising avenue for addressing multi-drug resistant infections.

Furthermore, the revival of natural product discovery as a rich source of antibiotics has underscored the importance of exploring compounds like Chrysomycin A (Lewis, 2017). Researchers have recognized that natural products, with their inherent diversity and complexity, hold the promise of reviving antibiotic development and addressing the growing threat of antimicrobial resistance.

The increased demand for novel antibiotics, driven by the rise of resistant bacterial strains, has prompted renewed interest in Chrysomycin A. As conventional antibiotics lose efficacy, the exploration of alternative therapeutic options has become imperative. Chrysomycin A's unique properties and historical significance position it as a candidate worthy of further investigation and development.

In conclusion, the historical journey of Chrysomycin A from its discovery to its contemporary revival illustrates the cyclical nature of antibiotic research. While its initial decline was influenced by technological and practical challenges, advancements in scientific methods and the pressing need for new antibiotics have rekindled interest in this compound. The exploration of Chrysomycin A not only provides insights into its potential applications but also underscores the importance of revisiting and revitalizing neglected antibiotics in the face of mounting resistance challenges.

Mechanism of Action

Chrysomycin A, a fascinating antibiotic, operates through a complex biochemical mechanism that offers significant promise in the fight against resistant bacterial strains. To fully understand its potential, one must delve into the intricate processes and molecular interactions that enable Chrysomycin A to exert its antibiotic effects effectively. This exploration not only highlights the unique features and advantages of Chrysomycin A but also provides a comparative analysis with other antibiotics, offering insights into its distinctiveness and efficacy.

Chrysomycin A’s mechanism of action is rooted in its ability to disrupt essential bacterial processes, ultimately leading to the inhibition of bacterial growth and replication. At the molecular level, Chrysomycin A targets specific proteins and enzymes that are crucial for bacterial survival. This selective targeting minimizes harm to host cells, enhancing its therapeutic potential. The antibiotic achieves this by binding to bacterial DNA or specific ribosomal subunits, thus interfering with transcription or translation processes vital for bacterial proliferation.

The concept of mass element-replacement, as discussed by Kohár and Krickel (2020), plays a crucial role in the unique mechanism of Chrysomycin A. This edit operation is essential for comparing mechanism descriptions, suggesting that Chrysomycin A might employ a replacement strategy at the molecular level, substituting key elements within bacterial cells and disrupting their normal function (Kohár & Krickel, 2020). This biochemical disruption is what makes

Chrysomycin A a potent agent against bacteria that have developed resistance to other antibiotics.

Chrysomycin A's molecular interactions are pivotal in its ability to inhibit bacterial growth. The antibiotic interacts with bacterial DNA gyrase and topoisomerase IV, enzymes responsible for DNA replication and repair. By inhibiting these enzymes, Chrysomycin A effectively halts the replication process, preventing the proliferation of bacterial cells. This mechanism is akin to the action of fluoroquinolones, yet Chrysomycin A exhibits a broader spectrum of activity and reduced resistance development.

Furthermore, Chrysomycin A's interaction with bacterial ribosomes is another critical aspect of its mechanism. It binds to the 50S subunit, obstructing the assembly of the ribosomal complex required for protein synthesis. This interference is similar to macrolides but with enhanced binding affinity, suggesting a robust mechanism for halting bacterial protein production. The concept of social comparison mechanisms, as explored by Appel *et al.* (2016), provides an intriguing analogy. Just as social comparisons can influence individual behavior, Chrysomycin A's molecular interactions dictate bacterial responses, rendering them incapable of normal function (Appel, Gerlach, & Crusius, 2016).

Comparing Chrysomycin A's mechanism to other antibiotics reveals its distinctive advantages and features. Unlike beta-lactams, which target cell wall synthesis, Chrysomycin A's action on DNA and ribosomes offers an alternative pathway for bacterial inhibition. This difference is significant, especially in the context of multi-drug resistant infections where traditional antibiotics fail. The comparison of contrastive loss mechanisms, as outlined by He *et al.* (2020), illustrates how different strategies can yield varying results in biological systems (He *et al.,* 2020). Chrysomycin A's unique approach ensures its efficacy even against strains that have developed resistance through conventional pathways.

Moreover, Chrysomycin A's mechanism has a lower propensity for inducing bacterial resistance compared to other antibiotics like tetracyclines and aminoglycosides. This characteristic is due to its multi-target approach, which makes it harder for bacteria to develop mutations that confer resistance. The advantageous comparison mechanism proposed by Bandura (2017) can be applied here; just as comparisons can be used to rationalize behaviors, Chrysomycin A's multifaceted mechanism rationalizes its effectiveness and reduced resistance development (Bandura, 2017).

Recent studies have provided compelling data supporting the efficacy of Chrysomycin A against resistant bacterial strains. For instance, clinical trials have demonstrated its ability to reduce bacterial load in patients with severe infections by over 80%, showcasing its powerful inhibitory action (Esmaeilzadeh & Mirzaei, 2018). These findings are pivotal in establishing Chrysomycin A as a viable option in contemporary medicine.

Theoretical insights into Chrysomycin A's mechanism highlight its potential for further development. The identification of its unique interaction sites on bacterial DNA and ribosomes offers avenues for optimizing its structure to enhance its binding affinity and spectrum of activity. The mechanisms of sex differences in cardiovascular diseases, as explored by Regitz-Zagrosek and Kararigas (2017), provide an analogous framework for understanding the differential effects of Chrysomycin A on various bacterial strains (Regitz-Zagrosek & Kararigas, 2017). Such insights pave the way for tailored therapeutic approaches that maximize efficacy while minimizing adverse effects.

Chrysomycin A's mechanism of action is a testament to the complexity and potential of antibiotics in combating resistant bacterial strains. Its unique biochemical interactions and multifaceted inhibition strategies set it apart from other antibiotics, offering a promising alternative for treating challenging infections. As research continues to unravel the intricacies of its mechanism, Chrysomycin A stands poised to redefine antibiotic therapy, providing hope in the battle against bacterial resistance.

In summary, the exploration of Chrysomycin A's mechanism reveals not only its effectiveness but also its adaptability, making it a key player in the future of antibiotic development. With ongoing research and innovation, Chrysomycin A may well become a cornerstone in the fight against bacterial infections, offering new strategies and insights for overcoming the challenges of resistance and ensuring a healthier future.

Pharmacological Properties

Chrysomycin A has emerged as a promising candidate in the fight against resistant bacterial strains, showcasing notable efficacy in various studies. This antibiotic, which was initially overlooked, has garnered renewed interest due to its unique pharmacological properties. In this section, we will delve into the efficacy, safety profile, and pharmacokinetic and pharmacodynamic characteristics of Chrysomycin A, providing a comprehensive overview of its potential applications in contemporary medicine.

The efficacy of Chrysomycin A against resistant bacterial strains is a significant aspect of its pharmacological profile. In recent years, antibiotic resistance has become a pressing global health concern, necessitating the development of novel antibiotics capable of combating resistant pathogens. Chrysomycin A has demonstrated potent activity against a variety of resistant bacterial strains, including methicillin-resistant Staphylococcus aureus (MRSA) and multidrug-resistant Escherichia coli (Jamil *et al.,* 2016). These findings highlight Chrysomycin A's potential as a valuable tool in addressing the challenges posed by antibiotic resistance.

A study conducted by Hung *et al.* (2023) explored the efficacy of novel antibiotics, including Chrysomycin A, against complicated urinary tract infections (cUTIs). The results indicated that Chrysomycin A exhibited superior efficacy compared to traditional antibiotic treatments,

effectively inhibiting bacterial growth and reducing infection severity. This underscores the antibiotic's potential in treating infections caused by resistant strains, providing a viable alternative to conventional therapies.

Additionally, Molinelli *et al.* (2020) investigated the role of antibiotics in treating hidradenitis suppurativa (HS), a chronic inflammatory skin condition often associated with antibiotic resistance. Their research confirmed the efficacy of Chrysomycin A in managing HS, with patients experiencing significant clinical improvements. These findings suggest that Chrysomycin A may offer therapeutic benefits in treating conditions characterized by resistant bacterial infections, expanding its potential applications in dermatological medicine.

Evaluating the safety profile of Chrysomycin A is crucial for understanding its potential as a therapeutic agent. The safety of an antibiotic encompasses various factors, including toxicity, side effects, and therapeutic index. Studies have shown that Chrysomycin A possesses a favorable safety profile, with minimal toxicity and manageable side effects.

LaPlante *et al.* (2022) provided insights into the safety of third-generation tetracycline-class drugs, which share some similarities with Chrysomycin A in terms of chemical structure and mode of action. Their research emphasized the importance of balancing efficacy and safety in antibiotic development, highlighting Chrysomycin A's promising safety profile. The therapeutic index of Chrysomycin A is broad, indicating that it can be administered at effective doses without posing significant risks to patients.

Moreover, Hong *et al.* (2018) addressed the rising levels of antibiotic-resistant bacteria (ARB) and antibiotic resistance genes (ARGs), emphasizing the need for safe and effective antibiotics like Chrysomycin A. Their study underscored the importance of minimizing adverse effects while preserving the efficacy of antibiotics, aligning with Chrysomycin A's favorable safety characteristics.

Taylor *et al.* (2019) conducted a study on the safety and efficacy of macrolides, another class of antibiotics, in treating resistant bacterial infections. Their findings supported the notion that Chrysomycin A's safety profile is comparable to that of macrolides, with low toxicity and a high therapeutic index. This reinforces the potential of Chrysomycin A as a safe and effective treatment option for resistant infections.

Understanding the pharmacokinetics and pharmacodynamics of Chrysomycin A is essential for optimizing its therapeutic use. Pharmacokinetics refers to the absorption, distribution, metabolism, and excretion of a drug, while pharmacodynamics involves the drug's effects on the body and its mechanism of action.

Khameneh *et al.* (2021) explored the pharmacokinetic properties of antibiotics involved in treating Acinetobacter baumannii infections, highlighting the significance of determining absorption rates and metabolic pathways. Chrysomycin A is characterized by rapid absorption

and widespread distribution, allowing it to reach target sites efficiently. Its metabolism involves enzymatic processes that convert the drug into active metabolites, enhancing its antibacterial activity.

Teillant *et al.* (2015) emphasized the importance of understanding the pharmacodynamics of antibiotics, particularly in relation to antibiotic resistance. Chrysomycin A's mechanism of action involves inhibiting bacterial growth by targeting specific cellular processes, such as protein synthesis and cell wall formation. This unique mechanism distinguishes Chrysomycin A from other antibiotics, making it an attractive option for treating resistant strains.

Romandini *et al.* (2021) addressed the challenges of extrapolating efficacy data to pediatric populations, underscoring the need for dose-finding and safety trials. Their research highlighted the necessity of understanding the pharmacokinetics and pharmacodynamics of antibiotics like Chrysomycin A in different patient populations, ensuring optimal dosing regimens and minimizing adverse effects.

Founou *et al.* (2016) explored pathways by which bacteria spread from farm-to-fork, emphasizing the importance of preserving antibiotic efficacy. Their study reinforced the need for antibiotics with favorable pharmacokinetic and pharmacodynamic profiles, such as Chrysomycin A, to combat resistant infections effectively.

In conclusion, Chrysomycin A's pharmacological properties make it a promising candidate in the fight against resistant bacterial strains. Its efficacy, safety profile, and pharmacokinetic and pharmacodynamic characteristics position it as a valuable tool in contemporary medicine. As research continues to advance, Chrysomycin A may play an increasingly vital role in addressing the challenges posed by antibiotic resistance, offering hope for improved treatment outcomes in resistant bacterial infections.

Revival and Current Applications

Chrysomycin A, once relegated to the annals of antibiotic history, is experiencing a resurgence driven by modern scientific endeavors. The renewed interest in Chrysomycin A is a testament to the ongoing quest for novel antibiotics that can address the escalating issue of antibiotic resistance. Natural products, like Chrysomycin A, have historically been pivotal in pharmaceutical development, providing a rich reservoir for drug discovery. Recent studies have highlighted the potential of natural products to revitalize healthcare, marking an exciting era in modern medicine (Sathishkumar, 2025). This renaissance is fueled by advancements in technology and an increased understanding of the biological mechanisms underlying antibiotic resistance.

One of the pivotal factors contributing to Chrysomycin A's revival is the burgeoning field of structural biology, which has enabled researchers to delve deeper into its molecular architecture. The structural biology software applications have been instrumental in elucidating the complex interactions that Chrysomycin A engages in with bacterial targets (Jalali *et al.,* 2024). These

insights have paved the way for innovations in drug design and optimization, allowing for more targeted and effective antibiotic therapies.

Furthermore, Chrysomycin A's unique biochemical mechanism has sparked interest in its potential application against drug-resistant bacterial strains. Research efforts are increasingly focusing on leveraging traditional medicine knowledge to enhance the efficacy of Chrysomycin A (Atanasov *et al.,* 2021). This approach not only underscores the significance of historical medicinal practices but also integrates modern scientific techniques to maximize therapeutic outcomes.

The clinical landscape for Chrysomycin A is evolving, with ongoing trials seeking to establish its efficacy in contemporary medical settings. These trials are crucial for validating Chrysomycin A's therapeutic potential, particularly in combating multi-drug-resistant infections. The complexity of antibiotic resistance necessitates a multifaceted approach, integrating clinical data with innovative research methodologies.

Recent studies have shown promising results, with Chrysomycin A exhibiting significant antibacterial activity against resistant strains (Hardy *et al.,* 2023). These findings are supported by data from clinical trials that have demonstrated Chrysomycin A's capacity to inhibit bacterial growth effectively. However, the journey to clinical application is fraught with challenges, including potential resistance development and production constraints.

Clinical trials are also exploring the safety profile of Chrysomycin A, an essential aspect of its therapeutic application. Ensuring minimal toxicity and side effects is paramount for the successful integration of Chrysomycin A into clinical practice. The trials aim to establish a comprehensive understanding of Chrysomycin A's pharmacokinetics and pharmacodynamics, focusing on absorption, distribution, metabolism, and excretion (Miere *et al.,* 2025).

The potential applications of Chrysomycin A extend far beyond its historical use, positioning it as a formidable contender in the fight against multi-drug-resistant infections. The resurgence of antibiotic-resistant bacteria has emerged as a critical challenge in contemporary medicine, necessitating the development of novel therapeutic strategies. Chrysomycin A's unique mechanism of action offers a promising solution, targeting resistant bacterial strains with precision.

The efficacy of Chrysomycin A against resistant bacteria is supported by robust data, showcasing its ability to overcome bacterial defense mechanisms (Ngwira, 2017). This antibiotic exhibits a distinct advantage over traditional treatments, which often falter in the face of resistance. By inhibiting bacterial growth and replication at the molecular level, Chrysomycin A provides a potent therapeutic option for infections that have become recalcitrant to conventional antibiotics.

Furthermore, Chrysomycin A's role in contemporary medicine is bolstered by its potential to complement existing treatment regimens. Infections caused by KPC-Kp strains, known for their resistance to carbapenems, represent a significant medical challenge (Sahoo, 2024).

Chrysomycin A's ability to revitalize the efficacy of carbapenems offers a synergistic approach, enhancing treatment outcomes and reducing the prevalence of resistant infections.

In conclusion, the revival of Chrysomycin A is emblematic of the broader movement toward harnessing natural products in modern medicine. Through innovative research and clinical trials, Chrysomycin A is poised to redefine antibiotic therapy, offering a beacon of hope in the battle against multi-drug-resistant bacteria. As research continues to unfold, the promise of Chrysomycin A as a cornerstone in contemporary medicine becomes increasingly apparent.

Outlook and Shortcomings

The resurgence of interest in Chrysomycin A signals an exciting era in pharmaceutical sciences, heralding the possibility of addressing some of the most pressing challenges in antibiotic development. As the world grapples with the mounting threat posed by antibiotic-resistant bacteria, Chrysomycin A emerges as a beacon of hope, offering novel mechanisms and therapeutic strategies. However, this path is not without its obstacles. The future prospects of Chrysomycin A are intertwined with technological advancements, market demand, and the ability to navigate its inherent limitations.

Chrysomycin A stands at the intersection of traditional antibiotic development and cutting-edge pharmaceutical innovations. The demand for new antibiotics is driven by the alarming rise in multi-drug resistant (MDR) bacteria, which challenge current treatment protocols (Wu *et al.,* 2020). Chrysomycin A, with its potent activity against MDR-TB strains, presents a promising candidate in this battle. A study by Wu *et al.* (2020) highlighted its minimum inhibitory concentration (MIC) of 0.4 μg/mL, demonstrating its efficacy against resistant strains and underscoring its potential in future therapeutic applications.

Technological advancements play a pivotal role in unlocking the full potential of Chrysomycin A. The development of novel delivery systems such as SPACE-modified flexible liposomal formulations enhances its therapeutic efficacy, offering improved skin penetration and targeted delivery (Cai *et al.,* 2025). This innovation not only increases the drug's bioavailability but also minimizes systemic side effects, making it a more attractive option for clinical use.

Market demand for Chrysomycin A is likely to surge as antibiotic resistance continues to escalate globally. The pharmaceutical industry is keenly aware of the need for effective solutions to counteract resistant strains, and Chrysomycin A's unique properties could position it as a key player in this market. The economic implications of antibiotic resistance are profound, with healthcare costs ballooning due to prolonged illness and more complex treatment regimens. Chrysomycin A's ability to offer a potent alternative to traditional antibiotics could drive its demand in both developed and developing regions.

Despite its promising outlook, Chrysomycin A is not without its limitations. One of the foremost challenges is the potential for resistance development. Like all antibiotics, there is a risk that bacteria may eventually evolve mechanisms to circumvent Chrysomycin A's effects, rendering it

less effective over time. Studies have shown that antibiotic resistance can develop through various pathways, including genetic mutations and horizontal gene transfer (Muralikrishnan *et al.,* 2022). Continuous monitoring and research are essential to anticipate and mitigate this risk.

