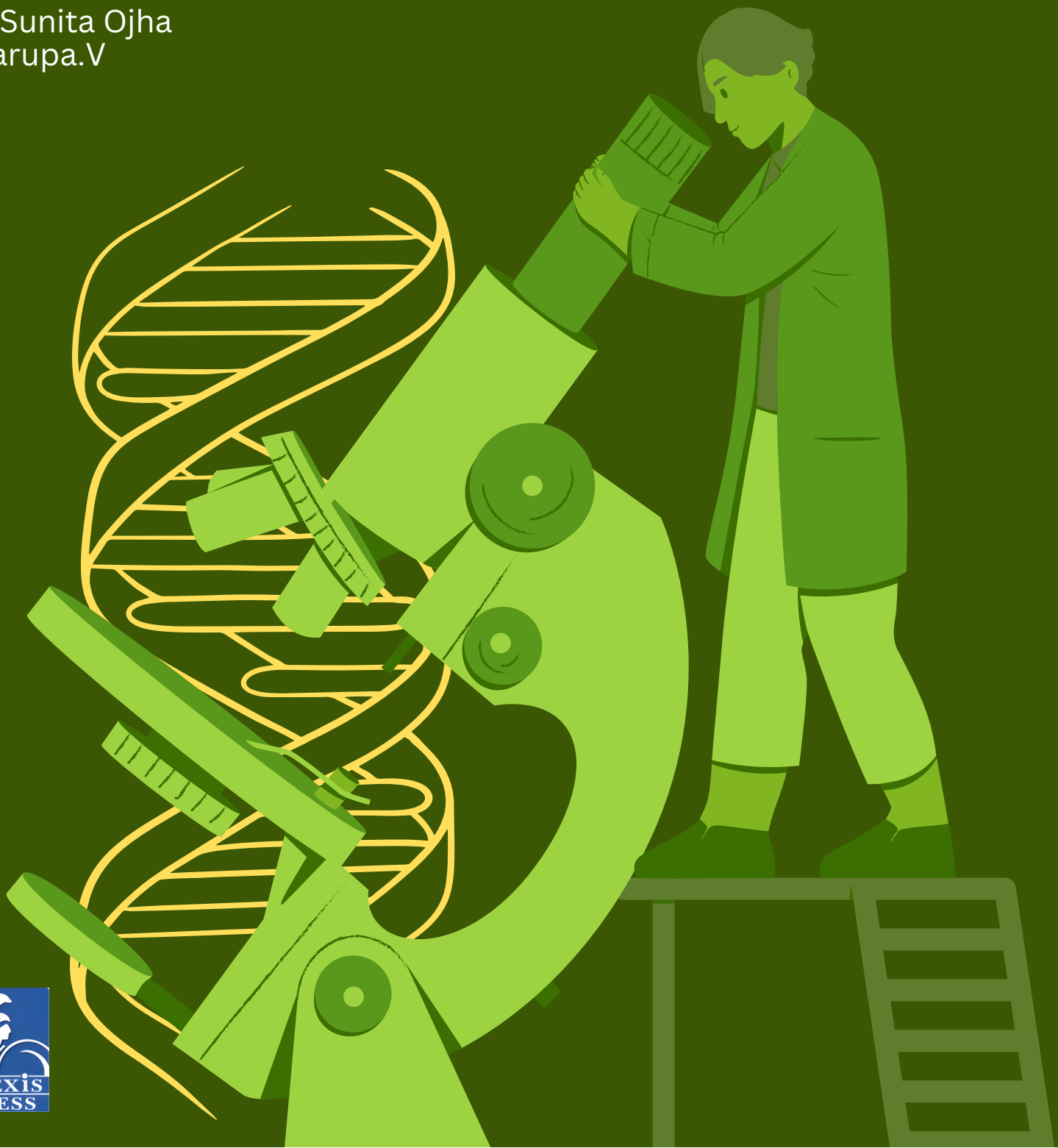
BASIC OF BIOTECHNOLOGY

Dr. Sunita Ojha
Swarupa.V



ALEXIS PRESS

BASICS OF BIOTECHNOLOGY

BASICS OF BIOTECHNOLOGY

Dr. Sunita Ojha

Swarupa. V

ALEXIS PRESS

ALEXIS PRESS

Published by: Alexis Press, LLC, Jersey City, USA
www.alexispress.us

First Published 2022

A catalogue record for this publication is available from the British Library

Library of Congress Cataloguing in Publication Data

Includes bibliographical references and index.

Basics of Biotechnology by *Dr. Sunita Ojha, Swarupa. V*

ISBN 978-1-64532-383-9

CONTENTS

CHAPTER 1

A STUDY ON NANOMATERIAL-BASED THERAPY FOR EFFECTIVE WOUND HEALING

Dr. Sunita Ojha, Assistant Professor,
Department of Biotechnology, Jaipur National University, Jaipur, India,
Email Id-ojhasunita@jnujaipur.ac.in

ABSTRACT: The "optimal" method for wound healing has undergone extensive research to ensure function retention while achieving quick healing and minimal scarring. Topical therapies, such as antibacterial or colloidal agents, are used in the traditional method of managing wounds to stop the infection and encourage a healthy healing process. Nanotechnology examines very small particles with a maximum diameter of 100 nm and associated phenomena.Due to its numerous benefits over more traditional forms of therapy, wound healing based on nanomaterials holds considerable potential for the treatment and prevention of wound infections. Such in-depth analyses of wound-healing applications are made feasible by the physiochemical characteristics of nanoparticles.With a focus on liposomes, polymeric nanoparticles, inorganic nanoparticles, lipid nanoparticles, nanofibrous structures, and nanohydrogel, this study described and addressed the present nano-drug delivery methods with significant promise for wound healing and skin regeneration.It also examines recent discoveries about the possibilities and problems of using nanomaterials in the therapy of chronic wounds. Thus, the application of nanotechnologies has enormous promise and might provide tangible benefits in boosting wound healing and rejuvenation, sustaining skin cell populations under unfavorable circumstances, and adopting therapeutic choices already employed in clinics.

KEYWORDS: Clinics, Infection, Nanomaterial, Therapy, Wound Healing.

1. INTRODUCTION

The skin is the body's biggest organ and a vital barrier with important immunologic, sensory, and defensive functions. The skin is constantly exposed to the elements, making it susceptible to a wide range of environmental conditions that may cause a wide variety of skin damage and injuries. It's important to note that, as the rates of obesity and chronic illnesses like diabetes, venous insufficiency, and arterial occlusion have skyrocketed in recent years, the number of persons suffering from chronic wounds has increased considerably as well [1].The skin is the biggest organ in the body and plays a crucial barrier role with its immunologic, sensory, and protective capabilities. Skin is susceptible to damage and harm from a wide range of sources due to its constant contact with the air, water, and soil. It's important to note that, as the rates of obesity and chronic illnesses like diabetes, venous insufficiency, and arterial insufficiency continue to skyrocket, the number of persons suffering from chronic wounds has also increased considerably in recent years [2].

When compared to the current standard of care (SOC), wound healing based on nanomaterials offers some benefits in both the treatment and prevention of wound infections. Patients' QoL is negatively impacted by wounds, making them a "silent pandemic." An estimated eight million users had either an acute wound or a chronic wound and an associated infection in 2018.The hemostatic cascade begins instantly after an injury. A person's life may be punctuated more than once by a wound. About a billion individuals throughout the globe will become hurt either temporarily or permanently. The natural, albeit intricate, biological

process of wound healing consists mostly of four stages (hemostasis, inflammation, proliferation, and maturation). Following injury, inflammation sets in and may last for up to 6 days [3]. During the proliferation stage, angiogenesis and extracellular matrix production begin (ECM). The recovery process, known as the maturation phase, typically starts three weeks after injury and may last for up to two years.

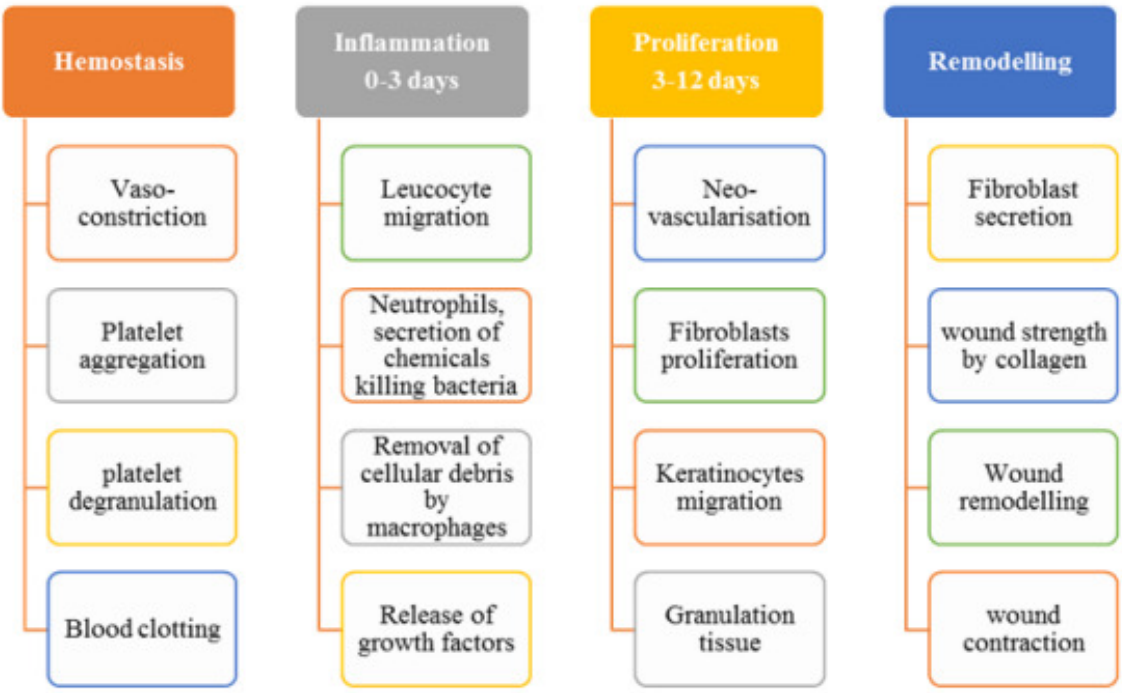


Figure 1: Displays The Events And Phases Of The Healing Process For Wounds [4]**.**

Nanotechnology is a globally expanding and intellectually demanding scientific area. Nanomaterials are now widely used in a variety of fields, from engineering to medicine. Nanotechnology's potential applications in the field of wound healing are now the subject of many studies. Due to their unique physical and chemical characteristics, nanomaterials have garnered a lot of studies. Because of their distinct chemical, physical, and biological features, biomaterials have attracted increased research into their impact on wound healing. Figure 1 displays several forms of nanoparticles that aid in the healing process.

There has been a dramatic rise in the number of individuals with chronic wounds due to the prevalence of chronic conditions like vascular dysfunction, obesity, and diabetes. Chronic abscesses are more common in diabetes patients, with a risk of 15-25%. Malignant skin tumors, sporotrichosis, autoimmune skin illnesses, Dermatomyositis, and physical skin disease are just a few examples of communicable skin conditions that may leave patients susceptible to chronic wounds. Chronic and nonhealing wounds leave the hypodermic tissue exposed to the outside environment for a long time, putting the patient in danger of hemorrhage and osteomyelitis, and, in extreme cases, death[5].

The process of wound healing is becoming more challenging for physicians, making any new materials or methods highly sought after. Significant advances in nanotechnology, primarily in nanochemistry and nanomanufacturing, have changed the pharmaceutical and biotechnology sectors. Small size, surface, and macroscopic quantum tunneling processes cause nanomaterials (those with at least one dimension below 100 nm) to exhibit unusual physicochemical features. Due to their enhanced adsorption capacity, antibacterial

characteristics, and medication loading, nanoparticles have also recently seen widespread use in wound healing [6].

2. LITERATURE REVIEW

Moist, breathable, and antimicrobial milieu may increase cell proliferation and migration, which is favorable to wound healing, as indicated in research by Miao Zhang et al. Here, utilizing aldehydated sodium alginate (SA), chitosan oligosaccharide (COS), and zinc oxide (ZnO) nanoparticles, researchersfabricated a novel sodium alginate-chitosan oligosaccharide zinc oxide (SA-COS-ZnO) composite hydrogel by spontaneous Schiff base reaction, which can provide a moist and antibacterial environment for wound healing. SA-COS-ZnO hydrogel has a porosity of 80%, a swelling degree of 150%, and a water vapor permeability of 682 g/m2/24h. The composite hydrogel was shown to be antibacterial activity against Escherichia coli, Staphylococcus aureus, Candida albicans, and Bacillus subtilis, and was biocompatible with blood cells, 3T3 cells, and 293T cells. In a scale model of rats, the hydrogel also accelerated wound healing. The results of the current investigation show promise for the use of marine carbohydrate composite hydrogels in the treatment of wounds [7].

Andrei V. Zvyagin et al. conducted a study that the penetration of nanoparticles into the sub-dermal layers of human skin after topical application of ZnO, utilizing multiphoton microscopy (MPM) imaging using a combination of scanning electron microscopy (SEM) and an energy-dispersive x-ray (EDX) approach.First off, the endogenous skin fluorophores NADPH and FAD dominate the "silent" spectral range of skin autofluorescence where the ZnO main photoluminescence occurs at 385 nm. Secondly, compared favorably to NADPH and FAD, ZnO-nano has a large two-photon action cross-section ZnO 0.26 GM; a diameter, of 18 nm that is 500 times greater than that anticipated from its bulk third-order nonlinear susceptibility.These observations indicate that the kind of ZnO-nano examined here is unlikely to raise safety concerns since the nanoparticles don't penetrate beyond the SC and the SC's outermost layers rotate quickly [8].

David D. Evanoff and George Chumanov stated in their study that chemically pure silver nanoparticles in water were tested for 16 distinct sizes ranging from 29 to 136 nm, and the extinction, scattering, and absorption cross sections and efficiencies were determined. Efficiency measurements show that particles interact with light at a rate four orders of magnitude higher than predicted by the geometric cross-section. The visible spectral region was used to independently quantify the absorption and scattering components of the plasmon resonance. It is proposed that standard subtraction be used as a quick and accurate way to calculate particle concentrations regardless of particle size, shape, or aggregation [9].

According to the research by Hongli Ye et al., a novel composite may be made by combining silver nanoparticles (AgNPs), chitosan (CS), crosslinking with tannic acid, and then freeze-drying. Gelatin was utilized as a reducing agent and stabilizer to restore the AgNPs in situ.UV visible spectrophotometry, XRD, and electron microscopy all provided definitive proof of the presence of AgNPs. Excellent mechanical characteristics, water absorption, and moisture retention were all observed in a gelatin/cellulose/silver composite. Antibacterial tests were conducted, and the results showed that the Gelatin/CS/Ag combination had a significant inhibitory impact on the bacteria. Co-culturing L929 cells with gelatin/collagen/saponin/ag showed no cytotoxicity. Finally, Gelatin/CS/Ag was shown to be biocompatible and effective in fostering wound healing. Therefore, Gelatin/CS/Ag shows promise as an antibacterial and wound-healing agent [10].

3. DISCUSSION

The economic toll of chronic wounds in affluent nations is substantial and is only projected to rise as the population ages. Infections and incomplete wound closure are only two examples of issues that might arise from subpar healing that aren't adequately addressed by current therapy. Therefore, novel biomolecules and treatments that enhance wound healing, and minimize wound infections, or inflammation, among others, are required. Several multi-functional and mechanism-specific nanotechnological techniques have shown promise in wound animal models and may represent the next generation of wound nanotherapies [11].

Nanodevices are cutting-edge tools that have the potential to improve many aspects of drug delivery, from the biocompatibility, bioavailability, and safety profiles of drugs to the ability of nanoparticles to enter the cytoplasmic space across cellular barriers like Trojan horses and activate specific transport mechanisms. In addition, it is becoming more feasible to pick therapies that are specific to each patient's profile. Nanotherapies provide a promising new way to boost the effectiveness of existing medical treatments, potentially boosting the quality of care and the prognosis for serious medical conditions including slow wound healing.

Physiology of Healing Wounds:

Targeting the intricacy of the natural wound-healing process, cell type specificity, an abundance of regulatory molecules, as well as the pathophysiology of chronic wounds, is made possible by nanotechnology-based diagnostics and therapy techniques. The use of nanotherapeutics for cutaneous wound healing provides significant benefits conceptually. It might be multifactorial, cell-type specific, necessitates topical application, and the therapeutic substance is utilized for a brief period or until the wound has healed. Restoring skin is a physiologically complex process that requires the sequential organization of many different cell types, chemokines, and growth hormones. Traditional models divide the healing process into four stages: Figure 2 displays the processes of hemostasis (a), inflammation (b), proliferation (c), and remodeling (d) throughout the body.

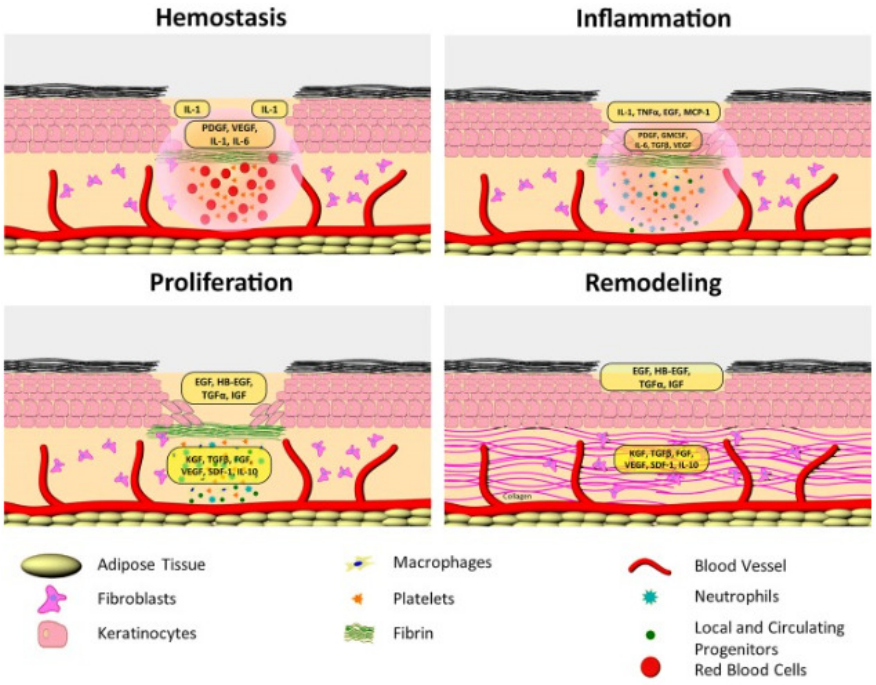


Figure 2: Skin wound healing stages that show the molecules and cells in charge of reestablishing a healthy barrier [12]**.**

Hemostasis Phase:

Hemostasis, which stops bleeding and reduces hemorrhaging, is the first reaction to damage, followed by vascular injury. Three phases of hemostasis vasoconstriction, primary hemostasis, and secondary hemostasis are achieved by a quick, coordinated, and mechanically connected process. Additionally, they extend the next step of the wound healing process by activating epithelial cells, using fibroblasts to deposit collagen, and promoting the repair of damaged tissue [13].

Inflammation Phase:

The inflammation begins very immediately after the accident and often continues for up to three days after that. Following the intense vasoconstriction that occurs during early hemostasis, the degranulation of platelets sets off a complement cascade and results in the production of potent complement peptides. This, in turn, causes basophils and mast cells to release histamine, serotonin, proteases, and other cellular intermediaries into the bloodstream. Vasodilation increased vascular permeability, and increased blood flow is all side effects of this, along with inflammation and heat [14].After three to four days of the wound developing, macrophages remove fatigued neutrophils via a process called efferocytosis. This prevents the tissue from breaking down in a way that isn't particular and keeps inflammation going.

Proliferation Phase:

A proliferation stage starts four days after wound creation and lasts for around 21 days in chronic wounds. The size of the wound and the patient's condition, however, both have an impact on the timeframe. Granulation of tissue, healing of the wound, and angiogenesis are the main categories for the proliferation stage. Angiogenesis is crucial for granulation because the production of TGF-β, PDGF, and FGF by the platelets during hemostatic plug activates tissue development. Additionally, the main tissue that forms during inflammation, the granulation tissue, gradually replaces the clot at the wounded location [15].

Nanomaterials for Healing Wounds:

Different nanomaterial structures, such as nanoparticles, nanospheres, nanocapsules, nanoemulsions, nanocarriers, and nanocolloids, may be produced for use in tissue regeneration. Nanoparticles, nanospheres, nanocapsules, nanoemulsions, nanocarriers, and nanocolloids are only a few of the shapes that might be used to create nanomaterials for tissue regeneration. Nanoparticles (NPs) are widely utilized in wound treatment, with two primary categories: (1) NPs with inherent features that help wound closure, and (2) NPs used as delivery vectors for medicinal drugs. Nanomaterials are often classified into two groups, metallic and nonmetallic, as illustrated in Figure 3.

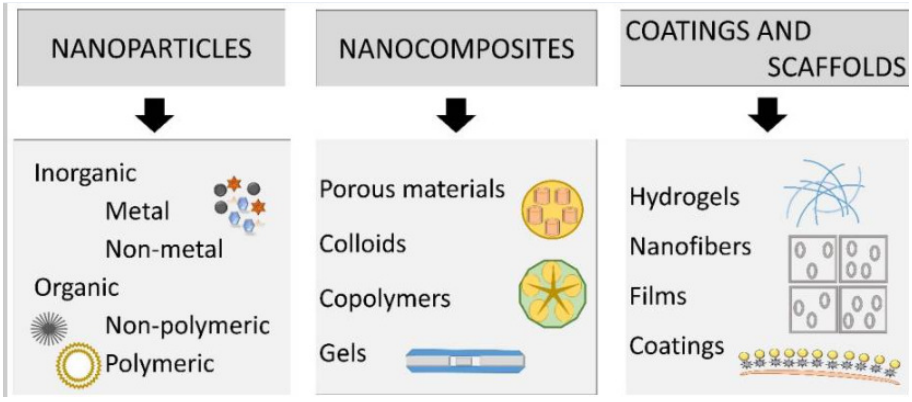


Figure 3: Shows The Primary Kinds Of Nanomaterials That May Be Utilized To Heal Wounds [16]**.**

Nanospheres are tiny polymeric matrix systems made up of a fixed porous polymer that may bind to active materials like amino acids, minerals, or chemical compounds. Nanoemulsions are homogenous, thermally stable oil-in-water emulsions with a maximum droplet size of 100 nm that also contain a surfactant and can conveniently integrate biologically active substances, preventing their sedimentation. As a result, active compounds become much more stable and exhibit enhanced biocompatibility and pharmaceutical properties. They also have a high capacity for solubilization, are fluid, and have a low viscosity. Their drawback would be the unchecked buildup of active ingredients in the subcutaneous fat or reticular dermis [17].

- *Silver Nanoparticles(AgNps):*

The antibacterial properties of silver have made it a popular choice for treating burns, open wounds, and many chronically infected wounds [18]. Indirect evidence for the importance of AgNPs and their antimicrobial action has been gathered from some research. When applied topically, AgNPs outperform control formulations in antibacterial effectiveness by interacting with proteins in bacterial membranes that contain sulfur and phosphorus. Even at low concentrations, AgNPs are more effective.Some strains of Staphylococcus aureus, Escherichia coli, and Bacillus subtilis, among other skin pathogens, are inhibited by AgNPs' antimicrobial.

- *Gold nanoparticles (AuNPs):*

Biologically active materials and cancer diagnostic agents, AuNPs show great promise. Based on the work of Leu et al. Evidence presented in [19] demonstrated that wound healing in mice was dramatically sped up when AuNPs were combined with substances high in antioxidants (epigallocatechin gallate and -lipoic acid). The topical administration of the product has been shown to hasten the healing of wounds in both healthy individuals and those with diabetes, thanks to the activating effects of anti-oxidant agents and AuNPs.Recent ex vivo permeation research has shown that AuNPs may be effective in the treatment of burns because they are transdermally active, promote healing, and prevent microbial colonization.

- *Zinc Oxide, Copper (Cu), and Titanium Dioxide (TiO_2) Nanoparticles:*

The skin bacteria that cause diabetic foot ulcers and burn wound infections are no match for CuNPs. Nanoparticles of TiO2 and ZnO are often utilized in sun protection and wound healing products in the cosmetics and pharmaceutical industries. Excision wound model evaluation of Origanum vulgare-containing TiO2 nanoparticles showed considerable wound healing activity.Inducing bacterial cell membrane perforations, zinc oxide nanoparticles (ZnONPs) is an effective antibacterial agent. Hydrogel-based wound dressings improve the total contact duration, which in turn encourages keratinocyte migration and betters re-epithelialization. Another recent research found that a microporous chitosan hydrogel/ZnONPs dressing had a high capacity for absorbing wound exudates, promoted the development of hemostatic blood clots, and showed antibacterial activities with low cytotoxicity.

Therefore, their use in wound healing therapy is restricted due to their inherent high toxicity. For instance, keratinocytes exposed to high levels of ZnONPs exhibit mitochondrial malfunction, leading to the secretion of lactate dehydrogenase. Furthermore, ZnONPs induce oxidative stress and death in human keratinocytes because they create reactive oxygen species and block the expression of superoxide dismutase and glutathione peroxidase genes. Furthermore, it has been reported that ZnONPs cause carcinogenic alterations.

3.1.Nanotechnology's Potential And Current Use In Skin Wound Healing:

Outstanding characteristics of electrospun nanofibers have made the process appealing for creating cutting-edge, multifunctional wound dressings and other medicinal materials. As a result, during the last 10 years, an increasing number of scholarly publications and patents have been published. Among the principal applicants for these published patents are multinational corporations like Dupont, 3M, and Procter & Gamble as well as illustrious universities like the University of Akron, the University of California, and the University of Columbia.Only a few businesses globally are now focused on manufacturing machinery and electrospun nanofibers. There are still issues to be solved about the affordability, homogeneity, and efficiency of mass manufacturing. Before additional effective treatments based on nanofibers for wounds can be created from this developing technology, regulatory concerns, and clinical studies must be completed.Additionally, there are several cutting-edge uses for nanoemulsions in the area of dermatology. The nanoemulsion system benefits from the tiny size of its droplets in several ways, including uniform skin dispersion, a large surface area, targeted and controlled drug release, occlusive qualities, and increased stability. Despite all these benefits, the majority of commercially available nanoemulsions are only used for aesthetic purposes.

4. CONCLUSION

Systems for delivering drugs using nanoparticles have excellent therapeutic potential for both biological and synthetic molecules. Although new drugs based on nanotechnology have shown promising results, the true therapeutic effects of nanomaterials must be carefully considered, assessed, and evaluated before being used in clinical settings. The objective of wound healing research, despite advancements in wound care, is full regeneration and restoration of skin structure and function with no, or minimum, scarring. Nanostructured scaffolds for skin regeneration, colloidal drug delivery systems including polymeric nanoparticles, micelles, nanoemulsions, liposomes, and cyclodextrins, and antibacterial inorganic nanoparticles are just a few of the possibilities made possible by recent breakthroughs in nanotechnology.Despite its acknowledged relevance, neither systematic research nor global guidelines on the toxicity and biocompatibility of nanoparticles have been developed. Researchers hope that more studies will be done on nanotechnology as an applied science. International criteria on their biocompatibility must be created to fully realize the revolutionary promise of nanoscale therapies in wound healing. Care for chronic wounds and ulcers is a global problem that demands a useful usage that is both safe and focused.

REFERENCES:

[1] B. M. Kuehn, “Chronic Wound Care Guidelines IssuedChronic Wound Care Guidelines Issued,” *JAMA J. Am. Med. Assoc.*, vol. 297, no. 9, p. 938, Mar. 2007, doi: 10.1001/jama.297.9.938.

[2] S. Chakrabarti, P. Chattopadhyay, J. Islam, S. Ray, P. S. Raju, and B. Mazumder, “Aspects of Nanomaterials in Wound Healing,” *Curr. Drug Deliv.*, vol. 16, no. 1, pp. 26–41, Nov. 2018, doi: 10.2174/1567201815666180918110134.

[3] S. Ellis, E. J. Lin, and D. Tartar, “Immunology of Wound Healing,” *Curr. Dermatol. Rep.*, vol. 7, no. 4, pp. 350–358, Dec. 2018, doi: 10.1007/s13671-018-0234-9.

[4] D. K. Chellappan, Y. Yenese, C. C. Wei, and G. Gupta, “Nanotechnology and Diabetic Wound Healing: A Review,” *Endocrine, Metab. Immune Disord. - Drug Targets*, vol. 17, no. 2, Sep. 2017, doi: 10.2174/1871530317666170421121202.

[5] S. F. Spampinato, G. I. Caruso, R. De Pasquale, M. A. Sortino, and S. Merlo, “The Treatment of Impaired Wound Healing in Diabetes: Looking among Old Drugs,” *Pharmaceuticals*, vol. 13, no. 4, p. 60, Apr. 2020, doi: 10.3390/ph13040060.

[6] M. Berthet, Y. Gauthier, C. Lacroix, B. Verrier, and C. Monge, "Nanoparticle-Based Dressing: The Future of Wound Treatment?," *Trends Biotechnol.*, vol. 35, no. 8, pp. 770–784, Aug. 2017, doi: 10.1016/j.tibtech.2017.05.005.

[7] M. Zhang, X. Qiao, W. Han, T. Jiang, F. Liu, and X. Zhao, "Alginate-chitosan oligosaccharide-ZnO composite hydrogel for accelerating wound healing," *Carbohydr. Polym.*, vol. 266, p. 118100, Aug. 2021, doi: 10.1016/j.carbpol.2021.118100.

[8] A. V. Zvyagin, X. Zhao, A. Gierden, W. Sanchez, J. A. Ross, and M. S. Roberts, "Imaging of zinc oxide nanoparticle penetration in human skin in vitro and in vivo," *J. Biomed. Opt.*, vol. 13, no. 6, p. 064031, 2008, doi: 10.1117/1.3041492.

[9] D. D. Evanoff and G. Chumanov, "Size-Controlled Synthesis of Nanoparticles. 2. Measurement of Extinction, Scattering, and Absorption Cross Sections," *J. Phys. Chem. B*, vol. 108, no. 37, pp. 13957–13962, Sep. 2004, doi: 10.1021/jp0475640.

[10] H. Ye, J. Cheng, and K. Yu, "In situ reduction of silver nanoparticles by gelatin to obtain porous silver nanoparticle/chitosan composites with enhanced antimicrobial and wound-healing activity," *Int. J. Biol. Macromol.*, vol. 121, pp. 633–642, Jan. 2019, doi: 10.1016/j.ijbiomac.2018.10.056.

[11] A. Clapp, "Potential clinical applications of quantum dots," *Int. J. Nanomedicine*, p. 151, Jun. 2008, doi: 10.2147/IJN.S614.

[12] S. Hamdan *et al.*, "Nanotechnology-Driven Therapeutic Interventions in Wound Healing: Potential Uses and Applications," *ACS Cent. Sci.*, vol. 3, no. 3, pp. 163–175, Mar. 2017, doi: 10.1021/acscentsci.6b00371.

[13] M. Rodrigues, N. Kosaric, C. A. Bonham, and G. C. Gurtner, "Wound Healing: A Cellular Perspective," *Physiol. Rev.*, vol. 99, no. 1, pp. 665–706, Jan. 2019, doi: 10.1152/physrev.00067.2017.

[14] T. Velnar, T. Bailey, and V. Smrkolj, "The Wound Healing Process: An Overview of the Cellular and Molecular Mechanisms," *J. Int. Med. Res.*, vol. 37, no. 5, pp. 1528–1542, Oct. 2009, doi: 10.1177/147323000903700531.

[15] S. Singh, A. Young, and C.-E. McNaught, "The physiology of wound healing," *Surg.*, vol. 35, no. 9, pp. 473–477, Sep. 2017, doi: 10.1016/j.mpsur.2017.06.004.

[16] A. Pormohammad, N. K. Monych, S. Ghosh, D. L. Turner, and R. J. Turner, "Nanomaterials in Wound Healing and Infection Control," *Antibiotics*, vol. 10, no. 5, p. 473, Apr. 2021, doi: 10.3390/antibiotics10050473.

[17] K. Niska, E. Zielinska, M. W. Radomski, and I. Inkielewicz-Stepniak, "Metal nanoparticles in dermatology and cosmetology: Interactions with human skin cells," *Chem. Biol. Interact.*, vol. 295, pp. 38–51, Nov. 2018, doi: 10.1016/j.cbi.2017.06.018.

[18] M. Rai, A. Yadav, and A. Gade, "Silver nanoparticles as a new generation of antimicrobials," *Biotechnol. Adv.*, vol. 27, no. 1, pp. 76–83, Jan. 2009, doi: 10.1016/j.biotechadv.2008.09.002.

[19] J.-G. Leu *et al.*, "The effects of gold nanoparticles in wound healing with antioxidant epigallocatechin gallate and α-lipoic acid," *Nanomedicine Nanotechnology, Biol. Med.*, vol. 8, no. 5, pp. 767–775, Jul. 2012, doi: 10.1016/j.nano.2011.08.013.

CHAPTER 2

AN ANALYSIS OF BLOCKCHAIN TECHNOLOGY'S APPLICATION IN HEALTHCARE

Dr. Sunita Rao, Assistant Professor,
Department of Biotechnology, Jaipur National University, Jaipur, India,
Email Id-sunita.rao@jnujaipur.ac.in

ABSTRACT: In this age of advanced technologies, blockchain technology has emerged over the last several years. Blockchain technology is attracting a lot of attention from the domains of finance, government, energy, health, and other industries. This research report offers a detailed examination of blockchain's applicability and efficacy in this newly developing area of health care. Researchers are eager to pursue the ongoing blockchain technology research that is emerging in this field very quickly.. This study provides a thorough overview of blockchain technology's use in the healthcare industry. In truth, the field's continuous study is advancing quickly. As a result, authors have found some current use cases for blockchain technology, including the sharing of electronic medical data, remote patient monitoring, medication supply chains, etc.The assessment also identifies the state-of-the-art blockchain application development for healthcare, as well as its shortcomings and potential future research topics. To further comprehend, define, and assess the usefulness of blockchain in healthcare, additional study is still required.

KEYWORDS: Healthcare, Blockchain, Blockchain Technology, Technologies.

1. INTRODUCTION

New technologies, such as the Internet of Things and big data, have aided in the building of a more advanced healthcare system all over the globe. Utilizing the Internet of things (IoT), data transmission, and exchange technologies to construct medical and health services and optimal management, "smart healthcare" is a medical system with medical cloud data at its core that combines the electronic medical record, electronic health archive, and the medical Internet of Things. Even though advancements have been made quickly in the field of smart healthcare, issues with data and network security persist. Blockchain is the foundational technology of the Fourth Industrial Revolution [1] because of its potential to be decentralized, anonymous, tamper-proof, and auditable [2].

As healthcare continues to embrace technology, huge amounts of patient information are being stored digitally. The need to secure healthcare information during transmission and usage has never been greater. Blockchain's emergence as a trustworthy and transparent data storage and distribution method has opened up exciting new possibilities for addressing healthcare's longstanding problems with patient data privacy, security, and integrity. Over the last several years, blockchain technology has received a great deal of interest from both businesses and academia. Every day, new blockchain-related use cases and academic studies are developed [3].

In the years since the Bitcoin white paper was released in October 2008 [4], blockchain has become more popular as a distributed ledger system. Because it is the technology behind Bitcoin, blockchain's primary benefit is that it allows users on a decentralized network to send and receive digital currency without relying on a central authority. Banks and other TTP

have long played an intermediary role in facilitating the transfer of digital currency between individuals and businesses. There are several reasons why a TTP shouldn't be relied on.There are three key parts to the healthcare system: (i) primary healthcare service providers, this includes healthcare providers (doctors, nurses, technicians, and administrators), (ii) emergency services, and (iii) patients (i.e., people who utilize these services) who are focused on health and wellness. This research project investigates the expansion of constituent service providers' technologically-based remote-control health maintenance to promote, protect, and recover beneficiaries' health [5].

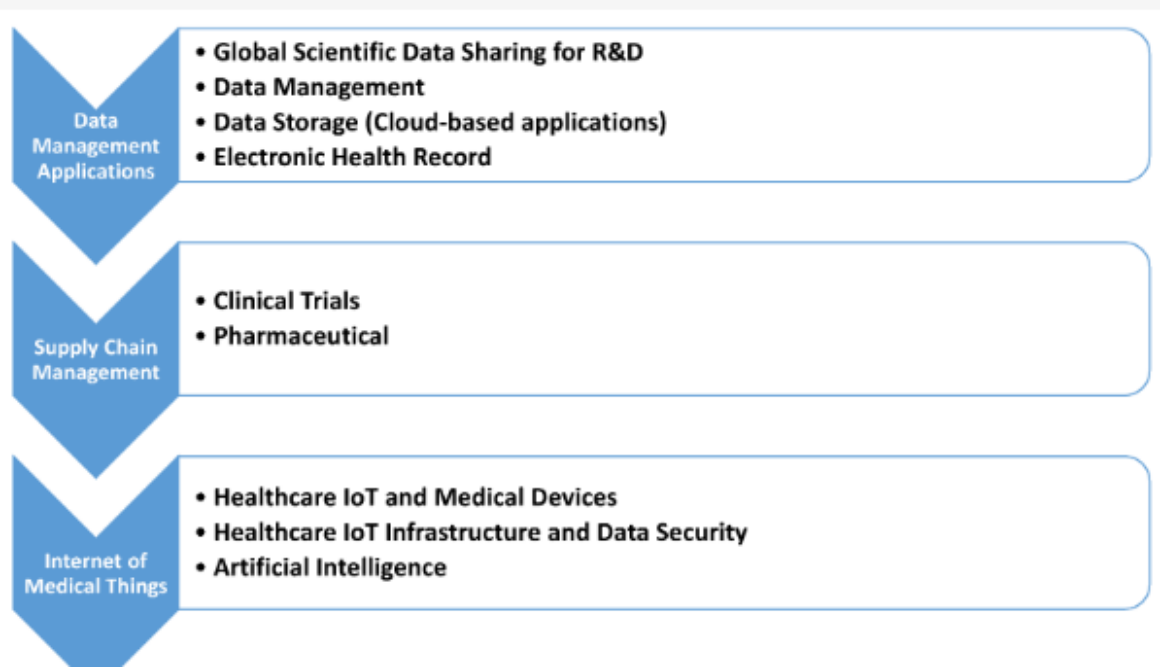


Figure 1: Displays The Applications In The Medical Industry Based On The Blockchain.

The following step, which comes after the platform has been produced via the use of blockchain technology, is to make certain that the apps are connected with the whole system. Three primary categories may be used to categorize blockchain-based healthcare applications. To begin, there is the issue of data management, which encompasses worldwide scientific data exchange for research and development (R&D), data administration, data storage (such as apps hosted in the cloud), and electronic health records (EHRs). The applications of SCM are the focus of the second class. This includes clinical trials and medications. In the third and final class, Internet of Medical Things (IoMT) topics is discussed. These topics include a convergence of healthcare IoT and medical devices, healthcare IoT infrastructure and data security, and AI. Applications of the blockchain in the healthcare industry are shown in Figure 1. Stakeholders, including business users, researchers, and patients, are included in this layer, which sits atop the hierarchy at the last and highest level. This layer is comprised of parties that stand to gain from blockchain-based healthcare applications. Users at this layer's primary concerns revolve on properly sharing, processing, and managing data without compromising the data's confidentiality or integrity in any way[6].

Patients throughout the world would be safer if there was a way to prevent the distribution of fake medications, and blockchain technology might make that a reality. Data storage, device connection, and internet of medical things security are just some of the healthcare use cases where blockchain technology is now being investigated (IoMT). The majority of the

stakeholders and end users—patients, caregivers, researchers, pharmaceutical firms, and insurance companies—reported an improvement in QoE as a result of the implementation of blockchain technology in the aforementioned application domains. To develop a more intelligent healthcare system and enhance the quality of healthcare services and the user experience, it is crucial to be able to exchange healthcare data without endangering users' privacy and data security. This study aims to give a current analysis of blockchain applications in healthcare, focusing on their effects on healthcare economics, quality of experience (QoE), and new business prospects.

2. LITERATURE REVIEW

The research by Deepa Elangovan et al. aimed to assess the feasibility of using blockchain technology in healthcare and to characterize existing blockchain-based studies. The authors of this study conducted a systematic review to compile relevant literature on the subject of blockchain technology's application in healthcare settings. PubMed, Springer Link, IEEE Xplore, Embase, Scopus, and EBSCO host were scoured for relevant articles. The 22 papers were subjected to a credibility and applicability evaluation to determine their overall quality as literature.Twenty-two articles passed the rigorous first review. The evidence was organized into a table, and the findings from the chosen publications were discussed. An evaluation of the publications' quality was obtained and scored results were interpreted. In a total of 22 publications, 3 were deemed to be of excellent quality (14%), 9 were deemed to be of moderate level (41%), and 10 were deemed to be of poor quality (45%). The results may provide the scientific community with a better grasp of the blockchain's practical implications. The findings of this research contribute to an understanding of blockchain technology's applicability and use in the healthcare industry.

To assess how people with diabetes feel about current permission procedures and the Dovetail blockchain-based digital consent application, George Despotou et al. performed research. Diabetic patients at a family doctor's office were enlisted. The researchers used questionnaires and focus groups to compile their data. Both the focus group transcripts and the questionnaires were subjected to thematic analysis and descriptive statistics.Few patients had any idea how permission was obtained or documented, and many could not recall ever having provided it. Patients were generally positive about the digital consent application, citing its usefulness for its unique capabilities. People who used the digital consent app were more likely to be satisfied than those who used the traditional method.Patients mostly approve of digital consent since it improves upon the present approach in key respects. Suggestions were heard about how things might be better. Confirmation of results in a larger demographic sample and across multiple conditions is an area where future research needs to focus [7].

Pouyan Esmaeilzadeh and Tala Mirzaei conducted a study by researchers who devised 16 information exchange scenarios for controlled Web-based studies to better understand the possible uses of blockchain technology in healthcare practices from the perspective of healthcare consumers. There were a total of 16 online surveys conducted with 2013 participants. There were two categories of health information exchanged (sensitive and nonsensitive) and four types of exchange methods (direct, lookup, patient-centered, and blockchain) outlined in each trial (weak vs strong).The results reveal that patients' impressions of different exchange channels vary in terms of privacy concerns, faith in competence and integrity, opt-in intention, and readiness to give information. Participants embrace blockchain-based trading methods for privacy, coordination, and information sharing. This research explored the blockchain's possibilities and limits in HIE.This work

may add to blockchain research and HIE blockchain literature. Practitioners may use blockchain to promote HIE nationally [8].

According to Saurabh Rahurkar et al., they examined 27 scientific publications, collected key features from each, and conducted a meta-analysis of these characteristics to look for patterns in how HIE has influenced healthcare indicators including cost, service utilization, and quality. In all, 57 percent of studies that were published noted some advantages of Health information exchange (HIE). However, studies using randomized controlled trials or quasi-experiments, which have high internal validity, were much less likely than others to link HIE with advantages. Six publications with high internal consistency found no impact, two claimed advantages from HIE, one reported paradoxical negative effects, and three found no effect. These two studies also had more constrained objectives than the others. Overall, there isn't much data that can be generalized about the advantages of HIE yet [9].

3. DISCUSSION

The data is kept on a decentralized node network called a blockchain. It is a great piece of technology for keeping system-wide private data safe. Important data may be sent using this technology while maintaining its confidentiality and security. It is the ideal solution for securely storing all relevant papers in one place. Using a single patient database, blockchain also expedites the search for candidates who meet particular trial requirements. The Blockchain is a decentralized peer-to-peer (P2P) network of nodes or individual computers that maintain, saves, and records transaction or historical data.Since all participants in the network share and preserve data, as well as keep track of previous and present experiences, the network facilitates trustworthy cooperation. Using this technology, formerly separate networks may be brought together to better understand the significance of each patient's care. Because of this, Blockchain has earned a reputation for being both secure and immutable. The core concepts of Blockchain are blocks, nodes, and miners. With blockchain, information is not stored in a central repository. Instead, the Blockchain is replicated and disseminated throughout a network of computers. As soon as a new block is added to the Blockchain, the Blockchain on every computer in the world is automatically updated. The fundamental processes of Blockchain technology are shown in Figure 2 [10].

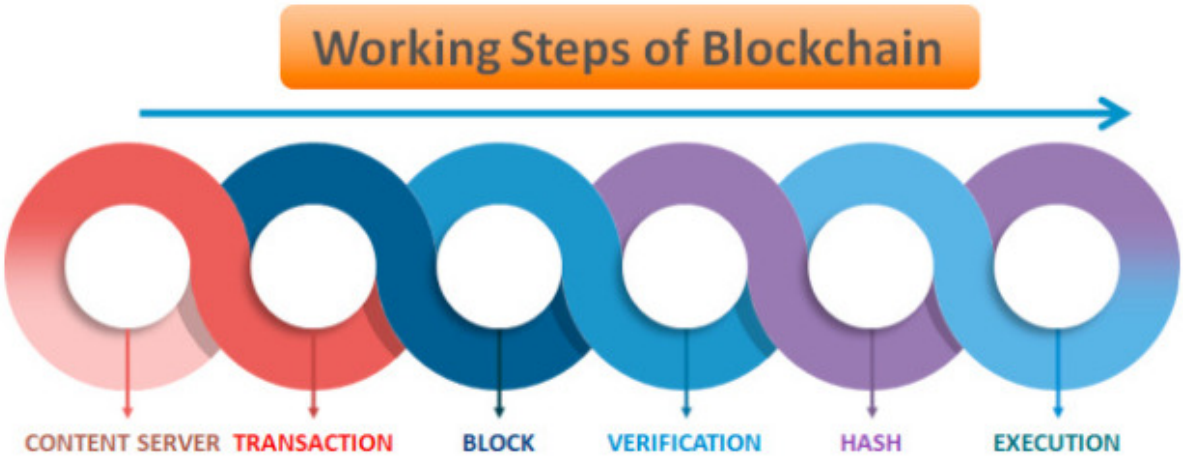


Figure 2: Displays the stages involved in the operation of Blockchain Technology [11]**.**

3.1.Applications in Healthcare Using Blockchain:

Healthcare research has been a hot topic for decades, and scientists are still looking for better, more efficient solutions to improve people's health and the healthcare system overall. Health

records must be organized, accessed, and shared in a safe and interoperable manner by a wide range of stakeholders (practitioners, medical experts, hospitals, therapists, patients, payers, etc.). Data provenance is also critical for establishing the credibility of data. The healthcare industry has some pressing problems, and blockchain technology can solve them. However, a more concentrated study is required before this technology may be deployed in real-time applications.

Figure 3: A flowchart of apps based on the blockchain that is used in healthcare [12]**.**

The use of blockchain technology is changing data modeling and governance in a variety of applications within the healthcare industry. This is mostly attributable to its versatility as well as its segment capabilities, protect, and exchange medical data and services in a manner that has never been seen before. The use of blockchain technology lies at the heart of many of the most recent breakthroughs in the medical sector. Data sources, blockchain technology, healthcare applications, and stakeholders are the four layers that make up the conceptual structure of emerging blockchain-based healthcare systems. A process based on a blockchain is shown here in Figure 3, which highlights its use in the healthcare industry.

In the beginning, all the data from medical devices, labs, social media, and many other places is put together to make raw data, which then grew to become big data. This data is the most important part of the blockchain-based healthcare system as a whole, and it is the main part that makes up the first layer of the stack. Blockchain technology sits on top of the raw data layer, which is considered the core framework for creating a four-part, secure healthcare architecture. Consensus algorithms and protocols are different for each blockchain platform [13].

- *Electronic Medical Records(EMR):*

Health data management, which might benefit from the opportunity to link disparate systems and boost Electronic Health Record (EHR) accuracy, should be prioritized in the quest to

revolutionize healthcare. While EHRs and EMRs may seem synonymous, there is a distinct distinction between the two. First arose the phrase "electronic medical records," which refers to electronic versions of traditionally paper-based medical charts. All of a clinic's patients' medical records are kept in one place in an electronic medical record. But EHRs take a far wider picture of a patient's treatment than just the traditional clinical data gathered in a provider's office.Better health data management, made possible by the opportunity to link disparate systems and improve the precision of Electronic Health Records (EHRs), is a key factor in bringing about a fundamental shift in healthcare delivery. While EHRs and EMRs may seem synonymous, there is a distinct distinction between the two. First arose the phrase "electronic medical records," which refers to electronic versions of traditionally paper-based medical charts. All of a clinic's patients' medical records are kept in one place in an electronic medical record. In contrast, electronic health records (EHRs) consider the whole patient, not just the information gathered in a doctor's office [14].

- *Remote Patient Monitoring:*

Remote patient monitoring encompasses the collecting of medical data using mobile devices, body area sensors, and IoT (Internet of Things) devices to remotely monitor the patient's state. Blockchain technology is vital for the safekeeping, dissemination, and retrieval of remotely gathered biological data. Ichikawa et al. [15] offer a use case in which mobile devices send information to a blockchain application running on Hyperledger Fabric.

3.2.Blockchain technology enablers for revitalizing healthcare services:

The blockchain has the potential to improve healthcare by expanding the field of view and fostering growth in the industry as a whole. Blockchain techniques in healthcare and its core areas are being researched and investigated by some affiliated industrial/medical-care supporters or providers. There are just a few companies actively providing and advocating for the use of Blockchain technology at the ground level, and they go by names like BurstIQ, Guardtime, Robomed, Simply vital, Encrypgen, Chronicled, Tieion, etc [16].Medical professionals at different facilities will need to create new patient data cards as part of the blockchain implementation. It's a serious fault of the health system when newly added information is redundant and causes time loss. Depending on their position in the supply chain, people may have varying levels of access and privileges. Additionally, a hash would be created linking any block holding the medical information to another block.

Clinical trials are now being undertaken in the medical field to determine how well these medicines work in treating or alleviating the symptoms of a certain condition. Results from tests, participant counts, patient histories, and other information may all be recorded for future reference by scientists. Clinical trial data has to be verified for scientists, pharmaceutical companies, and politicians to trust the findings. More trustworthiness and traceability in clinical trials may be possible with the use of Blockchain technology. Given that the blocks are made accessible to physicians and patients, and that medical history is processed with an awareness of patient concerns, the health care Blockchain has great record-keeping potential. With its widespread use in the supply chain, blockchain is a natural match for the healthcare industry, particularly the distribution of medications [17].

4. CONCLUSION

Since its introduction to the world via Bitcoin, blockchain technology has matured into a general-purpose technology with applications across many sectors, including healthcare. Our evaluation, which used the systematic mapping study approach to construct a map of all relevant studies, shed light on where things are with the use of blockchain technology in

healthcare. The study set out to do a few things: identify the healthcare use cases for blockchain technology, the applications that have been built to support those use cases as examples, the difficulties and restrictions of blockchain-based healthcare applications, the methods currently used to create such applications, and potential avenues for future study.

REFERENCES:

[1] M. H. Miraz and D. C. Donald, "Application of Blockchain in Booking and Registration Systems of Securities Exchanges," in *2018 International Conference on Computing, Electronics & Communications Engineering (iCCECE)*, IEEE, Aug. 2018, pp. 35–40. doi: 10.1109/iCCECOME.2018.8658726.

[2] Z. Zheng, S. Xie, H. N. Dai, X. Chen, and H. Wang, "Blockchain challenges and opportunities: a survey," *Int. J. Web Grid Serv.*, vol. 14, no. 4, p. 352, 2018, doi: 10.1504/IJWGS.2018.095647.

[3] H. Min, "Blockchain technology for enhancing supply chain resilience," *Bus. Horiz.*, vol. 62, no. 1, pp. 35–45, Jan. 2019, doi: 10.1016/j.bushor.2018.08.012.

[4] S. Squarepants, "Bitcoin: A Peer-to-Peer Electronic Cash System," *SSRN Electron. J.*, 2008, doi: 10.2139/ssrn.3977007.

[5] S. A. Talesh, "Data Breach, Privacy, and Cyber Insurance: How Insurance Companies Act as 'Compliance Managers' for Businesses," *Law Soc. Inq.*, vol. 43, no. 02, pp. 417–440, Dec. 2018, doi: 10.1111/lsi.12303.

[6] D. V. Dimitrov, "Blockchain Applications for Healthcare Data Management," *Healthc. Inform. Res.*, vol. 25, no. 1, p. 51, 2019, doi: 10.4258/hir.2019.25.1.51.

[7] G. Despotou, J. Evans, W. Nash, A. Eavis, T. Robbins, and T. N. Arvanitis, "Evaluation of patient perception towards dynamic health data sharing using blockchain based digital consent with the Dovetail digital consent application: A cross sectional exploratory study," *Digit. Heal.*, vol. 6, p. 205520762092494, Jan. 2020, doi: 10.1177/2055207620924949.

[8] P. Esmaeilzadeh and T. Mirzaei, "The Potential of Blockchain Technology for Health Information Exchange: Experimental Study From Patients' Perspectives," *J. Med. Internet Res.*, vol. 21, no. 6, p. e14184, Jun. 2019, doi: 10.2196/14184.

[9] S. Rahurkar, J. R. Vest, and N. Menachemi, "Despite The Spread Of Health Information Exchange, There Is Little Evidence Of Its Impact On Cost, Use, And Quality Of Care," *Health Aff.*, vol. 34, no. 3, pp. 477–483, Mar. 2015, doi: 10.1377/hlthaff.2014.0729.

[10] X. Yue, H. Wang, D. Jin, M. Li, and W. Jiang, "Healthcare Data Gateways: Found Healthcare Intelligence on Blockchain with Novel Privacy Risk Control," *J. Med. Syst.*, vol. 40, no. 10, p. 218, Oct. 2016, doi: 10.1007/s10916-016-0574-6.

[11] U. Padmavathi and N. Rajagopalan, "A Research on impact of Blockchain in Healthcare," *Int. J. Innov. Technol. Explor. Eng.*, vol. 8, no. 9S2, pp. 35–40, Aug. 2019, doi: 10.35940/ijitee.I1007.0789S219.

[12] S. Khezr, M. Moniruzzaman, A. Yassine, and R. Benlamri, "Blockchain Technology in Healthcare: A Comprehensive Review and Directions for Future Research," *Appl. Sci.*, vol. 9, no. 9, p. 1736, Apr. 2019, doi: 10.3390/app9091736.

[13] C. Saraf and S. Sabadra, "Blockchain platforms: A compendium," in *2018 IEEE International Conference on Innovative Research and Development (ICIRD)*, IEEE, May 2018, pp. 1–6. doi: 10.1109/ICIRD.2018.8376323.

[14] T. Ahram, A. Sargolzaei, S. Sargolzaei, J. Daniels, and B. Amaba, "Blockchain technology innovations," in *2017 IEEE Technology & Engineering Management Conference (TEMSCON)*, IEEE, Jun. 2017, pp. 137–141. doi: 10.1109/TEMSCON.2017.7998367.

[15] D. Ichikawa, M. Kashiyama, and T. Ueno, "Tamper-Resistant Mobile Health Using Blockchain Technology," *JMIR mHealth uHealth*, vol. 5, no. 7, p. e111, Jul. 2017, doi: 10.2196/mhealth.7938.

[16] R. Kumar, N. Marchang, and R. Tripathi, "Distributed Off-Chain Storage of Patient Diagnostic Reports in Healthcare System Using IPFS and Blockchain," in *2020 International Conference on COMmunication Systems & NETworkS (COMSNETS)*, IEEE, Jan. 2020, pp. 1–5. doi: 10.1109/COMSNETS48256.2020.9027313.

[17] I. A. Omar, R. Jayaraman, M. S. Debe, K. Salah, I. Yaqoob, and M. Omar, "Automating Procurement Contracts in the Healthcare Supply Chain Using Blockchain Smart Contracts," *IEEE Access*, vol. 9, pp. 37397–37409, 2021, doi: 10.1109/ACCESS.2021.3062471.

CHAPTER 3

AN INVESTIGATION PHARMACOLOGICAL PROPERTIES OF *WITHANIA SOMNIFERA*

Dr. Manish Soni, Assistant Professor,
Department of Biotechnology, Jaipur National University, Jaipur, India,
Email Id-manishsoni@jnujaipur.ac.in

ABSTRACT: Withania somnifera is a medicinal plant that grows all over the world, from the Atlantic Ocean to South East Asia, as well as from Mediterranean region to South Africa. Traditional medicine practitioners regularly use medicinal plants in their everyday practice to treat a wide range of diseases. Withania somnifera, popularly known as Ashwagandha in Hindi, is a tiny plant found all throughout India. It has long been used as an liver tonic, anti-inflammatory agent,aphrodisiac, and astringent, as well as a cure for bronchitis, asthma, emaciation, sleeplessness, senile dementia, ulcers, and other ailments. As a stress-related adaptation for patients with nervous weariness, sleeplessness, and weakness as well as an immunological stimulant for those with low blood levels of white blood cells, ashwagandha is also utilized therapeutically. In a group of substances known as withanolides, steroidal alkaloids as well as steroidal lactones make up the majority of the ashwagandha root's biochemical components. The literature was specifically searched for studies discussing toxicity, therapeutic advantages, or chemical features. This study goal is to evaluate the research on the plant Withania somnifera, often known as ashwagandha, which is frequently used in Ayurvedic treatment. In the future this study will aware the people about various medicinal importance of Withania Somnifera.

KEYWORDS: Anti-inflammatory, Diseases, Herb, Medicinal, Withania Somnifera.

1. INTRODUCTION

One of the most significant sources of medications in the world is plants. Many of the medications that are currently prescribed come from plants, such as morphine from eugenol from Ocimum sanctum, atropine from Atropa belladonna, ephedrine from Ephedra vulgaris, Papaver somniferum, and respin from Roulphia serpentina, among others. The therapeutically significant secondary metabolites or essential oils are abundant in the medicinal plants. In addition to being affordable, efficient, and readily available, medicinal plants' major benefits for therapeutic usage in treating various illnesses include safety. Due to these benefits, traditional medical practitioners frequently employ medicinal plants in their daily practices.

Withania somnifera, commonly referred to as Indian ginseng or Indian Winter Cherry, is a significant ancient plant whose roots have been used in Ayurveda and Unani, two of the oldest medical systems in India as shown in Figure 1. The primary Ashwagandha-producing states in the nation include Madhya Pradesh, Haryana, Maharashtra, Rajasthan, Gujarat, Punjab, and Uttar Pradesh. Given that India produces more than 1500 tonnes of ashwagandha roots year and that the country needs over 7000 tonnes annually, more of the herb must be cultivated [1]. The Ayurvedic or indigenous medicinal systems have employed ashwagandha, also known as Indian ginseng as well as winter cherry, as a useful herb for over 4,000 years. The berry's roots, leaves, and fruits are incredibly valuable as medicines. Commonly sold as a churna, or finely sieved powder that may be combined with water, ghee or honey, ashwagandha is a well-known herb. It helps memory and the way the brain or nervous system work. It promotes a healthy reproduction and sexual balance by enhancing

the reproductive system's functionality. Due to its potent adaptogenic properties, it increases the body's resistance to stress. Ashwagandha enhances cell-mediated immunity, which strengthens the body's resistance to illness [2], [3]. Additionally, it has strong antioxidant qualities that help prevent cellular damage brought on by free radicals. Indian medicinal plants have been successfully used in traditional medical systems to treat a variety of disease conditions, including bronchial asthma, cold, malaria, dysentery, cough, convulsions, diarrhea, arthritis, diabetes, emetic syndrome, insect bites, skin diseases, etc. as well as disorders of the gastrointestinal, cardiovascular, hepatic, or immune systems.

Figure 1: Illustrating the pictorial representation of Withania Somnifera (Ashwagandha), a) plant, b) Fruit, c) Flower.

1.1. Withania Somnifera as a Medical Herb:

One of the most effective revitalizing ingredients in Ayurveda is ashwagandha. Ayurvedic and Unani treatments make use of the plant's roots, seeds, and leaves. The medicine made from the ashwagandha root has a significant role in the management of epilepsy, neurological diseases, and joint or rheumatic pain. Dried roots are utilized as a sedative, to treat senile debility, ulcers, and other conditions as well as a tonic for hiccups, colds, coughs, and feminine diseases. Carbuncles, irritation, and edema are treated with leaves [4], [5]. Conjunctivitis can benefit from leaf juice. For bed sores as well as asthma, bark decoction is administered topically. Its extracts and ashwagandha are used to make herbal tea, powders, pills, and syrups. Ashwagandha possesses characteristics that include anti-inflammatory, anti-stress, anti-tumor, antioxidant, immune-boosting, or rejuvenating. Sex-enhancing qualities have also been linked to ashwagandha root. The ancient Kama Sutra refers to ashwagandha as a plant that may be used to enhance sexual enjoyment. Ashwagandha has the power to promote general vitality, including sexual health, as well as foster a peaceful state of mind. According to a laboratory experiment conducted in 2002, ashwagandha promotes the formation of both dendrites and axons. According to a 2001 research on rats, ashwagandha can improve memory [6], [7].

Ashwagandha was found to have anti-depressive and anti-anxiety properties in a 2000 mouse research. The herb has historically been used to treat ulcers, sleeplessness, asthma, and senile dementia as well as a liver tonic, aphrodisiac, and anti-inflammatory. Ashwagandha is effective for treating inflammation, anxiety, Parkinson's disease, or neurological and cognitive impairments, according to human and animal studies. The consumption of ashwagandha may stop or slow the growth of cancers in people. For a variety of health issues including aging, anemia and poor development, arthritis, weariness, failing memory, sports

fitness, and stress problems, it aids in delivering gradual, long-lasting improvements [7], [8]. Figure 2 as hows the Ashwagandha has been shown to have antitumor, anti-stress, antioxidant, hemopoeitic, and rejuvenating activities in pharmacological investigations or research to date. It is also a superb nerve tonic that feeds the nerves and enhances nerve performance to keep calm under pressure. Additionally, it supports the vital mind-body link and psychological immune system.

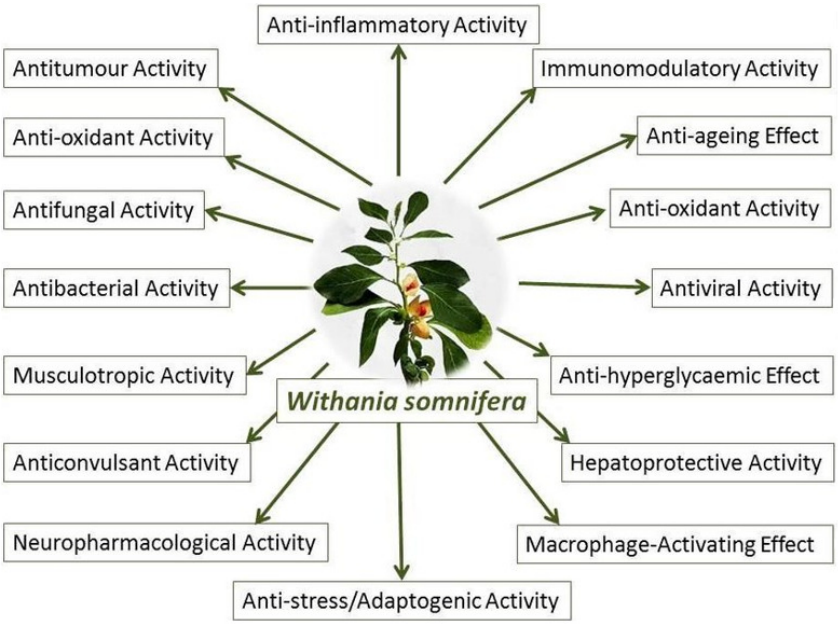


Figure 2: Illustrate the Pharmacological activities of Ashwagandha (W. somnifera).

Ayurvedic medicine in India frequently uses the plant Withania somnifera Dunal. It has been of tremendous interest to researchers due to its pharmacological usefulness and endless source of new physiologically active chemicals. Anti-inflammatory, immunomodulatory, anti-stress, antioxidant, and hemopoetic activities of the plant are well documented. The steroidal lactones known as withanolides, which were isolated from W. somnifera, were recognized to have a great therapeutic value. The species has been divided into several chemotypes according to differences in the substitutions patterns of withanolides. In this paper author discussed about various medicinal benefits of Ashwagandha.

2. LITERATURE REVIEW

M. Umadevi et al. studied about the Withania somnifera is used medicinally. It has sedative, diuretic, and anti-inflammatory properties, is well-known for boosting endurance and energy levels and functions as an adaptogen with potent immunostimulatory or anti-stress effects. It has a substantially greater steroidal content than hydrocortisone, a typical therapy for cancer. Due to Ashwagandha's potent immunostimulatory properties, diseases includes TB, chronic upper respiratory illnesses, or HIV have been added to the variety of ailments it can treat. It is also known as a blood tonic, particularly in cases of gynecological problems like anemia or irregular menstruation. Ashwagandha has additional benefits for those with anxiety [9].

Kaur Narinderpal et al. studied about medicinal use use of Withania somnifera. Ashwagandha, also known as Withania somnifera, is an herb that has been utilized in traditional Indian medicine since the time of Ayurveda. The plant's dried roots are used to treat neurological and sexual issues. According to studies, ashwagandha has anti-

inflammatory, anticancer, anti-parkinsonian, memory enhancing, adaptogen, antioxidant, anxiolytic activities. There have also been studies on a number of other effects, including immunomodulation, hypolipidemia, antimicrobial, cardiovascular protection, sexual behavior, tolerance, and dependency. These results are quite positive and indicate that further research should be done on this herb to support these findings and uncover other potential medicinal properties [10].

Vikas Kumar et al. studied about Withania somnifera pharmacology and chemistry. It is employed as a tonic in the conventional Indian medical system to promote lifespan and bodily renewal. Various plant components have been utilized in Ayurvedic medicines to treat a wide range of illnesses that have an impact on human health. Furthermore, the plant's dried roots are commonly used to diagnose sexual or psychological diseases. Withanolides, one of this plant's main active chemical components, are in charge of a variety of its biological functions. These pharmacological investigations were conducted to describe the ways in which they prevent illness [11].

Jinu John studied about Ashwagandha, or Withania somnifera, is a member of the Solanaceae family. By regulating the endocrine, cardiac, central nervous system, but also sexual behavior without causing any harm, ashwagandha demonstrates a wide spectrum of therapeutic qualities. The root has already been used most commonly for medicinal purposes as well as being a component of more than 200 Ayurvedic, Siddha, or Unani medicinal formulations. This paper provides a thorough overview of Withania somnifera's diverse traditional applications, phytochemical makeup, and pharmacological qualities. These traits are a result of the plant's distinctive bioactive phytochemicals, including alkaloids or phytosterols [12].

3. DISCUSSION

A database search on PubMed, Google Scholar, Research Gate, Science Direct, and other sites was used to conduct the current review study. Combining keywords like “Anti-inflammatory, Diseases, Herb, Medicinal, Withania Somnifera” were used in the review technique. Title and abstract screening were used for the records preliminary review. Additionally, non-extractable data, duplicate research, and inadequate information were grounds for excluding the Records. Figure 3 below provides more information on the methodology utilized to conduct the review study

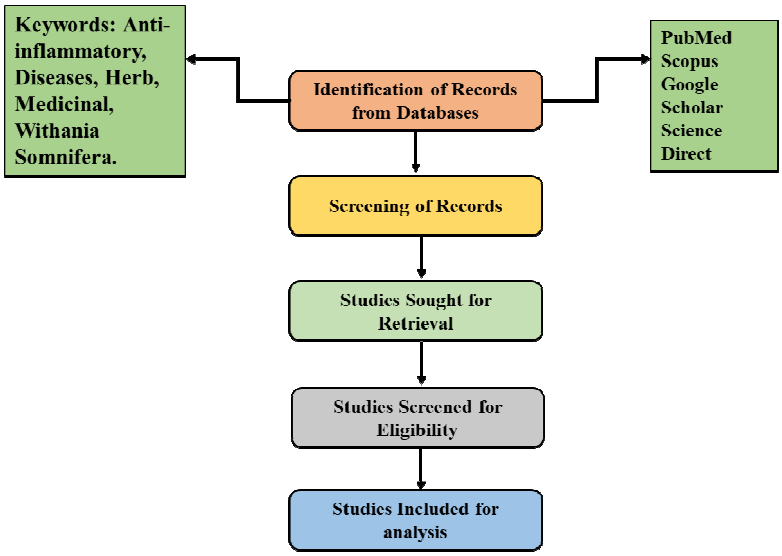


Figure 3: Illustrate the Design of Methodology of Current Review Work.

3.1. Uses for Withania Somnifera in Medicine:

One of the main botanical ingredients of geriatric tonics described in Indian system of medicine is Withania somnifera. According to the ancient medical system Ayurveda, this plant has strong aphrodisiac, rejuvenative, and life-extension effects. It is used, among other things, to treat nervous weariness, memory-related disorders, sleeplessness, tiredness potency troubles, skin problems, or coughing. It also has general animating or even regenerating properties. It enhances memory and learning capability. Ashwagandha has traditionally been used to boost vitality, young vigor, strength, endurance, health, nourish the time elements of the body, and stimulate the production of muscle fat, semen, vital fluids, blood, lymph, and cells [13], [14]. It aids in reducing muscular tension, chronic tiredness, weakness, dehydration, bone deterioration, loose teeth, thirst, impotence, early aging, debility, or emaciation. Similar to how a tree gets revitalized by feeding the roots, it aids in reviving the reproductive organs in the body.

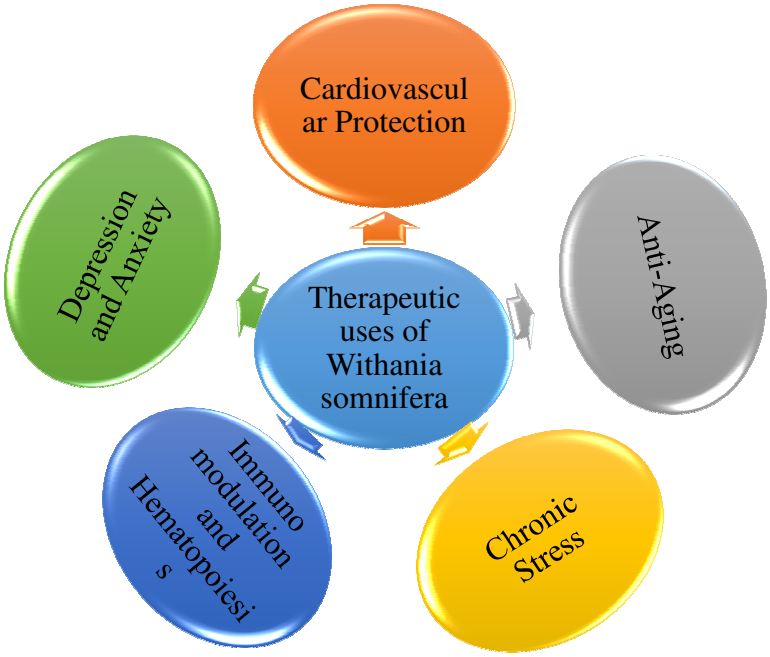


Figure 2: Illustrate the Therapeutic Use of Withania Somnifera (Ashwagandha).

3.1.1. Hematopoiesis and Immunomodulation.

Ashwagandha acts as an immunoregulator as well as a chemoprotective agent, and a number of animal studies have demonstrated that it has major impacts on the hematopoietic system. Administration of an ashwagandha root powder extract was observed to increase the overall white blood cell count in a mouse research. Additionally, as compared to a control group, this extract reduced delayed-type hypersensitivity responses and increased macrophage phagocytic activity [15].

A plausible explanation for the enhanced cytotoxicity of macrophages exposed to W. somnifera extracts has been suggested by recent study. It has been discovered that nitric oxide has a major impact on macrophage cytotoxicity against microbes and tumor cells. According to Iuvone et al, withania somnifera has grown. No production in a concentration-dependent way in mouse macrophages. Inductive nitric oxide synthase, an enzyme produced in response to proinflammatory cytokines or known to suppress the development of numerous

pathogens, was thought to be responsible for this impact. Ashwagandha shows the ability to inhibit tumor growth by stimulating the development of cytotoxic T cells both in vitro and in vivo. In comparison to the control group, a substantial reduction in incidence and the average number of skin lesions was seen. In addition, injection of the extract caused levels of reduced glutathione, catalase, superoxide dismutase, or glutathione reductase in the exposed tissue to restore to almost normal levels [16], [17].

3.1.2. Cardiovascular Safety:

Ashwagandha root's hypoglycemic, hypocholesterolemic and diuretic, properties were studied in humans. For 30 days, a powder extract was administered to six people with type 2 diabetes and six people who had mild hypercholesterolemia. Blood glucose levels were shown to drop in a manner like those of an oral hypoglycemic medication. Significant rises in urine salt and volume as well as falls in serum triglycerides, lipoproteins, low-density and lipids were also seen.