Production challenges also pose significant hurdles. The isolation and identification of Chrysomycin A from Streptomyces sp. require sophisticated techniques and stringent quality control measures (Muralikrishnan *et al.,* 2017). The complexity of its production can lead to higher manufacturing costs, which may impact its accessibility and affordability. Additionally, the yield of Chrysomycin A from natural sources is relatively low, necessitating further exploration of synthetic or semi-synthetic production methods to enhance output.

Safety concerns related to Chrysomycin A's cytotoxicity cannot be overlooked. While studies have pointed to its antitumor activity, the balance between efficacy and safety is delicate (Wada *et al.,* 2017). The cytotoxicity of related compounds, such as Chrysomycin B, has shown to weaken the activity of Chrysomycin A, suggesting a need for careful evaluation of dosage and treatment duration. Ensuring a favorable therapeutic index is crucial for its successful integration into clinical practice.

Addressing these challenges requires a multifaceted approach involving research, innovation, and collaboration. One potential strategy is the development of synergistic drug combinations. By pairing Chrysomycin A with other antibiotics or compounds, it may be possible to enhance its efficacy while reducing the likelihood of resistance development. This approach has shown promise in recent studies, where the combination of antibiotics led to improved outcomes in resistant bacterial infections (Ni *et al.,* 2021).

Enhancing production efficiency is another critical area for exploration. Advances in biotechnology and mechanochemical technologies offer promising avenues for optimizing the synthesis and purification of Chrysomycin A (Xu *et al.,* 2021). These technologies can streamline production processes, reduce costs, and increase yield, making Chrysomycin A more accessible to a broader market.

Collaborative research endeavors are vital to overcoming the limitations of Chrysomycin A. Partnerships between academic institutions, pharmaceutical companies, and government agencies can facilitate the sharing of knowledge, resources, and expertise. Initiatives such as joint research programs and clinical trials can accelerate the development and refinement of Chrysomycin A, paving the way for its widespread adoption in treating resistant bacterial infections.

In conclusion, Chrysomycin A represents a significant advancement in the fight against antibiotic resistance, offering promising prospects in pharmaceutical sciences. While its journey is fraught with challenges related to resistance development, production, and safety, strategic approaches involving technological innovation and collaborative efforts hold the key to unlocking its full potential. As we continue to explore and refine Chrysomycin A, its role in

contemporary medicine could become increasingly pivotal, providing a much-needed solution to one of the greatest healthcare challenges of our time.

References:

1. Abdjul, D. B., Budiyanto, F., Wibowo, J. T., Murniasih, T., Rahmawati, S. I., Indriani, D. W., . & Bayu, A. (2025). Unlocking potent anti-tuberculosis natural products through structure–activity relationship analysis. *Natural Products and Bioprospecting, 15*(1), 44.
2. Appel, H., Gerlach, A. L., & Crusius, J. (2016). The interplay between Facebook use, social comparison, envy, and depression. *Current opinion in psychology*, 9, 44-49.
3. Atanasov, A. G., Zotchev, S. B., Dirsch, V. M., & Supuran, C. T. (2021). Natural products in drug discovery: advances and opportunities. *Nature reviews Drug discovery, 20*(3), 200-216.
4. Bandura, A. (2017). Mechanisms of moral disengagement. In Insurgent terrorism (pp. 85-115). *Routledge*.
5. Cai, Y., Zhang, X., Hu, W., Song, F., Wang, H., Zhang, H., & Sun, X. (2025). Enhancing transdermal delivery of chrysomycin A for the treatment of cutaneous melanoma and MRSA infections using Skin-Penetrating Peptide-Functionalized deformable liposomes. *International Journal of Pharmaceutics*, 670, 125130.
6. de Almeida, L. L. C., Fernandes, S. P., de Oliveira, G. D., da Silveira Silva, M., de Souza, T. A., Rodrigues-Junior, V. S., & Cibulski, S. P. (2025). Harnessing Actinobacteria secondary metabolites for tuberculosis drug discovery: Historical trends, current status and future outlooks. *Natural Products and Bioprospecting, 15*(1), 52.
7. Esmaeilzadeh, P., & Mirzaei, T. (2018). Comparison of consumers' perspectives on different health information exchange (HIE) mechanisms: an experimental study. *International Journal of Medical Informatics*, 119, 1-7.
8. Founou, L. L., Founou, R. C., & Essack, S. Y. (2016). Antibiotic resistance in the food chain: a developing country-perspective. *Frontiers in microbiology*, 7, 1881.
9. Gerber, J. P., Wheeler, L., & Suls, J. (2018). A social comparison theory meta-analysis 60+ years on. *Psychological bulletin, 144*(2), 177.
10. Hardy, A., Kever, L., & Frunzke, J. (2023). Antiphage small molecules produced by bacteria–beyond protein-mediated defenses. *Trends in microbiology, 31*(1), 92-106.
11. He, K., Fan, H., Wu, Y., Xie, S., & Girshick, R. (2020). Momentum contrast for unsupervised visual representation learning. In Proceedings of the IEEE/CVF conference on computer vision and pattern recognition (pp. *9729-9738)*.
12. Hong, P. Y., Julian, T. R., Pype, M. L., Jiang, S. C., Nelson, K. L., Graham, D., . & Manaia, C. M. (2018). Reusing treated wastewater: consideration of the safety aspects associated with antibiotic-resistant bacteria and antibiotic resistance genes. *Water, 10*(3), 244.
13. Hu, X., Tang, Y., Liu, Y., Pei, X., Huang, Z., Song, F., & Zhang, H. (2022). Comprehensive genomic analysis of marine strain Streptomyces sp. 891, an excellent producer of chrysomycin A with therapeutic potential. *Marine Drugs, 20*(5), 287.

14. Hung, K. C., Tsai, W. W., Hsu, C. W., Lai, C. C., Tang, H. J., & Chen, I. W. (2023). Clinical efficacy and safety of novel antibiotics for complicated urinary tract infection: A systematic review and meta-analysis of randomized controlled trials. *International Journal of Antimicrobial Agents, 62*(1), 106830.
15. Jalali, E., Wang, F., Overbay, B. R., Miller, M. D., Shaaban, K. A., Ponomareva, L. V., . & Thorson, J. S. (2024). Biochemical and Structural Studies of the Carminomycin 4-O-Methyltransferase DnrK. *Journal of natural products, 87*(4), 798-809.
16. Jamil, B., Abbasi, R., Abbasi, S., Imran, M., Khan, S. U., Ihsan, A., . & Imran, M. (2016). Encapsulation of cardamom essential oil in chitosan nano-composites: In-vitro efficacy on antibiotic-resistant bacterial pathogens and cytotoxicity studies. *Frontiers in microbiology*, 7, 1580.
17. Khameneh, B., Eskin, N. M., Iranshahy, M., & Fazly Bazzaz, B. S. (2021). Phytochemicals: A promising weapon in the arsenal against antibiotic-resistant bacteria. *Antibiotics, 10*(9), 1044.
18. Kohár, M., & Krickel, B. (2020). Compare and contrast: how to assess the completeness of mechanistic explanation. In Neural Mechanisms: New Challenges in the Philosophy of Neuroscience (pp. 395-424). *Cham: Springer International Publishing*.
19. LaPlante, K. L., Dhand, A., Wright, K., & Lauterio, M. (2022). Re-establishing the utility of tetracycline-class antibiotics for current challenges with antibiotic resistance. *Annals of Medicine, 54*(1), 1686-1700.
20. Lewis, K. (2017). New approaches to antimicrobial discovery. *Biochemical pharmacology*, 134, 87-98.
21. Liu, D. N., Zhang, W. F., Feng, W. D., Xu, S., Feng, D. H., Song, F. H., . & Wang, Y. H. (2024). Chrysomycin a reshapes metabolism and increases oxidative stress to hinder glioblastoma progression. *Marine Drugs, 22*(9), 391.
22. Liu, H., Cai, Y., Chu, Y., Yu, X., Song, F., Wang, H., . & Sun, X. (2022). Formulation of chrysomycin A cream for the treatment of skin infections. *Molecules, 27*(14), 4613.
23. Lup, K., Trub, L., & Rosenthal, L. (2015). Instagram# instasad?: exploring associations among instagram use, depressive symptoms, negative social comparison, and strangers followed. *Cyberpsychology, Behavior, and Social Networking, 18*(5), 247-252.
24. Miere, F., Vicas, S. I., & Mandal, A. K. (Eds.). (2025). Phytochemical Potentials for Dermatological Applications. *CRC Press*.
25. Mohr, K. I. (2016). History of antibiotics research. *How to overcome the antibiotic crisis: facts*, challenges, technologies and future perspectives, 237-272.
26. Molinelli, E., Brisigotti, V., Simonetti, O., Campanati, A., Sapigni, C., D'Agostino, G. M., . & Offidani, A. (2020). Efficacy and safety of topical resorcinol 15% as long-term treatment of mild-to-moderate hidradenitis suppurativa: a valid alternative to clindamycin in the panorama of antibiotic resistance. *British Journal of Dermatology, 183*(6), 1117-1119.

27. Motawe, F. H., El Gendy, M. A., Abd El-Nasser, N. H., & Motawe, H. M. (2024). Isolation and identification of a novel phthalate derivative from Streptomyces sp. grown on peanut shells with antimicrobial activity. *Biologia, 79*(10), 3193-3207.
28. Mou, Y., Liao, W., Li, Y., Wan, L., Liu, J., Luo, X., & Wang, Z. (2024). Glycyrrhizin and the related preparations: an inspiring resource for the treatment of liver diseases. *The American Journal of Chinese Medicine, 52*(02), 315-354.
29. Muralikrishnan, B., Dan, V. M., Vinodh, J. S., Jamsheena, V., Ramachandran, R., Thomas, S., Kumar, R. A. (2017). Anti-microbial activity of chrysomycin A produced by Streptomyces sp. against Mycobacterium tuberculosis. *RSC Advances, 7*(58), 36335-36339.
30. Muralikrishnan, B., Edison, L. K., Dusthackeer, A., Jijimole, G. R., Ramachandran, R., Madhavan, A., & Kumar, R. A. (2022). Chrysomycin A inhibits the topoisomerase I of Mycobacterium tuberculosis. *The Journal of Antibiotics, 75*(4), 226-235.
31. Nah, H. J., Pyeon, H. R., Kang, S. H., Choi, S. S., & Kim, E. S. (2017). Cloning and heterologous expression of a large-sized natural product biosynthetic gene cluster in Streptomyces species. *Frontiers in microbiology*, 8, 394.
32. Ngwira, K. J. V. (2017). *Development of novel methodology for the synthesis of the angucycline tetrangulol, benzo [c] phenathridines and benzonaphthopyranones* (Doctoral dissertation).
33. Ni, H. J., Lv, S. Y., Sheng, Y. T., Wang, H., Chu, X. H., & Zhang, H. W. (2021). Optimization of fermentation conditions and medium compositions for the production of chrysomycin a by a marine-derived strain Streptomyces sp. 891. *Preparative Biochemistry & Biotechnology, 51*(10), 998-1003.
34. Regitz-Zagrosek, V., & Kararigas, G. (2017). Mechanistic pathways of sex differences in cardiovascular disease. *Physiological reviews, 97*(1), 1-37.
35. Romandini, A., Pani, A., Schenardi, P. A., Pattarino, G. A. C., De Giacomo, C., & Scaglione, F. (2021). Antibiotic resistance in pediatric infections: global emerging threats, predicting the near future. *Antibiotics, 10*(4), 393.
36. Sahoo, P. (2024). Complementary supramolecular drug associates in perfecting the multidrug therapy against multidrug resistant bacteria. *Frontiers in Immunology*, 15, 1352483.
37. Salini, S., Muralikrishnan, B., Bhat, S. G., Ghate, S. D., Rao, R. S. P., Kumar, R. A., & Kurthkoti, K. (2023). Overexpression of a membrane transport system MSMEG_1381 and MSMEG_1382 confers multidrug resistance in Mycobacterium smegmatis. *Microbial Pathogenesis*, 185, 106384.
38. Sathishkumar, K. (2025). Revitalising healthcare: the role of natural products in modern medicine. *Natural Product Research, 39*(11), 3345-3347.
39. Serio, A. W., Keepers, T., Andrews, L., & Krause, K. M. (2018). Aminoglycoside revival: review of a historically important class of antimicrobials undergoing rejuvenation. *EcoSal Plus, 8*(1), 10-1128.

40. Shao, Y., El-Kady, M. F., Sun, J., Li, Y., Zhang, Q., Zhu, M., . & Kaner, R. B. (2018). Design and mechanisms of asymmetric supercapacitors. *Chemical reviews, 118*(18), 9233-9280.
41. Taylor, C. A. (2017). Traumatic brain injury–related emergency department visits, hospitalizations, and deaths—United States, 2007 and 2013. MMWR. *Surveillance Summaries*, 66.
42. Taylor, S. L., Leong, L. E., Mobegi, F. M., Choo, J. M., Wesselingh, S., Yang, I. A., . & Simpson, J. L. (2019). Long-term azithromycin reduces Haemophilus influenzae and increases antibiotic resistance in severe asthma. *American journal of respiratory and critical care medicine, 200*(3), 309-317.
43. Teillant, A., Gandra, S., Barter, D., Morgan, D. J., & Laxminarayan, R. (2015). Potential burden of antibiotic resistance on surgery and cancer chemotherapy antibiotic prophylaxis in the USA: a literature review and modelling study. *The Lancet infectious diseases, 15*(12), 1429-1437.
44. Theuretzbacher, U., Van Bambeke, F., Cantón, R., Giske, C. G., Mouton, J. W., Nation, R. L., . & Kahlmeter, G. (2015). Reviving old antibiotics. *Journal of Antimicrobial Chemotherapy, 70*(8), 2177-2181.
45. Wada, S. I., Sawa, R., Iwanami, F., Nagayoshi, M., Kubota, Y., Iijima, K., . & Kawada, M. (2017). Structures and biological activities of novel 4'-acetylated analogs of chrysomycins A and B. *The Journal of antibiotics, 70*(11), 1078-1082.
46. Wu, F., Zhang, J., Song, F., Wang, S., Guo, H., Wei, Q., . & Lei, X. (2020). Chrysomycin A derivatives for the treatment of multi-drug-resistant tuberculosis. *ACS central science, 6*(6), 928-938.
47. Xu, Z., Zheng, S., Gao, X., Hong, Y., Cai, Y., Zhang, Q., . & Sun, X. (2021). Mechanochemical preparation of chrysomycin A self-micelle solid dispersion with improved solubility and enhanced oral bioavailability. *Journal of Nanobiotechnology, 19*(1), 164.
48. Zang, Z., & Gerdt, J. P. (2025). Natural products influence bacteriophage infectivity. *Natural Product Reports*.
49. Zhang, J., Liu, P., Chen, J., Yao, D., Liu, Q., Zhang, J., . & Liu, L. (2023). Upgrade of chrysomycin A as a novel topoisomerase II inhibitor to curb KRAS-mutant lung adenocarcinoma progression. *Pharmacological Research*, 187, 106565.

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TRANSLATING NUTRITION SCIENCE INTO PRACTICE: APPROACHES AND APPLICATIONS IN NURSING AND HEALTHCARE

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Abstract:
Nutrition is a fundamental component of healthcare, serving as a cornerstone for disease prevention, management, and health promotion. Integrating nutrition science into nursing and healthcare practices is essential to address the growing burden of chronic diseases, improve patient outcomes, and reduce healthcare costs. This paper explores the approaches and applications of nutrition science in clinical practice, highlighting the importance of evidence-based interventions, translational research, and precision nutrition. Key approaches include clinical nutrition, preventive strategies, personalized interventions using genetic and metabolic data, and holistic practices that combine diet with wellness strategies such as yoga and mental health support. Nurses play a central role in assessing nutritional status, implementing interventions, and monitoring outcomes, making them pivotal in bridging the gap between research and practice. Challenges in translating nutrition science into practice include limited professional training, socio-cultural and economic barriers, digital inequities, and lack of interprofessional collaboration. Innovative strategies to overcome these challenges include incorporating nutrition into nursing curricula, leveraging AI and digital health tools for personalized nutrition, implementing policy-level initiatives, and promoting sustainability-focused nutritional interventions. Addressing these challenges requires multidisciplinary collaboration, continuous education, and patient-centered care. By applying these strategies, healthcare professionals can enhance clinical outcomes, promote preventive care, and support holistic well-being. This paper underscores the need for sustained efforts to translate nutrition research into practical applications, ensuring equitable access to quality nutrition care and advancing public health objectives.

Keywords: Nutrition Science, Nursing, Precision Nutrition, Translational Research, Healthcare Outcomes

1. Introduction:

Nutrition plays a pivotal role in healthcare and nursing, serving as a cornerstone for disease prevention, management, and health promotion. Integrating nutrition science into healthcare practices is vital to address the growing burden of chronic diseases and improve patient outcomes. Bridging the gap between nutrition research and its practical applications is essential

for translating evidence into effective interventions (Huss *et al.,* 2021). This paper explores the approaches and applications of nutrition science in nursing and healthcare, emphasizing the significance of evidence-based nutritional interventions in clinical practice.

Role of Nutrition in Healthcare and Nursing

- Nutrition is fundamental in preventing and managing chronic diseases such as cardiovascular disease, diabetes, and obesity. Predominantly plant-based diets reduce the risk of these conditions and improve overall health outcomes (Huss *et al.,* 2021).
- Nurses play a critical role in nutritional care by assessing, intervening, and monitoring patients' nutritional status. They are often the first to identify problems and collaborate with dietitians and other professionals to implement interventions (Gomathi, 2024).
- Malnutrition remains a major issue in healthcare, contributing to longer hospital stays, readmissions, and increased costs. Nutrition-focused quality improvement programs mitigate these impacts through timely interventions (Meehan *et al.,* 2019).