3.1.3. Anti-Aging:

Ashwagandha was examined in a double-blind clinical research on 101 healthy guys between the ages of 50 and 59 who took 3 grams per day for a whole year. Hemoglobin, hair melanin, red blood cell count, and sitting stature all showed considerable improvement. Nail calcium was retained while serum cholesterol fell. Significantly less erythrocyte sedimentation occurred, and 71.4 percent of people reported improved sexual performance.

3.1.4. Long-Term Stress:

Chronic stress (CS) can cause a variety of harmful physiological conditions, such as changes in plasma corticosterone levels, sexual dysfunction, immunosuppression, stomach ulcers, or cognitive deficits. Withania somnifera as well as Panax ginseng extracts were tested for their capacity to mitigate the consequences of chronic stress in a rat model. Both plants were able to lessen the frequency and severity of ulcers brought on by CS, undo the suppression of male sexual activity brought on by CS, and prevent the negative effects of CS on memory retention. CS-induced immunosuppression was likewise reversed by both plants, but only the Withania extract led to an increase in peritoneal macrophage activity in the rats [18]. The Panax ginseng extract and the Withania extract both had about the same amount of activity. Moreover, Withania somnifera differs from Panax ginseng in that it does not seem to cause ginseng misuse syndrome, which is characterized by increased blood pressure, muscular tension, water retention, and sleeplessness.

3.1.5. Anxiety and Depression:

An extract of the root was given orally to rats once daily for five days as part of a study comparing the anxiolytic or antidepressive effects of ashwagandha to those of frequently prescribed medications. The outcomes were contrasted with those of a group given the benzodiazepine lorazepam for anxiolytic activity as well as the tricyclic antidepressant imipramine for an inquiry into antidepressants. Both the lorazepam and ashwagandha groups showed decreased levels of a clinical anxiety marker in the brain. In the forced swim-induced behavioral despair or learned helplessness tests, ashwagandha also demonstrated an antidepressant effect equivalent to that caused by imipramine. These findings, supported by previous research, support the utilization of ashwagandha as a stress-reduction adaptogen. According to studies, ashwagandha is useful for treating conditions including inflammation, stroke, osteoarthritis, or tardive dyskinesia. Ashwagandha has been shown in studies to have

antifungal and mild antibacterial properties against Escherichia coli and Pseudomonas aeruginosa, respectively.

Due to its numerous pharmacological actions, such as its anti-stress, antitumor, neuroprotective, anti-arthritic, anti-inflammatory and analgesic, properties, Ashwagandha is indeed a real potent regenerative tonic (Rasayana of Ayurveda). This conclusion is supported by the scientific data that is currently available. It is beneficial for treating a variety of illnesses, including Parkinson's, memory loss, dementia, disorders brought on by stress, malignancies, as well as others. Indians utilize ashwagandha as a common home treatment because they believe it to be the ideal tonic for children and the elderly, as well as a potent aphrodisiac. It is one of Ayurveda's greatest nervine tonics, the oldest branch of medicine [19]. Our clinical experience has demonstrated that, in addition to the neurological diseases listed above, brain strokes that result in paralysis and neuronal deficiency also get better with continued Ashwagandha use. Additionally, we use it to treat many types of cancer, include lung or prostate tumors, especially in their latter stages, providing the patients with several health advantages. Humans have several lung cancer instances that have rejected conventional treatment and have responded well to our Ashwagandha therapy clinically as well as radiologically. It was envisioned as one of the six critical medicinal herbs at a recent symposium on the notion of essential drugs. Thus, it is abundantly obvious from the aforementioned studies that Ashwagandha's traditional uses have both a scientific and logical basis. Large-scale clinical investigations are required to demonstrate the effectiveness of this plant, particularly in the treatment of cancer, neurological disorders, and illnesses associated with stress.

One of the best cancer treatment options is chemotherapy. But the main problems with standard chemotherapy are cancer recurrence, making chemotherapeutic agents worthwhile, cost, late-stage detection, negative health effects, and accessibility. Therefore, there is a critical need for novel, inexpensive drugs that can target multiple gene products with very few side effects. A large fraction of potential therapeutic drugs are natural phytochemicals derived from plants. In this research, we investigated the development and prospects of anticancer or immunomodulatory chemicals from Withania somnifera (WS). Preclinical research has suggested that WS may be able to stop or delay the spread of cancer in a number of different organs, including the liver, brain, cervix, breast, colon, lung, skin, and prostate. The best effectiveness against medication resistance in cancer is provided by WS extracts, which act through a variety of routes. Durability, bioavailability, or target specificity, however, are significant barriers to combination treatment and have restricted their use. The cutting-edge nanotechnology methods enable solubility, absorption, stability, protection from early deterioration in the body, and prolonged circulation duration, which inevitably leads to a high differentiated created to facilitate in the phytochemical's target tissue.

4. CONCLUSION

The applications of herbal remedies grow together with contemporary medicine. Withania somnifera has a lot of promise as a secure and efficient immunomodulator and hematopoietic growth factor. The ability of Withania somnifera to reproduce this action in people and the ideal dose range for producing these effects both require more investigation. The potential therapeutic benefits of withania in conditions including anxiety, Parkinson's disease, or cognitive and neurological impairments. Utilizing the herb Withania somnifera, skilled practitioners of natural medicine might improve effectiveness and lessen adverse effects of conventional therapies while collaborating with oncologists. Due to the vastly different methodologies used in each study, no statistical pooling of outcomes or assessment of the quality of something like the studies was carried out. Instead, this review is narrative in

nature and includes all publications pertinent to ashwagandha that the authors were able to locate through a thorough search of significant computerized medical databases.

According to studies, ashwagandha has qualities that include hemopoietic, anti-inflammatory, anticancer, anti-stress, immunomodulatory, or antioxidant. The endocrine, cardiovascular, and central neurological systems also seem to benefit from it. Humans still don't completely understand how these qualities work. According to toxicology tests, ashwagandha looks to be a safe substance. According to preliminary investigations, different ashwagandha components show a range of therapeutic benefits with little to no related harm. This plant should be further evaluated in order to validate these findings and elucidate further possible therapeutic properties, according to these extremely positive results. Additionally, ashwagandha clinical trials for a range of ailments should be carried out. Studies addressing toxicity, therapeutic benefits, or chemical characteristics were explicitly sought out in the literature. The purpose of this study is to assess the literature on the Withania somnifera plant, also referred to as ashwagandha and utilized extensively in Ayurvedic medicine. This study will raise public awareness about Withania Somnifera's numerous medical benefits in the future.

REFERENCES:

[1] R. Dutta, R. Khalil, R. Green, S. S. Mohapatra, and S. Mohapatra, "Withania somnifera (Ashwagandha) and withaferin a: Potential in integrative oncology," *International Journal of Molecular Sciences*, vol. 20, no. 21. 2019. doi: 10.3390/ijms20215310.

[2] F. Mehmood, Abdullah, I. Shahzadi, I. Ahmed, M. T. Waheed, and B. Mirza, "Characterization of Withania somnifera chloroplast genome and its comparison with other selected species of Solanaceae," *Genomics*, vol. 112, no. 2, pp. 1522–1530, 2020, doi: 10.1016/j.ygeno.2019.08.024.

[3] S. Paul *et al.*, "Withania somnifera (L.) Dunal (Ashwagandha): A comprehensive review on ethnopharmacology, pharmacotherapeutics, biomedicinal and toxicological aspects," *Biomedicine and Pharmacotherapy*, vol. 143. p. 112175, Nov. 2021. doi: 10.1016/j.biopha.2021.112175.

[4] Q. X. Ng *et al.*, "A systematic review of the clinical use of Withania somnifera (Ashwagandha) to ameliorate cognitive dysfunction," *Phytotherapy Research*, vol. 34, no. 3. pp. 583–590, 2020. doi: 10.1002/ptr.6552.

[5] P. K. Mukherjee, S. Banerjee, S. Biswas, B. Das, A. Kar, and C. K. Katiyar, "Withania somnifera (L.) Dunal - Modern perspectives of an ancient Rasayana from Ayurveda," *J. Ethnopharmacol.*, vol. 264, p. 113157, Jan. 2021, doi: 10.1016/j.jep.2020.113157.

[6] B. Ganguly, M. Mrigesh, P. Chauhan, and S. K. Rastogi, "Dietary supplementation with Withania somnifera root powder ameliorates experimentally induced Infectious Bursal Disease in chicken," *Trop. Anim. Health Prod.*, vol. 52, no. 3, pp. 1195–1206, 2020, doi: 10.1007/s11250-019-02104-9.

[7] P. Sengupta, A. Agarwal, M. Pogrebetskaya, S. Roychoudhury, D. Durairajanayagam, and R. Henkel, "Role of Withania somnifera (Ashwagandha) in the management of male infertility," *Reproductive BioMedicine Online*, vol. 36, no. 3. pp. 311–326, 2018. doi: 10.1016/j.rbmo.2017.11.007.

[8] N. Singh *et al.*, "Review on anticancerous therapeutic potential of Withania somnifera (L.) Dunal," *Journal of Ethnopharmacology*. 2021. doi: 10.1016/j.jep.2020.113704.

[9] K. P. S. Kumar, D. Bhowmik, S. Duraivel, and M. Umadevi, "Traditional and Medicinal Uses of Banana," vol. 1, no. 3, pp. 51–63, 2012.

[10] K. Narinderpal, N. Junaid, and B. Raman, "Research and Reviews□: Journal of Botanical Sciences A Review on Pharmacological Profile of Withania somnifera (Ashwagandha).," *Res. Rev. J. Bot. Sci.*, vol. 2, no. 4, pp. 6–14, 2013.

[11] V. Kumar, A. Dey, M. B. Hadimani, T. Marcovic, and M. Emerald, "Chemistry and pharmacology of withania somnifera: An update," *TANG [HUMANITAS Med.*, vol. 5, no. 1, pp. 1.1-1.13, 2015, doi: 10.5667/tang.2014.0030.

[12] J. J., "Therapeutic potential of Withania somnifera: A report on phyto-pharmacological properties," *Int. J. Pharm. Sci. Res.*, vol. 5, no. 6, pp. 2131–2148, 2014, doi: 10.13040/IJPSR.0975-8232.5(6).2131-48.

[13] T. Kuboyama, C. Tohda, and K. Komatsu, "Effects of Ashwagandha (Roots of Withania somnifera) on neurodegenerative diseases," *Biological and Pharmaceutical Bulletin*, vol. 37, no. 6. pp. 892–897, 2014. doi: 10.1248/bpb.b14-00022.

[14] M. K. Tripathi, P. Singh, S. Sharma, T. P. Singh, A. S. Ethayathulla, and P. Kaur, "Identification of bioactive molecule from Withania somnifera (Ashwagandha) as SARS-CoV-2 main protease inhibitor," *J. Biomol. Struct. Dyn.*, vol. 39, no. 15, pp. 5668–5681, Oct. 2021, doi: 10.1080/07391102.2020.1790425.

[15] B. M. Biswal, S. A. Sulaiman, H. C. Ismail, H. Zakaria, and K. I. Musa, "Effect of withania somnifera (Ashwagandha) on the development of chemotherapy-induced fatigue and quality of life in breast cancer patients," *Integr. Cancer Ther.*, vol. 12, no. 4, pp. 312–322, 2013, doi: 10.1177/1534735412464551.

[16] N. J. Dar, A. Hamid, and M. Ahmad, "Pharmacologic overview of Withania somnifera, the Indian Ginseng," *Cellular and Molecular Life Sciences*, vol. 72, no. 23. pp. 4445–4460, 2015. doi: 10.1007/s00018-015-2012-1.

[17] T. Iguchi, M. Kuroda, M. Ishihara, H. Sakagami, and Y. Mimaki, "Steroidal constituents isolated from the seeds of Withania somnifera," *Nat. Prod. Res.*, vol. 35, no. 13, pp. 2205–2210, 2021, doi: 10.1080/14786419.2019.1667351.

[18] N. G. Dumore, M. J. Umekar, B. G. Taksande, M. M. Aglawe, and N. R. Kotagale, "Effects of Withania somnifera nicotine induced conditioned place preference in mice," *Pharmacogn. J.*, vol. 11, no. 1, pp. 43–47, 2019, doi: 10.5530/pj.2019.1.8.

[19] V. Alagesan and S. Venugopal, "Green Synthesis of Selenium Nanoparticle Using Leaves Extract of Withania somnifera and Its Biological Applications and Photocatalytic Activities," *Bionanoscience*, vol. 9, no. 1, pp. 105–116, Mar. 2019, doi: 10.1007/s12668-018-0566-8.

CHAPTER 4

AN EVALUATION OF BIO-FORTIFICATION TECHNIQUES FOR MICRONUTRIENT IMPROVEMENT IN CROP PLANTS

Prof. Kapilesh Jadhav, Professor,
Department of Biotechnology, Jaipur National University, Jaipur, India,
Email Id-kapilesh@jnujaipur.ac.in

ABSTRACT:A practical, affordable method of providing micronutrients to communities who may not have easy access to a variety of supplements, diets, or professionally fortified foods is bio-fortification, the procedure of breeding nutrients into food crops. Minerals fertilization or plant breeding are two methods that may be used to bio-fortify or enhance the number of micronutrients in the edible sections of plants. In certain nations that used selenium-containing fertilizers as a temporary fix to increase wheat's selenium content, bio-fortification by mineral fertilization is a widespread technique. a lack of micronutrients Significant populations are affected by nutritional shortages from standards for important elements including zinc, iron, vitamin B_{12}, vitamin A, or iodine, yet bio-fortification is too organic, cost-effective, and lucrative to completely eradicate starvation. It is a food-based strategy, and prior study has shown that it dramatically raises nutritional levels. The main objective of learns more about the various strategies of Bio-fortification for crop improvement. In the Future this paper will aware people of the importance of Bio-fortification for crop improvement.

KEYWORDS:Agriculture,Bio-fortification, Crop Improvement, Genetic Engineering, Nutritional, Micronutrient, Vitamin.

1. INTRODUCTION

Breeding practices are adopted to improve the level of nutritional values among crops plant products, especially higher concentrations of micronutrients or their precursors, is known as bio-fortification. Instead of increasing the nutritional density of crops after food processing, bio-fortification tries to do so during plant development. A procedure known as bio-fortification seeks to improve the nutritional content of crops. This may be accomplished using both traditional selective breeding and genetic engineering. Bio-fortification focuses on making fruits and vegetables more nutrient-rich while they are developing, as opposed to standard fortification, which adds nutrients to meals after they have been digested [1], [2]. This is a major advance over traditional fortification in terms of supplying nutrients to the rural poor, who rarely have access to truly economically treated food. Therefore, treating micronutrient deficiencies in low- or middle-income countries with bio-fortification is viewed as a novel approach. Since the advent of agriculture thousands of years ago, people have modified crops to produce desired traits. Traditional breeding, however, necessitates multiple generations and is ineffective in enhancing a single quality. Precision technologies, like genetic engineering or genome engineering, could speed up the genetic improvement or add rice qualities that would be difficult to significantly enhance through conventional breeding [3], [4].

2. LITERATURE REVIEW

The Bio-fortification Plan recommends that all family members regularly consume the recommended daily amounts of dietary staples, with a focus on women and children who are

most at risk for nutritional deficiencies. This method indirectly targets low-income households due to the prevalence of dietary staples in the diets of the poor. Recurring expenses are modest when an initial investment is made to produce seed that can support itself, although germplasm may very well be shared internationally. The cost-effectiveness of plant breeding in time and area is due to this multiplier effect [5], [6]. Once established, bio-fortified cropping systems are highly sustainable. Even if government funding or interest in micronutrients wanes, however, varieties with enhanced nutrition will continue to be planted and eaten year after year. Furthermore, bio-fortification provides a practical way to feed malnourished individuals in remote rural areas who have little access to the commercially promoted fortified foods that are more widely available in metropolitan areas.

Up until recently, improving crop production or grain output has been our agricultural system's top priority rather than protecting human health. Due to this method, dietary grains now contain far fewer micronutrients than they once did, which has worsened consumer micronutrient deficiency [7], [8]. Agriculture is currently shifting from producing adequate nutrient-rich crops to growing more food crops in larger numbers. This would help fight "micronutrient malnutrition" or hidden hunger, especially in developing and impoverished countries where the majority of the basic foods consumed are deficient in micronutrients.

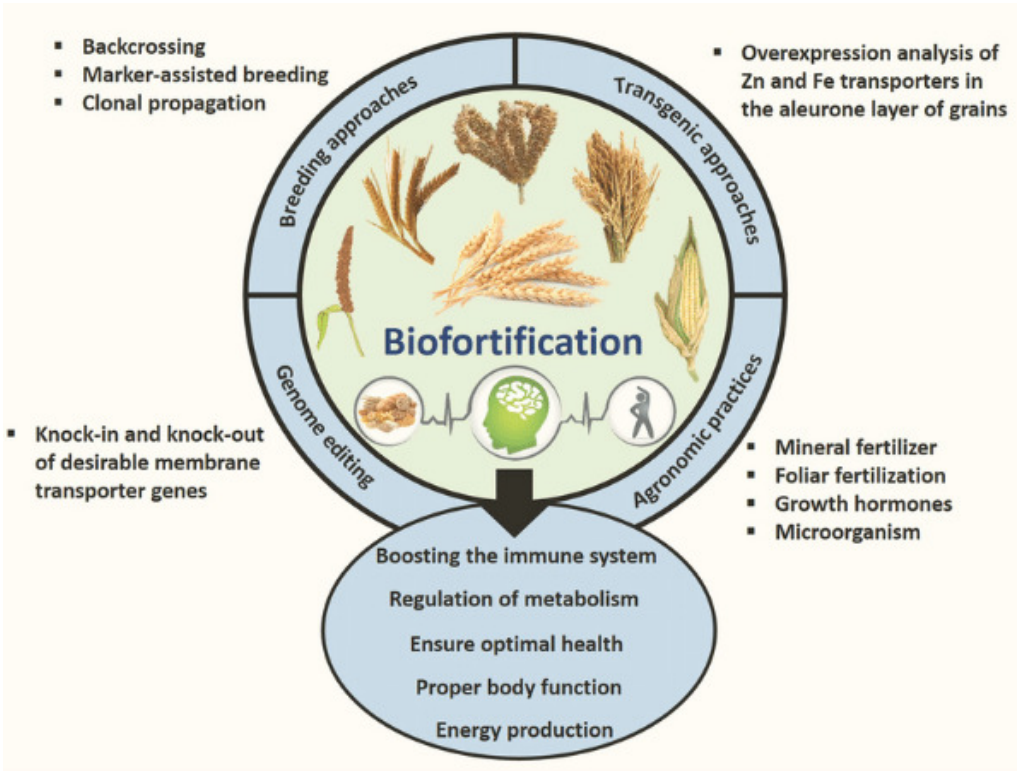


Figure 1: Techniques used for bio-fortification of agricultural plants [9]**.**

As seen in Figure 1, successful bio-fortification strategies include genome editing, plant breeding, agronomic methods, and transgenic technology. By boosting the expression of Iron and Zinc transporters in crop plants, it is possible to fortify Zn and Fe to edible grains using the transgenic approach. Through backcrossing, marker-assisted breeding, clonal propagation, as well as other methods, the breeding process also aids in the production of crop varieties that are bio-fortified. Foliar sprays of Zn or Fe-based fertilizer, microscopic organism bio-fertilizer, and delivery of appropriate fertilizer and growth hormone dosages are all agronomic strategies that can assist enhance Zn or Fe bioavailability in crop related products. [10].

Enhancing food crops nutritional value can be achieved through bio-fortification. Other methods like Agronomic techniques, traditional breeding, gene manipulation and genome editing are frequently used to enrich nutritional value of crop related products. Bio-fortification is also known as "biological fortification and can described as nutrient-improved food crops with a better bioavailability to humans by utilizing contemporary biotechnological techniques, traditional plant breeding and agronomic practices. [11], [12]. Around 792.6 million people worldwide suffer from malnutrition, 780 million of them are in developing countries, as reported by the “United Nations Food and Agriculture Organization”. In addition, despite increasing food crop output, almost two billion people globally experience hidden hunger, which would be characterized by an inadequate intake of essential micronutrients daily. In addition, concerns about over nutrition are growing.

To combat micronutrient deficiencies, emerging economies are also contemplating or committing to food fortification methods. The major objectives of the “Food Fortification Program” (FFP) as well as the “Global Alliance for Improving Nutrition” (GAIN) initiatives, both of which have been launched in Pakistan, are to fortify wheat flour as well as an edible oil with micronutrients. Generating adequate nutrient-rich food is the goal of bio-fortification. Various methods are used to fortify food nowadays. Several techniques can be used to fortify food. Figure 2 illustrates the most prevalent strategies, which are further examined below.

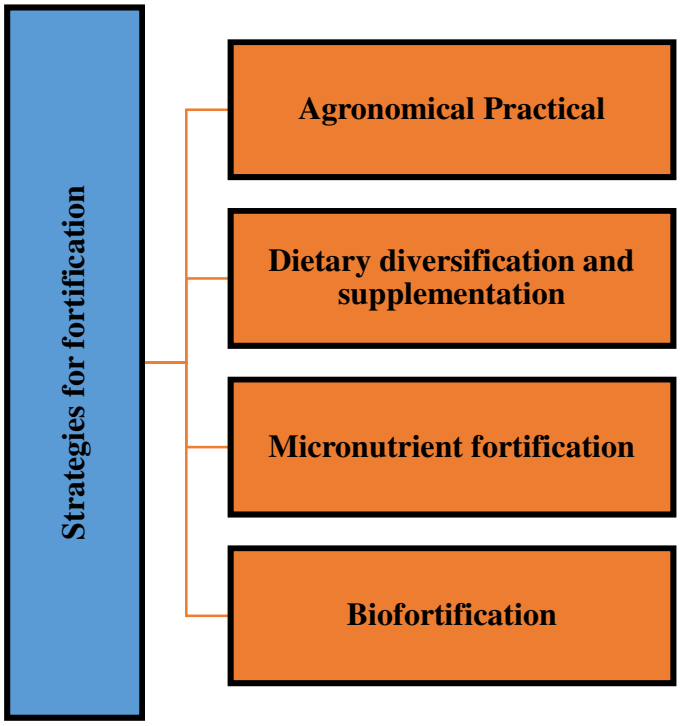


Figure 2: Methods of Micronutrient Enhancement through Food Fortification.

2.1. Using Micronutrients to Fortify:

The technique of adding one or more vitamins to everyday consumer goods including milk, cereals, oil, as well as sauces is known as micronutrient fortification. Additionally, it is possible to massively fortify goods consumed by a specific group, including common items such as wheat flour as well as edible oil, along with additional food for displaced persons or young children. Particular fortification Food producers can also increase the quality of products that are offered in open markets. Products made from wheat were fortified by

adding a variety of micronutrients, such as zinc, riboflavin, and iron. The meal is provided the nutrients in its best form to maintain its appearance, consistency, or flavor.

The ultimate objective of bio-fortification is to produce adequate quantities of safe, wholesome meals that are produced sustainably. The 3 fundamental technologies for bio-fortifying essential micronutrients in crop plants are three different methods: transgenic, conventional, and agronomic. These methods employ biotechnology, fertilization methods, or crop breeding, respectively. In Figure 3, it is shown that common food crops including rice, wheat, sorghum, maize, lupins, sweet potatoes, common beans, potatoes, and tomatoes make up the majority of crops targeted by conventional breeding, agronomic techniques, and transgenic techniques. Transgenic methods have targeted more crops, while breeding techniques have increased the practical application of bio-fortification [11], [12].

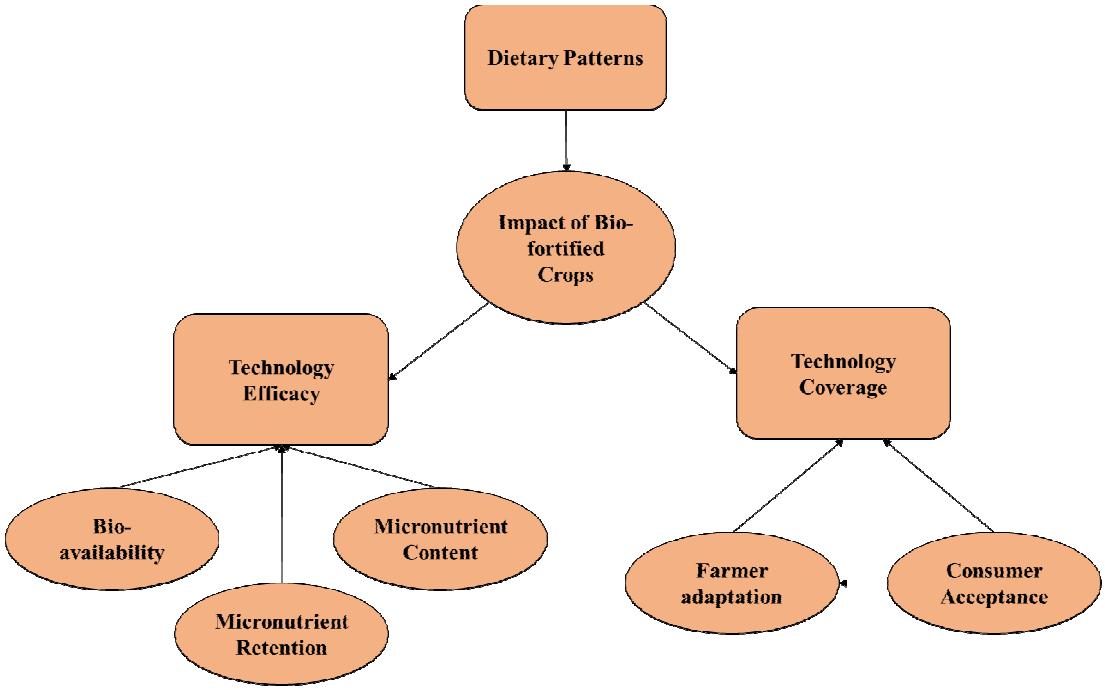


Figure 3: Illustrate Factors Affecting How Bio-fortified Crops Perform.

The elements that will determine the future effects of Bio-fortified crops might or might not assist improve nutritional and health conditions in underdeveloped countries, depending on the circumstances of each situation. Local eating patterns, technology efficacy, or technological coverage are important variables affecting the effects in a certain environment. The agricultural species to be targeted must be determined by local eating habits. Only when the crop in issue is a significant local staple food that is routinely consumed in reasonably big amounts can bio-fortification be effective [13], [14]. As a result, the optimum crop selection may differ by area. The quantity of the micronutrient in the crops, its retention after processing, as well as its bioavailability will all affect how effective the technology is. Coverage, which is measured as the proportion of bio-fortified varieties in the total amounts of the crop consumed, is primarily influenced by farmer adoption and consumer acceptability.

In many countries, the bulk of the undernourished lives in these more distant areas. When production surpluses are sold, bio-fortified crops provide a rural-based therapy that, by design, reaches these groups before spreading to urban populations. As a result, bio-fortification initiatives complement fortification or supplementation efforts, which are most effective in concentrated metropolitan areas before expanding into rural regions with adequate infrastructure. As adaptive bio-fortified cultivars become broadly accessible in

nations over time at low recurrent costs, initial expenditures in agricultural research at a central site can provide significant recurring advantages at a cheap cost [15], [16].

Phool Chand Meena *et al.* studied both traditional and contemporary breeding techniques, it is possible to use a genetic variety to improve the concentration of micronutrients. Increasing the mineral content of crops while also raising their bioavailability by lowering anti-nutritional chemicals and/or increasing concentrations of mineral absorption boosters is the most promising strategy for successfully treating micronutrient deficits. To stimulate farmers' production of them as well, eventually, their utilization by end users, it will be necessary to solve several socioeconomic as well as sociopolitical difficulties to successfully battle hidden hunger [17].

Matin Qaim *et al.* studied about monetary aspects of bio-fortification. In many poor nations, micronutrient malnutrition is a severe public health issue. Various therapies are now in use, although their total reach is somewhat constrained. A novel agriculture-based strategy called bio-fortification, which entails developing staple food crops for greater micronutrient levels, is yet mostly unexplored. Here, the key determinants of success are examined, and a technique for evaluating the economic effect is provided. Ex-ante studies from India and other nations indicate that bio-fortified crops, when aimed at certain circumstances, might minimize the issue of micronutrient deficiency cost-effectively. Additional investigation is required to confirm these findings and address several unsolved difficulties [18].

Joana Diaz-Gomez *et al.* studied regarding nutrient bio-fortification of crops. Food fortification involves the synthesis or absorption of nutrients by plants at the source, in contrast to traditional fortification using synthetic chemicals. In terms of nutritional bioavailability or bio-accessibility, it is unknown how important synthetic fortification is alongside bio-fortification. What matters most is the nutrient's biochemical composition, which can affect how effectively various nutrients are transported, stored, and utilized through the blood. This may result in an increase or decrease in absorption. Current knowledge of nutrient utilization and absorption is reviewed, along with recent studies on nutrient transfer from bio-fortified crops and the effects of food processing, storage, or matrix [19].

3. DISCUSSION

3.1. Iodine-boosting Techniques using Transgenic Plants:

Iodine supplementation in sodium chloride is a common way to avoid iodine deficiency, but bio-fortification of plants with iodine, which is more ecologically and financially feasible than other fortification techniques, is a better way to prevent mineral malnutrition. Scientists have successfully supplemented basic crops with micronutrients like zinc, iron, or folate in recent years. Published research state that recombinant DNA technology has not yet been used to bio-fortify iodine in crops. This is due to the paucity of studies on iodine physiology in plants. Iodine is assumed to pass through hypothesized H+/halides transporters but also anion channels to reach the cell membrane of root cells. Such transporter molecules have not yet been identified, though. The process of iodine volatilization from above-ground plant components like the root or leaf is more well-known in some species. Various Techniques for Vegetable Bio fortification those shown in Figure 4.

3.2. The following are key benefits of bio-fortification:

3.2.1. Getting to the hungry in remote areas:

The micronutrient-dense feature is intended to be included in as many released varieties as is practical, as well as the most lucrative, highest-yielding variety aimed at farmers. Additionally, these crops' marketing surpluses find their way into retail establishments, where they are purchased by customers in both rural and urban locations.

3.2.2. Affordability and low cost:

Recurrent expenses are modest when a one-time investment is made to create seeds that can bolster themselves, or germplasm might well be exchanged worldwide. The cost-effectiveness of plant breeding is due to this multiplier effect that occurs over time and space.

3.2.3. Behavior Modification:

In milled rice, 5–10 parts per million of the physical mass of the seed is made up of mineral micronutrients. So many more as 100 parts per million may be present in dense bean seeds. It is necessary to research if such minute amounts will change how meals look, taste, or are prepared. Consumers may not notice the higher mineral and vitamin densities, therefore the trace mineral distribution approach may be based on already-established producer and consumer behavior.

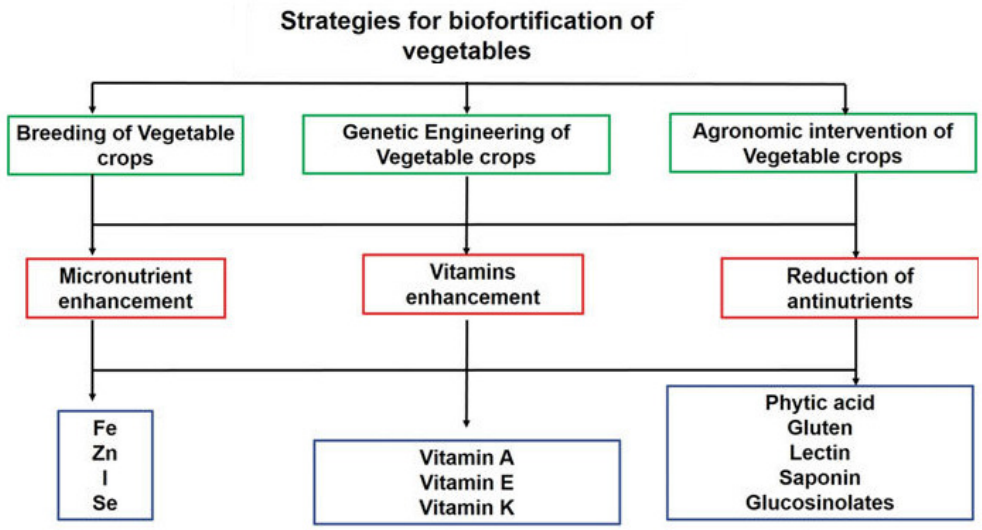


Figure 4: Strategies for the Bio-fortification of Vegetables.

3.3. A sustainable Bio fortification Strategy:

Bio-fortified farming systems are extremely sustainable. The development and use of nutritionally superior varieties will continue, even if the issue of micronutrients receives less government attention or international funding. Relies on the physiological (mineral) or biosynthetic (vitamin) capabilities of the plant; policy changes or inadequate financing have no impact.Strong new studies that assess the effectiveness of bio-fortified crops for a wider variety of genders and age groups, including newborns, and over a longer period, such as before conception throughout infancy, are areas that require additional investigation. Other research will look at the efficacy of consuming a range of bio-fortified crops, each of which enriches the food supply with a distinct set of vitamins or minerals. Nutritionists agree that bio-fortified crops may help people that are deficient in micronutrients, but more study is needed to properly understand how eating bio-fortified foods may affect one's health. Other, more acute biochemical markers should be used in this study in addition to functional indications [20], [21].

3.4. Current methods for Preventing Malnutrition:

Having a balanced diet high in micronutrients is the greatest strategy to avoid and even completely eradicate micronutrient deficiency. Malnutrition and micronutrient deficiencies can be treated in a variety of ways, including food fortification, supplementation, farmstead food production, or bio-fortification of crops. The most practical method of reducing vitamin deficiencies in individuals is food fortification with micronutrients. With food fortification, an approach to close the nutrition gap, significant portions of the population can receive nutrients without having to drastically alter their eating habits.

A long-standing practice, fortification of butter, margarine, or sugar with vitamin A, salt with iodine, milk with vitamins, and cereals with vitamin B is already being used in various nations. It has been effectively used for decades throughout the world. Mandatory food fortification is more effective than voluntary fortification. Fortification of milk and oil is required in 14 and 27 nations, respectively. Similarly to this, iodine and fluoride fortification of salt is required in 134 nations. Currently, 83 nations make use of fortification laws to supplement basic foods with micronutrients. However, there are still issues with the ways that food is currently fortified. Food fortification is often only possible in nations with sophisticated food and pharmaceutical processing industries that are effectively controlled and supervised. The fact that supplementation or fortification methods involve recurring expenditures every year and rely on financing is another significant disadvantage.

This strategy is particularly successful in nations where the poorest citizens typically supplement their meals with modest amounts of processed food. However, consumption of industrial applications processed foods is sadly very low in the world's most underdeveloped nations, where the bulk of the poor, particularly the agricultural population, depend on their products for nourishment. The impact of these food fortification initiatives may thus be rather limited, particularly in developing nations' rural regions, where the majority of the world's poor reside. In India, the mandatory fortification was first introduced in 1953 when vitamins A and D were added to hydrogenated vegetable oil. To reduce goiter, salt fortification by iodization was used later, in 1998. Wheat flour fortification began in West Bengal in 2000, then moved to the Andaman and Nicobar Islands.

Micronutrient deficits in industrialized civilizations are treated through supplements and fortification. The broad implementation of dietary diversification or dietary fortification/supplementation programs, however, is hampered in developing nations by low-income levels as well as the inadequate market access of both the target population. However, none of these methods stemming from socioeconomic development can effectively combat micronutrient deficiency. Additionally, for the aforementioned tactics to be successful, society's behavior must change. This requires literacy, communications, social marketing, or sustained commitment.

The combined experience of many researchers has shown that preventing nutrient deficiencies requires a combination of different cost-effective alternatives rather than a single more expensive alternative. Therefore, plant scientists are focusing on developing methods for applying fertilizers or using plant breeding strategies to improve the bioavailability of essential minerals in the nutrient content of crop plants to address the occurrence of nutritional deficiencies in modern humans. Levels of bioavailability can be increased. These methods are called agronomic, which depends on fertilization, or genetic, which depends on breeding.

To increase the number of micronutrients in agricultural products, a technique known as bio-fortification is used. This technique includes tactics to target and improve circulation routes

root uptake, remobilization, transport, and storage as well as increased bioavailability of mineral nutrients or nutrients from the soil. In the functional portions of plants, they are present in their bioavailable forms. Genetic engineering, conventional plant breeding, and agronomic bio-fortification are the three main approaches used to date to bio-fortify food crops. The primary goals of the agronomical approach are to enhance the solubility or mobility of mineral elements in the soil or optimize the use of mineral fertilizers. By reducing anti-nutrient concentrations, the latter two strategies aim to generate and/or enhance plant cultivars with improved micronutrient accumulation capability and higher levels of their bioavailability. In this paper author discussed about importance of bio-fortification to improve the nutrient value of crops.

4. CONCLUSION

An emerging, promising, affordable, and sustainable method of providing micronutrients to something like a population with limited access to varied meals as well as other micronutrient therapies is bio-fortification. Main food crops, however, are poor suppliers of the micronutrients necessary for healthy human growth. Three basic methods transgenic, conventional, or agronomic involve the use of such biotech, crop breeding, or fertilization techniques, respectively, to bio-fortify vital micronutrients into crops. When risk-free options are available with the advantages demonstrated, political issues shouldn't stand in the way of human efforts to liberate “polyvinyl alcohol” (PVA) crops. However, even if transgenic PVA crops were effective at preventing “Vitamin A Deficiency” (VAD), if a full proactive plan wasn't put in place to take into consideration those important consequences, political limitations would be difficult to reach market shelves from research facilities. It is a food-based approach, and earlier research has demonstrated that it significantly boosts nutritional levels. Understanding the various methods of bio-fortification for crop development is the major goal. This study may provide a platform for designer food through bio-fortification technique for further research.

REFERENCES:

[1] A. Homayouni Rad, A. Yari Khosroushahi, M. Khalili, and S. Jafarzadeh, “Folate bio-fortification of yoghurt and fermented milk: a review,” *Dairy Science and Technology*, vol. 96, no. 4. pp. 427–441, Jul. 23, 2016. doi: 10.1007/s13594-016-0286-1.

[2] B. Loedolff, “Diversification of health-promoting phytochemicals in radish (Raphanus raphanistrum) and kale (Brassica oleracea) micro-greens using high light bio-fortification,” *Funct. Foods Heal. Dis.*, vol. 10, no. 2, p. 65, Feb. 2020, doi: 10.31989/ffhd.v10i2.681.

[3] R. Chomchan, S. Siripongvutikorn, and P. Puttarak, “Selenium bio-fortification: an alternative to improve phytochemicals and bioactivities of plant foods,” *Funct. Foods Heal. Dis.*, vol. 7, no. 4, p. 263, Apr. 2017, doi: 10.31989/ffhd.v7i4.323.

[4] M. U. Hassan *et al.*, “Agronomic Bio-Fortification of Wheat to Combat Zinc Deficiency in Developing Countries,” *Pakistan J. Agric. Res.*, vol. 34, no. 1, pp. 201–217, 2021, doi: 10.17582/journal.pjar/2021/34.1.201.217.

[5] M. Adnan, “Role of Micro Nutrients Bio- Fortification in Agriculture: A Review,” *Int. J. Environ. Sci. Nat. Resour.*, vol. 24, no. 4, May 2020, doi: 10.19080/IJESNR.2020.24.556141.

[6] R. Chomchan, S. Siripongvutikorn, P. Puttarak, and R. Rattanapon, “Influence of selenium bio-fortification on nutritional compositions, bioactive compounds content and anti-oxidative properties of young ricegrass (Oryza sativa L.),” *Funct. Foods Heal. Dis.*, vol. 7, no. 3, pp. 195–209, 2017, doi: 10.31989/ffhd.v7i3.321.

[7] L. Jiang, S. Strobbe, D. Van Der Straeten, and C. Zhang, “Regulation of Plant Vitamin Metabolism: Backbone of Biofortification for the Alleviation of Hidden Hunger,” *Molecular Plant*. 2021. doi: 10.1016/j.molp.2020.11.019.

[8] D. K. Saini, P. Devi, and P. Kaushik, “Advances in genomic interventions for wheat biofortification: A review,” *Agronomy*, vol. 10, no. 1, p. 62, 2020. doi: 10.3390/agronomy10010062.

[9] I. Cakmak and U. B. Kutman, “Agronomic biofortification of cereals with zinc: a review,” *Eur. J. Soil Sci.*, vol. 69, no. 1, pp. 172-180, 2018, doi: 10.1111/ejss.12437.

[10] Q. Ali, C. Muhammad Bilal, and M. N. Subhani, "Zinc application improves the productivity and grain bio-fortification of fine rice," *Pakistan J. Agric. Sci.*, vol. 58, no. 1, pp. 95–102, 2021, doi: 10.21162/PAKJAS/21.9108.

[11] K. Bashir, T. Nozoye, Y. Ishimaru, H. Nakanishi, and N. K. Nishizawa, "Exploiting new tools for iron bio-fortification of rice," *Biotechnol. Adv.*, vol. 31, no. 8, pp. 1624–1633, Dec. 2013, doi: 10.1016/j.biotechadv.2013.08.012.

[12] M. F. Ali *et al.*, "Agronomic zinc bio-fortification in rice production systems," *Plant Cell Biotechnol. Mol. Biol.*, vol. 22, no. 25–26, pp. 103–113, 2021.

[13] Q. Wang, C. Zhong, and H. Xiao, "Genetic Engineering of Filamentous Fungi for Efficient Protein Expression and Secretion," *Frontiers in Bioengineering and Biotechnology*, vol. 8, article no. 293, 2020. doi: 10.3389/fbioe.2020.00293.

[14] S. Zhang *et al.*, "Recent Advances of CRISPR/Cas9-Based Genetic Engineering and Transcriptional Regulation in Industrial Biology," *Frontiers in Bioengineering and Biotechnology*, vol. 7, article no. 459, 2020. doi: 10.3389/fbioe.2019.00459.

[15] T. Mulualem, "Application of Bio-fortification through Plant Breeding to Improve the Value of Staple Crops," *Biomed. Biotechnol.*, vol. 3, no. 1, pp. 11–19, 2015, [Online]. Available: http://pubs.sciepub.com/bb/3/1/3/index.html

[16] B. Bhushan, S. K. Tomar, and A. Chauhan, "Techno-functional differentiation of two vitamin B12 producing Lactobacillus plantarum strains: an elucidation for diverse future use," *Appl. Microbiol. Biotechnol.*, vol. 101, no. 2, pp. 697–709, Jan. 2017, doi: 10.1007/s00253-016-7903-z.

[17] P. C. Meena, A. Choudhary, P. C. Meena, and C. Meena, "Biofortification of cereal crops: An emerging strategy to overcome hidden Hunger," ~ *776* ~ *Int. J. Chem. Stud.*, vol. 6, no. 3, pp. 776–785, 2018.

[18] M. Qaim, A. J. Stein, and J. V. Meenakshi, "Economics of biofortification," *Agric. Econ.*, vol. 37, pp. 119–133, Dec. 2007, doi: 10.1111/j.1574-0862.2007.00239.x.

[19] J. Díaz-Gómez *et al.*, "Biofortification of crops with nutrients: factors affecting utilization and storage," *Curr. Opin. Biotechnol.*, vol. 44, pp. 115–123, Apr. 2017, doi: 10.1016/j.copbio.2016.12.002.

[20] A. Kumar, A. K. Choudhary, and V. K. Suri, "Agronomic bio-fortification and quality enhancement in okra–pea cropping system through arbuscular mycorrhizal fungi at varying phosphorus and irrigation regimes in Himalayan acid alfisol," *J. Plant Nutr.*, vol. 40, no. 8, pp. 1213–1229, May 2017, doi: 10.1080/01904167.2016.1267208.

[21] B. Blasco *et al.*, "Study Of The Interactions Between Iodine And Mineral Nutrients In Lettuce Plants," *J. Plant Nutr.*, vol. 35, no. 13, pp. 1958–1969, Oct. 2012, doi: 10.1080/01904167.2012.716889.

CHAPTER 5

A COHERENT STUDY ON NANOMATERIALS FOR CANCER THERAPY

Dr. Sunita Ojha, Assistant Professor,
Department of Biotechnology, Jaipur National University, Jaipur, India,
Email Id-ojhasunita@jnujaipur.ac.in

ABSTRACT: The main cause of mortality and low quality of life worldwide is cancer. Even while many methods have been developed to lower mortality rates, ease chronic pain, and enhance the quality of life, these cancer medicines still fall short in several respects. Early cancer cell diagnosis and highly targeted medicine administration to minimize side effects are essential elements in assuring optimum cancer therapy.This study will methodically examine different nanomaterial uses in cancer treatment and biomedical imaging. Optical imaging, ultrasound, photoacoustic imaging, computed tomography, positron emission tomography, single photon emission computerized tomography, and magnetic resonance imaging are some of the medical imaging modalities. Additionally, several cancer treatment modalities such as photothermal therapy, photodynamic therapy, chemotherapy, and immunotherapy will be covered.New ideas on cancer therapy have been opened up by the therapeutic implications of nanoformulations. The majority of research, however, is restricted to in vivo and in vitro experiments, and the number of authorized nanodrugs has not increased much over time. This study covers a wide range of nanoparticle kinds, targeting strategies, and authorized nanotherapeutics for use in the treatment of cancer. We also provide a summary of the pros, disadvantages, and present state of clinical translation.

KEYWORDS: Cancer, Cancer Therapy, Cell Diagnosis, Nanomaterials, Treatment.

1. INTRODUCTION

Cancer is a category of illnesses characterized by aberrant and uncontrolled cell division and malignant activity, including invasion and metastasis. Cancer is a prominent cause of mortality across the globe (accounting for around 13% of all deaths) despite tremendous breakthroughs in contemporary medical sciences. Cancer deaths have increased steadily over the last seven decades, outpacing the more modest increases in deaths from cardiovascular disease, stroke, and pneumonia. Today, radiation and chemotherapy are the mainstays of treatment for inoperable, metastatic solid cancers [1].The problem with these techniques is that they destroy cancer cells and normal cells alike due to their non-specific mechanism of action. The most prevalent chemotherapeutic drugs, such as paclitaxel and doxorubicin, have anti-cancer effects by triggering the apoptotic death of fast-proliferating cells; however, they may also kill various kinds of normal cells that divide quickly under normal conditions. Current chemotherapy relies heavily on administering chemotherapeutic agents systemically, which may lead to serious adverse effects because of the drugs' non-selective cytotoxic action [2].

Nanotechnology has advanced fast in recent years, leading to the discovery of an increasing number of nanomaterials with highly desirable electrical, magnetic, and optical characteristics. Researchers in the area of biomedicine have utilized a wide variety of nanomaterials. Nanomaterials with photothermal conversion capabilities, for instance, are employed to treat tumors; mesoporous materials, for drug administration; magnetic

nanomaterials, for superior superparamagnetic properties; carbon nanomaterials, for wide absorbance areas [3].Applications of nanomaterials, such as cellular imaging, drug delivery, and cancer diagnosis/therapy, have been shifting from the cellular level to the tissue level. Most nanomaterials accumulate in a specific area due to the enhanced permeability and retention (EPR) effect. Several methods have been proposed to enhance the stability and biocompatibility of nanomaterials, as well as their ability to flow through the bloodstream.

The therapeutic effectiveness of the loaded chemotherapeutic medications will be significantly enhanced, while non-specific toxicity will be greatly reduced, thanks to the use of these synthetically designed nanomaterials. The development of multi-functional theragnostic Nanosystems for cancer detection and treatment, which may deliver medications selectively to tumors and concurrently monitor their therapeutic response by viewing tumor legions throughout the body, has also received a lot of attention in recent years [4].Cancer treatment is set to undergo a dramatic shift in the not-too-distant future as nanotechnology and biological sciences collide. The goals of this study are to provide a foundational understanding of tumor vasculature and angiogenesis, to highlight the unique benefits of nanoparticulate drug carriers and the molecular mechanisms underlying their selective cancer targeting effects, and to introduce several cutting-edge examples of current nanomaterials for cancer diagnosis and therapy.

2. LITERATURE REVIEW

To combine photothermal treatment, chemotherapy, and radiation, Zahra Alamzadeh et al. reported using multifunctional nanoplatforms consisting of alginate hydrogel co-loaded with cisplatin and gold nanoparticles (thermo-chemo-radio therapy).The effectiveness of ACA in treating KB human oral epidermal carcinoma cells was evaluated in conjunction with a 532 nm laser and 6 MV X-ray. The data showed that ACA-assisted tri-modal thermo-chemo-radiation therapy was more effective against cancer than either mono- or bi-modality therapies. Tri-modal treatment resulted in a 4.4-fold rise in the intracellular level of reactive oxygen species (ROS) in KB cells compared to untreated cells. A 4.5-fold increase in the expression of the pro-apoptotic protein Bax and a corresponding decrease in the expression of the anti-apoptotic factor Bcl-2 were seen in the gene expression study (by 0.3-fold). The micrograph of KB cells confirmed the extensive cellular damage and the emergence of apoptotic morphological features that were brought on by the thermo-chemo-radiation treatment. As a result, the ACA nano complex may be provided as a potentially useful platform to integrate photothermal therapy with chemoradiotherapy, providing a new tool for treating malignancies that have become resistant to conventional treatments [5].

Research by Nahla Rizk et al. examined the effectiveness of multifunctional gold nanoparticles (AuNPs) coupled with three anti-cancer drugs: TGF-1 antibody, methotrexate, and folic acid. A metastatic human breast cancer cell line, MDA-MB-231, was used to determine the optimal size and shape of the AuNPs. The research focused on spherical AuNPs (S-AuNPs) with a size of 100 nm. S-AuNP (3.8 108 particles/ml) was conjugated with either folic acid-BSA or methotrexate-BSA in a constant volume (900 l). Cellular toxicity was caused by S-AuNP treated with methotrexate, and 500 l of methotrexate-BSA (2.83 mM) was shown to be optimal. The conjugation of folate, which binds to folate receptors that are overexpressed in MDA-MB-231, increased the absorption of S-AuNPs, with the optimal uptake occurring at 500 l of folic acid-BSA (2.83 mM). Antibody against transforming growth factor 1 (TGF1) bound to S-AuNP decreased cancer cell-derived TGF1 by 30%. We expect several therapeutic uses of multifunctional gold nanospheres in treating breast cancer due to their potency and tenability [6].

In their research, TianyuLi and Huaping Xu found that selenium-containing nanoparticles are among the most promising biomaterial candidates of the recent decade. Since selenium is a necessary trace element in the human body, nanomaterials that include selenium tend to be biocompatible. Nanomaterials containing selenium may be made highly responsive to redox stimuli and have anticancer action with careful engineering. In this study, researchers explore the potential of nanomaterials containing selenium as medication delivery vehicles and anticancer medicines in the treatment of cancer. Nanomaterials that show promise in both in vitro and in vivo may be developed into treatments [7].

3. DISCUSSION

Cancer is the second biggest cause of mortality worldwide, making it a major public health issue. New cases are expected to reach 1.9 million by 2021, as reported by the American Cancer Society. Surgery, chemotherapy, radiation therapy, targeted therapy, immunotherapy, and hormone therapy are all examples of traditional therapeutic techniques utilized in the treatment of cancer. Chemotherapy and radiation can cause cytostatic and cytotoxicity, respectively, but they also come with some unpleasant side effects and a significant danger of cancer coming back. Neuropathies, suppression of bone marrow, gastrointestinal and skin diseases, hair loss, and weariness are among the most often seen adverse effects. Anthracycline- and bleomycin-induced cardiotoxicity and pulmonary toxicity are two examples of drug-specific adverse effects shown in Figure 1 [8].

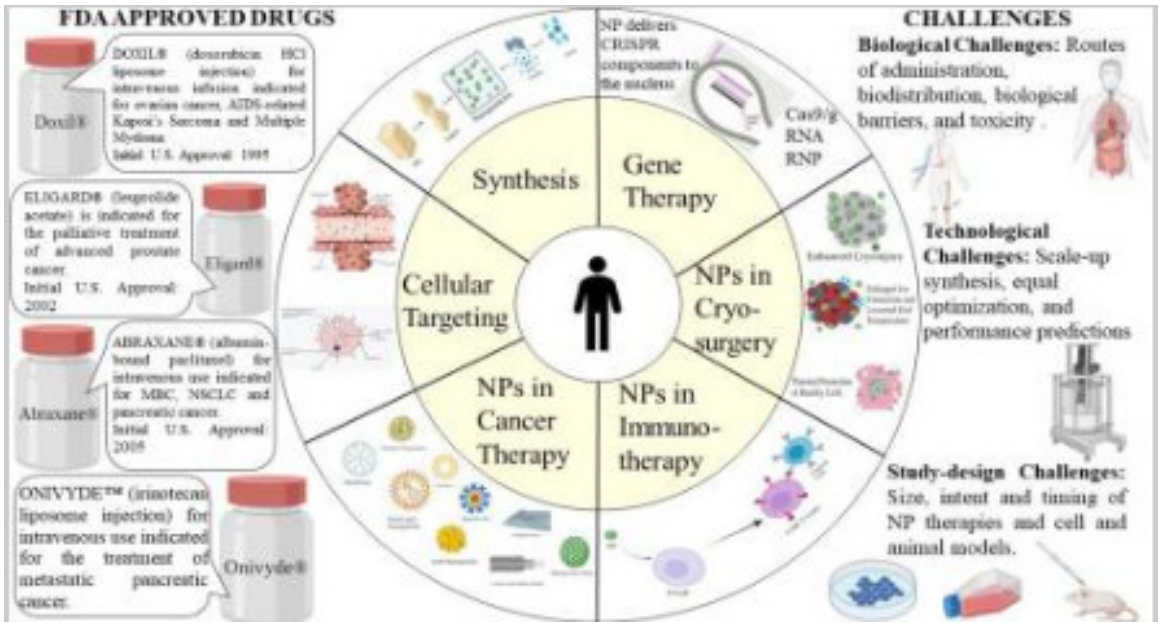


Figure 1: Displays the Therapeutic use of nanoparticles for the treatment of cancer [9]**.**

Precision medicine has progressed with the development of focused therapies. Multi-drug resistance is only one of the numerous unavoidable side effects that reduce the effectiveness of treatment [8]. Positive outcomes have been shown with immunotherapeutic drugs, which not only cure the underlying tumor but also stop it from spreading and reduce the likelihood of relapse. Immunotherapy has some benefits, but autoimmune illness is one of the biggest downsides. It has been suggested by studies and pieces of evidence that immunotherapy is less successful against solid tumors than lymphoma. Infiltration of immune cells is hindered by the abnormal extracellular matrix (ECM) produced by these malignancies [10].In this study, the author will discuss the many functions of nanomaterials in biomedical imaging and cancer treatment, including contrast agents and dosage enhancers. The review also included

the physical, chemical, and biological factors that underpin nanomaterials. Nanomaterials are being investigated for potential novel uses as theranostic agents. As a result of the author's in-depth familiarity with the most up-to-date developments in biomedical imaging and cancer treatment using nanomaterials, promising new avenues for the improvement and therapeutic transformation of these materials have been uncovered.

3.1.Medical Imaging:

The accuracy with which anatomical information may be obtained through various medical imaging modalities has increased greatly in recent decades. As will be seen below, nanoparticles play a crucial role in the field of medical imaging.

3.1.1. Magnetic Resonance Imaging(MRI):

Magnetic resonance imaging (MRI) is a non-invasive imaging method that may offer multiparametric and comprehensive data. Magnetic resonance imaging (MRI) was developed in the 1980s and fundamentally changed the way doctors saw their images. It rose to prominence as a top paraclinical diagnostic and monitoring tool. An estimated 17 million MRI scans including contrast chemicals were done in the United States in 2015. In magnetic resonance imaging, the contrast agent is used to improve the quality of the picture. While there is little doubt that many present contrast agents have unwanted side effects such as allergic responses, nephrotoxicity, gadolinium deposition, and physiologic reactions, the ideal contrast agent would be given and then removed from the body without any problems. Recent developments in NPs demonstrate their potential for use as a contrast agent in MRI and reduce many of the possible negative effects [11].

- *Gadolinium (GD):*

Over the last three decades, gadolinium-based contrast agents have been utilized in diagnostic MRI, and their potential for other, more useful uses has been investigated extensively. The r1 relaxivity of Gd has recently been shown to increase when it is exposed to Zn+2 ions. There are some uses where this quality shines. Zn+2 ions may be employed as a biomarker for insulin release in -cells since they play a crucial role in the biological process involving the enzyme catalytic reaction. Zn+2 is abundant in the prostate and may be utilized to improve MRI contrast. Diseased cells and cancer cells have collagen synthesis that is out of whack, and common liver disorders like alcohol and drug addiction are associated with an increase in collagen production. Gd nanoparticles (NPs)-based contrast agents may be employed in magnetic resonance imaging to identify areas with excessive collagen [12].

Dendrimers are artificially branched macromolecules that take on a specified form and size. Monodispersity describes these formations. Chemical processes and physical manipulations may be used to alter their surface. Dendrimers are used to create complicated or capsule-like structures that may then be filled with drug compounds. The pharmaceutical industry's first dendrimer NP system, Vivagel®, was released in 2005. Antiviral medications like those made by Vivagel® are used topically to stop the spread of viruses including herpes and the human immunodeficiency virus. This product blocks the virus from attaching to the host by its dendrimer structure.Further research demonstrated the efficacy of gadolinium oxide as an MRI contrast agent and cell marker when combined with diethylene glycol polymer and magneto liposome NPs in Hepa 1-6 cell lines. For a long time, clinicians could utilize gadolinium chelates with a high degree of confidence in their safety. Recent investigations, however, have shown a link between the use of a Gd-based contrast agent that is currently licensed for clinical use and the onset of nephrogenic systemic fibrosis. Studies have shown that even in healthy individuals with appropriate renal function, a Gd-based contrast agent may lead to Gd accumulation in bone and brain tissue [13].

3.1.2. Computed Tomography:

Computerized tomography creates pictures by using an x-ray source and a detector array. It has a long history of usage in clinical imaging and the ability to provide a picture with great spatial and temporal resolution. Various organs and systems, including the heart, intestines, liver, and lungs, may be mapped out in 3D with this technique, and no tissue or organ is harmed in the process. CT's lack of sensitivity to contrast agents is a limitation compared to other modalities, such as MRI. Contrast agents for CT are desperately needed, however, there are currently just a few that show promise [14].

- *Gold Nanoparticles:*

Gold nanoparticles may be easily modified on the surface and have exceptional x-ray attenuation characteristics. Functionalizing Au NPs with glucosamine makes them a potent contrast agent. Due to their high x-ray absorption coefficient, gold nanoparticles facilitate tumor-specific CT imaging via improved permeability and retention (EPR). To study breast cancer, Au NPs were paired with PEG chains and tumor biomarkers in a lab (human epidermal growth factor 2). The ability to precisely target an area allowed them to generate a better CT picture. Mesenchymal stem cells are a kind of adult stem cell with great promise in cellular-based regenerative therapy for the treatment of a wide range of diseases and ailments, including autoimmune, neurodegenerative, and cardiovascular disorders. Cartilage and bone damage may also be treated using them. Their ability to spread into new tissues is the most surprising feature, and researching metastases requires careful tracking of this process.

3.2. Using NPS in cancer diagnostics and therapy:

Nanoparticles (NPs) made from lipids, polymers, inorganic materials, viruses, and drugs are just some of the platforms being studied for their potential as nanocarriers in cancer treatment (Figure 2). In addition, a few of these NP systems have received clinical approval. One of the most exciting and cutting-edge approaches to developing new cancer treatments is nanomedicine.

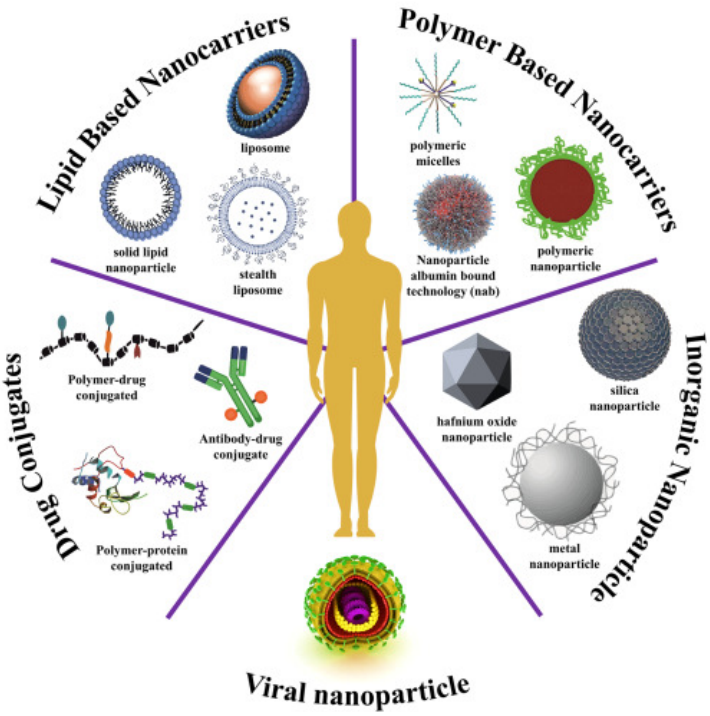


Figure 2: Displays the list of recognized nanomedicine for the treatment of cancer [15].

One of the most promising and cutting-edge approaches to the creation of novel cancer treatments is nanomedicine. The majority of scientific literature indicates that nanomedicine therapeutics are successful in treating cancer both in vitro and in vivo. The ability to deliver anticancer agents to specific tumors, tumor imaging, the capacity of NPs to store a thousand drug molecules, and the ability to overcome solubility, stability, and resistibility issues are the main benefits of NPS as anticancer agent carriers. Additionally, some NP-related diagnostic and therapeutic agents that are examined by clinical tests have been approved. Some of them already had Food and Drug Administration approval. NPS of the types Daunoxome, Doxil, Depocyt, Abraxane, and Oncaspar have also received FDA approval. These medications are effective in treating cancers such as ovarian, breast, lung, renal, and others.

4. CONCLUSION

Different types of NPs with diverse architectures have been created as a result of the advancement of nanotechnology and its integration with other disciplines. They both have certain benefits and drawbacks. However, they are regarded as a successful step in enhancing particle functionality. In DDS, NPs serve their most effective role. They serve as polymer, lipid, metal, ceramic, and other types of carriers for the delivery of drugs to treat many illnesses, particularly resistant disorders like cancer. Drug delivery, biomedical imaging, and the detection and treatment of illnesses are all possible uses for NPs. As nanotechnology develops, there will be more options to target several tumor samples' molecules at once and to use the best treatment approaches. The use of NPS treating in vivo cancers is quickly advancing. Targeting malignant antigens may be viable as a result of these advancements. Nanotechnology research will soon bring about a significant transformation in cancer as well as all other medical specialties.

REFERENCES:

[1] Y. Liu, D. Liu, J. Shi, and R. S. Langer, “Cancer Nanotechnology,” in *Holland-Frei Cancer Medicine*, Hoboken, NJ, USA: John Wiley & Sons, Inc., 2017, pp. 1–7. doi: 10.1002/9781119000822.hfcm070.

[2] J.-H. Park *et al.*, “Cooperative nanomaterial system to sensitize, target, and treat tumors,” *Proc. Natl. Acad. Sci.*, vol. 107, no. 3, pp. 981–986, Jan. 2010, doi: 10.1073/pnas.0909565107.

[3] J. Liu, C. Detrembleur, M.-C. De Pauw-Gillet, S. Mornet, C. Jérôme, and E. Duguet, “Gold Nanorods Coated with Mesoporous Silica Shell as Drug Delivery System for Remote Near Infrared Light-Activated Release and Potential Phototherapy,” *Small*, vol. 11, no. 19, pp. 2323–2332, May 2015, doi: 10.1002/smll.201402145.

[4] M. E. Davis, Z. Chen, and D. M. Shin, “Nanoparticle therapeutics: an emerging treatment modality for cancer,” *Nat. Rev. Drug Discov.*, vol. 7, no. 9, pp. 771–782, Sep. 2008, doi: 10.1038/nrd2614.

[5] Z. Alamzadeh *et al.*, “Gold nanoparticles promote a multimodal synergistic cancer therapy strategy by co-delivery of thermo-chemo-radio therapy,” *Eur. J. Pharm. Sci.*, vol. 145, p. 105235, Mar. 2020, doi: 10.1016/j.ejps.2020.105235.

[6] N. Rizk, N. Christoforou, and S. Lee, “Optimization of anti-cancer drugs and a targeting molecule on multifunctional gold nanoparticles,” *Nanotechnology*, vol. 27, no. 18, p. 185704, May 2016, doi: 10.1088/0957-4484/27/18/185704.

[7] T. Li and H. Xu, “Selenium-Containing Nanomaterials for Cancer Treatment,” *Cell Reports Phys. Sci.*, vol. 1, no. 7, p. 100111, Jul. 2020, doi: 10.1016/j.xcrp.2020.100111.

[8] L. Zitvogel, L. Apetoh, F. Ghiringhelli, and G. Kroemer, “Immunological aspects of cancer chemotherapy,” *Nat. Rev. Immunol.*, vol. 8, no. 1, pp. 59–73, Jan. 2008, doi: 10.1038/nri2216.

[9] S. Gavas, S. Quazi, and T. M. Karpiński, “Nanoparticles for Cancer Therapy: Current Progress and Challenges,” *Nanoscale Res. Lett.*, vol. 16, no. 1, p. 173, Dec. 2021, doi: 10.1186/s11671-021-03628-6.

[10] A. M. Williams, Y. Liu, K. R. Regner, F. Jotterand, P. Liu, and M. Liang, “Artificial intelligence, physiological genomics, and precision medicine,” *Physiol. Genomics*, vol. 50, no. 4, pp. 237–243, Apr. 2018, doi: 10.1152/physiolgenomics.00119.2017.

[11] T. Yousaf, G. Dervenoulas, and M. Politis, “Advances in MRI Methodology,” in *International Review of Neurobiology*, 2018, pp. 31–76. doi: 10.1016/bs.irn.2018.08.008.

[12] A. C. Esqueda *et al.*, “A New Gadolinium-Based MRI Zinc Sensor,” *J. Am. Chem. Soc.*, vol. 131, no. 32, pp. 11387–11391, Aug. 2009, doi: 10.1021/ja901875v.

[13] J. Ramalho, R. C. Semelka, M. Ramalho, R. H. Nunes, M. AlObaidy, and M. Castillo, “Gadolinium-Based Contrast Agent Accumulation and Toxicity: An Update,” *Am. J. Neuroradiol.*, vol. 37, no. 7, pp. 1192–1198, Jul. 2016, doi: 10.3174/ajnr.A4615.

[14] Y. C. Dong *et al.*, “Effect of Gold Nanoparticle Size on Their Properties as Contrast Agents for Computed Tomography,” *Sci. Rep.*, vol. 9, no. 1, p. 14912, Dec. 2019, doi: 10.1038/s41598-019-50332-8.

[15] A. Aghebati□Maleki *et al.*, “Nanoparticles and cancer therapy: Perspectives for application of nanoparticles in the treatment of cancers,” *J. Cell. Physiol.*, vol. 235, no. 3, pp. 1962–1972, Mar. 2020, doi: 10.1002/jcp.29126.

CHAPTER 6

AN INVESTIGATION OF PHARMACOLOGICAL PROPERTIES OF *SARACA ASOCA*

Dr. Sunita Rao, Assistant Professor,
Department of Biotechnology, Jaipur National University, Jaipur, India,
Email Id-sunita.rao@jnujaipur.ac.in

ABSTRACT: The Caesalpiniaceae family includes the rain forest tree Saraca indica (Ashoka) Linn. The name Ashoka, which means "without sadness" or "tree without grief," alludes to its bark's well-known ability to keep women young and healthy. With so many individuals looking for treatments and health strategies free from negative effects brought on by synthetic pharmaceuticals, medicinal plants are transitioning from being used on the periphery to being more widely accepted. According to reports, saraca asoca includes glycoside, tannins, flavanoids, or saponins.The goal of the current study is to provide a thorough explanation of the botanical elements, phytochemical components, therapeutic applications, or pharmacological research. It has antibacterial, anti-progestational, anti-implantation, anti-tumor, antiestrogenic action against menorrhagia, or anti-cancer properties in addition to its spasmogenic, oxytocic, but also uterotonic properties. This review includes a pharmacognostic analysis of numerous plant sections, phytochemical components, and various claimed pharmacological activities. In the Future this paper will aware the people about the pharmacological importance of Saraca asoca (Ashok).

KEYWORDS: Diseases, Medicine, Pharmacology, Skin Cancer, Saraca Asoca.

1. INTRODUCTION

The Flame of the Forest trees also include the Saraca Indica tree species. This particular tree helps individuals feel less pain and grief. When people view the tree's remarkable beauty, they are pleased. The tree's official scientific name is Saraca Indica. It is a member of the Leguminosae family and the Coesalpineae subfamily. These trees go by a variety of names among the Indians. People who speak Bengali or Hindi refer to it as Asok, and Vanjulam, respectively [1], [2]. In Tamil, it is Asok, Ashoka, or Asogam, and in Sinhalese, it is Diyaratmal. It is referred to as either Gapis as well as Tengalan in Malayalam. There are many questions and disagreements over the etymology of the name Saraca Indica. The tree is supposed to keep its previous Sanskrit name of Ashoka after the respect it received from Indian botanists, who described him as the wisest of the sons of humanity. But it would be difficult to argue that this is an advancement of rulers like Ashoka.

With a growing number of individuals seeking treatment and health methods free of the side effects brought about by synthetic pharmaceuticals, medicinal plants are transitioning from niche to mainstream use. One of the oldest trees in India, Ashoka is often referred to as the “Ashoka tree”. The Caesalpiniaceae family includes Saraca asoca (Roxb.) Wilde and Saraca indica. All plant components are thought to have therapeutic qualities. It is known that the leaves of Saraca asoca contains proteins, tannins, carbohydrates, or saponins as well as possessing antibacterial properties. Glycosides, steroids, saponins, sugars, and tannins are all present in bark [3], [4]. The flowers are also seen to be a crucial component of the plant from a medical standpoint and are employed as a therapeutic agent in the management of uterine diseases including menorrhagia, cancer, diabetes, or hemorrhagic dysenteryas shown in Figure 1. Additionally, it is effective for bacillary dysentery and bleeding piles. According to

reports, dried flower buds contain antimicrobial properties. In albino rats, Saraca indica flower aqueous solution possesses antiulcer action. The bark and blossoms of Saraca asoca have anti-tumor properties against the cancer cell lines DLA, S-180, or Ehrlich ascites carcinoma [5], [6]. The flavonoid fraction of S. asoca has been shown to have chemopreventive effect in the development of skin cancer. Women consume the flower buds orally throughout ashoka-sasthi. Despite the fact that phytoconstituents have previously been recorded for the plant's bark and leaves flowers have not yet undergone a detailed qualitative phytochemical examination. The current study makes an effort to fill this gap by assessing associated with a greater standardization criteria in flowers that may be helpful for identifying the medication in its dry form. There is no information on gallic acid's presence in Saraca leaf, however the antioxidant molecule's known existence in Saraca asoca flowers [7], [8]. The HPTLC technique has been developed for the conventional gallic acid qualitative test. Saraca asoca flowers and leaves are tested for gallic acid using a simple "high-performance thin layer chromatography" (HPTLC) technique (Figure 1).

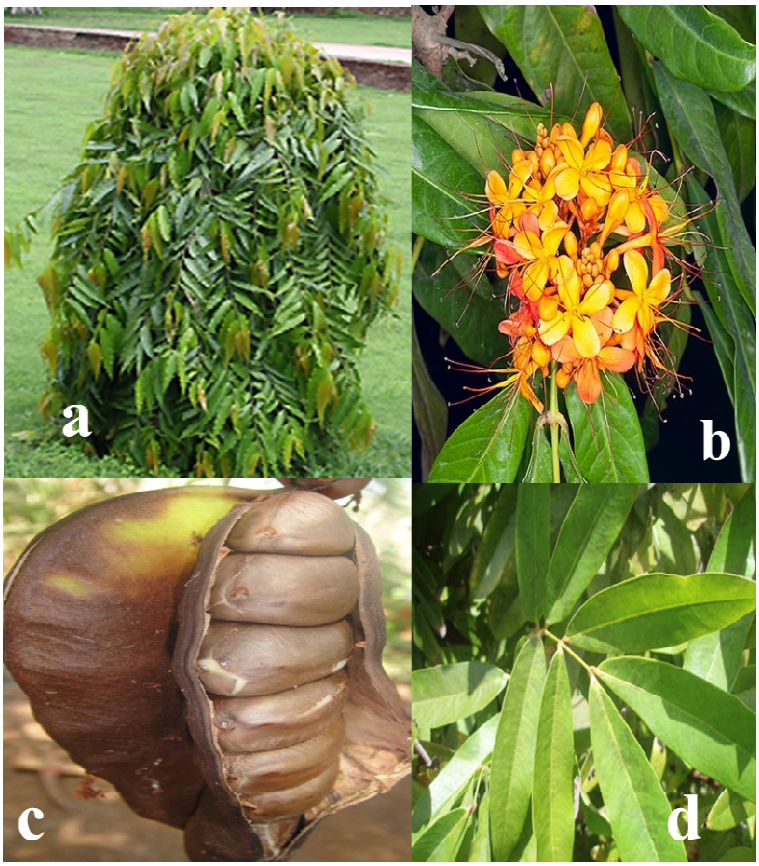


Figure 1: Illustrating the pictorial representation of different part of Saraca asoca Plant.

One of the most important Unani or Ayurvedic medicinal herbs, Saraca indica, is used to treat a variety of female problems, including menorrhagia and gynecological disorders. Its bark keeps a lady healthy and youthful and has an astringent, bitter, and sweet flavor. The ovarian or endometrial tissues are stimulated by it. Internal bleeding, ulcers, uterine diseases, hemorrhoids, menorrhagia especially those caused by uterine fibroids menometrorrhagia, leucorrhoea, or pimples might all benefit from it, and Showing the Classification of Saraca asoca Plant Table 1. The plant has several medical benefits and is

used extensively in Unani or Ayurvedic medicine to treat a variety of ailments, including inflammation or blood diseases, discomfort, as well as to enhance digestion and absorption as well as the body's appearance as well as excessive thirst.

Table 1: Illustrate the classification Saraca asoca Plant.

Classification	
Kingdom	Plantae
Division	Magnoliophyta
Class	Mgnoliopsida
Order	Fabales
Family	Caesalpinaceae
Genus	Saraca
Species	Indica

2. LITERATURE REVIEW

Jayita Saha et al. studied about HPTLC analysis of phytoconstituents in saraca asoca. The current study makes an effort to look into the qualitative phytochemical components from extraction of Saraca asoca (Roxb.) Wildde's flower. In various floral extracts, substances including tannin, flavonoids, carbohydrates, proteins, and steroids have been discovered.

Analysis of the phytochemical and physicochemical components of the raw medication form is helpful in determining its legitimacy. Gallic acid, a pharmacologically significant active component, has been determined qualitatively in dried Saraca asoca. Wilde flowers or leaves using a sensitive and trustworthy high performance thin layer chromatographic (HPTLC) technique [9].

Satpal Singh et al. studied about the therapeutic value of Saraca asoca. Numerous commercial S. asoca formulations are now available and are advised for a variety of indications thanks to extensive folkloric usage or ethnobotanical uses of this plant, while adulteration of these products is still a major worry. Here, they explore potential barriers to using the stated phytomedicinal value of this recommended Ayurvedic medicinal plant, define socio-ethnobotanical utilization, present the available therapeutic status. Moreover, they consider the potential course of drug development and pharmaceutical R&D initiatives aimed at investigating its pharma legacy [10].

Navneet Kumar Yadav et al. studied about One of the oldest holy plants with therapeutic qualities is Saraca indica (family Caesalpiniaceae), which has a variety of pharmacological effects. Due to their affordability and accessibility, medicinal plants are utilized as alternatives and complementary medicine in the treatment of many illnesses, including cancer, around the world. Due to their affordability and accessibility, medicinal plants are employed as supplementary or alternative medicine in many countries to treat illnesses like cancer[11].

Satish a Bhalerao studied on Saraca asoca's pharmacological profile, phytochemistry, and medicinal effects. According to reports, the stem bark, which is mostly utilized in medicine, contains compounds including glycoside, flavanoids, saponins, tannins, esters, alkanes, or

primary alcohols. Traditional medicine for women's issues, including menorrhagia, bleeding hemorrhoids, leucorrhoea, dysfunctional uterine hemorrhage, etc., has made extensive use of saraca asoca [12].

3. DISCUSSION

A database search on PubMed, Google Scholar, Research Gate, Science Direct, and other sites was used to conduct the current review study. Combining keywords like "Diseases, Medicine, Pharmacology, Skin Cancer, Saraca Asoca", were used in the review technique. Title and abstract screening were used for the records preliminary review. Additionally, non-extractable data, duplicate research, and inadequate information were grounds for excluding the Records. Figure 2 below provides more information on the methodology utilized to conduct the review study.

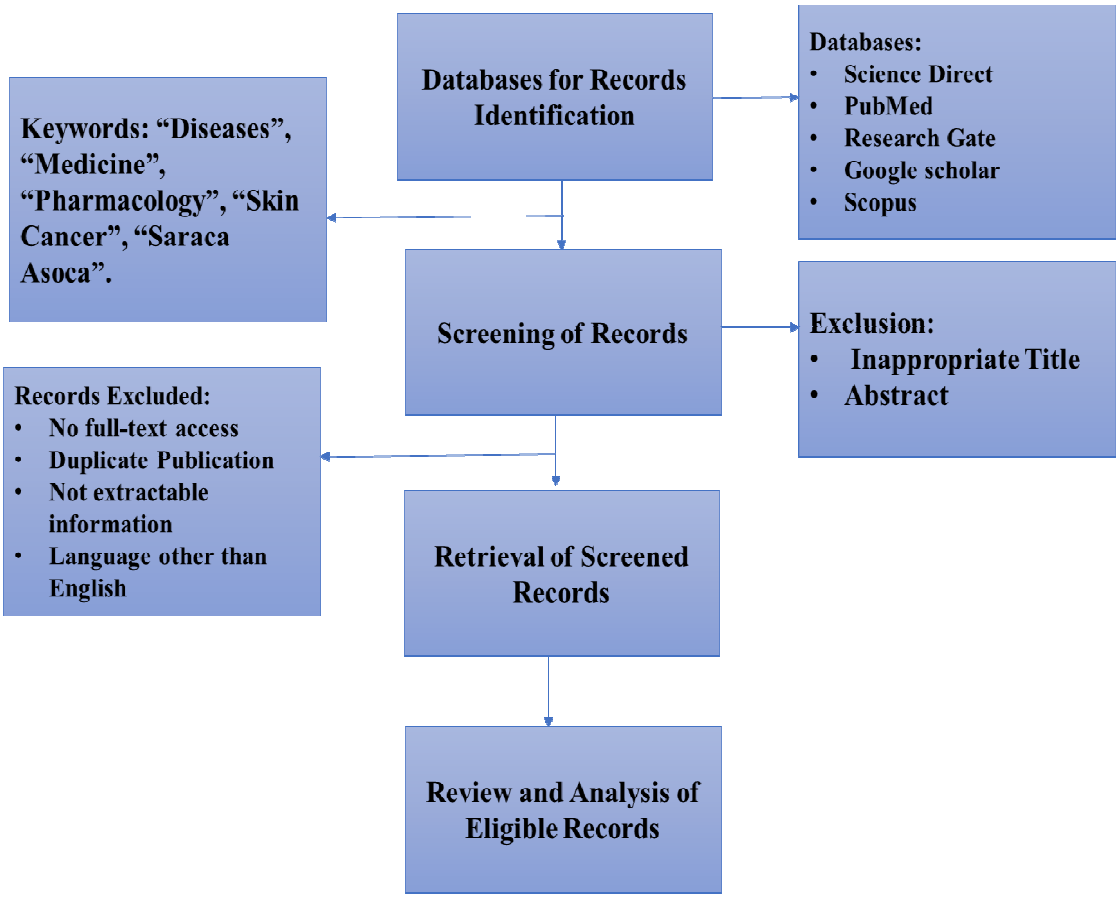


Figure 2: Illustrate The Design Of Methodology Of Current Review Work.

There has been a lot of research in recent years that has solidified the therapeutic use of antioxidants in the treatment of many diseases, including cancer, neurodegeneration, inflammation, or heart disease. Superoxide and peroxyl radicals are examples of free radicals that can form during normal metabolic activity. These radicals are extremely short-lived and reactive, damaging biomolecules but having negative effects on human health. They can also cause serious illness.

3.1. Saraca asoca's biological and pharmaceutical effects:

Ayurveda is an ancient medical system that made extensive use of herbal treatments. The indigenous plant known as Ashokai, or Sarraca asoca (Roxb.), is a member of the Legume family's Caesalpinaceae subfamily and has significant cultural value. All of this plant's

components are thought to have medicinal value, and they have been used to treat a variety of gynecological conditions, including menorrhagia, leucorrhea, and abnormal uterine bleeding [13], [14]. According to reports, saraca asoca contains a variety of phytoconstituents including flavonoids, steroids, glycosides, saponins, tannins, carbohydrates, and proteins. It also reportedly has a number of pharmacological properties including spasmogenic, uterotonic, oxytocic, anti-menorrhagic, anti-cancer, anti-estrogenic, anti-bacterial, dermatoprotect, anti-progestational, Information about gaps in enhancing Ashok's pharmaceutical value, such as the absence of tissue culture procedures in Ashoka planting, has also been acquired.

The best choice for screening Saraca asoca's endophytes for pharmaceutically relevant substances is this plant. It is believed that this study will offer sufficient, ideal, and distinct information under one roof and will also provide fresh guidance for the pharmaceutical business and research community to increase the Pharma worth of this natural substance. Figure 3, shows the Saraca asoca's biological and pharmacological activity.

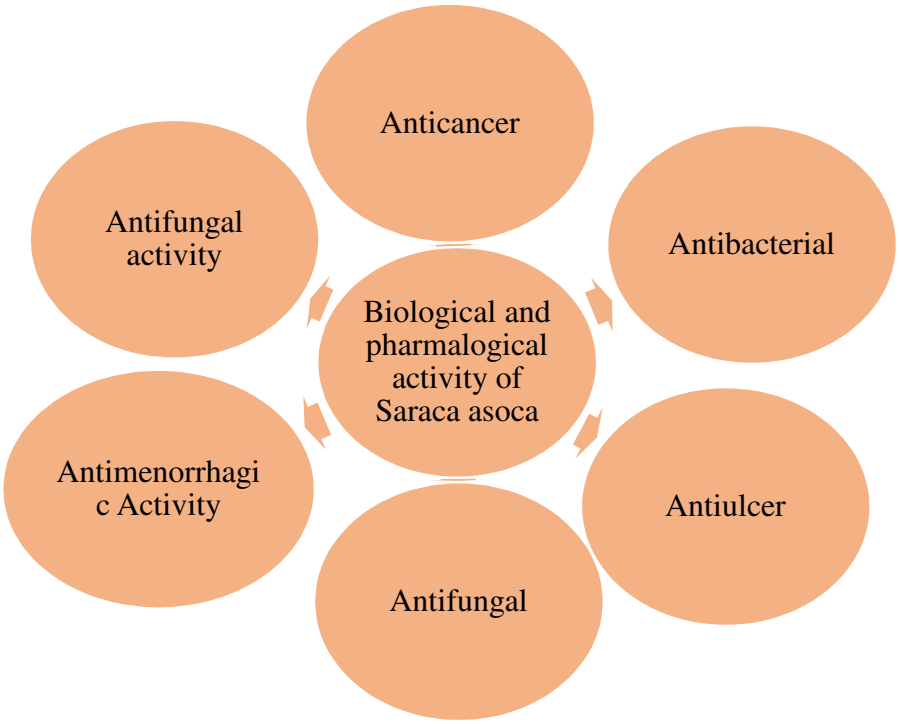


Figure 3: Illustrate the Biological and Pharmalogical activity of Saraca asoca.

3.1.1. Anticancer:

In the past, natural compounds have offered some of the most potent anticancer leads, with a number of them now in successful commercial production. According to ethnobotanical research of S. asoca, its flavonoid fraction (derived from flowers) inhibits the development of two stages of skin cancer and acts selectively against Sarcoma or Dalton's lymphoma ascites while being non-toxic to healthy lymphocytes. It has been demonstrated that the ethanolic S. indica extract inhibits breast cancer. In a recent in vitro experiment, it was shown that the lectin saracin extracted from the seed integument caused human T cells to undergo apoptosis.

3.1.2. Antifungal:

Although fungal disease outbreaks have been on the rise in the past, they have historically been thought to be caused by a person's weakened immune system and not to pose a substantial threat to the general populace. The clinical microbiology community has

consequently made it a top priority to discover novel antifungal medications. The antifungal properties of hot aqueous and methanolic extracts of S. Alternaria alternata, Drechlera specifera, Alternaria cajani, Colletotrichum gloeosporioides, Helminthosporium sp., Bipolaris sp., Aspergillus flavus, or A. asoca leaves, flowers, as well as bark. Fusarium sp. but also fumigates have allegedly been shown by many organizations. These might be the topic of more thorough research to find the bioactive principles.

3.1.3. Antifungal:

Although fungal disease outbreaks have been on the rise in the past, they have historically been thought to be caused by a person's weakened immune system and not to pose a substantial threat to the general populace. The clinical microbiology community has consequently made it a top priority to discover novel antifungal medications. The antifungal properties of hot aqueous and methanolic extracts of S. Alternaria alternata, Alternaria cajani, Drechlera specifera, Colletotrichum gloeosporioides, Helminthosporium sp., Bipolaris sp., Aspergillus flavus, or A. asoca leaves, flowers, as well as bark. Fusarium sp. but also fumigates have allegedly been shown by many organizations. These might be the topic of more thorough research to find the bioactive principles. The mechanisms by which the molecules responsible for ulcer reduction work are thought to be inhibition of basal gastric secretion, stimulation of mucus secretion, endogenous gastric mucosal secretions triggered by prostaglandin E2 and I2 synthesis, or antioxidant activity of the flavonoids present in the aqueous extract of S. indica, which combat the reactive oxidants present in the gastrointestinal lumen [15].

3.1.4. Active Antimenorrhagic Effect:

In India, dried bark from Saraca asoca has been used to treat menorrhagia. In India, Saraca asoca dry bark and flower are given to women suffering from uterine diseases as a tonic. All conditions related to the menstrual period are also treated using the stem bark of Saraca asoca. In Sri Lanka, saraca asoca bark is used to treat menstruation irregularities or menorrhagia. In India, saraca asoca bark is used to relax the uterus, or hot water extracts given to adult female humans stimulate the uterus similarly to ergot without causing tonic contraction. Additionally used for menorrhagia, as such an emmenagogue, as a uterine sedative, for uterine diseases, and in a number of female health remedies. In Pakistan, the bark of the saraca indica tree is used to treat menorrhagia and uterine discomfort [16]. The dried bark of Saraca indica is utilized as an astringent in menorrhagia to control excessive uterine bleeding. It is also used as a refrigent and demulcent for uterine abnormalities and regular monthly discomfort in the belly. According to reports, the bark's aqueous extract contains active components, one of which relaxes and the other of which stimulates the guinea pigs ileum's plain muscle. According to reports, the medication stimulates the uterus, increasing the frequency and duration of contractions. Another claim about the crystalline glycoside molecule is that it causes uterine contractions.

3.1.5. Anti-fungal Properties:

Fungal infections have traditionally been considered to be caused by a person's weakened immune system and not to represent a severe threat to the general populace, although there have been a growing number of fungal infectious diseases in the past. The diagnostic laboratories community has consequently made it a top priority to discover novel antifungal medications. Saraca indica leaves, flowering, or bark extracts' antifungal efficacy against Colletotrichum gloeosporioides, Alternaria alternata, or Drechlera specifera [17].

3.1.6. Indications:

In cases of paralysis, hemiplegia, or visceral numbness, dried root is utilized. Transient delirium caused by the neurological system. It works as a vulnerary and speeds up the recovery process for broken bones as well as skin wounds. Root paste is effective for treating skin conditions such as ulcers, rashes, and freckles. Utilized especially to purify, chill, and clarify the blood. used to treat itching caused by herpes-kushta/visarpa, psoriasis, eczema, and dermatitis. It is a preferred plant for treating pruritis. Applied to scabies or tinea pedis as well. Utilize it as a wash or as a cream for this condition's external advantages. It improves skin tone or complexion and could be used for pigment loss or discolouration. Root is also used to treat ammenorrhea and blockage of the urinary tract. After giving birth, it is drank to encourage profuse lochial discharge. It has the ability to dissolve kidney-related oxalic tones. Useful for symptoms of endometriosis, difficult periods, fixed discomfort, clots, and uterine congestion. Rickets, delayed bones consolidation, or calcium insufficiency can all be treated with decoction.

3.1.7. Dermatologically Safe:

Various skin conditions, including eczema, acne, psoriasis, dermatitis, herpes-kushta/visaropa, pruritis, tinea pedis, scabies, or skin cancer, are treated with the bark, root, as well as seed preparations of Saraca indica. It has been demonstrated that 7, 12-dimethyl benzanthracene-induced skin tumors can be reduced by Saraca indica flower preparations, which contain flavonoids. It is also known to improve the appearance of the skin, hasten the healing of skin wounds, and lessen freckles or external skin inflammations. It has been observed that seed extracts are beneficial against dermatophytic fungus.

The above-discussed medicinal value of the tree is clear evidence that Saraca indica is one of the most significant medicinal plants with many therapeutic benefits, particularly for female problems. According to reports, the stem bark, which is mostly utilized in medicine, contains compounds including glycoside, tannins, saponins, flavanoids, esters, or primary alcohols. Traditional medicine has made extensive use of Saraca indica to treat women's health issues, including leucorrhea, bleeding hemorrhoids, menorrhagia, dysfunctional uterine hemorrhage, etc.

3.2. Traditional uses:

Leucorrhoea, menorrhagia, dysfunctional uterine hemorrhage, etc. have all been treated with ashoka traditionally as a medication. Biliousness, dysentery, dyspepsia, colic, piles, ulcers, piles, and acne are all said to be cured by bark. The juice from the leaves, when combined with cumin seeds, is used to treat stomachaches and has blood-purifying qualities. Flowers that have been dried are used to treat diabetes and haemorrhagic dysentery, respectively. Flowers are seen as being beneficial for biliousness, syphilis, or the uterus. Fruits are chewed instead of areca nuts in Assam. Pods are said to produce excellent cow feed. Assam uses light, reddish-brown, soft wood to make ploughs and shafts, whereas Ceylon uses it to build homes.

The seeds are beneficial for urinary excretions. The bark is frequently used for uterine conditions, particularly menorrhagia. Typically, a bark decoction in milk is given. Bark, fruits, and flowers, according to aacharya Sushruta, are given in conjunction with other medications for the treatment of snakebite or scorpion sting. However, Mhaskar and Caius have determined that the fruits, flowers, and bark are equally ineffective for treating snakebite as well as scorpion sting. The Ashoka plant is useful as a uterine tonic for irregular menstrual periods or miscarriage because it improves the endometrium and uterine muscles.

Females with Pradara roga benefit from the use of a 6 gm bark powder of Ashoka ksheerapaka, which is also useful for uterine inertia, uterine discomfort, urinary calculi, and dysuria. Bark paste used locally for pain should be beneficial [18]. To avoid gynecological diseases, Chhattisgarh women boil the bark of Ashoka in cow's milk, add sugar, or ingest it once daily for three days. They then repeat this procedure three months later. Married Hindu women in India consume the blossom buds of Ashoka herbs on "Ashoka Shasthi day" in order to shield their kid from sadness and suffering. It is recommended for those with mental illnesses to bathe beneath the Ashok tree's shade. The locals make a unique "Herbal Mala" for mental peace using bits of Sita Ashok's root and feed it to the sick. Patients are instructed to fill the Pan (Betel) with powdered seeds or consume it on an empty stomach. The bark of Ashok is prepared into a decoction by the healers and used as an exterior wash. The bark is boiled in a cultured buttermilk mixture but then administered to Safed pani (leucorrhoea) patients after the water has evaporated. When the nerves are agitated by vata dosha, the unique analgesic characteristics of Ashoka can be employed to soothe them. The ashoka plant is also good at preventing skin allergies or naturally purifying blood. Additionally, this herb might help to enhance the skin's tone.

CONCLUSION

In ayurveda medicine, saraca asoca is regarded as a universal cure-all. It is one of the many plants with universal medical properties. This adaptable plant is the origin of many different kinds of chemicals. Currently, a wide variety of plants are utilized to cure a wide variety of ailments. However, because Ashoka is an old and trustworthy source of medicine, it is employed in several pharmacological activities including those that fight cancer, menorrhagia, oxytoxin, and microbes. It also has extensive uses in ayurveda, unani, or homeopathy. It can be used to treat skin problems, "central nervous system" (CNS) functioning, and genitor-urinary processes, among other things. The development of new drugs from Saraca asoca must be prioritized for the treatment of different ailments as the worldwide situation is now shifting toward the usage of nontoxic plant products having traditional medical use. The pharmacognostic evaluation of diverse plant parts, phytochemical elements, and variously reported pharmacological properties are all included in this paper. This paper will educate people on the medicinal value of Saraca asoca in the future (Ashok).

REFERENCES:

[1] M. A. Ali *et al.*, "Plastome of Saraca asoca (Detarioideae, Fabaceae): Annotation, comparison among subfamily and molecular typing," *Saudi J. Biol. Sci.*, vol. 28, no. 2, pp. 1487–1493, 2021, doi: 10.1016/j.sjbs.2020.12.008.

[2] N. K. Yadav *et al.*, "Saraca indica bark extract shows in vitro antioxidant, antibreast cancer activity and does not exhibit toxicological effects," *Oxid. Med. Cell. Longev.*, vol. 2015, p. 205360, 2015, doi: 10.1155/2015/205360.

[3] T. Dhanani, R. Singh, and S. Kumar, "Extraction optimization of gallic acid, (+)-catechin, procyanidin-B2, (–)-epicatechin, (–)-epigallocatechin gallate, and (–)-epicatechin gallate: their simultaneous identification and quantification in Saraca asoca," *J. Food Drug Anal.*, vol. 25, no. 3, pp. 691–698, 2017, doi: 10.1016/j.jfda.2016.08.004.

[4] S. Hegde *et al.*, "Population genetic and phytochemical dataset of Saraca asoca: A traditionally important medicinal tree," *Data Br.*, vol. 25, 2019, doi: 10.1016/j.dib.2019.104173.

[5] S. Lahiry, D. Bhattacharyya, A. Chakraborty, M. Sudarshan, and M. Manna, "Saraca asoca seed extract treatment recovers the trace elements imbalances in experimental murine visceral leishmaniasis," *J. Parasit. Dis.*, vol. 44, no. 1, pp. 131–136, 2020, doi: 10.1007/s12639-019-01173-9.

[6] A. Sharma, R. Tilak, and N. Sisodia, "Evaluation of bioactivity of aqueous extracts of Bougainvillea spectabilis, Saraca asoca, and Chenopodium album against immature forms of Aedes aegypti," *Med. J. Armed Forces India*, vol. 75, no. 3, pp. 308–311, 2019, doi: 10.1016/j.mjafi.2018.07.013.

[7] S. Fatema, M. Farooqui, M. Ubale, and P. M. Arif, "Physicochemical, phytochemical, biological and chromatographic evaluation of saraca asoca plant leaves," *Rasayan J. Chem.*, vol. 12, no. 2, pp. 616–624, 2019, doi: 10.31788/RJC.2019.1222065.

[8] M. Kundu, S. Tiwari, and M. Haldkar, "Collection, germination and storage of seeds of Saraca asoca (Roxb.) Willd," *J. Appl. Res. Med. Aromat. Plants*, vol. 16, p. 100231, Mar. 2020, doi: 10.1016/j.jarmap.2019.100231.

[9] J. Saha, T. Mitra, K. Gupta, and S. Mukherjee, "Phytoconstituents and HPTLC analysis in Saraca asoca (Roxb.)Wilde," *Int. J. Pharm. Pharm. Sci.*, vol. 4, no. SUPPL.1, pp. 96–99, 2012.

[10] S. Singh, T. H. Anantha Krishna, S. Kamalraj, G. C. Kuriakose, J. M. Valayil, and C. Jayabaskaran, "Phytomedicinal importance of Saraca asoca (Ashoka): An exciting past, an emerging present and a promising future," *Curr. Sci.*, vol. 109, no. 10, pp. 1790–1801, 2015, doi: 10.18520/v109/i10/1790-1801.

[11] N. K. Yadav *et al.*, "Saraca indica Bark Extract Shows In Vitro Antioxidant, Antibreast Cancer Activity and Does Not Exhibit Toxicological Effects," *Oxid. Med. Cell. Longev.*, vol. 2015, pp. 1–15, 2015, doi: 10.1155/2015/205360.

[12] N. Teli, S. A. Bhalerao, D. R. Verma, V. S. Didwana, and N. C. Teli, "OPEN ACCESS Saraca asoca (Roxb.), De. Wild: An overview," no. April, pp. 770–775, 2014, [Online]. Available: www.annalsofplantsciences.com

[13] J. Saha, K. Gupta, and B. Gupta, "Phylogenetic analyses and evolutionary relationships of Saraca asoca with their allied taxa (Tribe-Detarieae) based on the chloroplast matK gene," *J. Plant Biochem. Biotechnol.*, vol. 24, no. 1, pp. 65–74, 2015, doi: 10.1007/s13562-013-0237-3.

[14] G. Swar, S. Shailajan, and S. Menon, "Activity based evaluation of a traditional Ayurvedic medicinal plant: Saraca asoca (Roxb.) de Wilde flowers as estrogenic agents using ovariectomized rat model," *J. Ethnopharmacol.*, vol. 195, pp. 324–333, 2017, doi: 10.1016/j.jep.2016.11.038.

[15] A. Choudhary, P. Elumalai, S. Raghunandhakumar, T. Lakshmi, and A. Roy, "Anti-Cancer Effects of Saraca asoca Flower Extract on Prostate Cancer Cell Line," *J. Pharm. Res. Int.*, pp. 330–338, Dec. 2021, doi: 10.9734/jpri/2021/v33i62B35621.

[16] S. C. T., J. C. K., J. K. U. G., P. K.M., and I. Balachandran, "Identification of validated substitute for Asoka (Saraca asoca (Roxb.) Willd.) by phytochemical and pharmacological evaluations," *Futur. J. Pharm. Sci.*, vol. 6, no. 1, p. 10, Dec. 2020, doi: 10.1186/s43094-020-00024-2.

[17] M. Gill, M. Kinra, A. Rai, M. R. Chamallamudi, and N. Kumar, "Evaluation of antidepressant activity of methanolic extract of Saraca asoca bark in a chronic unpredictable mild stress model," *Neuroreport*, vol. 29, no. 2, pp. 134–140, 2018, doi: 10.1097/WNR.0000000000000944.

[18] S. Kumar, S. Narwal, D. Kumar, G. Singh, S. Narwal, and R. Arya, "Evaluation of antihyperglycemic and antioxidant activities of Saraca asoca (Roxb.) De Wild leaves in streptozotocin induced diabetic mice," *Asian Pacific J. Trop. Dis.*, vol. 2, no. 3, pp. 170–176, Mar. 2012, doi: 10.1016/S2222-1808(12)60041-3.

CHAPTER 7

A STUDY ON VOXELOTOR FOR THE TREATMENT OF SICKLE CELL DISEASE

Dr. Manish Soni, Assistant Professor,
Department of Biotechnology, Jaipur National University, Jaipur, India,
Email Id-manishsoni@jnujaipur.ac.in

ABSTRACT: The presence of thick, sickle cells is diagnostic of sickle cell disease, which leads to hemolysis of blood cells, anemia, organ failure, and, in the most severe instances, death. Studies documenting SCD's clinical symptoms and its diagnosis with monitoring, which is the need of the hour, have shown heterogeneity.More than 100,000 people in the United States are affected by the genetic illness known as sickle cell disease, which shortens their lifespan significantly. Anemia, vasoocclusion, and tissue destruction are hallmarks of this illness, which is caused by the synthesis of aberrant, sickle-shaped hemoglobin.The first medicine of its sort, Voxelotor, may change the underlying disease pathophysiology (by enhancing the affinity between Hb and oxygen) and suppress the sickling of red blood cells simply by changing how it is delivered. The effectiveness and safety of voxelotor treatment have been shown in many clinical studies and case reports involving sickle cell disease. Nursing implications are discussed, along with information on voxelotor potential side effects and its usage with vulnerable groups.

KEYWORDS:Cell, Disease, Sickle, Treatment, Voxelotor.

1. INTRODUCTION

Erythrocytes (which store hemoglobin or transport oxygen throughout the body) become elongated or sickle-shaped in people with sickle cell disease (SCD) due to a mutation in the Hemoglobin Sickle-Beta (HBB) gene. A mutant type of beta-globin called Hemoglobin-S is produced as a consequence (HbS). Sickle cell anemia (SCA), a hereditary blood ailment, is one of the most common hematological disorders, affecting a sizable percentage of the population in many countries. It is more common in people of South or Central American, Saudi Arabian, or Indian ancestry than in those with African or Sub-Saharan ancestry. About 72,000 Americans, or about one in every 500 African-American newborns and about one in every 1000-1400 American kids, are born with the disease [1].

Millions of individuals throughout the globe suffer from sickle cell disease (SCD), a chronic condition that is difficult to treat. The onset, frequency, and severity of SCD's clinical symptoms may vary widely, and the disease can impact more than one body system. The physical and social functioning, general health, and emotional well-being of patients are all impacted negatively by disease-related symptoms and consequences, which in turn contribute to a worse health-related quality of life (QOL) [2]. Therefore, it is essential to evaluate whether clinical advantages transfer to changes in a patient's health status as a whole, in addition to monitoring treatment-related physiological and symptomatic consequences.In SCD, erythrocytes take on a rigid crescent or sickle shape due to the polymerization of deoxygenated sickle hemoglobin (HbS), which disrupts the cell membrane. Repetitive trauma

makes these cells more prone to bleeding within the blood vessels. The increased stickiness of damaged erythrocytes is another possible cause of vaso-occlusive crises (VOCs). Hydroxyurea and regular blood transfusions were the cornerstones of SCD treatment until quite recently. Even though there have been great strides in both identifying and treating the symptoms of SCD, very few treatments that alter the course of the illness have been licensed [3].

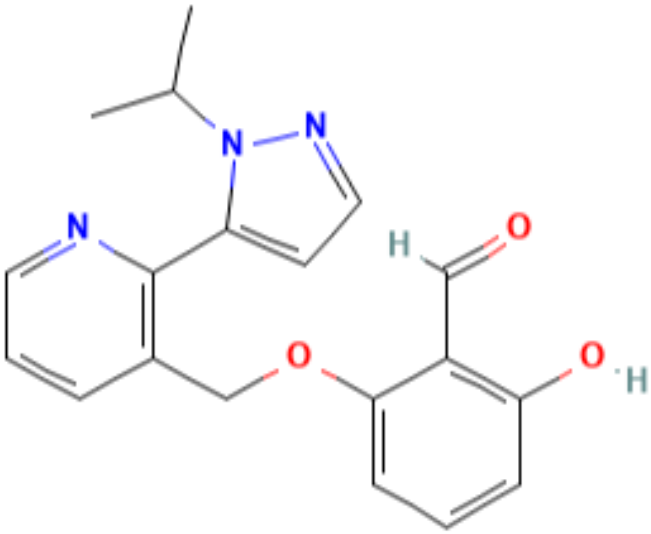


Figure 1: Shows the chemical structure of Voxelotor.

For patients with sickle cell disease, the oral inhibitor of hemoglobin S polymerase known as voxelotor has been effective in treating the condition. Rarely, substantial blood enzyme increases have been reported in patients using voxelotor, however, the drug has not been connected to cases of idiopathic acute liver damage or the chemical structure shown in Figure 1. Key indicators of RBC health have been demonstrated to improve in individuals with SCD after treatment with voxelotor, a new sickle hemoglobin (HbS) polymerization inhibitor. Hemoglobin (Hb) concentrations and indicators of hemolysis improved rapidly and persistently in individuals treated with voxelotor in phase III clinical study. The Clinical Global Impression of Change (CGI-C), a validated evaluation of the clinician's perception of the patient's global functioning before and after commencing a study drug, was used to evaluate the effect of voxelotor on patient disease status in the same research [4].Voxelotor alters hemoglobin, protecting patients against sickle cell crises, which may cause severe pain, hospitalization, and even death if left untreated. By stopping the destruction of sickled blood cells, which is a common complication of sickle cell disease, it prevents hemoglobin levels from dropping too low. In clinical studies, voxelotor resulted in a 40% rise in hemoglobin.

The most prevalent among hereditary diseases is sickle cell anemia. Those living in Sub-Saharan Africa, South Asia, the Middle East, and the Mediterranean are disproportionately affected by the illness. Roughly 100,000 Americans already have sickle cell disease, and that number is expected to rise. Heterozygous disorders such as hemoglobin sickle beta zero thalassemias, hemoglobin sickle beta plus thalassemia, and hemoglobin sickle cell disease are more prevalent than homozygous hemoglobin SS (HbSS) itself (HbSC)[5].There have been new medications identified to treat SCD that work by modifying its pathophysiology, hence reducing the occurrence of problems. The HbS polymerization inhibitor voxelotor (Oxbryta) has been licensed by the U.S. Food and Drug Administration for the treatment of sickle cell disease in adults and children over the age of 12.

2. LITERATURE REVIEW

According to research by Modupe Idowu et al., patients with sickle cell disease (SCD) suffer from a wide variety of clinical symptoms, such as acute and chronic pain, fatigue, and respiratory problems; in addition, SCD can cause chronic organ complications, which can cause disability and increased mortality.Treatment of SCD in patients aged 4 and older in the US, the EU, and the UAE; treatment of SCD in children aged 12 and older in these regions. Here, we provide a single-center analysis of the effects of voxelotor on 27 patients who were all given the drug for a minimum of 8 weeks, with positive results noted by both clinicians and patients. The effects of voxelotor on patients' health-related quality of life were measured using the Clinical Global Impression of Change and Patient Global Impression of Change rating scales, respectively. Clinical response to therapy was measured by both observational and objective laboratory data. Patients treated with voxelotor showed increases in hemoglobin concentrations and decreases in indicators of hemolysis, consistent with findings from other clinical investigations. The majority of patients reported significant reductions in illness symptoms, which corresponded positively with the evaluations made by medical professionals. These results imply that the use of voxelotors improves outcomes for patients with SCD, despite the limitations imposed by the retrospective open-label trial design.

Patient-reported outcome measures assessing the quality of ambulatory and ED treatment for individuals with SCD were developed by Christian T. Evensen et al. Following the Consumer Assessments of Healthcare Providers and Systems surveys, they drafted and field tested questions on the quality of care for SCD patients. Scientists used psychometric techniques to create ratings and assess their validity and reliability. Sixty-three percent of the study's participants were between the ages of 18 and 34; sixty-four percent of the participants were female, and sixty-four percent of the participants had SCD-SS. The Adult Sickle Cell Quality of Life Measurement information system Quality of Care survey was utilized as the instrument for this study.90% of subjects experienced at least 1 severe pain episode (7.8 2.3, 0–10 scale) in the prior year. Most (81%) selected home pain management over the ED, citing unpleasant experiences (83%). Access, Provider Interaction, and ED Care composites had reliable scores (Cronbach 0.70–0.83) and construct validity (r = 0.32–0.83 correlations with global care evaluations). Other studies have shown inadequacies in ED treatment for SCD adults. The Adult Sickle Cell Quality of Care Measurement is a self-report tool for recording and monitoring SCD care discrepancies [6].

Study authors Matthew P. Smeltze et al. stated that the SCD Implementation Consortium aimed to survey providers in the areas of 6 clinical centers across the USA, concentrating on non-emergency care from the providers' perspective, to examine the perceptions and level of comfort of providers regarding evidence-based care to identify barriers to treating individuals with SCD.105 SCD clinicians responded. Pediatrics (24%) and hematology/SCD (24%). 77% reported being comfortable managing acute pain, and 63% chronic pain. Hematologists and SCD specialists were more comfortable prescribing opioids (100% vs 67%, p=0.004) and using hydroxyurea (90% vs 51%, p=0.005) than other clinicians. 33% of providers didn't know the 2014 NHLBI recommendations. 63% of clinicians believed patients' medical needs were satisfied, compared to 22% for mental health.Many medical professionals are unaware of the SCD care recommendations established by the NHLBI. Providers' specialization, education, and experience in caring for patients with SCD all had a role in the prevalence and nature of barriers to treatment. If providers knew more, they could better use hydroxyurea, control pain, and aid patients with mental health issues [7].

According to the research by Mira Yang et al., people with SCD who adhere to their disease-modifying medications have a higher quality of life.Both SCD patients and their parents or

other caretakers were included in the 788 people studied over 12 studies. Self-report questionnaires, test indicators (such as fetal hemoglobin and mean corpuscular volume), and mHealth medicine trackers were all used to assess adherence. The quality of life was evaluated by utilizing self-report questionnaires to assess HRQOL.Greater HU adherence has consistently been linked to higher health-related quality-of-life ratings across all investigations. Better physical HRQOL results were seen in those who adhered to HUs more closely, as measured by reduced pain impact, decreased pain episode frequency, reduced exhaustion, and enhanced physical function and mobility. Improved emotional reaction, reduced anxiety and depression, enhanced social functioning, and strengthened peer interactions were all related to higher adherence.The author concludes that enhancing HRQOL in SCD patients is possible via optimizing HU adherence, which also has the potential to lessen healthcare utilization and boost patient satisfaction with therapy. Improving patient outcomes may be possible with the elimination of obstacles to HU adherence [7].

3. DISCUSSION

The mutated gene disclosed here causes the hemoglobin molecule to become polymerized, which in turn changes the erythrocyte's structure and its capacity to deform. Due to enhanced erythrocyte adhesion and the subsequent development of heterocellular aggregates, small vessel blockage and subsequent local hypoxia are physically induced. This mechanism initiates a cascade of events that lead to reperfusion damage by increasing his production, releasing inflammatory mediators, and generating free radicals. Hemoglobin may also release oxygen when bound to nitric oxide (NO), a powerful vasodilator. Sickling and rigidity of erythrocytes are increased by dehydration. Variations in cation homeostasis notably increased potassium and water efflux mediated by potassium-chloride cotransport and Gardos channels, which play a significant role in this process (calcium-dependent potassium channel). Increased neutrophil adhesiveness, nitric oxide binding, platelet activation, and hypercoagulability are all related pathological outcomes.

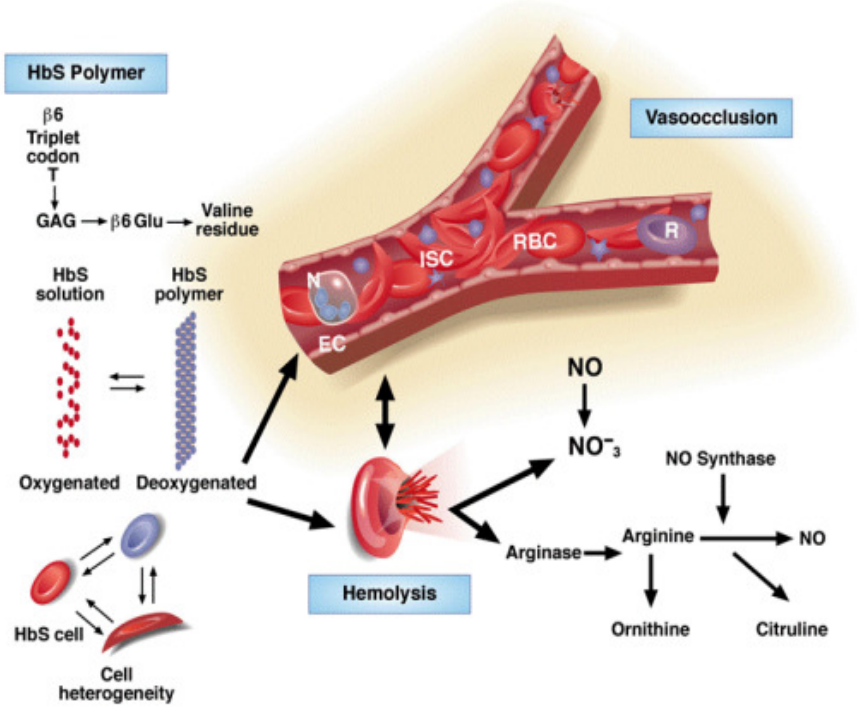


Figure 2: Pathophysiology of Sickle Cell Disease, Diagrammatically Represented[8]**.**

The Apo protein of hemoglobin, globin, shields the heme ring of the iron-bearing porphyrin, where reversible oxygen binding occurs, allowing the molecule to function effectively not just in oxygen transport but also in a wide variety of other physiological roles. Inherited changes to the main amino acid sequence of globin polypeptides may lead to hemoglobinopathies, which are serious medical diseases. Sickle cell illness is one instance of such a disease. It is only the HbS-replaced varieties of hemoglobin that will polymerize in the absence of oxygen. Sickle cell disease is characterized by hemolysis with vas-occlusion, as depicted in Figure 2, and occurs when an erythrocyte generates a critical quantity of HbS polymer, causing cellular death [9].

Voxelotor is prescribed for patients aged 4 and above who suffer from sickle cell disease, a genetic blood disorder. Hemoglobin S (HbS) polymerization inhibitors, like voxelotor, are a kind of drug. It prevents hemoglobin (a protein in red blood cells) from becoming malformed and aids in hemoglobin's ability to bind to more oxygen. You may take Voxelotor as either a tablet or a tablet for oral suspension.

Once daily, with or without meals. Voxelotor should be taken daily, at around the same time. Carefully adhere to the instructions on your prescription label, and if there is anything you do not understand, please see your doctor or pharmacist. Use voxelotor precisely as prescribed. Do not adjust your dosage or increase or decrease the frequency of administration without consulting the doctor.

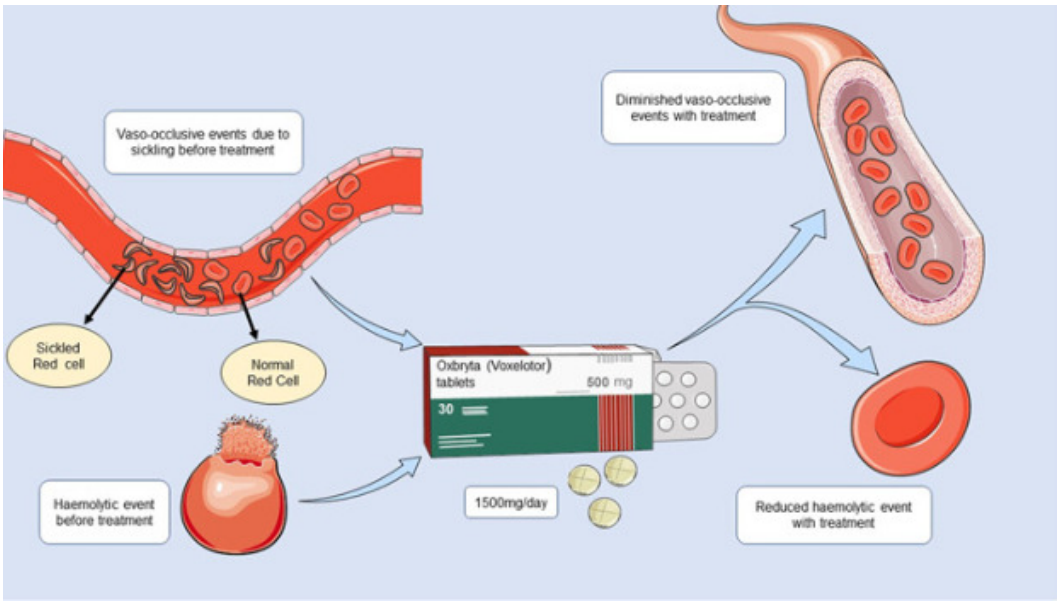


Figure 3: SCD-related hemolytic and sickling episodes both before and after the injection of voxelotor.

Voxelotor, also marketed under the trade name Oxbryta®, is an oral medication that inhibits the polymerization of hemoglobin S (HbS). Voxelotor is the first of a series of Hb oxygen affinity modifiers that binds to the N-terminal valine of Hb's alpha chains reversibly and covalently. Within 2 weeks of its initial dosage, a 1 g/dl increase in blood Hb concentration and a reduction in hemolytic episodes were seen. Reducing hypoxemic episodes lessens RBC sickling, which in turn lessens hemolysis and vaso-occlusive infarction in SCD patients shown in Figure 3. Voxelotor was shown to be well tolerated in a clinical study up to a dosage of 2800 mg, although the recommended dose for SCD patients with no concomitant conditions was 1500 mg once a day [10].

3.1.Mechanism Of Action:

By enhancing hemoglobin's affinity for oxygen via reversible binding to hemoglobin, voxelotor stabilizes the oxygenated hemoglobin state and inhibits HbS polymerization. Voxelotor improves hemoglobin's affinity for oxygen and reduces HbS polymerization in a dose-dependent way, according to preclinical research. Voxelotor may prevent the sickling of red blood cells, enhance red blood cell deformability, and decrease whole blood viscosity, all of which affect hemolysis and anemia [11].

3.2.Clinical Trials:

Phase 1/2 randomized, double-blind, placebo-controlled, single and multiple ascending dosage trial of voxelotor reported by Howard and colleagues [11]. Patient participants with sickle cell disease were paired with healthy controls. A six-month open-label, single-arm extension trial was conducted after the first research. Results showed that voxelotor improved clinical parameters of anemia, bouts of hemolysis, and proportion of malformed RBCs, and the research produced proof of concept (sickled).Voxelotor comes in 500-milligram capsules. Voxelotor has a suggested daily intake of 1,500 mg. The capsules should be swallowed whole, with or without meals, and not crushed or chewed. Individuals with severe hepatic impairment taking the maximum prescribed dosage of voxelotor showed up to a 90% increase in voxelotor concentration in clinical studies. Individuals with mild to moderate hepatic impairment do not need dosage adjustments, however, those with severe hepatic impairment should take just 1,000 mg orally once a day [12].

3.3.Contraindications:

There is a possibility that Voxelotor will interfere with certain laboratory measurements. When determining hemoglobin type by the use of high-performance liquid chromatography, voxelotor caused interference with the readings of different hemoglobin types (hemoglobin A, HbS, hemoglobin). Because the impact of voxelotor on subtype readings is not lasting, individuals and clinicians have the option to choose to temporarily stop using the medication when it is necessary to take such measures [13].

4. CONCLUSION

Pharmacological treatments for SCD have not yet been shown to be effective in curing the disease. Acute complications related to SCD have been the only ones demonstrated to be reduced by presently licensed medicines in randomized controlled studies. When used in individuals aged 12 and up, the new HbS polymerization inhibitor voxelotor is effective in treating SCD. To our knowledge, this is the only treatment available that directly attacks the underlying pathophysiology of SCD. The vaso-occlusive crises that are a typical side effect of SCD do not seem to be greatly reduced by voxelotor. The extent to which public and private health insurance and prescription drug programs will pay the high cost of the medicine is still up in the air. The new drug voxelotor lowers anemia in SCD patients by inhibiting the production of Q5 of HbS. For those with SCD, this novel method of therapy adds a new line of defense. Vasoocclusive crises are a typical side effect of SCD, although voxelotor doesn't seem to help avoid them. The extent to which the government and commercial health insurance and prescription drug programs will fund the high cost of the medicine is yet unclear.

REFERENCES:

[1] C. Spier, “Wintrobe’s Atlas of Clinical Hematology,” *Am. J. Surg. Pathol.*, 2008, doi: 10.1097/pas.0b013e31816955c5.

[2] D. K. McClish *et al.*, "Health related quality of life in sickle cell patients: The PiSCES project," *Health Qual. Life Outcomes*, vol. 3, no. 1, p. 50, Dec. 2005, doi: 10.1186/1477-7525-3-50.

[3] J. Howard, "Sickle cell disease: when and how to transfuse," *Hematology*, vol. 2016, no. 1, pp. 625–631, Dec. 2016, doi: 10.1182/asheducation-2016.1.625.

[4] J. Busner and S. D. Targum, "The clinical global impressions scale: applying a research tool in clinical practice.," *Psychiatry (Edgmont).*, vol. 4, no. 7, pp. 28–37, Jul. 2007.

[5] M. Arigliani *et al.*, "Lung function in children with sickle cell disease from Central Africa," *Thorax*, vol. 74, no. 6, pp. 604–606, Jun. 2019, doi: 10.1136/thoraxjnl-2018-212720.

[6] C. T. Evensen *et al.*, "Quality of care in sickle cell disease," *Medicine (Baltimore).*, vol. 95, no. 35, p. e4528, Aug. 2016, doi: 10.1097/MD.0000000000004528.

[7] M. P. Smeltzer *et al.*, "Identifying barriers to evidence-based care for sickle cell disease: results from the Sickle Cell Disease Implementation Consortium cross-sectional survey of healthcare providers in the USA," *BMJ Open*, vol. 11, no. 11, p. e050880, Nov. 2021, doi: 10.1136/bmjopen-2021-050880.

[8] M. H. Steinberg, "Sickle Cell Anemia, the First Molecular Disease: Overview of Molecular Etiology, Pathophysiology, and Therapeutic Approaches," *Sci. World J.*, vol. 8, pp. 1295–1324, 2008, doi: 10.1100/tsw.2008.157.

[9] C. Ibiapina, C. Alvim, and A. K. Vieira, "Nasal inspiratory peak flow in sicke cell disease," in *1.5 Diffuse Parenchymal Lung Disease*, European Respiratory Society, Sep. 2015, p. PA818. doi: 10.1183/13993003.congress-2015.PA818.

[10] A. Hutchaleelaha *et al.*, "Pharmacokinetics and pharmacodynamics of voxelotor (GBT440) in healthy adults and patients with sickle cell disease," *Br. J. Clin. Pharmacol.*, vol. 85, no. 6, pp. 1290–1302, Jun. 2019, doi: 10.1111/bcp.13896.

[11] J. Howard *et al.*, "A phase 1/2 ascending dose study and open-label extension study of voxelotor in patients with sickle cell disease," *Blood*, vol. 133, no. 17, pp. 1865–1875, Apr. 2019, doi: 10.1182/blood-2018-08-868893.

[12] M. Vissa and E. Vichinsky, "Voxelotor for the treatment of sickle cell disease," *Expert Rev. Hematol.*, vol. 14, no. 3, pp. 253–262, Mar. 2021, doi: 10.1080/17474086.2021.1893688.

[13] T. Boafor *et al.*, "Pregnancy outcomes in women with sickle-cell disease in low and high income countries: a systematic review and meta-analysis," *BJOG An Int. J. Obstet. Gynaecol.*, vol. 123, no. 5, pp. 691–698, Apr. 2016, doi: 10.1111/1471-0528.13786.

CHAPTER 8

A COHERENT STUDY ON MEDICINAL PROPERTIES OF *VITEX NEGUNDO* AS AN ALTERNATIVE MEDICINE

Prof. Kapilesh Jadhav, Professor,
Department of Biotechnology, Jaipur National University, Jaipur, India,
Email Id-kapilesh@jnujaipur.ac.in

ABSTRACT: Hardy plant Vitex negundo Linn. (Verbenaceae), is frequently distributed in the Indian subcontinent and is frequently used as an alternative medicine in Ayurveda. It is described as a potential herb for many illness, however these is a wide research gap between traditional medicine and its application due to lack of valid research on this herb. The current review aims to compile available scientific knowledge amalgamated with tradition knowledge to explore possible applications of V. negundo. Data are collected for its therapeutic characteristics, phytochemical or pharmacological activities, existing conventional applications using scientific approach established through research through the cutting-edge scientific knowledge and techniques. Plant extracts are frequently used to treat a wide range of human ailments. The chemical constituents of this plant have the potential to use as anti-diabetic, antibacterial, antifungal, antinociceptive, anti-inflammatory, anticonvulsant and antioxidant agent. In Unani and Siddha medicine, the seeds are recommended for delaying ejaculation and boosting male lidibo. Vitex negundo relieves aches and relief pains in the joints and muscles. In present study an attempt was made to explore possible medicinal use of V. negundo. This paper may provide a plateform for further research to explore the benefits of V. negundo.

KEYWORDS:Anti-inflammatory,Antibacterial, Ayurveda, Diseases, Herb, Phytochemicals Vitex negundo.

1. INTRODUCTION

Vitex negundo Linn. (Verbenaceae), often referred to as Nirgundi locally, is a woody, fragrant deciduous shrub that can grow to be a small tree. It is a significant medicinal value plant. It is an upright, 2–5 m tall, thin tree with branchlets that are quadrangular in shape. The leaves contain five palmately arranged, lanceolate, 4–10 cm long, hairy underneath, and pointed leaflets that are pointed at both ends. Afghanistan, outside of Africa, Pakistan, Malaysia, India, Thailand, and Madagascar have all been reported to have it. In wastelands or mixed open forests, it thrives in humid conditions or next to watercourses. It is grown commercially as a crop in some Asian, North American, European, and West Indian locations. Additionally, it is utilized to produce food and timber [1], [2].

Historically this herb was used to manage plant diseases and pests since ancient times, *V. negundo* has been used to treat plant illnesses and prevent tree wind damage. To get successful results in the treatment of wind disorders, Vishvavallabha refers to fumigation with a mixture of nigundika, guggul *Commiphora wightii*, as well as oil cake at the root. A frostbitten tree can develop a lot of sprouts if it is treated using cow dung ash and by being sprinkled with a nirgundika decoction, according to Vishvavallabha [3].

Approximatelytwenty five percent(25%) of all medications that are given in industrialized nations contain substances that are either directly or indirectly obtained from plants. It has been discovered that *Vitex negundo* has a variety of phytochemicals as well as biologically active ingredients that are widely used in the pharmaceutical sectors.

Typically, phytochemicals as well as secondary metabolites take the shape of intricate combinations that vary depending on the organs and developmental stages of plants. A thorough description of the many phytochemical components that have been identified from various *Vitex negundo* sections [4]–[6].

2. LITERATURE REVIEW

Vitex negundo is a plant that is indigenous to tropical Eastern or Southern Africa, Asia, or Europe. It is a small, upright tree or shrub that grows anywhere between 2 and 8 meters tall. Its bark has a rusty brown color. It has digitated leaves with five lanceolate leaflets, sometimes three. The center leaflet, which is the biggest and has a stalk, is the longest and ranges in length from 4 to 10 cm. The underside of the leaf is hair-covered and has toothed or serrated edges. The many, white to blue blooms are produced in panicles. The fruit is an egg-to-round, 4 mm-diameter, juicy drupe. When ripe, it is dark purple or black [7].

The herbal medication vitex may be made from the plant's leaves, seeds, flowers, or roots. When treating skin conditions, a decoction of Vitex roots and leaves is applied topically to wounds as well as an aromatic bath. When its paste is applied topically, it soothes pain, treats edema or swelling, cleans and mends ulcers or wounds, as well as reduces swelling. It is an anthelmintic that eradicates bacteria and worms. It treats itching and is anti-dermatosis. It treats diseases of the eyes, nose, or otorrhoea. The root of the *Vitex negundo* plant is very useful for the treatment of rheumatism, and the leaves of *Vitex negundo* are for the treatment of skin disease.

2.1. Medicinal Plants:

Infectious and chronic illnesses can be treated using a variety of compounds found in plants that are employed in traditional medicine. A survey conducted by the World Health Organization found that more than 80% of people worldwide rely on traditional medicine to meet their basic medical needs. As a result, the demand for drugs made from plants is rising. Therefore, it is important to conduct thorough research on the plants used in traditional medicine to treat a range of ailments. Consequently, it's important to assess medicinal plants for any potential biological action [8], [9].

Although practically all of the components of *V. negundo* are employed, the extract from either the leaves or roots is most significant in the field of phytomedicine since it is the one that is used to make medications. The Ayurvedic and Unani systems of medicine employ leaf extract. Fresh mature leaf water extract had anti-inflammatory, analgesic, or antihistamine effects. Lignans, a group of organic substances found in *V. negundo*, showed *in-vitro* anti-cholinesterase action. However, no research has been done to examine the effectiveness of *V. negundo* extracts against memory loss in living organisms [10], [11].

To preserve pulses against insects, *Vitex negundo* leaf extract is typically used as a grain preservative. The best part of the plant to utilize medicinally is the leaves. It is used to treat a variety of conditions, including bronchitis, gonorrhea, rheumatoid arthritis, toothache, inflammation, leucoderma, and skin ulcers. Along with these other uses, they serve as tonics, vermifuges, galactagogues, emmenagogues, antipyretic, antibacterial, or antihistaminic agents. It is used to make oil that is used on scrofulous sores and sinuses. Additionally, Ehrlich ascites tumor cells were sensitive to its extract's anticancer properties. Rheumatism, dysentery, dyspepsia, or piles are treated with the roots, which are also used as tonics, febrifuges, expectorants, anthelmintics, and diuretics [12], [13]. The astringent blossoms are

used for liver problems, fever, and diarrhea. The bark is used to treat toothaches, while the dried fruits are vermifuges. According to chemical analysis of the essential oil extracted from *V. negundo* leaves, vivid floral is the main component. According to reports, the plant contains therapeutic qualities that can treat rheumatic pain or lessen joint swelling. It has been utilized to treat chronic bronchitis in traditional Chinese medicine. An infusion of the twigs is said to be a successful treatment for headaches, vertigo, convulsions, coughing, or mental restlessness. It is also believed to encourage alertness [14], [15].

Its leaves and seeds, which are also said to have insecticidal effects, are frequently applied topically to treat rheumatism and joint pain. Internally, its leaves are used as a decoction for diuretic, vermifuge, tonic, expectorant, or febrifuge purposes. The chemical makeup of the leaf essential oils produced from *V. negundo* or other Vitex species has been the subject of several research in the past. Its essential oil has demonstrated efficacy in treating sores and ulcers. According to reports, *V. negundo* leaves have pesticide, antifungal, and antibacterial capabilities. This plant's leaves have been demonstrated to have the ability to deter mosquitoes as well as possess antiparasitic, antibacterial, antiulcerogenic, or hepatoprotective properties. The methanolic root extract has strong anti-snake venom properties. A toxic lepidopteran insect pest was shown to be susceptible to the insecticidal, ovicidal, growth-inhibiting, and morphogenetic actions of the methanolic extracts of *V. negundo*. The leaves of *Vitex negundo* have shown notable analgesic or anticonvulsant action against strychnine or leptazole in petroleum ether extract. Rats treated with *Vitex negundo* dried leaf powder demonstrated anti-arthritic efficacy.

In Bangladesh's traditional medical system, *V. negundo* is used for a variety of medical purposes. In addition to being used by local doctors and healers for traditional medicine, this plant also reportedly exhibited a variety of pharmacological properties, such as analgesic, antihyperglycemic effect, antinociceptive, anti-fertility, antifeedant, anti-inflammatory, anti-antioxidant, cytotoxicity for human cancer cell line, antibacterial activities against liver damage caused by d-galactosamine, frequently used tubercular drugs, and. The plant components are claimed to have significant impacts on preventing the lethal activity caused by the venom of the Vipera Russell or Naja kaouthia in both in vitro and in vivo. These effects include being anti-microfilariae, anti-viral, anti-bacterial, anti-fungal, insecticidal, and larvicidal.

According to reports, the plant contains effective and cutting-edge medicinal compounds for scavenging NO and controlling pathological diseases brought on by excessive NO production and peroxynitrite, its oxidation result. Administration of *V. negundo* extracts significantly enhanced the anti-inflammatory, sedative-hypnotic, and anti-convulsant effects of widely used medications. Additionally, it has been shown that *V. negundo* inhibits the activity of the enzymes lipoxygenase, xanthine-oxidase, chymotrypsin, butyrylcholinesterase, and tyrosinase. In Asia, particularly India, China, and Malaysia, folkloric medical systems have used medicinal herbs and diverse plant components for a variety of ailments. Numerous pharmacological, as well as ethnobotanical effects of *V. negundo*, have been documented, including analgesic as well as anti-inflammatory effects, enzyme inhibitions, antioxidant activity, antiandrogenic effects, CNS effects, nitric oxide scavenging effects, anti-bacterial effects, antifungal effects, hepatoprotective effects, larvicidal effects, as well as mosquito-repellent effects. NSAID-like activity was detected in the leaves of *V. negundo*. Traditional uses of the plant include the treatment of rheumatism, leprosy, cough, asthma, fever, eye illness, inflammation, intestinal worms, and skin ailments. Roots have diuretic, febrifuge, tonic, febrifuge, anodyne, and febrifuge properties. To lessen phlegm in coughs, asthma, and chronic bronchitis, leaves are decocted and served as a drink. Despite a recent review finding

that there is no evidence to imply that such treatments create any meaningful effectiveness, cough medications are among the most often used over-the-counter medications in the world.

P. Renuka Devi, *et al.* reported on the anti-microbial properties of several *Vitex negundo* Linn leaf extracts. Three microorganisms were used as test subjects to determine the antibacterial effectiveness of *Vitex negundo* leaves. For example, *Staphylococcus aureus, Escherichia coli*, as well as *Klebsiella pneumonia* were employed to test the antibacterial properties of fresh aqueous, chloroform, heated aqueous, as well as methanolic extracts of leaves. The three bacteria were shown to be resistant to the antibacterial activity of the fresh or aqueous leaf extracts in different dilutions [16].

KambhamVenkateswarlu studied that this *Vitex negundo* Linn is an Indian plant with extensive traditional usage against several ailments. The study was created through research utilizing cutting-edge scientific methods. Similarly to this, it has been established that many plant components, including leaves, fruits, seeds, etc., contain nutrients and health-promoting substances that may be used in food for humans. Another Indian herb with extensive historical applications against several ailments is *Vitex negundo Linn.* The current study seeks to summarize the medical benefits of *Vitex negundo* discovered via research employing cutting-edge scientific methodologies [17].

Ajay Kumar Meena *et al*, studied plants and the active ingredients in them are crucial in the prevention of many diseases. Especially in Ayurveda and Siddha, the majority of Vitex species have medicinal uses in conventional Indian medicine. The genus Vitex has over 270 different species that may be found all over the world. Most of these species have analgesic, antibacterial, antioxidant, hepatoprotective, anti-inflammatory, and anti-asthmatic properties. The pharmacology evidence for the benefits of Vitex plant extracts is reviewed in this article, along with an outline of the identified phytochemical components and the most extensively researched biological effects [18].

3. METHODOLOGY

For this study, a database search on PubMed, Google Scholar, Research Gate, Science Direct, and other sites was used to find current review studies. A combination of keywords such as "anti-inflammatory, antibacterial, disease, therapy, *Vitex negundo*" were used in the review technique. Title and abstract screening were used for the initial review of records. Additionally, non-extractable data, duplicate research, and insufficient information were grounds for excluding records. Figure 1 below provides more information on the methodology used to conduct the review study.

A member of the Verbenaceae family, *Vitex negundo* is also known as the "five-leaved chaste tree" as well as grows to a height of approximately 3 meters. It has branchlets that are quadrangular, thickly white, and tomentose. It may be found all across India, up to a height of 1500 meters, in damp areas, and frequently on riverbanks. It is also grown in Central Asia and the Mediterranean region. It is said to provide several medical benefits, particularly for the treatment of fungal, antioxidant, inflammatory, or hepatoprotective conditions. In South and Southeast Asia in especially, it is frequently utilized in folk medicine. Alternative medicine that derives from plants and plant extracts is known as herbal medicines. The predecessor to modern medicine, herbal remedies have been used for centuries. They are used to treat physical and mental health issues as well as sicknesses and diseases. A wide range of natural resources, such as plant leaves, berries, flowers, bark, as well as roots, are used to make herbal treatments.

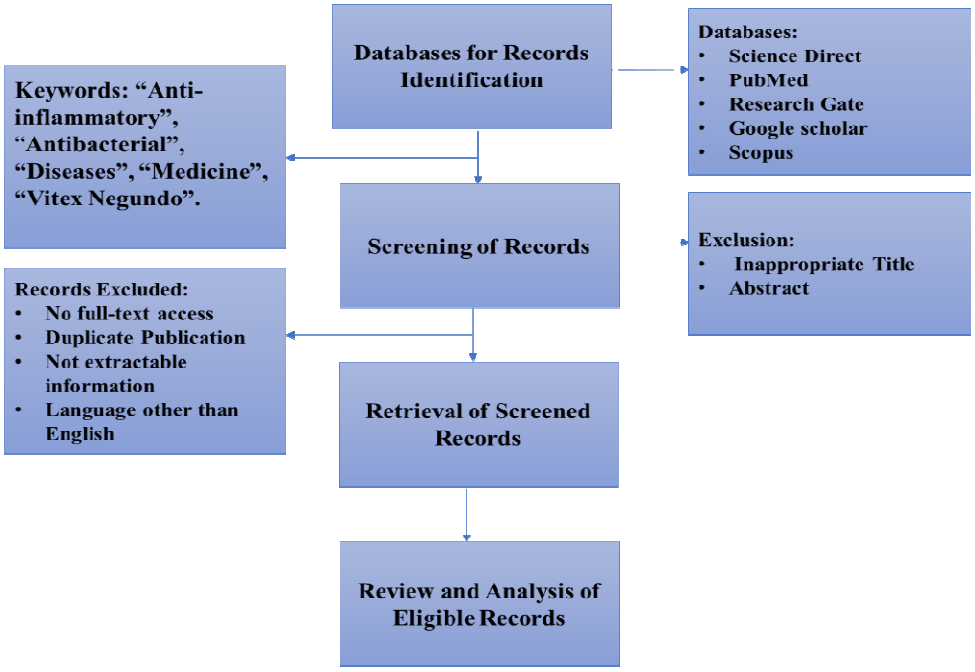


Figure 1: Flow Diagram of Methodology.

4. DISCUSSION

4.1. Benefits of Vitex negundo:

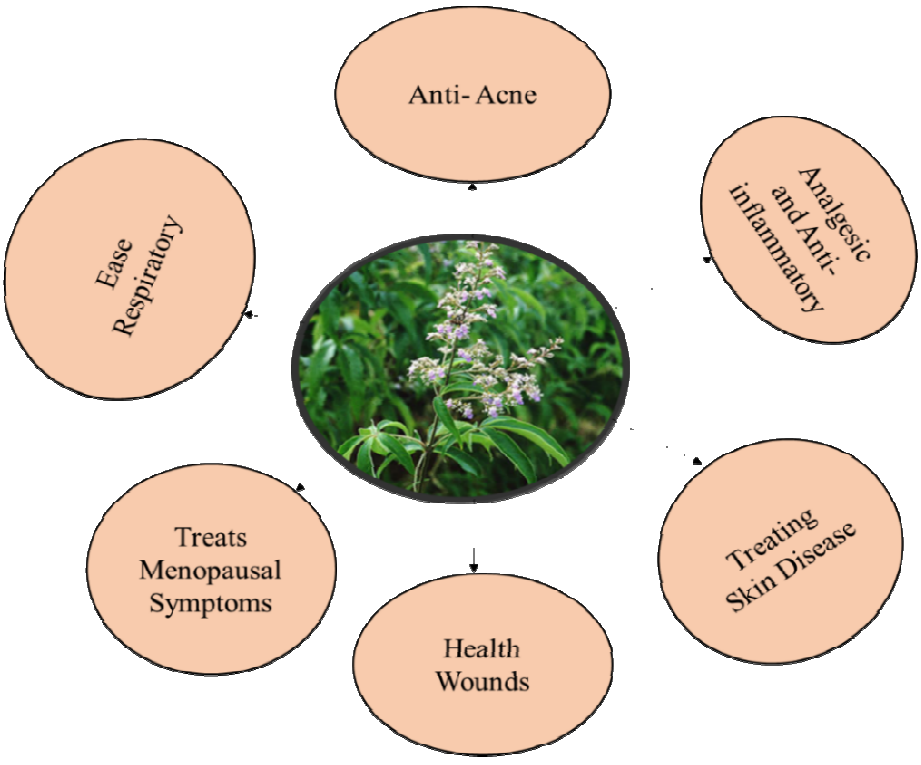


Figure 2: Health Advantage of *Vitex negundo*.

4.1.1. Nirgundi Oil's Analgesic or Anti-Inflammatory Properties:

Nirgundi oil is effective at relieving pain. It lessens muscular and joint pain and inflammation brought on by injuries as well as interior illnesses, which are shown in figure 2. Fractures can also be healed with Nirgundi Ras. Nirgundi products can be used to treat ulcers as well.

4.1.2. Natural remedy Nirgundi Helps Fertility:

For many women, fertility is a serious problem. It restricts not only a person's physical and emotional well-being but also her social and emotional circumstances. Nirgundi oil use has been seen to increase fertility levels in several women and aid in conception. Nirgundi leaves oil can be used to treat a variety of skin conditions. Leprosy, leukoderma, and vitiligo are all treated using this plant's components.

4.1.3. Nirgundi Oil for PMS Management:

In the days leading up to the commencement of their period, women frequently go through intense mental, emotional, and physical upheaval. Nirgundi can help with PMS symptoms including anxiety, melancholy, and fluid retention more easily. Regularly, a person might even fully recover and have no more PMS symptoms.

4.1.4. Nirgundi Helps in Digestion

A great treatment for intestinal issues is nigundi ras. It aids in bolstering and enhancing the digestive system's performance. It enhances appetite while reducing gas production. Nirgundi plant extracts work well for treating stomach pain brought on by poor digestion and bloating that causes gas buildup. The digestive system is cleansed.

4.1.5. The respiratory system is more easily:

By eliminating mucus from the respiratory tract, nirgundi plant tea aids in decongesting it. This facilitates the opening of air passageways, improves ventilation, and normalizes breathing. Because of this quality, nirgundi is a popular component in Ayurvedic remedies that treat respiratory conditions including bronchitis, asthma, and pneumonia.

4.1.6. Nirgundi Oil's anti-acne properties

Many individuals take acne quite seriously. A pimple can appear at any time, and they hurt as well as look bad. Many women get acne and pimples as a result of PMS. Nirgundi has been seen to have a therapeutic impact on acne brought on by hormonal fluctuations.

4.1.7. Heal Wounds with Nirgundi:

Nirgundi leaves oil is a great component for treating wounds since it has anti-bacterial, anti-inflammatory, and analgesic, properties. It shields the wounds from infection and helps keep the area odor-free. It eases discomfort and swelling in the afflicted region.

4.2.Nirgundi's uses:

It is quite advantageous to use nigundi. In addition to its medical purposes, this plant also has a variety of additional uses, such as preventing insects from ruining long-term stored clothing by placing dried leaves between them. Burning the leaves of this plant also acts as a very powerful mosquito repellant. Nirgundi leaves are employed as natural insecticides and pesticides. It is always preferable to utilize natural alternatives to pest or insect repellents rather than the chemicals that are commonly employed because they are terrible for both the environment and human health.

4.3. Nirgundi Side Effects & Allergies:

Consumption of nirgundi is associated with several negative side effects and issues, particularly in females. It is not a good choice for pregnant women because of its capacity to

control hormone secretion. It disrupts oral contraceptives and might lessen their effectiveness. If a person has any cardiac problems, they should only take nigundi under medical supervision since it changes the way the heart works. The menstrual cycle may change, and it may also cause allergies to flare up. Additionally, it has been shown that breastfeeding mothers have seen changes in their milk output. There is no doubt that a change occurs, notwithstanding the dispute around its nature.

Dry mouth, headaches, nausea, tachycardia, upset stomach, or urticaria are common side effects of nigundi use. These negative effects have been observed to be rare, mild, and reversible. The important biological discoveries and known phytochemical components of the Vitex genus are summarized in this paper. Several physiologically active chemicals with anti-inflammatory, antibacterial, antioxidant, analgesic, antiimplantation, antihistamine, hepatoprotective, or antiasthmatic actions are present in the plants of the Vitex genus, according to investigations done to date. As a result, more research into the Vitex genus as a source of hepatoprotective compounds is warranted. There is a present demand for novel plant-derived bioactive molecules; as a result, the genus Vitex might be a significant natural source for the creation of new medications and may offer a practical way to treat cardiac issues and other serious ailments in the developing world.

Nirgundi helps maintain good eye function, helps the lungs, relieves rheumatic inflammations, but also encourages the growth of hair. According to Ayurveda, nigundi can also aid with hard teething, hypopigmented skin and spleen enlargement. Additionally, nirgundi increases overall urine production and supports healthy menstrual flow in females. According to contemporary practice, Nirgundi Leaves Powder is beneficial when applied with hot water to rheumatic growths of the bones or sprains.