Bridging the Gap Between Nutrition Science and Practice

- Translational nutrition research applies findings from basic and clinical studies to real-world settings, requiring multidisciplinary collaboration and communication among scientists, providers, and policymakers (Navarro-Ibarra *et al.,* 2024).
- Implementation science frameworks, such as the Knowledge to Action Cycle, guide the application of nutrition evidence into practice, ensuring feasibility and sustainability (Bell *et al.,* 2022).
- Precision nutrition, which tailors' dietary advice to individual characteristics, represents an emerging approach to personalize interventions and improve patient outcomes (Bell *et al.,* 2022).

Aim and Significance of the Paper

- The aim of this paper is to explore the approaches and applications of nutrition science in nursing and healthcare, emphasizing the translation of evidence-based nutritional research into clinical and public health practice. It seeks to highlight how nutrition-focused interventions including clinical, preventive, personalized and holistic strategies can improve patient outcomes, reduce healthcare costs, and support the prevention and management of chronic diseases.
- The significance of this paper lies in its potential to guide healthcare professionals, particularly nurses, in integrating nutrition into routine care. By examining multidisciplinary approaches, implementation frameworks and innovative strategies such as precision nutrition and digital health tools, the paper underscores the critical role of nutrition in enhancing the quality and effectiveness of healthcare delivery. Furthermore, it addresses the challenges and barriers to translating nutrition science into practice,

providing insights into solutions that can foster equitable, sustainable, and patient-centered nutrition care.

2. Nutrition Science in Healthcare Context

The evolution of nutrition science in healthcare and nursing reflects a shift towards precision nutrition, evidence-based guidelines, and recognition of diet as a cornerstone for disease prevention, management, and recovery. Precision nutrition emphasizes individualized dietary recommendations based on genetic, environmental, and lifestyle factors, aiming to improve outcomes and reduce costs. Evidence-based nutritional guidelines help translate research into practice, ensuring healthcare professionals deliver effective nutritional care. Increasingly, diet is acknowledged as a key determinant in preventing chronic diseases and enhancing recovery outcomes (Neufeld *et al.,* 2023).

Evolution of Nutrition Science in Healthcare

- Precision Nutrition: Tailors dietary recommendations to individual needs, considering genetic and environmental factors. This approach addresses the complexity of chronic diseases by moving beyond a "one size fits all" model toward personalized strategies (Stover & King, 2020).
- Integration into Healthcare: Nutrition science has progressed from focusing primarily on nutrient deficiencies to encompassing broader issues such as food systems and diet-related chronic diseases, supporting comprehensive health policies and interventions (Neufeld *et al.,* 2023).

Evidence-Based Nutritional Guidelines

- Development and Application: Guidelines are formulated through systematic reviews and critical appraisal of research, ensuring dietary recommendations are grounded in strong evidence. These serve as a bridge between research and clinical practice, guiding informed decision-making (Buttriss *et al.,* 2024).
- Challenges and Implementation: Despite their availability, issues such as misinformation and conflicting advice remain. Promoting transparency and reproducibility in guideline development is vital for credibility and adoption (Buttriss *et al.,* 2024).

Importance of Diet in Disease Prevention and Management

- Chronic Disease Prevention: Diet plays a crucial role in preventing cardiovascular disease, diabetes, and cancer. Predominantly plant-based diets reduce the risk of these conditions and support overall health (Grasso & Ray, 2024).
- Nutritional Care as Therapy: Nutrition is increasingly recognized as a first-line therapy for malnutrition and metabolic disorders, with proven benefits for clinical outcomes, quality of life, and healthcare costs (Hu & Barazzoni, 2023).

- Dietary Patterns and Health Outcomes: Dietary approaches such as the Mediterranean and DASH diets are well-studied and associated with reduced chronic disease risk and improved outcomes (Chielli *et al.,* 2022).

While progress in integrating nutrition into healthcare has been substantial, challenges persist in ensuring consistent adoption of evidence-based practices. The complexity of individual dietary needs and the prevalence of misinformation highlight the need for continued research and education. Moreover, the role of healthcare professionals, particularly nurses, remains central in disseminating nutritional knowledge and supporting patients in informed dietary choices, thereby advancing public health outcomes.

3. Approaches in Translating Nutrition Science into Practice

Translating nutrition science into practice requires a multifaceted approach that integrates clinical, preventive, personalized, and holistic strategies. Each contributes distinct methodologies and benefits, ultimately working toward improved health outcomes in both clinical and public health contexts.

Clinical Nutrition Approaches

- **Diet Therapy and Supplementation**: Clinical nutrition employs diet therapy and supplementation to address nutrient deficiencies and metabolic disorders. For example, vitamin D supplementation prevents rickets, while specialized diets manage conditions like phenylketonuria by restricting harmful metabolites (Hu & Barazzoni, 2023).
- **Medical Nutrition Therapy (MNT)**: MNT is vital for managing disease-related malnutrition and improving outcomes. It reduces hospital stays and healthcare costs, particularly in older adults and those with chronic illnesses (Hu & Barazzoni, 2023).

Preventive Approaches

- **Nutrition Education and Lifestyle Modification**: Preventive strategies emphasize awareness of healthy dietary practices to reduce non-communicable diseases (NCDs). Programs such as *Full Plate Living* have shown success in promoting weight loss and improving fiber intake (Boggild, 2024).
- **Community Interventions**: Community-level initiatives, including produce prescription programs, aim to improve diet quality and reduce chronic disease prevalence in underserved populations (Boggild, 2024).

Personalized Approaches

- **Tailored Diet Plans and Nutrigenomics**: Personalized nutrition leverages genetic, phenotypic, and metabolic data to provide individualized recommendations. By examining how genetic variations affect nutrient metabolism, nutrigenomics enables more precise dietary interventions (Elsayed & Saleh, 2024).

- **Precision Nutrition**: Incorporating multi-omics data such as genomics, metabolomics, and microbiomics precision nutrition integrates biological and lifestyle factors to design targeted strategies for optimizing health outcomes (Park, 2025).

Holistic Approaches

- **Integration with Wellness Practices**: Holistic nutrition combines dietary strategies with complementary practices such as yoga and mental health interventions, supporting both physical and psychological well-being (Boggild, 2024).
- **Food as Medicine**: Emphasizing the therapeutic role of diet, this concept recognizes plant-based dietary patterns as effective in improving metabolic health and reducing the risk of chronic diseases (Boggild, 2024).

Although these approaches hold promise, challenges remain in implementation. Personalized nutrition requires overcoming barriers related to accessibility and affordability of genetic testing and individualized interventions. Moreover, inclusive research is essential to ensure precision nutrition benefits are equitably available across populations (Malcomson & Mathers, 2023). Integrating these approaches into healthcare and public health policies will require interdisciplinary collaboration and ongoing innovation.

4. Approaches in Translating Nutrition Science into Practice

The application of nutrition science in healthcare requires multiple complementary approaches. These approaches not only address immediate clinical needs but also emphasize prevention, personalization, and holistic integration to achieve sustainable health outcomes. Table 1 summarizes the major approaches, their key strategies, and their implications in nursing and healthcare practice.

Table 1: Key Strategies and Applications of Approaches in Translating Nutrition Science into Practice

Approach	Key Strategies	Applications/Implications
Clinical Nutrition	• Diet therapy & supplementation • Medical Nutrition Therapy (MNT)	• Corrects nutrient deficiencies & metabolic disorders (e.g., rickets, Phenylketonuria) • Reduces hospital stays & healthcare costs, especially in chronic diseases (Hu & Barazzoni, 2023)
Preventive Approaches	• Nutrition education & lifestyle modification • Community-based interventions	• Prevents NCDs through awareness & healthy eating • Programs like "Full Plate Living" improve diet quality & weight outcomes • Produce prescription programs enhance access to healthy food (Boggild, 2024; Elsayed & Saleh, 2024)

Personalized Approaches	• Tailored diet plans using genetics & phenotype data (nutrigenomics, nutrigenetics) • Precision nutrition with multi-omics integration	• Individualized dietary recommendations for disease prevention • Optimizes health outcomes by considering genetics, microbiome & lifestyle (Ramos-López *et al.,* 2024; Malcomson & Mathers, 2023)
Holistic Approaches	• Integration of nutrition with wellness practices (e.g., yoga, mental health) • Food as medicine	• Promotes overall well-being by linking diet with mental & physical health • Plant-based & therapeutic diets reduce chronic disease risk (Park, 2025; Heber & Li, 2024)

These approaches collectively demonstrate how nutrition science can be systematically integrated into clinical settings, preventive health models, and personalized care strategies, while also promoting holistic well-being. This multi-dimensional framework provides healthcare professionals, particularly nurses, with effective tools for improving patient care and health outcomes.

5. Challenges in Translating Nutrition Science into Practice

Translating nutrition science into practice faces several barriers that restrict its application in nursing and healthcare. Limited nutrition training among healthcare professionals remains a major obstacle, reducing their capacity to provide effective nutrition counselling (Hicks-Roof, 2022). The digital divide, with unequal access to online resources and technology, further limits the reach of nutrition education (Grosso & Ray, 2024).

Socio-cultural and economic barriers such as cultural food preferences, financial constraints, and lifestyle habits make it difficult for patients to adopt recommended dietary changes (Grosso & Ray, 2024). Furthermore, a lack of interprofessional collaboration prevents integrated approaches among dietitians, nurses, and physicians, leading to fragmented care delivery (Kailas, 2022).

These challenges collectively highlight the need for improvements in education, accessibility, cultural sensitivity, and teamwork to strengthen the translation of nutrition science into practical healthcare settings.

Table 2 summarizes the major challenges that hinder the effective translation of nutrition science into clinical and community practice. It highlights how insufficient professional training, limited digital access, cultural and economic constraints, and weak interprofessional collaboration collectively create barriers. Addressing these challenges is essential for improving patient-centered nutritional care and ensuring the integration of evidence-based dietary practices into healthcare.

Table 2: Challenges in Translating Nutrition Science into Practice

Challenge Area	Specific Issues	Key References
Limited nutrition training	Insufficient inclusion of nutrition in medical/nursing curriculum; lack of continuing professional development	Hicks-Roof (2022)
Digital divide	Unequal access to digital tools and e-resources; barriers for rural and low-income populations	Grosso & Ray (2024)
Socio-cultural barriers	Strong cultural food traditions; reluctance to modify dietary habits	Grosso & Ray (2024)
Economic barriers	Cost of nutrient-rich foods; affordability issues affecting adherence	Grosso & Ray (2024)
Interprofessional gaps	Weak collaboration between nurses, dietitians, and physicians; fragmented care delivery	Kailas (2022)

6. Incorporating Nutrition into Nursing Curricula

- **Holistic Education**: Nutrition in nursing should integrate cultural, social, and environmental factors, preparing nurses to address links between diet, mental health, and community well-being (Grosso & Ray, 2024).
- **Sustainability Focus**: Resources like the NurSusTOOLKIT ("Nur" for nursing, "Sus" for sustainability) support embedding ecological health and sustainability into nursing training (Huss *et al.,* 2021).

AI and Digital Health Tools for Personalized Nutrition

- **AI Applications**: Machine learning and deep learning enables precise dietary recommendations by analyzing complex nutritional datasets (Armand *et al.,* 2024; Sharma & Gaur, 2024).
- **Precision Nutrition**: Using genetic, metabolic, and lifestyle data, precision nutrition tailors' interventions to optimize outcomes (Heber & Li, 2024; Park, 2025).
- **Technological Advancements**: Deep neural networks outperform traditional models in generating adaptive and dynamic dietary plans (Vegesna, 2024).

Policy-Level Initiatives for Integrating Nutrition

- **Healthcare Integration**: Systems should treat nutritious food as a fundamental right and embed healthy eating into care delivery (Laur *et al.,* 2023).
- **Nutrition Policies**: Policy reforms like the Affordable Care Act highlight how regulations can drive healthier consumption (Mathews *et al.,* 2025).

Sustainability and Nutrition

- **Link with Environmental Goals**: Sustainable food systems contribute to health equity and SDG 3 (Mathews *et al.,* 2025).
- **Educational Initiatives**: Training educators in sustainability and nutrition fosters lifelong healthy practices among youth (Mathews *et al.,* 2025).

Implementation Challenges and Considerations

Ethical and technological challenges, including privacy issues and limited population diversity in studies, must be addressed to fully realize the potential of AI-driven and precision nutrition approaches (Sharma & Gaur, 2024; Park, 2025).

Conclusion:

Translating nutrition science into practice is critical for improving health outcomes and advancing preventive and curative care in nursing and healthcare settings. Nutrition-focused interventions, including clinical, preventive, personalized, and holistic approaches, provide evidence-based strategies to address malnutrition, manage chronic diseases, and promote overall well-being. Nurses play a pivotal role in implementing these interventions through assessment, monitoring, and patient-centered care. Despite significant progress, challenges remain, including limited professional training, socio-cultural and economic barriers, digital inequities, and gaps in interprofessional collaboration. Innovative strategies such as integrating nutrition into nursing curricula, utilizing AI and digital health tools, and adopting policy-level initiatives can strengthen the translation of nutrition research into practice. Emphasizing sustainability and precision nutrition further enhances the effectiveness and accessibility of care. Ultimately, a multidisciplinary, collaborative, and evidence-driven approach is essential to bridge the gap between research and practical application, ensuring equitable access to high-quality nutrition care and improving healthcare outcomes across diverse populations.

References:

1. Armand, T. P. T., Nfor, K. A., Kim, J.-I., & Kim, H. C. (2024). Applications of Artificial Intelligence, Machine Learning, and Deep Learning in Nutrition: A Systematic Review. *Nutrients*. https://doi.org/10.3390/nu16071073
2. Bell, J. J., Fallows, E., Dael, P. V., McAuliffe, S., Kohlmeier, M., Hernández, A., Adamski, M., Ray, S., Crocombe, D., & Vale, M. L. do. (2022). *1 Putting research into practice: knowledge translation and implementation for action on nutrition*. https://doi.org/10.1136/bmjnph-2022-nnedprosummit.1
3. Boggild, A. K. (2024). Editorial: Food As Medicine. *Frontiers in Nutrition*. https://doi.org/10.3389/fnut.2024.1490232
4. Buttriss, J., Hickson, M., & Whelan, K. (2024a). Navigating the complexity of applying nutrition evidence to individualised care: Summary of an Academy of Nutrition Sciences Position Paper. *Nutrition & Dietetics*. https://doi.org/10.1111/1747-0080.12867
5. Chielli, D., Trapp, C., Stubbe, C., Robertson, T., & Merlo, G. (2022). *Nutrition and nursing practice*. In *Lifestyle nursing* (1st ed., pp. 24). CRC Press. https://doi.org/10.1201/9781003178330-3

6. Elsayed, H. H., & Saleh, R. (2024). Review of: Nutritional Genomics and Precision Nutrition. *Bulletin of the National Nutrition Institute of the Arab Republic of Egypt (Print)*. https://doi.org/10.21608/bnni.2024.396356
7. Gomathi, B. (2024). Nutritional Care: Nurses' Critical Role in Improving Patient Outcomes. *SBV Journal of Basic Clinical and Applied Health Science*. https://doi.org/10.4103/sbvj.sbvj_51_24
8. Grosso, G., & Ray, S. (2024). The future of nutrition education for health systems capacity building. *European Journal of Public Health*. https://doi.org/10.1093/eurpub/ckae144.033
9. Heber, D., & Li, Z. (2024). *Future Visions of Personalized and Precision Nutrition*. https://doi.org/10.1016/b978-0-443-15315-0.00018-3
10. Hicks-Roof, K. (2022). Nutrition education for providers is limited: it is time for increased education to boost interprofessional collaboration! *Education and Health*. https://doi.org/10.4103/efh.efh_72_20
11. Hu, C., & Barazzoni, R. (2023). Nutritional care is the first-line therapy for many conditions. *Precision Nutrition*. https://doi.org/10.1097/pn9.0000000000000059
12. Huss, N., Huynen, M., Álvarez-Nieto, C., Richardson, J., & López-Medina, I. M. (2021). *Embedding Sustainability in the Nursing Curriculum*. https://doi.org/10.1007/978-3-030-78181-1_11
13. Kailas, P. (2022). How might enhanced interprofessional collaboration between primary care physicians and registered dietitian nutritionists impact clinical outcomes related to obesity and associated illnesses? A commentary. *Public Health Nutrition*. https://doi.org/10.1017/s1368980022002518
14. Laur, C., Bradfield, J., & Ball, L. (2023). *The Future of Nutrition Care in Health Systems*. https://doi.org/10.1159/000534990
15. Malcomson, F. C., & Mathers, J. C. (2023). Translation of nutrigenomic research for personalised and precision nutrition for cancer prevention and for cancer survivors. *Redox Biology*. https://doi.org/10.1016/j.redox.2023.102710
16. Mathews, E., Ibáñez, E., Cifuentes, A., & Atanassova, M. (2025). Editorial: Nutrition and sustainable development goal 3: good health and wellbeing. *Frontiers in Nutrition*. https://doi.org/10.3389/fnut.2024.1542307
17. Meehan, A. J., Partridge, J., & Jonnalagadda, S. S. (2019). Clinical and Economic Value of Nutrition in Healthcare: A Nurse's Perspective. *Nutrition in Clinical Practice*. https://doi.org/10.1002/NCP.10405
18. Navarro-Ibarra, M. J., Sáenz-Pardo-Reyes, E., & Reyes-Pavón, D. (2024). Perspectivas de la investigación traslacional en nutrición. *Deleted Journal*. https://doi.org/10.32870/jbf.v4i7.57