5. CONCLUSION

The pharmacognostic, phytochemical, or medicinal functions of the leaves of *Vitex negundo Linn,* a plant in the Lamiaceae family, is compiled in this paper. A thorough analysis of the research in the area shows that Nirgundi is clearly of the highly importance in the traditional medical system. To make herbal medications, almost every component of the plant is utilized. The plant has been shown to have analgesic, anti-cancer, anti-microbial, hepatoprotective, antifeedant, anti-hyperpigmentation, anti-inflammatory, or related properties. According to in-depth scientific investigations, the plant's therapeutic characteristics and chemical components play a part in the treatment of several human diseases. Numerous scientific studies have shown that *V. negundo* has a wide variety of biological activities. It stands for a class of herbal remedies having a dependable theoretical base. As a result, the pharmaceutical industry has a lot of promise for this plant to be developed into a medication. However, clinical research is still required to prove the plant's medicinal potential before it can be recommended for use in certain circumstances. In recent years, pharmacological research has concentrated heavily on medicinal plants, the basis of conventional medicine. This research has looked at the potential of medicinal plants as innovative therapeutic chemical sources or as sources of lead compounds for pharmaceutical development. Consequently, to provide the groundwork for more pharmacological study, it is vital to look for bioactive compounds in medicinal plants.

REFERENCES:

[1] T. Chandrasekaran, A. Thyagarajan, P. G. Santhakumari, A. K. B. Pillai, and U. M. Krishnan, “Larvicidal activity of essential oil from Vitex negundo and Vitex trifolia on dengue vector mosquito Aedes aegypti,” *Rev. Soc. Bras. Med. Trop.*, 2019, doi: 10.1590/0037-8682-0459-2018.

[2] N. Kakadia, P. Patel, S. Deshpande, and G. Shah, “Effect of Vitex negundo L. seeds in letrozole induced polycystic ovarian syndrome,” *J. Tradit. Complement. Med.*, 2019, doi: 10.1016/j.jtcme.2018.03.001.

[3] M. Zargar *et al.*, “Green synthesis and antibacterial effect of silver nanoparticles using Vitex negundo L.,” *Molecules*, 2011, doi: 10.3390/molecules16086667.

[4] K. Sharma, M. Yadav, and K. Attri, “Pharmacognostic studies on methanolic extract of leaves of vitex negundo linn,” *Pharmacogn. J.*, 2020, doi: 10.5530/pj.2020.12.83.

[5] T. H. T. Nguyen *et al.*, “Further terpenoids from Vitex negundo L. growing in Vietnam,” *J. Saudi Chem. Soc.*, 2021, doi: 10.1016/j.jscs.2021.101298.

[6] D. M. Alegado-Bagaoisan, M. C. R. Castro, and J. M. Purificacion, “A systematic review on Vitex negundo (NIRPROMP formulations) for the treatment of acute cough of mild to moderate severity in pediatric patients,” *Acta Medica Philippina*. 2020. doi: 10.47895/amp.v54i1.1096.

[7] B. S. Gill, R. Mehra, Navgeet, and S. Kumar, “Vitex negundo and its medicinal value,” *Molecular Biology Reports*. 2018. doi: 10.1007/s11033-018-4421-3.

[8] A. Khan *et al.*, “Bioactive chromone constituents from Vitex negundo alleviate pain and inflammation,” *J. Pain Res.*, 2018, doi: 10.2147/JPR.S145551.

[9] M. S. Rabeta and Z. A. An Nabil, “Total phenolic compounds and scavenging activity in Clitoria ternatea and Vitex negundo linn,” *Int. Food Res. J.*, 2013.

[10] L. L. Tang *et al.*, “Distribution and species diversity patterns of Vitex negundo var. Heterophylla shrublands in North China,” *Chinese J. Plant Ecol.*, 2019, doi: 10.17521/cjpe.2018.0162.

[11] G. Rana, “Inhibition efficiency of a newly isolated flavonoid compound from Vitex negundo L. leaves against cattle-endosymbiont Setaria cervi: Phytomedicine for lymphatic filariasis,” *Parasite Epidemiol. Control*, 2018, doi: 10.1016/j.parepi.2018.03.002.

[12] D. Anusha, S. Sharanya, Ramya, and D. C. David, “Anticancer Screening of the Phytochemicals Present in the Medicinal Plant Vitex Negundo against Mutant Anaplastic lymphoma Kinase (ALK) Protein: A in-silico Approach,” *Biomed. Pharmacol. J.*, 2019, doi: 10.13005/bpj/1727.

[13] M. Issa *et al.*, “Appraisal of phytotoxic, cytotoxic and genotoxic potential of essential oil of a medicinal plant Vitex negundo,” *Ind. Crops Prod.*, 2020, doi: 10.1016/j.indcrop.2019.112083.

[14] Y. Huang, G. Y. Ding, and P. Hu, “Vitexnegheteroin M, a new phenolic glycoside from Vitex negundo var. heterophylla,” *Nat. Prod. Res.*, 2021, doi: 10.1080/14786419.2019.1656628.

[15] S. Shah, T. Dhanani, and S. Kumar, “Validated HPLC method for identification and quantification of p-hydroxy benzoic acid and agnuside in Vitex negundo and Vitex trifolia,” *J. Pharm. Anal.*, 2013, doi: 10.1016/j.jpha.2013.09.008.

[16] V. Linn and R. Kokilavani, “Anti Microbial activity of the various leaf extracts of,” *Anc. Sci. Life*, vol. 28, no. 2, pp. 15–18, 2008.

[17] K. Venkateswarlu, “Vitex negundo□: Medicinal Values , Biological Activities , Toxicity Studies , Phytopharmacological Actions,” no. April, 2016.

[18] A. Kumar, U. S. Niranjan, M. M. Rao, M. M. Padhi, and R. Babu, “A review of the important chemical constituents and medicinal uses of Vitex genus,” *Asian J. Tradit. Med.*, vol. 6, no. 2, pp. 54–60, 2011.

CHAPTER 9

AN ANALYTICAL STUDIES OF PHARMACOLOGICAL PROPERTIES OF *THYMUS VULGARIS*

Dr. Sunita Ojha, Assistant Professor,
Department of Biotechnology, Jaipur National University, Jaipur, India,
Email Id-ojhasunita@jnujaipur.ac.in

ABSTRACT: Thymus vulgaris Linn. is a medicinal and culinary plant from Southern Europe. T. vulgaris is a well-recognized medicinal plant having gastroprotective, anti-infective, anti-inflammatory, and immunomodulatory properties. A mixture of monoterpenes found in T. vulgaris oil. The oil has antibacterial, antitussive, antispasmodic, antimicrobial, and antioxidative properties. Many modern medicines are inadvertently made from medicinally innovative medicinal herbs. The number of species of flowering plants is estimated to be 250,000. There are many benefits to studying medicinal plants, including helps to understand plant toxicity or protecting humans and animals from natural toxins. Our findings can provide a platform for further studies. The therapeutic application documented, points to possible use for this carvacrol-rich T. vulgaris in the prevention and treatment of fungal infections or topical irritation. Additionally, the mode of action is mostly unknown and has to be explored. The objective of this paper is to present a thorough analysis of pharmacological features of T. vulgaris. In future, this paper may provide a background for physicochemical characterization of their bioactive compounds and experimental validation of various therapeutic use of T. vulgaris.

KEYWORDS: Antibacterial, Anti-Inflammatory, Antioxident, Diseases Medicine, Immunomodulator, Thymus vulgaris (T. vulgaris).

1. INTRODUCTION

A plant from the mint family called thyme (*Thymus vulgaris*) is frequently used as an ingredient of spices. The plant is said to offer therapeutic benefits in addition to its flavor-enhancing qualities. Anti-inflammatory, antibacterial, or antioxidant properties are well-known for their potential utility in treating everything from skin disorders to intestinal infections. Thyme is versatile and may be used fresh, dried, or distilled into a lavender oil for aromatherapy. Thyme is also offered as a liquid or capsule-based nutritional supplement. Even teas, face masks, popular mouthwashes, and nose sprays contain thyme [1]. The best-known species in the genus Thymus (family Lamiaceae) is *Thymus vulgaris* (Tv), often called thyme. It is especially common in the Mediterranean region, North Africa, Asia, and Europe. The biological and natural uses of members of the thymus family, such as their use as food additives, traditional medicinal remedies, or pharmaceutical preparations, are well known [2], [3].

The herb commonly known as thyme has been utilized for ages as a spice, home medicine, medication, perfume, or pesticide. It may have first been used as incense. Based on its historical, fragrant, and therapeutic qualities, it is regarded as one of the most distinguished plants. Thyme was employed for numerous medicinal uses by the Sumerian or Egyptian cultures in antiquity to prevent people from dying. The Romans cooked the thyme to provide the cheese taste as well as to keep away hazardous animals. In addition, Tv has been used for a while to cure a variety of illnesses like intestinal problems, dermatophyte poisoning, pneumonia, or dental plaque [4].

The essential oil of Tv, which is used in meals for taste, fragrance, and preservation as well as in traditional medicine, is responsible for the plant's medicinal properties. Additionally, essential oils are among the most widely utilized essential oils in the food sector as well as in cosmetics as antioxidants but also preservatives. Numerous investigations on the biological effects of essential oils have been conducted. This research served as the foundation for this analysis, which sought to examine some of the possible health advantages of Tv essential oil (TVEO), focusing on the gastrointestinal system [5], [6].

1.1. Thymus vulgaris (TV's) Genesis and Development:

The genus Thymus contains over 300 different kinds of fragrant herbs and subshrubs. These plants may be found all over the world, particularly in regions with Mediterranean Sea coastlines, Asia, North Africa, and Southern Europe. Tv is a member of the "Lamiaceae" family. Thymoma, an antiquated Greek word for anger, was presented to the gods in temples because of its odor. Due to its pharmacological and biological characteristics, thymus species have been used as medicines since ancient times [7], [8]. Their leaves are commonly for use as herbal tea, a stimulating, an antiflatulent, a cough suppressant, a therapy for the common cold, as well as an antibacterial agent. Traditional Yemeni medicine states that fresh or dried leaves of Tv can be used as a dry powder in hot milk or as sesame oil to treat several ailments, including tonsillitis, gastritis, pharyngitis, and kidney disease.

1.2. Thymus vulgaris Plant Description:

T. vulgaris is a small evergreen ground cover that grows to a maximum height of about 40 cm. It gradually grows up to a height of 0.2 m. The stem of the plant becomes woody as it ages. As shown in Figure 1, the small leaves have a wide variety of forms and are covered with hairs, and vary in size from 2.5 to 5 mm. The technique of producing the oil by condensation mostly uses slightly fleshy aerial components and ovate quadrangular leaves. Thyme can grow in any sunny climate. Additionally, experiments 23 and 24 showed that thyme requires 5 to 8 pH or well-drained soils to develop.

Figure 1: Pictorial Representation of *Thymus vulgaris*, a) Leafs, b) flowers, c) Fruits.

Thyme is a small perennial shrub that grows both horizontally and vertically. Rarely it grow taller than 40 cm. The stem becomes woody after ripening. Thyme leaves vary widely in size and hair cover and are typically only 2.5 to 5.00 mm long. Additionally, each species has a unique fragrance. Volatile oils are mostly extracted from fleshy leaves that vary in form from oval to oblong. It has culinary usage in the modern and dried herb markets. Thyme thrives in

conditions that range from mild to hot, dry, and sunny, as well as in any location where the plants don't appear to be shaded [9], [10]. To reach its maximum capacity, it needs full sunlight. Thyme dislikes too much moisture since it will get rot illnesses as a result of its health. Thyme loves pH ranges of 5.0 to 8.0 in light, well-drained soils. Thyme species thrive on abrasive, grit-laden soils that can be unsuitable for many other plants. Processing is required to separate the stems or leaves from the dried product. The product must then be filtered to eliminate debris or provide a consistent result [9], [10]. There are several methods, ranging from the sun to elegant dryers. The quality of both volatile oils suffers as a result of sun-drying techniques. Artificial drying techniques provide better product quality management. To dry higher-quality leaves, a forced air-flow dryer would be the best option. Thyme should be dried at temps under 40 °C to preserve a good, fresh color and reduce flavor loss from volatile oil volatilization. The leaves should be sieved, removed from the stems, or arranged in a hierarchy after drying. Fresh produce must be free of foreign matter, appear recent and soft, and have acceptable color and flavor.

2. LITERATURE REVIEW

Devansh Mehta *et al.* studied newer pharmacological properties and the latest chemical composition present in them. Medicinal plants have the properties to treat various diseases and ailments which are present in humans as well as animals. Traditional medicines which have again gained importance in recent times utilize the advantages of healing properties of Phyto-constituents present in herbal or medicinal plants and heal the respective disease or ailment. Medicinal plants have the properties and capabilities to treat almost all diseases. It is because of these reasons that again latest research is happening in this field of medicinal sciences. Plant medicines have a big advantage, that they have very minute or no side effects on the human body. *Thymus vulgaris* (wild zebra) is one such medicinal plant of importance that has properties to treat microbial infections and ailments related to the gastric region of the human body [11].

Abdulaziz Almanea *et al.* studied the potential TVE essential Oil (TVEO) health benefits for the gastrointestinal tract. Many chemical substances, which are obtained from various medicinal plants, have a wide range of biological effects. A flowering plant with a fragrant odor known as *Thymus vulgaris* (Tv) is widely used in traditional medicine, culinary additives, or phytopharmaceutical remedies. It is acknowledged to have encouraging therapeutic potential for the treatment of a wide variety of disorders. The essential oil from TV, which has been extracted, has antioxidant and antibacterial properties because of its high flavonoid content [12].

Tamas-Krumpe *et al.* studied about Apart from its nutritional benefits, *Thymus vulgaris* essential oil has therapeutic properties that may be used to find new, alternative treatments for illnesses that affect both people and animals. *Thymus vulgaris* L., generally known as common or garden thyme, is a tiny perennial herb that has been utilized for a number of diseases as well as a beneficial culinary addition throughout the years. *Thymus vulgaris's* essential oil, a blend of monoterpenes, is thought to be responsible for the plant's therapeutic effects.

Additionally, the terpenoid thymol as well as its phenol isomer carvacrol, which are the essential oil's major constituents, are what give it its medicinal qualities. Thyme oil has been shown to have potent antiseptic, antibacterial, antifungal, or antioxidant properties. As a result of all the aforementioned qualities, this essential oil has great promise in the domains of veterinary and human medicine [13].

3. METHODOLOGY

The present review study was carried out using a database search on PubMed, Google Scholar, Research Gate, Science Direct, and other websites. In the review process, keywords were combined like "Antibacterial, Anti-Inflammatory, Diseases Medicine, *Thymus vulgaris*". The records preliminary review employed title and abstract screening. Insufficient information, redundant research, and non-extractable data were some reasons to exclude the Records. More details about the review study's methodology are provided in Figure 2 below.

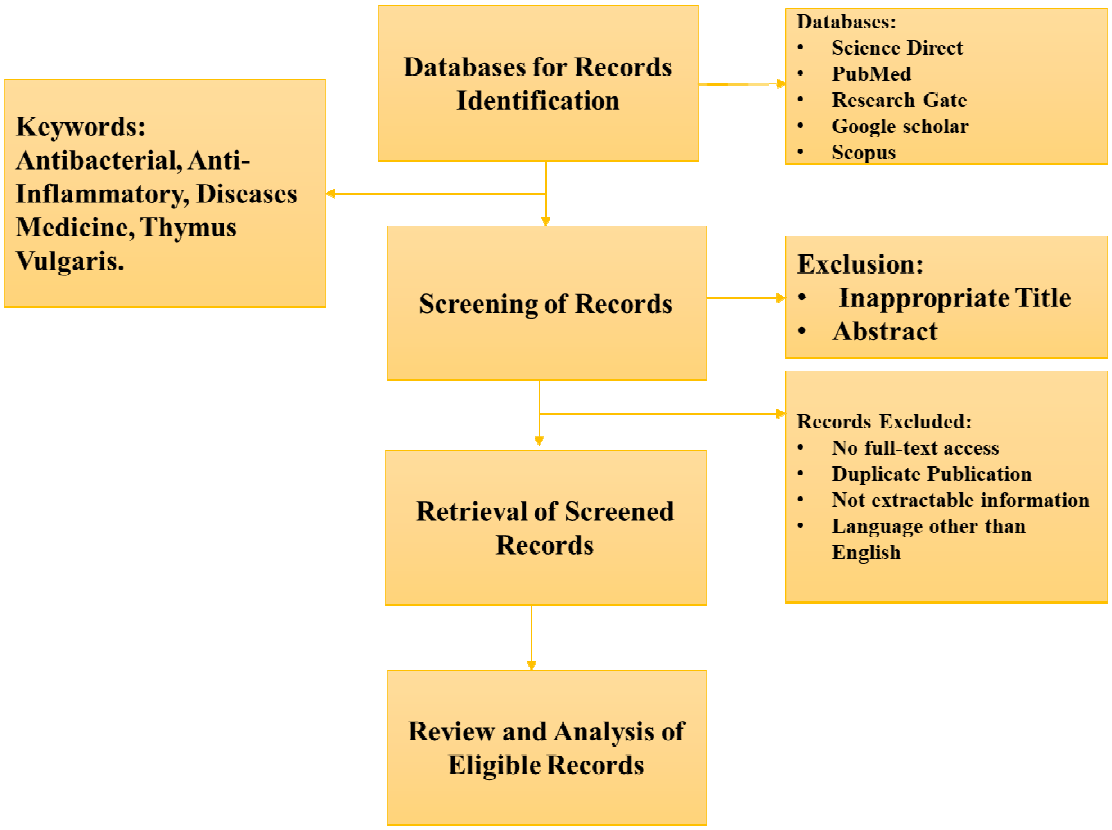


Figure 2: Flow diagram of Methodology.

4. DISCUSSION

4.1. Uses for Medicines:

Thyme has been used as a tonic, antiseptic, antibiotic, astringent, anthelmintic, therapeutic medicine, and as a carminative and disinfectant. Thyme is quite effective against a variety of intestinal illnesses and infestations, including *Candida albicans*, hookworms, ascarids, hookworms, gram-negative or gram-positive bacteria, fungi, as well as yeasts. *Enterobacteria* or *cocci* bacteria are both resistant to thymol, the substance that makes it active. Additionally, thyme may enhance liver performance and stimulate hunger. It will be utilized to treat infections of the bronchi, urinary tract, and cartilaginous tubes. Thyme can be used as a gargle to relieve inflammation as well as laryngitis [14], [15]. Thymol, the primary constituent of thyme's volatile oil, has anti-enterobacterial and anti-cocci bacterial properties. It is applied to treat insect bites, acne, greasy skin, dermatitis, sciatica, and other skin conditions. Aromatherapy uses a variety of thymol compounds, including "red thyme oil," linalool for its exceedingly mild action, or thuyanol for its antiviral properties. Also used is white thyme oil, a refined product that is gentler on the skin. Thyme may be administered topically to relieve rheumatic or neuralgic pain as well as insect bites and stings.

4.1.1. Antibacterial Activity:

The essential oils from *Thymus vulgaris L.* obtained at four different phases of the biological process were evaluated for their biological activity or chemical makeup. Humans looked at the thyme volatile oils' inhibitory effects on nine gram-negative bacteria strains or six gram-positive bacteria strains. The bioimpedance technique was employed to ascertain the bactericidal activity of the essential oils, and the detection time was chosen as the criteria for characterizing and evaluating the antibacterial activity of the thyme oils. The inhibitory impact of direct exposure was studied using the plate counting approach. Considerable bacteriostatic activity was detected in all of the thyme essential oils evaluated against the tested bacteria. Further markings against gram-positive bacteria were added to this activity. The oil obtained from fully blossomed thyme was the most effective in preventing the growth of the tested microorganism species [16], [17].

4.1.2. Anti-Inflammatory property:

Monoterpenes are the major constituents of *T. vulgaris* oil. The natural terpene thymol as well as its phenol chemical component carvacrol, which have antimicrobial, antibacterial, antitussive, or antispasmodic properties, make up the majority of this oil's constituents. In addition, *Thymus spp.* included terpenoids, flavonoid aglycones, flavonoid glycosides, or synthetic resin acids as an ingredient.

Insecticide use “Thyme volatile oil, thymol”, and also carvacrol were tested in a lab against several lesser mealworm larval stages for their insecticidal effects. On meals containing one or two acetone solutions of the investigated substances, the earlier and later larval stages were raised. The dosage and age of the larvae were important factors in the insecticidal efficacy of thyme volatile oil or pure monoterpenes towards diaperinus larvae. Younger larvae had a significant impact on their growth. However, older larvae had less of an impact and were solely affected by pure essential oils. Implementation of 1% thyme oil, thymol, or carvacrol to immature larvae resulted in death rates of 50.0, 86.68, or 85.00%, respectively.

4.1.3. Antioxidant Properties:

A substance known as an antioxidant stops other molecules from oxidizing. A substance contributes electrons or hydrogen to an oxidizing agent during an oxidation process. The oxidation processes will result in the production of free radicals. A chain reaction would then be initiated by these radicals. A chain reaction will cause harm or death to a cell. Antioxidants interrupt these chain reactions by removing the free radical intermediates, which limit a variety of oxidation processes. The leafy components of thyme as well as the oil are used in traditional remedies as well as in recipes for flavor, aroma, or preservation.

4.2. Health advantages of Thymus vulgaris:

Many products available in the market now contain thyme herb, which is an excellent plant with antifungal and antibacterial properties, as shown in figure 3. After looking at its nutritional benefits, let's look at some of thyme's healing abilities.

4.2.1. Help in vision improvement:

Vitamin A, an antioxidant or fat-soluble vitamin, is abundant in thyme oil. For forming and sustaining healthy mucous membranes or skin, it is crucial. So thyme aids in encouraging improved vision. Use thyme oil but rather thyme tea to treat dry eyes.

4.2.2. Thyme treats cough colds, and sore throat:

Due to its antibacterial or antibiotic properties, thyme herb is an excellent cold and cough remedy. Bronchitis can also be treated with thyme. Since thyme oil is one of nature's most powerful antiseptics, it is often used to heal sore throats. Its high concentration of carvacrol is a significant factor in its popularity as one of the best essential oils for treating sore throat.

4.2.3. Thyme for acne and blemishes:

Thyme is highly efficient in warding off the bacteria that cause acne as it has great antibacterial properties. Thyme helps maintain healthy skin by getting rid of germs that are the root cause of many skin problems. Thyme essential oil may be used as a toner to tighten aging skin by diluting it with water.

4.2.4. Thyme helps to develop hair:

For hair to grow, nutrients must be delivered to the hair follicles. Thyme promotes the development of hair by increasing blood flow to the scalp. Employing thyme essential oil or a combination containing thyme makes it easier for vital nutrients to reach the scalp, which promotes the development of hair. Due to its antimicrobial qualities, thyme oil is also beneficial in treating dandruff and preventing hair loss and hair thinning.

4.2.5. Thyme is used to treat respiratory issues:

Thyme is a plant that has antiseptic and antibacterial characteristics that make it a useful treatment for colds, sore throats, coughs, and bronchitis. The ability of thyme to effectively cure bronchitis has been demonstrated.

4.2.6. Thyme Supports Strong Bones:

Thyme is a superb source of vitamin K as well as calcium, iron, and manganese. These thyme-derived minerals are essential for bone health because they encourage healthy bone development and growth and lower the risk of bone diseases. As a result, thyme supports strong, healthy bones but also guards against bone illnesses.

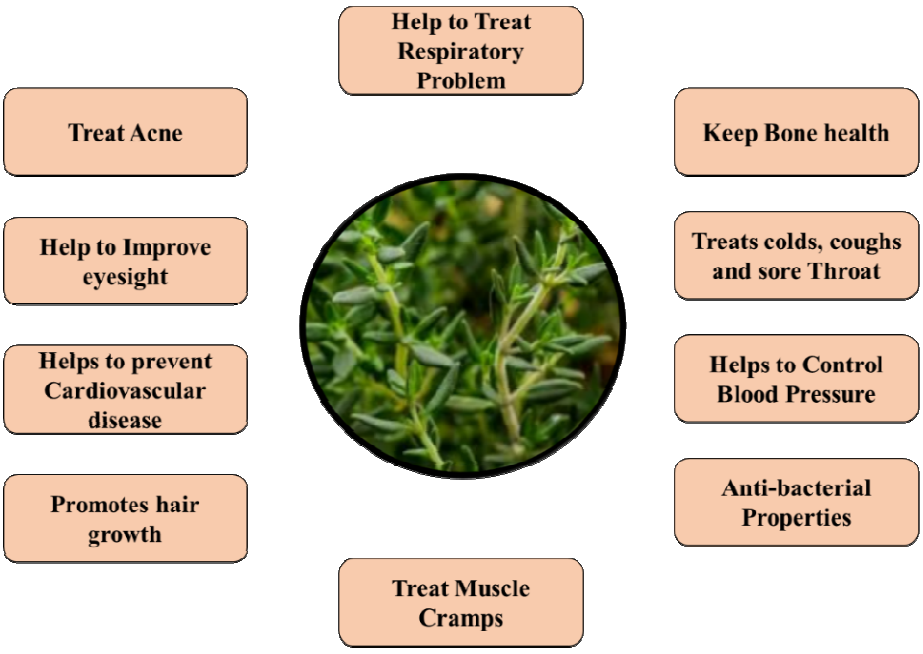


Figure 3: Various Health Benefits of *Thymus vulgaris*.

4.2.7. Thyme Reduces the Risk of Heart Disease:

The anti-inflammatory or antioxidant properties of thyme work together to reduce chronic inflammation which is the main contributor to cardiovascular illnesses. Particularly thyme oil is renowned for its anti-spasmodic qualities, which afterward support heart health. It relaxes the veins and arteries, allowing the cardiac valves to operate properly, lowering blood pressure, and bolstering the heart.

4.2.8. Thyme aids with Blood Pressure Regulation:

Potassium, a vital element of bodily fluids that helps regulate blood pressure and heart rate, is abundant in thyme leaves. Thyme extracts have also been seen to lower blood pressure in hypertension-related circumstances. Menstrual cramps and other types of bodily spasms can be effectively treated with thyme because of its powerful anti-inflammatory qualities. Women with PMS are frequently advised to drink thyme tea.

4.2.9. Thyme is Quite Effective against Bacteria.

Thyme is frequently used to treat infections or disorders brought on by fungi and bacteria, such as E. coli since it contains anti-bacterial qualities. According to studies, thyme essential oil can combat bacteria strains that are resistant to various antibiotics. Both within and outside the body, it is capable of eliminating microorganisms. Furthermore, thyme tea is employed for cleaning surfaces such as skin.

4.2.10. Herb thyme for Anemia:

A particularly good source of iron is thyme. For both the body's red blood cells to form and expand, iron is essential. Including thyme in your diet regularly will help avoid anemia because iron deficiency could result in anemia.

4.2.11. Thyme uses:

Thyme leaves are primarily utilized in cooking and the brewing of teas. Thyme is frequently used as an insect repellent by sandwiching the leaves between layers of linen to protect the cloth from bug bites. Thyme oil is used in a variety of products, such as scented soaps as well as deodorants [18]. Thyme has long been used to preserve meat and vegetables and is an excellent antimicrobial. Although thyme's fresh leaves can be eaten, the essential oil that is derived from them should never be applied directly to the skin without first diluting it with carrier oil or water. Thyme is used medicinally to cure and prevent conditions including arthritis, sore throat, colic, diarrhea, whooping cough, and stomachaches. It's also frequently employed as a diuretic.

4.2.12. Thyme Side-Effects & Allergies:

Thyme has several adverse effects, much like other plants do. Thyme includes substances including thymol or carvacrol, which could also irritate mucous membranes in sensitive individuals. The safety of this plant has not been proven for pregnant or lactating women, and there are no known contraindications. However, because thyme has a long history of use as a menstruation-inducing medicine, there is a risk that pregnant women may experience a miscarriage.

Thyme herbs should not be given to children under 10 years of age. Thyme is known to react adversely with anti-thyroid as well as thyroid replacement medications, reducing their effectiveness, thus those taking these treatments should avoid using them [19].

Although it originated in the western Mediterranean region, thyme is now extensively grown in temperate regions. The ancient Greeks made great use of thyme. Thyme served as a symbol of temperament and sophistication for the Greeks. It was the medieval equivalent of chivalry. It stood for the republican spirit of France. It was employed as a cheese and liqueur flavoring. On the battlefield in World War I, it served as an antiseptic and was used medicinally to cure a plague, depression, and epilepsy. In a warm, sunny location with well-drained soil, thyme grows nicely. It is often cultivated in the spring, but after that, it becomes a perennial. It may be multiplied by cuttings, seeds, or division of the plant's rooted portions. It performs well in arid environments.

5. CONCLUSION

The results of the current investigation demonstrated that *Thymus vulgaris* plant extract had significant flavonoid content and showed antioxidant and antibacterial activities. Therefore, thyme may be employed as a readily available source of naturally occurring antibiotics or antioxidants in foods and medications. Despite several studies showing the *T. vulgaris* plant's ability to treat a variety of ailments, additional pathological and medical research must be done to fully explore this plant's potential. This paper seeks to present a comprehensive analysis of or pharmacological characteristics of *T. vulgaris*. This paper may provide a complete account for medicinal properties of *T. vulgaris* and also provide various health advantages of *T. vulgaris* to design and develop as a bioactive drug.

REFERENCES:

[1] S. M. Patil, R. Ramu, P. S. Shirahatti, C. Shivamallu, and R. G. Amachawadi, “A systematic review on ethnopharmacology, phytochemistry and pharmacological aspects of Thymus vulgaris Linn.,” *Heliyon*, vol. 7, no. 5, 2021, doi: 10.1016/j.heliyon.2021.e07054.

[2] M. Fani and J. Kohanteb, “In Vitro Antimicrobial Activity of Thymus vulgaris Essential Oil Against Major Oral Pathogens,” *J. Evidence-Based Complement. Altern. Med.*, vol. 22, no. 4, pp. 660–666, 2017, doi: 10.1177/2156587217700772.

[3] C. Catella *et al.*, “Virucidal and antiviral effects of Thymus vulgaris essential oil on feline coronavirus,” *Res. Vet. Sci.*, vol. 137, pp. 44–47, 2021, doi: 10.1016/j.rvsc.2021.04.024.

[4] P. Reddy V, “Review on Thymus vulgaris Traditional Uses and Pharmacological Properties,” *Med. Aromat. Plants*, vol. 03, no. 03, 2014, doi: 10.4172/2167-0412.1000164.

[5] L. Capatina, E. Todirascu-Ciornea, E. M. Napoli, G. Ruberto, L. Hritcu, and G. Dumitru, “Thymus vulgaris essential oil protects zebrafish against cognitive dysfunction by regulating cholinergic and antioxidants systems,” *Antioxidants*, vol. 9, no. 11, pp. 1–18, 2020, doi: 10.3390/antiox9111083.

[6] A. K. Al-Asmari, M. T. Athar, A. A. Al-Faraidy, and M. S. Almuhaiza, “Chemical composition of essential oil of Thymus vulgaris collected from Saudi Arabian market,” *Asian Pac. J. Trop. Biomed.*, vol. 7, no. 2, pp. 147–150, 2017, doi: 10.1016/j.apjtb.2016.11.023.

[7] M. Mahmoodi *et al.*, “Beneficial effects of Thymus vulgaris extract in experimental autoimmune encephalomyelitis: Clinical, histological and cytokine alterations,” *Biomed. Pharmacother.*, vol. 109, pp. 2100–2108, Jan. 2019, doi: 10.1016/j.biopha.2018.08.078.

[8] S. Sardari, A. Mobaien, L. Ghassemifard, K. Kamali, and N. Khavasi, “Therapeutic effect of thyme (Thymus vulgaris) essential oil on patients with covid19: A randomized clinical trial,” *J. Adv. Med. Biomed. Res.*, vol. 29, no. 133, pp. 83–91, 2021, doi: 10.30699/jambs.29.133.83.

[9] R. Aitfella Lahlou, M. Bounechada, A. Mohammedi, L. R. Silva, and G. Alves, “Dietary use of Rosmarinus officinalis and Thymus vulgaris as anticoccidial alternatives in poultry,” *Anim. Feed Sci. Technol.*, vol. 273, p. 114826, Mar. 2021, doi: 10.1016/j.anifeedsci.2021.114826.

[10] M. Moazeni *et al.*, “In vitro antifungal activity of Thymus vulgaris essential oil nanoemulsion,” *J. Herb. Med.*, vol. 28, p. 100452, Aug. 2021, doi: 10.1016/j.hermed.2021.100452.

[11] S. Rastogi, D. Mehta, and S. Sharma, “Review on Thymus Vulgaris Objective Review of Thymus vulgaris□: A Review with Latest Updates on Pharmacological Properties and Phytoconstituents,” *Inven. Journals*, vol. 2021, no. January, pp. 9–12, 2021.

[12] A. Almanea, G. S. Abd El-Aziz, and M. M. M. Ahmed, "The potential gastrointestinal health benefits of Thymus vulgaris essential oil: A review," *Biomed. Pharmacol. J.*, vol. 12, no. 4, pp. 1793–1799, 2019, doi: 10.13005/bpj/1810.

[13] O. Tamas-Krumpe, C. D. Abălaru, R. Grosu, A. Buta, R. MĂRGĂOAN, and L. Ognean, "Medicinal properties of Thymus vulgaris essential oil: a review," *Lucr. Ştiinţifice Ser. Med. Vet.*, vol. 63, no. 2, pp. 129–135, 2020.

[14] C. Gonçalves da Rosa *et al.*, "Application in situ of zein nanocapsules loaded with Origanum vulgare Linneus and Thymus vulgaris as a preservative in bread," *Food Hydrocoll.*, vol. 99, p. 105339, Feb. 2020, doi: 10.1016/j.foodhyd.2019.105339.

[15] C. Moisa *et al.*, "Variation of the chemical composition of Thymus vulgaris essential oils by phenological stages," *Rev. Chim.*, vol. 70, no. 2, pp. 633–637, 2019, doi: 10.37358/rc.19.2.6973.

[16] J. Rojas-Armas *et al.*, "Acute and repeated 28-day oral dose toxicity studies of Thymus vulgaris L. essential oil in rats," *Toxicol. Res.*, vol. 35, no. 3, pp. 225–232, 2019, doi: 10.5487/TR.2019.35.3.225.

[17] T. Liu, J. Kang, and L. Liu, "Thymol as a critical component of Thymus vulgaris L. essential oil combats Pseudomonas aeruginosa by intercalating DNA and inactivating biofilm," *LWT*, vol. 136, p. 110354, Jan. 2021, doi: 10.1016/j.lwt.2020.110354.

[18] L. Almasi, M. Radi, S. Amiri, and L. Torri, "Fully dilutable Thymus vulgaris essential oil:acetic or propionic acid microemulsions are potent fruit disinfecting solutions," *Food Chem.*, vol. 343, p. 128411, May 2021, doi: 10.1016/j.foodchem.2020.128411.

[19] M. A. C. De Oliveira, M. R. Da C Vegian, F. L. Brighenti, M. J. Salvador, and C. Y. Koga-Ito, "Antibiofilm effects of Thymus vulgaris and Hyptis spicigera essential oils on cariogenic bacteria," *Future Microbiol.*, vol. 16, no. 4, pp. 241–255, 2021, doi: 10.2217/fmb-2020-0181.

CHAPTER 10

AN EXPLORATORY STUDY ON VISION LOSS IN A HEALTHY PERSON DUE TO VITAMIN A DEFICIENCY

Dr. Sunita Rao, Assistant Professor,
Department of Biotechnology, Jaipur National University, Jaipur, India,
Email Id-sunita.rao@jnujaipur.ac.in

ABSTRACT: The problem of vision loss in adults as well as in childhood is increasing day by day. Vitamin A deficiency occurs when your body does not get enough vitamin A to maintain health. Blindness and visual impairment can result from vitamin A deficiency. Additionally, it may result in problems with your immune system, skin, heart, tissues, lungs, skin, or skin. "Vitamin A deficiency" (VAD) is more prevalent in underdeveloped countries than in countries with abundant resources. In wealthy countries, behavioral problems and malabsorption are the most prevalent causes of VAD. In the present example, a healthy young man experienced ocular symptoms as a result of vitamin A deficiency among cultural factors and psychological pressures. The main objective of the study is to learn more about the importance of Vitamin A, due to vitamin A deficiency and vision loss. In the future, this paper will aware people of the nutritional value of a healthy life.

KEYWORDS: Corneal, Disease, Blindness, Deficiency, Vitamin A.

1. INTRODUCTION

Vitamin A must be taken from food because the human body is unable to generate it. A crucial fat-soluble micronutrient is vitamin A. There are two types of it: Carotenoids, also known as provitamin A, are phytonutrients that are present in meals derived from plants, including orange, yellow, or red fruits and vegetables but also dark green leafy or non-leafy vegetables. Foods derived from animals, including fish liver oil, liver (from sheep, goats, or ox), egg yolks, or dairy products, include preformed vitamin A, also known as retinoids [1], [2].Retinol, another name for vitamin A, is a necessary fat-soluble vitamin that is important for many physiologic functions, including vision, immunity, cellular communication, and reproduction. Up to 30% of children under the age of five are at risk of developing vitamin A deficiency (VAD), which is one of the major causes of avoidable blindness worldwide [3], [4]. In civilized nations, VAD is uncommon and generally caused by behavioral or physical disorders that lead to restricted eating habits, such as malabsorption (i.e., autism or anorexia). As an essential micronutrient, vitamin A cannot be synthesized by the human body and has to be consumed through food sources. Green leafy vegetables, mangoes, carrots, tomatoes, or sweet potatoes are some examples of foods high in vitamin A. Anemia, a compromised immune system, visual problems, or blindness can all be consequences of VAD. The term for serum retinol concentrations below 0.35 mol/L is xerophthalmia. Night blindness, such as conjunctival and corneal xerosis, are frequent consequences of xerophthalmia. If left untreated, VAD can eventually result in blindness and atrophic changes called keratomalacia [5], [6].

The most frequent preventable cause of corneal scarring, which is mostly brought on by vitamin A deficiency, is the fact that over a million children in Asian and African countries are blind. Measles infection is frequently linked in Africa to ocular ulceration that results in scarring, while severe diarrhea in Asia can cause an acute vitamin A deficit that results in

blindness. Ophthalmia neonatorum, and herpes virus infection, including the use of dangerous conventional eye medications, are other causes of corneal scarring. All of these factors may be avoided or treated [7], [8].

Congenital or developmental cataracts are becoming comparatively more significant in many developing nations where measles infection and vitamin A deficiency are under good control. Children who get cataracts can recover from their blindness. Services for preterm newborns have developed in many middle-income nations, notably in Latin America or Eastern Europe. Retinopathy of prematurity is the most prevalent cause in many of these nations [9], [10]. This illness can be properly treated and may be avoided. In developed nations, preterm delivery but also inherited genetic conditions that result in cataracts or retinal dystrophies are also significant causes of childhood blindness. The majority of youngsters in industrialized nations are blind due to problems that are difficult to prevent. Figure 1, Show Examples of Childhood Blindness Causes.

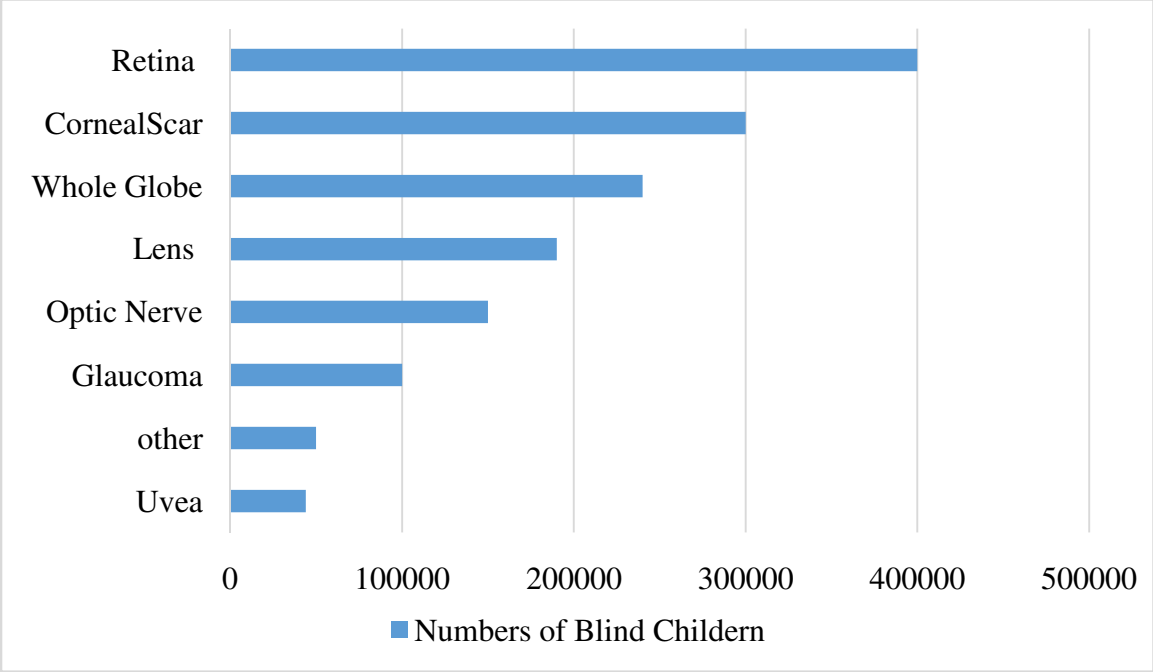


Figure 1: Illustrate the Causes of Childhood Blindness.

Our patient's symptoms of visual abnormalities and worsening eye nodules led to an evaluation. Before it was determined that he had VAD, he was seen by several healthcare professionals and given several various ophthalmologic diagnoses. This situation is special since it wasn't brought on by either malabsorption or maybe even a developmental disorder. This previously healthy but also developmentally adequate youngster developed VAD as a result of the social and cultural forces that formed his surroundings. This instance highlights the importance of acquiring a full history to properly evaluate and manage a patient, even if physical exam results and current symptoms are vital components of medicine [11], [12]. Figure 2, shows attention to the various ratios according to the poverty line in each area.

Our patient is an eight-year-old Hmong boy who was previously healthy and went to the emergency room complaining of vision loss and red, sensitive bumps around his eyes. His physical examination revealed bilateral lower eyelids with 3-millimeter erythematous papules. Since the mother could speak a little English but it wasn't her first language, the history of the presentation was pieced together via chart review and with the help of a Hmong interpreter. He developed a fear of bright lights four months before his presentation. The

patient was given warm compresses to take home after being diagnosed with styles at that time. He was directed to an ophthalmologist who administered Polytrim eye drops at his initial primary care follow-up. He was seen by many ophthalmologists over the following few months, who once more determined that he had styes and gave him a prescription for prednisolone eye drops [13], [14]. His mother brought him back to the emergency room at this point since his symptoms were becoming worse. His physical examination indicated bilateral cloudiness of his eyes and little white patches over his right iris. People were also now having night vision loss. When he saw a third ophthalmologist, the examination he had there revealed bilateral xerosis, bilateral corneal.

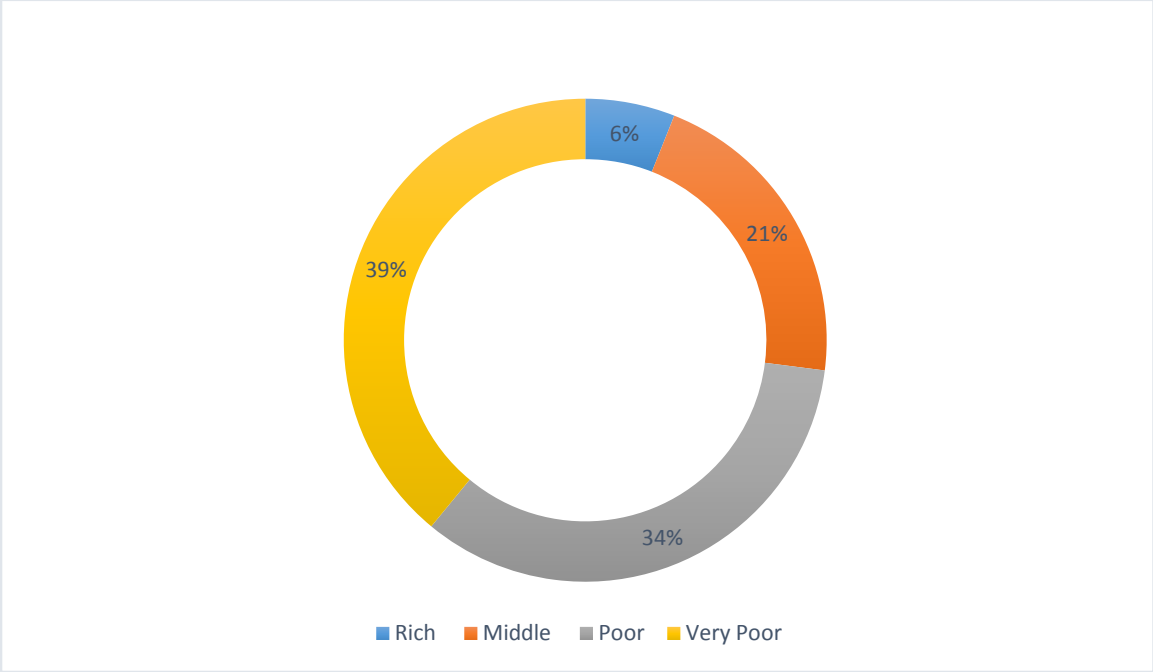


Figure 2: Illustrate the Different Proportion as per their Area of Poverty Line.

To understand the progression of his illness and the failure of his therapy, a complete history was gathered at the ED presentation. The patient's mother said that he was having trouble as a result of losing his father recently. According to their tradition, the eldest male takes on the role of the family head. The patient, who at age 8 was the eldest male in the household, considered himself to be the boss and was in charge of his diet. Since his father's passing, the youngster had primarily consumed instant noodles, always picking the vegetables. His only noticeable symptoms were severe eye discomfort, and throughout the previous few months, his weight had not significantly changed [15], [16]. The patient was immediately hospitalized at our facility for additional symptom evaluation and an anesthetic eye exam due to the suspicion of VAD.

2. LITERATURE REVIEW

Wiseman et al. studied aboutvitamin A insufficiency vicious cycle. Additionally, especially in underdeveloped nations, it is linked to higher rates of fatal illnesses. Researchers have spent the last 35 years examining vitamin A's many functions in the body's many tissues. VAD can cause a variety of visual symptoms, anemia, or weakened infection resistance, which could also worsen infectious infections and raise the chance of mortality. Among the essential functions that are inadequately maintained by VAD are proper metabolism, growth, as well as cell development. This model incorporates consequences including inflammation, malnutrition, and inappropriate development processes, as well as potential reasons, starting

with inadequate intake and its connection to lower digestion and absorption. These clinical and laboratory symptoms work together to perpetuate VAD's vicious cycle [17].

Saliha Rizvi et al. studied vitamin e's effects on human health as well as certain diseases. Because of its antioxidant action, it plays a variety of significant roles in the body. Vitamin E has been demonstrated to be beneficial against these since oxidation has been connected to a wide range of potential ailments and diseases, including aging, arthritis, cancer, or cataracts. Vitamin E can also assist to inhibit the formation of prostaglandins like thromboxane, which promote platelet clumping, as well as platelet hyper aggregation, which can result in atherosclerosis. The tocopherol class of vitamins is the primary subject of the review [18].

Eusterman et al. studied about symptoms of vitamin a deficiency in humans. Some of these views are both prescient and startlingly true. Today, it has been conclusively demonstrated from the perspectives of either human experience or laboratory study that a natural food supply provides and that adequate nutrition requires various components in addition to fats, proteins, carbs, water, as well as salts. The current understanding of these auxiliary dietary components, or vitamins, is more the result of development than of any one discovery, and most of this progress occurred before the name vitamin was ever coined [19].

3. DISCUSSION

A database search on PubMed, Google Scholar, Research Gate, Science Direct, and other sites was used to conduct the current review study. Combining keywords like “Corneal, Disease, Blindness, Deficiency, and Vitamin A” were used in the review technique. Title and abstract screening were used for the record's preliminary review. Additionally, non-extractable data, duplicate research, and inadequate information were grounds for excluding the Records. Figure 3 below provides more information on the methodology utilized to conduct the review study.

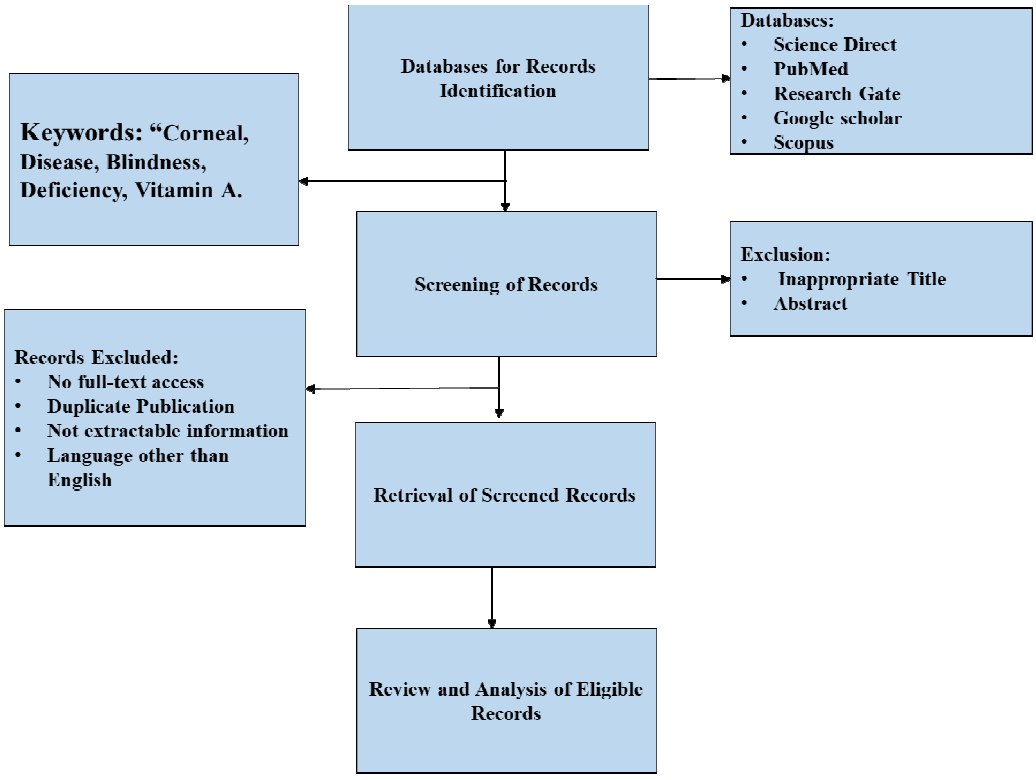


Figure 3: Illustrate the Design of the Methodology of the Current Review Work.

Due to food insecurity and a lack of foods high in vitamin A, VAD is a widespread problem in underdeveloped countries. VAD can cause lifelong visual loss if neglected. This deficiency is uncommon and is typically caused by an underlying medical problem, such as malabsorption, or behavioral issues that result in restricted eating practices, such as anorexia and autism, in industrialized nations where vitamin-enriched foods are more widely available. To ascertain the cause of any patient's primary symptoms, it is crucial to first gather a complete history. This is what the current instance demonstrates. This must always include a thorough history of nutrition and eating patterns, with an emphasis on any customs based on culture. VAD is probably both underdiagnosed but more prevalent than we presently realize in affluent nations. Unfortunately, our patient suffered from eye problems for months before the right diagnosis was discovered after two trips to the emergency room, two independent ophthalmologist assessments, several visits to primary care providers, a hospital stay, and a thorough review.Even though our patient had no history of behavioral or mental health issues, his VAD is probably connected to psychological pressures that led to an extremely limited diet. For a child, losing a parent is a traumatic experience since children mourn differently than adults and have various behavioral and emotional difficulties. Generally speaking, cultural experience may mediate how children deal with loss; there may be more cultural factors that contributed to our patient's VAD.

The patient had altered his eating habits, which signaled that he need bereavement counseling. The Hmong ethnic group, with roots in Southeast Asian locales, included our patient. Health is defined by focus groups among the Hmong population in California as family harmony, emotional and mental stability, and consuming a variety of fruits and vegetables. Children need to learn from adults how to consume a nutritious diet. Hmong children also claim that their father shares cooking responsibilities equally with them. Our patient's eating habits were probably impacted by the passing of his father [20]. When they are too exhausted or pressed for time to prepare dinner, families frequently turn to the convenience of fast food and other readily available meals. A freshly bereaved mother would probably face several difficulties, including doing all of the meals for our patient or his siblings. As her son and perhaps other children are continually exposed to American food, which is often richer in sugar, trans fatty acids, saturated fat, or salt, the mother must also fight the acculturation of her son's and even other children's eating habits.

The eldest man has responsibility for family leadership in the Hmong culture. After his father passed away, our patient the eldest son began to see himself as the leader of the home. His mother claims that is when he decided to eat anything he wanted. It would be simple to presume that our patient disobeyed orders by eating whatever he pleased. Avoiding these suppositions is advisable. Even though it might be useful to comprehend how cultural factors can affect a patient's atmosphere, it is impossible to know the patient's genuine objectives, his access to resources, or the strength of his family's support or guidance. We must comprehend the effects of cultural influences as well as the intricate relationships between nutrition, familial dynamics, mortality, and mourning. It's also noteworthy that this family asked for a Hmong interpreter to be there.

Although it was not her first tongue, the mother spoke a little bit of English. Although it is uncertain if she required an interpreter for any of the earlier presentations, this might be one factor in the delayed diagnosis. Although the socioeconomic class did not appear to have a significant role in this instance, it is nevertheless crucial to take into account since it might add another barrier to gaining access to foods high in vitamins. Low-income communities lack nutritional resources, and the ease of access to nutritious meals often varies depending on the socioeconomic aspects of the neighborhood.

3.1. Advantages of Vitamin A:

One of the fundamental vitamins that are very necessary for the human body is vitamin A. It is necessary for a person's general health. The natural versions of these vitamins present in plants or animals are always an option. It is also simple for the body to assimilate this fat-soluble vitamin. This vitamin's significance has long been understood. This vitamin is essential for maintaining eye health among its several other advantages. Additionally, it guarantees the strength of your bones and teeth. Additionally, the antioxidant property maintains the skin healthy but also acne-free. Both the immune system and red blood cell production are strengthened by it. This vitamin slows down the aging process by preventing the creation of free radicals. Fruits having a higher vitamin A content can also be used to treat urinary tract infections. Getting enough vitamin A every day from the correct sources keeps the body's systems functioning normally. Figure 4, shows the positive effects of vitamin a on human health.

Figure 4: Illustrate the Advantage of Vitamin A, for Human Health.

3.1.1. Eliminates Cancer:

One of the worst illnesses humans have ever met, cancer still lacks a cure. We must use preventative measures to combat this illness. A study conducted by the University of York revealed that increasing vitamin A consumption helps cure a variety of cancer types. This is made feasible by the vitamin's capacity to limit the development of cancerous cells. Still, taking too many vitamins is not advised. The first step should be to see a doctor and modify your diet.

3.1.2. Enhances Immunity:

Numerous health advantages of vitamin A are especially true for young people. Vitamin A promotes fetal development which is safe, and raises the mortality rate. Children who lack vitamin A are more susceptible to measles and diarrhea. Additionally, it could cause blindness. Foods having higher Vitamin A in them may be found at the top of a list of foods for kids and adults that increase immunity.

3.1.3. Enhancement of Vision:

This vitamin not only promotes clear eyesight but also better eye health. This vitamin makes the difference between light and dark more noticeable.

Additionally, eye diseases are avoided. Children, adults, and older people can all suffer from vitamin A insufficiency. Glaucoma, Cataracts, and night blindness are just a few of the conditions that may be caused by insufficient vitamin A.

3.1.4. Decreases Acne:

The production of sebum by the skin is the cause of acne. The extra oil draws dust, which promotes the growth of germs. Sebum production is reduced by vitamin A, which also maintains the integrity of the skin's barrier layers. This will guarantee that the skin stays clear of acne or is healthy. Vitamin A-rich meals are necessary to cleanse the body or remove impurities. The antioxidant quality is in charge of this.

3.1.5. Vitamin A uses:

A substance called vitamin A helps to maintain healthy skin, eyes, or immune systems. A diet rich in fruits, vegetables, dairy products, and meat will provide you with sufficient levels. Additionally, it is important for healthy prenatal development and to avoid iron deficiency. You may rely on the antioxidant qualities to protect you from difficulties associated with inflammation and allergies. Studies have demonstrated its effectiveness in battling particular cancer types. Increased vitamin C consumption strengthens the structure of the bones and muscles.

3.1.6. Vitamin A Side Effects & Allergies:

Night blindness is the first symptom of vitamin A insufficiency. The body is unable to sense light in the same manner when this vitamin is deficient. If you consume enough vitamin A, people can recover from it. As your immune system deteriorates, you'll also be more prone to illness. If this vitamin is lacking and there is an iodine shortage, goiter or thyroid problems will follow. The skin might exhibit symptoms as well. The deficit leads to the emergence of hyperkeratosis-related lesions. An overdose may cause osteoporosis, itching, or skin redness.

3.1.7. Sources and Methods of Vitamin A Production:

Night blindness is the first symptom of vitamin A insufficiency. The body is unable to sense light in the same manner when this vitamin is deficient. If you consume enough vitamin A, people could recover from it. As your immune system deteriorates, you'll also be more prone to illness. If this vitamin is lacking and there is an iodine shortage, goiter and thyroid problems will follow. The skin might exhibit symptoms as well. The deficit leads to the emergence of hyperkeratosis-related lesions. An overdose may cause osteoporosis, itching, or skin redness.

4. CONCLUSION

Children are still learning how to control their eating habits at such a young age. The parent's job is to encourage and direct their development in this way. Pediatricians should inform families about proper diet and keep an eye out for any possible inadequacies. To recognize social factors and psychological stresses that could be influencing a patient's presentation, it is also critical to conduct a detailed history. To further comprehend these cultural dynamics as well as how they impact behavior and nutrition, more research is required. Due to vitamin A insufficiency and eyesight loss, the study's major goal is to understand the significance of

vitamin A. This study will educate readers in the future on the importance of nutrition to a healthy lifestyle.

REFERENCES:

[1] E. K. Addo *et al.*, "Prevalence and associated factors of vision loss in the South African National Health and Nutrition Examination Survey (SANHANES-1)," *BMC Ophthalmol.*, 2021, doi: 10.1186/s12886-020-01714-4.

[2] Y. T. Y. Wu *et al.*, "The risk of vision loss in contact lens wear and following LASIK," *Ophthalmic Physiol. Opt.*, 2020, doi: 10.1111/opo.12663.

[3] S. Ge, E. S. McConnell, B. Wu, W. Pan, X. Q. Dong, and B. L. Plassman, "Longitudinal Association Between Hearing Loss, Vision Loss, Dual Sensory Loss, and Cognitive Decline," *J. Am. Geriatr. Soc.*, 2021, doi: 10.1111/jgs.16933.

[4] K. M. Kapoor, P. Kapoor, I. Heydenrych, and D. Bertossi, "Vision Loss Associated with Hyaluronic Acid Fillers: A Systematic Review of Literature," *Aesthetic Plastic Surgery*. 2020. doi: 10.1007/s00266-019-01562-8.

[5] J. Amsler *et al.*, "Vision loss in patients with giant cell arteritis treated with tocilizumab," *Arthritis Res. Ther.*, 2021, doi: 10.1186/s13075-021-02480-4.

[6] N. Chen, K. Shin, R. Millin, Y. Song, M. Y. Kwon, and B. S. Tjan, "Cortical reorganization of peripheral vision induced by simulated central vision loss," *J. Neurosci.*, 2019, doi: 10.1523/JNEUROSCI.2126-18.2019.

[7] G. Deshpande and P. Giri, "Acute monocular vision loss as presenting symptom of delayed stroke from internal carotid occlusion in COVID-19," *Indian J. Ophthalmol.*, 2021, doi: 10.4103/ijo.IJO_439_21.

[8] A. R. Morse and W. H. Seiple, "Decreasing avoidable vision loss: Identifying antecedents of adherence," *Clinical Ophthalmology*. 2020. doi: 10.2147/OPTH.S278627.

[9] C. Smith-Morris, G. H. Bresnick, J. Cuadros, K. E. Bouskill, and E. R. Pedersen, "Diabetic Retinopathy and the Cascade into Vision Loss," *Med. Anthropol. Cross Cult. Stud. Heal. Illn.*, 2020, doi: 10.1080/01459740.2018.1425839.

[10] M. Maniglia, K. M. Visscher, and A. R. Seitz, "A method to characterize compensatory oculomotor strategies following simulated central vision loss," *J. Vis.*, 2020, doi: 10.1167/JOV.20.9.15.

[11] A. R. Morse and W. Seiple, "Activation in individuals with vision loss," *J. Health Psychol.*, 2021, doi: 10.1177/1359105320922303.

[12] V. Silvestri *et al.*, "Reading with central vision loss: binocular summation and inhibition," *Ophthalmic Physiol. Opt.*, 2020, doi: 10.1111/opo.12726.

[13] J. Foreman *et al.*, "Future burden of vision loss in Australia: Projections from the National Eye Health Survey," *Clin. Exp. Ophthalmol.*, 2020, doi: 10.1111/ceo.13776.

[14] R. C. H. Jeffery, F. K. Chen, and C. J. Lueck, "Blackout: Understanding transient vision loss," *Aust. J. Gen. Pract.*, 2021, doi: 10.31128/AJGP-03-20-5271.

[15] W. Thanasarnaksorn, S. Cotofana, C. Rudolph, P. Kraisak, N. Chanasumon, and A. Suwanchinda, "Severe vision loss caused by cosmetic filler augmentation: Case series with review of cause and therapy," *J. Cosmet. Dermatol.*, 2018, doi: 10.1111/jocd.12705.

[16] S. T. L. Chung and J. B. Bernard, "Bolder print does not increase reading speed in people with central vision loss," *Vision Res.*, 2018, doi: 10.1016/j.visres.2018.10.012.

[17] E. M. Wiseman, S. Bar-El Dadon, and R. Reifen, "The vicious cycle of vitamin a deficiency: A review," *Crit. Rev. Food Sci. Nutr.*, vol. 57, no. 17, pp. 3703–3714, Nov. 2017, doi: 10.1080/10408398.2016.1160362.

[18] S. Rizvi, S. T. Raza, F. Ahmed, A. Ahmad, S. Abbas, and F. Mahdi, "The role of vitamin e in human health and some diseases.," *Sultan Qaboos Univ. Med. J.*, vol. 14, no. 2, pp. e157-65, May 2014, [Online]. Available: http://www.ncbi.nlm.nih.gov/pubmed/24790736

[19] G. B. EUSTERMAN, "CLINICAL FEATURES OF VITAMIN A DEFICIENCY," *J. Am. Med. Assoc.*, vol. 98, no. 24, p. 2054, Jun. 1932, doi: 10.1001/jama.1932.27320500001008.

[20] J. H. Pula, K. Kwan, C. A. Yuen, and J. C. Kattah, "Update on the evaluation of transient vision loss," *Clinical Ophthalmology*. 2016. doi: 10.2147/OPTH.S94971.

CHAPTER 11

AN EXPLORATORY STUDY ON THE ROLE OF PROBIOTICS IN IMPROVING HUMAN HEALTH

Dr. Manish Soni, Assistant Professor,
Department of Biotechnology, Jaipur National University, Jaipur, India,
Email Id-manishsoni@jnujaipur.ac.in

ABSTRACT: Probiotics are certain bacteria that have had a significant positive impact on people's health; because of this, they have been added to many different diets for many years. The effect of probiotics against microorganisms is connected to their capacity to alter the immune response of the host, combat pathogenic bacteria, or compete against competing for adhesion sites with them. Probiotics can be used to treat or prevent conditions including cystic fibrosis, irritable bowel syndrome, lactose intolerance, urogenital tract infections, allergies, and several malignancies. They can lessen adverse reactions to different antibodies. According to the results of numerous of these clinical investigations, probiotics may be helpful in the treatment and prevention of a wide range of illnesses and health problems. Before the outcomes may be used in the clinical context, a considerable number of clinical investigations need to be validated. Clinical trials are a crucial component of these investigations, but in the not-too-distant future, the results of these studies will establish the efficacy of probiotics in the treatment of disease. The purpose of this page is to attempt to summarize the information on the advantages of various probiotics for health and illness.

KEYWORDS: Disease, Inflammatory Bowel Disease, Human Health,Microorganisms, Probiotics.

1. INTRODUCTION

Every day, a sizable number of pathogens, mostly bacteria, are consumed by humans. Due to their beneficial benefits on human health, probiotic bacteria have been included in many diets for several years. Probiotics were described in 2001 by the United States Department of Agriculture and the World Health Organization as microorganisms that, when given to a host in sufficient quantities, enhance their health. The most popular genera for probiotics are Lactobacillus and Bifidobacterium. Unlike typical pathogens, these bacteria may live in the body to treat and prevent illnesses, leading to the popular perception that they are benign. Additionally, for a very long time, these microbes have been crucial in the processes of fermenting milk or food preservation [1], [2]. Probiotic strains are both effective and safe in providing users with their advantages in several randomly chosen clinical experiments. Acute diarrhea, Crohn's disease, dental caries, cardiovascular or urogenital infections, cancer, cystic fibrosis, lactose intolerance, or oral disorders are among the conditions that can be prevented by these advantages. Additionally, bacteria may help heal periodontal disease, reduce tooth decay, and lessen bad breath. The number of probiotics' beneficial effects in avoiding inflammatory diseases is constantly growing [3].

Scientists have been increasingly curious about finding, examining, and researching organisms with probiotic qualities over time. In this article, the probiotics' function in health and disease is outlined using data from evaluated research. Probiotics can help to enhance human gut health. Prebiotics in combination has also been suggested. As a result, the probiotics sector has expanded quickly to include probiotics in food and supplements.

Probiotics have been suggested as a way to boost overall health and immunity [4], [5]. It is now known that the commensal microorganisms in the human gut may have a role in the development of metabolic diseases such as diabetes, obesity, or inflammatory bowel disease. It's interesting to note that probiotics use greatly improves the prognosis and treatment of such illnesses. This review provides a clear description of the concept, aim, and the relationship between probiotics and illnesses associated with the gut microbiota [6], [7].

1.1. Probiotics' Sources:

Probiotics are live bacteria or yeasts, which could benefit one's health. They are present in several foods, dietary supplements, as well as the human digestive system. Beneficial probiotic microorganisms exist. Even though they are present throughout the body, most people mainly associate them with the intestines and the stomach. Probiotics may be found in yogurt and kimchi, two examples of fermented foods. Probiotic supplements are furthermore offered. Figure 1.

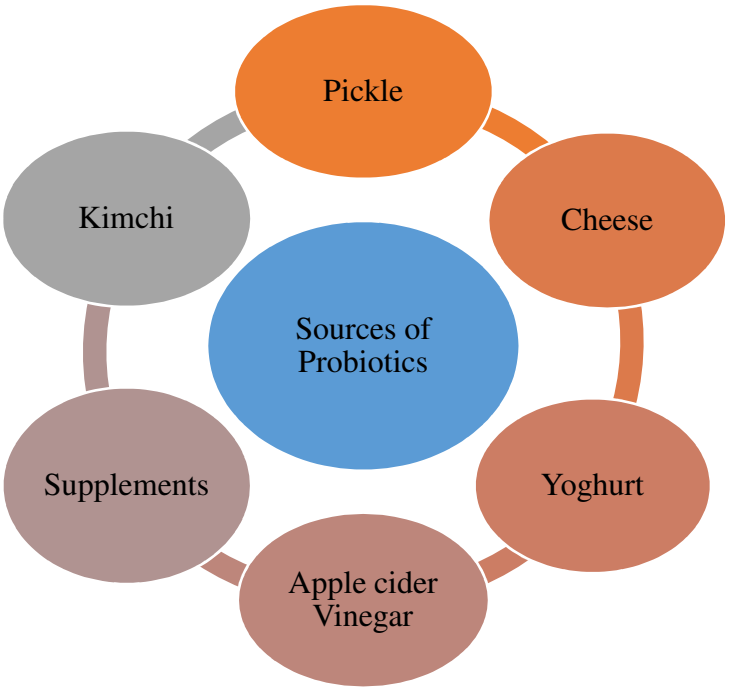


Figure 1: Illustrate the Various sources of Probiotics.

This study is divided into several sections such as introduction, literature view, discussion, and conclusion. In the introductory part, the author discussed a general overview of probiotics, sources of probiotics, etc. In the literature view section, the author discussed the previous study on probiotics. In the discussion, the author talks about various benefits of probiotics for human health, and at the end, the author concludes the entire study as per the observation about the use of probiotics for human health.

2. LITERATURE REVIEW

Maria Kechagia et al. studied about benefits of probiotics for health. Due to the growing body of scientific data supporting the positive benefits of probiotic bacteria on human health, they have gained more and more attention during the past 20 years. The food industry has been highly active in investigating and promoting them as a result, leading to their application as varied products. Probiotics have been added to a variety of items in this sector, mostly fermented dairy products. Further study is required to develop them, assess their safety, and

determine the nutritional features of these microbes due to this persistent tendency and despite the compelling scientific evidence linking them to numerous health advantages [8].

Ravinder Nagpal et al. studied Probiotics and their potential use in functional foods for better nutrition and wellness in society. The most important and often used functional food components are probiotics and prebiotics, which are occasionally referred to as symbiotic compounds. Since dairy products already have a good reputation for being healthy, using them to make nutrient-rich foods seems to be a wonderful idea. These probiotic dairy foods have positive effects on the host by selectively boosting the development or stimulating the catabolism of one or a limited number of health-promoting intestinal bacteria systems and by improving the microbial balance of the digestive tract [9].

H S Gill and F Guarner studied using probiotics to enhance human health Probiotics are also showing promise in the diagnosis and intervention of pouchitis or pediatric atopic illnesses, as well as in the control of surgical infections. Additionally, there is compelling evidence that some probiotic strains can improve immune function, particularly in people with subpar immune systems, like the elderly. Probiotics have not yet been demonstrated to be effective in preventing traveler's diarrhea, sepsis linked to severe acute pancreatitis, malignancies, managing ulcerative colitis, or decreasing blood cholesterol. Major information gaps remain about the processes by which probiotics affect numerous physiological systems and the ideal dose, frequency, or duration of treatment for distinct probiotic strains, in addition to clear proof of efficacy [10].

3. DISCUSSION

Probiotics are certain bacteria that have had a significant positive impact on people's health; because of this, they have been added to many different diets for many years. The effect of probiotics against microorganisms is connected to their capacity to alter the immune response of the host, combat pathogenic bacteria, or compete for adhesion sites with them. Probiotics can be used to treat or prevent conditions including cystic fibrosis, irritable bowel syndrome, lactose intolerance, allergies, urogenital tract infections, and several malignancies. They can lessen adverse reactions to different antibodies [11], [12]. Probiotics can be used to prevent or treat oral health issues such as poor breath, periodontal disease, and tooth cavities. According to the results of numerous of these clinical investigations, probiotics may be helpful in the treatment and prevention of a wide range of illnesses and health problems. Before the findings of many of these clinical studies may be used in a therapeutic context, they must first be validated. Clinical trials are a crucial component of these investigations, as in the not-too-distant future, the results of these studies will establish the efficacy of probiotics in the treatment of disease. The purpose of this page is to attempt to summarize the information on the advantages of various probiotics for health and illness [13], [14].

3.1. Probiotics and their Advantages:

A few advantages of probiotics for human health are listed in Figure 2. These cover a wide range of applications for practically every portion of our body, not just one specific area. Their well-known advantages of enhancing our digestion and lowering cholesterol are located in the gastrointestinal system. Their additional applications include the management of diarrhea and defense against inflammatory bowel conditions. Additionally, the advantages will include reducing tooth cavities and boosting our immune systems, particularly in times of allergy. Probiotics can somewhat prevent the dangerous germs' continual development. The production of glutamine by Bifidobacterium enhances the mucosal barrier's resistance as

well as maintains the integrity of the mucosa [15], [16]. Probiotics have been shown in several trials to be effective in treating various types of diarrhea, including rotavirus-related diarrhea in young children, antibiotic-induced diarrhea, or travelers' diarrhea. Because the origin of irritable bowel syndrome is not well known, treating these patients can be difficult. However, patients' health conditions improved after receiving the oral probiotic Enterococcus strain PR88. Probiotics have been the subject of persistent research, which has produced some fascinating findings on their usage in illnesses that are complicated.