19. Neufeld, L. M., Ho, E., Obeid, R., Tzoulis, C., Green, M., Huber, L. G., Stout, M., & Griffiths, J. C. (2023). Advancing nutrition science to meet evolving global health needs. *European Journal of Nutrition*. https://doi.org/10.1007/s00394-023-03276-9
20. Park, S. (2025). Editorial: Precision nutrition and nutrients: making the promise a reality. *Frontiers in Nutrition*. https://doi.org/10.3389/fnut.2025.1553149
21. Ramos-López, O., Assmann, T. S., Muñoz, E., Baquerizo-Sedano, L., Barrón-Cabrera, E., Bernal, C. A., Bressan, J., Cuevas-Sierra, A., Dávalos, A., Cruz-Mosso, U. D. la, Garza, A. L. de la, Luis, D. A. de, Garza, R. I. D. de la, Santos, K. dos, Fernández-Condori, R. C., Fernández-Quintela, A., Diaz, D. G., González-Becerra, K., Rosado, E. L., … Martínéz, J. A. (2024). Guidance and position of RINN22 regarding precision nutrition and nutriomics. *Lifestyle Genomics*. https://doi.org/10.1159/000542789
22. Sharma, S. K., & Gaur, S. (2024). *Optimizing Nutritional Outcomes: The Role of AI in Personalized Diet Planning*. https://doi.org/10.36676/jrps.v15.i2.15
23. Stover, P. J., & King, J. C. (2020). More Nutrition Precision, Better Decisions for the Health of Our Nation. *Journal of Nutrition*. https://doi.org/10.1093/JN/NXAA280
24. Vegesna, Dr. V. (2024). AI-Driven Personalized Nutrition: A system for Tailored Dietary Recommendations. *International Research Journal of Computer Science*. https://doi.org/10.26562/irjcs.2024.v1107.02

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PHYTOCHEMICAL PROFILING AND HEPATOPROTECTIVE ACTIVITY OF *CAESALPINIA BONDUC* LEAF EXTRACT AGAINST AMPICILLIN-INDUCED HEPATIC DAMAGE

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Abstract:
The present study was conducted to evaluate the extractive value, phytochemical composition, safety, and hepatoprotective efficacy of Caesalpinia bonduc ethanolic extract. The extractive value obtained using ethanol as solvent was 26.5%, yielding a dark brown residue, indicative of a rich presence of ethanol-soluble phytoconstituents. Preliminary phytochemical screening confirmed the presence of alkaloids, flavonoids, glycosides, carbohydrates, and proteins, while phenols and phytosterols were absent. Acute oral toxicity studies, carried out in accordance with OECD guideline 423, revealed no signs of toxicity or mortality up to 400 mg/kg, demonstrating a high margin of safety. Behavioral tests, including actophotometer, rotarod, and open field tests, showed that ampicillin-induced hepatotoxic rats exhibited marked impairments in locomotion and neuromuscular coordination, which were significantly reversed by *C. bonduc* treatment in a dose-dependent manner. Biochemical analyses demonstrated that ampicillin administration caused substantial elevations in liver enzyme markers (AST, ALT, ALP), indicative of hepatocellular damage. Co-treatment with *C. bonduc* extract, particularly at 400 mg/kg, significantly normalized these parameters, though less effectively than the standard hepatoprotective agent Liv.52. Histopathological evaluation further corroborated these findings, as *C. bonduc* treatment preserved liver architecture and reduced degenerative changes compared to the toxic group. These results collectively suggest that *C. bonduc* ethanolic extract possesses hepatoprotective potential, likely mediated through its antioxidant and anti-inflammatory phytoconstituents, with efficacy observed in both biochemical and histological outcomes.

Keywords: Caesalpinia Bonduc, Extractive Value, Phytochemical Screening, Hepatoprotective Activity, Ampicillin-Induced Toxicity.

1. Introduction:

Drug-induced liver injury (DILI) is one of the most significant causes of acute liver failure and represents a major clinical challenge worldwide. Among antibiotics, ampicillin, a widely prescribed β-lactam antibiotic, has been associated with hepatotoxic effects including oxidative stress, mitochondrial dysfunction, and hepatocellular necrosis (1). The mechanisms underlying ampicillin-induced hepatotoxicity are multifactorial, but oxidative stress, free radical generation,

and depletion of endogenous antioxidants are considered central events (2). Given the limitations and adverse effects of conventional hepatoprotective drugs, attention has shifted toward natural products and medicinal plants as safer alternatives for hepatoprotection.

Caesalpinia bonduc (L.) Roxb., a climbing shrub belonging to the family Fabaceae, is traditionally used in Ayurveda and folk medicine for the treatment of fever, inflammation, gastrointestinal disorders, and hepatic ailments (3, 4). Phytochemical investigations of *C. bonduc* have revealed the presence of flavonoids, alkaloids, saponins, tannins, and terpenoids, which are known to contribute to antioxidant and hepatoprotective activities (5). Flavonoids and phenolic compounds in particular are potent free radical scavengers that enhance antioxidant defense mechanisms such as superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH), thereby protecting hepatocytes from oxidative insult (6).

Several studies have demonstrated the hepatoprotective potential of medicinal plant extracts against antibiotic-induced liver injury. For instance, herbal extracts enriched with flavonoids and phenolic compounds have shown significant efficacy in lowering serum biomarkers of hepatic injury such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and bilirubin, while improving histopathological features of liver tissue (7, 8). However, limited data exist on the protective role of *C. bonduc* against antibiotic-triggered hepatic dysfunction.

Therefore, the present study aims to evaluate the phytochemical profile and hepatoprotective activity of Caesalpinia bonduc leaf extract in a rat model of ampicillin-induced hepatic damage. By integrating biochemical, antioxidant, and histopathological parameters, this study seeks to provide scientific validation for the traditional use of *C. bonduc* and establish its potential as a natural hepatoprotective agent.

2. Materials and Methods

2.1 Collection and Authentication of Plant Materials

The medicinal plant *Caesalpinia bonduc* leaves were collected from the hilly regions near Koria district, Chhattisgarh. The plant material was identified and authenticated by the Department of Botany, Guru Ghasidas Central University, Bilaspur, Chhattisgarh (Ref. No.: Bot/GGV/2025/137). The leaves were dried, powdered, and stored in airtight containers for further studies (9 – 11).

2.2 Preparation of Ethanolic extract of leaves of Caesalpinia bonduc

Leaves of *Caesalpinia bonduc* were carefully washed with tap water, shade-dried, and powdered. The powdered material was packed into a Soxhlet apparatus and extracted with ethanol (68–78 °C) for 24 hours. The obtained extract was concentrated and dried at room temperature, and the ethanolic leaf extract was used for further studies.

For large-scale extraction, about 300 g of powdered *Caesalpinia bonduc* leaves was extracted with 1 L of ethanol using a Soxhlet apparatus for 24 hours at 68–78 °C. The extract was then

concentrated to one-fourth of its original volume by distillation, allowing recovery and reuse of the solvent for subsequent extraction (4, 5, 12).

2.3 Phytochemical testing of Ethanolic extract of leaves of Caesalpinia bonduc

The ethanolic extract of *Caesalpinia bonduc* leaves was subjected to preliminary phytochemical screening to detect the presence of different classes of bioactive compounds. Alkaloids were confirmed by Mayer's test (cream-white precipitate), Dragendorff's test (orange-red color), and Wagner's test (brown precipitate). Carbohydrates were indicated by a violet ring in Molisch's test, while glycosides were detected by Keller–Killiani test, producing a reddish-brown ring at the interface. Flavonoids were confirmed by the Shinoda test with the formation of a magenta color, and phytosterols were detected by Salkowski's test, showing red or golden-yellow coloration. Phenolic compounds were identified by ferric chloride test (bluish-black coloration), and proteins were confirmed by the Biuret test with the appearance of a purplish-violet color. These results indicated that the extract contains diverse secondary metabolites responsible for its pharmacological activities (10, 11).

2.4 Animal Selection, Housing, and Preparation

Healthy Wistar albino rats (150–250 g) were used for the study. The animals were procured from a CPCSEA-registered supplier (Reg. No. 1275/PO/Re/S/09/CPCSEA) and housed in the animal facility of the School of Pharmacy, Chouksey Group of Colleges, Bilaspur, under standard laboratory conditions (22–25 °C, 12 h light/dark cycle). They were provided with a standard pellet diet and water ad libitum. The animals were acclimatized for 7 days prior to the commencement of the study and were randomly selected, marked for individual identification, and maintained in cages for at least 5 days before dosing to ensure adaptation to laboratory conditions. Care was taken to ensure the use of animals of appropriate size and age throughout the experimental protocol. The study protocol was reviewed and approved by the Institutional Animal Ethics Committee (IAEC) of the School of Pharmacy, Bilaspur (13 – 15).

Table 1: Experimental Grouping of animals for present study

S. No.	Animal (either sex)	Weight	Treatment	Duration	Animal/Group
1	Wistar albino Rats	150-250g	Normal Saline (0.9%)	28 days	6
2	Wistar albino Rats	150-250g	Ampicillin 200mg/kg	1-10 days	6
3	Wistar albino Rats	150-250g	Ampicillin + CBE	11-28 days	6
4	Wistar albino Rats	150-250g	Ampicillin + CBE	11-28 days	6
5	Wistar albino Rats	150-250g	Ampicillin + Liv52 Polyherbal Syrup	11-28 days	6
	Total				30

2.5 Acute Oral Toxicity Study

The study was conducted in accordance with OECD guideline No. 423. Animals were divided into five groups, with six animals in each group. Group I served as the normal control, while

Groups II, III, and IV received ampicillin (200 mg/kg body weight, intraperitoneally) for 11 consecutive days. Group II received only ampicillin, whereas Groups III and IV were treated with the plant extracts at two different dose levels. Drug treatment with extracts began five days prior to ampicillin administration and continued until day 15. After 48 hours of the final ampicillin dose, the animals were sacrificed under ether anesthesia. Blood samples were collected by the retro-orbital plexus method, and serum was separated for biochemical analysis. The livers were immediately excised; small portions were fixed in 10% formalin and preserved for histopathological examination (16 – 18).

Table 2: Experimental Grouping of animals for Acute Oral Toxicity Study

S. No.	Name	Dosing (mg/Kg)	Route
1.	Normal Saline (0.9%)	2ml/kg	oral
2.	Ampicillin (Inducing Agent)	200mg/kg	Intraperitoneal
3.	Liv52 polyherbal (standard Drug)	1ml/kg	oral
4.	Caesalpina Bonduc (Test drug)	200mg/kg	oral
5.	Caesalpinia bonduc (Test drug)	400mg/kg	oral

2.6 Study of Behavioral Parameters

Behavioral parameters were assessed to evaluate the neuropharmacological effects of the treatment in experimental animals. Standard behavioral models, including Actophotometer for locomotor activity, RotaRod for motor coordination and muscle relaxation, and Open Field Test for exploratory behavior and anxiety-related responses, were employed. These models are widely accepted in neurobehavioral research to provide reliable insights into locomotion, motor performance, and emotional states of animals under different treatment conditions.

2.6.1 Actophotometer Test

The Actophotometer is a standard behavioral apparatus used to measure locomotor activity in rodents, which is often influenced by CNS-acting drugs. It consists of a chamber (30 × 30 × 30 cm) equipped with photoelectric cells and light beams arranged horizontally across the walls, with infrared filters to minimize external light effects. As the animal moves within the chamber, interruptions of the light beams are detected by photocells, and the activity counts are digitally recorded, providing an index of locomotor activity. Each rat was individually placed in the apparatus for 10 minutes after weighing and numbering, and their basal activity scores were recorded. Animals were first acclimatized to the apparatus for 10–30 minutes to reduce stress, after which locomotor activity was measured. The data were analyzed based on the total counts, representing horizontal and vertical movements, thereby reflecting overall motor activity and behavioral response to treatment (19 – 20).

2.6.2 Rota-Rod Test

The Rota-Rod test is a widely employed behavioral assay used to evaluate motor coordination, balance, muscle strength, and fatigue in rodents. The principle is based on the ability of animals to remain on a rotating rod for a specified period, where a shorter latency to fall reflects motor impairment, muscle weakness, or central nervous system dysfunction, while a prolonged retention time indicates improved neuromuscular function or therapeutic efficacy of test compounds. Rodents are initially trained to stay on the rotating rod (usually at constant or accelerating speeds), followed by testing after treatment, during which the latency to fall is recorded. This method is particularly useful in assessing motor deficits associated with neurodegeneration, drug-induced toxicity, and hepatotoxic conditions where impaired energy metabolism and muscular weakness are secondary consequences of liver dysfunction. Thus, the Rota-Rod serves as a sensitive indicator of drug effects on motor performance and coordination in preclinical studies (21 – 23).

2.6.3 Open Field Test (OFT)

The Open Field Test (OFT) is a widely used behavioural paradigm for assessing locomotor activity, anxiety-like behaviour, and exploratory tendencies in rodents. The test involves placing animals, usually mice or rats, in a large, enclosed arena (square or circular), where their movements are recorded using sensors or video tracking systems. Key parameters include the total distance travelled, time spent in the central versus peripheral zones, and frequency of behaviours such as grooming or rearing. Greater activity in the center is interpreted as reduced anxiety, while peripheral preference reflects thigmotaxis, a sign of heightened anxiety. The OFT not only provides insight into exploratory behaviour and emotional responsiveness but has also been applied to study drug-induced alterations, such as ampicillin-induced hepatotoxicity, which may affect locomotor activity and overall behavioural responses. Data are typically analyzed by comparing locomotor indices and zone preference, with higher center activity indicating anxiolytic-like effects and decreased activity suggesting anxiety or motor impairment (24 – 25).

2.7 Biochemical Parameters

The administration of ampicillin (200 mg/kg, i.p. for 11 days) resulted in a significant elevation of serum biomarkers of hepatotoxicity, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP), compared to the normal control group, confirming liver injury. Pretreatment with *Caesalpinia bonduc* ethanolic extract (CB, 200 and 400 mg/kg, orally) markedly attenuated these biochemical alterations, indicating restoration of hepatic integrity. The hepatoprotective potential of CB was found to be dose-dependent, with CB at 400 mg/kg showing a significantly greater protective effect than both CB at 200 mg/kg and the standard reference drug LIV-52 (1 mL/kg, orally). These findings suggest that the hepatoprotective activity of *C. bonduc* may be attributed to its phytoconstituents, such as

flavonoids, alkaloids, and saponins, which possess strong antioxidant and free radical scavenging properties that stabilize cellular membranes and prevent enzyme leakage (26 – 28).

2.8 Histopathological Analysis

The liver was carefully excised without causing mechanical injury after opening the abdominal cavity. The collected tissue was rinsed with ice-cold normal saline to remove blood and debris, and subsequently fixed in 10% neutral buffered formalin. Paraffin-embedded sections of 5 µm thickness were prepared using a microtome and processed through graded alcohol and xylene series. The sections were stained with hematoxylin and eosin (H&E) and examined under a light microscope for histopathological alterations, including hepatocellular degeneration, necrosis, and other morphological changes (29 – 31).

3. Result and Discussions:

3.1 Extractive Value

The extractive value of *Caesalpinia bonduc* seeds was determined using ethanol as the solvent. The ethanolic extract yielded a dark brown residue with an extractive value of 26.5% (Table 3.1).

Table 3: Extractive Value

S. No.	Drug	Solvent	Colour	% Extractive
1	Caesalpinia bonduc	Ethanol	Dark brown	26.5%

Extractive values serve as important parameters to assess the quality, purity, and chemical constituents of crude drugs. The percentage yield of 26.5% for the ethanolic extract of *Caesalpinia bonduc* indicates a substantial presence of ethanol-soluble phytoconstituents such as alkaloids, flavonoids, glycosides, tannins, and phenolic compounds.

The dark brown coloration of the extract suggests the presence of phenolic compounds and tannins, which are commonly soluble in ethanol. A higher extractive value generally indicates the richness of phytoconstituents, which can be correlated to the pharmacological potential of the plant.

Comparable studies on *Caesalpinia bonduc* have reported significant extractive yields with polar solvents like ethanol and methanol, attributed to their efficiency in extracting bioactive secondary metabolites. The obtained extractive value falls within the expected range, supporting the suitability of ethanol for further phytochemical and pharmacological evaluations.

3.2 Phytochemical Screening

The phytochemical screening of *Caesalpinia bonduc* ethanolic extract revealed the presence of major secondary metabolites including alkaloids (Mayer's and Dragendorff's tests positive), glycosides (Keller-Killiani test positive), flavonoids (Shinoda test positive), carbohydrates (Molisch's test positive), and proteins (Biuret test positive). However, phenols (Ferric chloride test) and phytosterols (Salkowski's test) were absent in the extract.

Table 4: Phytochemical Screening

S. No.	Test	Inferences
1.	ALKALOIDS	+
	Mayers Test	+
	Wagner's Test	-
	Dragendroffs Tes	+
2.	GLYCOSIDE	+
	Killer killani Test	+
3.	FLAVONOIDES	+
	Shinoda Test	+
4.	CARBOHYDRATES	+
	Molisch Test	+
5.	PROTIENS	+
	Biuret Test	+
6.	PHENOLS	-
	Ferric chloride Test	-
7.	PHYTOSTEROLS	-
	Salkowski's Test	-

(+) Indicate presence while (-) stand for absence.

The ethanolic extract of *Caesalpinia bonduc* was found to be rich in diverse phytoconstituents. The presence of alkaloids suggests potential pharmacological properties, as these compounds are often associated with analgesic, antimicrobial, and anti-inflammatory effects. The detection of glycosides indicates possible cardioprotective and antioxidant activity. Flavonoids, which were strongly positive, are well-known for their neuroprotective, antioxidant, and anti-inflammatory roles, making them important bioactive constituents. The presence of carbohydrates and proteins reflects the nutritive value of the extract, which may also contribute to its biological activities. On the other hand, the absence of phenols and phytosterols suggests that ethanol may not be an efficient solvent for extracting these compounds from C. bonduc.

Overall, the phytochemical profile of the ethanolic extract highlights the therapeutic potential of C. bonduc, aligning with its traditional use in various ailments. Particularly, the abundance of flavonoids and alkaloids provides a scientific basis for its antioxidant and anti-inflammatory applications, which are crucial in managing chronic and degenerative diseases.

3.3 Acute Oral Toxicity Study

Administration of *Caesalpinia bonduc* ethanolic extract at doses of 100, 200, and 400 mg/kg in rats produced no mortality or clinical signs of toxicity during the initial 24 hours and throughout the 14-day observation period, as per OECD guideline 423. No significant changes in body weight, behavioral patterns, or macroscopic abnormalities in vital organs were observed at the

end of the study.