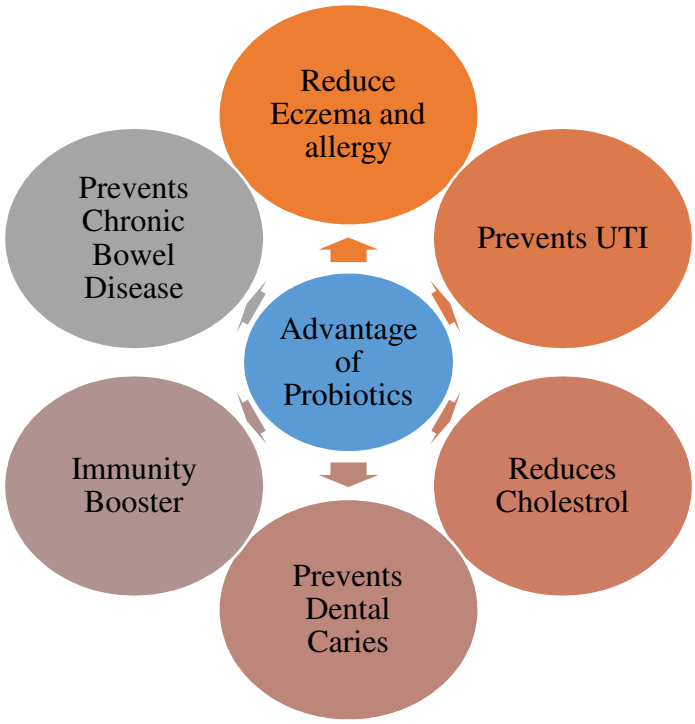


Figure 2: Illustrate some major advantages of probiotics.

Probiotics' beneficial benefits on food allergy sufferers are due to their cumulative effects on the non-immunologic or immunologic defensive barriers in the gut. Lactobacilli modify the immunomodulatory properties of the natural dietary protein. By activating the lymphoid cells in the gastrointestinal lymphoid tissue, probiotics have an impact on the immune system. The impact of probiotics on atopic dermatitis has been well investigated. With the ingestion of live and heat-neutralized probiotic bacteria, the severity of eczema and the number of distinct processes in the given population reduced [17], [18]. Women are protected from getting urinary tract infections by lactobacilli (UTIs). Researchers discovered that taking one or more two capsules vaginally each week for a year can help avoid UTI recurrence. Probiotics for humans lower cholesterol. Direct digestion of lipids by probiotics affects the generation of cholesterol. No study found that cholesterol levels changed statistically significantly.

The outer coating of our teeth is academically decalcified in dental caries, a multifactorial bacterial infection. A probiotic has to be able to adhere to tooth surfaces and blend in with the microbial flora that makes up the dental biofilm to help prevent dental caries. It also needs go to combat and repel cariogenic germs to stop their spread. Only Streptococcus thermophilus or Lactobacillus lactis ssp. lactis were discovered to be able to establish a biofilm on hydroxyapatite surfaces, preventing the growth of the cariogenic species Streptococcus sobrinus there. Recent studies have shown that W. cibaria isolates can suppress S. mutants' ability to produce germs both in vitro and Vivo, as well as stop this microbe from spreading. Gingivitis and periodontitis are the two types of periodontal disorders. Contrary to

periodontitis, gum disease is a temporary, non-debilitating gum inflammation that only affects the unattached gingiva but not the alveolar bone [19]. Most initiatives to stop periodontal disease and ensure a full recovery center on eliminating germs and fortifying the outer border, which also reduces the likelihood that a person would get ill. If these beneficial bacteria can establish themself in dental biofilm and stop the development and metabolism of bad bacteria right once, periodontal health may be enhanced. Probiotic microorganisms have been discovered to be safe through a variety of data analyses. There isn't much published clinical research on the potential benefits of these probiotics for treating periodontal disease. Therefore, the main source of information on probiotics that specifically target periodontal tissues is lab research. Patients with periodontal disease had better periodontal health after using gum or lozenges containing probiotics. Halitosis, often known as foul breath or foetor ex ore, is a frequent condition. The major cause of foul breath in the oral cavity is volatile sulfur compounds (VSCs), which are predominantly formed by Gram-negative anaerobes in dental plaque as well as on the surface of the tongue. It has also been demonstrated that bacterial treatment works effectively for this condition. As a supplement to prevention and therapy, probiotic strains of bacteria from the natural oral microbiota of healthy people might be utilized to begin replacing the bacteria thought to be responsible for halitosis.

3.2. Probiotics impact dental health:

Probiotics' effects, when taken orally, are unclear. The usage of probiotics results in a small decrease in gum disease. Inflammation is brought on by lactic acid bacteria products. The majority of research demonstrates that probiotics can get rid of illnesses by competing with bacteria for nutrition and connecting surfaces. The author's analysis of the literature revealed no evidence that bacteriotherapy is dangerous. According to Taipale et al., two patients from the probiotic intervention group and two from the placebo control group, however, were dropped owing to gastrointestinal discomfort or atopic eczema. Bacteriotherapy is effective in boosting immune function in those with cancer and HIV.

3.3. Probiotics' Function in Illnesses of the Human Gut's Microbiome:

3.3.1. Dysbiosis of the Human Gut Microbiota:

An imbalance in the composition and operation of gut bacteria is known as microbial dysbiosis. The issue, which is increasingly common in the current period, is a result of the use of antibiotics, bacterial infections, and dietary changes. The lack of beneficial bacteria in the stomach is linked to irritable bowel syndrome (IBS), celiac disease, or other intestinal disorders. By competing for resources and space, healthy probiotics inside the gastrointestinal system prevent pathogenic microorganisms from trying to invade and spread. One of the most important applications of probiotics is the restoration of healthy commensal microorganisms and the attempt to avoid infections in patients after antibiotic therapy. They are typically employed to treat antibiotic-associated diarrhea (AAD), a condition that develops anytime the microbial population is upset.

One of the main causes of AAD is the disease-causing bacteria Clostridioides difficile (formerly Clostridium difficile), which is carbapenem-resistant. Probiotics can assist patients of any age group to prevent AAD when administered in combination with other therapies, according to prior studies and meta-analyses. Both adults and children who have diarrhea brought on by C. difficile can benefit from probiotics. Probiotic diagnosis might lower AAD incidence by 51%, according to this study's findings, however, there was no discernible increased risk of side effects. Additionally, a study on this subject revealed that Saccharomyces boulardii as well as Lactobacillus rhamnosus are considered to be quite efficient in defending against AAD.

3.3.2. Frequent Bowel Disorder Inflammatory Bowel Disease:

The digestive system is impacted by the chronic inflammatory disorder known as inflammatory bowel disease (IBD). In IBD, three different types of colitis may be distinguished depending on the location of the GI tract inflammation: Crohn's disease (CD), ulcerative colitis (UC), and indeterminate colitis (IC). Although the precise etiology of IBD is still unknown, stress and an imbalanced diet are cited as potential factors. IBD is thought to be caused by an abnormal immune system response. Studies have suggested that the pathophysiology of IBD may be responsible for the existence of gut pathogens. Numerous studies have also shown that the microbiome of people with IBD is different from that of healthy people. Keeping the equilibrium of gut microorganisms may also be essential for avoiding IBD, according to some theories. Probiotics have received a lot of interest recently as a possible therapy to change the beneficial effects of the microorganism on IBD. For example, probiotics have been used to treat ulcerative colitis or bring about remission. Probiotic supplementation, according to a new study, appears to be an effective adjuvant treatment for UC but not for CD in people with inflammatory bowel diseases.

3.3.3. Diarrheal Conditions:

After receiving antibiotic therapy, probiotics are showing promise in preventing and controlling diarrhea. Diarrhea is treated using Bifidobacteria species such as S. boulardii, Lactobacillus GG, or Lactobacillus reuteri. Probiotics can also prevent rotavirus-induced diarrhea in young children and travelers' diarrhea. Lactobacillus spp., Lactobacillus casei, Bifidobacterium bifidum, L. Reuters, S. boulardii, or S. thermophilus are among the probiotic species used for children. By competing with harmful viruses or bacteria, stopping them from adhering to epithelial cells, by creating bacteriocins like nisin, probiotics may be able to inhibit germs that cause diarrhea.

The whole gastrointestinal system is affected by Crohn's disease (CD), an irritable bowel ailment that causes weight loss, constipation, fever, lethargy, and abdominal discomfort (GIT). Although the precise etiology of CD is still unknown, several variables, including genetic, ecological, or microbial influences its start.

Various drugs can be used to alleviate CD's symptoms, but there is currently no recognized treatment for the condition. Immunosuppressants and steroid medicines can be used to treat intestinal inflammation and decreased resistance to disease. Probiotics might provide an additional treatment method to conventional medicine. Early treatment is superior to postoperative probiotic feeding in CD patients. Meanwhile, a more recent study discovered that administering adjuvant multi-strain probiotic medication had little to no effect on CD patients' inflammatory responses. Due to differences in the results of clinical trials using probiotic supplements to treat CD, further research is needed to establish how probiotics work.

3.4. Probiotics for Better Health

Probiotics' contribution to bettering health is one of the topics covered in this review. In actuality, this is the most crucial point, where we anticipated that healthy individuals would be the first in need of using probiotics, leading to an improvement in their overall health and, as a consequence, protecting them from various illnesses. Improving our health will be a wise move to keep us safe from various illnesses. However, how could probiotics accomplish that? The idea of how probiotics might directly or indirectly help our health will be highlighted in the paragraphs that follow.

3.5. Probiotics' Function in Illness Therapy:

Probiotics have the potential to cure and manage actual diseases in addition to enhancing our health and reducing pathogenic infections. The same ideas concerning probiotic functions that are discussed in the aforementioned sections serve as a foundation for some of these duties. But how many probiotics aid in the management and treatment of actual diseases? Knowing the behavior of the illness and its underlying causes is crucial. For instance, conditions linked to hereditary illnesses will result in shortages like lactose intolerance. Probiotics' function in these situations is to address these deficiencies through a variety of mechanisms, including

Supplying our system with the gene products that were lost.

- The best course of action in the event of a deficiency of one or more genes that may block a particular pathway is to provide our body with the end product of a complete pathway since no metabolic intermediates from the broken pathway accumulate in our cells. Will not be done.
- Probiotics may be able to maintain a partially defective rather than defective pathway, which may be caused by a deficiency in one rather than both alleles. Similar to how patients with retinoblastoma are affected. In such a scenario, the crucial mechanism underlying Knudson hypnosis will be entirely disrupted, yet no one gene would experience an excessive amount of stress that can result in mutation.
- The best assistance for us as humans age will be probiotics.

This would lighten the stress on our biological system as well as free us up to engage in more activities, particularly those that will enhance how effectively we utilize food. Here are a few ways that probiotics can help us stay healthy and treat and prevent illness:

- Treating the condition causing diarrhea. For the treatment of several diarrheal illnesses, Saccharomyces cerevisiae var. boulardii was frequently used.
- Enhancing gut health.
- Improving the bioavailability of minerals, synthesis, as well as the immunological system.
- Reducing the prevalence of allergies in sensitive people and lactose intolerance symptoms.
- Lowering the danger of certain malignancies.
- Lowering the amount of serum cholesterol.
- Improved lactose digestion when compared to meals that contain lactose.
- Probiotics might even affect the intestinal mucosa's defense mechanisms, such as the production and release of antimicrobial peptides.
- Control of hypertension and blood pressure.
- State of the genitourinary system.

The initial species that colonizes a kid's body and influences his or her health throughout life is determined by the mother's health and the environment in which the child is born. Healthy microbial strain communities of microflora will promote excellent health and provide us with a variety of advantages. Exo-sources should be employed in situations where our beneficial microflora is disturbed by a variety of variables in daily living. Probiotics are beneficial microorganisms that may be found in a variety of meals, including fermented foods, or milk products. The quick development of next-generation sequencing (NGS) technology has

allowed for a clearer understanding of the functions that certain probiotics perform in the maintenance and improvement of human health. These probiotics most likely have something to do with both the regulation of intestinal problems and the balance of bacteria in the intestines. Our understanding of the selection and isolation of appropriate probiotic strains, the verification of their genuine probiotic effect or the mechanisms involved, and the assessment of an individual's health consequences in vitro and in vivo experiments has improved thanks to these different omics technologies, including microbial genetic analysis, metagenomics, transcriptomics, and occasionally even metabolomics. This has increased our understanding of various areas of probiotic research. Therefore, current knowledge on bacteria or their effects on people at an omics level, which has just lately begun to become available, is needed to create novel probiotic strains or perhaps pharmabiotic therapies. When some microorganisms, including L. rhamnosus, are used improperly, people who already have indications of inflammation of both digestive organs may develop septicemia, endocarditis, and septic shock. Because of this, it's crucial to employ the right dosage of probiotics when treating certain individuals.

3.6. Additional Health Benefits:

The list of health advantages mediated by probiotics goes beyond those already listed and includes a variety of potential outcomes that, however, need more human investigations to be confirmed. There is proof that probiotic bacteria are dietary elements that might help reduce the occurrence of cancer. Studies have shown that certain Lactobacillus as well as Bifidobacterium spp. reduce the levels of common in later life enzymes produced by colonic flora by normalizing intestinal permeability but rather microflora balance, producing antimutagenic organic acids, and boosting the host's immune system. The precise mechanisms are still being studied. Additionally, evidence indicates that by reducing serum cholesterol levels, meals containing probiotic bacteria may help control blood pressure and prevent coronary heart disease. Some of the hypothesized processes include direct cholesterol assimilation, but also interfere with cholesterol absorption from the stomach. These processes affect systemic blood levels of lipids and mediate an antihypertensive effect. These probiotic benefits, nevertheless, still need to be investigated further in extensive human studies. Not to mention, probiotic strains added to dairy products were shown to enhance treatment outcomes for women with bacterial vaginitis. The probiotics' preservation of the beneficial vaginal lactobacilli flora is probably what caused this improvement.

4. CONCLUSION

Probiotics-related medical research is just recently beginning to explore the complex relationships between food and health. Nevertheless, good early data from several research institutes. This research will enable the selection of the best probiotics for a certain application as well as the best delivery methods, such as food products like cheese, milk, and yogurt or supplements like chewing gum and lozenges. Since these bacteria have the advantage of being perfectly suited to the human oral ecology, it is important to investigate if probiotics are present in the natural human microflora. Promising results from earlier research on probiotics' effects on the human intestinal microbiota have been reported for the treatment of illnesses of the digestive system. There has also been more research in recent years that look at the role that bacteria play in patients' digestive ailments. There is a chance that probiotics might be used as treatment alternatives or preventative measures for disorders that are tied to a person's unique gut flora, however much more hypothesis-driven research is necessary. Additionally, science, researchers, and contemporary businesses give us a variety of probiotics to treat various illnesses. Early human observations, scientific studies, and many uses for probiotics in their various forms demonstrate just how much these amazing bacteria

can do to support our health, keep us safe, and assure the treatment or management of disorders. The fact that probiotics are available in natural forms and perform safe, natural functions may be their most important virtue. This overview provides a brief list of the many probiotic strains, types, applications, and some of the firms participating in these topics, in addition to identifying common categories of foods high in probiotics. In the future, probiotics, promising bacteria, will attract more and more attention.

REFERENCES:

[1] A. Staniszewski and M. Kordowska-Wiater, "Probiotic and potentially probiotic yeasts—characteristics and food application," *Foods*, 2021, doi: 10.3390/foods10061306.

[2] G. Wieërs *et al.*, "How Probiotics Affect the Microbiota," *Frontiers in Cellular and Infection Microbiology*. 2020. doi: 10.3389/fcimb.2019.00454.

[3] C. Maldonado Galdeano, S. I. Cazorla, J. M. Lemme Dumit, E. Vélez, and G. Perdigón, "Beneficial effects of probiotic consumption on the immune system," *Ann. Nutr. Metab.*, 2019, doi: 10.1159/000496426.

[4] M. Cunningham *et al.*, "Shaping the Future of Probiotics and Prebiotics," *Trends in Microbiology*. 2021. doi: 10.1016/j.tim.2021.01.003.

[5] M. Yao, J. Xie, H. Du, D. J. McClements, H. Xiao, and L. Li, "Progress in microencapsulation of probiotics: A review," *Comprehensive Reviews in Food Science and Food Safety*. 2020. doi: 10.1111/1541-4337.12532.

[6] J. Suez *et al.*, "Post-Antibiotic Gut Mucosal Microbiome Reconstitution Is Impaired by Probiotics and Improved by Autologous FMT," *Cell*, 2018, doi: 10.1016/j.cell.2018.08.047.

[7] C. de Simone, "The Unregulated Probiotic Market," *Clinical Gastroenterology and Hepatology*. 2019. doi: 10.1016/j.cgh.2018.01.018.

[8] M. Kechagia *et al.*, "Health Benefits of Probiotics: A Review," *ISRN Nutr.*, vol. 2013, pp. 1–7, Jan. 2013, doi: 10.5402/2013/481651.

[9] R. Nagpal, A. Kumar, M. Kumar, P. V. Behare, S. Jain, and H. Yadav, "Probiotics, their health benefits and applications for developing healthier foods: a review," *FEMS Microbiol. Lett.*, vol. 334, no. 1, pp. 1–15, Sep. 2012, doi: 10.1111/j.1574-6968.2012.02593.x.

[10] H. S. Gill, "Probiotics and human health: a clinical perspective," *Postgrad. Med. J.*, vol. 80, no. 947, pp. 516–526, Sep. 2004, doi: 10.1136/pgmj.2003.008664.

[11] K. Śliżewska, P. Markowiak-Kopeć, and W. Śliżewska, "The role of probiotics in cancer prevention," *Cancers*. 2021. doi: 10.3390/cancers13010020.

[12] E. Ringø, "Probiotics in shellfish aquaculture," *Aquaculture and Fisheries*. 2020. doi: 10.1016/j.aaf.2019.12.001.

[13] M. E. Sanders, D. Merenstein, C. A. Merrifield, and R. Hutkins, "Probiotics for human use," *Nutrition Bulletin*. 2018. doi: 10.1111/nbu.12334.

[14] J. M. A. Khaled, "Probiotics, prebiotics, and COVID-19 infection: A review article," *Saudi Journal of Biological Sciences*. 2021. doi: 10.1016/j.sjbs.2020.11.025.

[15] M. Bermudez-Brito, J. Plaza-Díaz, S. Muñoz-Quezada, C. Gómez-Llorente, and A. Gil, "Probiotic mechanisms of action," *Annals of Nutrition and Metabolism*. 2012. doi: 10.1159/000342079.

[16] W. Morovic and C. R. Budinoff, "Epigenetics: A New Frontier in Probiotic Research," *Trends in Microbiology*. 2021. doi: 10.1016/j.tim.2020.04.008.

[17] C. S. Kim *et al.*, "Probiotic supplementation improves cognitive function and mood with changes in gut microbiota in community- dwelling older adults: A randomized, double-blind, placebo-controlled, multicenter trial," *Journals Gerontol. - Ser. A Biol. Sci. Med. Sci.*, 2021, doi: 10.1093/GERONA/GLAA090.

[18] Y. Zhu, Z. Wang, L. Bai, J. Deng, and Q. Zhou, "Biomaterial-based encapsulated probiotics for biomedical applications: Current status and future perspectives," *Mater. Des.*, 2021, doi: 10.1016/j.matdes.2021.110018.

[19] S. Stojanov, A. Berlec, and B. Štrukelj, "The influence of probiotics on the firmicutes/bacteroidetes ratio in the treatment of obesity and inflammatory bowel disease," *Microorganisms*. 2020. doi: 10.3390/microorganisms8111715.

CHAPTER 12

AN EXPLORATORY STUDY ON CAUSES, CONTROL, AND PREVENTION OF CHILDHOOD OBESITY

Swarupa. V, Assistant Professor, Department of Chemistry,
School of Sciences, B-II, Jain (Deemed to be University),JC Road, Bangalore-560027.,
Email Id- v.swarupa@jainuniversity.ac.in

ABSTRACT: Obesity among children has reached epidemic proportions in both developed and developing nations. Childhood overweight and obesity are known to negatively affect both mental and physical well-being. Children who are overweight and obese are more likely to be overweight into maturity and to experience non-communicable illnesses like diabetes and cardiovascular disease earlier in life. It is thought that obesity is an illness with several underlying causes since the process behind its development is not entirely understood. The global rise in obesity prevalence is mostly due to environmental variables, lifestyle choices, and cultural context. In general, it is believed that increased calorie and fat intake causes overweight or obesity. Over the past several years, there have been substantial changes in lifestyle throughout the world that have resulted in more calorie-dense food consumption and decreased physical exercise. Obesity in children has been linked to metabolic syndrome, hypertension, cardiovascular disease, and a higher prevalence of diabetic complications. New approaches to preventing and treating childhood obesity must be created. The prevalence of pediatric obesity, its numerous causes and effects, and potential therapies are all examined in this study. In the future this paper will aware the people about harmful effect of childhood obesity.

KEYWORDS: ***Health, Fast Food, Physical Activity, Obesity, Overweight.***

1. INTRODUCTION

As demonstrated by the frequency of anemia, stunting, and zinc or iron shortages, the globe is going through a fast epidemiological and nutritional change that is marked by chronic nutritional deficits. The incidence of obesity, diabetes, as well as other nutrition-related chronic diseases (NCDs) like these, as well as cardiovascular disease and several types of cancer, is rising concurrently. In wealthy nations, obesity has reached pandemic proportions. Although affluent nations have the greatest incidence rates of kid obesity, emerging nations are also seeing an increase in this condition. Due to innate hormonal differences, women are more prone than men to be fat [1], [2].

It is becoming increasingly clear that childhood obesity has a significant role in the development of Type 2 Diabetes or Coronary Heart Disease. In the past 40 years, especially in the industrialized world, there has been an astounding increase in the percentage of youngsters who are obese. Studies that have come out of various sections of India over the past ten years also point to a similar pattern. In light of subsequent challenges to this theory, we now see them as distinct manifestations of the worldwide malnutrition issue. By concurrently addressing the underlying causes of nutritional deficiencies, this new approach enables us to regulate undernutrition or avoid obesity, diabetes, as well as other NCDs. With a life-course perspective on nutrition and child growth, this brief offers a public health overview of a few critical themes connected to the prevention of obesity and chronic illnesses [3].

Although the definition of overweight and obesity has evolved, an excess of body fat can still be considered one (BF). There is no agreement on a threshold for excessive fatness, overweight, or obesity in kids and teenagers.

1.1. Causes of Childhood Obesity:

It is generally accepted that the increase in obesity is caused by an imbalance between calorie intake and expenditure, with increases in a positive balance of calories strongly correlated with lifestyle choices and food preferences. In addition, there is growing evidence that suggests that a person's genetic history plays an important role in predicting their obesity risk. Our knowledge of the factors that contribute to obesity has greatly benefited from research. Age and gender are two characteristics that can reduce the effect of such risk factors. Parenting practices and parents' lives also have an impact on the family. Environmental aspects including school rules, demography, and parental job obligations also have an impact on eating and exercise patterns [4], [5]. As a result, the epidemic had a major impact on childhood obesity in recent years. The numerous causes of childhood obesity are depicted in Figure 1.

Increased fast food intake has recently been linked to an increase in obesity. These locations are chosen by several families, especially those with two parents who have jobs outside the home, as they are frequently preferred by their kids and are both practical and affordable. Fast food restaurants typically provide foods that are high in calories and low in nutritional value. Teenagers who were lean or overweight were compared in research to see what they ate at fast food outlets. The lean group adjusted their caloric intake either before or during the meal of fast food in anticipation of or compensation for the excess calories consumed even during fast food meal, according to the researchers, who discovered that both groups consumed more calories while eating fast food than they would typically do at home [6], [7]. Although several studies have demonstrated that eating fast food often causes weight gain, it is challenging to establish a link between eating fast food and obesity.

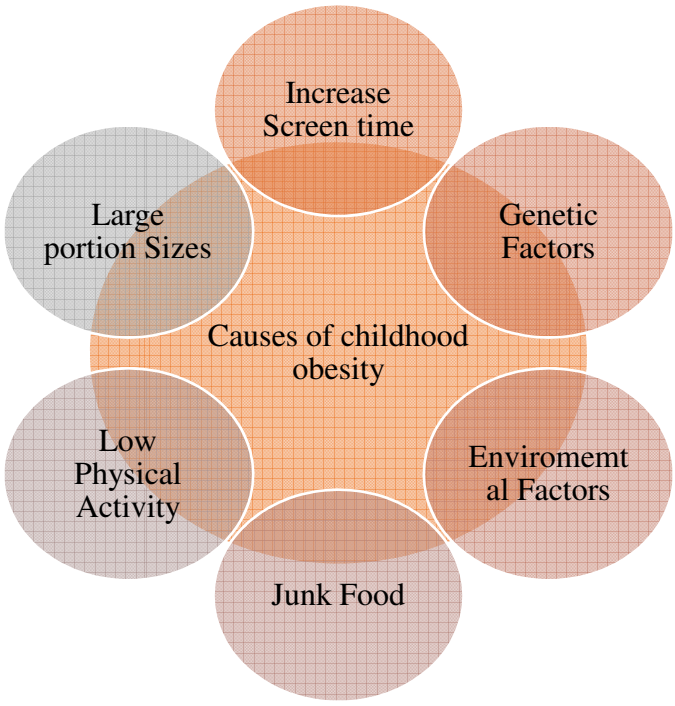


Figure 1: Illustrate the Some Major Causes of Childhood Overweight or Obesity.

1.1.1. Snack Food:

The eating of snack foods has also been investigated as a potential contributor to childhood obesity. Foods like chips, candy, and baked goods, are examples of snack foods. To determine if these foods are to blame for the rise in childhood obesity, several research has

been carried out. Although studies have indicated that snacking increases calorie consumption overall, no correlation between snacking and being overweight has been found. One of the main things being researched as an obesity cause is genetics. According to some research, "Body Mass Index" (BMI) has a 25–40% heritability. To have an impact on weight, meanwhile, genetic predisposition frequently has to be combined with supportive behavioral and environmental variables. Less than 5% of occurrences of childhood obesity are hereditary. As a result, while genetics may contribute to the onset of obesity, it is not to blame for the sharp rise in juvenile obesity [8].

Additionally investigated as a potential contributor to obesity is basal metabolic rate. The body uses its basal metabolic rate, often known as metabolism, to carry out routine testing processes. In inactive individuals, 60.00% of total energy consumption is accounted for by basal metabolic rate. According to a popular theory, obese people have a lower basal metabolic rate. The increased rates of obesity, however, are unlikely to be due to changes in basal metabolic rates.

1.1.2. External Variables:

Other environmental conditions have resulted in decreased likelihood of physical exercise, even though excessive consumption of television and use of other electronic media has led to sedentary living. In recent years, there have been fewer opportunities for physical activity and less safe environments to engage in. In the past, most children rode their bikes to school walking. According to 2002 research, 53% of family members take their children to school. Since their residences were too distant from the school, 66% of these parents claimed they drove their kids there. Parents also cited the lack of a safe walking path, concern about child predators, but also convenience for the child as additional justifications for driving their kids to school. Children have fewer possibilities to be physically active if they reside in dangerous regions or do not have access to adequate, well-lit walking paths [9], [10].

1.1.3. Psychiatric Variables:

Both anxiety and depression According to a recent study, the majority of studies uncover a potential link between eating disorders and depression. But there is more to this link than meets the eye; sadness may both contribute to and result from obesity. Moreover, in comparison to non-obese controls, a clinical sample of obese teenagers showed a greater prevalence rate of anxiety disorders. Even though certain research finds no connection between elevated BMI and elevated anxiety symptoms [11], [12]. Consequently, the link between fat and anxiety might not be direct and is surely not definitive.

2. LITERATURE REVIEW

Sameera Karnik and Amar Kanekar studied and explores the causes that contribute to childhood obesity, the many solutions and governmental initiatives addressing obesity, as well as the difficulties in controlling this pandemic. It results from an imbalance between calories consumed and burned. Family-based, community-based, school-based, play-based, or hospital-based interventions were among those that were implemented. Physical exercise and healthy eating instruction were the two main focuses of the successful school-based initiatives. These therapeutic initiatives confront significant financial difficulties in addition to stigmatizing fat youngsters. In conclusion, sustainable interventions connected to promoting healthy eating habits and physical exercise can be used to combat pediatric obesity at the population level [13].

Alvina R. Kansra et al. studied Obesity in children and adolescents. Obesity is a serious public health issue and is a complex disorder involving biological, environmental, developmental, behavioral, and hereditary components. Clinicians have mostly depended on advising dietary modifications and exercise because there isn't a single therapy option for obesity. This strategy could backfire because of the psychological problems with bodily habitus that may come along with puberty. However, there is little information available on the effectiveness and security of various weight-loss drugs in children and adolescents. The topic of bariatric surgery as a potential solution for almost 6% of seriously obese teenagers in the United States will be covered. The etiology, clinical consequences, psychological effects, and therapy choices for obese adolescent and childhood patients are all summarized in this study [14].

Krushnapriya Sahoo et al. studied Childhood obesity and overweight are known to negatively affect both physical and mental health. Children who are overweight or obese are more likely to stay that way into adulthood and are also at an earlier age to acquire non-communicable illnesses including diabetes and cardiovascular disorders. It is thought that obesity is an illness with several underlying causes since the process behind its development is not entirely understood. The global rise in obesity prevalence is mostly due to environmental variables, lifestyle choices, and cultural context. Additionally, it is linked to a child's poorer quality of life and poor academic achievement. Childhood obesity is also associated with several co-morbid illnesses, including metabolic, hepatic, pulmonary, neurological, cardiovascular, orthopedic, and renal problems [15].

3. DISCUSSION

3.1. Effects of Childhood Obesity:

3.1.1. Leptin:

To prevent excessive energy storage or to maintain a healthy balance of energy, leptin is crucial. This action is supported by the relationship between leptin concentrations as well as lipid oxidation, satiety, and increased energy expenditure. Rather than each element separately, leptin is more closely related to a balance between calorie intake and energy expenditure. People's plasma leptin concentrations are significantly influenced by their adipose tissue mass; variations in body fat and caloric intake regulate human leptin mRNA or protein. The body mass index and fat mass have been shown to positively correlate with leptin, whereas the fat-free mass has indeed been found to negatively correlate with leptin. Leptin is also frequently greater in obese children than that in lean children. Leptin resistance is the primary risk factor for obesity. Numerous factors, like inflammation or stress just on the endoplasmic reticulum, contribute to leptin resistance (ER). In obese persons, leptin levels are exceptionally high. Due to a condition called “leptin resistance”, which occurs when certain obese people's brains do not respond to leptin, they continue to eat even when they have enough or excessive fat storage. As a result, leptin production by fat cells increases [16].

3.1.2. Ghrelin

An endogenous ligand of both the orphan G-protein associated receptor, ghrelin performs this activity. Among the many metabolic consequences of ghrelin are an increase in appetite, the release of growth hormone, and fat accumulation. Ghrelin affects the hypothalamic circuits that regulate hunger, which has an anorexigenic effect. At the same time, it encourages the development of adipose tissue but has a diabetogenic impact on peripheral organs including the kidneys and liver. Plasma ghrelin levels are influenced by body mass index or eating

patterns. In general, ghrelin levels are often lower in obese and insulin-resistant individuals. Growth hormone hyposecretion may be exacerbated by obesity's reduced ghrelin secretion.

3.1.3. Sweetened Drinks:

Sugary beverages have also been investigated as a possible obesity risk factor. Contrary to popular assumption, the term "sugary drinks" include not just soda but also juice and other liquids with added sugar. It has been found that consuming sugary drinks and being overweight are related. Sugary drinks are less satisfying than meals and can be eaten more rapidly. If these beverages are drunk more frequently, the link between genetic predisposition and obesity may be impacted. Children who consume beverages with added sugar are twice as likely to be obese as their average classmates. Children who were obese drank far more sugary drinks than kids who were of normal weight. Due to their little nutritional value, these beverages provide more empty calories than 100% fruit juices [17].

3.1.4. Insulin

Insulin is a peptide hormone secreted by the pancreatic islets of Langerhans cells that controls the metabolism of proteins, fatty acids, and carbohydrates while also promoting growth and cell division through its mitogenic actions. Insulin maintains appropriate blood sugar levels by assisting cells in absorbing glucose. Insulin resistance often and significantly worsens childhood and teenage obesity. Insulin resistance is characterized by a loss in insulin's capacity to increase glucose uptake by muscles or adipose tissue as well as to lower hepatic glucose production and output. It also clarifies why insulin has less of an effect on lipid and protein metabolism, gene expression, or vascular endothelial cell function. Furthermore, insulin resistance has been associated with the development of impaired glucose tolerance or type 2 diabetes in obese children and adolescents.

3.1.5. Consumption of Fast Food:

Being surrounded by a lot of fast food restaurants is thought to make childhood obesity more common because it deters people from following good eating habits and encourages exposure to locations that provide unhealthy food, which prompts compensatory intake of unhealthy foods. The prevalence of overweight and obesity might considerably rise as a result of eating bad food, which exposes kids to enormous food portions with excessive calories or glucose loading. These locations are popular with families, especially those of us with two working parents, due to their being convenient for them and their kids, as well as affordable.

3.1.6. Active Inactivity:

The relationship between obesity and sedentary activity is greatest. Today, more young kids and teens watch television than ever before. Instead of playing outside, children are becoming more engrossed in technology, computers, and video games. Both during and after school, physical exercise has decreased. Even for shorter distances, kids are now more likely to use cars than bicycles. Children who live in risky areas or who lack access to safe, well-lit walking trails have fewer opportunities to engage in physical activity.

3.1.7. External variables:

It has been highlighted that growing urban traffic congestion has led to several issues, including noise pollution from industry and other ecological issues. These issues can affect children's psychology, sleep, physical activity, or endocrine systems all of which are linked to the obesity epidemic. Due to extensive quarantine and home confinement during the coronavirus illness 2019 epidemic, which has exacerbated childhood obesity, children have

been exposed to new and unexpected stresses. Lack of access to any outside spaces for school closings, and physical activity, as well as the ensuing home confinement restrictions, had a severe influence on children's emotional and physical well-being [18].

Childhood obesity can have a substantial negative influence on a child's physical health, emotional and social well-being, or self-esteem. Additionally, it's linked to a kid's poorer level of life and poor academic achievement. Comorbidities including metabolic, orthopedic, neurological, pulmonary, cardiovascular, hepatic, or renal diseases are usually present in children who are obese. Children who were overweight had higher rates of various clinically important connected psychosocial disorders, an increase in conduct issues such as disruptive, aggressive, disobedience, and catastrophic behavior, as well as both physical and verbal abuse, compared to their healthy-weight peers. Other issues include peer issues, attention issues, and emotional symptoms. The stigma associated with being overweight might take the form of bullying and taunting. Older obese kids are more likely to have depression as well as other internalizing disorders like anxiety and paranoid thoughts. Non-alcoholic fatty liver disease in children is a kind of pediatric liver disease that is growing more prevalent as childhood obesity rises in prevalence.

Children who are obese typically have irregular periods. Obese girls are said to experience menarche earlier, usually before the age of 10, following the hypothesis that body weight and fatness are important physiologic triggers of menarche. However, oligomenorrhoea as well as amenorrhoea is also connected to obesity since obese teenage girls commonly have polycystic ovarian syndrome or hyperandrogenism, which are both fueled by metabolic syndrome brought on by visceral adiposity.

The onset of adult cardiovascular disease or total cardiovascular risk is both strongly correlated with childhood obesity. The atherosclerosis process, which has been shown to begin in infancy, has been connected to several childhood variables that cause adult cardiovascular disease. The cardiovascular effects of obesity include insulin resistance, dyslipidemia, and hypertension. Childhood obesity increases the risk of cancer, infertility, depression, diabetes, dyslipidemia, or cardiovascular disease mortality. It can also harm future health outcomes. Therefore, childhood obesity may be a risk factor for adult morbidity. The implications of childhood obesity are depicted in Figure 2.

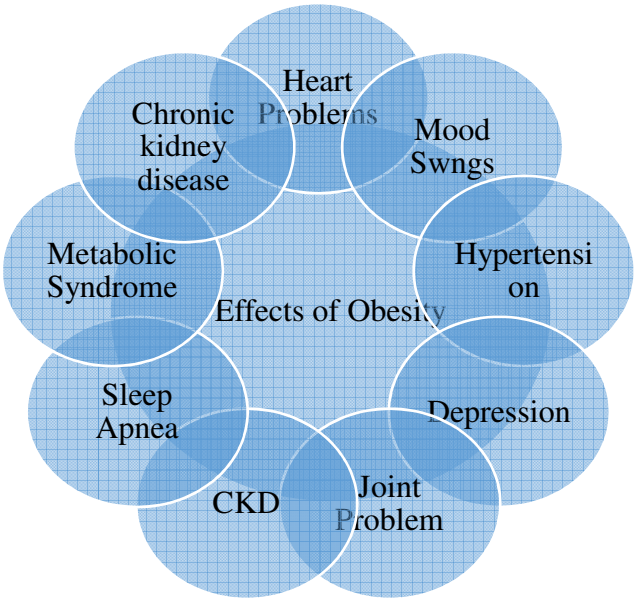


Figure 2: Illustrate the Effects of Obesity on Children.

3.2. Prevention:

Over the past several years, there has been a marked rise in the prevalence of pediatric obesity, which is becoming a serious public health concern. The treatment of childhood obesity by various sorts of interventions does seem to hold promise because it is extremely difficult to cure once it has been established. Reduced sedentary behavior, family support, and the encouragement of physical activity in conjunction with dietary education appear to be important factors in reducing juvenile obesity. It is possible to begin nutritional and activity change strategies at home, in preschool settings, in classrooms, or in institutions that provide after-school care.When creating these strategies, consideration should be given to the sociodemographic makeup, ethnic makeup, and cultural background of the target audience. Reduced use of sugary foods, prepackaged snacks, soft drinks, and fast food may help slow the growth of childhood obesity. To encourage the majority of kids to engage in prolonged physical exercise, interventions must adequately grasp and take into account the effects of this attitude, especially considering that many kids are overweight. Children's physical activity behavior is often influenced by biological, social, and psychological aspects as well as how they interact. Most recent research is in favor of the hypothesis that certain psychosocial traits, such as self-perception and physical competency, may operate as powerful pillars for boosting overweight and obese kids' participation in unstructured physical activity. Interventionists ought to prioritize improving these human qualities instead of probable biological and developmental reasons. To feel better about themselves, children who live with obesity might benefit from developing their motor skills.

Globally, the prevalence of pediatric obesity has increased in recent years. A buildup of adipose tissue that is significant enough to harm health is referred to as obesity. Obesity has a seriously detrimental effect on a child's health, both during childhood and into adulthood. Due to the rising frequency of childhood obesity, both developed and industrialized countries face serious hazards to their public health. Children who are overweight are more likely to become obese than adults. Children that are overweight have trouble exercising. Children should be encouraged to engage in physical exercise of any kind regularly. To raise a child in a healthy atmosphere, parents are crucial. It is crucial to evaluate the kid's nutritional status concerning what the youngster consumes and the advised diet. Being overweight, or obese is up to four times more common than malnutrition in some parts of the world, where it formerly predominated. On the other hand, there is evidence to show that larger portion sizes, excessive sugar consumption in soft drinks, and a continuous drop in physical activity have been contributing significantly to the global rise in obesity rates. Children's physical health, emotional well-being, and self-esteem can all be significantly impacted by childhood obesity. Additionally, it is linked to a child's poorer quality of life and poor academic achievement. Childhood obesity is frequently accompanied by several co-morbid illnesses, such as metabolic, orthopedic, cardiovascular, neurological, pulmonary, hepatic, and renal problems.

If society focuses on the causes, it may be possible to curb the growth of the kid obesity problem. Several factors contribute to childhood obesity, some of which are more important than others. Prevention of obesity or overweight is more successful with a community-based, school-based combined nutrition and physical activity strategy. However, several obesity issues may be prevented if parents encouraged a healthy lifestyle at home. Children's home-based instruction in nutrition, exercise, and good eating will ultimately translate to other facets of their lives. This is going to have the most impact on how kids decide what to eat at school, in fast food restaurants, and whether or not to exercise. By concentrating on these factors, childhood obesity may eventually decline or society as a whole seems to become healthier.

4. CONCLUSION

The improvement in a positive energy balance is directly associated with lifestyle decisions and food preferences. It is now known that an imbalance between energy intake and expenditure is the root cause of juvenile obesity. The prevalence of childhood obesity is expected to increase further. Therefore, it is vital to take into account its effects on both physical and mental health. Obesity in children and adolescents has a wide range of negative impacts. They cover both psychological, social, as well as behavioral outcomes, including an increased likelihood of issues with body image, self-esteem, socioeconomic discrimination and exclusion depression, and a lower quality of life. They also cover physical health outcomes, including metabolic syndrome, high blood pressure, high cholesterol, insulin resistance diabetes, asthma, sleep apnea, orthopedic issues, and hepatic steatosis. A clear and strategic approach is needed to combat the obesity epidemic by putting in place extensive programs that encourage kids and teenagers to eat healthy meals and reduce their consumption of processed foods and beverages with sugar added. This growing trend, which threatens the health and very well of the younger generation and includes a significant negative impact on resources and monetary cost, must be stopped. These treatments for children and teens require more attention. Parents should make sure their children develop healthy habits and grow up appropriately by encouraging them to eat well, get enough sleep, and exercise while they are young. Governments should create and execute policies that promote healthy school settings, active living amongst adolescents and youth, nutrition and health education, and comprehensive weight-management programs for obese children and adolescents.

REFERENCES:

[1] J. D. Smith, E. Fu, and M. A. Kobayashi, “Prevention and Management of Childhood Obesity and Its Psychological and Health Comorbidities,” *Annual Review of Clinical Psychology*, vol. 16. pp. 351–378, 2020. doi: 10.1146/annurev-clinpsy-100219-060201.

[2] R. An, “Projecting the impact of the coronavirus disease-2019 pandemic on childhood obesity in the United States: A microsimulation model,” *J. Sport Heal. Sci.*, vol. 9, no. 4, pp. 302–312, 2020, doi: 10.1016/j.jshs.2020.05.006.

[3] B. J. Deal, M. D. Huffman, H. Binns, and N. J. Stone, “Perspective: Childhood Obesity Requires New Strategies for Prevention,” *Advances in Nutrition*, vol. 11, no. 5. pp. 1071–1078, 2020. doi: 10.1093/advances/nmaa040.

[4] J. L. Warnick, S. Pinto, K. Ding, and D. M. Janicke, “Childhood obesity,” in *Adherence and Self-Management in Pediatric Populations*, 2020, pp. 85–105. doi: 10.1016/B978-0-12-816000-8.00004-9.

[5] W. K. H. Mok, N. N. Hairi, C. M. H. Chan, F. I. Mustapha, T. A. Saminathan, and W. Y. Low, “The implementation of childhood obesity related policy interventions in malaysia—a non communicable diseases scorecard project,” *Int. J. Environ. Res. Public Health*, vol. 18, no. 11, 2021, doi: 10.3390/ijerph18115950.

[6] J. Lanigan, L. Tee, and R. Brandreth, “Childhood obesity,” *Medicine (United Kingdom)*, vol. 47, no. 3. pp. 190–194, 2019. doi: 10.1016/j.mpmed.2018.12.007.

[7] C. S. González-González, N. G. Del Río, P. A. Toledo-Delgado, and F. J. García-Peñalvo, “Active game-based solutions for the treatment of childhood obesity,” *Sensors (Switzerland)*, vol. 21, no. 4, pp. 1–23, 2021, doi: 10.3390/s21041266.

[8] M. Vilar-Compte *et al.*, “Migration as a determinant of childhood obesity in the United States and Latin America,” *Obes. Rev.*, vol. 22, no. S3, 2021, doi: 10.1111/obr.13240.

[9] L. Ronan, A. Alexander-Bloch, and P. C. Fletcher, “Childhood Obesity, Cortical Structure, and Executive Function in Healthy Children,” *Cereb. Cortex*, vol. 30, no. 4, pp. 2519–2528, 2020, doi: 10.1093/cercor/bhz257.

[10] T. J. Kauh *et al.*, “Childhood Obesity Declines Project: An Effort of the National Collaborative on Childhood Obesity Research to Explore Progress in Four Communities,” *Child. Obes.*, vol. 14, pp. S1–S4, 2018, doi: 10.1089/chi.2018.0018.

[11] E. Argelich *et al.*, “Paediatric teams in front of childhood obesity: a qualitative study within the STOP project,” *An. Pediatr.*, vol. 95, no. 3, pp. 174–185, 2021, doi: 10.1016/j.anpedi.2020.11.009.

[12] O. Scudiero *et al.*, "Childhood obesity: An overview of laboratory medicine, exercise and microbiome," *Clinical Chemistry and Laboratory Medicine*, vol. 58, no. 9. pp. 1385–1406, 2020. doi: 10.1515/cclm-2019-0789.

[13] S. Karnik and A. Kanekar, "Childhood Obesity: A Global Public Health Crisis," in *School Nutrition and Activity*, Apple Academic Press, 2015, pp. 3–15. doi: 10.1201/b18227-3.

[14] A. R. Kansra, S. Lakkunarajah, and M. S. Jay, "Childhood and Adolescent Obesity: A Review," *Front. Pediatr.*, vol. 8, Jan. 2021, doi: 10.3389/fped.2020.581461.

[15] K. Sahoo, B. Sahoo, A. Choudhury, N. Sofi, R. Kumar, and A. Bhadoria, "Childhood obesity: causes and consequences," *J. Fam. Med. Prim. Care*, vol. 4, no. 2, p. 187, 2015, doi: 10.4103/2249-4863.154628.

[16] D. Berrigan *et al.*, "Measurement challenges for childhood obesity research within and between Latin America and the United States," *Obes. Rev.*, vol. 22, no. S3, 2021, doi: 10.1111/obr.13242.

[17] M. M. Kelsey, A. Zaepfel, P. Bjornstad, and K. J. Nadeau, "Age-related consequences of childhood obesity," *Gerontology*, vol. 60, no. 3. pp. 222–228, 2014. doi: 10.1159/000356023.

[18] S. Allender *et al.*, "Whole of systems trial of prevention strategies for childhood obesity: WHO STOPS childhood obesity," *Int. J. Environ. Res. Public Health*, vol. 13, no. 11, 2016, doi: 10.3390/ijerph13111143.

CHAPTER 13

APPLICATIONS AND SIDE EFFECTS OF FOOD PRESERVATIVES AND FOOD ADDITIVES

Dr. Subbulakshmi Ganesan, Assistant Professor, Department of Chemistry,
School of Sciences, B-II, Jain (Deemed to be University),JC Road, Bangalore-560027.,
Email Id- g.subbulakshmi@jainuniversity.ac.in

ABSTRACT: Food additives are natural or synthetic compounds that can be incorporated into food in small quantities to fulfill technical purposes such as sweetness, color, or shelf life enhancement. Preservatives also referred to as antimicrobial agents, are food additives that help food last longer by protecting it from degradation caused by bacteria. The purpose of this study is to evaluate the existing literature on the different impacts of food preservatives and additives as a consequence of their indiscriminate usage by food producers and food consumers. It has been noted and revealed that the indiscriminate consumption and use of food preservatives and food additives are associated with cancer, multiple sclerosis (MS), nausea, food intolerance, food allergies, brain damage, attention deficit hyperactivity disorder (ADHD), and heart illness.

KEYWORDS: Bacteria, Foods, Food Additives, Preservatives, Skin.

1. INTRODUCTION

Food additives are substances that food producers consciously put into foods in minute quantities throughout production or preparations to improve the food's quality and flavor. Compounds, which can be of synthetic or natural origin and usually lack significant nutritional value, are introduced to the food in small amounts throughout processing (industrial change or during packing). Maintaining the homogeneity, health, and purity of the product, helps to increase the food's shelf life. They truly make a variety of simple foods accessible without the stress of regular purchasing or preparation. The introduction of food additives must be done so in carefully monitored quantities and within the acceptable daily intakes (ADIs), since doing so might have severe effects on the consumers. Any substance used throughout the production, handling, processing, packaging, transportation, or storage of food falls under this definition. Compounds called additives are also added to food to preserve taste or enhance its taste and appearance. Since ancient times, certain additives have been employed to preserve food, including pickling (preserving with vinegar), salting (as with bacon), preserving sweets, and utilizing sulfites (such as in certain wines). In the second half of the 20th century, as packaged foods became more popular, several more additives of both natural and artificial origin were added[1]–[6].

Preservatives and additives must be used to preserve food for a long period to maintain its quality, wholesomeness, taste, appearance, and flavor. The additional moisture in food may lead to the growth and proliferation of bacteria, fungi, and yeasts, which will ultimately cause food to deteriorate. Due to the growth of germs and fungi, the use of chemicals and preservatives prevents food from decaying. Preserving the consistency and quality of the meals are additives and preservatives. Additionally, they maintain the food's nutritional content, control the pH level, provide leavening and color, and improve flavor while also maintaining palatability and wholesomeness.

Due to the characteristics of the food product or just because the additives themselves might decay and need to be stabilized by other additives, it is usually necessary to utilize many additives at once. Additionally, numerous chemicals may be used in conjunction to boost a certain activity (synergistic effect). The technical functions of several food additives might vary. In this regard, a variety of chemicals are used as anti-microbial agents as the growth of fungus and bacteria might degrade the quality of food when combined with other processes, including hermetically sealed packaging and freezing. These substances are labeled (according to their technical purpose) as preservatives, and the EU regulates their use. As a result, this research evaluates the qualities, uses, and drawbacks of food additives employed as preservatives (antimicrobial agents).

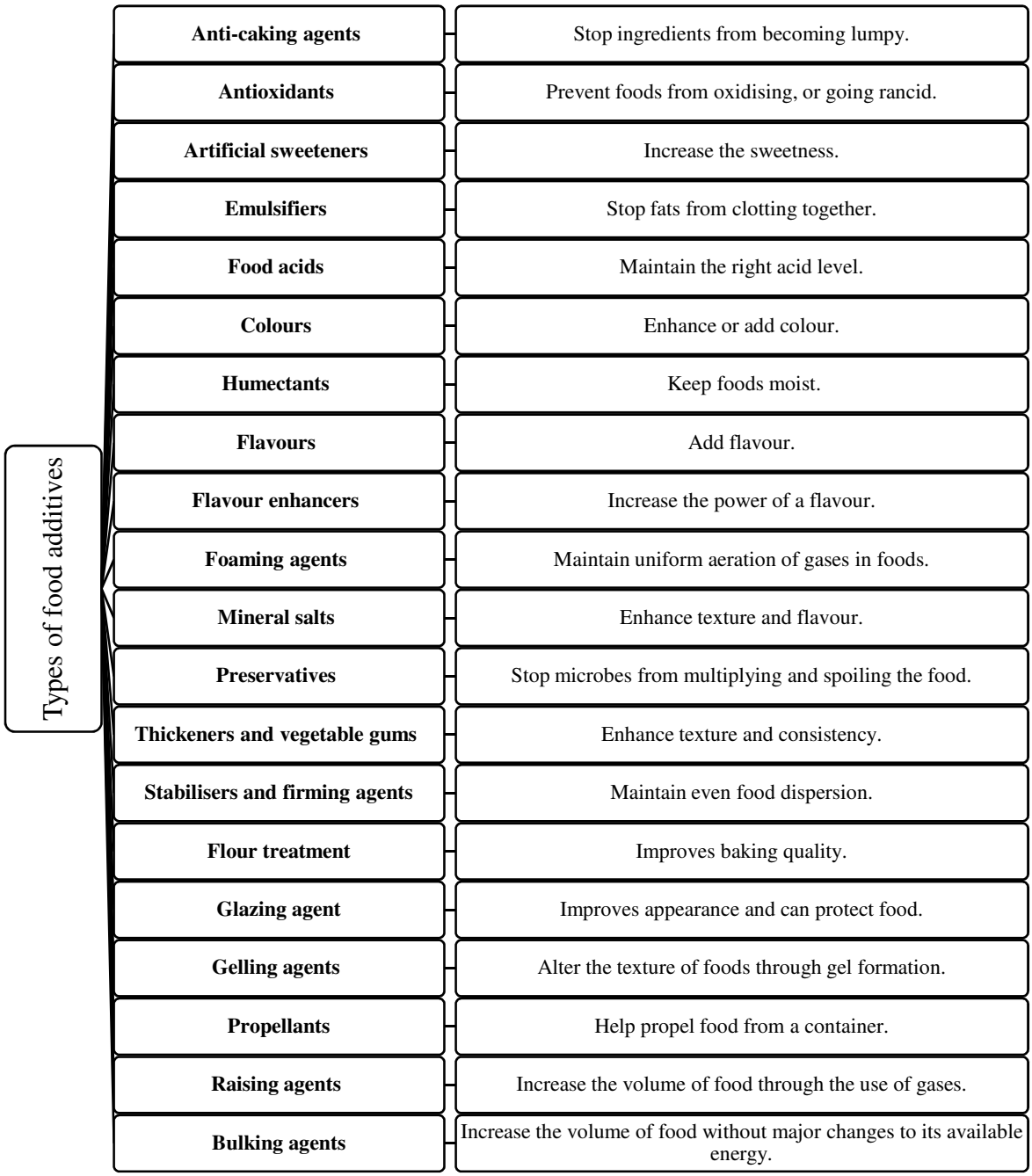


Figure 1: Illustrating the different types of food additives and their functions.

2. LITERATURE REVIEW

Helal et al. examined the negative impacts of several dietary additives in male laboratory rats as well as their detrimental effects on metabolic indicators. The results of their study evidenced altitude in tiers of “fasting glucose”, “actions of ALT”, “urea”, “triglycerides (TG)”, “total cholesterol (TC)”, “AST”, “creatinine”, and “high-density lipoprotein cholesterol (HDL-C)”, “VLDL”, and “proportion of LDL-C/HDL-C (risk factors)” and “TC/HDL-C”, as well as globulin/albumin ratio and serum thyroid hormones (T4 & T3), preceded with sharp decrease in levels of testosterone, serum total proteins, albumin, globulin, albumin/ creatinine ratio and HDL-C in all treated groups in versus the control group [7].

The effects of several food additives on male adult albino rats were examined by Tawfek et al. in terms of toxicology and biochemistry. A very large increase in GPx, MDA, and a sizable increase in CAT activity was seen in rats given tartrazine, according to the results. Additionally, they showed a significant increase in serum total bilirubin, ALT, LDL-cholesterol, serum albumin, AST, serum albumin, ALP, HDL-cholesterol, serum urea and total lipids, creatinine, serum potassium, total cholesterol, and sodium concentrations, alpha-fetoprotein, and protein kinase C levels, fasting blood glucose level, showing that all these additives alter various biochemical parameters, e.g. liver and kidney and that sunset yellow have the lowest negative impacts in contrast with the other food additives [8].

To determine if the use of artificial food colors and additives (AFCA) affected children's behavior, McCann et al. conducted a crossover experiment that was randomized, double-blinded, and controlled for many variables. The results of their research showed that, in the general population, children aged 8/9 and 3 years old who consume food with artificial coloring or a sodium benzoate preservative (or even both) exhibit increased hyperactivity [9].

The effects of frequently used preservatives and synthetic food colorings on the transcription of NFB, GADD45, and MAPK8 (JNK1) in liver tissues were examined by Raposa et al. The study's findings suggested that Tartrazine itself may have an impact on how NFB and MAPK8 are expressed. Apoptosis was also induced by azorubine in line with MAPK8 expression. Preservatives turned shown to be anti-apoptotic at high dosages. Sodium benzoate dose-dependently reduced MAPK8 expression (from low to high concentrations). At half-fold ($p = 0.002$) and fivefold dosages, the two preservatives worked together to dramatically increase MAPK8 expression [10].

3. METHODOLOGY

The evidence for this review investigation was obtained using a particular search terms technique in an electronic database ("PubMed," "Scopus," "Google Scholar," and "Science Direct.") A screened search was used to find and organize relevant materials. "Food Additive," "Preservatives," "Food," "Preservative agents," "Preservation," "contamination," "side effects," and "Heath effects" were the keywords employed. The technique of the present review research is shown in Figure 2 below.

In the modern food supply, food additives are necessary. They make it possible for the growing urban population to eat a variety of meals throughout the year and access a wide selection of foods without having to go shopping every day. Often neglected, food additives serve a variety of crucial functions in meals. Additives keep food appealing and nutrient-rich while it travels to markets hundreds of miles from the farms or processing facilities since the majority of people no longer live on farms. Additionally, by enhancing a product's flavor, consistency, texture, or color, additives increase its attractive properties and increase the

nutritional value of particular meals. The importance of food preservation is that it extends a food's shelf life and prevents food from going bad due to germs on hands that touched it before putting it inside a container or bacteria found in the container itself. Food preservation is important so that food does not deteriorate or cause sickness. Although preservatives are necessary for food safety, too much of a good thing is unhealthy. In addition to allergies, these foods may induce stomach discomfort, vomiting, breathing difficulties, hives, and skin rashes. Some of the most dangerous additives are benzoates, which may cause skin rashes, asthma, and perhaps brain damage.

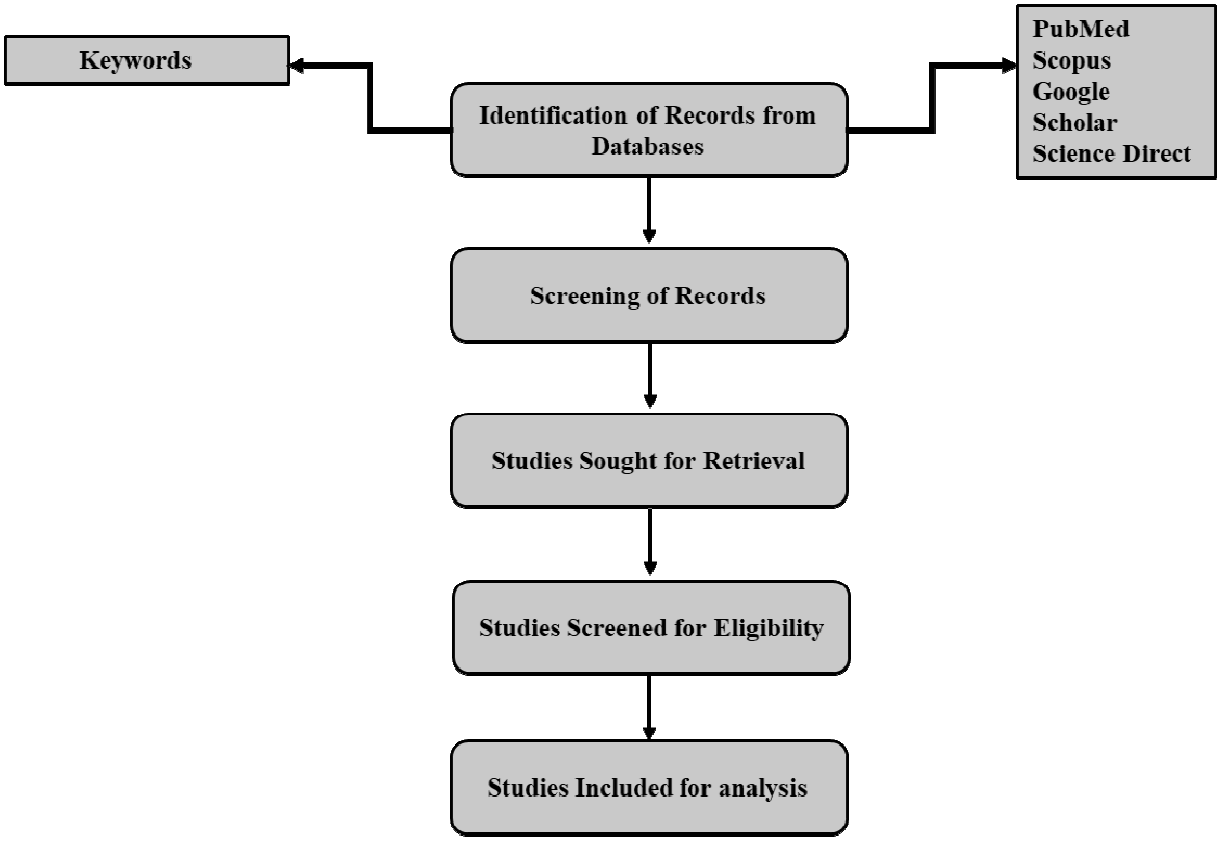


Figure 2: Illustrating the Methodology used to carry out the review study.

4. DISCUSSION

The importance of food preservation lies in the fact that it extends a food's shelf life and prevents food from going bad due to germs found in the container it was stored in or on the hands that touched it before putting it inside. Food preservation is important to prevent food from going bad or spreading illness. Preservatives are required for food safety, but consuming too much of anything is unhealthy. These foodstuffs not only cause sensitivity but also vomiting, respiratory problems, stomach pain, hives, and skin rashes. Benzoates are one of the most hazardous chemicals since they may lead to asthma attacks, rashes, and even brain damage. Bromates can cause nausea and diarrhea. In addition to tumors and bladder cancer, saccharin may cause adverse reactions in the heart, gastrointestinal tract, and blood vessels. Red Dye 40 may have contributed to several birth defects. Sodium chloride has been linked to high blood pressure, kidney failure, heart attacks, and strokes. Due to these problems, many medical professionals now advise against drinking diet sodas since they contain chemicals and favor sugar-sweetened sodas.

Bromates have the potential to produce nausea and diarrhea. Saccharin may produce harmful responses in the gastrointestinal system and the heart, as well as tumors and bladder cancer.

Various birth abnormalities may be caused by Red Dye 40. High blood pressure, renal failure, stroke, and heart attack may all be caused by sodium chloride.

4.1. Beneficial applications/features of Food additives and Preservatives

Additives are used in foods for five main reasons as illustrated in Figure 3:

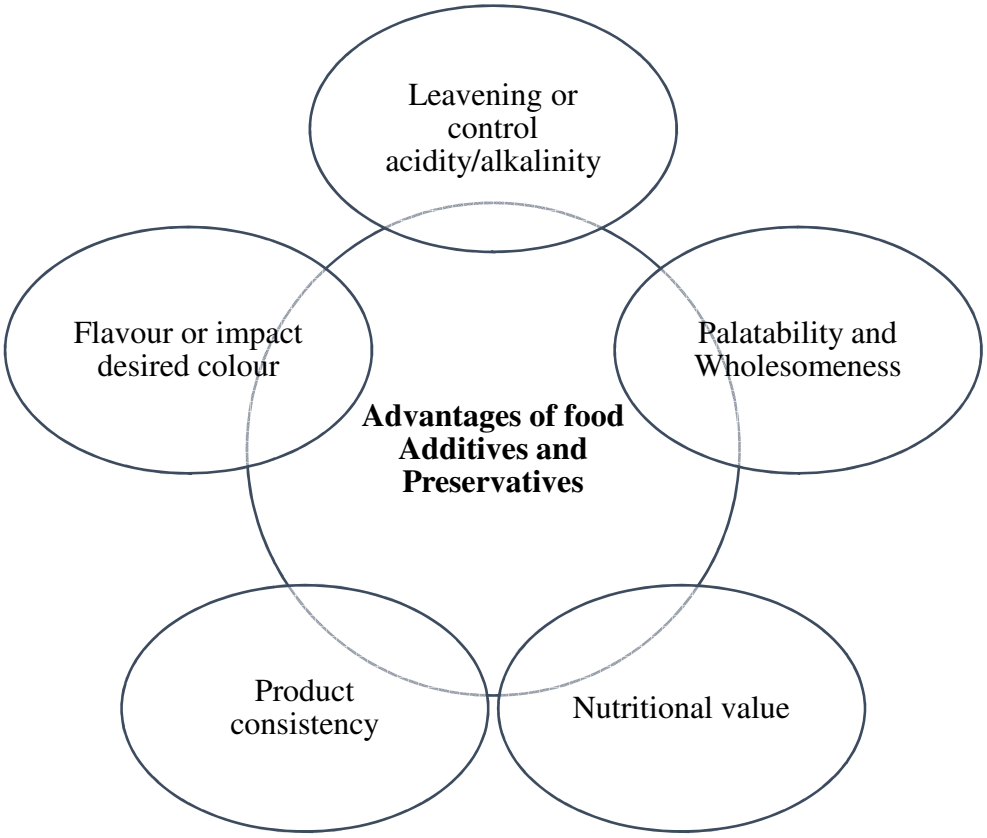


Figure 3: Illustrating Five Main Reasons for Which Additives are Used in Foods.

- Emulsifiers give goods a uniform texture and keep them from separating. Stabilizers and thickening agents provide a smooth, homogeneous texture. Anti-caking substances allow things such as salts to flow freely.
- To increase or preserve nutritional value: Minerals and vitamins are introduced to several popular foods such as milk, cereal, wheat, and butter to compensate for nutrients that are likely to be lacking in a balanced lifestyle or lost during manufacturing. Nutritional fortification and supplementation have helped to decrease malnutrition in the United States. All items with additional nutrients must be properly labeled.
- Preservatives prevent product spoiling caused by mold, air, bacteria, fungus, or yeast. Microbial contamination in foodstuff may result in food contamination, potentially life-threatening botulinum. Antioxidants are preservatives that keep oils and fats in baked products as well as other foodstuffs from going rancid or acquiring an off-flavor. They also keep chopped fresh fruits like apples from turning brown when exposed to air.
- To give seasoning or manage acidity/alkalinity: Leavening agents that produce acids while heated can interact with sodium bicarbonate to assist biscuits, cakes, and other baked products rise during baking. Other additions serve to change the acidity and alkalinity of meals for optimum flavor, taste, and color.

- To improve flavor or effect desired color: Many spices, natural and synthetic flavors enhance the taste of dishes. Colors, for example, contribute to improving the look of some meals to fulfill customer expectations.
- To preserve product consistency and quality: They aid to increase or maintain nutritional value, palatability, and wholesomeness, offer to leaven, adjust pH, enhance taste, or give color.

4.2. Disadvantages of Food additives and preservatives

Despite being necessary for food preservation, chemicals and preservatives have the potential to cause some health issues. For those who are allergic to certain chemicals, they may result in a variety of diseases including hyperactivity as well as attention deficit disorder. Aside from rashes, vomiting, headaches, and tightness in the chest and hives, meals with additives may aggravate eczema and cause asthma and hay fever. Following are some of the recognized risks associated with food additives and preservatives:

- Benzoates are thought to be causing brain damage as well as allergies including skin problems and asthma, among others.
- Bromates deplete dietary sources of their nutrition. It may result in diarrhea and motion sickness. High blood cholesterol levels, as well as compromised liver and renal function, are brought on by butylates
- High blood pressure, renal failure, a migraine, and cardiac arrest may all be brought on by sodium chloride. One must stay away from foods that include chemicals and preservatives to reduce the chance of becoming sick from eating such things. Examine the ingredients of the canned food before buying it. One should purchase organic foods since they don't include artificial ingredients. Eat as many freshly made meals as you can instead of processed or canned ones.
- Caffeine is a flavoring and coloring agent with stimulant and diuretic characteristics. Anxiousness, tachycardia, and possibly heart abnormalities are possible effects.
- Red dye 40 is thought to contribute to certain cancers and birth abnormalities.
- Birth abnormalities, genetic alterations, and cancer may all be brought on by mono- and di-glycerides.
- A popular flavoring and coloring ingredient known to deplete vitamin B6 levels is caramel. It may potentially result in cancer and certain genetic abnormalities.
- The skin, digestive system, and heart are all negatively impacted by toxic responses and adverse reactions caused by saccharin. Tumors and bladder may also be brought on by it.

The major side effects of food additives that are common with all additives are preservatives are illustrated in Figure 4.

With the use of food additives, consumers may enjoy and tolerate food on an organoleptic level. No longer is there a single food business that uses these compounds to improve the quality of food. Food additives are a vast area of specialty and a popular topic of study for scientists.

Demand for food additives has recently outpaced supply, necessitating a change in the way they are produced. To achieve this, research in this area is necessary to meet the demands of consumers, merchants, and producers. A big focus should be placed on adhering to the relevant requirements of food safety authorities to prevent or eliminate any health concerns when utilizing food additives since they have effects on one's health as well.

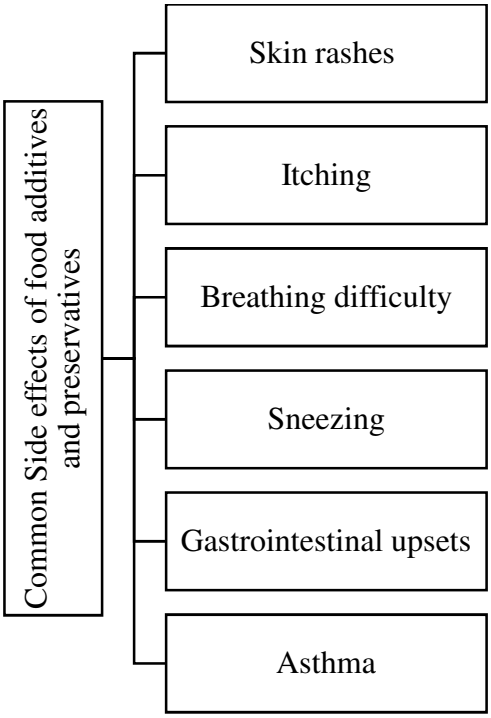


Figure 4: Illustrating the common side effects of food preservatives and Additives.

5. CONCLUSION

There are several food preservatives (anti-microbial compounds) that shield food from the actions of microbes (fungi and/or bacteria) and so prolong its shelf life. Preservatives are indisputable components of food science, alongside methods like chilling and hermetically sealed packing. Preservatives are used by agro-food businesses in so many different foods, including pre-cooked meals, processed meats, condiments, canned fish, cheese, vegetables, meat, vegetables, and fruits, cooked confectionery, packaged bread, frozen crustaceans, and many others. In these cases, the EU regulates all additives and their uses. The usage of certain such food additives does not, nevertheless, come without potential negative health repercussions. Preservatives such as potassium and sodium nitrates, nitrites, different benzoates, orthophenylphenol, diphenyl, sulfites, and hexamethylenetetramine have significant negative effects and should only be used in the lowest amounts feasible while keeping the essential technical characteristics.

REFERENCES:

[1] M. M. Silva and F. C. Lidon, “Food preservatives - An overview on applications and side effects,” *Emirates Journal of Food and Agriculture*. 2016. doi: 10.9755/ejfa.2016-04-351.

[2] E. Stoleru and M. Brebu, “Stabilization techniques of essential oils by incorporation into biodegradable polymeric materials for food packaging,” *Molecules*. 2021. doi: 10.3390/molecules26206307.

[3] S. A. Adefegha, B. M. Okeke, and G. Oboh, “Antioxidant properties of eugenol, butylated hydroxylanisole, and butylated hydroxyl toluene with key biomolecules relevant to Alzheimer’s diseases—In vitro,” *J. Food Biochem.*, 2021, doi: 10.1111/jfbc.13276.

[4] R. H, “Rosmarinus officinalis (Rosemary): A Novel Therapeutic Agent for Antioxidant, Antimicrobial, Anticancer, Antidiabetic, Antidepressant, Neuroprotective, Anti-Inflammatory and Anti-Obesity Treatment,” *Herb. Med. Open Access*, 2017, doi: 10.21767/2472-0151.100028.

[5] L. Martínez-Zamora, R. Peñalver, G. Ros, and G. Nieto, “Olive tree derivatives and hydroxytyrosol: Their potential effects on human health and its use as functional ingredient in meat,” *Foods*. 2021. doi: 10.3390/foods10112611.

[6] Ç. E. D., "FoodWiki: a Mobile App Examines Side Effects of Food Additives Via Semantic Web," *J. Med. Syst.*, 2016.

[7] E. G. E. Helal, R. A. A. El-Sayed, and M. A. Mustafa, "Adverse Effects of Two Kinds of Food Additive Mixtures (Flavor Enhancer, Food Preservative or Food Coloring Agent) on Physiological Parameters in Young Male Albino Rats," *Egypt. J. Hosp. Med.*, vol. 67, no. 1, pp. 344–351, Apr. 2017, doi: 10.12816/0036646.

[8] N. S. Tawfek, H. M. Amin, A. A. Abdalla, and S. H. M. Fargali, "Adverse Effects of Some Food Additives in Adult Male Albino Rats," *Curr. Sci. Int.*, vol. 04, no. 04, pp. 525–537, 2015.

[9] D. McCann *et al.*, "Food additives and hyperactive behaviour in 3-year-old and 8/9-year-old children in the community: a randomised, double-blinded, placebo-controlled trial," *Lancet*, vol. 370, no. 9598, pp. 1560–1567, Nov. 2007, doi: 10.1016/S0140-6736(07)61306-3.

[10] B. Raposa *et al.*, "Food additives: Sodium benzoate, potassium sorbate, azorubine, and tartrazine modify the expression of NFκB, GADD45α, and MAPK8 genes," *Physiol. Int.*, vol. 103, no. 3, pp. 334–343, Sep. 2016, doi: 10.1556/2060.103.2016.3.6.