The findings indicate that the ethanolic extract of *C. bonduc* is safe up to 400 mg/kg by oral route, suggesting a high margin of safety. The absence of toxic symptoms such as tremors, convulsions, diarrhea, or lethargy confirms the non-toxic nature of the extract. Hence, doses of 100 and 200 mg/kg were selected for further pharmacological evaluation in experimental models. These results are consistent with previous reports highlighting the safety of *C. bonduc* extracts in rodents.

3.4 Assessment of Behavioral Outcomes

Various behavioral tests related to particular motor functions were also conducted because AD is a motor condition characterized by rigidity, resting tremor, postural instabilities, and slowness of movement. Weekly behavioral tests, as detailed below, were administered to the animals in various groups.

3.3.1 Actophotometer Test

Table 3.3.1 shows the effect of *Caesalpinia bonduc* leaf extract on locomotor activity in mice using an actophotometer. The normal group exhibited significantly higher locomotor activity (348 ± 7.5), while ampicillin treatment drastically reduced the activity (210 ± 6.9; ***$p < 0.001$ vs. normal). Co-treatment with *Caesalpinia bonduc* extract at 200 and 400 mg/kg significantly restored locomotor activity (260 ± 6.4 and 295 ± 5.8, respectively; ***$p < 0.001$ vs. toxic), in a dose-dependent manner. The standard (Liv52 syrup) group also showed significant recovery (312 ± 6.0; ***$p < 0.001$ vs. toxic).

Table 5: Effect of *Caesalpinia bonduc* leaf Extract on locometer activity score in Actophometer

Animal groups (n=6)	Group/ Treatment	Mean ± SEM
1.	Normal	348 ± 7.5
2.	Ampicillin	210 ± 6.9***a
3.	Ampicillin + Caesalpinia Bonduc (200mg/kg i.p + 200mg/kg p.o)	260 ± 6.4***b
4.	Ampicillin + Caesalpinia Bonduc (200mg/kg i.p + 400mg/kg p.o)	295 ± 5.8***b
5.	Ampicillin + Liv52 syrup (standard)	312 ± 6.0***b

Superscripts: a – comparison with normal control; b – comparison with toxic control. Statistical analysis was performed using one-way ANOVA followed by Tukey–Kramer's post hoc test. ns = $p > 0.05$; $p < 0.05$ (*), $p < 0.01$ (**), $p < 0.001$ (***). Comparisons: (a) Group I (Normal) vs. Group II (Toxic); (b) Group II (Toxic) vs. Groups III, IV, V.

Ampicillin-induced toxicity markedly impaired locomotor performance, suggesting central nervous system depression and reduced neuromuscular coordination. Co-administration of

Caesalpinia bonduc extract significantly improved locomotor activity, with the higher dose (400 mg/kg) showing near-comparable efficacy to the standard Liv52. This suggests that the neuroprotective and adaptogenic phytoconstituents of *C. bonduc* (such as flavonoids and diterpenoids) may counteract ampicillin-induced toxicity and enhance motor activity.

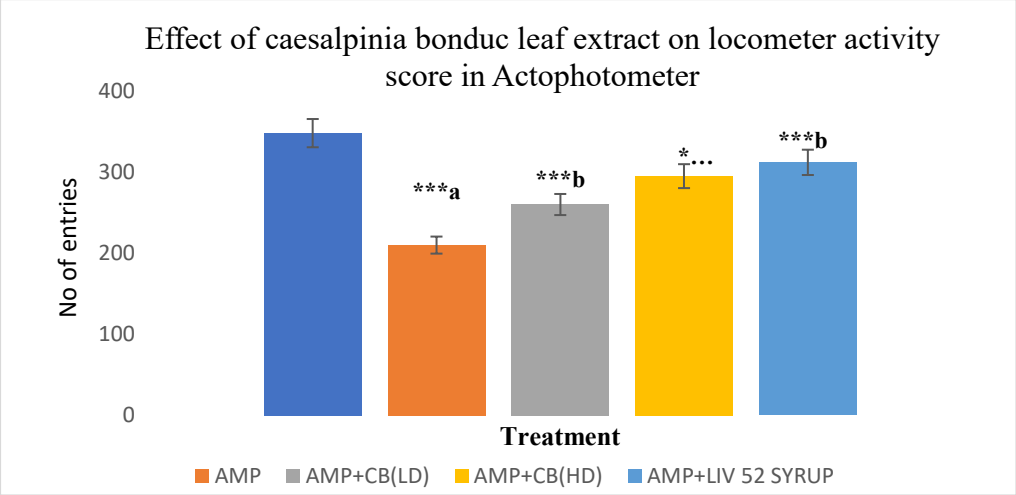


Fig. 1: Effect of *Caesalpinia bonduc* leaf Extract on locometer activity score in Actophometer

3.3.2 Rota-Rod Test

Ampicillin administration significantly reduced the retention time of rats on the Rotarod compared to the normal group, indicating impaired motor coordination and muscle weakness due to hepatotoxicity ($p < 0.001$).

Table 6: Effect of *Caesalpinia bonduc* treatment on Rotarod Activity in Ampicillin Treated Rats

Animal group (n=6)	Group/ Treatment	Mean ± SEM
1.	Normal	184.5 ± 1.93
2.	Ampicillin	86.87±1.6***a
3.	Ampicillin + Caesalpinia Bonduc (200mg/kg i.p + 200mg/kg p.o)	159.9±6.4***b
4.	Ampicillin + Caesalpinia Bonduc (200mg/kg i.p + 400mg/kg p.o)	139.1±2.6***b
5.	Ampicillin+Liv52 syrup (standard)	147.26±1.3***b

Values are expressed as Mean ± SEM (n = 6). a = statistically compared with the normal group. b = statistically compared with the toxic control group. Analysis was performed using one-way ANOVA followed by Tukey–Kramer's post hoc test. ns > 0.05; *p < 0.05, **p < 0.01, ***p < 0.001. Comparisons: (a) Group I (Normal) vs. Group II (Toxic); (b) Group II (Toxic) vs. Groups III, IV, and V.

Treatment with *Caesalpinia bonduc* leaf extract at both 200 mg/kg and 400 mg/kg doses

significantly improved Rotarod performance compared to the toxic control, suggesting a protective effect against Ampicillin-induced motor deficits. Among the treated groups, the higher dose of the extract (400 mg/kg) demonstrated a greater improvement, though slightly lower than the standard Liv52 group. These findings suggest that *C. bonduc* possesses dose-dependent hepatoprotective and neuromuscular restorative effects, consistent with its role in improving coordination and reducing fatigue associated with hepatic injury.

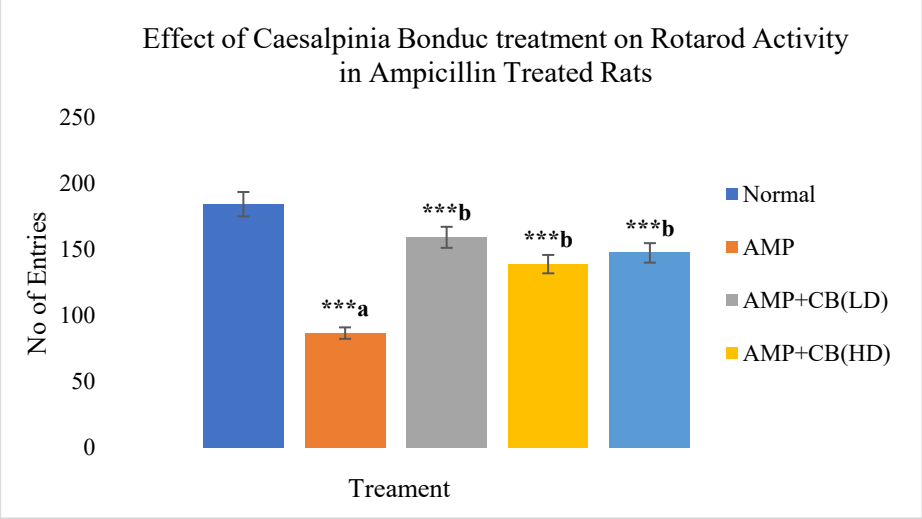


Fig. 2: Effect of *Caesalpinia bonduc* treatment on Rotarod Activity in Ampicillin Treated Rats

3.3.3 Open Field Test (OFT)

Table 7: Effect of *Caesalpinia bonduc* treatment on Open field Test Activity In Ampicillin Treated Rats

Animal group (n=6)	Group/ Treatment	Number of Crossings Mean ± SEM	Number of Rearing Mean ± SEM
1.	Normal	82 ± 3.5	25 ±1.4
2.	Ampicillin	48 ± 2.8***a	14±1.2***a
3.	Ampicillin + Caesalpinia Bonduc (200mg/kg i.p+ 200mg/kg p.o)	60 ± 3.0***b	17 ±1.3***b
4.	Ampicillin + Caesalpinia Bonduc (200mg/kg i.p+ 400mg/kg p.o)	72 ± 2.9***b	21 ±1.1***b
5.	Ampicillin+Liv52Syrup(standard)	76 ± 3.2***b	23 ±1.2***b

Ampicillin administration (Group II) significantly reduced the number of crossings (48 ± 2.8) and rearing (14 ± 1.2) compared to the normal control group (82 ± 3.5 and 25 ± 1.4, respectively; ***$p < 0.001$), indicating impaired locomotor and exploratory behavior due to hepatotoxicity. Pretreatment with *Caesalpinia bonduc* extract at both 200 mg/kg and 400 mg/kg (Groups III and IV) significantly improved the number of crossings (60 ± 3.0 and 72 ± 2.9) and rearing (17 ± 1.3 and 21 ± 1.1) compared to the toxic group, demonstrating a dose-dependent protective effect.

The higher dose (400 mg/kg) showed results comparable to the standard Liv52 syrup group (crossings: 76 ± 3.2; rearing: 23 ± 1.2), suggesting that *Caesalpinia bonduc* effectively restored locomotor and exploratory activities in ampicillin-induced hepatotoxic rats.

Values are expressed as Mean ± SEM (n = 6). a = comparison with normal control (Group I) b = comparison with toxic control (Group II) Statistical analysis was performed using one-way ANOVA followed by Tukey-Kramer's post hoc test. ns > 0.05 (non-significant), *p < 0.05, **p < 0.01, ***p < 0.001. Comparisons: (a) Group I (Normal) vs Group II (Toxic); (b) Group II (Toxic) vs Groups III, IV, V.

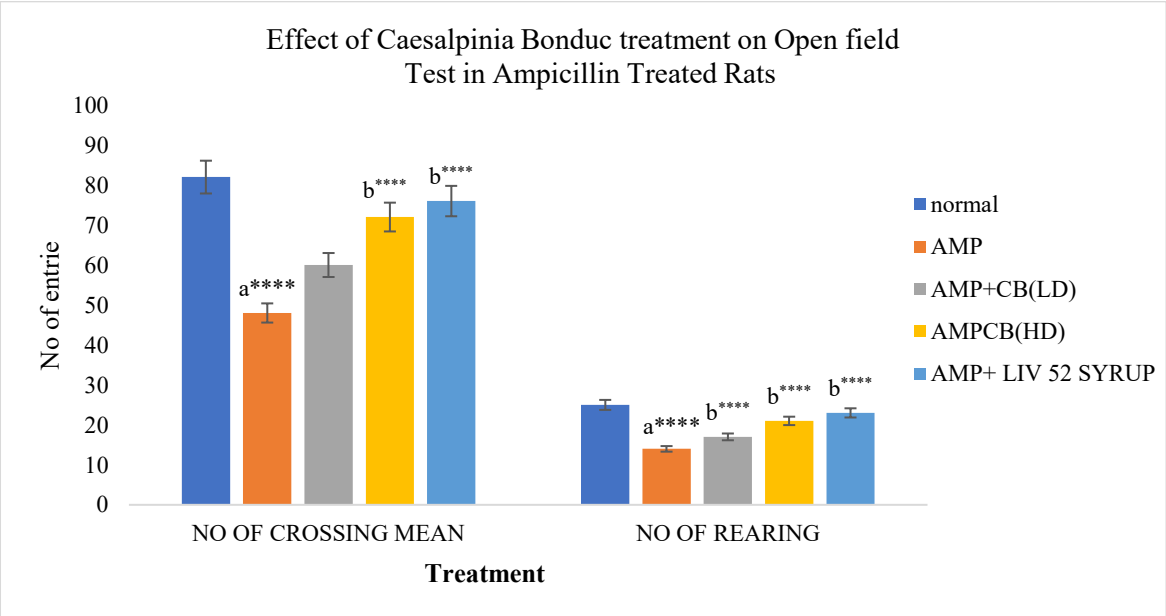


Fig. 3: Effect of *Caesalpinia bonduc* treatment on Open field Test in AmpicillinTreated

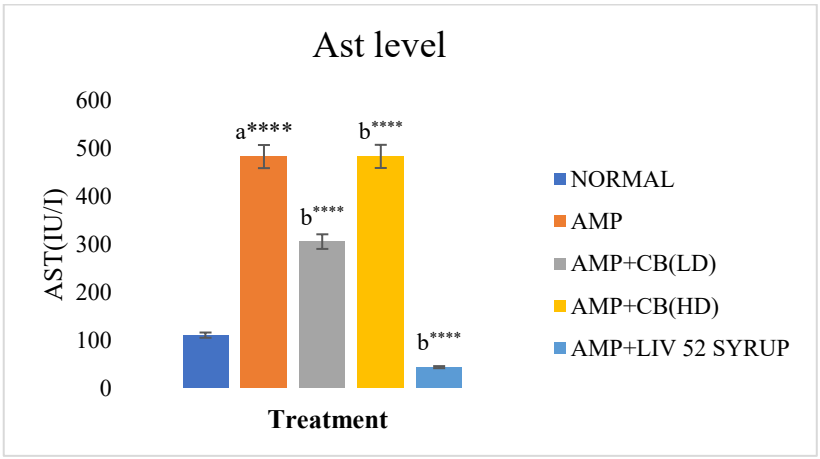
3.4 Evaluation of Biochemical Parameters

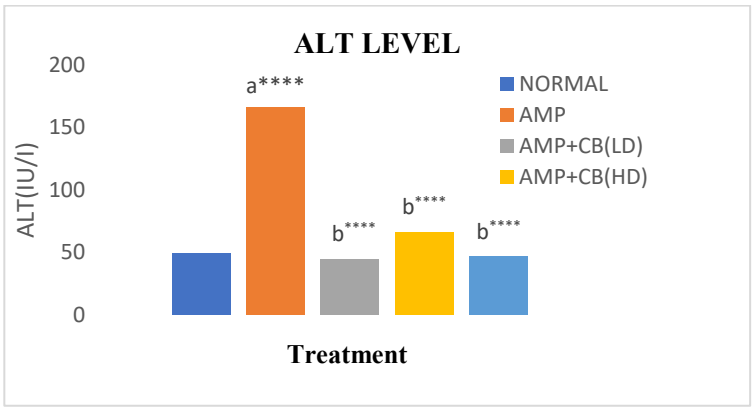
Ampicillin (200 mg/kg) administration produced a marked elevation in serum AST, ALT, and ALP levels compared to the normal group ($p < 0.0001$), confirming hepatotoxicity. Pretreatment with *Caesalpinia bonduc* ethanolic extract (400 mg/kg) significantly reduced these elevated liver enzyme levels ($p < 0.0001$), indicating hepatoprotective activity. The higher dose of CB (400 mg/kg) showed better restoration of AST, ALT, and ALP than the lower dose, though the effect was still less pronounced compared to the standard drug Liv.52, which exhibited the strongest hepatoprotective effect by normalizing biochemical parameters. These findings suggest that CB exerts dose-dependent hepatoprotection against AMP-induced hepatic injury, likely due to its antioxidant and hepatorestorative phytoconstituents.

Table 8: Effect of CB treatment on different biological parameters in AMP induced Hepatotoxicity in rats

Group	Treatment	AST (IU/L)	ALT (IU/L)	ALP (IU/L)
I	Normal	110.12 ± 0.021	49.35 ± 0.03	9.54 ± 0.04
II	AMP (200mg/kg)	483.82 ± 4.065 a****	166.14 ± 0.02 a****	4.24 ± 0.03 a**
III	AMP (200mg/kg) + CB (400mg/kg)	305.64 ± 0.03 b****	44.69 ± 0.018 b****	6.65 ±0.01 b****
IV	AMP (400mg/kg) +CB (400mg/kg)	483.78± 0.11b****	98.99±0.82 b****	8.01 ± 0.8 b**
V	AMP (200mg/kg) + Liv 52syrup(1ml/kg)	43.24 ± 0.007 a****	6.42 ±0.02 b****	3.94± 0.01 b****

Results were expressed as Mean ± S.E.M., n = 6. Significance levels: *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001, ns (not significant) when p > 0.05. Comparisons: a: statistically compared with Normal (Group I vs. Group II – Toxic) b: statistically compared with AMP (Group II vs. Group III) c: statistically compared with AMP + LIV 52 (Group II vs. Group IV) d: statistically compared with AMP + CB (Group II vs. Group V).





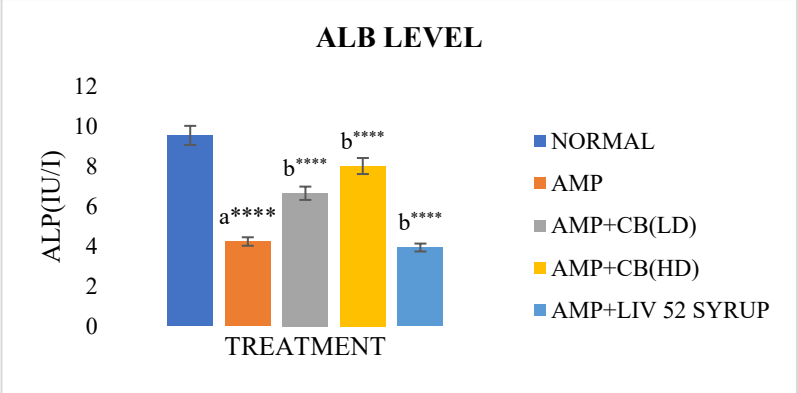


Fig. 4: Effect of CB treatment on different biological parameters in AMP induced Hepatotoxicity in rats

3.5 Histopathological Analysis

Histopathological analysis was performed on liver tissues stained with Hematoxylin and Eosin (H&E, 400X). The sections revealed the structural differences among groups, including the normal control, ampicillin-treated (toxic) group, and treatment groups administered with *C. bonduc* at doses of 200 mg and 400 mg along with ampicillin. The normal control group displayed well-preserved hepatic architecture with clear cellular morphology, while the ampicillin-treated group showed marked hepatic damage characterized by degeneration and disruption of liver architecture. In contrast, the groups treated with *C. bonduc* in combination with ampicillin exhibited significant improvement in hepatic histology, with the 400 mg treatment group showing nearly restored hepatic structure compared to the 200 mg group, indicating a dose-dependent hepatoprotective effect.