CHAPTER 14

AN INVESTIGATION OF PHARMACOLOGICAL PROPERTIES OF NIGELLA SATIVA

Dr. Krupa. S, Assistant Professor, Department of Chemistry,
School of Sciences, B-II, Jain (Deemed to be University),JC Road, Bangalore-560027.,
Email Id- Krupa.s@jainuniversity.ac.in

ABSTRACT: N. sativa has been utilized since antiquity before there was a scientific understanding of how to use medicinal plants to heal human ailments and lessen their suffering. Black cumin is an annual herbaceous plant of the Ranunculaceae family. Around the world, herbal medicine uses the seeds of Nigella sativa Linn. (Ranunculaceae), often known as black cumin or black seed, to cure and prevent various diseases and ailments such as diarrhea, asthma, and dyslipidemia. Proteins, alkaloids, fixed or essential oils, as well as saponins, are all present in the seeds. Thymoquinone, a constituent of the essential oil but also found in a fixed oil, has been demonstrated to be responsible for a large part of the bioactivity of the seeds. Kalonji oil is rich in antioxidants and may have many health benefits. These include managing blood sugar or cholesterol levels, treating asthma and various skin problems, promoting weight loss, and protecting brain health. The medicinals, phytochemicals, characteristics, ayurvedic benefits, and traditional applications of Nigella sativa are briefly discussed in this paper.

KEYWORDS:Disease, Kalonji Nigella sativa Linn., Phytochemical, Pharmacological.

1. INTRODUCTION

In human history, plants have served as the foundation for both conventional treatments and the creation of contemporary medications. The World Health Organization (WHO) reports that since more than 60% of cultures lack access to and/or cannot afford allopathic medications, more than three-fourths of communities in resource-constrained nations depend on medicinal plants for their basic healthcare requirements. There is now a revival of interest in the use of plants as an source of food or medicine, which is in line with the recent advancements in the field of optimal nutrition. Because of its affordability and ease of use, as well as the perception that natural therapies have fewer negative side effects than synthetic ones, the use of phytomedicine for many disorders has recently increased significantly.

Figure 1: Illustrate the representation of Nigella sativa. A) Flower, b) seeds.

Nigella sativa, also known as kalonji or shoniz, has been used medicinally for thousands of years. Additionally, the herb is used as a spice. The plant is a perennial herb that grows between 30 and 60 cm tall and is a member of the Ranunculaceae family, as shown in figure 1. The foliage is delicately split, and the blooms are either white or light blue-purple [1]. The Black seed develops into a fruit capsule with several white trigonal seeds within. When the fruit capsule is fully developed, it opens, exposing the seeds within, which are then exposed to the air and become black.

1.1. Geographical Distribution:

The plant is extensively cultivated across the globe. It is mostly found in Pakistan and India. The plant is cultivated in Bangladesh, South Europe, Israel, Syria, Lebanon, and Lebanon. Like wheat, N. Sativa is grown throughout the winter months. It is cultivated specifically in Punjab, Himachal Pradesh, the Gangetic plains, Assam, Bihar, and Maharashtra in India [2], [3].

Studies on both humans and animals revealed that black seed and TQ may be used to treat male infertility. Their antioxidant properties have lately drawn more attention since they are safe to use as dietary supplements. Additionally, they have synergistic effects when taken with various conventional chemotherapeutic drugs, which may result in a decrease in the dose of the concurrently used medications and an improvement in efficacy against toxicity as well as the elimination of the issue of drug resistance. Therefore, it would be a prospective herbal therapy to be evaluated under clinical research for a variety of disorders since it has larger safety margins and commendable effectiveness against a wide range of ailments. Additional recommendations include the isolation of new bioactive components from black cumin and its oil and research of those components' therapeutic benefits utilizing particular clinical models.

2. LITERATURE REVIEW

Md FaruqueAhmad et al. studied the plant's pharmacological effects and claimed chemical makeup. Given that it is referenced in both Christian and Islamic sacred texts, it has a profound religious importance. It is referenced in ancient medicine in addition to having historical and religious value. Many ailments, such as asthma, bronchitis, fever, coughing, disorientation, paralysis, back pain, persistent headache, chest congestion, and inflammation are treated with it in traditional medical systems[4].The scientific community conducted substantial phytochemical or biological research on N. sativa as a result of this plant's significance. N. sativa's anti-diabetic, anti-cancer, anti-tussive, antioxidant, neuroprotective, hepatoprotective, immunomodulator, spasmolytic, analgesic, gastroprotective, antibacterial, anti-inflammatory, and bronchodilator action has been shown in pharmacological research

WesamKootie et al. studied Southwest Asia as the natural home of the annual blooming plant known as black seed (Nigella sativa). The findings demonstrated that N. sativa has a wide range of biological benefits, including actions that are anti-inflammatory, anti-microbial, anti-hyperlipidemic, anti-cancer, anti-diabetic, anti-hypertensive, anti-oxidant, or wound healing. It also has impacts on the immunological, digestive, and reproductive, but also central neurological systems, as well as an analgesic or anticonvulsant properties. In conclusion, it is a useful plant for the development of novel medications for the treatment of a variety of ailments [5].

Bahare Salehi et al. examined the in vitro, in vivo, or human pharmacological trials. The fact that Nigella seeds are high in the omega-6 fatty acid linoleic acid and provide an additional supply of dietary phytochemicals, such as the bioactive thymoquinone and distinctive saponins, alkaloids, and flavonoids, is one of its key advantages. The Nigella species N. Sativa L. has undergone the greatest research. The seeds and seed oils from this plant may be regarded as promising candidates to create functional components based on folklore or scientific knowledge because of the phytochemical composition and pharmacological capabilities. The key conclusions, however, are that more research, particularly clinical trials, is needed to standardize the findings, to determine, for example, active molecules, long-term effects, dose, chemical profile, and the influence of cooking/incorporation into meals [6].

Ebrahim M. Yimer et al. studied about explores the functional food or nutraceutical potential of this prized plant by focusing on the profile of higher-value elements as well as traditional medical and biological concepts of N. Sativa seed or its oil. Despite the few studies that have been done so far, after proving its complete therapeutic effectiveness, the potential efficacy of N. Sativa against HIV/AIDS might be investigated as a different option for the treatment of this pandemic illness. As a possible dietary supplement with little adverse effects, this prized seed's high antioxidant properties have lately attracted growing interest [7].

Hala Gali-Muhtasib et al. studied Nigella sativa, the black seed, which has therapeutic promise.The seeds of this plant have undergone the greatest pharmacological or phytochemical research. It has been shown that the seeds' aqueous and oil extracts contain antioxidant, anti-cancer, anti-inflammatory, analgesic, or antibacterial properties. Black seed essential oil's most prevalent component, thymoquinone, has been discovered to be the active ingredient behind many of the seed's health benefits. The seed, its chemical components, and its common use in traditional medicine are described in this review study [8].

Alyaa Majid studied nigella sativa's chemical components or pharmacological effects. The presence of several pharmacologically active components, including thymohydroquinone, thymoquinone, thymoquinone, nigellone, thymol, and many other phytochemicals, is largely responsible for the black cumin seed's medicinal potential. Additionally, it was discovered that using the seed as a feed supplement improved various elements of chicken products like feed conversion rate, bodyweight performance, carcass features, egg production, or egg quality [9].

George A. Burdock studied the black cumin plant, Nigella sativa L. Additionally, there is growing evidence that the seed or its extracts are effective medicinal agents, with effectiveness often linked to the presence of the potent antioxidant thymoquinone. But even so, quantitative analysis of the seed, particularly the volatile fraction, produces highly variable results.

This could be because of a single or a combination of factors, such as the origin of the crop, potential varietal differences, adulteration or contamination, the method of extraction, the venue of the extracted seed's maturation, as well as others.

Mohammed Dalli et al. studied about photochemistry or pharmacological activities of Nigella sativa L.Numerous research publications published between 2019 and 2021 were retrieved from several databases (Science Direct, Scopus, PubMed, or Web of Science), researched, and evaluated to study the various pharmacological characteristics of various Nigella sativa extracts. In addition to exploring the pharmacological activities displayed by several identified compounds in Nigella sativa, the assessment of the gathered articles enables us to classify the phytochemical constituents and the pharmacological activities through their underlying molecular mechanisms [10].

3. DISCUSSION

The previous several decades have seen much research on Nigella sativa, and those investigations have shown that it has a variety of therapeutic benefits and pharmacological effects. Using different search phrases like “Nigella sativa” and or “Black seed” and “Black cumin” and the appropriate illness conditions, people have utilized PubMed, Scopus, Google Scholar, Science Direct, or grey works of literature to retrieve the pertinent literatures with corresponding subtopics. We have utilized the appropriate "Mesh" keywords and text words "tw" in the context of PubMed searches to obtain all related papers regardless of time constraints.

In this study for the data base search author used various websites such as PubMed, google scholar, research gate, science direct, and different others sites were used to conduct this study. The author uses some keywords like “Disease, Kalonji Nigella sativa Linn. Phytochemical, Pharmacological”, were used in this review work. Abstracts and titles were employed to document the early work. Insufficient information, redundant research, and non-extractable data were some reasons to exclude the Records. Figure 2, shows the design of the methodology of the current review work.

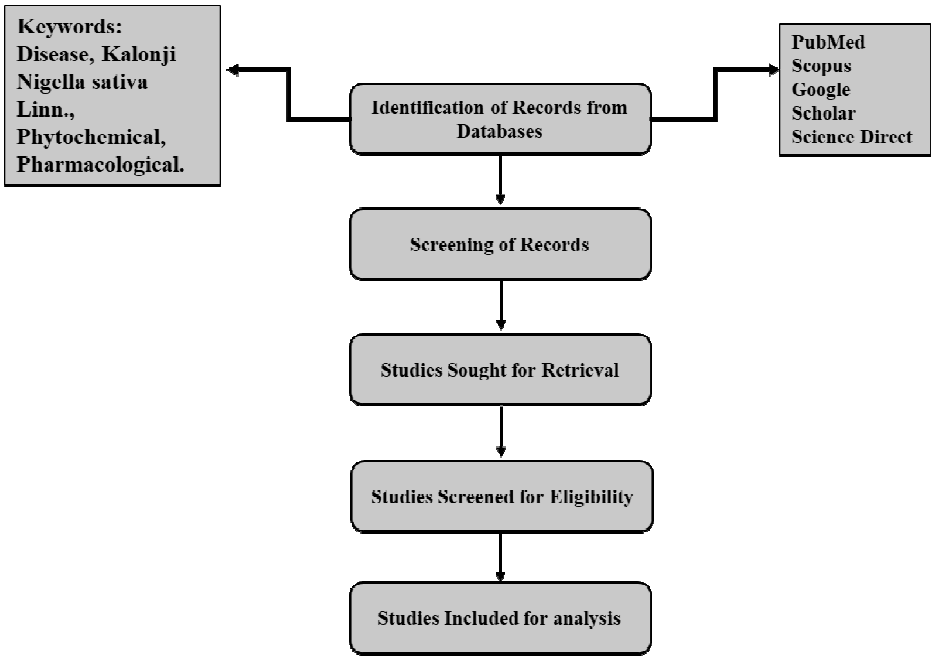


Figure 2: Illustrate the design of the methodology of the current work.

Kalonji uses traditional medicine using seeds greek-Arabic/Unani medicine since the first century BC, when Discoroides, a Unani physician and botanist, detailed Kalonji and its medicinal uses in his book, Kalonji (Nigella sativa of Family-Ranunculaceae) has been used. An excellent source of dietary fiber, which encourages bowel movement, is the polysaccharide component. The seeds are also abundant in important fatty acids like linoleic acid, which must be taken from the diet since they cannot be synthesized by the body. Black seed is crucial for the body since it contains nutrients including calcium, salt, iron, and potassium [6], [11].

3.1. Kalonji Uses & Benefits:

3.1.1. Bad Breath, or halitosis

The usage of kalonji is advised by Ayurveda for foul breath. It helps to reduce halitosis. Its antibacterial and antimicrobial effects in the mouth are thought to be responsible for its antihalitosis qualities. Take a half teaspoon of kalonji seeds and chew them twice a day to treat foul breath. It is used for one month to permanently cure halitosis [4].

3.1.2. Anorexia, Indigestion, and Flatulence:

Kalonji aids in anorexia, indigestion, and flatulence due to its stimulant, digestive, and carminative characteristics. It enhances liver function, enhances digestive juice output, and enhances appetite in anorexic patients. It helps with wind release and stops the growth of intestinal gas. Therefore, it aids in the relief of stomach discomfort, gastric distention, and flatulence. You may chew a half teaspoon of kalonji seeds just before consuming meals if you have these conditions [12], [13].

- *Dysmenorrhea:* Kalonji seeds are used in Ayurveda and traditional medicine to increase menstrual flow and lessen menstrual discomfort.
- *Galacotogenic Activity:* Kalonji seeds also contain galactagogic action, much as cumin seeds do. It increases breastfeeding production and reduces abnormalities in breast milk. It permeates breastmilk and aids in the infant's better digestion. However, in rare circumstances, it may also make newborns constipated.
- *Asthma:* Kalonji controls mucus output and lowers airway inflammation. According to several Ayurvedic research, kalonji decoction lessens asthmatic wheezing's intensity and frequency.

3.2. Reports of Nigella sativa Therapeutic Studies:

Numerous investigations have been done on this plant to determine its potential usefulness in medicine and therapy. To demonstrate the therapeutic effectiveness of this herb, particularly in conditions affecting the immune system and cancer, large-scale clinical investigations are still required [14].

Antibacterial Activity: N. sativa has been linked in several studies to antibacterial activity, as shown in figure 3. The primary chemical component of this plant that has been identified is thymoquinone. The majority of bacteria, particularly Gram-positive cocci like Staphylococcus aureus or Staphylococcus epidermidis, were shown to be resistant to it.

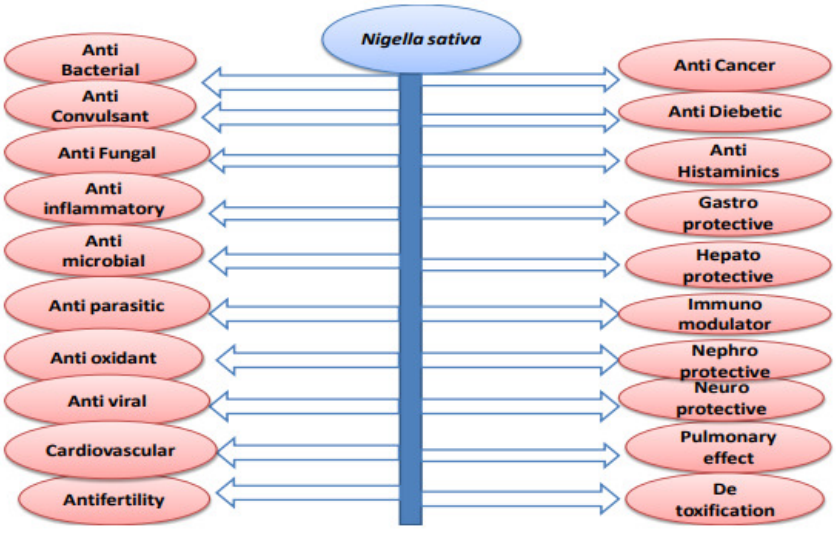


Figure 3: Illustrate the therapeutic use of Nigella Sativa.

3.2.1. Fungicide activities:

It is evident from the research that Nigella sativa has an antiviral effect against the majority of pathogenic fungi. The antifungal efficacy of thymoquinone was tested against the majority of fungal strains. According to a comparison study, Nigella sativa has stronger antifungal properties than the medication Amphotericin B. (an antifungal drug). Another investigation revealed N. sativa's antifungal properties. On several harmful fungi strains, the effects of methanolic and ethanolic extract from N. Sativa seeds were studied. Aspergillus, Cryptococcus, Candida, and Issatchenkia species comprised these strains [15]–[17]. The decoction was made using the cold maceration method, and it was then evaluated using a method developed by the National Committee of Clinical Laboratory Science (NCCLS). It was discovered that the plant's ethanolic and methanolic extracts both significantly inhibited the development of Issatchenkia Orientalis and Candida parapsilosis fungi, as well as Candida parapsilosis, respectively. In a different investigation, the effectiveness of N. sativa's essential oil and several extracts against the dermatophyte fungi Trichophyton mentagrophytes, Microsporum canis, and Microsporum gypsum was assessed. Using the disk diffusion technique, N. sativa's antifungal activity was investigated. The results on T. mentagrophytes, M. canis, and M. gypseum demonstrated a strong antifungal impact.

3.2.2. Viricide Activity:

Recent research has been conducted on the antiviral properties of Nigella sativa. In 2013, research on the effectiveness of N. Sativa oil against the hepatitis C virus was conducted (HCV). Thirty HCV patients who were not eligible for IFN/ribavirin treatment participated in clinical research. N. Sativa oil was taken orally three times a day at dosages of 450 mg in each capsule. After three months, a diabetic patient's clinical state and glycemic control improved, and there was a decrease in total virus levels.

3.3. Anti-inflammatory:

3.3.1. Psoriasis:

The antipsoriatic potential of Nigella sativa seed ethanolic extract was examined. To screen the extract, a mouse tail model for psoriasis was used. When compared to the control group, the findings demonstrated an increase in relative epidermal thickness. the antipsoriatic effects of the ethanolic extract of N. Sativa. Two dose forms for seed oil were used: ointment and oral. Individuals with palmoplantar psoriasis and mild to moderate plaque were chosen. The outcome showed that Nigella sativa has an antipsoriatic effect and caused a satisfactory reaction in patients when taken orally.

3.3.2. Vulgar acne:

One of the most pervasive illnesses in people. Numerous scientific investigations have been conducted, and it has been shown that Nigella sativa oil is effective in treating acne vulgaris. In their investigation, Hadi and Ashok looked at the effectiveness of incorporating 20% N. Sativa oil extract into lotion formulations. 62 acne sufferers were chosen for the research. Results indicated that benzoyl peroxide lotion, which is used to treat mild to moderate acne vulgaris, is less hazardous than Nigella sativa. Another investigation was done to compare the antibacterial effects of amoxicillin and nigella Sativa oil. With the aid of carbopol 940, the gel was created from the oil. When this mix was utilized as treatment, positive results were attained. However, Nigella sativa is a useful herbal remedy for treating skin conditions including psoriasis, dermatitis, acne, and rashes that are caused by infection, irritation, or rashes.

3.3.3. Gastro-protective activity:

To justify its usage by herbal and Unani medicine practitioners, the anti-ulcer potential of Nigella sativa aqueous suspension on experimentally produced stomach ulcers and basal gastric secretion in rats was investigated. Different toxic substances caused acute gastrointestinal ulcers in Wistar albino rats. Antisecretory research was conducted on a different set of rats. In addition to estimating the amount of nonprotein sulfhydryl in the stomach wall mucus and histopathologically analyzing the gastric tissue, N. sativa's anti-ulcer effects may be caused by prostaglandins, as well as by its antioxidant and anti-secretory properties.

3.3.4. Effects that Prevent Asthma:

The impact of nigellone and thymoquinone on respiratory clearance as well as their antispasmodic effects on the trachea. Using a microdialysis approach, the effects of Ba++ carbachol- and leukotriene-induced trachea contractions and the transfer of the fluorescent dye rhodamin B on ciliary activity in the tracheal region were examined. When the trachea was being squeezed by the depolarizing impact of Ba2+, nigellone and high doses of thymoquinone had a concentration-dependent inhibitory effect on it. Thymoquinone and nigellone both prevented the trachea's d (4) LT4-induced contractions. According to the research, nigellone has an antispasmodic effect and increases mucociliary clearance, but thymoquinone does not. The conclusion is that nigellone, but not thymoquinone, may be helpful in the treatment of various respiratory illnesses.

3.3.5. Anti-inflammatory Action:

In a Long-Evans rat model created to test the impact of N. Sativa seeds on specific immunological components, the immunomodulating and cytotoxic activities of the volatile oil of N. Sativa seeds were studied. In Long-Evans rats, a specific antigen (typhoid TH) was administered, and the rats were then treated with N. Sativa seeds. Treatment with N. Sativa oil caused a 2-fold reduction in the production of antibodies in response to typhoid vaccination compared to control rats, but there was a significant increase in peripheral lymphocyte and monocyte counts in these animals. These findings suggested that N. Sativa seeds may be used as a possible cytotoxic immunosuppressive agent.

4. CONCLUSION

The immune system is the only system with the capacity to fight off illnesses and generate cells that destroy viruses, according to scientific evidence. These data lead us to the conclusion that the Kalonji/Black Seed may be a remedy for any illness since it boosts the immune system, which is in charge of fighting off illnesses and infections. Numerous lifestyle diseases, such as arthritis, hypertension, diabetes mellitus, heart disease, and others, as well as life-threatening illnesses, such as cancer, tumors, and AIDS, may be treated by doing a significant clinical study on Kalonji.

REFERENCES:

[1] B. H. Ali and G. Blunden, “Pharmacological and toxicological properties of Nigella sativa,” *Phytotherapy Research*, vol. 17, no. 4. pp. 299–305, Apr. 2003. doi: 10.1002/ptr.1309.

[2] E. Z. Dajani, T. G. Shahwan, and N. E. Dajani, “Overview of the preclinical pharmacological properties of Nigella sativa (Black seeds): A complementary drug with historical and clinical significance,” *Journal of Physiology and Pharmacology*, vol. 67, no. 6. pp. 801–817, 2016.

[3] S. Thakur, H. Kaurav, and G. Chaudhary, “Nigella sativa (Kalonji): A Black Seed of Miracle,” *Int. J. Res. Rev.*, vol. 8, no. 4, pp. 342–357, 2021, doi: 10.52403/ijrr.20210441.

[4] M. F. Ahmad *et al.*, "An updated knowledge of Black seed (Nigella sativa Linn.): Review of phytochemical constituents and pharmacological properties," *J. Herb. Med.*, vol. 25, p. 100404, Feb. 2021, doi: 10.1016/j.hermed.2020.100404.

[5] W. Kooti, Z. Hasanzadeh-Noohi, N. Sharafi-Ahvazi, M. Asadi-Samani, and D. Ashtary-Larky, "Phytochemistry, pharmacology, and therapeutic uses of black seed (Nigella sativa)," *Chin. J. Nat. Med.*, vol. 14, no. 10, pp. 732–745, 2016, doi: 10.1016/S1875-5364(16)30088-7.

[6] B. Salehi *et al.*, "Nigella Plants – Traditional Uses, Bioactive Phytoconstituents, Preclinical and Clinical Studies," *Front. Pharmacol.*, vol. 12, Apr. 2021, doi: 10.3389/fphar.2021.625386.

[7] A. A. Mariod, M. E. Saeed Mirghani, and I. Hussein, "Nigella sativa L. Black Cumin," *Unconv. Oilseeds Oil Sources*, vol. 2019, pp. 73–80, 2017, doi: 10.1016/b978-0-12-809435-8.00013-5.

[8] H. Gali-Muhtasib, N. El-Najjar, and R. Schneider-Stock, "The medicinal potential of black seed (Nigella sativa) and its components," *Adv. Phytomedicine*, vol. 2, no. C, pp. 133–153, 2006, doi: 10.1016/S1572-557X(05)02008-8.

[9] A. Majid, "The Chemical Constituents and Pharmacological Effects of Nigella sativa," *J. Biosci. Appl. Res.*, vol. 4, no. 4, pp. 389–400, 2018, doi: 10.21608/jbaar.2018.151793.

[10] M. Dalli, O. Bekkouch, S. Azizi, A. Azghar, N. Gseyra, and B. Kim, "Nigella sativa L. Phytochemistry and Pharmacological Activities: A Review (2019-2021).," *Biomolecules*, vol. 12, no. 1, p. 20, Dec. 2021, doi: 10.3390/biom12010020.

[11] H. Tabassum, A. Ahmad, and I. Z. Ahmad, "Nigella sativa L. and Its Bioactive Constituents as Hepatoprotectant: A Review," *Curr. Pharm. Biotechnol.*, vol. 19, no. 1, pp. 43–67, 2018, doi: 10.2174/1389201019666180427110007.

[12] K. Fatima Shad, W. Soubra, and D. J. Cordato, "The role of thymoquinone, a major constituent of Nigella sativa, in the treatment of inflammatory and infectious diseases," *Clinical and Experimental Pharmacology and Physiology*, vol. 48, no. 11. pp. 1445–1453, 2021. doi: 10.1111/1440-1681.13553.

[13] H. Shirvani, F. Rostamkhani, E. Arabzadeh, F. Mohammadi, and F. Mohammadi, "Potential role of Nigella sativa supplementation with physical activity in prophylaxis and treatment of COVID-19: a contemporary review," *Sport Sciences for Health*, vol. 17, no. 4. pp. 849–854, 2021. doi: 10.1007/s11332-021-00787-y.

[14] A. Sandhya and G. Kannayiram, "Pharmacological, bioactive screening of medicinal plant nigella sativa and the derived compound thymoquinone: An invitro study," *Int. J. Res. Pharm. Sci.*, vol. 11, no. 2, pp. 2458–2465, 2020, doi: 10.26452/ijrps.v11i2.2239.

[15] M. R. Khazdair, "The Protective Effects of Nigella sativa and Its Constituents on Induced Neurotoxicity," *Journal of Toxicology*, vol. 2015. pp. 1–7, 2015. doi: 10.1155/2015/841823.

[16] A. F. Zulkefli, R. Bt Hj Idrus, and A. A. Hamid, "Nigella sativa as a Galactagogue: A Systematic Review," *Sains Malaysiana*, vol. 49, no. 7, pp. 1719–1727, 2020, doi: 10.17576/jsm-2020-4907-22.

[17] P. N. Dubey, B. Singh, B. K. Mishra, K. Kant, and R. K. Solanki, "Nigella (Nigella sativa): A high value seed spice with immense medicinal potential," *Indian Journal of Agricultural Sciences*, vol. 86, no. 8. pp. 967–979, 2016.

CHAPTER 15

AN INVESTIGATION OF PHARMACOLOGICAL ACTIVITY OF MOMORDICA CHARANTIA

Dr. Ruby Varghese, Assistant Professor, Department of Chemistry,
School of Sciences, B-II, Jain (Deemed to be University),JC Road, Bangalore-560027.,
Email Id-v.ruby@jainuniversity.ac.in

ABSTRACT: Momordica charantia also called as bitter karela, melon, bitter gourd, and balsam pear, is a well-known plant that is frequently utilized by the native inhabitants of South America, Asia, India, the East Africa and Caribbean, to treat diabetes-related diseases. This plant is used worldwide in folk medicine to cure a variety of maladies, mostly diabetes but also cancer as well as other disorders associated with inflammation, as it contains many bioactive chemicals, among which some have strong biological effects. It has been well established that M. charantia extract helps type 2 diabetics by lowering blood sugar levels. This review objective is to give a comprehensive overview of the bitter melon's pharmacological activity for treatment of different disease, and also its usage in cancer treatment. There is a ton of information regarding the anti-diabetic qualities of bitter melon, but very little is written about just the plant's anti-inflammatory or anti-cancer characteristics. In the future this paper will aware the people about the importance of momordica charantic.

KEYWORDS: Momordica Charantia, Medical System, Pharmacological Activity, Phenolic, virus.

1. INTRODUCTION

Inherent to human civilisation are plants. Nearly 80.00% of the world's population also relies on medicinal plants for their fundamental medical system. Drugs made from plants are essential for many treatments in traditional and contemporary medicine all over the world, and they also serve as a replacement for medication supplies in modern medicine. Due to their abundance of bioactive phytochemical components that have therapeutic properties, medicinal plants are utilized to treat a variety of infectious illnesses in humans [1], [2]. The existence of secondary metabolites such as cardiac glycosides, saponins, tannins, alkaloids, flavonoids, reducing agents, minerals, or vitamins is primarily responsible for the therapeutic effects of plants. Human illnesses and disorders include heart disease, diabetes mellitus, atherosclerosis, HIV/AIDS, inflammation, stroke, cancer, malaria, etc. are caused by reactive oxygen species that lead to oxidative stress [3], [4]. The phenolics found in plant-based antioxidants have a wide range of biological effects, including anti-cancer, anti-inflammatory, or antibacterial properties. By scavenging free radicals and preventing peroxidation and other processes mediated by radicals, plants can also protect the organism from oxidative harm.

Momordica charantia (M. charantia), a member of the Cucurbitaceae family of medicinal plants, is also called as bitter melon, bitter gourd, karela, or balsam pear. It is mostly grown in Africa, Asia, or South America. Due of the fruit's bitter flavor, which intensifies as it ripens, it is also known as bitter guard or melon. Although well recognized for its anti-diabetic properties, bitter melon is a medicinal plant with a variety of advantageous benefits [5], [6]. The several bioactive components of M. charantia, including vicine, glycosides, polypeptide-p, charantin, karavilosides, or plant insulin, are responsible for the anti-diabetic benefits. These bioactive substances include triterpene,steroids, protein, alkaloids, lipid, inorganic, or phenolic compounds [7], [8]. They are all members of the large class of phytochemicals. Both type 1 or type 2 diabetes mellitus have been linked to M. charantia's anti-diabetic properties. Additionally, all of M. charantia's morphological components showed hypoglycemic action in normal animals, streptozotocin-induced diabetic animals, alloxan-

induced diabetic animals, and diabetes genetic animal models. M. charantia has demonstrated positive effects in avoiding diabetes mellitus or delaying the progression of diabetic sequelae, including as neuropathy, waterfall, gastroparesis, nephropathy, and insulin blockage, in experimental animal models. Figure 1, shows the diferent part of Momordica Charantia plant.

a b c

Figure 1: Illustrate the Pictorial Representation of Momordica Charantia.

1.1. Used in Traditional:

For a very long time, momordica charantia has been employed in several Asian traditional medical systems as a means of both disease prevention and disease treatment. Fruits: Momordica charantia is used to treat ulcers, wounds, gout, leprosy, fever (malaria), burning, helminthiases, constipation, diabetes, colic, cough, and asthma. In both animal and human investigations, it has been reported to have hypoglycaemic (antidiabetic) effects. Momordica charantia leaf juice is utilized to completely cure piles [9], [10]. Momordica charantia's bitter tonic characteristics make it useful as a blood cleanser. It can treat skin conditions including boils as well as other blood-related issues. Momordica charantia juice is helpful in both prevention and treatment of liver disease.

1.1.1. Seeds:

Momordica charantia is used to treat a variety of conditions, including stomachaches, wound healing, liver and spleen issues, diabetes, intestinal parasites, high cholesterol, or intestinal gas.

1.1.2. Root:

Momordica charantia roots are employed in the treatment of prolapsus vagenae, syphilis, ulcer, boils, rheumatism, or septic swellings. Juice from Momordica charantia aids in the reduction of the Pyorrhea issue (bleeding from the gums). For the management of diabetes, viruses, colds, flu, excessive cholesterol, tumors, cancer, or psoriasis, momordica charantia capsules or tinctures are readily available in the United States.

1.1.3. Leaves:

Momordica charantia has been used to treat menstruation problems, infections, worms, fever (malaria), burns, constipation, colic, or parasites, as an emmenogogue, helminthiases and

measles, hepatitis. Leaf tea is used in Guyana traditional medicine to treat diabetes, expel intestinal gas, stimulate menstruation, but as an antivirus for hepatitis, measles, and febrile conditions. It is used topically to treat ulcers, wounds, and infections, as well as externally and internally to treat worms or parasites.

1.1.4. Photochemistry:

The bulk of M. charantia is composedof glycosides, sterols, fatty acids, proteins, or volatile components. Momordicine is one of two alkaloids found in the plant's leaves and fruit. Contributing approximately, an aromatic volatile oil, a substance like soponin, a resin with a disagreeable taste, and glycoside are all present in the plant. The seeds' germ contains an alkaloid, an anthelmintic component, as well as urease. The fruit contains ascorbigen, a kind of ascorbic acid. The fruit contains the following free amino acids: serine, glutamic acid, aspartic acid, threonine, g-amino butyric acid, alanine, or pipecolic acid. Luteolin, which is one of the main carotene pigments, is found in green fruit. Soluble pectin however no free pectic acid can be found in the fruit pulp [11], [12]. According to research, the leaves are an excellent source of calcium, phosphorus, potassium, magnesium, and iron. The delicious fruit and leaves are also both excellent sources of vitamin B.

According to a recent WHO report, primary healthcare is provided through herbal medicine for almost 80% of the world's population. Some legally prescribed medications, including anthracyclines (doxorubicin, daunorubicin, epirubicin, and idarubicin), vinca alkaloids (vincristine, vinblastine, vinorelbine and vindesine), taxanes, podophyllotoxin and its derivatives or taxanes (paclitaxel Numerous epidemiological studies point to the significant functions that vegetables and fruits play in lowering the risk of cancer. The combination of several bioactive phytochemicals, proteins, vitamins, minerals, or otherwise fibers in vegetables and fruits may be to blame for this. Numerous plant products, whether complete extracts or bioactive parts, have the ability to reduce the development of cancer, at least in experimental animals. The safety and effectiveness of natural substances in treating or preventing cancer are now being tested in several clinical studies.

Updated details on cancer prevention, treatment, and underlying processes for bitter melon have been the main emphasis of this review. The Cucurbitaceae family includes bitter gourd, bitter melon, balsam pear, or karela, all of which are widely farmed in Africa, Asia, as well as South America. Since the dawn of time, toothaches, diarrhea, furuncles, and diabetes have all been treated using the therapeutic benefits of bitter melon. Lowering diabetes and lipidemia, as well as anti-bacterial, anti-HIV activities, and anti-fungal, are connected with the positive benefits of bitter melon crude extract or isolated components. Various in vitro and in vivo investigations on bitter melon have revealed promising anticancer effects. Furthermore, we provide a summary of the molecular pathways behind bitter melon treatment and cancer prevention.

Therefore, this analysis has broad implications for the treatment of disease that might facilitate the development of clinical research [13], [14].Traditional or ethnobotanical applications of natural substances, particularly those with plant origins, have drawn a lot of interest in recent years since they have undergone extensive effectiveness testing and are widely regarded as safe for use by humans. Further in-depth study is essential given the potency and flexibility of these plants' medicinal potential. The production of several phytochemicals, many of which have substantial medicinal effect, along with the plant's extensive harvesting for various purposes make it potentially significant. The presence of phytochemicals in the plant suggests importance for extensive harvesting, chemical alterations, and usage.

2. LITERATURE REVIEW

Subhayan Sur et al. studied about the bitter melon's ability to treat and prevent cancer, with an emphasis on the underlying molecular pathways. A nutrient-rich medicinal plant called bitter gourd or bitter melon (Momordica charantia) is grown in several nations' tropical and subtropical climates. The bitter melon has historically been used as a folk remedy and includes a variety of bioactive substances, such as triterpene glycoside, triterpenoids, phenolic acids, lectins, sterols, flavonoids, and proteins, which may have anticancer properties without causing any discernible side effects. By increasing the production of reactive oxygen species, inhibiting the cancer cell cycle, glucose cancer stem cells, and lipid metabolism, hypoxia, invasion, metastasis, or angiogenesis, likely to induce apoptosis or autophagy cell death, and boosting immune defense, the methanolic extracts as well as its components prevent several more types of cancers. As a result, bitter melon has promise as a cancer preventative and treatment [15].

Mozaniel et al. studied about focused on producing a solvent-free extract while emphasizing supercritical fluid extraction (SFE), high selectivity, variable fractions in terms of mass yields, and achieved chemical composition. Momordica charantia L.'s bioactive content, supercritical fluids extraction, or biological activity over the last five years. Numerous substances, such phytosterols, fatty acids, phenolic acids, terpenoids, phenolic compounds, and flavonoids that have been found in M. charantia preparations were also discussed. These biological properties of M. charantia extracts have a direct impact on human health. The results of this review are significant because they can direct future research on extracting bioactive chemicals from M. charantia and its uses [16].

Agrawal Mala, and Tyagi Tulika studied about effectiveness of momordica charantia as a medicine. Due to its abundance of natural resources, India is referred to as the botanical garden of the globe. In India, folk, traditional, or herbal medicine employ around 6000 plants. 500 of the 1500 herbal medicines classified by the Indian medical system are utilized often. The conventional medical system still views plants as a promising source of medication despite their vast medicinal history spanning thousands of years. The primary pharmaceutical population has resorted to study on medicinal plants because of the effectiveness and safety of herbal treatment [17].

3. DISCUSSION

3.1. Considerations and Toxicity

charantia momordica According to studies, eating bitter melon fruit by mouth is harmless. According to studies, eating bitter melon fruit by mouth is harmless. P-insulin derived from Momordica charantia appeared to be safe for subcutaneous injection, although intravenous administration of Momordica charantia extract is far more toxic but it is not advised. Given that bitter melon seeds have momorcharin, which has been demonstrated to have antifertility actions in female mice, bitter gourd seeds can induce pregnancy.

3.2. Pharmacy Activity:

According to a literature review, M. Charantia Linn's entire plant, including its fruits and leaves is used to cure a number of ailments. Figure 2, shows the Momordica Charantia, Pharmacological Activity.

3.2.1. Biological Activity:

The MAP30 protein homolog, obtained from the seeds of Momordica charantia extracts, and bitter melon extracts both exhibit broad-spectrum antibacterial action, according to in vitro investigations. Extracts of the momordica charantia prevent the spread and infection of several viruses, including the Epstein-Barr virus or HIV. Momordica charantia therapy resulted in a stabilization of CD4/CD8 ratios in three HIV patients, according to a preliminary research on the effect of the herb on 2 A and 24 Herpes simplex. Momordica charantia extracts are thought to limit HIV replication by reducing the production of syncytials and cell-to-cell infection. Several gram-negative or gram-positive bacteria, including Salmonella, Shigella, E. coli, Staphylococcus, Streptococcus, Pseudomonas, and H. pylori, as well as the parasites E. histolytica or Plasmodium falciparum, appear to be inhibited by momordica charantia extracts.

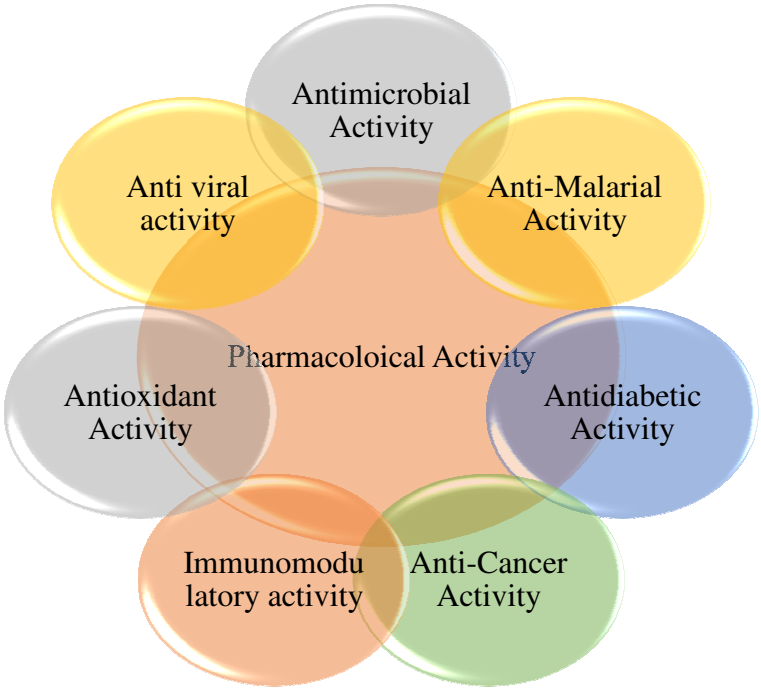


Figure 2: Illustrate the various Pharmacological Activity of Momordica Charantia.

3.2.2. Diabetes Prevention:

Momordica charantia includes bitter compounds that are hypoglycemic in action and lower blood sugar levels by continuing to increase glucose uptake as well as gluconeogenesis in the liver, fat cells or muscles. These compounds include vicine, glycosides, charantin, or karavilosides, as well as polypeptide-p plant insulin. According to certain study findings, they also enhance the release of insulin by pancreatic beta cells as well as repair or encourage the proliferation of beta cells that secrete insulin. P-Insulin, a polypeptide from fruits and seeds significantly reduced and restored normal blood sugar levels in rats [18], [19]. Another bioactive substance, called lectin, found in bitter melon exhibits insulin-like effects.

The bioactivity of lectin, which resembles that of insulin, results from the binding of two insulin receptors. By activating on peripheral tissues and, like insulin's actions in the brain, decreasing hunger, this lectin reduces blood glucose levels. When Momordica charantia is consumed, a hypoglycemic effect occurs in large part due to this lectin. When treating diabetes, the mixed steroid compound charantin, which would be extracted using alcohol, is occasionally used to reduce blood sugar levels.

3.2.3. Malaria Prevention:

Panamanians, Asians, and Colombians all have a long-standing belief that momordica charantia is a beneficial herb for avoiding and treating malaria. Several Momordica charantia species have been shown to have anti-malarial efficacy in laboratory trials. Tea made from leaves that have been steeped in hot water to cure malaria.

3.2.4. Activity of Antioxidants:

charantia momordica Other than diabetes, the plant's various components have been employed in Indian medicine for a variety of illnesses. The phenolic component from bitter melon that was isolated has been reported to have antioxidant properties. The Momordica charantia's antioxidant properties the effects of Momordica charantia seeds on rats with streptozotocin-induced diabetes have been researched, and the findings strongly imply that these seeds may successfully correct the compromised antioxidant status in this condition.

3.2.5. Antiviral Defenses:

This in vitro antiviral activity was against Epstein-Barr, herpes, and HIV viruses, among other viruses. A leaf extract has been shown in an in vivo investigation to boost both human and animal immune systems and enhance resistance to viral infections (increasing interferon production and natural killer cell activity). The anti-viral properties of M. charantia ribosome inactivating proteins lead to the emergence of an intriguing paradigm that may be employed to safely treat viral illnesses. According to a research, single chain ribosome inactivating proteins (SCRIPs), which operate permanently on the ribosome by deleting the adenine residue from eukaryotic ribosomal RNA, are ribosome inactivating proteins. Ribonuclease and deoxyribonuclease are a few of the functions of ribosome inactivating proteins, along with anti-tumor and wide antiviral.

3.2.6. Anti-inflammatory Action:

Momordica charantia's immunomodulatory activity shown that it has a varied impact on the immune system in diseases like allograft rejection, where it was proven to have immunosuppressive effects in some instances or immunostimulant effects in others. Interferon synthesis or natural killer cell activity have been linked to immunomodulatory action.

3.2.7. Cholesterol-lowering Behavior:

Studies on both healthy and diabetic animals have revealed that Momordica charantia has hypocholesterolemic effects. Program is made up octadecatrienoic fatty acid from Momordica charantia seeds was given to rats fed sunflower for four weeks in a research. These rats demonstrated a considerable reduction in nonenzymatic liver tissue lipid peroxidation, erythrocyte membrane lipid peroxidation, or plasma lipid peroxidation after 4 weeks.

3.2.8. Cancer and Bitter Melon Activity:

Clinical research on malignancies are sparse, however bitter melon extract and its active components have been investigated in pre-clinical animal models or cancer cell line-based models in the laboratory [20]. Using primarily a crude product of bitter melon made from water, ethanol, or methanol, preventative investigations on animal models of stomach, liver, head and neck, and stomach cancers were carried out. In vitro or in vivo models of blood, gastric, breast, brain, colon, the head and neck, liver, kidney, lung, ovary, pancreatic, skin, prostate, or uterine cervical malignancies have been used in therapeutic research employing

crude extracts or identified drugs. Figure 3 provides a summary of the impact of bitter melon on cancer chemoprevention or treatment.

3.3. Future Scope

Despite having a harsh flavor, bitter melon extracts is regarded as a popular health beverage. Nutrients and bioactive ingredients abound in bitter melon. In cell culture or pre-clinical animal studies, the crude extract as well as certain crude extracts have been investigated against various malignancies; however, it is still unclear whether or not these separated compounds have the same anti-cancer benefits as the crude bitter melon extract. Additionally, we are unsure of whether combining some of those substances will increase their effectiveness. For a thorough assessment of therapy effectiveness, further preclinical research is required. Due to varying extraction techniques, fruit varietals, and dosages, there are some uncertainties in various research. The metabolism or bioavailability of the chemicals found are not well understood.

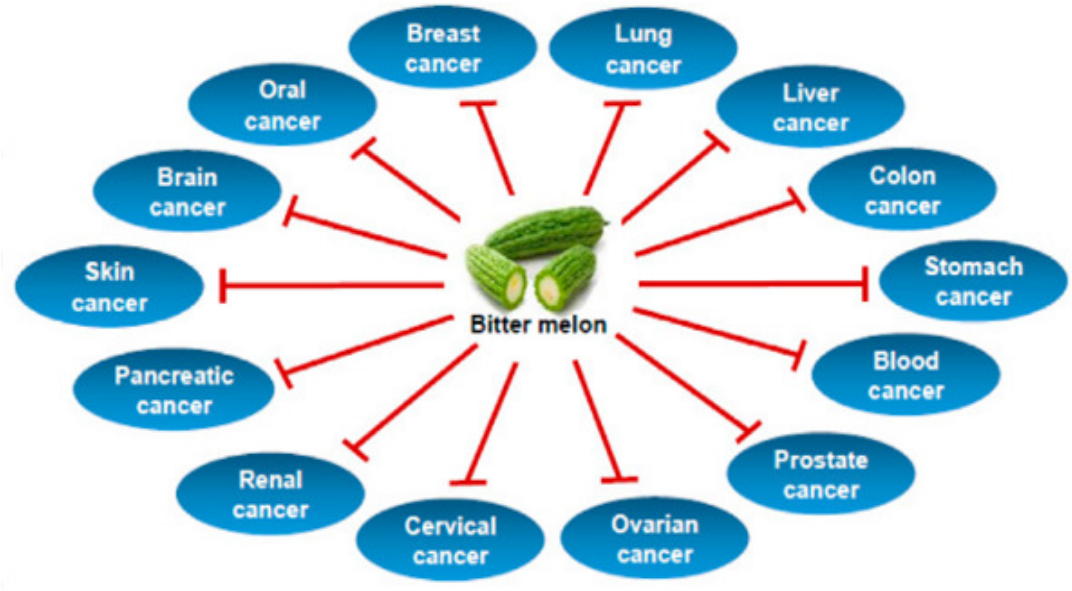


Figure 3: Illustrate the Types of cancer that bitter melon prevents.

Additionally, there aren't many studies employing the same purified substances in various cancer preclinical models, which raises concerns regarding the specificity of the active ingredients. In pre-clinical models, bitter melon has been extensively investigated for its potential to prevent the development of numerous malignancies; however, there are few anticancer trials that combine bitter melon with conventional treatment. Consequently, there is a chance to investigate these research topics and properly plan clinical studies to combat cancer.

4. CONCLUSION

The Cucurbitaceae plant Momordica charantia is also referred to as bitter melon, pare or karela, from ancient times till the present, momordica charantia has offered several treatments for numerous ailments. It has been used in many ancient Asian remedies to treat conditions like cholera, anemia, ulcer, diarrhea, blood illnesses, worms, colic, rheumatism, gonorrhea, liver or spleen problems, cancer, or diabetes. Researchers came to the conclusion

that Momordica charantia Linn. is a promising herb. M. charantia is one of the most effective plants for treating diabetes as well as a beneficial medicinal and vegetable plant. To discover many more uses for this plant, additional research is necessary.

REFERENCES:

[1] M. Fan, E. K. Kim, Y. J. Choi, Y. Tang, and S. H. Moon, "The role of momordica charantia in resisting obesity," *Int. J. Environ. Res. Public Health*, vol. 16, no. 18, 2019, doi: 10.3390/ijerph16183251.

[2] S. Jia, M. Shen, F. Zhang, and J. Xie, "Recent Advances in Momordica charantia: Functional Components and Biological Activities," *Int. J. Mol. Sci.*, vol. 18, no. 12, p. 2555, Nov. 2017, doi: 10.3390/ijms18122555.

[3] M. Bortolotti, D. Mercatelli, and L. Polito, "Momordica charantia, a nutraceutical approach for inflammatory related diseases," *Front. Pharmacol.*, vol. 10, no. MAY, 2019, doi: 10.3389/fphar.2019.00486.

[4] F. Chen, G. Huang, Z. Yang, and Y. Hou, "Antioxidant activity of Momordica charantia polysaccharide and its derivatives," *Int. J. Biol. Macromol.*, vol. 138, pp. 673–680, Oct. 2019, doi: 10.1016/j.ijbiomac.2019.07.129.

[5] S. Desai, P. Tatke, T. Mane, and S. Gabhe, "Isolation, characterization and quantitative HPLC-DAD analysis of components of charantin from fruits of Momordica charantia," *Food Chem.*, vol. 345, p. 128717, May 2021, doi: 10.1016/j.foodchem.2020.128717.

[6] S. K. Singh, S. Singh, and R. Singh, "Targeting novel coronavirus SARS-CoV-2 spike protein with phytoconstituents of Momordica charantia," *J. Ovarian Res.*, vol. 14, no. 1, 2021, doi: 10.1186/s13048-021-00872-3.

[7] T. INDRAWATI, I. HAJARD, and D. K. PRATAMI, "Skincare Cream Preparation And Evaluation Of Pare (Momordica Charantia) Leaves Using Three Difference Base," *Int. J. Appl. Pharm.*, pp. 162–166, Sep. 2020, doi: 10.22159/ijap.2020v12i6.37921.

[8] L. Soo May, Z. Sanip, A. Ahmed Shokri, A. Abdul Kadir, and M. R. Md Lazin, "The effects of Momordica charantia (bitter melon) supplementation in patients with primary knee osteoarthritis: A single-blinded, randomized controlled trial," *Complement. Ther. Clin. Pract.*, vol. 32, pp. 181–186, Aug. 2018, doi: 10.1016/j.ctcp.2018.06.012.

[9] P. Daniel, U. Supe, and M. G. Roymon, "A review on Phytochemical analysis of Momordica charantia," *Nternational J. Adv. Pharm. , Biol. Chem.*, vol. 3, no. 1, pp. 214–220, 2014.

[10] N. Valarmathi, R. Subha Sree, and T. S. Rajan, "Neuroprotective effects of momordica charantia: A review from preclinical studies," *Int. J. Res. Pharm. Sci.*, vol. 11, no. 2, pp. 1902–1907, 2020, doi: 10.26452/ijrps.v11i2.2105.

[11] M. Cortez-Navarrete, E. Martínez-Abundis, K. G. Pérez-Rubio, M. González-Ortiz, and M. Méndez-Del Villar, "Momordica charantia administration improves insulin secretion in type 2 diabetes mellitus," *J. Med. Food*, vol. 21, no. 7, pp. 672–677, 2018, doi: 10.1089/jmf.2017.0114.

[12] J. T. Efird, Y. Ming Choi, S. W. Davies, S. Mehra, E. J. Anderson, and L. A. Katunga, "Potential for improved glycemic control with dietary Momordica charantia in patients with insulin resistance and pre-diabetes," *International Journal of Environmental Research and Public Health*, vol. 11, no. 2. pp. 2328–2345, 2014. doi: 10.3390/ijerph110202328.

[13] H. Gao *et al.*, "Polysaccharide from fermented Momordica charantia L. with Lactobacillus plantarum NCU116 ameliorates type 2 diabetes in rats," *Carbohydr. Polym.*, vol. 201, pp. 624–633, 2018, doi: 10.1016/j.carbpol.2018.08.075.

[14] S. Jiang *et al.*, "Antidiabetic effect of Momordica charantia saponins in rats induced by high-fat diet combined with STZ," *Electron. J. Biotechnol.*, vol. 43, pp. 41–47, 2020, doi: 10.1016/j.ejbt.2019.12.001.

[15] S. Sur and R. B. Ray, "Bitter Melon (Momordica Charantia), a Nutraceutical Approach for Cancer Prevention and Therapy," *Cancers (Basel).*, vol. 12, no. 8, p. 2064, Jul. 2020, doi: 10.3390/cancers12082064.

[16] S. de O. Mozaniel, A. da C. Wanessa, W. F. B. Fernanda, E. A. Marilena, C. F. Gracialda, and N. de C. J. Raul, "Phytochemical profile and biological activities of Momordica charantia L. (Cucurbitaceae): A review," *African J. Biotechnol.*, vol. 17, no. 27, pp. 829–846, 2018, doi: 10.5897/ajb2017.16374.

[17] A. Mala and T. Tulika, "Therapeutic efficacy of Centella asiatica and Momordica charantia: As Traditional Medicinal Plant," *J. Plant Sci.*, vol. 3, no. 1–1, pp. 1–9, 2015, doi: 10.11648/j.jps.s.2015030101.11.

[18] M. Fan *et al.*, "Comparative analysis of metabolite profiling of momordica charantia leaf and the anti-obesity effect through regulating lipid metabolism," *Int. J. Environ. Res. Public Health*, vol. 18, no. 11, 2021, doi: 10.3390/ijerph18115584.

[19] J. K. Grover and S. P. Yadav, “Pharmacological actions and potential uses of Momordica charantia: A review,” *J. Ethnopharmacol.*, vol. 93, no. 1, pp. 123–132, 2004, doi: 10.1016/j.jep.2004.03.035.

[20] K. N. K. Ranasinghe *et al.*, “In vivo anticancer effects of Momordica charantia seed fat on hepatocellular carcinoma in a rat model,” *J. Ayurveda Integr. Med.*, vol. 12, no. 3, pp. 435–442, Jul. 2021, doi: 10.1016/j.jaim.2021.03.001.

CHAPTER 16

AN ANALYSIS OF 3D-PRINTING TECHNOLOGY AND ITS FUTURE PERSPECTIVE

Dr. Parvathi Jayasankar, Assistant Professor, Department of Chemistry,
School of Sciences, B-II, Jain (Deemed to be University),JC Road, Bangalore-560027.,
Email Id- parvathi.jaysankar@jainuniversity.ac.in

ABSTRACT: A three-dimensional object is created from a CAD model or digital 3D model through 3D printing or manufacturing techniques. This can be accomplished through a number of techniques in which the material is brought together, often layer by layer, and then deposition, bonding or crystallization are all controlled by algorithms. This study investigates state-of-the-art polymer-based bioinks already employed in 3D printing for tissue engineering and therapeutic applications. This section outlines fundamental guidelines for selecting effective bioinks for additive manufacturing processes and creating 3D tissue or organ architectures using microfluidic devices such as mixtures of cells, biomedical materials and bio signals. Various bioink polymers are examined at length, and their mechanical, printability and cytocompatibility characteristics are included, which have been previously reported for 3D printing. In the future there is the potential for access to 3D-printed implantable organs to reduce waiting lists and increase the number of lives saved. Even though rapid prototyping for the healthcare industry is still in its infancy, it is already being used in various capacities in the healthcare industry to cut costs as well as perform at the highest level. Already under tremendous pressure. The industry will benefit from this powerful technology as key determinants.

KEYWORDS: 3D-Printing, Bioprinting, Healthcare, Manufacturing Industry, Print Technology.

1. INTRODUCTION

By adding material in layers, 3D-printing may translate geometric approximations into actual physical products. Many 3D processes have also shown amazing growth in recent years. Charles Hull first made 3D printing technologies widely available in the year 1980. PGA rocket engines, 3D printed professionals are able, steel bridges in Amsterdam, artificial heart pumps, jewelry-collections, and other equipment for the food and automotive industries are among the current applications of 3D printing [1]. The layer-by-layer effective collaborations of three-dimensional (3D) structures immediately from computer-aided design (CAD) drawings is the ancestor of 3D printing technology. The advancement of 3D printing technology has been very ingenious and adaptable. For organizations trying to increase operational effectiveness, it offers up new options and quite the for many others. Currently, 3D printing techniques may be used to generate conventional injection molded parts, ceramics, materials based on grapheme, and metal [2]. The manufacturing method might shift and be modernized by 3D printing technology. Utilizing 3D printing technology will speed up manufacture while cutting expenses. The business's demand will also have a stronger impact on production at the exact same time.

Customers should request that a product be developed according to their specification and have a bigger say in the final production [3]. In the meantime, 3D printing facilities will be positioned nearer to the customer, enabling a more adaptable and quick production system as well as greater quality control. Additionally, the use of 3D printing technology dramatically reduces the requirement for foreign travel. This is due to the fact that inventory monitoring technology can perform all transmission when production lines are situated close to the final destination, minimizing both energy and time [4]. The infrastructure of the business may also alter as a result of the implementation of 3D printing technology. The logistics of the

enterprises may oversee so this whole procedure and provide more thorough, end-to-end products. Today, 3D printing is increasingly employed around the globe, and it is becoming more and more widespread to produce any form of open source design in the fields of agriculture, healthcare, the automotive manufacturing, and aerospace. However, there are a range of disadvantages to the use of 3D printing in the industrial sector. For instance, the adoption of 3D printing technology would diminish the need for manufacturing jobs, which will immediately have a significant effect on the economies of nations that largely depend on low-skill occupations [5]. Additionally, users of 3D printing technology may generate a wide variety of things, including knives, firearms, and other hazardous goods. As a result, the usage of 3D printing should be restricted to a small group of individuals in order to stop terrorists and criminals from bringing firearms into the country undetected [6]. In consequence, anybody with access to a blueprints will be able to produce fake goods equally ease. This is due to the convenience of use of 3D printing technology, which just requires a drawing and the setting of data for mechanical printing of 3D items. In summation, 3D printing technology has become an efficient and versatile tool in the smart factories sector in recent years. Many nations have adopted this technology widely, especially in the commercial sector [7]. As a result, this paper provides a look at the various 3D printing methods, their applications, and finally the components that are used in the construction sector.

In this way, 3D printing has the opportunity to significantly enhance the research knowledge and surgical skills of the next millennium of surgeons, the patient-surgeon relationship, the level of understanding of the underlying disease, the design of implant materials and surgical tools those are patient-specific, and the efficiency and cost of surgical intervention [8]. Different printing materials and techniques are now developed to better replicate the architecture of the patient. Unlike human tissues, as is shown in Figure 1, most printing materials are hard and therefore not ideal for flexibility and elasticity. As a result, there still are materials available at the moment that may bridge the difference between the actual and recreated anatomy, in particular when it comes to soft tissue [9]. An overview of 3D printing's usage mostly in medical sector is included in this study, along with a discussion of its advantages and drawbacks and the ways in which surgeons would find it advantageous.

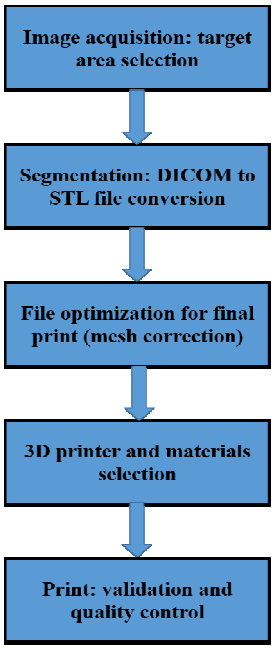


Figure 1: Illustrated that the 3D-printing Workflow.

1.1.Methods and Processes for 3D-printing:

The construction of a virtual model of the thing to be printed is the first step in the 3D printing process. This might be accomplished using Design software, a three-dimensional printer, or photogrammetry, where another model is created by fusing together a number of photos of the item taken from various angles. The 3D model must be transformed to the once it has been built. Prototype surface information is saved in the STL file format as a collection of three dimensional section coordinates. This file type is widely adopted since every 3D printer software can read it and, during a "slicing" procedure, convert the information to a G-code file. The process of "slicing" means creating a number of 2D cross section layers of the total item. As seen in Figure 2, the printer begins injecting material after building repeated chains of these 2D layers on top of each other's until a 3D item is produced [10]. A plethora of 3D printing technologies have been developed, each with a procedure known for deposition the 2D layers of material. These can be grouped into four main categories based on their respective common mechanism or principle:

i. Photo-polymerization;

ii. Extrusion;

iii. Powder based;

iv. Lamination

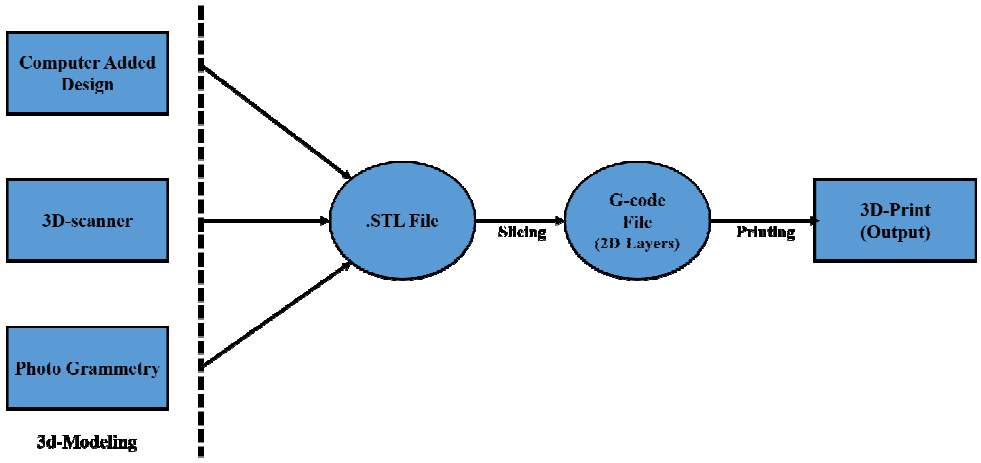


Figure 2: Illustrated that the Digital model of the Object is obtained through CAD-Software, a 3D-Scanner, or a Photogrammetry Procedure.

i. *Photopolymerization:*

One of the first 3D printing methods was photopolymerization. The actual approach was created in the 1980s. Hideo Kodama managed to come up with a technique to create three-dimensional objects in 1981 that included curing a photo-hardening polymer using UV radiation. UV radiation induces the liquid polymer to solidify at the surface. By carefully sinking this hardened layer, further layers may solid and be piled one on top each other with high adherence to produce the final 3D shape. Charles Hull created the first business system based on this technique in 1984. The process has now become referred to as stereo lithography [11]. Additionally, he developed 3D Systems, Corp. Hull not only made the first 3D printer available for purchase, but he also created and popularized the .STL file format, which integrates digital design to 3D printing systems. Still widespread now is the .STL file format. The UV curing system may either utilize a digital mirror device or a laser that travels

over the polymer surface in accordance with the layer design. The laser UV curable system projects UV light one time for each layer in accordance with the design. When it comes to the polymerization process, it may either take effect at the liquid surface, where the platform moves higher as each layer solidifies, or it can be acquired from the bottom but use an optical fiber is a flexible window, where the stage moves lower as layers cement (layer configuration or bat configuration. When the resin polymerization is only accessible in tiny quantities, this second process is beneficial since a smaller volume will operate just well [12]. Polyjet-technology, which is based on the same photopolymerization concept, employs inkjet technologies to deposit photopolymer resin material at a precise position as determined by the layer design, followed by full area UV light irradiation to harden the layer. For intricate patterns, a support material is further deposited to facilitate the ability for the printed architecture to stand alone.

ii. Extrusion:

Model material or support material is often directly transferred from a nozzle head dispenser employing extrusion-based 3D printing techniques going to follow material preparation, such as melting. Fused deposition modelling, the most popular 3D technology adopting this technique, produces 3D things using thermoplastic materials. Powder bed fusion modelling, introduced by Scott Crump in 1989, creates 3D things by layer-by-layer depositing thermoplastic polymers that have been heated to a semimolten condition before becoming extruded at the dispenser nozzle. In conformity with the sliced model design, the compound hardens after deposition to produce a uniformly hard layer that stacks on top of the base layer. This technology is now the most widely used 3D printing technology due to the way easy it is to use and how readily available equipment's are at reasonable pricing [13]. Thermoplastic materials include polylactic acid, acrylonitrile butadiene styrene (ABS), polycarbonate, polyamide, etc. are frequently utilized and delivered as feeding spools in filament form. Multi-material structures may be produced by continuously using nozzles with several materials during such a single printing operation. Additionally, materials may be employed to create a supporting or sacrifice structure that will be immediately taken out of the completed product. The controlled grand jury testimony of a much wider range of materials or a combination of materials is made possible by direct ink writing technology using a very similar principle, so long as the materials are in "ink" form, that is, in some kind of a highly viscous liquid state that can maintain its shape after deposition [14]. An almost unlimited choice of materials, including ceramic, polymers, food, and live cells, may be deposited with this 3D printing process, make it very adaptable. The kind of dispenser you choose depends on the kind of substrate, the viscosity, density, and particle shape of the ink.

iii. Powder-Based:

The building blocks for the 3D item manufactured using this additive assembly process are solid materials with a particle size range of 50 to 100 m. The printing procedure is obviously related to SLA, except that powder though rather than liquid photopolymer was being used, and it is afterwards deposited to the construction stage in different thicknesses using rollers or brooms. At this stage, a binding system is applied to the layer thickness, joining the grains precisely where the cross-sectional design approach dictates they should be. In order to apply a second coat of powder on top of the previous one in preparation for the subsequent binding operation, the stage is lowered once the uniform layer has developed [15]. Given relatively minute particle forms of plaster, ceramic, acrylic, wood, marble, and transition metals are easily accessible, a diverse range of materials might theoretically be used. The ability of the residual non-bonded powder to serve as a support material all throughout printing process is a substantial benefit of this technique. Therefore, co-printing doesn't need any additional

materials. Additionally, when the procedure is finished, any extra powder may be collected and utilized for a separate printing job, greatly decreasing the amount of material waste. According to the model design, the simplest binding system makes use of a conventional inkjet-based dispenser to accurately deposit liquid gluing inks onto the powder bed. Binder jetted is the name given to this inkjet printing [16]. Alternately, it is possible to fuse the powders particles together via sintering by selective lasers (SLS), which uses high-energy beams of light to sinter the particles somewhere below their melting point.

iv. Lamination:

The laminating procedure following defining a layer contour without cutting tools, 3D printing entails stacking laminated material components that are accessible in sheets on top of one another. A sheet of material is first put onto a staging, after which it is cut using a laser or a sword in line with a particular CAD design, specifying the layer's cross-sectional form. A subsequent sheet is put on top of the original one and once again traced after the superfluous material has been trimmed. Each layer is joined to the previous one before it using adhesives or welding technologies, depending according to the type of material, which might be paper, metal, plastic, etc. Until the 3D item is eventually constructed, the method is repeated several times [17].

1.2.The Uses of 3D Printing in the Manufacturing Industry:

i. Aerospace Industry:

The creative flexibility offered by 3D printing in component and manufacture is unmatched. The adoption of 3D printing in the automotive and aerospace industries offers the ability to accomplish these objectives with enhanced and complicated geometry that are lightweight while consuming less resources and energy. Using technology for 3D printing may also result in fuel savings since it can utilize less material to create aeronautical components. Furthermore, the production of replacement parts for many aircraft components, such engines, has made heavy use of 3D printing technology. Parts of the powertrain are readily damaged and need to be updated often. Therefore, the use of 3D printing technology to get such replacement batteries is an excellent suggestion. The tensile characteristics, oxidation or corrosion resistance, especially damage tolerance of nickel-based alloys end up making them increasingly common in the aviation industry [18].

ii. Automotive Industry:

Today's 3D-printing technology has significantly altered our industry's ability to create, develop, and create a new product. The 3D-printing movement has brought new shines to the vehicle industry by enabling lighter and far more complex constructions in a small amount of time. For instance, Local Motor manufactured the first electric vehicle printed in three components in 2014. By producing a 3D-printed bus dubbed OLLI, Local Motors expanded the breadth of uses for the 3D-printing process beyond only automobiles. OLLI is a 3D-printed, electric, recyclable, and very intelligent bus. Ford is a pioneer in the adoption of 3D-printing technology and uses it to create experiments and engine components. BMW also employs 3D-printing to create wire cutters for testing and assembling motors. In the meanwhile, SLM Solution Group AG and AUDI worked together through 2017 to develop prototypes and spares components. As a result, the use of 3D-printing technology in the automotive market allows businesses to try out different ideas and focus early on in the development process, leading to the creation of optimal and efficient car designs. Furthermore addition, technology for 3D-printing helps cut down on chemical use and waste. However, 3D-printing technology may save money and time, allowing people to test new ideas swiftly [19].

iii. Food Industry:

The food business has access to 3D printing technologies as well as the aviation industry. Presently, there is a really growing demand for manufacturing custom designed foods for people with genuine dietary needs, such as athletes, children, pregnant women, service users, and others who require enhanced nutrient levels. Decreasing requires a different amount of nutrients. Promoting unhealthy ingredients and corresponding presence of nutrients. However, creating personalized food requires careful planning and innovative production, which is where the use of 3D-food printing comes into play. Edible layer manufacturing, sometimes referred to as 3D-edible printing, is created by depositing successive layers one at a time that are produced directly from desktop design data. Specialized materials can be combined and manufactured into a variety of complex structures and shapes using 3D printing technology. It is possible to create novel food dishes with intricate and delectable patterns and shapes using sugar, chocolate, pureed foods, and flat foods such as spaghetti, pizza, and crackers. Manufacturing food using 3D printing technology is highly energy efficient, cost effective and ecologically friendly. Because of its ability to generate new methods for food modification and adapt to the tastes and needs of each individual, 3D printing of food can be beneficial and healthy for humans [20]. One could imagine diets that impose themselves without the need for exercise if it were possible to automatically prepare food and ingredients according to the consumer's knowledge.

iv. Healthcare and Medical Industry:

The technology of 3D-printing can also be used to create models for 3D skin, bones and cartilage, organs, replacement tissues, tissues for cancer research and ultimately for perception, instruction and communication. The following are some of the benefits of 3D-printing for biomedical products: The process of 3D-printing can be used to create models for 3D skin, bones and cartilage, organs, replacement tissues, tissues for cancer donation and ultimately for observation, instruction. Could and communication. The following appear to be some of the benefits of 3D-printing for biomedical products:

- At low cost, 3D printing technology can mimic the natural structure of the skin. Chemical, cosmetic and medicinal products can be tested on 3D printed skin. Therefore, there is no need to test items on animals. By employing duplicates of the skin, researchers would be able to obtain accurate results.
- By employing 3D printing technology to print drugs, efficiency can be increased along with the ability to create dosage forms with precise dose and size control, excellent repeatability, and complex drug-release patterns.
- Gaps in cartilage or bone in bone caused by trauma or disease can be filled with printed cartilage and bone, thanks to 3D printing technology. Because it focuses on generating bone, maintaining it, or improving its function in vivo, this therapy differs from others that include auto-grafts and allografts.
- Using 3D printing technology, tissue function can be improved, maintained or replaced. The 3D-printed replacement tissues have a connected pore network, are biocompatible, have the correct surface chemistry, and have acceptable mechanical properties.
- Similar organ failure caused by serious issues including disease, accidents and congenital malformations can also be printed using 3D printing technology.

- 3D printing technologies have the potential to greatly accelerate cancer research because they can create highly controlled models of cancer tissue. By using 3D printing technology, patients can receive more reliable and accurate information.
- 3D printing models can be used to teach neurosurgeons how to practice different surgical approaches. As a 3D model simulates an actual patient's pathological condition, it can increase accuracy, reduce instructor time when performing diagnostic procedures, and provide hands-on training opportunities for surgeons.

In this paper, the author has highlighted about 3d-printing technology and its features. According to the author, 3D-printing is happening today on a large scale in every industry. This paper shows the methods and process of 3D printing along with the workflow of 3D-printing.

2. LITERATURE REVIEW

Z. Chen et al. illustrated that the 3D printing of ceramics is the emergence of social to get attention, after years of intensive investigation on the 3D printing of both metals and polymers. Without the use of 3D printing, constructing ceramic parts with arbitrary complicated has proven to be quite difficult. This article examines the most recent developments in ceramic 3D printing all the while outlining the development of each relevant technology across time. There is also discussion of the key technical elements, such as material qualities, process management, post-treatments, and relationships between forms of energy and materials. The technological challenges are discussed, along with suggestions about how to handle them. In order to choose the best procedures for actual application, analyses between the techniques are done. A study of exemplary 3D printing uses for different ceramic materials is also done. The improvement of materials and manufacturing techniques for the production of high-performance materials and structures are highlighted as future trends [21].

J. Li et al. stated that In place of conventional molding or machining, 3D-printing, also commonly known as additive industrial production, may convert 3D virtual items made by computer-aided design (CAD) into actual 3D items by stacking multiple one at a time. Since its conception, great strides have been made in our awareness of the 3D printing process and how the components, structures, properties, and applications of the manufactured things relate with each other. This review focuses on innovative hydrogel-based biomaterial inks and bionics for 3D printing since hydrogels represent one of the most practical classes of ink substances for this technology and because it has been expanding rapidly. It includes a wide range of 3D printing processes, namely laser, extrusion, inkjet, 3D, 4D, and 4D-printing. It gives a thorough analysis and explanation of how improved hydrogel designs for 3D printing may be made possible by the materials, economic, physical, chemical, and biological aspects of moisturizers. Biopolymers, synthetic materials, polymer blends, nano-composites, functional-polymers, and cell-laden systems are all included in the list of polymer matrix that may form hydrogels. Hydrogel-based 3D printing is playing a crucial role in the design and fabrication of sophisticated functional systems in a configurable fashion that is unequaled by thermoplastics, thermosets, ceramics, and metallurgy [22].