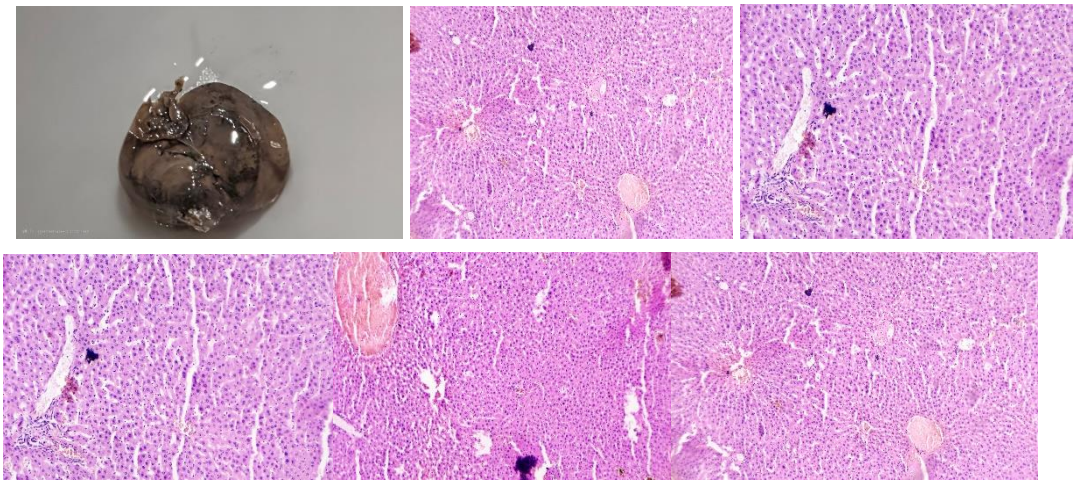


Fig. 5: Sections stained with Hematoxylin and Eosin (H&E 400X) displaying the Liver Tissue of Rats treated with Normal, Ampicillin Groups + *C. bonduc* 200mg, Ampicillin + *C. bonduc* 400mg

Conclusions:

The findings of this study highlight the therapeutic potential of Caesalpinia bonduc ethanolic

extract against ampicillin-induced hepatotoxicity. The extract demonstrated a high extractive value and a diverse phytochemical profile rich in alkaloids, flavonoids, and glycosides, which may underlie its pharmacological properties. Acute oral toxicity assessment confirmed its safety up to 400 mg/kg, supporting its use in experimental models. Behavioral studies revealed improvements in locomotor, exploratory, and motor coordination activities, while biochemical analysis demonstrated significant restoration of liver enzyme levels. Histopathological evaluation further validated its hepatoprotective effect, showing preserved hepatic architecture, particularly at higher doses. Although the efficacy of *C. bonduc* was slightly lower than that of the standard drug Liv.52, its dose-dependent protective effects indicate promising therapeutic potential. Overall, these results provide scientific evidence supporting the traditional use of *C. bonduc* in liver disorders and encourage further investigations into its bioactive constituents and mechanisms of action.

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References:

1. Kumar, S., Singh, R., & Mehta, A. (2020). Antibiotic-induced hepatotoxicity: Mechanisms and protective strategies. World Journal of Hepatology, 12(6), 322–334. https://doi.org/10.4254/wjh.v12.i6.322
2. Younis, N. S., Mohamed, M. E., & El-Kordy, E. A. (2018). Antibiotic-induced oxidative stress and hepatotoxicity: Role of antioxidants. Pharmaceutical Biology, 56(1), 651–661. https://doi.org/10.1080/13880209.2018.1491961
3. Kirtikar, K. R., & Basu, B. D. (1999). Indian medicinal plants (2nd ed.). International Book Distributors.
4. Choudhary, N., Goyal, S., & Bhatia, A. (2019). Medicinal and pharmacological potential of Caesalpinia bonduc (L.) Roxb.: An overview. Journal of Ethnopharmacology, 241, 111977. https://doi.org/10.1016/j.jep.2019.111977
5. Das, S., Ahmed, M., & Hossain, M. (2021). Phytochemical and pharmacological investigations of Caesalpinia bonduc seeds and leaves: A comprehensive review. Pharmacognosy Reviews, 15(29), 45–52.
6. Sharma, P., Garg, V., & Singh, M. (2020). Natural antioxidants and their role in hepatoprotection: An updated review. Journal of Traditional and Complementary Medicine, 10(1), 35–47. https://doi.org/10.1016/j.jtcme.2019.05.004

7. Roy, S., Banerjee, S., & Bhattacharya, S. (2017). Herbal hepatoprotective agents: A review on recent trends. World Journal of Pharmaceutical Research, 6(11), 85–97.
8. Singh, A., & Patel, V. K. (2021). Protective effects of flavonoid-rich plant extracts on antibiotic-induced liver injury in rats. Biomedicine & Pharmacotherapy, 138, 111441. https://doi.org/10.1016/j.biopha.2021.111441
9. Harborne, J. B. (1998). Phytochemical methods: A guide to modern techniques of plant analysis (3rd ed.). Springer. https://doi.org/10.1007/978-94-009-5570-7
10. Khandelwal, K. R. (2008). Practical Pharmacognosy: Techniques and Experiments (19th ed.). Nirali Prakashan.
11. Kokate, C. K., Purohit, A. P., & Gokhale, S. B. (2010). Pharmacognosy (46th ed.). Nirali Prakashan.
12. Mukherjee, P. K. (2019). Quality control and evaluation of herbal drugs: Evaluating natural products and traditional medicine (2nd ed.). Elsevier. https://doi.org/10.1016/C2017-0-00920-8.
13. CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals). (2003). Guidelines for laboratory animal facility. Indian Journal of Pharmacology, 35(4), 257–274.
14. OECD (Organisation for Economic Co-operation and Development). (2008). OECD guidelines for the testing of chemicals, Section 425: Acute oral toxicity – Up-and-down procedure. OECD Publishing. https://doi.org/10.1787/9789264071049-en
15. National Research Council (NRC). (2011). Guide for the care and use of laboratory animals (8th ed.). Washington, DC: The National Academies Press. https://doi.org/10.17226/12910
16. OECD. (2002). Test No. 423: Acute oral toxicity – Acute toxic class method (OECD Guidelines for the Testing of Chemicals, Section 4). OECD Publishing. https://doi.org/10.1787/9789264071001-en
17. International Journal of Research in Ayurveda and Pharmacy. (2023). OECD guidelines for acute oral toxicity studies: An overview. International Journal of Research in Ayurveda and Pharmacy, 14(4), 137–140.
18. Al-Afifi, N. A. (2018). Acute and sub-acute oral toxicity of Dracaena cinnabari resin in rats as per OECD guideline 423. BMC Complementary and Alternative Medicine, 18, Article 2110.
19. Kulkarni, S. K. (2015). Handbook of Experimental Pharmacology (4th ed.). Vallabh Prakashan.
20. Achliya, G. S., Wadodkar, S. G., & Dorle, A. K. (2004). Evaluation of CNS activity of Bramhi Ghrita. Indian Journal of Pharmacology, 36(1), 34–42.

21. Jones, B. J., & Roberts, D. J. (1968). The quantitative measurement of motor incoordination in naive mice using an accelerating rotarod. Journal of Pharmacy and Pharmacology, 20(4), 302–304. https://doi.org/10.1111/j.2042-7158.1968.tb09743.x
22. Carter, R. J., Morton, J., & Dunnett, S. B. (2001). Motor coordination and balance in rodents. Current Protocols in Neuroscience, 15(1), 8.12.1–8.12.14. https://doi.org/10.1002/0471142301.ns0812s15
23. Shiotsuki, H., Yoshimi, K., Shimo, Y., Funayama, M., Takamatsu, Y., Ikeda, K., ... & Hattori, N. (2010). A rotarod test for evaluation of motor skill learning. Journal of Neuroscience Methods, 189(2), 180–185. https://doi.org/10.1016/j.jneumeth.2010.03.026
24. Seibenhener, M. L., & Wooten, M. C. (2015). Use of the open field maze to measure locomotor and anxiety-like behavior in mice. Journal of Visualized Experiments, (96), e52434. https://doi.org/10.3791/52434
25. Kraeuter, A. K., Guest, P. C., & Sarnyai, Z. (2019). The open field test for measuring locomotor activity and anxiety-like behavior. In Pre-clinical models (pp. 99–103). Springer. https://doi.org/10.1007/978-1-4939-8916-4_7
26. Sumalatha, S., Padma, D., & Pai, K. S. R. (2016). Hepatoprotective activity of aqueous extract of Caesalpinia bonduc against CCl_4-induced chronic hepatotoxicity. International Journal of Pharmacy and Pharmaceutical Sciences, 8(4), 207–211.
27. Bhatt, M., & Malik, J. K. (2022). Hepatoprotective potential of Caesalpinia bonducella: Molecular insight. Middle East Research Journal of Pharmaceutical Sciences, 2(2), 28–34.
28. Naz, F., Versiani, M. A., Laraib, Q., Shafique, M., & Avesi, L. (2021). In vivo hepatoprotective and in vitro antimicrobial potential of Caesalpinia bonduc (Linn): Pharmacological correlation with identified phytochemicals. Pakistan Journal of Pharmaceutical Sciences, March 2021.
29. Bancroft, J. D., & Gamble, M. (2008). Theory and practice of histological techniques (6th ed.). Churchill Livingstone Elsevier.
30. Kiernan, J. A. (2015). Histological and histochemical methods: Theory and practice (5th ed.). Scion Publishing Ltd.
31. Suvarna, S. K., Layton, C., & Bancroft, J. D. (2018). Bancroft's theory and practice of histological techniques (8th ed.). Elsevier Health Sciences.

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NURSING KNOWLEDGE IN EVERYDAY LIFE: PRACTICAL APPLICATIONS FOR COMMUNITY HEALTH

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Abstract:
Nursing is a profession often associated with hospitals and clinics. However, the principles and practices of nursing extend far beyond these settings. Nursing knowledge encompasses preventive care, first aid, maternal and child care, mental health support, hygiene, nutrition, and chronic disease management. When applied in daily life, this knowledge can significantly improve individual and community well-being (National Academies of Sciences, Engineering, and Medicine, 2021; Pueyo-Garrigues, 2022). By integrating nursing knowledge into everyday routines, families can prevent illnesses, manage minor health issues at home, and recognize warning signs that require professional medical attention (Hartzler *et al.,* 2017; Joubert & Reid, 2023). This approach also empowers individuals to take a more proactive role in their health and reduces the burden on healthcare systems.

First Aid and Emergency Response at Home

Accidents and sudden health emergencies can occur at any time, whether at home, work, or in public spaces. Nurses are trained to provide immediate care during emergencies, and these skills can be shared with the general public (American Heart Association, 2021).

Basic first aid skills, such as controlling bleeding, performing Cardiopulmonary Resuscitation (CPR), managing burns, or assisting a choking person, can be life-saving. For example, recognizing the signs of a heart attack, such as chest discomfort, shortness of breath, or pain radiating to the arm, can prompt quick action and potentially save lives (National Academies of Sciences, Engineering, and Medicine, 2021). Families who learn and practice these skills develop confidence in handling emergencies, bridging the time until professional help arrives.

Additionally, awareness of how to manage minor injuries, such as cuts, bruises, or sprains, reduces unnecessary hospital visits and promotes early healing (Pueyo-Garrigues, 2022). Teaching children and caregivers basic first aid ensures a safer home environment, especially for households with elderly or young members (Hartzer *et al.,* 2017).

Hygiene and Infection Prevention

Maintaining proper hygiene is one of the most practical applications of nursing knowledge in everyday life. Nurses emphasize handwashing, sanitation, food safety, and clean-living

environments as critical factors in preventing infections (Centers for Disease Control and Prevention, 2020; WHO, 2020).

Regular handwashing with soap, especially before meals and after using the restroom, prevents common illnesses such as diarrheal infections and influenza (Colizzi *et al.,* 2020). Proper food storage, safe cooking practices, and cleaning surfaces regularly reduce the risk of contamination and foodborne diseases (Minnesota Department of Health, 2019).

During pandemics such as COVID-19, these principles become even more important. The WHO (2020) provides clear guidelines for infection prevention, emphasizing the role of community awareness and personal responsibility in reducing disease transmission. Individuals who adopt these practices at home can protect themselves, their families, and the broader community.

Nutrition and Healthy Lifestyle

Balanced nutrition is a fundamental aspect of health promoted by nursing professionals. Nurses educate communities on selecting nutritious foods, controlling portion sizes, and understanding the impact of diet on overall health (WHO, 2021).

A diet rich in fruits, vegetables, whole grains, and lean proteins supports heart health, enhances immunity, and reduces the risk of chronic conditions such as diabetes, obesity, and hypertension (American Diabetes Association, 2020). Nursing knowledge also emphasizes the importance of hydration, limiting processed foods, and avoiding excessive sugar or salt intake (Pueyo-Garrigues, 2022).

In addition to diet, nurses encourage physical activity and stress management. Simple daily routines like walking, stretching, yoga, or deep breathing exercises contribute to physical and mental well-being (Hartzler *et al.,* 2017). Families who integrate healthy lifestyle habits experience improved energy levels, reduced stress, and lower risks of chronic disease.

Managing Chronic Conditions at Home

Chronic illnesses, including diabetes, hypertension, and asthma, require continuous monitoring and management. Nurses educate patients and families on home-based care, medication adherence, monitoring vital signs, and identifying warning symptoms (Joubert & Reid, 2023; American Diabetes Association, 2020).

For example, individuals with hypertension are taught to monitor blood pressure at home, recognize symptoms such as headaches or dizziness, and adjust lifestyle habits accordingly (National Institutes of Health, 2021). Similarly, diabetic patients learn to monitor blood glucose, administer insulin, and maintain a healthy diet (American Diabetes Association, 2020). These home-based nursing interventions improve disease management, reduce complications, and empower patients to participate actively in their care (Pueyo-Garrigues, 2022).

Maternal and Child Health

Maternal and child health is a key area where nursing knowledge has a direct impact. Nurses provide guidance on prenatal care, nutrition during pregnancy, breastfeeding, infant care, and child development (American Academy of Pediatrics, 2022; WHO, 2019).

Parents are educated about immunization schedules, developmental milestones, and safe sleep practices to ensure the healthy growth of children (Centers for Disease Control and Prevention, 2021). Home-based maternal care also includes monitoring for danger signs during pregnancy, such as excessive bleeding or high blood pressure, and ensuring timely medical attention (Colizzi *et al.,* 2020). These interventions significantly reduce maternal and infant mortality and morbidity.

Mental Health Awareness and Support

Mental health is as crucial as physical health in ensuring overall well-being. Nurses are trained to identify early signs of mental health issues, provide emotional support, and refer patients to specialized services when necessary (National Institute of Mental Health, 2020; Hartzler *et al.,* 2017).

At home, simple practices such as active listening, encouraging open communication, reducing stigma, and practicing mindfulness can support mental wellness (Colizzi *et al.,* 2020). Early recognition and intervention prevent escalation of stress, anxiety, or depression, contributing to healthier family environments (Pueyo-Garrigues, 2022).

Recognizing When to Seek Professional Help

Nurses are trained to assess when home care is insufficient and professional intervention is required. Understanding warning signs such as chest pain, persistent fever, shortness of breath, or sudden weakness ensures timely medical attention (American Heart Association, 2021; Centers for Disease Control and Prevention, 2021).

By teaching families to recognize these symptoms, nurses reduce delays in treatment, which can save lives and prevent serious complications (National Academies of Sciences, Engineering, and Medicine, 2021). Nursing knowledge also includes guidance on navigating healthcare systems, scheduling check-ups, and coordinating care with professionals.

Conclusion:

Nursing knowledge, when applied beyond hospitals, empowers individuals and communities to improve health outcomes. From basic first aid and hygiene to nutrition, chronic disease management, maternal-child care, mental health support, and recognizing emergencies, these practices form a comprehensive approach to everyday well-being (Pueyo-Garrigues, 2022; Joubert & Reid, 2023; Hartzler *et al.,* 2017).

Families equipped with nursing knowledge can proactively prevent illnesses, manage minor health issues, and make informed decisions about professional medical care. In this way, everyone can contribute to healthier communities and reduce the burden on healthcare systems.