J. Gopinathan and N. Nsup illustrated that the need for bone regeneration and organ replacement is increasing globally. Advances in bioengineering now have the potential to repair such damaged human organs into functioning organs or tissues, using 3D printing. Bioink, the primary component in 3D printing, is critical for the creation of functioning organs or physical structures. The selection of a bioink to be used in 3D printing should

possess a large number of essential properties. To create more effective bioinks for 3D-printing of organs or tissue architectures, several techniques and properties need to be improved. For use in cell transplantation, a variety of bioink formulations have been described, including cell-biomaterials-based bioink and cell-based biomimetic such as cell aggregates and tissue spheroids. Interestingly, with the support of functional compatibles, their transformation, and mixtures of cells and nano-fibers, more tunable biopolymers are being developed that are compatible to living cells, printable, and extremely robust after printing. Huh. These methods underscore the immense potential of bioink for use in future 3D printing of incredibly complex tissue and organ architecture [23].

3. DISCUSSION

The use of printing technology across several industries provides a number of obstacles along with benefits. The usage of printing technology will rise as a result of the ongoing research and development in the field. Manufacturing has undergone significant transformation. Health is the most desired thing for a person, and 3D-printing has a significant impact in this area. Another aspect of food printing that is beneficial for the body is the ability to supply customized meals and manage diets. The 3D-printing technology is offering the finest advantages compared to conventional manufacturing and designing techniques for the building, housing, and jeweler industries. The use of 3D-printing in education benefits both students and educators. Therefore, this technology is essential in every stage of the production process. Authors want to assemble knowledge about this technology that is currently accessible in many elements of real world applications that may enhance human lives. As a result, humans have limited our focus to a small variety of applications rather than a broad range.

4. CONCLUSION

Organ structures can be created automatically using 3D printing, although improvements are still needed in a variety of areas, notably bioink and the sale of 3D-printed items. This technique could make it easier to fabricate more complex, patient-specific 3D structures for critical medical need. This offers many advantages including design freedom, fabrication options, use of certain cell lines, biodegradability and management of mechanical properties, etc. Cell-containing hydrogels are a popular technique for fabricating such 3D structures, among other methods. In this review, several microfluidic devices that are available and their specific selection process as well as characteristics were included. Creation of Optimum Bioink is still ongoing, but thanks to significant foreign contributions, it may one day be viable to use this technology for profitable purposes. While cell-laden biomaterial bioinks are widely employed, bioinks based on sub-dermal bioinks, cell aggregates, and spheroids also show potential for the application of 3D printing technology to create operable tissues or organs. However, the use of these approaches in many organs and tissue types is limited by the need for exceptionally high amounts of certain cells. In addition to bioink, it is envisaged that the development of sophisticated, low-cost printers with excellent resolution could dramatically improve the prospects of this field of study. More promising are the use of innovative nanomaterial with supramolecular reactivity, reversible crosslinking polymers and stimuli-responsive hydrogels in terms of bioink selection and application. Advanced agriculture in patient-specific devices is on the horizon because of the potential of bioink and 3D printing.

REFERENCES

[1] H. Guo, R. Lv, and S. Bai, “Recent advances on 3D printing graphene-based composites,” *Nano Mater. Sci.*, 2019, doi: 10.1016/j.nanoms.2019.03.003.

[2] V. M. Vaz and L. Kumar, “3D Printing as a Promising Tool in Personalized Medicine,” *AAPS PharmSciTech*, vol. 22, no. 1, p. 49, Jan. 2021, doi: 10.1208/s12249-020-01905-8.

[3] J. Z. Gul *et al.*, “3D printing for soft robotics–a review,” *Science and Technology of Advanced Materials*. 2018. doi: 10.1080/14686996.2018.1431862.

[4] J.-Y. Lee, J. An, and C. K. Chua, “Fundamentals and applications of 3D printing for novel materials,” *Appl. Mater. Today*, vol. 7, pp. 120–133, Jun. 2017, doi: 10.1016/j.apmt.2017.02.004.

[5] T. D. Ngo, A. Kashani, G. Imbalzano, K. T. Q. Nguyen, and D. Hui, “Additive manufacturing (3D printing): A review of materials, methods, applications and challenges,” *Composites Part B: Engineering*. 2018. doi: 10.1016/j.compositesb.2018.02.012.

[6] M. A. Azad, D. Olawuni, G. Kimbell, A. Z. M. Badruddoza, M. S. Hossain, and T. Sultana, “Polymers for extrusion-based 3D printing of pharmaceuticals: A holistic materials–process perspective,” *Pharmaceutics*. 2020. doi: 10.3390/pharmaceutics12020124.

[7] H. Agrawaal and J. E. Thompson, “Additive manufacturing (3D printing) for analytical chemistry,” *Talanta Open*, vol. 3, p. 100036, Aug. 2021, doi: 10.1016/j.talo.2021.100036.

[8] S. Wasti and S. Adhikari, “Use of Biomaterials for 3D Printing by Fused Deposition Modeling Technique: A Review,” *Frontiers in Chemistry*. 2020. doi: 10.3389/fchem.2020.00315.

[9] Z. Chen, M. Yang, M. Ji, X. Kuang, H. J. Qi, and T. Wang, “Recyclable thermosetting polymers for digital light processing 3D printing,” *Mater. Des.*, 2021, doi: 10.1016/j.matdes.2020.109189.

[10] G. Bai, L. Wang, F. Wang, and G. Ma, “In-process reinforcing method: dual 3D printing procedure for ultra-high performance concrete reinforced cementitious composites,” *Mater. Lett.*, 2021, doi: 10.1016/j.matlet.2021.130594.

[11] M. Sangermano, I. Roppolo, and A. Chiappone, “New horizons in cationic photopolymerization,” *Polymers*. 2018. doi: 10.3390/polym10020136.

[12] A. Andreu *et al.*, “4D printing materials for vat photopolymerization,” *Addit. Manuf.*, vol. 44, p. 102024, Aug. 2021, doi: 10.1016/j.addma.2021.102024.

[13] X. Zhao *et al.*, “Efficient 3D printing via photooxidation of ketocoumarin based photopolymerization,” *Nat. Commun.*, 2021, doi: 10.1038/s41467-021-23170-4.

[14] K. Classens, T. Hafkamp, S. Westbeek, J. J. C. Remmers, and S. Weiland, “Multiphysical modeling and optimal control of material properties for photopolymerization processes,” *Addit. Manuf.*, 2021, doi: 10.1016/j.addma.2020.101520.

[15] M. Sangermano, “Recent advances in cationic photopolymerization,” *J. Photopolym. Sci. Technol.*, 2019, doi: 10.2494/photopolymer.32.233.

[16] F. Jasinski, P. B. Zetterlund, A. M. Braun, and A. Chemtob, “Photopolymerization in dispersed systems,” *Progress in Polymer Science*. 2018. doi: 10.1016/j.progpolymsci.2018.06.006.

[17] F. Zhang *et al.*, “The recent development of vat photopolymerization: A review,” *Additive Manufacturing*. 2021. doi: 10.1016/j.addma.2021.102423.

[18] S. Mantihal, R. Kobun, and B. B. Lee, “3D food printing of as the new way of preparing food: A review,” *International Journal of Gastronomy and Food Science*. 2020. doi: 10.1016/j.ijgfs.2020.100260.

[19] M. Idrees, A. M. H. Ibrahim, E. Tekerek, A. Kontsos, G. R. Palmese, and N. J. Alvarez, “The effect of resin-rich layers on mechanical properties of 3D printed woven fiber-reinforced composites,” *Compos. Part A Appl. Sci. Manuf.*, 2021, doi: 10.1016/j.compositesa.2021.106339.

[20] N. A. Sukindar *et al.*, “Implementation of 3D Printing Technology in the Food Industry,” *Guigoz. Sci. Rev.*, 2021, doi: 10.32861/sr.74.50.54.

[21] Z. Chen *et al.*, “3D printing of ceramics: A review,” *J. Eur. Ceram. Soc.*, vol. 39, no. 4, pp. 661–687, Apr. 2019, doi: 10.1016/j.jeurceramsoc.2018.11.013.

[22] J. Li, C. Wu, P. K. Chu, and M. Gelinsky, “3D printing of hydrogels: Rational design strategies and emerging biomedical applications,” *Mater. Sci. Eng. R Reports*, vol. 140, p. 100543, Apr. 2020, doi: 10.1016/j.mser.2020.100543.

[23] J. Gopinathan and I. Noh, “Recent trends in bioinks for 3D printing,” *Biomater. Res.*, vol. 22, no. 1, p. 11, Dec. 2018, doi: 10.1186/s40824-018-0122-1.

CHAPTER 17

A SPECIAL EMPHASIS ON VITILIGO WITH ASSOCIATED PROBLEMS AND POSSIBLE SOLUTIONS

Dr. Rekha MM, Assistant Professor, Department of Chemistry,
School of Sciences, B-II, Jain (Deemed to be University),JC Road, Bangalore-560027.,
Email Id- mm.rekha@jainuniversity.ac.in

ABSTRACT: The loss of epidermal melanocytes occurs as a result of the chronic inflammatory skin condition known as vitiligo. The majority of vitiligo treatments currently available are based on the off-label use of immunosuppressant therapy like systemic or topical steroids or topical calcineurin inhibitors in conjunction with the application of UV irradiation, are scarce, lack sustained efficacy, and are currently ineffective. Herbal medications of various natures and impacts have been utilized in the treatment of vitiligo from antiquity. Therefore, the study aims at providing a summary of the herbal products that may be used to treat pigmentary disease. Vitiligo treatment is usually problematic since patient cooperation is low. Patients often stop their treatments because the results are so slowly-acting. Therefore, the present study aims at exploring the fundamentals of Vitiligo with its treatments along with the problems and possible solutions.

KEYWORDS: Lesions, Skin, Topical, Treatments, Vitiligo.

1. INTRODUCTION

Spots of skin lose color due to the condition known as vitiligo. Any area of your body with the skin might be affected. Additionally, the tongue and hair may be impacted. Skin and hair colour are often influenced by melanin. Vitiligo happens when cells that produce melanin die or cease functioning [1]. All skin types are susceptible to vitiligo, however, those with darker complexion may see it more readily. Typically, 1% of people worldwide are affected with vitiligo. Racial, sexual, or geographical diversity among the populace is not accepted. According to certain intelligence, India, Egypt, and Japan may have greater vitiligo incidence rates. From 1.25 to 6 percent of the population. The most prevalent form is non-segmental generalized vitiligo, often known as vitiligo, which manifests as widely spread, frequently symmetric, and progressing lesions [2]. Patients with vitiligo have a significant decline in quality of life that is unmistakably connected with the disease's early age of beginning, as well as a clear effect on their physical and mental health, including loss of skin UV protection and reduced cutaneous immunity.

With an approximate prevalence of 0.5–2% in both children and adults globally, vitiligo is by far the most prevalent depigmenting skin condition. On the Danish archipelago of Bornholm, wherein vitiligo was estimated to afflict 0.38% of the population, one of the first and biggest epidemiological studies ever published was carried out in 1977. There is no preference in the ethnic groups or skin tones that vitiligo affects [3]. Furthermore, there seem to be significant spatial disparities. For example, research in China's Shaanxi Province found an incidence of only 0.093%, but 8.8% was observed in certain parts of India. Figure 2 shows how common vitiligo is all around the globe. This high number may be due to the presence of cases involving toxic and pharmacological depigmentation, or it may simply be a result of the dominance of one skin institute in Delhi. Furthermore, there could be a discrepancy in the prevalence estimates because more people report their lesions in areas with a high incidence of social and cultural stigma or because lesions are more obvious in people with darker skin. According to a thorough analysis of prevalence data from more than 50 international research, the prevalence of vitiligo varies from a base of 0.06% to a peak of 2.28%. Different types of vitiligo have been classified as shown in Figure 1 below [4].

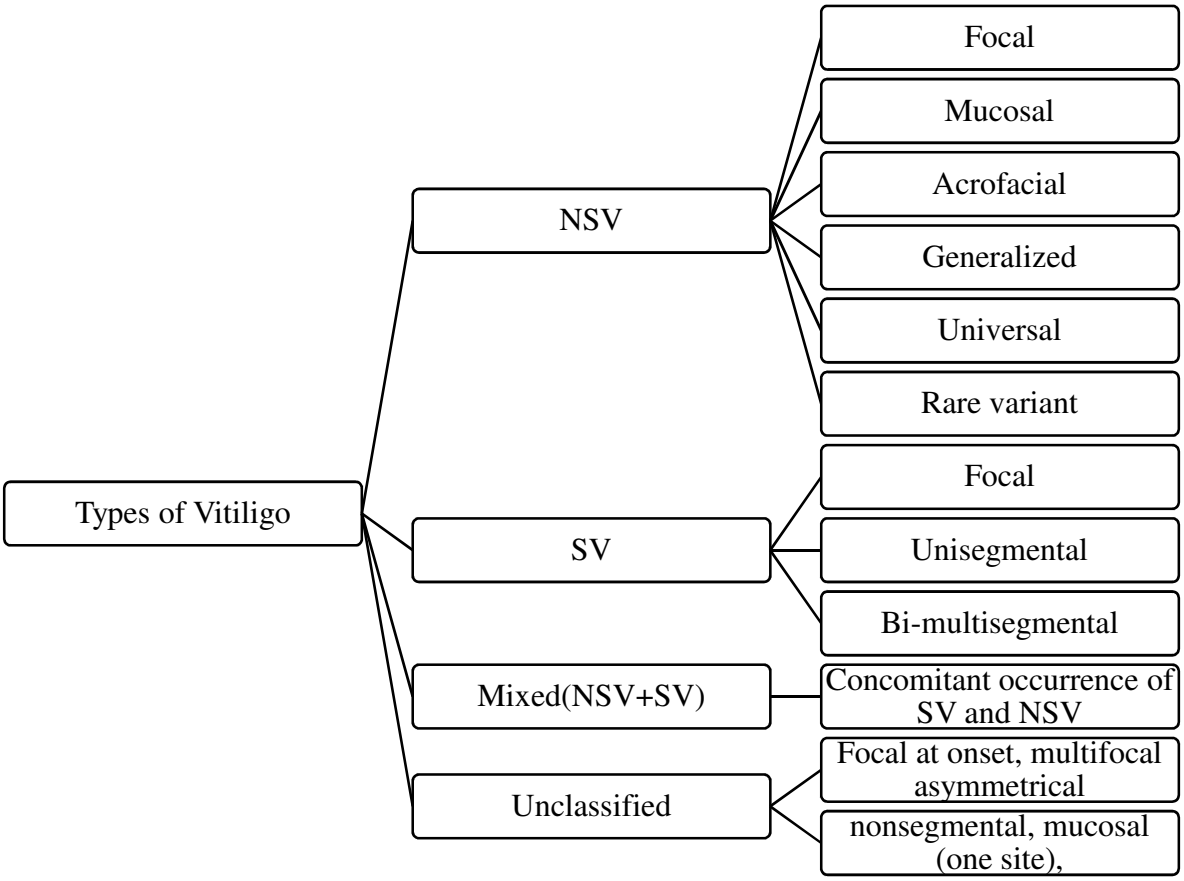


Figure 1: Illustrating the classification of different types of Vitiligo.

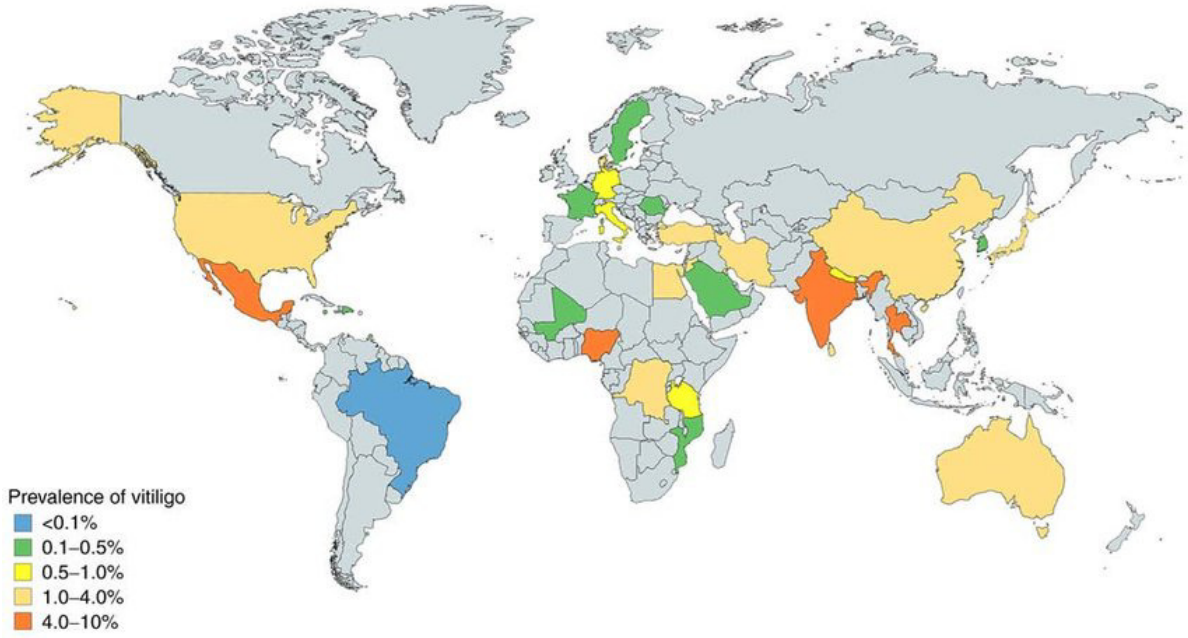


Figure 2: Worldwide prevalence of vitiligo. Estimated prevalence rates at all ages were obtained from studies conducted globally [5]**.**

The location of Vitiligo might provide information about its triggers or causes. Skin lesions caused by stress are often limited to the seborrheic region. Lesions of traumatic forms are typically restricted to areas of pressure or damage. Depigmented lesions often develop in regions with a particular pre-existing dermatitis in dermatitis-related kinds. Doctors often make assumptions about risk factors and aggravating variables that might help them determine the cause of vitiligo, and they then counsel patients to change modifiable lifestyle choices[6], [7].

In the management of vitiligo, diet is not seen as being especially significant. Vitiligo can benefit from a nutritious, diversified diet that includes elements from a range of sources[8], [9]. There are a few foods that complementary and alternative medicine (CAM) practitioners believe to be either helpful for vitiligo or detrimental, however, they disagree in their opinions on these meals and frequently lack the scientific proof to support their claims [10]. The amount of vitamins, microelements, and antioxidants in a food is often taken into account when making recommendations. The negative effects of foods or food additives, in contrast, hand, are frequently predicated on the possibility of allergic reactions and discomfort, both of which might cause or aggravate vitiligo.

2. LITERATURE REVIEW

Orest Szczurko & Heather S Boon stated that while natural health products are effective for treating vitiligo, the studies that have been done on them have low methodological quality and serious reporting errors. The combination of L-phenylalanine and phototherapy, as well as Ginkgo biloba taken orally as a single therapy, both show potential and need more research [11]

In light of upcoming issues, Saeedinezhad assessed the individuals' vitiligo experiences. A descriptive phenomenology method was used in this qualitative study. With use of targeted sampling, it was carried out in 2015 with 10 patients who had been sent to dermatological clinics at the hospitals in Zabol and Zahedan. The data were analyzed via the Colaizzi approach. The findings indicated that several problems impact and risk the future of those who have vitiligo. To create a culture and raise consciousness, family and society are seen as the primary forces that shape people's futures[12].

Kovacs et al. revealed a disordered keratinocyte differentiation with changed lipid composition using cellular and lipidomic methods, which was connected to compromised energy metabolism and elevated expression of glycolytic enzymes. As a result of minor mechanical stress, vitiligo keratinocytes released even more inflammatory mediators, demonstrating immunological activation. The findings point to internal changes in the nonlesional epidermis, which could be the main driver of the localized inflammatory environment that prompts immune responses directed against melanocytes.

High-degree complications diseases in vitiligo patients were explored by Khattri et al., and Firooz et al.. Vitiligo, which is substantially more frequent in women than in males, is thought to be the cause of severe depressive episodes in around 31% of those who have the disorder. Because of age-related characteristics, this issue is more severe in younger women. Young ladies who are single and approaching marriageable age are particularly affected. Because young women who have vitiligo signs are less likely to get married. For women, the disease is a huge source of stress. Married women with progressive vitiligo have also experienced marital issues, divorce, and subsequent remarriages [13], [14].

The vitiligo condition was described by Fatani et al. as a barrier to a person's socializing. Marriage is often hampered by socialization issues. Of the study's participants, 42% had an average marital status. Interaction between people is essential for a happy marriage since it helps couples understand one another better. Women struggle with a lot in this area, which makes marriage a rare occasion for them [15].

3. METHODOLOGY

The information in this review is obtained from searching electronic databases such as Scopus, Science Direct, Research Gate, Google Scholar, and PubMed. To search relevant records, a combination of keywords was used involving; “Vitiligo ”, “Pigmentation”, ”Treatments”, “Skin”,

"Diagnosis" and "Natural products". pertinent records for analysis, although only English-language records are included in this process. Figure 3 below provides an overview of the methodology used to carry out the review study.

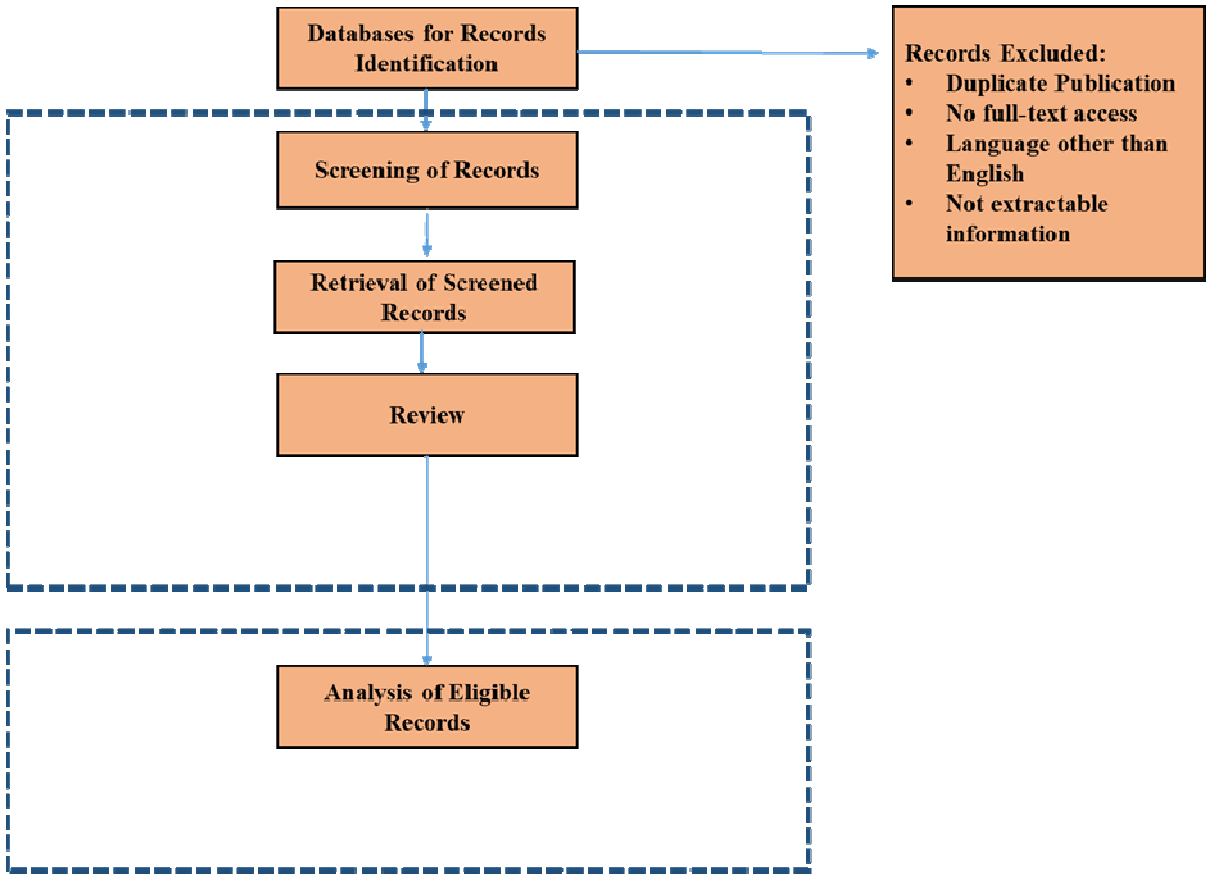


Figure 3: Illustrating the Methodology used to carry out the review study.

4. DISCUSSION

One of the dermatology's most challenging problems is still treating vitiligo. The goal of care ought to be to prevent the immune system from stopping depigmentation, destroying melanocytes, stabilizing depigmented lesions, promoting repigmentation, and afterward avoiding relapses after repigmentation has been accomplished. Very crucial first measures include understanding that vitiligo is more than simply a cosmetic issue and resolving concerns of patients about deformity and social embarrassment.

4.1. Treatments

There are several secure and efficient therapies for vitiligo as shown in Figure 4, and the treatment regimen must take the patient's preferences and needs into account, even though no particular medication has yet been licensed for the condition. These remedies include surgery, systemic and topical immunosuppressive agents, and photodynamic therapy. Because most therapeutic choices are time-consuming and need long-term follow-up, therapy involves an individualized therapeutic strategy wherein patients are at the center of the decision-making.

There is currently no recognized cause for vitiligo. However, other theories are involved, including those involving genetics, free radicals, cytotoxicity, neurological triggering, and autoimmunity. In moderate cases, the medicine can be administered orally or topically; however, in extreme situations of vitiligo, these methods are not sufficient. To boost skin pigmentation, light treatment is also provided together with the use of medications. To achieve an equal distribution of the typical quantity of cutaneous coloration, the treatment for leukoderma or vitiligo needs not only the deposit of pigmentation in the depigmented regions but also the redistribution of pigment from border areas that are too pigmented. The sort of cell present and its presence are both factors. The existence of

keratinocyte stem cells in the area where melanocytes may potentially grow in the inter-follicular epidermis reduces that likelihood. Vitiligo presently has no known cause. However, there are additional hypotheses at play, such as those involving heredity, neurological triggering, cytotoxicity, free radicals, and autoimmune. Oral or topical administration of the medication is effective in mild instances of vitiligo, however, both approaches fall short in severe cases. Along with the usage of drugs, light therapy is frequently used to improve skin pigmentation. Treatments for vitiligo or leukoderma require not only the deposition of pigment in the hypopigmented areas but also the distribution of pigmentation from border regions that are overly pigmented to establish an efficient allocation of the usual amount of cutaneous coloration. Both existence and the kind of cell present are elements. The possibility of melanocytes developing in the region of the inter-follicular epidermis wherein keratinocyte stem cells are present is diminished.

To properly comprehend the genesis of vitiligo, additional study is required to clarify the reasons for melanocyte degeneration. Understanding the biological messengers and molecular mechanisms behind metabolic irregularities, melanocyte degeneration, and autoimmune diseases is crucial to developing innovative therapeutic targets and drugs that might potentially reverse the disease's progression and cure vitiligo. Psoriasis and vitiligo have both been successfully treated with natural cytokine-targeting therapies. Therefore, it is tempting and exciting to target the interferon (IFN)-chemokine axis using existing or upcoming drugs. It may sometimes be frustrating to see therapy success for vitiligo that is uneven and recurrent. Based on the kind of vitiligo, whether it is active, and the drug's adverse effects, specific treatment regimens must be created. Only a few vitiligo therapies are available, and none of them consistently induce repigmentation in every patient. To create novel treatment approaches and learn more about the causes of vitiligo, further scientific and medical study is needed. The bulk of information on upcoming medications is given through case studies or actual incidents. To adequately determine their efficacy, further randomized controlled studies are needed.

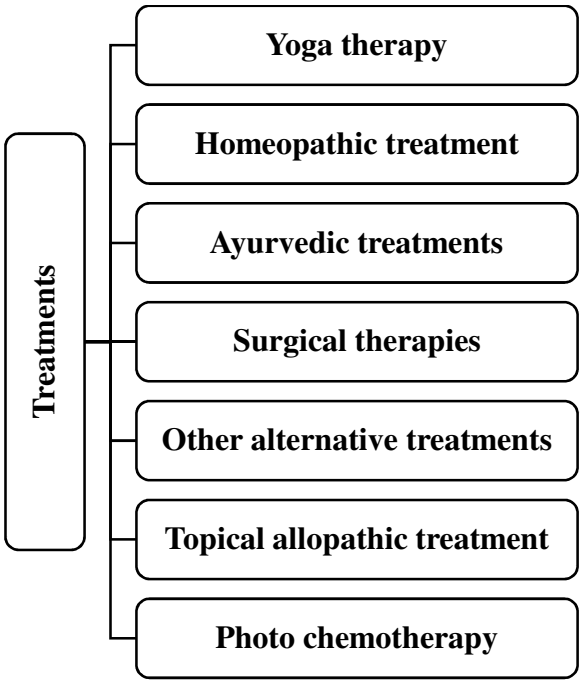


Figure 4: Illustrating different treatment Avenues of Vitiligo.

For Vitiligo, the aforementioned treatments are available. But the effectiveness of these therapies is questionable. Such therapies are being used for extended periods, possibly up to or even including two years. These factors cause patients to lose patience and stop receiving therapy. Additionally, less of the medicine psoralen is absorbed after being administered orally, which reduces the efficiency of the treatment. Additionally, it also has several extra symptoms and negative consequences. Gastric discomfort, skin photosensitivity response, burning, itching, sunburn, tanning, nausea, and severe erythema are examples of other symptoms that might occur together with drug side effects. A stressful

existence and other elements, such as clothing choices and smoking habits, have a detrimental impact on the course of therapy.

4.2. Problems with the Treatment of Vitiligo

Topical therapies are quicker than oral treatments because, with topical creams, the medication directly enters the epidermis. In oral treatments, the medication first enters the bloodstream and then travels via the blood to the epidermis. It is now challenging for drugs to penetrate the skin when used topically. Permeability enhancers may be added to the formula to address this issue. By lowering the skin's particle size, the medicine may be delivered quickly. New formulation delivery may be made to get tiny particles. Phospholipid-structured delivery systems such as ethosomes, lecithin organogels, liposomes, transferosomes, and lipid emulsions among others may be created. Because of this new method of distribution, skin penetration of the medicine may be improved. Extra medicines may be used in conjunction with the therapy or separately to address the additional symptoms.

To treat itching and burning, soothing agents may be administered, and other antacid tablets, such as proton pump inhibitors or substances that lower the amount of stomach Hydrochloric acid, can be used to treat gastrointestinal disturbances. Because of damage to the skin cells, inflammation of the skin might sometimes develop during therapy. Anti-inflammatory drugs may be administered together with therapy to treat this kind of disease. The condition may be lessened by having individuals modify their lifestyles following their unique clinical presentations of vitiligo. Since extreme stress worsens lesions, adopting a positive outlook and minimizing stress may assist. It's crucial for people with lesions in a seborrheic distribution to get enough rest and eat antioxidants. Smoking must be cut out for patients who have a smoking habit since it depletes the body's supply of healthy antioxidant properties. If Vitiligo developed as a result of stress or friction, tight-fitting clothing like pants and shoes must be prevented.

4.3. Challenges in Socialization

Marriage and socialization are key components of this issue and a major life problem. Marriage success and a couple's ability to understand one another better are both connected with socialization and being an active part of society. Because vitiligo sufferers often struggle in social situations, marriage may not work out for them now or in the future. Everyone who has had vitiligo signs since childhood worries about getting married. Since it affects women more severely, many choose to avoid dissatisfaction by choosing to remain unmarried forever. However, males take marriage more seriously and search for a spouse who can accept them as they are. To this aim, people choose marriage with family because they believe they can handle it better and because their chances of a successful marriage are greater given their prior familiarity. Relative marriage increases the likelihood of illness appearing in the next generations if it is believed that inheritance also contributes to disease. Before and after getting married, persons with vitiligo must also consider how they will raise their children. Parents' primary worry throughout their children's formative years is the possibility of illness developing in them, and they respond to even the most minor skin signs. Due to the primary concerns of families being their entrance into society and marriage, this sensitivity is greater when it comes to female children.

5. CONCLUSION

A skin condition known as vitiligo occurs when the melanocytes are destroyed in various ways. To treat this disease, there are now available overheaddeliberated therapies. Current medical and surgical treatments for vitiligo, especially when combined, have shown some success in stabilizing and depigmenting the condition. The future for vitiligo is promising, and new treatments are on the horizon. Additionally, these initiatives will be aided by global partnerships to create standard outcome criteria. Further understanding of the disease targets and the most effective treatment strategy will come from ongoing studies into the pathophysiology of this complicated and multifaceted illness.

REFERENCES:

[1] C. Bergqvist and K. Ezzedine, “Vitiligo: A Review,” *Dermatology*, vol. 236, no. 6, pp. 571–592, 2020, doi: 10.1159/000506103.

[2] J. Stiegler and S. Brickley, “Vitiligo: A Comprehensive Overview,” *J. Dermatol. Nurses. Assoc.*, 2021, doi: 10.1097/JDN.0000000000000589.

[3] R. Gaafar, “Screening for Psychological Burden of Vitiligo Using Vitiligo Impact Scale,” *Egypt. J. Hosp. Med.*, vol. 70, no. 8, pp. 1289–1294, Jan. 2018, doi: 10.12816/0044637.

[4] S. Paavai and J. Thomas, “Clinical Types of Vitiligo,” *Indian J. Public Heal. Res. Dev.*, vol. 10, no. 8, p. 1520, 2019, doi: 10.5958/0976-5506.2019.02309.X.

[5] S. Said□Fernandez *et al.*, “Novel immunological and genetic factors associated with vitiligo: A review,” *Exp. Ther. Med.*, vol. 21, no. 4, p. 312, Feb. 2021, doi: 10.3892/etm.2021.9743.

[6] A. I. Eltaweel, R. M. Salem, A. M. Abdelrahman, and H. A. Hegazy, “Provocating factors of vitiligo,” *Benha J. Appl. Sci.*, vol. 6, no. 4, pp. 279–282, Aug. 2021, doi: 10.21608/bjas.2021.197962.

[7] R. C. Zuo *et al.*, “Risk factors and characterization of vitiligo and alopecia areata in patients with chronic graft-vs-host disease.,” *JAMA dermatology*, vol. 151, no. 1, pp. 23–32, Jan. 2015, doi: 10.1001/jamadermatol.2014.1550.

[8] P. E. Grimes and R. Nashawati, “The Role of Diet and Supplements in Vitiligo Management,” *Dermatol. Clin.*, vol. 35, no. 2, pp. 235–243, Apr. 2017, doi: 10.1016/j.det.2016.11.012.

[9] A. Shakhbazova, H. Wu, C. J. Chambers, and R. K. Sivamani, “A Systematic Review of Nutrition, Supplement, and Herbal-Based Adjunctive Therapies for Vitiligo,” *J. Altern. Complement. Med.*, vol. 27, no. 4, pp. 294–311, Apr. 2021, doi: 10.1089/acm.2020.0292.

[10] P. M. Herman, B. M. Craig, and O. Caspi, “Is complementary and alternative medicine (CAM) cost-effective? A systematic review,” *BMC Complementary and Alternative Medicine*. 2005. doi: 10.1186/1472-6882-5-11.

[11] O. Szczurko and H. S. Boon, “A systematic review of natural health product treatment for vitiligo,” *BMC Dermatol.*, vol. 8, no. 1, p. 2, Dec. 2008, doi: 10.1186/1471-5945-8-2.

[12] F. Saeedinezhad, M. Firouzkouhi, A. Abdollahimohammad, and M. Rahnama, “The challenges facing with vitiligo: a phenomenological research,” *Int. J. Pharm. Res. Allied Sci.*, vol. 5, no. 3, pp. 356–364, 2016.

[13] A. Firooz, N. Bouzari, N. Fallah, B. Ghazisaidi, M. R. Firoozabadi, and Y. Dowlati, “What patients with vitiligo believe about their condition,” *Int. J. Dermatol.*, vol. 43, no. 11, pp. 811–814, Nov. 2004, doi: 10.1111/j.1365-4632.2004.02059.x.

[14] I. Ahmed, S. Ahmed, and S. Nasreen, “Frequency and pattern of psychiatric disorders in patients with vitiligo.,” *J. Ayub Med. Coll. Abbottabad*, vol. 19, no. 3, pp. 19–21, 2007.

[15] M. I. Fatani, R. M. Aldhahri, H. O. Al Otaibi, B. B. Kalo, and M. A. Khalifa, “Acknowledging popular misconceptions about vitiligo in western Saudi Arabia,” *J. Dermatology Dermatologic Surg.*, vol. 20, no. 1, pp. 27–31, Jan. 2016, doi: 10.1016/j.jdds.2015.09.001.

CHAPTER 18

ANALYSES OF GLOBAL HEALTH SECURITY EFFECTS THROUGHOUT THE WORLD

Dr. Bhaskar Gaonkar, Assistant Professor, Department of Chemistry,
School of Sciences, B-II, Jain (Deemed to be University),JC Road, Bangalore-560027.,
Email Id-g.bhaskar@jainuniversity.ac.in

Abstract: Global health stability refers to the ability of public health systems to identify, prevent, and respond to threats from infectious diseases wherever they may arise. Health security one of the major concerns throughout the world and its creates good impact on the accuracy of any nation system. The study focuses on the effects of global health security throughout the word. The outcome of the study is help to find out how health security system give results globally and by this system what is the impact of the nations are going through. In future health security will needs to be more promising and super active throughout the world.

Keywords:Global Health Security, Health, Public Health, Security.

1. INTRODUCTION

Global health security is the presence of solid and resilient healthcare systems that are capable of preventing, detecting, and responding to infectious disease threats anywhere in the world. The Centers for the Prevention and Control of Diseases (CDC) works around the clock to safeguard the well-being, safety, and security of Americans and to combat global health threats so that we don't have to fight them here at home. A malady threat anywhere is an illness threat everywhere in today's globalised society.

Global public health security is defined as the proactive and reactive activities required to reduce the danger and impact of acute public health events that endanger people's health across geographical regions and international borders.Population growth, rapid urbanisation, environmental degradation, and antimicrobial misuse are all disrupting the microbial world's equilibrium. New diseases, such as COVID-19, are emerging at an alarming rate, disrupting people's health and starting to cause social and economic consequences. Every year, billions of passengers travel by plane, increasing the chances of infectious agents and their vectors spreading quickly across borders.

Chemical dependence has grown, as has public awareness of potential health and environmental risks such as air pollution and changing the climate. As food production becomes more globalised, so does the risk of contaminated ingredients and foodborne diseases. As the world's population has become more mobile and economic interdependence grows, so do global health threats, and typical defences at national borders could indeed protect against disease or vector invasion.The revised International Health Regulations aim to protect it against international spread of pandemics and other public health emergencies while minimising disruptions to international travel and trade. To that end, the regulations provide official guidelines to member states on a variety of issues The regulations' fundamental premise is that preparation, early detection, and response are required to protect against global health emergency cases. As a result, the regulations require member states to assess their fundamental capacity for successful health oversight and response within two years and to meet core capacity requirements within three years.

The new regulations make it a priority to ensure that public health emergencies are reported to the World Health Organization (WHO) in a timely manner. The previous version of the regulations only addressed three diseases: plague, cholera, and yellow fever. Instead, the new regulations include the concept of a "public health emergency of international concern." The new regulations include a mechanism for determining whether incidents are potential international threats, which will aid countries in defining what events should be reported. 3,7 Within 48 hours, member states must assess any event occurring on their territory and determine whether it is a health emergency for the public using an automated system A disease outbreak, such as SARS (severe acute respiratory syndrome), is always considered to be a possible public health emergency of concern worldwide.

1.1Challenges to compliance:

Despite these criticisms, WHO member states unanimously approved the new regulations. Unless they expressly object by the end of 2007, all member states are bound by their requirements. 15 As of February 2008, no member state had rejected the regulations, 188 had designated National Focal Points, 76 had already assessed their national core capacities, and 50 had nominated persons to the International Health Regulations Roster of Experts.

Australia, Syria, Finland, Sweden, Columbia, France, Georgia, and Germany are among the countries that have already recognised the regulations as domestic law or have incorporated elements of the agreement into their public healthcare legislation.Other countries, including Argentina, Spain, Brazil, South Africa, and the European Union, have enacted administrative regulations citing the new International Health Standards. Other countries, including the United Kingdom18, are considering "all-hazards" approaches to public health legislation reform.Despite these efforts and the recognition of the regulations' importance, several factors may prevent truly federal compliance. This is especially true when compliance may expose nations or areas within countries to risk.

Limited capacity in developing countries

Developed countries have a vested interest in the regulations' success. Many developed countries will be geographically separated from areas where public health emergencies, such as a flu pandemic, could occur. It is in their best interests for countries in high-risk areas to follow the regulations in order to provide early warning so that developed countries can take reasonable action to protect their populations. However, for many developing countries, early detection and reporting of a health crisis may be ineffective.

2. LITERATURE REVIEW

Deliana Richter, [1] et al. discussed the role of noncommunicable diseases in the pursuit of global health security which is Noncommunicable diseases as well as their risk factors are critical for all aspects of infection preparedness and response, influencing factors such as host susceptibility, disease virulence, and health system capacity. This conceptual examination has two goals. First, we employ the Haddon matrix paradigm to develop a framework for evaluating the importance of noncommunicable diseases to health security efforts at all stages of the disaster life cycle: before, while in, and after an event. Second, we use this framework to identify six technological action areas in global health security programmes that are ideal for integrating global health security and non - communicable disease objectives: surveillance, employment services, lab systems, immunisation, risk communication, and sustainable financing.

,Sanjana J. Meyer, [2] et al. establishing a theoretical foundation for measuring global health security explained Since the 2014-2016 West African Ebola epidemic, the concept of measuring health security capacity has grown in importance within the broader context of strengthening health systems, improving responses to public health emergencies, and reducing international catastrophic biological risks. Efforts to track the advancement of health security capabilities and abilities over time, while accounting for political, social, and ecological impacts, could aid countries in their efforts to eliminate sources of health insecurity. We aimed to collect evidence-based principles that capture a country's base - line public health and healthcare capabilities, health security system performance prior to and during infectious disease crises, and the country's broader social, political, security, and environmental risk environments. Methods: To identify evidence- and practice-based identifiers and proxies for measuring health security at the great nation level over time, we conducted a scoping review of British scholarly and grey literature.

Kyle E. Kirkpatrick, [3] et al. explained the crispr revolution and its potential impact on global health security nfectious diseases pose a constant threat to global health security. Despite biotechnology advances that have improved disease diagnosis and treatment, delays in detecting outbreaks and a lack of countermeasures for some bioweapons continue to pose serious challenges to global health security. In this review, we discuss some of the challenges that global health security faces, as well as how genome editing technologies can help to address them. We show how the genome-editing tool CRISPR is being employed to create new tools for characterising pathogenic agents, diagnosing infectious disease, and developing vaccines and therapeutics to counteract the effects of an outbreak. The article also discusses a few of the challenges associated with genetic technologies, as well as the efforts being made by scientists to mitigate them. Overall, CRISPR and genetic technologies have the potential to have a significant positive impact on global health security in the coming years.

Clare Katz, [4] et al. explained Global health security and universal health coverage which is Global health security and universal health coverage have been widely considered as "two separate coins." However, more research is needed to determine whether or not these two ideals collide, as well as what significant differences exist. As a result of ignoring their individual characteristics, global and local health priorities are distorted in an effort to streamline policymaking but also funding activities. This paper investigates the both conceptual and empirical consolidation and divergence between international health safety and universal health coverage. We believe that the analytical concepts of risk and human rights are fundamental to both goals, but we also see differences in priorities between the positive illusions.

Eizabeth Juma, [5] et al. explained Kenyan programmes have helped to develop diagnostic expertise and laboratory capacity. In 2004, the CDC's Global Disease Detection (GDD) programme within Kenya's Division of Global Health Protection (DGHP-Kenya) began close collaboration with the Kenya Medical Research Institute (KEMRI) and established the Testing and Diagnostic Systems Program (DLSP). DLSP supported the expansion of diagnostic expertise and potential in Social communication and interaction and the Ministry of Health, building on previous efforts by malaria, HIV, and tuberculosis (TB) programmes.

Wenham, Clare [6] explained Feminist global health security which Through engagement with feminist concepts of visibility, social and stratified reproduction, intersectionality, and structural violence, Feminist Global Health Confidentiality highlights the ways in which women are disadvantaged by international development security policy. The book contends that a focus on short-term response efforts to health emergencies ignores the differential effects of outbreaks on women. This feminist critique tends to focus on the policy response to

the Zika outbreak, which centred on limiting the vector's spread through civic participation and asking women to postpone foetus, actions that are inherently gendered and reveal a distinguishable lack of consideration for women's daily lives.

Lyttleton, Chris [7] explained Vigilance and Sentinels in Global Health Security which Vigilance is becoming increasingly important in providing early warning of transnational health threats. In theory, this approach requires sentinels to deliver timely alerts of impending risk in communities most affected by new or resurging contagious diseases. Medicalizing global safety implies that specific types of insecurity must be addressed in order to prevent disease spread. I investigate vigilance in the context of the spread of drug-resistant malaria in Southeast Asian border zones, arguing that in order to serve as sentinels, marginalised groups vulnerable to infection have to be able to articulate what social and behavioural factors contribute to the spread of disease risks.

Xia, Han and Yuan, Z6iming discussed high-containment facilities and the role they play in global health security which Biological threats, whether naturally occurring or intentionally released, have the potential to endanger person's life and disrupt economies around the world. Thus, when handling phyto that can cause serious, highly contagious diseases, high-containment security precautions should be implemented; otherwise, devastating pandemics can occur. High-containment facilities play an important role in preventing, detecting, and reacting to threats to global health security in scientific research, healthcare, and product development. In this paper, we provide an overview of the various kinds of high-containment facilities, as well as their applications, obstacles, and future recommendations.

Banda A. Abbey [8] et al. explained the global health security index is not predictive of vaccine rollout responses among oecd countries which The purpose of this study was to assess the usefulness of the Global Health Security (GHS) index in forecasting the start of COVID-19 vaccine rollout by Organization for the Cooperation and Development of Nations (OECD) member countries. Methods: The GHS index was used to collect country-level data on preparedness to reply to dangers from infectious diseases through vaccination rollout. The OECD member states were ranked according to the portion of their population numbers fully immunised against COVID-19. The countries were ranked from lowest to highest, with a score of one to 33 assigned to each. A Spearman's rank correlation was also performed between the GHS index and the number of people that is fully vaccinated. Results: Israel, currently ranks 34th in the world for pandemic preparedness on the GHS index, had the highest number of people fully vaccinated against COVID-19 within two months of the global vaccine rollout. The Spearman correlation coefficient between the GHS index and the percentage of fully vaccinated population was -0.1378, with a p-value of 0.43. Conclusion: The findings indicate a lack of correlation between the Globally harmonized index rating and OECD countries' COVID-19 vaccine rollout, implying that the GHS index may not accurately reflect OECD countries' preparedness for infectious disease threats.

3. DISCUSSION

The idea of global health is based on research from the last several decades. The term "global health" first appeared in scientific literature in the 1940sIt was later used as guidance and theoretical basis by the World Health Organization (WHO). Until the 1990s, few scholars discussed the concept of global health, and the number of papers on this topic has risen rapidly in the following decade when global health was promoted under the Global Health Initiative - a global health plan signed by U.S. President Barack Obama Global health in the United States has promoted collaborations across countries to deal with challenging medical and health issues via government money, development aids, building capacity, education,

scientific research, policymaking, and implementation as a key part of the national strategy in economic globalisation, security, and international policies.

Dr. Chen presented his own thoughts on the definition of healthcare system to the 2019 GHRP Editorial Board Meeting based on his experience working with Professor Zongfu Mao, the lead Editor-in-Chief, who established the Global Health School at Wuhan University in 2011 and launched the GHRP in 2016.

Dr. Chen described global health in three dimensions in a nutshell. To begin, global health can be viewed as a guiding principle, a splinter group of biomedical sciences, and a specialised discipline within the larger arena of public health and medicine . According to many researchers, global health first serves as a central tenet for persons who want to contribute to the health of the all the people worldwide

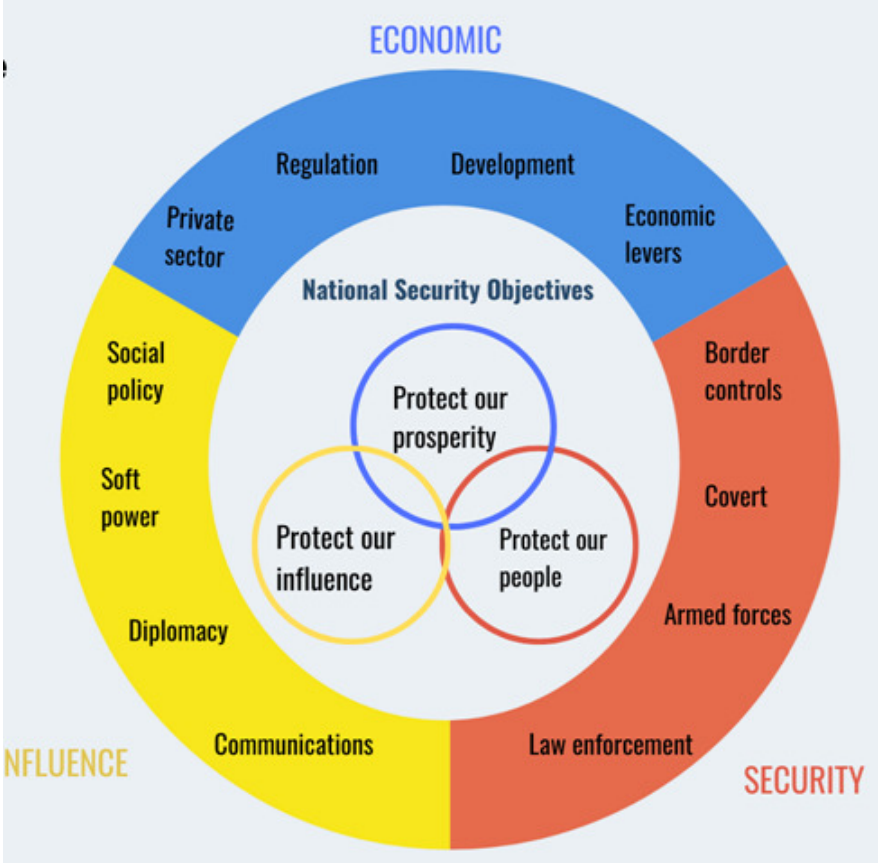


Figure 1: represents the factors of global health security

Second, Dr. Chen's understanding of global health is consistent with that of many other scholars. Global health, as a branch of science, focuses on medical and health issues that have a global impact or can be managed effectively through global solutions As a result, the goal of global health science is to comprehend global medical and health issues and to devise global solutions and implications

Third, Dr. Chen believes that in order to develop global health as a branch of science in the fields of public health and medicine, a specialised discipline, including academic institutions, research entities, and academic societies, must be established. Only with such infrastructure can global health professionals and students receive academic training, undertake global health research, exchange and spread information research findings, and promote global health practices.We have learned and will continue to learn about global health from the

WHO, both historically and developmentally WHO projects are frequently ambitious, involving multiple countries or even having a global scope. The WHO has established a solid base of knowledge, theories, models, methodologies, important data, and a wealth of experiences through research and action projects that can be directly applied in developing global health Examples include WHO's global HIV/AIDS control efforts and Primary Healthcare Programs to promote Health For All.Figure 1 represents the factors of global health security.

3.1 The concept of global impact

Global impact is an important concept in global health. Global health, unlike other public health and medical disciplines, can address any issue that has a global impact on human health, including health system problems that have already affected or will affect a large number of people or countries around the world.

The SARS epidemic that occurred in several areas of Hong Kong could spread globally in a short period of time to cause many medical and public health challengesthe global HIV/AIDS epidemic ; and the novel coronavirus epidemic that first broke out in December 2019 in Wuhan and quickly spread to many countries around the world

With the rapid and uneven pace of globalisation, economic growth, and scientific progress, an increasing number of medical and health issues with global implications emerge. Growing health disparities, migration-related medical and health issues, internet abuse, the spread of sedentary lifestyles and lack of physical activity, obesity, increasing rates of substance abuse, depression, suicide, and many other emerging mental health issues are typical examples. GHRP anticipates receiving and publishing more studies addressing these issues from a global health perspective, and it encourages more researchers to seek global answers to these issues.

3.2 The concept of global solution:

Global solution is another concept related to global impact. What do we mean when we talk about global solutions. Global health, in contrast to conventional public health and medical understanding, selectively targets difficulties with global implications.

Such problems are frequently only effectively addressed at the macro level through cross-cultural, globally, and/or global collaboration and cooperation among various entities and stakeholders.

Furthermore, as long as the problem is solved, it will benefit a large population This type of intervention is referred to as a global solution. For example, the WHO's 90-90-90 strategy is a global solution means of ending the HIV/AIDS epidemic ; the measures used to end the SARS epidemic are a global solution , as are the ongoing measures to control influenza , malaria , and the measures taken by China, WHO, and many countries around the world to control the new coronaviral outbreak that began in China

Many emerging health problems, such as cardiovascular disease, sedentary lifestyle, obesity, online abuse, drug addiction, tobacco smoking, suicidal behaviour, and other issues, require global solutions global solutions are frequently frameworks, policies, strategies, laws, and regulations rather than medical interventions or procedures for individual patients.Given its ability to penetrate physical barriers and reach a large audience quickly, using social media to deliver intervention strategies represents a promising approach in the establishment of global solutions.

3.3 Canada's role in global security:

Canada has the opportunity to lead in this new global approach to emerging threats to public health. However, its first responsibility is to become compliant with revised regulations. The ability of Canada to comply ought not to be taken for granted. It will be difficult to build the necessary core capacity as well as the necessary surveillance and reporting systems.The SARS outbreak revealed a shortage of capacity and appropriatesystems, as well as the ramifications of such gaps. The surveillance systems, in particular, were ineffective, and there were no information-sharing protocols in place. The failure to notify WHO in a timely manner resulted in the implementation of an avoidable travel advisory. When an affected care attendant travelled to the Philippines, Canada's lack of capacity endangered other countries with weaker health infrastructures.

The most recent report, released in May 2008, identified challenges that this country will face in adhering to the revised International Health Regulations. 4 Inability to comply endangers Canadians and sends a message to less developed countries that regulations are not a priority.

Canada has taken significant steps to comply with the regulations, including the designation of a National Focal Point and the passage of new quarantine legislation. However, the Auditor General identified two major challenges: the lack of an inclusive national surveillance system and mechanisms to ensure timely domestic journalism to allow the National Focal Point to meet its global notification requirements.Intergovernmental disagreements have hampered this country's efforts to develop monitoring systems. Despite its innovation in establishing the Global Public Health Intelligence Network — WHO's early-warning system Canada has failed to develop an integrated national surveillance system. This is primarily due to the fact that such a system would have to have interoperable features and data-sharing capabilities. Obtaining provincial contract on these issues remains a challenge.

4. CONCLUSION

The presence of solid and resilient healthcare systems capable of preventing, detecting, and responding to dangers from infectious diseases anywhere in the world is defined as global health security. The Centers for Disease Control and Prevention (CDC) works around the clock to protect Americans' health, safety, and security, as well as to combat world health threats so that we don't have to fight them now at home. In today's globalised society, a disease threat anyplace is an ailment threat everywhere.The Global Health Security Agenda (GHSA) objectives will necessitate not only a "One Health" approach to combat natural disease threats to humans, animals, and indeed the environment, in addition to a security focus to combat deliberate dangers to human, animal, and agricultural health, as well as to nations' economies.

REFERENCES:

[1] D. Kostova, P. Richter, G. Van Vliet, M. Mahar, and R. L. Moolenaar, "The Role of Noncommunicable Diseases in the Pursuit of Global Health Security," *Heal. Secur.*, 2021, doi: 10.1089/hs.2020.0121.

[2] S. J. Ravi, D. Meyer, E. Cameron, M. Nalabandian, B. Pervaiz, and J. B. Nuzzo, "Establishing a theoretical foundation for measuring global health security: A scoping review," *BMC Public Health*. 2019. doi: 10.1186/s12889-019-7216-0.

[3] K. E. Watters, J. Kirkpatrick, M. J. Palmer, and G. D. Koblentz, "The CRISPR revolution and its potential impact on global health security," *Pathogens and Global Health*. 2021. doi: 10.1080/20477724.2021.1880202.

[4] C. Wenham *et al.*, “Global health security and universal health coverage: From a marriage of convenience to a strategic, effective partnership,” *BMJ Glob. Heal.*, 2019, doi: 10.1136/bmjgh-2018-001145.

[5] E. Hunsperger *et al.*, “Building laboratory capacity to detect and characterize pathogens of public and global health security concern in Kenya,” *BMC Public Health*, 2019, doi: 10.1186/s12889-019-6770-9.

[6] C. Wenham, *Feminist global health security*. 2021. doi: 10.1093/oso/9780197556931.001.0001.

[7] C. Lyttleton, “Vigilance and Sentinels in Global Health Security,” *Med. Anthropol. Cross Cult. Stud. Heal. Illn.*, 2018, doi: 10.1080/01459740.2017.1423071.

[8] B. A. Khalifa *et al.*, “The Global Health Security Index is not predictive of vaccine rollout responses among OECD countries,” *Int. J. Infect. Dis.*, 2021, doi: 10.1016/j.ijid.2021.09.034.

CHAPTER 19

ANTI-MICROBIAL, ANTI-CANCER AND CARDIOPROTECTIVE ACTIVITY OF RESVERATROL

Dr. Soumya V. Menon, Assistant Professor, Department of Chemistry,
School of Sciences, B-II, Jain (Deemed to be University),JC Road, Bangalore-560027.,
Email id-v.soumya@jainuniversity.ac.in

ABSTRACT: Resveratrol (RV), a well-known polyphenolic substance found in many plants, such as grape, groundnuts, and berry fruits, is widely recognized for its interconnections to a number of health advantages, such as cardioprotective, anti-obesity, antitumor, anti-age effects, neuro-protective, antioxidants, antidiabetic, and glucose metabolism. Surprisingly many different bacterial, viral, and fungal species are susceptible to the antimicrobial effects of resveratrol. In addition to that, a variety of studies have also suggested the cardio protective and anti-cancer activity of Resveratrol. It has been noted that there are very less studies documenting the evidence on the anti-microbial, anti-cancer and cardio protective activity of resveratrol. Hence, the present study aims at developing the said gap. The study also provides a critical discussion on the challenges which comes while putting resveratrol from lab to clinic for patient use which involves the estimation of safe uses as well as more information of its interaction with other medications.

KEYWORDS: Antimicrobial, Anti-cancer, Disease Phytoalexin, Resveratrol .

1. INTRODUCTION

Plants are vulnerable to infections and diseases as a result of their evident exposure to microorganisms and related microbial assaults. Therefore, plants build up a stockpile of secondary metabolites that are anti-microbial, which they utilise as defence against harmful bacteria and to manage the illnesses and infections that occur from them. Those antimicrobial secondary metabolites are referred to as phytoalexins collectively. Antimicrobial compounds are phytoalexins. A class of low-molecular-weight photochemicals called phytoalexins accumulate in plants after interacting with microbes to suppress them. When the pathogen is discovered, the plant produces phytoalexins as a consequence of an induced response mechanism that secretes antibiotic substances to the diseased areas.

In this way, phytoalexins may function not just as plant defences but also as antimicrobials that fight human illness. One important phytoalexin found in tobacco plants, hydroxycoumarin scopoletin (6-methoxy-7-hydroxycoumarin), has antibacterial action. It caused reactive oxygen species to become more active in scavenging. They are fundamentally not biodegradable because of their stable architectures, which means that once created, they might bio-accumulate and have a long-lasting impact. Thus, plants have long been reliable suppliers of pharmaceuticals both directly and indirectly, including many of the medicines that are now on the market. For instance, a broad range of plant-derived active principles representing a variety of chemical compounds have shown activity consistent with their potential application in the treatment of diabetes mellitus. Numerous diseases that impact the general physiology of plants and the health of all living creatures are found in association with plants. When pathogen elicitors are detected, phytoalexins—constitutive chemical defences against microbial attacks—are often triggered.

Phytoalexins have a huge range of chemical properties and biological functions. Their different plant sources may be the source of the diversification. Therefore, resveratrol—a prototype of and a well researched phytoalexin—was investigated in order to fulfil the review's objective. Numerous studies have linked resveratrol to improved human health,

particularly cancer and heart disease prevention. Resveratrol functions primarily via processes connected to its ability to reduce oxidative stress, presumably by greatly increasing the production of nitric oxide, or NO, which may function as an antioxidants. Human disease has been linked to increased oxidative stress, and attempts to manage and control human disease have been centred on reducing (or avoiding the beginning of) oxidative stress.

This review may provide an update on the present uses of phytoalexins as shown by resveratrol and may also offer profound insight into potential uses for phytoalexins in the treatment of diseases and the prevention of human health problems in the future. The 2-D and 3D structure Resveratrol is provided in the Figure 1 and Figure 2 respectively and other details are enlisted in Table 1.

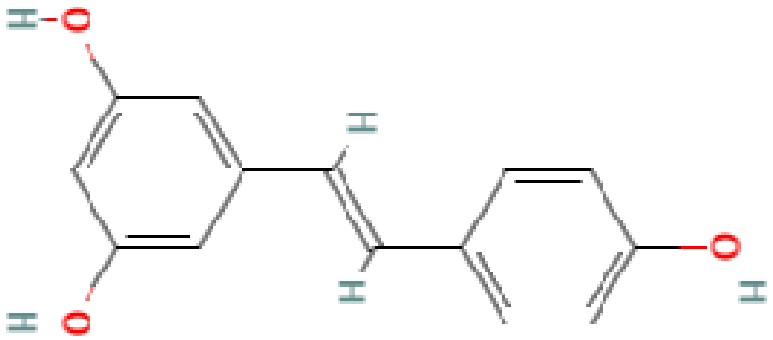


Figure 1: Illustrating the 2-Dimensional structure of Revesterol.

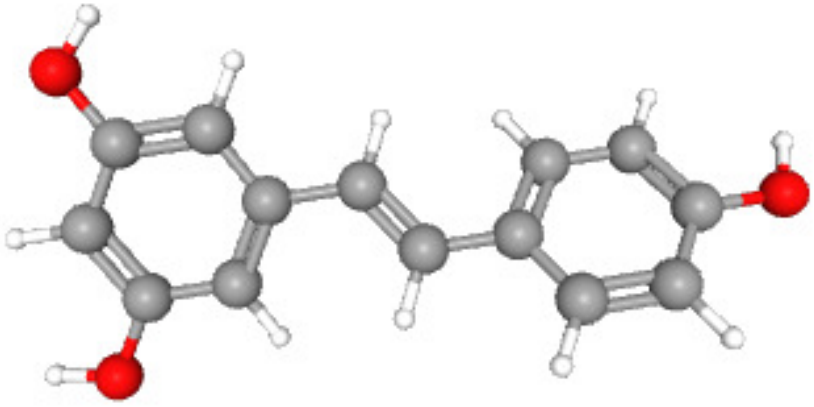


Figure 2: Illustrating the 3-Dimensional structure of Revesterol.

Table 1: Enlisting the details about PubChem ID, Synonyms, Molecular Weight and Chemical Formula.

PubChem ID	445154
Synonyms	trans-resveratrol, 3,4',5-Trihydroxystilbene, 3,5,4'-Trihydroxystilbene
Molecular Weight	228.24
Chemical Formula	$C_{14}H_{12}O_3$

Plants produce phytoalexins, which are toxic to the invading organism. They could pierce the cell wall of pathogen, postpone development, interfere with metabolism, or stop reproduction. Phytoalexins are substances produced by plants that are poisonous to the invader. They may disrupt metabolism, inhibit reproduction, delay development, or penetrate the cell walls of pathogens. In spite of the fact that phytoalexins are typically targeted at specific predators, a plant having anti-insect phytoalexins may not be able to resist a fungal assault. When a plant senses pathogen particles or particles from damaged cells, it responds in two ways: immediately with a general response and later with a specialised response. In order to eliminate invading cells as part of the induced resistance, or short-term responses, the plant employs free radicals, such as superoxide and hydrogen peroxide. The hypersensitive mechanism is a characteristic short-term response in pathogen contacts, in which apoptosis-impaired cells try suicide to create a physical barrier for the invader.

One of the phytoalexins is resveratrol, and it has been extensively studied in preclinical settings for use as a nutraceutical and a therapeutic agent for a wide range of diseases. Its applicability is especially fascinating for patients with cancer because of the significant risks associated with traditional medicines like surgery and chemotherapy. Because of the intricacy of the networks that cancer cells employ for communication, specific inhibitors that target just one network are unable to successfully treat cancer. The purpose of this review is to provide a thorough analysis of the compound's medicinal potential.

1.1.Anti-microbial activity

In their work, Vestergaard et al. discovered that resveratrol exhibits antibacterial activity against an astonishingly wide range of bacterial, viral, and fungal species. Resveratrol inhibits the development of virulence characteristics in bacteria at subinhibitory doses, which decreases the production of toxins, limits the formation of biofilms, slows motility, and disrupts quorum sensing (Figure 3). When used with conventional antibiotics, resveratrol boosts the deadly effects of fluoroquinolones on Escherichia coli and Staphylococcus aureus while decreasing the lethal effects of aminoglycosides on the same bacteria [1].

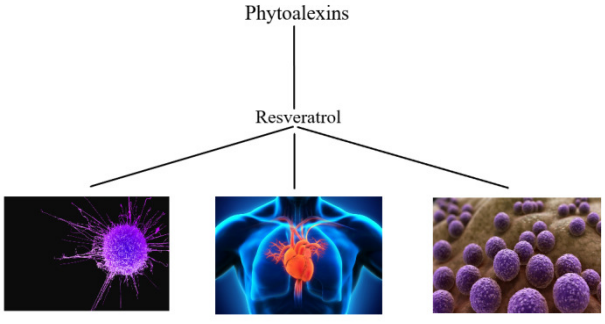


Figure 3: Illustrating the various pharmacologic effects of resveratrol.

The in vitro oligomerization of resveratrol by soybean peroxidase was carried out by Mauricio Mora-Pale et al. In thier study, the antibacterial activity of the two isomers (resveratrol-trans-dihydrodimer and pallidol) generated was evaluated. In vitro, the active dimer demonstrated >90% reduction of DNA gyrase activity by inhibiting the enzyme's ATP binding site suggesting that the resveratrol-trans-dihydrodimer operates to (1) disturb membrane potential and (2) limit DNA synthesis therefore providing the action mechanisms and preliminary assessment of an effective bactericide, as well as a platform for the synthesis of polyphenolic [2].

Resveratrol can cut the dose of itraconazole and ketoconazole to 1/64, according to research by J. Wang et al. Additionally, the synergistic anticandidal effect of resveratrol coupled with azoles was shown against even a panel of clinical C. albicans isolates, as well as the combination approach increased the sensitivity of three fluconazole-resistant isolates to azoles [3].

Chen et al. reviewed resveratrol's antiviral and anti-inflammatory doses and mechanisms. Researchers suggested that the NF-B signalling pathway is a crucial and frequent molecular pathway through which resveratrol exerts its anti-inflammatory and antiviral benefits since viral infections are frequently accompanied by inflammation. Future research should focus on the NF-B signalling pathway's upstream signalling molecules to better understand the anti-inflammatory and antiviral effects of resveratrol [4].

1.2. Cardio-protective activity

Cheng et al. summarised the extensive effects of resveratrol on lifespan regulation, stress resistance, circadian clock, energy metabolism, exercise mimicry, and microbiome makeup in their assessment of the most recent research on the molecular underpinnings of resveratrol-mediated beneficial properties. They also highlighted the unfavourable and erratic effects of resveratrol that have been seen in both preclinical and clinical research, as well as an update on resveratrol's ability to induce cardiac protection [5].

According to Micha Wiciski et al., resveratrol enhanced Sirtuin-1 levels, that also block the TLR4/NF-B/STAT signal cascade and reduce the cytokines production in activated microglia. TNF-alpha (tumour necrosis factor-alpha), histamine, and PAF (platelet-activating factor), that are pro-inflammatory compounds secreted by mast cells and macrophage, were decreased by resveratrol [6].

In rats with streptozotocin (STZ)-induced diabetic mellitus, N Bostanceri et al. examined the effects of the antioxidants resveratrol, quercetin, and melatonin, on apoptosis and cardiomyopathy. While the cardiac tissue of the Diabetes mellitus group showed necrosis, vacuolization, infiltration, congestion, and destruction of myofibrils, the heart tissue of the control group had normal histology. Comparing the DM group to the control group, apoptosis was considerably higher in the DM group.

1.3. Anti-cancer activity

The involvement of Reservatrol in the treatment and prevention of cancers, with an emphasis on colorectal and skin cancer, was emphasized by Elshaer et al. The molecular processes behind its therapeutic and chemopreventive effects are also covered. The difficulties of using resveratrol clinically are highlighted in our last section, along with efforts to address them [7].

Using the MDA-MB-231 cell line, Antoniraj et al. designed and assessed the anti-cancer efficacy of resveratrol-loaded nano-carriers with redox responsive disulfide. By using a

hemolytic experiment to test the NC's biocompatibility, it was determined that the NC was safe up to a level of 200 g/mL. Final findings highlighted the development of the R-applicability NC's for stimulus regulated redox and pH-responsive therapeutic agents in the treatment of cancer.

2. METHODOLOGY

This review research was conducted utilising an electronic database search that included Google Scholar, PubMed, Science Direct, Scopus, and Research Gate. A mixture of keywords was used to search a search strategy to get the relevant data. Records were excluded if they included non-extractable data, inadequate information, or duplicate research. Manual retrieval of the studies was also carried out in order to locate any missing pertinent information. Figure 4 depicts the approach utilised to carry out the review research.

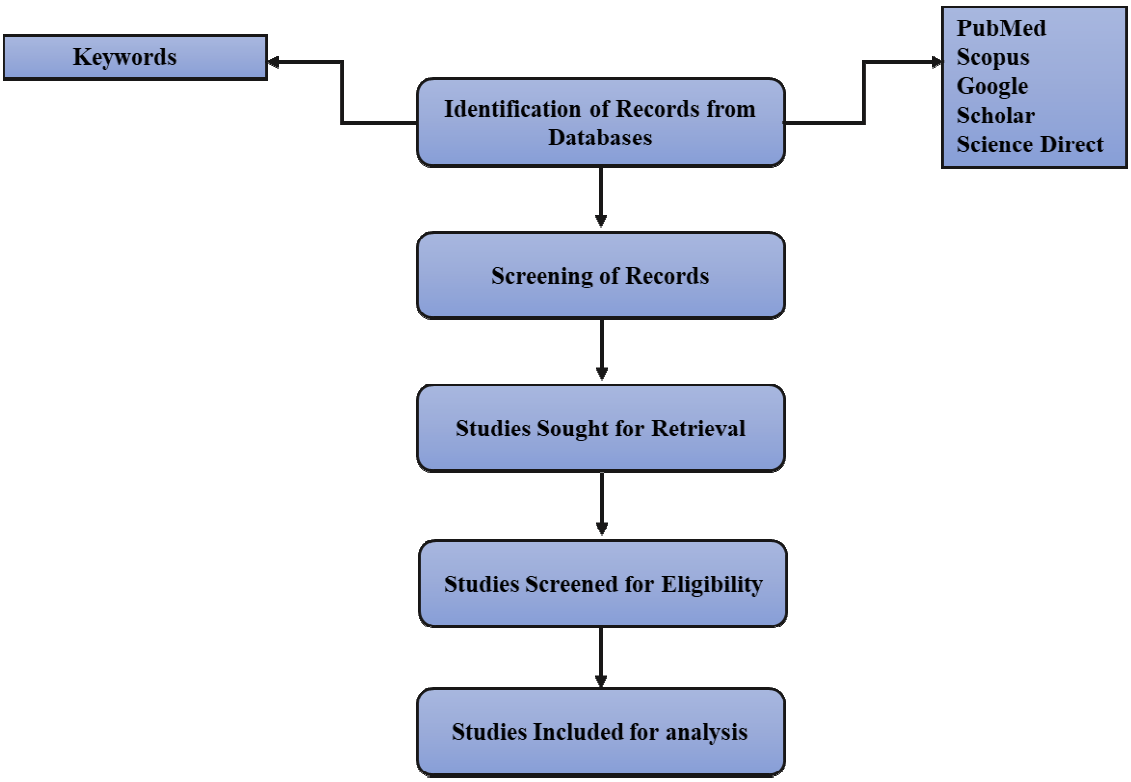


Figure 4: Illustrating the methodologies used to carry out the review study.