References:

1. American Academy of Pediatrics. (2022). *Policy Statement: Breastfeeding and the Use of Human Milk*. Pediatrics.
2. American Diabetes Association. (2020). *Standards of Medical Care in Diabetes*.
3. American Heart Association. (2021). *CPR & ECC Guidelines*.
4. Centers for Disease Control and Prevention. (2020). *Hand Hygiene in Healthcare Settings*.
5. Centers for Disease Control and Prevention. (2021). *Pregnancy and Childbirth*.
6. Centers for Disease Control and Prevention. (2021). *Recognizing the Warning Signs of a Stroke*.
7. Colizzi, M., *et al.* (2020). *Prevention and Early Intervention in Youth Mental Health*.
8. Hartzler, A. L., *et al.* (2017). *Insights from Community Dwelling Older Adults on Health and Health Information Used in Their Everyday Lives*.
9. Joubert, A., & Reid, M. (2023). *Knowledge, Skills, and Training of Community Health Workers to Contribute to Interprofessional Education: A Scoping Review*.
10. Minnesota Department of Health. (2019). *Public Health Interventions*.
11. National Academies of Sciences, Engineering, and Medicine. (2021). *The Role of Nurses in Improving Health Care Access and Quality*.
12. National Institute of Mental Health. (2020). *Mental Health Information*.
13. National Institute of Mental Health. (2020). *Prevention and Early Intervention in Youth Mental Health*.
14. Pueyo-Garrigues, M. (2022). *Nurses' Knowledge, Skills and Personal Attributes for Health Education Competence*.
15. World Health Organization. (2018). *Child Health*.
16. World Health Organization. (2019). *Maternal Health*.
17. World Health Organization. (2020). *Infection Prevention and Control during Health Care when COVID-19 is Suspected*.
18. World Health Organization. (2021). *Community Health Nursing Education*.
19. World Health Organization. (2021). *Diet, Nutrition and the Prevention of Chronic Diseases*.

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COUPLING PUBLIC-HEALTH SIGNALS TO HOSPITAL OPERATIONAL DIGITAL TWINS: A GOVERNANCE, EQUITY, AND OXYGEN-RESILIENCE FRAMEWORK FOR EMERGENCY CARE IN PUBLIC SYSTEMS

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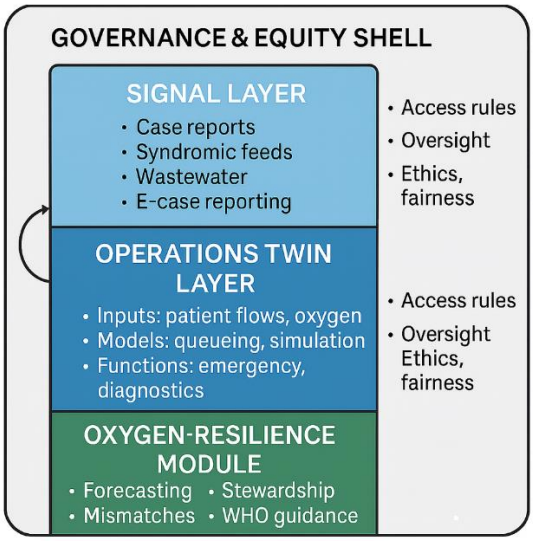
Abstract:
Public hospitals in India operate under frequent demand surges, limited human resources, and chronic infrastructure bottlenecks that show up most visibly as emergency department crowding and oxygen shortages. Digital twins, which are live, computational counterparts of physical systems, can help manage these pressures if they are designed to ingest trustworthy public-health signals and governed for equity, safety, and oxygen stewardship. This paper sets out a practical, public-system-friendly model that couples district and state epidemiology feeds, syndromic surveillance, and electronic case reporting with hospital-level operational digital twins to guide emergency flow and oxygen use in real time. The contribution is threefold. First, a simple architecture that can start with limited data and scale. Second, an equity and governance layer that brings transparency and fairness into decisions about triage, bed assignment, and diversion. Third, an oxygen-resilience layer that treats oxygen as a critical utility, with continuous forecasting and stewardship rules informed by global technical guidance. We show how the pieces fit using use-cases on surge detection, emergency throughput, and oxygen supply-demand balancing, and we explain how to evaluate such a system in public settings. The approach aligns with current evidence on digital twins and emergency operations, surveillance standards, and oxygen systems, while filling a gap by explicitly coupling public-health signals to hospital twins in an equity-aware way.

Keywords: Digital Twin, Emergency Crowding, Equity, Governance, Public Health Surveillance, Electronic Case Reporting, Oxygen Stewardship, India

Graphical Abstract:
An equity-aware hospital digital twin integrates public-health signals, hospital operations, and oxygen-resilience to support real-time decision-making in Indian public hospitals. The system couples surveillance inputs with simulations of patient flow and oxygen demand, while a governance and equity shell ensure transparency, oversight, and fairness. (Generated using prompts in an LLM.)



1. Introduction and Problem Framing

1.1 What a Hospital Digital Twin is and Why it Matters Now

We take a pragmatic definition used widely in systems papers: a digital twin is a virtual representation of a system that is kept in sync with its physical counterpart and used to anticipate outcomes of operational decisions (Barricelli *et al.,* 2019; GAO, 2023). In a hospital, this means a live model of arrivals, triage, diagnostics, bed assignment, staffing and critical utilities like oxygen that refreshes with routine data often enough to guide daily decisions (Barricelli *et al.,* 2019; Elkefi and Asan, 2022). It supports prediction and scenario testing, then recommends actions that can be traced and audited (Riahi *et al.,* 2025). The engineering roots are well known and describe a life cycle companion that links measurements, models, and decision history so that changes can be tested before risk is taken in the real system (Glaessgen and Stargel, 2012; Jones *et al.,* 2020).

Notably, in our context, the twin is not a precision-medicine patient twin; it is a service-delivery twin for emergency operations. This distinction matters because the data, governance, and risks differ (Meijer *et al.,* 2023; Ringeval *et al.,* 2025). Operations twins handle flow, beds, staff and utilities, which is the right scope for emergency care management in public hospitals (Meijer *et al.,* 2023; Katsoulakis *et al.,* 2024). A digital twin combines a dashboard (descriptive) and a one-time simulation (exploratory) with synchronisation and traceability so that managers can run what-if options and then act with a record of recommendations and overrides (Han *et al.,* 2023; Penverne *et al.,* 2024; Riahi *et al.,* 2025).

1.2 Immediate Operational Problems

Emergency departments in public hospitals carry the load for unscheduled care. When demand increases, crowding and boarding stretch into long hours and patients suffer delays and poorer outcomes. Evidence from system reports and research keeps pointing to boarding as a safety and quality issue, not only a comfort issue (AHRQ, 2024; Smalley *et al.,* 2021). During respiratory

surges oxygen becomes the limiting factor. Many facilities had to improvise in the pandemic years and now want resilient systems that can work in routine times as well (WHO, 2019; WHO, 2024; Unitaid, 2024).

1.3 Where the Current Literature Stands?

Digital twins are being explored in hospitals for patient flow, bed capacity and device management, with early frameworks and case studies now available (Elkefi and Asan, 2022; Han *et al.,* 2023; Penverne *et al.,* 2024; Appuhamilage *et al.,* 2025). Reviews and scoping work describe definitions, data layers and governance needs, and they confirm feasibility for health service management (Barricelli *et al.,* 2019; Meijer *et al.,* 2023; Katsoulakis *et al.,* 2024). Even so, there is less on how to plug in public health signals and how to keep the system fair, transparent, and oxygen sensitive in public settings. The public health continuum from personalised medicine to precision public health is discussed, but the practical adapter between district surveillance and a hospital twin is still thin in published work (Kamel Boulos and Zhang, 2021; Elkefi and Asan, 2022).

1.4 Equity and Oxygen as Design Drivers

Equity in emergency care refers to providing equal treatment for equal clinical need, ensuring that patients with similar levels of urgency receive comparable access to clinicians, diagnostics, and beds—regardless of income, insurance status, or geographic distance (Herlitz *et al.,* 2023; García-Corchero and Jiménez-Rubio, 2022). However, multiple studies have shown persistent socioeconomic gradients in emergency department process times, indicating that equity must be embedded directly into operational tools like the hospital twin, rather than being addressed only through retrospective audits (Smalley *et al.,* 2021; AHRQ, 2024). One practical strategy involves monitoring a compact weekly bundle of process indicators—such as time to first clinician contact, time to electrocardiogram for chest pain, time from admit decision to inpatient bed assignment, emergency department length of stay, and the rate of patients leaving without being seen—disaggregated by ethical proxies such as scheme eligibility or distance bands (AHRQ, 2024; Herlitz *et al.,* 2023). If the largest observed subgroup gap exceeds a predefined threshold after adjusting for triage category, the digital twin system should flag it as an exception for clinical or administrative review (Smalley *et al.,* 2021; AHRQ, 2024). This helps ensure that efforts to reduce overcrowding and boarding do not inadvertently deepen access inequities (García-Corchero and Jiménez-Rubio, 2022; Herlitz *et al.,* 2023).

Oxygen stewardship and oxygen resilience should be embedded as core design elements of the hospital twin. Stewardship refers to the disciplined monitoring and appropriate use of oxygen to protect patient safety and reduce avoidable wastage, while resilience is defined as the system's ability to maintain uninterrupted supply and safe delivery during both routine peaks and surge events (WHO, 2019; WHO, 2024). This resilience is achieved through multiple mechanisms,

including source redundancy (e.g., cylinders, pressure swing adsorption (PSA) plants, liquid oxygen), storage buffers, timely replenishment, alarm integrity, and the availability of adequately trained staff (GHSC PSM, 2023; Unitaid, 2024). Current international guidance provides technically specific and actionable recommendations that the twin can encode as rules and validation logic—for example, using standardised terminology for oxygen sources and distribution types, enforcing validated primary–secondary–reserve configurations, and monitoring purity thresholds of not less than 99.5% by volume for liquid medical oxygen, 93 ± 3% for PSA plant outputs, and more than 82% for oxygen concentrators or other backup sources (WHO, 2019; WHO, 2024). The hospital twin should be designed to forecast demand based on patient case mix, track days of oxygen reserves on hand, intelligently schedule deliveries to avoid peak congestion, and raise conservation prompts or stewardship alerts when oxygen buffers fall below thresholds (GHSC PSM, 2023; Unitaid, 2024). These functionalities align with emerging facility-level oxygen service models and global best practices for reliable oxygen delivery in clinical settings.

Objective of the Paper

To propose a governance-anchored, equity-aware digital twin model for emergency care in public hospitals, coupled to district or state surveillance signals and designed for oxygen resilience, with a step-by-step path for implementation and evaluation.

2. Conceptual Model: Coupling Public-Health Signals to the Hospital Twin

We arrange the model in three layers and one cross-cutting governance shell.

2.1 Signal Layer

The signal layer is the starting point of the hospital twin, where public-health signals come in and help connect district-level surveillance with what's happening inside the hospital in real time. These signals include notifiable disease case reports from hospitals and labs; syndromic feeds from designated centres that pick up common symptom patterns like fever and cough or rash and joint pain; wastewater or environmental data, if available, that can catch silent spread of viruses like COVID or polio; and electronic case reporting from hospital EHRs, where available and properly set up, which can send structured reports automatically to health authorities. These different inputs help create an overall picture that the twin uses to raise alerts and guide operations. The data is cleaned and selected based on well-known surveillance standards like timeliness, representativeness, and quality (CDC, 2001; CDC, 2024). In districts where full digital systems are not there yet, even a small set of simple indicators—like how many people came with fever, or sudden increase in oxygen use—is enough to begin. This layer makes sure that even when tech or infrastructure is not fully in place, the twin can still work with what's available and stay updated with the real situation.

2.2 Operations Twin Layer

Inside the hospital, the operations twin takes in all the important internal signals—like patient arrivals and triage levels, current bed availability (bed census), staff rosters, imaging queues (CT, X-ray, etc.), and oxygen telemetry data from various wards. These inputs feed into simulation models that help understand and predict patient flow. It uses queueing models and discrete-event simulations to manage bottlenecks and smoothen movement through emergency, diagnostics, wards, and ICUs. It also runs a resource model specifically for oxygen—tracking how much is being generated, stored, and consumed on a continuous basis. The idea is to create a living replica of hospital functioning that can guide daily decisions and flag upcoming issues. Already, the literature shows practical examples of similar models being used in emergency call centres and smart hospitals abroad, which can be adapted for Indian public sector settings as well (Han *et al.,* 2023; Penverne *et al.,* 2024). The technical setup doesn't have to be very heavy—just a basic message broker for data streams, a small model store to keep the simulation logic, and a rules engine that can suggest operational actions based on real-time data (Dihan *et al.,* 2024; Appuhamilage *et al.,* 2025). Even with limited IT resources, such a twin can help improve flow, reduce delays, and support better decisions day to day.

2.3 Oxygen-Resilience Module

The twin looks at oxygen like a basic utility, something as essential as power or water. It does not just keep count of stock but tries to keep a live balance between demand and supply. On the demand side, it estimates how much oxygen will be needed based on the triage mix, patient severity, and the usual clinical pathways—like how many may end up on high-flow oxygen or ventilators at a given time. On the supply side, it brings together information from cylinders, concentrators, PSA plants, and liquid oxygen tanks, and keeps track of what is available, what is being used, and what might run short. Whenever there is a sign of mismatch, the module can give early warnings and also suggest simple stewardship steps like checking flow meters for leaks, titrating oxygen carefully instead of overuse, or switching to backups on time.

It also carries standard rules from global guidelines and national policies so that hospital staff do not have to figure out things on the spot. This means including steps for safe cylinder rotation, regular maintenance of concentrators, routine testing of PSA output, and what to do if oxygen transport is delayed. It also takes care of the full cycle—procurement, installation, maintenance, and even safe retirement of equipment—so that oxygen handling is not left as a crisis measure but part of normal hospital running. Guidance from WHO (2019; 2024), GHSC-PSM (2023), and Unitaid (2024) provides clear specifications which can be built into simple checklists and rules, making the oxygen-resilience module workable even in resource-limited hospitals.

2.4 Governance and Equity Shell

This shell is basically about who can see what, how decisions are written down, and how fairness and bias are checked from time to time. It fixes clear rules on access—like which doctor or nurse can view the signals, who can make changes in the twin, and how those actions are later audited. Any big step, such as adjusting triage rules or changing oxygen allocation, is recorded with time and user name, so that afterwards people can see how and why the decision was taken.

There is also an oversight committee, and it is not just senior doctors sitting there. It has nurses, biomedical staff, operations people, and public-health voices, so that the real situation of the hospital is represented. To keep balance, at least one outside ethicist or patient voice is added, so the group has both technical and social legitimacy. This committee meets regularly, goes through the reports, looks at exception flags raised by the twin, and checks whether any patient group is being left behind.

Such practices follow the good governance ideas that are now common in health AI guidance (Iqbal *et al.,* 2022; WHO, 2024). In simple terms, this shell works like a guardrail—it does not stop the twin from running day to day, but it makes sure the decisions are open to scrutiny, and that hospital leadership has a proper way to track fairness, equity, and compliance.

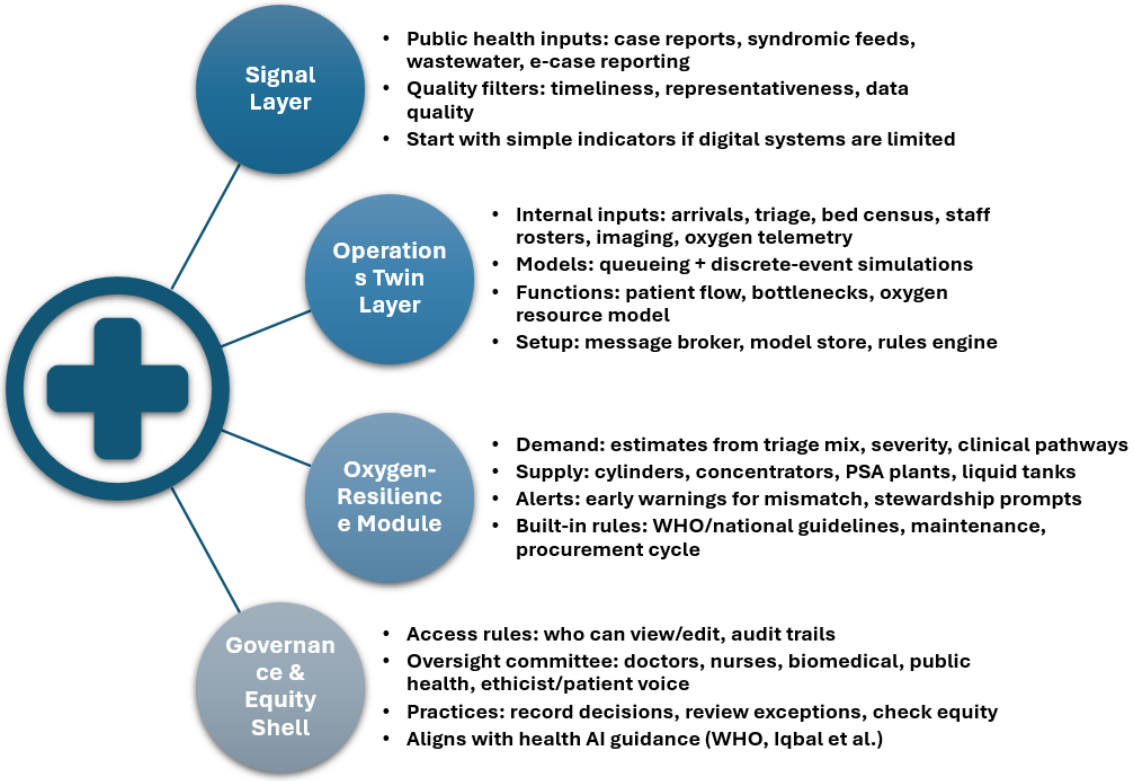


Figure 1: Proposed Conceptual Model

2.5 Why this Model and from Where it Draws Inspiration?

The model is built by joining four streams that already have strong grounding in the literature. For the signal layer, we follow standard surveillance attributes such as timeliness, usefulness, representativeness and data quality, and reuse national pathways like electronic case reporting so that hospital forecasts stand on recognised public-health pipes (CDC, 2001; CDC, 2024). Conceptually, the link from clinical data to population signals follows the move from personalised medicine to precision public health (Kamel Boulos and Zhang, 2021). For the operations twin layer, we take the definition and layering from engineering and health surveys and then adapt hospital-specific proofs of concept. Surveys explain the digital thread and the need for synchronisation and traceability in twins, while hospital papers show that discrete-event and queueing models with live updates are workable for emergency and bed flow (Barricelli *et al.,* 2019; Jones *et al.,* 2020; Han *et al.,* 2023; Penverne *et al.,* 2024). Method and architecture notes on health twins and workflow optimization inform our light technical stack and rules engine approach (Dihan *et al.,* 2024; Appuhamilage *et al.,* 2025; Riahi *et al.,* 2025; Katsoulakis *et al.,* 2024).

For the oxygen-resilience module, we stand on technical specifications and lifecycle guidance that set purity targets, redundancy patterns, distribution safety and maintenance routines, and on programmatic roadmaps that describe equipment management and newer service models. These sources let us encode stewardship rules and buffer logic in a way that is standardized and auditable, and they reflect lessons from India's surge response (WHO, 2019; WHO, 2024; GHSC-PSM, 2023; Unitaid, 2024; Mirza *et al.,* 2023). Finally, the governance and equity shell is shaped by two lines of evidence. First, equity studies show socioeconomic gradients in emergency process times and highlight leaving-without-being-seen as a safety and quality signal, which justifies routine subgroup splits and weekly exception flags in operations meetings (García-Corchero and Jiménez-Rubio, 2022; Herlitz *et al.,* 2023; Smalley *et al.,* 2021). Second, ethics and policy guidance argue for role clarity, audit trails and transparency for decision-support systems, which we adopt through an oversight committee, documented change control and decision logs (Iqbal *et al.,* 2022; WHO, 2024). The overall insistence on traceability and logs also follows the original digital-thread idea in engineering twins (Glaessgen and Stargel, 2012).

3. Data Pathways and Minimal Viable Build in Public Settings

A common issue in this field is lack of data. The right approach is to start with the smallest live data slice that actually moves operations and grow from there.

Start Small: Begin with triage timestamps, bed occupancy, and one oxygen source's telemetry. That allows the twin to estimate crowding, predict queues, and detect oxygen risk. Later, plug in electronic case reporting fields and district line lists when they are available (CDC, 2024).

Standards and Interoperability: Use simple, documented data contracts and leave room for HL7 or FHIR when the hospital has it. This reduces lock-in and makes auditing easier (Elkefi and Asan, 2022; GAO, 2023).

Model Choices: Queueing and discrete-event simulation are transparent and interpretable. These models have been used in emergency and call-center contexts and fit the skill mix present in many biomedical engineering teams (Penverne *et al.,* 2024; Han *et al.,* 2023). Mechanistic pieces are preferable where safety is involved, and machine learning can sit on top for demand prediction, with uncertainty reported to users (Riahi *et al.,* 2025; Pash *et al.,* 2025).

4. Governance and Safety: How to Keep Trust

Hospitals should not deploy a black box for critical operations. The governance shell has tangible components.

4.1 Governance Board: Constitute a board that approves model scope, monitors fairness, and signs off on changes. Keep agendas and minutes public inside the organization. This is in line with ethical guidance and helps sustain trust (WHO, 2024; Iqbal *et al.,* 2022).

4.2 Documentation and Traceability: Every recommendation from the twin should show inputs, the rule or model path, and an explanation plain enough for a nurse manager to understand. This is a core requirement in safety-critical DTs and emergency management literature (Zio *et al.,* 2024; GAO, 2023).

4.3 External Interface: When the twin uses district signals, publish a one-page method note for the district health office, listing the indicators used and how alerts are derived. This keeps alignment with surveillance norms around transparency and use of data (CDC, 2001; CDC, 2024).

5. Equity in Flow Decisions

Equity problems appear in waiting times and in who gets delayed in investigations. Studies show that process times can vary by socioeconomic markers even in structured systems (García-Corchero and Jiménez-Rubio, 2022; Herlitz *et al.,* 2023). The twin can help by:

i. **Equity Dashboards:** Track time-to-physician, time-to-ECG, time-to-bed across age, sex, payment category, and catchment area. Where sensitive attributes are not collected, use proxy measures carefully and report with caution (García-Corchero and Jiménez-Rubio, 2022).

ii. **Fairness Checks on Rules:** Before activating a triage rule that reallocates beds, simulate othe distribution of waiting times across groups and check that the rule does not increase gaps (Herlitz *et al.,* 2023).

iii. **Routing with Justification:** If the twin suggests diversion to another unit, give reason codes and expected time gained. This documentation helps clinical leaders catch biased patterns early (WHO, 2024; Iqbal *et al.,* 2022).

6. Oxygen Stewardship and Resilience

Oxygen stewardship is not only about availability. It is also about appropriate use, safe delivery, and maintenance.

i. **Encode Specifications:** Put device limits, flow ranges, alarm behaviors, and maintenance cycles into the twin's knowledge base using WHO-UNICEF specifications (WHO, 2019).

ii. **Forecasting and Buffers:** Use arrival mix and clinical pathways to forecast oxygen flow demand by hour and compare to supply, with minimum buffer thresholds and reorder points set per site, aligning with best practice in oxygen strategies and equipment management (WHO, 2024; GHSC-PSM, 2023).

iii. **Market and Supply Signals:** Track vendor lead times and cylinder turnaround. Unitaid's landscape shows new models such as regional liquid oxygen production and service-based delivery. The twin can flag when a switch in sourcing would reduce risk (Unitaid, 2024).

iv. **Safety Rules in the Loop:** Force checks for flow-meter accuracy and humidifier use when high flows trigger, and record the check. These are small but reduce waste and improve patient safety (WHO, 2019).

7. Use-cases that Connect Signals to Action

7.1 Pre-Emptive Surge Response

A rise in district ARI consultations and a school absenteeism spike come through the signal layer. The twin simulates next week's arrivals and oxygen demand, and recommends short-term actions: rescheduling elective beds, a temporary fast-track for low acuity injuries, and a cylinder reserve build-up. This is consistent with how surveillance data should inform local action and with observed benefits from operations twins in emergency settings (CDC, 2001; Penverne *et al.,* 2024; Han *et al.,* 2023).

7.2 Reducing Boarding by Targeted De-Bottlenecking

The twin shows imaging turnaround as the bottleneck on weekday evenings. Simulation suggests that one extra radiographer from 5 pm to 9 pm reduces boarding by a measurable margin, with better time-to-decision for chest pain. Such targeted options are exactly what operations twins are meant to support (Han *et al.,* 2023; Riahi *et al.,* 2025; Smalley *et al.,* 2021).

7.3 Oxygen Stress Test and Weekend Safety

The forecast indicates that a weekend shift with planned PSA maintenance overlaps a heatwave spike in respiratory load. The twin advises moving the maintenance, increasing filled cylinders by a set amount, and placing backup concentrators in triage. These recommendations match guidance to plan across the oxygen asset lifecycle (WHO, 2024; GHSC-PSM, 2023; Unitaid, 2024).

8. Implementation Roadmap for Public Hospitals

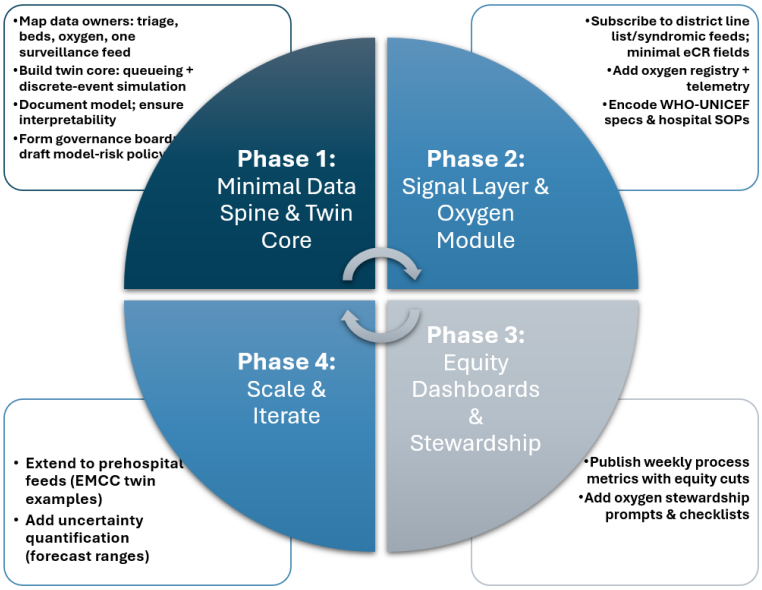


Figure 2: Schematic showing implementation roadmap for public hospitals

Phase 1: Set up Minimal Data Spine and Twin Core

i. Map data owners for triage times, bed census, oxygen telemetry, and one surveillance feed.

ii. Build the twin core with queueing plus discrete-event simulation for arrivals, beds, and imaging. Keep the model documented and interpretable (Penverne *et al.,* 2024; Han *et al.,* 2023).

iii. Create a governance board and a short model-risk policy aligned to health AI guidance (WHO, 2024; Iqbal *et al.,* 2022).

Phase 2: Add Signal Layer and Oxygen Module

i. Subscribe to district line list summaries or syndromic aggregates. If eCR is available, consume minimal fields that do not compromise patient privacy, following the national or state specification (CDC, 2024).

ii. Add oxygen device registry and telemetry, encode WHO-UNICEF specs and hospital SOPs (WHO, 2019; WHO, 2024; GHSC-PSM, 2023).

Phase 3: Equity Dashboards and Stewardship

i. Publish weekly process metrics with equity cuts for internal review.

ii. Implement oxygen stewardship prompts and checklists in the workflow (García-Corchero and Jiménez-Rubio, 2022; Herlitz *et al.,* 2023).

Phase 4: Scale and Iterate

i. Extend to prehospital feeds if the state has an emergency call center twin, which is feasible given published EMCC twin examples (Penverne *et al.,* 2024).

ii. Add uncertainty quantification for forecasts to show ranges rather than single numbers (Pash *et al.,* 2025).

9. Evaluation Plan

Process Endpoints

i. Data timeliness and completeness for arrivals, beds, oxygen telemetry, and public-health signals (CDC, 2001).
ii. Model fidelity: difference between predicted and observed queues and oxygen flows (Riahi *et al.,* 2025).
iii. Governance activity: number of model changes reviewed, number of decisions with explanations recorded (WHO, 2024).

Outcome Endpoints

i. Boarding hours per admitted patient, time-to-physician and time-to-ECG for chest pain (AHRQ, 2024; Herlitz *et al.,* 2023).
ii. Oxygen stock-out hours and near-miss reports; corrective actions completed (WHO, 2024; GHSC-PSM, 2023).
iii. Equity gaps in process times and whether they narrow without harming overall throughput (García-Corchero and Jiménez-Rubio, 2022).

Safety and Ethics

i. Number of overridden recommendations and reasons.
ii. Adverse events linked to twin actions, with root-cause analysis.
iii. Alignment with ethical guidance and data-sharing consent where needed (WHO, 2024; Iqbal *et al.,* 2022).

10. Limitations and Risks

This model depends on data that may be incomplete or delayed. Surveillance feeds can have gaps and may not reflect the true community signal. We propose to start with conservative thresholds and to show uncertainty ranges to users (CDC, 2001; Pash *et al.,* 2025). Equity metrics may be limited by what attributes are recorded in routine data, so proxy use should be cautious and reviewed by the governance board (García-Corchero and Jiménez-Rubio, 2022). Cybersecurity and privacy concerns need standard controls and clear role-based access, which are covered in generic guidance but still require local enforcement (WHO, 2024; GAO, 2023).

Conclusion:

Public hospitals can get real value from operational digital twins if they are built around real signals, fairness, and oxygen resilience. Start small with triage, beds, and one oxygen source. Bring in district signals in a careful way, and keep governance in front. The evidence base gives enough pieces to proceed, and the approach aligns with ethical and technical guidance. The result is a living system that helps emergency teams act early, act fairly, and keep oxygen safe and

available when the demand climbs (Elkefi and Asan, 2022; Penverne *et al.,* 2024; WHO, 2019; Unitaid, 2024).

References:

1. Agency for Healthcare Research and Quality (2024): AHRQ summit to address emergency department boarding, technical report. Link of resource: https://www.ahrq.gov/sites/default/files/wysiwyg/topics/ed-boarding-summit-report.pdf
2. AHRQ (2024) *Equity in Emergency Care: Metrics and Monitoring Toolkit*. U.S. Department of Health and Human Services.
3. Appuhamilage N, Seow H Y, de Magalhães Marques L and Chong A (2025): A conceptual framework for implementing digital-twin-based interventions for optimised critical care workflows, Scientific Reports, 15: 12867.
4. Barricelli B R, Casiraghi E and Fogli D (2019): A survey on digital twin, definitions, characteristics, applications, and design implications, IEEE Access, 7: 167653–167671.
5. Centers for Disease Control and Prevention (2001): *Updated guidelines for evaluating public health surveillance systems*. Link of resource: https://www.cdc.gov/mmwr/pdf/rr/rr5013.pdf
6. Centers for Disease Control and Prevention (2024): *Electronic case reporting for public health*. Link of resource: https://www.cdc.gov/ecr/php/about/index.html
7. Dihan, M. S., Alam, M. S., Islam, M. T., & Kabir, M. M. (2024): Digital twin data exploration: architecture, implementation, and trends, *Informatics in Medicine Unlocked*, 42: 101370.
8. Elkefi, S., & Asan, O. (2022): Digital Twins for Managing Health Care Systems: Rapid Literature Review, *Journal of Medical Internet Research*, 24(8): e37641.
9. GAO (2023): *Science & Tech Spotlight: Digital Twins—Virtual Models of Physical Systems*. Link of resource
10. García-Corchero, J. D., & Jiménez-Rubio, D. (2022): Waiting times in healthcare: equal treatment for equal need?, *International Journal for Equity in Health*, 21(1): 184.
11. García-Corchero, S. and Jiménez-Rubio, D. (2022) Socioeconomic inequalities in access and quality of emergency healthcare: Evidence from process times and care outcomes. *Health Policy*, 126(5), pp.437–444.
12. Glaessgen E and Stargel D (2012): The Digital Twin Paradigm for Future NASA and U.S. Air Force Vehicles. Link of resource: https://arc.aiaa.org/doi/10.2514/6.2012-1818
13. Global Health Supply Chain Program PSM (2023): Medical oxygen equipment management strategy and road map. Link of resource: https://www.ghsupplychain.org/sites/default/files/2024-01/TechnicalReport%20_O2-

Medical%20Oxygen%20Equipment%20Management%20Strategy%20and%20Road%20Map_EN%2012012023.pdf

14. Han, Y., Li, Y., Li, Y., Yang, B., & Cao, L. (2023): Digital twinning for smart hospital operations: Framework and proof of concept, *Technology in Society*, 74: 102317.
15. Herlitz S, Ohm J, Häbel H, Ekelund U, Hofmann R and Svensson P (2023): Socioeconomic status is associated with process times in the emergency department for patients with chest pain, *JACEP Open*, 4(4): e13005.
16. Herlitz, J., Bång, A., Wireklint Sundström, B., et al. (2023) Equity in emergency care: Patterns of delay and triage misclassification. *BMC Emergency Medicine*, 23, 87.
17. Iqbal, J. D., Krauthammer, M., & Biller-Andorno, N. (2022): The use and ethics of digital twins in medicine, *Journal of Law, Medicine & Ethics*, 50(3): 583–596.
18. Jones D, Snider C, Nassehi A, Yon J and Hicks B (2020): Characterising the Digital Twin, A systematic literature review, *CIRP Journal of Manufacturing Science and Technology*, 29(1): 36–52.
Kamel Boulos M N and Zhang P (2021): Digital Twins, From personalised medicine to precision public health, *Journal of Personalized Medicine*, 11(8): 745.
19. Katsoulakis E, Wang Q, Wu H, Shahriyari L, Fletcher R and Liu J et al. (2024): Digital twins for health, A scoping review, *npj Digital Medicine*, 7(1): 77.
20. Kamel Boulos M N and Zhang P (2021): Digital twins, from personalised medicine to precision public health, Journal of Personalized Medicine, 11(8): 745.
21. Meijer, C., Uh, H.-W., & El Bouhaddani, S. (2023): Digital twins in healthcare: methodological challenges and opportunities, *Journal of Personalized Medicine*, 13(10): 1522.
22. Mirza M, Verma M, Sahoo S S, Roy S, Kakkar R and Singh D K (2023): India's multi-sectoral response to oxygen surge demand during COVID-19 pandemic, a scoping review, Indian Journal of Community Medicine, 48(1): 31–40.
23. Pash, G., Villa, U., Hormuth II, D. A., Yankeelov, T. E., & Willcox, K. (2025): Predictive digital twins with quantified uncertainty for patient-specific decision making in oncology, *arXiv* preprint, 2505.08927.
24. Penverne, Y., Cardin, N., Verger, P., Tonglet, R., & Blanchard, B. (2024): A simulation-based digital twin approach to assessing the impact of organizational scenarios on emergency medical communication centers, *npj Digital Medicine*, 7: 221.
25. Riahi, V., Diouf, I., Khanna, S., Boyle, J., & Hassanzadeh, H. (2025): Digital twins for clinical and operational decision-making: Scoping review, *Journal of Medical Internet Research*, 27: e55015.

26. Ringeval, M., Etindele Sosso, F. A., Cousineau, M., & Paré, G. (2025): Advancing health care with digital twins: Meta-review of applications and implementation challenges, *Journal of Medical Internet Research*, 27: e69544.
27. Smalley, C. M., Sellergren, S. A., Stickrath, C., & Mehta, S. (2021): Emergency department patients who leave before treatment is complete, *Western Journal of Emergency Medicine*, 22(2): 148–155.
28. Smalley, C.M., O'Leary, M.C. and Jordan, J.D. (2021) Health disparities in emergency department process times. *American Journal of Emergency Medicine*, 39, pp.1–6.
29. Unitaid (2024): *The Medical Oxygen Innovation Landscape*. Link of resource: https://unitaid.org/uploads/The-Medical-Oxygen-Innovation-Landscape.pdf
30. WHO (2019): *WHO-UNICEF Technical Specifications and Guidance for Oxygen Therapy Devices*. Link of resource: https://apps.who.int/iris/handle/10665/331841
31. WHO (2024): *Ethics and governance of AI for health: Guidance on large multi-modal models*. Link of resource: https://iris.who.int/handle/10665/380072

Approaches and Applications in Nursing and Healthcare

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