3. DISCUSSION

The disparities between preclinical and clinical trial outcomes may be due to resveratrol's inability to penetrate the necessary tissues or cells. Despite the fact that resveratrol treatment has extraordinary beneficial effects in a wide range of cell types, the low resveratrol bioavailability during in vivo research (such as animal studies and human trials) may limit its therapeutic potential. Resveratrol concentrations in target tissues or cells must be raised in order to maximise therapeutic advantages. This calls for the creation of a better medicine delivery system. Different nanotechnologies, such as nanoparticles and liposomes, have been used to transport resveratrol to particular tissues in order to maximise its cardioprotective properties and minimise adverse effects. In a Phase I clinical trial, resveratrol was micronized, and patients with hepatic metastases had 3.6-fold greater plasma levels and more resveratrol transported to their livers. Nanocarriers and/or micronized resveratrol are two potential treatments for the low bioavailability of resveratrol in living organisms. Further study is required to optimise these delivery techniques. The synergistic effects of resveratrol

when taken with other supplements or exercise must be considered as compared to resveratrol given alone. Resveratrol, which has several beneficial impacts on health, is present in a variety of foods consumed by people. Despite encouraging results from in vitro activities and animal studies (preclinical), there remains ambiguity about safety when the predicted dose in people is administered. Although there is debate about their therapeutic effectiveness, resveratrol-based neutraceuticals are widely utilised worldwide. Even though the outcomes of all these studies on hypotheses have been very helpful, there has only been a limited amount of activity that has been verified in people. Resveratrol has been examined in human clinical studies for colon and colorectal cancer, type 2 diabetes, hepatic metastases, and cardio-protection, with promising results. Clinical research on resveratrol for a range of illnesses still has to be done in a number of different ways.

Numerous pharmacological investigations on resveratrol are being conducted in an effort to increase the drug's bioavailability, increase its stability, and lessen its toxicity. The present research offers in-depth information on the therapeutic potential of resveratrol, issues with drug administration, and different methods employed to boost the drug's bioavailability. It is thus expected that this discussion would spur scientists to develop the finest resveratrol medication delivery system.

The effects of Resveratrol have been inconsistently seen in studies conducted in preclinical and clinical settings. The conversion of preclinical discoveries into health benefits in clinical trials seems to be a challenging process. Studies back up the claims that resveratrol supplements may reduce LDL cholesterol, improve FMD, and lower systolic blood pressure. For instance, after taking a resveratrol-rich grape supplement containing 350 mg daily for six months, 75 persons using statins had lower levels of oxLDL and apolipoprotein B. Additionally, resveratrol administration did not always result in a better metabolic profile. It's interesting that a recent meta-analysis of randomised clinical trials with over 700 participants failed to find any significant differences in LDL and HDL levels after resveratrol treatment. To bridge the knowledge gap between animal research and human trials, consider the following factors.

Resveratrol may be able to prevent or delay the onset of a number of illnesses, including cancer, heart disease, damage brought on by ischemia events and chemicals, diabetes, pathological inflammation, and viral infection in animals. Although the medicine has a very low bioavailability and is swiftly removed from the bloodstream, these effects are still there. Since hazardous effects have been seen at or above 1 g per kg, it may not be possible to deliver higher doses to boost efficacy (body weight). Furthermore, to provide a daily dose of 100 mg per kg (body weight) of resveratrol to a 75 kg person would need 2.7 kg of resveratrol yearly, costing close to US$6,800. It will thus be more important than ever to block resveratrol from being metabolised, develop analogues with improved bioavailability, or find alternative, more potent compounds that mimic its actions.

Rats given doses of 300 mg/kg (body weight) showed no detrimental effects147, and studies on rodents often used doses of up to 100 mg/kg (body weight) despite the fact that the maximum tolerated dose of resveratrol has not yet been thoroughly determined (S1). As of right now, humans can expect peak serum concentrations of 2.4 nM unmodified resveratrol and 180 nM total resveratrol from a dose equivalent to two glasses of red wine, and 9 nM real resveratrol and 680 nM total resveratrol from a high, though pharmaceutically relevant, dosage of 100 mg per kg of resveratrol (predicated on rats and mice data). These predictions might be altered (body weight). Although it has been demonstrated that intestinal mucosa has a 30-fold enrichment of resveratrol above serum concentrations185 and that the bile, stomach, liver, and kidneys have a significant accumulation of resveratrol, there are

insufficient data to predict the peak concentrations in the majority of organs. In the long term, it will be important to focus on figuring out whether the metabolites portray inactive types of the drug, behave as a stream out of which free resveratrol can be released in different tissues, or are actively involved in promoting many of the medical benefits pertaining to resveratrol. This is because in vivo concentration levels of individual chemical compounds may be more than ten times more than those produced by the native compound.

Additionally, it's critical to consider any potential interactions between resveratrol and other dietary components. It has been demonstrated that resveratrol functions best when combined with other substances, such as quercetin and ellagic acid to cause apoptosis in human leukaemia cells, ethanol to suppress iNOS expression, vitamin E to prevent lipid peroxidation, catechin to protect PC12 cells from alpha-amyloid toxicity, as well as nucleoside analogues to prevent HIV-1 replication in cultured T lymphocytes. These results could help us comprehend how a little quantity of resveratrol from red wine or other dietary sources might have a significant positive impact on human health.

4. CONCLUSION

Due to its clear usefulness as a dietary component that prevents cancer, protects the heart, reduces inflammation, and antimicrobial action, resveratrol has appeared to be one of the most intriguing naturally occurring compounds with a tremendous therapeutic potential. The efficacy of diet or supplemental resveratrol in preventing cardiovascular disease, and delaying the onset of cancer and its prevention is being investigated in studies. Actually, resveratrol and its analogues exhibit pharmacological safety and can be combined with other medicines to improve therapeutic effectiveness and reduce side effects. Resveratrol has positive pharmacological activity, although its pharmacokinetic characteristics are not as good as they may be. According to a number of studies, trans-resveratrol is generally quickly absorbed, processed, and eliminated in both people and animals, showing a low bioavailability of resveratrol that impairs its biological effects. Resveratrol can accumulate to bioactive amounts in target organs, however this has to be shown. With conflicting outcomes, a number of research have attempted to provide an explanation. To solve this issue, resveratrol carriers and site-specific delivery methods have been created to safeguard and stabilise resveratrol as well as to improve its bioavailability, maintaining its biological and pharmacological properties. Despite the advancements gained, creating size-tuned carrier systems with improved lipophilicity is still necessary to transport resveratrol to harder-to-reach locations, such the brain.

REFERENCES:

[1] M. Vestergaard and H. Ingmer, “Antibacterial and antifungal properties of resveratrol,” *Int. J. Antimicrob. Agents*, vol. 53, no. 6, pp. 716–723, Jun. 2019, doi: 10.1016/j.ijantimicag.2019.02.015.

[2] M. Mora-Pale *et al.*, “Antimicrobial mechanism of resveratrol- trans -dihydrodimer produced from peroxidase-catalyzed oxidation of resveratrol,” *Biotechnol. Bioeng.*, vol. 112, no. 12, pp. 2417–2428, Dec. 2015, doi: 10.1002/bit.25686.

[3] J. Wang *et al.*, “The synergistic antifungal activity of resveratrol with azoles against Candida albicans,” *Lett. Appl. Microbiol.*, 2021, doi: 10.1111/lam.13458.

[4] J. Wang *et al.*, “The synergistic antifungal activity of resveratrol with azoles against Candida albicans,” *Lett. Appl. Microbiol.*, vol. 72, no. 6, pp. 688–697, Jun. 2021, doi: 10.1111/lam.13458.

[5] C. K. Cheng, J. Luo, C. W. Lau, Z. Chen, X. Y. Tian, and Y. Huang, “Pharmacological basis and new insights of resveratrol action in the cardiovascular system,” *Br. J. Pharmacol.*, vol. 177, no. 6, pp. 1258–1277, Mar. 2020, doi: 10.1111/bph.14801.

[6] M. Wiciński *et al.*, "Beneficial effects of resveratrol administration—Focus on potential biochemical mechanisms in cardiovascular conditions," *Nutrients*. 2018. doi: 10.3390/nu10111813.

[7] M. Elshaer, Y. Chen, X. J. Wang, and X. Tang, "Resveratrol: An overview of its anti-cancer mechanisms," *Life Sci.*, vol. 207, pp. 340–349, Aug. 2018, doi: 10.1016/j.lfs.2018.06.028.

CHAPTER 20

AN INVESTIGATION OF HEALTH BENEFITS AND POSSIBLE SIDE EFFECTS OF KETOGENIC DIET

Sujayaraj S, Assistant Professor, Department of Forensic Science,
School of Sciences, JAIN (Deemed-to-be University), Karnataka,
Email Id- samuel.sujayaraj@jainuniversity.ac.in

ABSTRACT: The ketogenic diet is a moderate protein, high fat, low carbohydrate diet where the source of energy is ketone bodies rather than glucose. It was originally intended to treat epileptic seizures but has proven to provide many other health advantages such as fat loss, weight loss, improved glucose, skin glow, and insulin levels, and many other therapeutic properties. The body will enter a condition of "ketosis" if individual follow a ketogenic diet. Given the scarcity of a complete, multidimensional assessment of the ketogenic diet (KD) in connection to health concerns, authors compiled research on the influence of ketogenic diet on the epigenome, diabetes, microbiome, weight reduction, cardiovascular health, and cancer. The KD diet may enhance the genetic diversity of the microbiome and the ratio. Therefore, the aim of this study is review on the health benefits of ketogenic diet. In addition to that, the author also provides a discussion on side effects of KD diet which further limits the application of KD.

KEYWORDS: Carbohydrate, Microbiome, Ketosis, Ketogenic Diet, Fat.

1. INTRODUCTION

The Ketogenic Diet is a high-fat diet that seems to assist certain epileptics, particularly youngsters. It is not a cure-all, but it is an alternative to the different anti-epileptic drugs that are now accessible. For certain children, the ketogenic diet provides better seizure management and, in some situations, increased mental alertness with less drugs. The ketogenic diet is sometimes seen as a tough regimen to adhere to; but, with experience and a knowledge of what the diet seeks to accomplish, it may be reduced to a reasonable routine. The main goal is to shift the body's major fuel source away from carbs (such as bread and sugar) and toward fats [1]–[3].

This is accomplished by increasing fat consumption while drastically lowering carbohydrate consumption. The main challenge is that the diet is so tight that all things consumed must be measured out to a tenth of a gram during meal preparation, and participants are not allowed to eat anything that has not been "approved" by the dietician. Because the quantity of carbs permitted is so minimal, even the little amount of sugar in most liquid or chewable drugs will prevent the diet from functioning. A typical dinner can consist of some form of meat with green veggies cooked in a mayonnaise sauce or with a lot of butter. Heavy cream may be served on the side as a drink. Another lunch may include bacon and eggs with plenty of butter or oil, as well as heavy milk to drink. To be effective, the diet must maintain an extremely high fat-to-carbohydrate ratio while consuming a low overall calorie intake [4].

Over the last several centuries, both internationally and in Asia, the prevalence of obesity and overweight concerns has increased quickly. Obese people are those whose BMI is 25 or above. Obesity often develops when calorie intake exceeds need and calorie expenditure is lower. Extra body fat increases the likelihood of developing major health conditions including hypertension, Type 2 diabetes, PCOS/PCOD, cardiovascular disease, arthritis, sleeping disorders, even certain types of cancer, as well as physiological difficulties like poor

self-esteem, sluggishness, and depression. Dietary adjustments and the addition of physical activities/exercises are part of the treatment for obesity. One such diet that aids in weight loss and is getting popular is the ketogenic diet.

The ketogenic diet was first created to treat epilepsy, and Rollin Turner originated the phrase in 1921. Since the 1920s and 1930s, patients with epilepsy have often used a ketogenic diet to manage their condition. This is because studies have shown that extended fasting reduces the frequency of seizures in epileptic patients. Although the exact mechanisms through which the ketogenic diet treats epilepsy are still not known. However, it is increasingly often used to treat obesity.

1.1. Different Types of Ketogenic Diets

1. Standard Ketogenic Diet (SKD): This is a diet that is rich in fat, moderate in proteins, and extremely low in carbohydrates. It comprises 5–10% carbohydrates, 20% protein, and 70–75% fat (Figure 1).

2. High-protein ketogenic diet: This diet has a higher protein intake and has a macronutrient composition of 35% protein, 60% fat, and 5% carbohydrates.

3. Cyclic Ketogenic Diet: This diet comprises regular intervals of days with a lot of carbs. For instance, a cycle of a 5-day ketogenic diet succeeded by 2-days of heavy carbs.

4. Targeted ketogenic diet: To boost training endurance and avoid muscle loss, this diet incorporates more carbohydrates around the time of an intense physical workout. However, the amount of carbs varies on the kind and length of exercise [5].

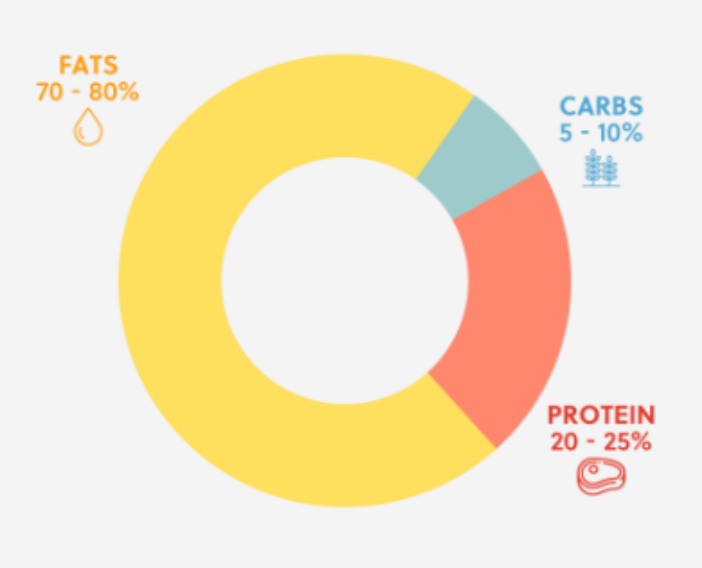


Figure 1: Illustrating the percentage or the proportion of fats, carbohydrates and proteins.

1.2. Ketosis Biochemistry

Fat from dietary fats and adipose tissue are both used in the formation of ketones bodies. Ketogenesis, sometimes referred to as the production of ketone bodies, takes place in the mitochondrial matrix of liver cells. The adipokine causes the release of fatty acids by sending signals to reduce insulin, higher glucagon, and epinephrine levels. Low glucose availability conditions, such as fasting or starvation, are correlated with high glucagon and low insulin levels. Following their bonding with coenzyme A, fatty acids are able to enter mitochondria.

Once within the mitochondria, the attached fatty acids are largely utilised as fuel by cells by -oxidation, which splits the Acyl-CoA molecule in half to generate acetyl-CoA in each cycle. AcetylCoA enters the citric acid cycle, where it engages in an aldol condensation with oxaloacetate to produce citric acid. After entering the krebs cycle, citric acid produces the original fatty acid per carbon high energy yield (Figure 2). Any cell may metabolise acetyl-CoA via the Krebs cycle, but the mitochondria of liver cells are also capable of ketogenesis [6].

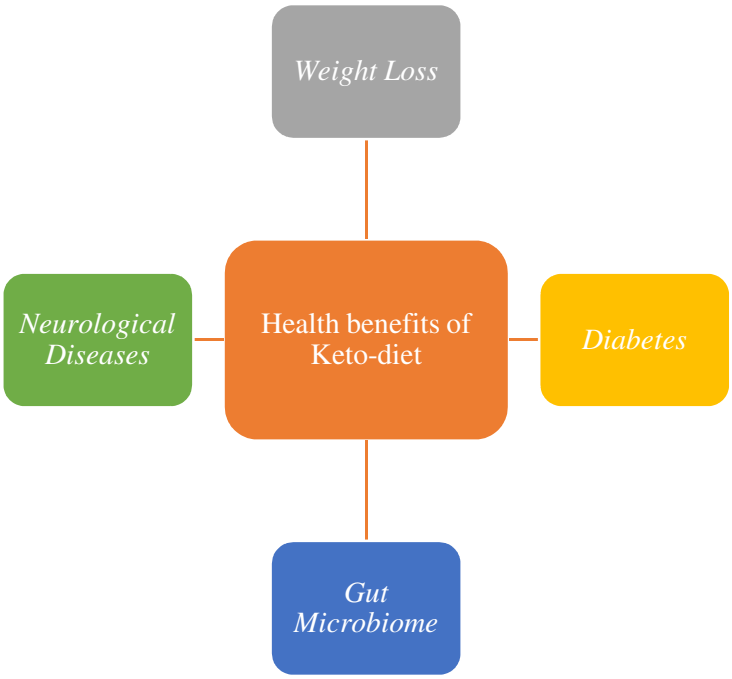


Figure 2: Illustrating the various Health benefits of Ketogenic diet.

1.3. Effect of Keto-diet on Gut Microbiome

In a recent research, Basciani et al. investigated the effects of isocaloric ketogenic diets with different protein sources on the intestinal microbiota of obesity, insulin-resistant individuals. The vegetable, whey, or animal foods were all included in the very low-calorie ketogenic diets (VLCKDs). Following 45 days, the findings showed that all groups exhibited a growth in Bacteroidetes and a drop in Firmicutes relative abundance. But, the group that ingested animals sources of protein had fewer obvious favourable improvements [7].The microbiota of individuals with normal cognition or moderate cognitive impairment was examined in a research by Nagpal et al. to compare the effects of a modified Mediterranean Ketogenic Diet (MMKD) with the American Heart Association Diet (AHAD). At 6 weeks, researchers discovered that the Firmicutes or Bacteroides phylas in the MMKD had not significantly changed. They did, though, observed a decline in the family Bifidobacteriaceae and an upsurge in the family Verrucomicrobiaceae, which was regarded as a favourable alteration. The MMKD also showed a rise in the advantageous SCFA butyrate. Butyrate has a reputation for improving gut health [8].

1.4. Effect of Keto-diet on Diabetes and Weight Loss

According to the investigation by Ellenbroek et al., a long-term KD led to a decreased ability to tolerate glucose, which was linked to inadequate insulin production by -cells. Mice receiving a KD after 22 weeks had decreased insulin-stimulated glucose uptake, decreased islet volume with an elevation in fewer islets, pro-inflammatory state, including hepatic steatosis symptoms [9].

In 56 patients with Type 2 diabetes in a Chinese population, Wang et al. examined the safety and effectiveness of an LCD vs. an LFD; individuals who followed an LCD decreased their HbA1c levels more than individuals who followed an LFD, with really no safety issues. In a large study, 115 obese individuals with Type-2 diabetes were randomized to follow either an low-fat diet for 52 weeks, isocaloric high-carbohydrate, high-unsaturated fat diet or a very-low-carbohydrate. Both diets led to a reduction in body weight and an improved performance in HbA1c, although there were no discernible difference between the two groups. Additionally, the LCD had substantial improvements in blood sugar variability, lipid profile (perhaps explained by the low-carb diet's high proportion of unsaturated fat and low proportion of saturated fat), and the need for diabetic medication [10].In a study by Hallberg et al., diabetic individuals were monitored on a ketogenic diet for a year. In the ketogenic treatment, 92% of the patients were obese at the start of the research. To keep BHB blood levels between 0.5 and 3.0 mmol/L, these individuals were told to consume no more than 30 g of total carbohydrates daily. With certain patients attaining as high as a 40% improvement, these patients' body weight decreased on average by 12%. The individuals who participated in the standard care of American Diabetes Association-recommended diet group did not see any appreciable changes in body weight [11].

1.5. Effect of Keto-diet on Neurological Diseases

According to Arora & Mehta et al., the ketogenic diet (KD) may be used to treat acute neurological diseases such status ischemic stroke, traumatic brain injury, epilepticus, and primary aggressive brain tumour. The theorised mechanism of the ketogenic is described together with a summary of the research literature, including both clinical as well as pre-clinical investigations. Along with the typical side effects and dose guidelines, they studied several commercially available ketogenic diet formulations [12].

2. METHODOLOGY

Google Scholar, PubMed, Science Direct, Scopus, and Research Gate were used to conduct the electronic database search for this review research. A search method was used to get the relevant information using a combination of keywords

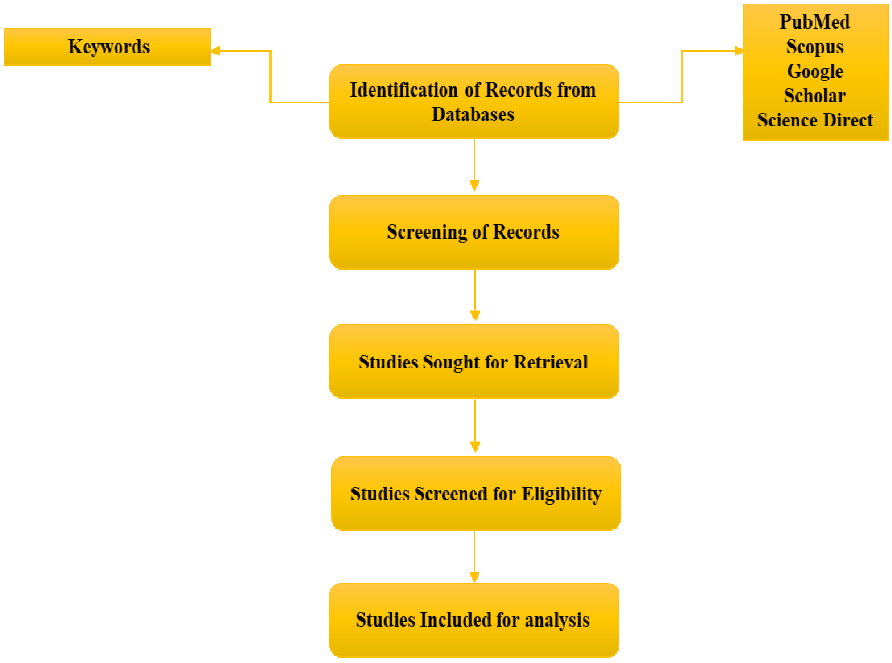


Figure 3: Illustrating the Block Diagram of Methodology used to carry out the review Study.

. Records were excluded if they had un-extractable data, inadequate information, or duplicate research. In order to find any pertinent records that may have been overlooked, manual retrieval of the studies was also done. Figure 3 below shows the approach that was employed to conduct the review research.

3. DISCUSSION

Studies have revealed that ketogenic diets often only function in the short term and may even be harmful. When the body enters ketosis, it also has a tendency to experience energy loss, extreme weakness, and eventually starvation. Losing weight is far more difficult in practise. stated he doesn't believe the ketogenic diet causes muscle loss. He cautioned that trying to build up strength wasn't the best course for everyone.

Many health support experts who were polled had more cautionary remarks. Ketogenic diets cannot be taken for shorter periods of time or when being directly observed. In the long term, it could be more harmful. Another organ that is vulnerable to damage is the heart. who, in specific circumstances, applied ketogenic diets to certain cancer patients, issued the following warning: "People are trying anything they can to reduce weight and keep it off. Any of them upped the ante on the ketogenic diet by using a feeding tube that was placed through the nose into the stomach. Dieters follow a strict 900-calorie, high-protein, low-carb diet that is provided via a pipe by a low-drip recirculation pump (Figure 4). Only coffee or tea, black coffee, or green tea drink is allowed in addition to the low carbohydrate diet. offered to support the claim that the ketogenic diet is beneficial and healthful, but only for people looking to shed a few pounds. An already healthy individual may have serious problems, such as infectious infections, whether the pipe gets infected, raised salt content, and might even result in vomiting, constipation, and diarrhoea, as stated in the article "It is a dumb way to reducing weight." As an alternative, anybody preparing to be married should take care of themselves, engage in a lot of physical activity, such as jogging, cycling, or riding a bike, and then improve their own health by consuming natural, nutrient-rich foods[13].

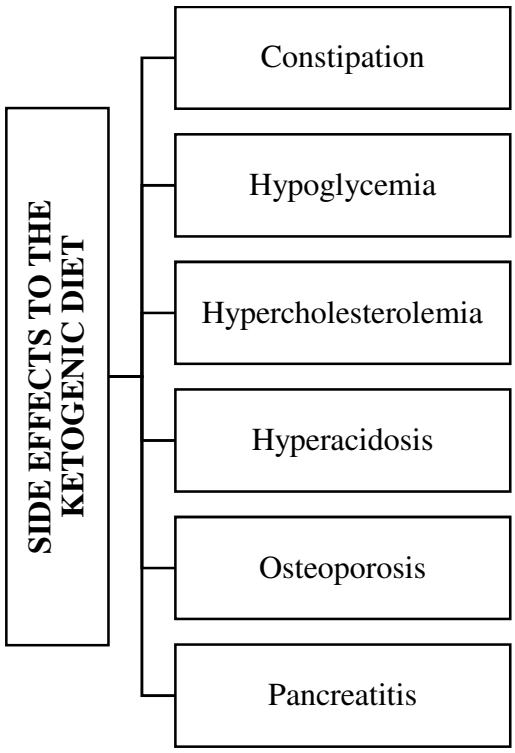


Figure 4: Illustrating the variety of common side effects of Ketogenic diet.

1. Constipation: Almost everyone who starts a diet has this. We have solutions to the issue, thus it has never been a justification for quitting the diet.

2. Hypoglycemia: This condition may be problematic for autonomous, energetic kids. The participant's family is instructed on the signs of hypoglycemia as well as what to do if you think the participant may be hypoglycemic. The dietician should be called to modify the diet if the person often experiences hypoglycemia.

3. Hypercholesterolemia: Some individuals have trouble metabolising the high quantities of fat in their diet, which causes their lipid (cholesterol and triglyceride) levels to rise. To reduce the blood lipid levels, we could advise a mineral supplement or try changing the cuisine. Diet is stopped if the lipid levels do not recover to a healthy level.

4. Hyperacidosis: Ketones of some participants may get excessively high if they become sick or become extremely active, which causes them to become dehydrated. They could get nauseous in this circumstance and turn down food. There might be some vomiting involved. Rehydrating would be the course of action. Dietary changes or the use of Bicitra may be necessary if the issue persists.

5. Osteoporosis: The diet has been linked to the disease. To decrease the severity of this issue, vitamin and calcium supplements are recommended for everyone starting the diet.

6. Kidney Stones: Participants in many ketogenic diet programmes around the nation are advised to limit their fluid consumption. We have opted not to impose a hydration restriction in New Mexico, and kidney stone development among participants has seldom been an issue. But this has to be taken into account if someone starts to complain of excruciating back pain, urinating problems, or blood in their urine. To attempt to address the issue, we could advise Bicitra, but if kidney stones reappear, the diet might need to be stopped.

7. Pancreatitis: The pancreas is an organ situated behind the kidneys in the belly. In order to break down fat, the pancreas is primarily responsible. The increased fat content of the ketogenic diet may be too much for the pancreas in some individuals. In certain situations, the pancreas swells or is inflamed, and the gastrointestinal (GI) system as a whole malfunctions. The patient has acute stomach pain, and the area is very sensitive to touch. Vomiting often follows. In this case, the patient has to be treated and diagnosed by medical professionals right away. The ketogenic diet is promptly abandoned and never tried again if a person contracts pancreatitis while following it. Pancreatitis may result in death.

There isn't a miracle pill to permanently lose weight, it is said. A Caribbean-style diet consisting of vegetables, fruits, whole grains, peas, fish, and vegetable oil that is acceptable for human consumption is recommended for long-term weight management. No one diet is suitable for everyone, especially given the wide range of individual metabolisms, genetics, body types, habits, and tastes. Additionally, ketogenic diets may be effective for those who are overweight, obese, or at risk for coronary heart disease. However, it may be difficult for individuals to stick to this diet if they favour high-fat foods but also love carbs. In the near future, ketogenic diets may be utilised to aid in weight loss and to improve health, mood, and other factors. However, this requires a lot of work, therefore eating healthfully must go along with it. Therefore, ketogenic diets may never be the best option for both serious weight-gainers and elite athletes.

Due to the key roles played by meat, poultry, fish, and fruits and vegetables, vegans and vegetarians may also struggle with such a diet. In contrast, switching to a ketogenic diet may sometimes result in unpleasant symptoms that are occasionally referred to as "keto flu". It may result in diminished energy, impaired mental clarity, decreased appetite, insomnia, diarrhoea, abdominal discomfort, and less effective exercise. Even if this is seldom the case, if someone starts out appropriately, it may give them the motivation to quit, especially because the first few weeks of any diet are the most difficult. Ketogenic diets might thus never be the best option for those who prefer to go on vacation due to the very low carbohydrate intake—less than 50 to 60 grammes per day.

It is crucial to remember that the ketogenic diet has sparked discussion, even though conventional dietary instruction has long highlighted the negative consequences of a high consumption of total fats, including trans fats. The misconception that a ketogenic diet necessitates a high consumption of animal products may have contributed to polarisation by causing concern among individuals who favour plant-based diets for ethical, ecological, or safety reasons. Additionally, the ketogenic diet can be vegetarian or organic (including poultry and meat products), and it can include plant-based foods like avocado, almonds, nuts, linseed, and coconut oil as well as foods high in protein like yoghurt, lupini, kimchi, tempeh, pumpkin, etc. Such versatility necessitates the individualism of food preferences on a ketogenic-diet for obesity and diabetes.

People who suffer renal failure (such as those with type 2 diabetes) and those who have or are at risk for cardiovascular disease, particularly breast-feeding mothers or pregnant women, do not follow the ketogenic diet. However, those with type 1 diabetes should avoid the menu because to the likelihood of hypoglycaemia (low); also, people who have previously had their gallbladder removed should avoid it since it is too high in fat. It is true that losing weight requires a diet, plan, and often a rethink of how people eat. Additionally, it could be good to attempt to lose weight or get some of the medical conditions that have been shown to get better. To be safe, it's important to see a doctor about whether the ketogenic diet is good for you and how you can drastically alter your eating habits. Although the keto diet has medical roots, it has only recently become widely popular, and physicians are aware of it. The following suggestions are made in light of the consequences of the ketogenic diet:

1) In addition to focusing on eating high-fat foods, it's important to include a variety of fish, meat, vegetables, berries, and leafy greens in your diet on a daily basis to ensure that you're getting the nutrition, minerals, and vitamins A, B, etc. (magnesium, zinc, iron) that are typically found in foods like whole wheat but are now restricted.

2) Potential symptoms of acute creatine supplementation, which may last weeks to months, should be addressed with medical evaluation by professionals as well as nutritionists, such as nausea, weariness, a bad attitude, fatigue, indigestion, vomiting, and constipation in the brain.

3) Diabetic patients who inject insulin or use oral hypoglycemic medications run the risk of significant hypoglycemia if their medicine is not taken as prescribed before starting a diet.

4. CONCLUSION

Low carbohydrate consumption may be achieved with a well-planned ketogenic diet that also includes sufficient fiber-rich foods including seeds, nuts, coconut, avocado, spinach, broccoli, cauliflower, and berries. All of these nutrient-dense pre-biotic meals would work in concert to enhance Bacteroides and Bifidobacterium while lowering Firmicutes. It is crucial to establish the safety, effectiveness, and potentially life-saving advantages of alternative diets given the fast rise in illness rates in the United States and other developed countries. It may

be found that patients need to be provided customised diets depending on the species that make up their microbiome. This would make it possible for patients to consume certain meals that will improve their capacity to maintain nutritional ketosis and their general health outcomes. The microbiome may need to be regularly monitored in order to continuously modify and vary dietary requirements for variety. Additionally, it may be found that faecal microbiota transplants are required to completely shift and transform the microbiome at the start of a new diet, which may then be further increased and adjusted by diet. However, much more study is required to establish the impact of the ketogenic diet on the microbiota.

REFERENCES:

[1] D. D. Weber, S. Aminzadeh-Gohari, J. Tulipan, L. Catalano, R. G. Feichtinger, and B. Kofler, "Ketogenic diet in the treatment of cancer – Where do we stand?," *Mol. Metab.*, vol. 33, pp. 102–121, Mar. 2020, doi: 10.1016/j.molmet.2019.06.026.

[2] A. Paoli, L. Mancin, A. Bianco, E. Thomas, J. F. Mota, and F. Piccini, "Ketogenic Diet and Microbiota: Friends or Enemies?," *Genes (Basel).*, vol. 10, no. 7, p. 534, Jul. 2019, doi: 10.3390/genes10070534.

[3] M. Ułamek-Kozioł, S. J. Czuczwar, S. Januszewski, and R. Pluta, "Ketogenic Diet and Epilepsy," *Nutrients*, vol. 11, no. 10, p. 2510, Oct. 2019, doi: 10.3390/nu11102510.

[4] A. Paoli, "Ketogenic Diet for Obesity: Friend or Foe?," *Int. J. Environ. Res. Public Health*, vol. 11, no. 2, pp. 2092–2107, Feb. 2014, doi: 10.3390/ijerph110202092.

[5] R. Dhamija, S. Eckert, and E. Wirrell, "Ketogenic diet," *Can. J. Neurol. Sci.*, 2013, doi: 10.1017/S0317167100013676.

[6] R. Bressler, "THE BIOCHEMISTRY OF KETOSIS*," *Ann. N. Y. Acad. Sci.*, vol. 104, no. 2, pp. 735–752, Dec. 2006, doi: 10.1111/j.1749-6632.1963.tb17705.x.

[7] S. Basciani *et al.*, "Very-Low-Calorie Ketogenic Diets With Whey, Vegetable, or Animal Protein in Patients With Obesity: A Randomized Pilot Study," *J. Clin. Endocrinol. Metab.*, vol. 105, no. 9, pp. 2939–2949, Sep. 2020, doi: 10.1210/clinem/dgaa336.

[8] R. Nagpal, B. J. Neth, S. Wang, S. Craft, and H. Yadav, "Modified Mediterranean-ketogenic diet modulates gut microbiome and short-chain fatty acids in association with Alzheimer's disease markers in subjects with mild cognitive impairment," *EBioMedicine*, vol. 47, pp. 529–542, Sep. 2019, doi: 10.1016/j.ebiom.2019.08.032.

[9] J. H. Ellenbroek *et al.*, "Long-term ketogenic diet causes glucose intolerance and reduced β- and α-cell mass but no weight loss in mice," *Am. J. Physiol. Metab.*, vol. 306, no. 5, pp. E552–E558, Mar. 2014, doi: 10.1152/ajpendo.00453.2013.

[10] Bolla, Caretto, Laurenzi, Scavini, and Piemonti, "Low-Carb and Ketogenic Diets in Type 1 and Type 2 Diabetes," *Nutrients*, vol. 11, no. 5, p. 962, Apr. 2019, doi: 10.3390/nu11050962.

[11] S. J. Hallberg *et al.*, "Effectiveness and Safety of a Novel Care Model for the Management of Type 2 Diabetes at 1 Year: An Open-Label, Non-Randomized, Controlled Study," *Diabetes Ther.*, vol. 9, no. 2, pp. 583–612, Apr. 2018, doi: 10.1007/s13300-018-0373-9.

[12] N. Arora and T. R. Mehta, "Role of the ketogenic diet in acute neurological diseases," *Clin. Neurol. Neurosurg.*, vol. 192, p. 105727, May 2020, doi: 10.1016/j.clineuro.2020.105727.

[13] M. Khatri, "Ketosis: Definition, Keto Diet, Symptoms, and Side Effects," *WebMD*, 2020.

CHAPTER 21

REASSESSMENT OF COMBINED ORAL CONTRACEPTIVES AND THEIR SIDE EFFECTS

Manashree Avinash Mane, Assistant Professor,
Department of Forensic Science, School of Sciences, JAIN (Deemed-to-be University), Karnataka,
Email Id- m.manashree@jainuniversity.ac.in

ABSTRACT: Oral contraceptives (OCs), often referred as "the pill," represent the most frequent contraceptive method among teenage females. Ovulatory inhibition is the principal action mechanism. Furthermore, contraceptive pills result in an endometrium that really is inhospitable to ovum implant and cervical mucus which thickens and then becomes hostile to sperm movement. The combination hormonal tablet containing oestrogen and progesterone is the most usually prescribed prescription. Progesterone is the hormone that inhibits conception, whereas oestrogen regulates monthly bleeding. Birth control tablets are generally used to prevent pregnancy. The efficiency of this method of birth control is referred to as normal and ideal usage. However, there are still side effects associated with the use of combined oral contraceptives. Here, the aim of the present paper is to discuss the side effects of these oral contraceptives with clear understanding of the avaialable evidence linking use of these form of contraception with different types of cancers.

KEYWORDS: Estrogen, Oral contraceptives, Pill, Progesterone.

1. INTRODUCTION

A means of preventing unintended pregnancy is contraception. Due to their effective contraception and favourable tolerability profile, combined oral contraceptives (COCs) have gained popularity as a birth control strategy. These tablets include hormones that influence a female reproductive system, producing contraceptives like progesterone and estrogen. OCs are either a progestin-only substance or an estrogen-progestin combo. Over time, OCs have evolved as a result of the introduction of 17-estradiol, different generations of progestin, and a steady decrease in the dosage of ethinylestradiol (EE). There are other varieties of progesterone and oestrogen that are utilised in tablets, including mestranol, a kind of oestrogen, and norethynodrel and 3-methyl ether of EE, a kind of progestin; its original dosage was 9.85 mg per tablet. Although the effectiveness in of the contraceptive clinical testing was great, the medication also produced a number of adverse effects, including nausea, dizziness, headaches, stomachaches, and vomiting. These symptoms were reported by 17% of the women participating in the clinical research. However, a woman who was using contraceptive pills was reported to have died in 1961. Despite the fact that different methods of administering COCs have been established after so many years, OCs have evolved due to lower oestrogen doses and the discovery of a new generation of progestins. The results of earlier study indicate that these medications have potentially serious negative effects. As a result, the emphasis of this brief research is on a general review of the female reproductive system and how it is regulated, hormonal contraceptive pills, how these medications work, and the adverse effects of OC pills [1], [2].

A total of 14% of women who use OCPs do so for non-contraceptive purposes, while the majority do so to avoid conception. Breakdown of conceptive use in U.S. population in illustrated in Figure 1. In example, menstrual-related illnesses such irregular menstruation, fibroids, menstrual pain, endometriosis-related pain, and menstrual-related migraines may all be treated with OCPs. For select brands, the FDA has officially authorised combination acne medications.

Compelling epidemiologic data suggests that women who have used combined OCs have a 50% lower chance of developing endometrial cancer than women who have never used combined OCs. Up to twenty years pass before this impact fades. Ovarian cancer risk is reduced by 27% with combined OC usage; the longer the use period, the higher the risk reductions. Additionally, OCs have been shown to significantly lower colon cancer risk, by 18%. Even hirsutism and acne are indicated for therapy with certain formulations [3].

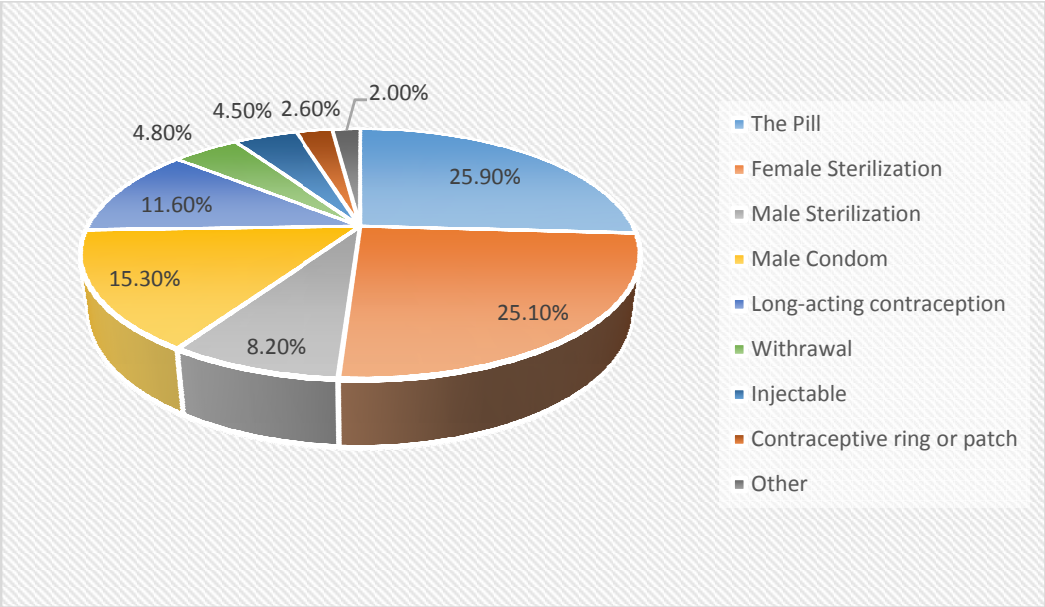


Figure 1: Illustrating the Percentage of Contraceptive Use by Types, National Centre for Health Statistics, CDC.

The main hormone that prevents pregnancy is progesterone. The primary method of action is ovulation suppression; they impede follicular growth and stop ovulation. The hypothalamus uses progesterone negative feedback to reduce pulse frequency of gonadotropin-releasing hormone. That, in return, will limit the release of follicle-stimulating hormone (FSH) as well as luteinizing hormone (LH). There will be no rise in estradiol levels if the follicles is not growing (the follicle makes estradiol). The mid-cycle LH surge is prevented by the progestogen negative feedback and the absence of oestrogen positive feedback. Ovulation is inhibited because no follicle has formed and no LH surge has occurred to liberate the follicle[4].

Since estrogen slows the ability of anterior pituitary to secrete FSH, it exerts a influence on folliculogenesis, but it is less pronounced than progesterone. The capacity of progesterone to prevent sperm from passing through into the upper and cervix vaginal canal by rendering the cervical mucus hostile is another major mode of action. Endometrial atrophy brought on by progesterone ought to prevent implantation, although there is no evidence to support this.

1.1. Combined Oral Contraceptive (COC)

A distinct generation of progestin ingredients with varying degrees of androgenic and progestogenic capability are coupled with the typical oestrogen component. The dosage of oestrogen plus progestin is given depending on the desired results, likelihood of adverse outcomes, and desired effects of the progestin ingredient.

Either ethinylestradiol, estradiol, or estetrol is an oestrogen component The classification of progestin is.

- Norethindrone acetate, Ethynodiol diacetate, Lynestrenol, and Norethynodrel are examples of first-generation progestins.
- dl-Norgestrel, and Levonorgestrel are a second-generation progestin
- Third-generation progestins: norgestimate, desogestrel, and gestodene
- Cyproterone acetate and drospirenone are unclassified progesterones.
- Progesterone-only prescription (POP)

While there are numerous other progestin pill varieties available in the US, norethindrone or drospirenone is most typically seen in compositions. In addition to suppressing ovulation, drospirenone possesses anti-mineralocorticoid properties. Although norethindrone predominantly prevents sperm entry by thickening cervical mucus, it also suppresses ovulation, lowers mid-cycle LH and FSH peaks, which delays the ovum's passage via fallopian tubes, and changes the thickness of the endometrium. Some progestins are more powerfully antiandrogenic than others, making them better at treating conditions including hirsutism, polycystic ovary syndrome, and acne.

2. LITERATURE REVIEW

According to recent research, HPV-positive women who take oral contraceptives for a prolonged period of time may be at an increased risk for cervical cancer. In a research by Jennifer S. Smith, findings from studies published examined combined to assess the connection between HPV infection and the frequency and length of hormonal contraception usage in relationship to in situ and invasive cervical cancer. The results of their research revealed that even though prolonged use of hormonal birth control is linked to a steadily increasing chance of developing cervical cancer, the global health consequences of these findings rely heavily largely on the degree to which the affiliations have persisted after use of hormonal birth control has stopped, and this cannot be properly assessed from published data [5].

Lundberg et al. looked at the likelihood of mammary and gynaecological malignancies in women who had been given an infertile diagnosis. Researchers discovered that there was a link between infertility and a higher incidence of endometrial cancer among 2,882,847 Swedish women. In particular, infertility was not related with a risk of developing breast cancer (aHR 0.96; 95% CI 0.92-1.01), but then was linked to a higher estimated incidence of endometrial cancer (aHR 1.25; 95% CI 1.11-1.40) and ovary (adjusted hazard ratio [aHR] 1.53; 95% CI 1.38-1.71) [6].

Amanual Getnet Mersha et al. conducted a comparative cross-sectional analysis comparing HIV-positive and HIV-negative women visiting the family planning clinic at the Gondar university referral hospital between January 2016 and August 2017. The most popular form of contraception among HIV patients, according to reports, is an intrauterine device. Additionally, among women with poor contraceptive use, unplanned pregnancies were rather prevalent. In order to prevent unplanned pregnancies and stop the spread of HIV, dual contraceptive usage should be encouraged for HIV-positive women [7].

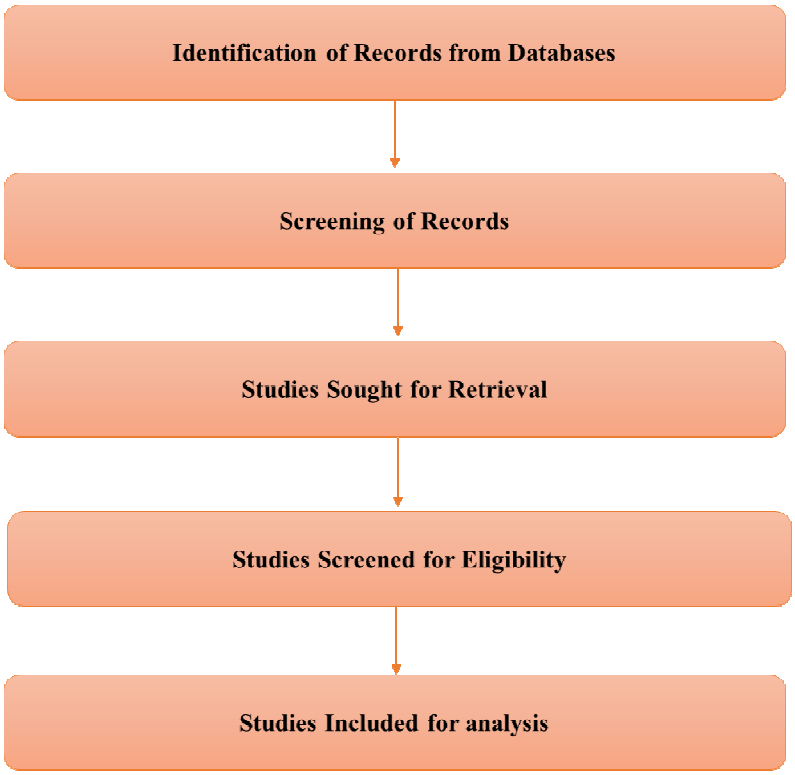
According to a research by Lieske H. Schrijver et al., mutation carrier with ovarian cancer were less likely to take contraceptive pills (ever use: 58.6% for BRCA1 and 53.5% for BRCA2) than unaffected carriers (ever use: 88.9% for BRCA1 and 80.7% for BRCA2) after receiving a diagnosis. In comparison to unaffected BRCA1 and BRCA2 carrier with ovarian cancer, the typical duration of usage was 7 years for both BRCA2 and BRCA1 carriers who had ovarian cancer and 9 and 8 years for those who did not. Univariate analysis for BRCA1

mutation carriers revealed that both an longer period of oral contraceptive usage and much more recent oral contraceptive use were linked to a lower risk of ovarian cancer [8].

Another research by Li-Wei Ji et al. revealed the existence of a substantial linear connection between the age of first OC usage and BC risk. Several BC subtypes determined by progesterone or ER status show no further persistent differences[9].

3. METHODOLOGY

Google Scholar, PubMed, Science Direct, Scopus, and Research Gate, were searched for this review study. To find the pertinent information, a search technique was applied using a variety of terms. Records that had unextractable data, insufficient information, or duplicate studies were eliminated. Additionally, the studies were manually retrieved in order to find any significant data that could have been missing. Figure 2 illustrates the methodology used to conduct the review study.



4. DISCUSSION

Nausea is only one example of a side effect that might be NUISANCE: Taking your medication with meals and eating a snack 4-6 hours after taking your medication may often help you avoid nausea. Some people find that taking the medication just before bed helps to prevent nausea from happening while they are asleep.

When you take your "active" (hormone) tablets and experience bleeding or spotting, this is known as breakthrough bleeding. Make an appointment for a pill follow-up and potential medication adjustment if this persists for two to three months and you have been taking your medications as directed. Set up a "pill follow-up" appointment over the phone if the bleeding is severe.

Breast alterations: You may need to adjust your medication if you have breast discomfort or enlargement that lasts for two to three cycles. There is nothing that has to be adjusted if you have enlarged breasts and this is not an issue for you.

When starting oral contraceptives, weight gain is not typical, although it is possible for some women to experience it while taking certain tablets. Schedule a consultation if you gain or lose more than 10 pounds, since you may need to adjust your medication. There is no medical significance to a gain of 3-5 pounds. Weight loss and weight gain will be equal.

Mood Issues: By ingesting 50–150 mg of vitamin B6 (pyridoxine) daily, mood issues such as fatigue, slight headaches, or malaise (feeling "blah") may be reduced. To determine if the B6 is going to work, give it two months. Health food shops, pharmacies, and supermarkets all have B6, which is quite reasonably priced. Urine will have a brilliant yellow hue since excess is discharged in it (Figure 3).

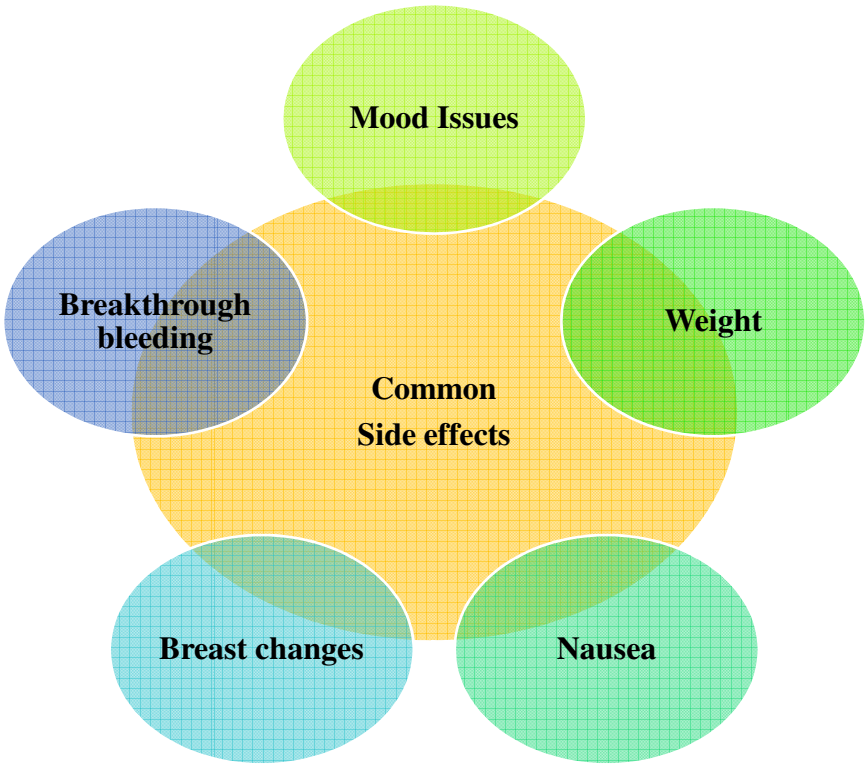


Figure 3: Common Side effects.

Safe and Suitable for Nearly All Women

Nearly all women can use COCs safely and effectively, including women who:

- Are living with HIV, whether or not on antiretroviral therapy
- Are of any age, including adolescents and women over 40 years old
- Are married or are not married
- Have or have not had children
- Have anemia now or had in the past
- Have just had an abortion, miscarriage, or ectopic pregnancy
- After childbirth and during breastfeeding, after a period of time
- Have varicose veins
- Smoke cigarettes—if under 35 years old

Avoid Unnecessary Procedures

Women can begin using COCs:

- Without any blood tests or other routine laboratory tests
- Without a breast examination
- Without cervical cancer screening
- Without a pelvic examination
- without using a pregnancy test. If a woman is relatively confident she isn't pregnant, she may start taking COCs whenever she wants, even if she isn't currently experiencing monthly bleeding (see Pregnancy Checklist, inside back cover).

By carefully advising a woman before prescribing a technique, most of her frustration due to monthly fluctuations may be avoided. To prevent the withdrawal that puts the woman at risk of an unwanted pregnancy, it is essential to have an open discussion about the possibility for bleeding abnormalities during this period. Although a gynecologist's professional, customised review may approve it, certain at-risk women's prescriptions for hormonal contraceptives may be seen as a danger.

Oral contraceptives, particularly those with low oestrogen levels or progestin-only formulations, are generally safe for use by most women with congenital heart disease. Oral contraceptives must categorically be managed to avoid in all patients who have a higher than average risk of developing thromboembolic complications due to Eisenmenger syndrome, pulmonary hypertension, rhythm problems, infectious complications (endocarditis), decreased ventricular function, severe arterial hypertension, or hyperlipidemia. Very successful, without biochemical side effects, and with just a negligible risk of endocarditis are intrauterine devices that release progestin.

5. CONCLUSION

The fundamental mechanism of action of oral contraceptives is the inhibition or postponement of ovulation, which to some degree also prevents fertilisation and implantation. COCs largely inhibits or delays ovulation, according to a number of clinical investigations. For the purpose of delaying pregnancy, millions of women between the ages of 14 and 45 use these medications. Administering COCs or POPs may cause adverse effects in many women, including spotting, weight gain or loss, severe headache, nausea, depression, breast tenderness, darkening of the skin, and vaginal infections. Combination oral estrogen-progesterone contraceptives have been shown to be naturally cancerous in people by significant evidence. Increased risk for cervical, liver, and breast cancer has led to this inference. The carcinogenicity of norgestrel, LNG, progesterone, or progestin-derived birth control tablets hasn't been well supported by animal experiments, however. With continued use, these contraceptives interact with the ovulatory cycle, leading to either delayed or premature ovulation. They do this by acting as progesterone hormone receptor (PGR) and LH receptor (LHR) inhibitors. Nevertheless, it has been shown that certain herbal components function as a small amount of LHR and PGR inhibitors. As a result, while these substances are being eliminated from the body, the ovulation cycle is maintained. We must all try to develop natural alternatives to modern contraceptives that are both potent and secure.

REFERENCES:

1] D. Vásquez-Awad and A. M. Ospino, “Combined oral contraceptives,” *Ginecol. Obstet. Mex.*, 2020, doi: 10.24245/gom.v88i-Supl1.3843.

[2] A. E. de Wit *et al.*, “Efficacy of combined oral contraceptives for depressive symptoms and overall symptomatology in premenstrual syndrome: pairwise and network meta-analysis of randomized trials,” *Am. J. Obstet. Gynecol.*, vol. 225, no. 6, pp. 624–633, Dec. 2021, doi: 10.1016/j.ajog.2021.06.090.

[3] J. Vrbíková and D. Cibula, "Combined oral contraceptives in the treatment of polycystic ovary syndrome," *Human Reproduction Update*. 2005. doi: 10.1093/humupd/dmi005.

[4] G. C. Di Renzo, I. Giardina, G. Clerici, E. Brillo, and S. Gerli, "Progesterone in normal and pathological pregnancy," *Horm. Mol. Biol. Clin. Investig.*, vol. 27, no. 1, Jan. 2016, doi: 10.1515/hmbci-2016-0038.

[5] J. S. Smith *et al.*, "Cervical cancer and use of hormonal contraceptives: A systematic review," *Lancet*, 2003, doi: 10.1016/S0140-6736(03)12949-2.

[6] F. E. Lundberg, A. N. Iliadou, K. Rodriguez-Wallberg, K. Gemzell-Danielsson, and A. L. V. Johansson, "The risk of breast and gynecological cancer in women with a diagnosis of infertility: a nationwide population-based study," *Eur. J. Epidemiol.*, 2019, doi: 10.1007/s10654-018-0474-9.

[7] A. G. Mersha, D. A. Erku, S. A. Belachew, A. A. Ayele, B. M. Gebresillassie, and T. M. Abegaz, "Contraceptive use among HIV-positive and negative women: implication to end unintended pregnancy," *Contracept. Reprod. Med.*, 2019, doi: 10.1186/s40834-019-0084-2.

[8] L. H. Schrijver *et al.*, "Oral contraceptive use and ovarian cancer risk for BRCA1/2 mutation carriers: an international cohort study," *Am. J. Obstet. Gynecol.*, vol. 225, no. 1, pp. 51.e1-51.e17, Jul. 2021, doi: 10.1016/j.ajog.2021.01.014.

[9] L. W. Ji, C. X. Jing, S. L. Zhuang, W. C. Pan, and X. P. Hu, "Effect of age at first use of oral contraceptives on breast cancer risk: An updated meta-analysis," *Medicine (United States)*. 2019. doi: 10.1097/MD.0000000000015719.

CHAPTER 22

MORPHOLOGY, PHOTOCHEMISTRY, AND PHARMACOLOGICAL PROPERTIES OF HIBISCUS

Shashidhar E S, Assistant Professor, Department of Forensic Science,
School of Sciences, JAIN (Deemed-to-be University), Karnataka,
Email Id- es.shashidhar@jainuniversity.ac.in

ABSTRACT: China rose, or Hibiscus rosa Sinensis, is a member of the Malvaceae family. In numerous tropical nations, this plant has a wide range of significant medical benefits for treating wounds, inflammation, fever and coughing, diabetes, infections caused by bacteria and fungus, hair loss, and stomach ulcers. The primary bioactive substances implicated in its therapeutic actions, according to a phytochemical study, include flavonoids, terpenoids, tannins, saponins, or alkaloids. Due to their many applications in recent decades, medicinal plants have drawn a lot of interest. Various kinds of extracts from all portions of H. rosa Sinensis have shown a broad variety of positive benefits in experiments conducted recently, including hypotensive, antipyretic, anti-inflammatory, antioxidant, anti-bacterial, wound-healing, anti-cancer, anti-diabetic, and abortifacient actions. The main objective of this study is to learn more about the pharmacological properties of Hibiscus. In the future through study people will be aware of the medicinal value of Hibiscus.

KEYWORDS: Hibiscus, Morphology, Pharmacological, Photochemistry Therapeutic.

1. INTRODUCTION

Given that it is mostly found in southeast China and a few islands in the Pacific and Indian Oceans, the lovely blooming plant Hibiscus rosa Sinensis is sometimes referred to as the "Queen of the Tropics or China rose. One of Hawaii's beloved national plants, hibiscus, is often worn in the hair for ceremonial purposes. This plant is a seed-producing vascular plant that is a member of the subkingdom Magnoliophyta as well as the class Magnoliopsida. One of the 300 species in the genus Hibiscus, it is a member of the Malvaceae family. Additionally, the juice obtained from the leaves and blossoms has long been utilized as an herbal cosmetic or a natural treatment for a variety of illnesses and uncomfortable sensations. The extract of dark flowers is used to produce eyeliners and to blacken shoes [1], [2]. It was thought that the eminent Swedish scientist Carolus Linnaeus named the species rose Sinensis, which translates to “Rose of China” in Latin, in the early 1750s.

Hibiscus blossoms have historically been used as analgesics, antipyretics, anti-asthmatics, and anti-inflammatory medicines. They have also been claimed to have anticancer qualities. Hibiscus rosa-Sinensis flower petals include anti-oxidant, anti-fungal, and antibacterial effects, according to several research, as shown in Figure 1. Studies using extracts of hibiscus stems, leaves, roots, and flowers have shown that the plant's photochemical elements have contributed to positive health effects for people, such as antioxidant activity, which is the elimination of free radicals that may cause DNA damage. Cassia, also known as Senna bicapsularis L. flower extracts, is another example of a plant source of antioxidants. In rural areas of India, the blossoms were also used as an abortifacient as well as a method of contraception for both sexes [3], [4].

More than 50% of today's therapeutic drugs, according to recent scientific research, are derived from natural products. Many of them have made substantial contributions to the pharmaceutical business and the creation of more effective treatments for different ailments. Due to its application in herbal goods and therapeutic purposes, this plant is quite important

commercially. There is not much scientific study or clinical testing on the chemical extracts of Hibiscus rosa-Sinensis that might be vital in examining its rapid prospective medical uses due to insufficient existing pharmacological knowledge.

Figure 1: Illustrate the pictorial representation of Hibiscus.

1.1. History:

India is where Hibiscus rosa-Sinensis most likely originated. Old Moors (Arabs) think Spain is where it first appeared. Others contend that Hibiscus rosa Sinensis is not a natural plant but rather a collection of artificial hybrids. The name "hibiscus" comes from the Greek word hibiscus, which means white or marshmallow.

1.2. Demographics and location

Hibiscus rosa-Sinensis is quite susceptible to freezing in even moderately cold temperatures. It grows most well in full sunlight and organically rich, well-drained soil. India (southwestern areas), Sri Lanka (tropical regions), Thailand, the Philippines, South Africa, China, Myanmar, and Pakistan are among the nations where it is commonly cultivated.

1.3.Botany and morphology

The perennial plant Hibiscus rosa-Sinensis has tap roots. 3 to 12 cm long and 2 to 5 cm broad describe its leaves. Simple ovate or lanceolate leaves with whole bases and coarsely serrated tips/margins make up the plant's leaves. Flowers are full, penicillate, pentamerous, or actinomorphic. Corolla is three inches in diameter and has five petals. Many types of corollas vary in size and color. Fruit is a 3 cm long capsule that very seldom develops. The optimal growing conditions for Hibiscus rosa Sinensis are well-drained, slightly acidic soils. It employs completely decomposed organic matter in sandy soils to preserve the soil's aeration, drainage, or water-holding capacity. Plants need direct sunshine because insufficient light prevents flowers from blooming. They can, however, endure some shade [5], [6].

2. LITERATURE REVIEW

Ishrat Mahmood Khan et al. studied about pharmaceutical use of Hibiscus. Due to their diverse use, medicinal plants have drawn a lot of interest in recent years. The shoe flower, also known as Hibiscus rosa Sinensis, is a widespread decorative plant throughout the globe. It has long been utilized in cosmetics, food, and medications. The main bioactive components include flavonoids, glycosides, terpenoids, and saponins. Plants are used in pharmacology for

a broad range of purposes, including their anti-fertility, anti-inflammatory, anti-microbial, anti-diabetic, or antipyretic properties. Studies on toxicology showed that using plant extracts in larger amounts is safe [7].

Raj Bala et al. studied the pharmacological and phytochemicals of Hibiscus. Hibiscus Rosa Sinensis Linn, a well-known medicinal shrub, belongs to the plant family Malvaceae. Most frequently, the Hibiscus Rosa Sinensis Linn plant is used to treat a wide range of illnesses, such as those that are anti-tumor, anti-ovulatory, anti-implantation, anti-fertility, anti-inflammatory, anti-estrogenic, analgesic, antipyretic, anti-fungal, anti-spasmodic, anti-viral, anti-fungal, hypoglycemic, anti-bacterial, spasmolytic, and CNS depressant. It will surely become a successful player in the market for herbal supplements, drugs, and the healthcare system because of its diverse pharmacological approach.

3. DISCUSSION

3.1. Applications of pharmaceuticals:

3.1.1. Anti-fertility activity:

Hibiscus rosa Sinensis flower extracts (alcohol, benzene, or chloroform) were tested on male albino rats to see how they affected them. For twenty days, extracts were given at two separate doses (125 mg and 250 mg/kg of body weight). After therapy, there was a noticeable decrease in the amount of sperm in the epididymis or spermatogenic components of the testicles. Because of a reduction in androgen production, the quantity of cholesterol in the testicles rose. In a different investigation, the impact of a crude aqueous extract of Hibiscus rosa-Sinensis on mouse reproductive organs was investigated [8], [9]. Model animals received the extract orally at a dosage of 500mg/kg body weight. The weight of the testis and epididymis both significantly decreased. Additionally, the amount of testosterone was decreased. It also investigated how female albino mice's reproductive systems responded to the benzene extract of Hibiscus rosa-Sinensis. The estrous cycle was disturbed by the thirty-day therapy. Ovarian, pituitary, and uterine weights were also reduced.

3.1.2. Pharmacological activities:

There are several pharmacological advantages to the leaves and flowers of Hibiscus Rosa Sinensis. Its aerial parts' aqueous-ethanolic extract has been suggested for the treatment of diarrhea and constipation. It is a blood purifier and aids in the treatment of cystitis, or bladder irritation. It is also used to treat syphilis and gonorrhea. It is a very excellent natural source of vitamin C. Similar to captopril, other hibiscus types have also been shown to help lower blood pressure [10].

3.1.3. Effect on hair growth:

Effect on hair growth: A 1% liquid paraffin extract was administered topically to the shaved skin of albino rats using an in vivo approach, and the results were monitored carefully for a while. At various intervals of time, the length of hair and the various cyclic stages of hair follicles, such as the anagen and telogen phases, were observed. The hair follicles from neonatal albino rats were separated and cultivated in DMEM with 0.01 mg/ml petroleum ether extract of leaves and flowers using an in vitro approach. It was shown that the leaf extract had more effectiveness on hair growth than the floral extract [11].

3.2. Effect on the estrous cycle:

The loss of implantation caused by ethanol extract was discovered to be caused by anti-zygotic, blastocytotoxic, or anti-implantation action. In ovariectomized immature female rats, oral treatment of the ethanol extract of Hibiscus Rosa Sinensis roots raises uterine weight and

promotes uterine development, indicating estrogenic action. Therefore, giving estrogen to young female rats and mice may have uterotropic consequences.

3.2.1. Effect on blood glucose level:

A hypoglycaemic effect has been seen after oral treatment of the extract combined with glibenclamide for a duration of 7 and 21 days. After 21 days, there has been a maximum reduction in blood glucose, which is 41-46%, as well as an insulin level of 14%. Additionally, it was discovered that the extract reduced blood triglycerides and total cholesterol by 22 or 30%, respectively. This extract's hypoglycaemic action is comparable to that of glibenclamide, however, it is not caused by an increase in insulin levels.

4. CONCLUSION

Rosa sinensis is a potent medicinal plant, and research has shown that it has a number of beneficial traits. Future study on hibiscus and its oil has a lot of potential, particularly in the areas of pharmacology and cosmeceuticals given its many uses. the therapeutic plant Numerous components of Hibiscus rosa sinensis, including the flowers, leaves, or roots, have been shown to have medical effects, including those for oral contraception, laxative, aphrodisiac, menorrhagic, and more. Therefore, the aforementioned plant might be the focus of the majority of research to uncover previously unsolved riddles that would aid the current pharmaceutical industry.

REFERENCES:

[1] I. Prabowo, Iskandarsyah, and R. Adriany, “Characterization and concentration optimization of hibiscus rosa-sinensis l. Mucilage powder as superdisintegrant,” *Int. J. Appl. Pharm.*, 2021, doi: 10.22159/ijap.2021.v13s2.09.

[2] S. Nuryanti, S. Matsjeh, C. Anwar, and T. J. Raharjo, “INDIKATOR TITRASI ASAM-BASA DARI EKSTRAK BUNGA SEPATU (Hibiscus rosa sinensis L),” *Agritech*, 2010.

[3] S. Z. Raduan, M. W. H. Abdul Aziz, A. H. Roslida, Z. A. Zakaria, A. Zuraini, and M. N. Hakim, “Anti-inflammatory effects of Hibiscus rosa-sinensis L. and Hibiscus rosa-sinensis var. alba ethanol extracts,” *Int. J. Pharm. Pharm. Sci.*, 2013.

[4] L. Hibiscus *et al.*, “INDIKATOR TITRASI ASAM-BASA DARI EKSTRAK BUNGA SEPATU (Hibiscus rosa sinensis L) Indicator of Acid-Base Titration from the Extract of Hibiscus rosa sinensis L Flower,” *J. Agritech*, 2012.

[5] D. Pakaya, M. Dewi, A. L. Antari, and I. Saraswati, “Ekstrak Hibiscus rosa-sinensis L. Memperbaiki Kadar Glukosa Darah Puasa dan Jumlah Sel Mast pada Model Tikus Diabetes Terinfeksi Mycobacterium tuberculosis,” *J. Farm. Galen. (Galenika J. Pharmacy)*, 2020, doi: 10.22487/j24428744.2020.v6.i1.13930.

[6] Y. Syaula, A. L. Antari, and D. A. Purbaningrum, “Pengaruh Perendaman Ekstrak Bunga Sepatu (Hibiscus rosa sinensis L.) terhadap Pertumbuhan Candida albicans pada Plat Resin Akrilik,” *e-GiGi*, 2021, doi: 10.35790/eg.9.2.2021.34104.

[7] I. M. Khan, R. Rahman, A. Mushtaq, and M. Rezgui, “Hibiscus rosa-sinensis L . (Malvaceae): Distribution , Chemistry and Uses,” no. October, 2019.

[8] H. M. Shen *et al.*, “The N-butyl alcohol extract from Hibiscus rosa-sinensis L. flowers enhances healing potential on rat excisional wounds,” *J. Ethnopharmacol.*, 2017, doi: 10.1016/j.jep.2017.01.016.

[9] R. Dwi Farasayu, M. Winnie Rachmawati, I. Dewi Ana, A. Syaify, and D. Listyarifah, “ The Effect of Hibiscus Flower Extract (Hibiscus rosa-sinensis L.) on the Growth of Streptococcus sanguinis Bacteria ,” *BIO Web Conf.*, 2021, doi: 10.1051/bioconf/20214107006.

[10] S. Singh, A. Gupta, A. Kumari, and R. Verma, “Antimicrobial and Antioxidant Potential of Hibiscus Rosa-Sinensis L. in Western Himalaya,” *Biol. Forum-An Int. J.*, 2019.

[11] I. Rostina, S. A. Kusumawati, and A. Salamah, “Comparative morphological analysis of ovaries in Hibiscus rosa-sinensis L. single pink, crested peach and double orange flowers,” in *Journal of Physics: Conference Series*, 2021. doi: 10.1088/1742-6596/1725/1/012044.

CHAPTER 23

AN EXPLORATORY STUDY OF BACTERIOPHAGE THERAPY AND ITS FUTURE POTENTIAL IN THE HEALTHCARE INDUSTRY

Dr. Vichar Mishra, Assistant Professor, Department of Forensic Science,
School of Sciences, JAIN (Deemed-to-be University), Karnataka,
Email Id- m.vichar@jainuniversity.ac.in

ABSTRACT: Bacteriophages, which are bacteria's natural predators, have recently been identified as having useful applications in contemporary biotechnology. For several bacterial strains that are resistant to antibiotics, they have been suggested as replacements. Phages may be employed as biocontrol agents in the oil sector and agriculture. Additionally, phages are employed as delivery systems for several proteins or antibodies, as well as DNA and protein vaccines, for the detection of harmful bacterial strains. Bacteriophages are a varied collection of viruses that are simple to handle, making them useful in biotechnology, exploration, and medicine. The main goal of this study about the future of bacteriophage therapy in the healthcare sector. In the future, this study will aware of the application of bacteriophage in the healthcare industry.

KEYWORDS: Bacteriophage, Bacterial Cells, Medicine, Therapeutic Agents, Vaccination.

1. INTRODUCTION

The most prevalent creatures on the planet are bacteriophages. These bacterial viruses are made up of genetic material that is encapsulated by a protein coat and may take the form of DNA or RNA. The fiber-filled tail of the capsid, which is connected to it, is employed to adhere to receptors on the surface of bacterial cells. Except for filamentous phages, the majority of phages contain polyhedral capsids. Phages may spread via two different life cycles lytic or lysogenic or infect bacteria. The term lytic life cycle refers to the phage's vegetative growth in which it kills its hosts. However, certain phages, referred to as temperate phages, can develop vegetatively and integrate their genome into the chromosome of the host, reproducing with the host for several generations.

If exposure to extreme circumstances, such as UV radiation, has a place, the prophage will elude detection by lysis of bacteria. Many scientists considered the bacteriophages' (phages') capacity to destroy bacteria after their discovery in the early 20th century, which surely made them potential therapeutic agents. However, this natural potential medicinal drug received little attention after World War II, when antibiotics were found and were solely thought of as a research tool for several years.

Bacteriophages continue to play a significant role in the fields of molecular biology and biotechnology. Bacteriophages can unravel many molecular biology puzzles. Bacteriophages are receiving a ton of interest in today's technologically sophisticated world owing to their potential to be utilized as phage display systems, or delivery systems for vaccinations as well as antibacterial. Phage typing has also been utilized to use them for diagnostic reasons. All of these apps have been compiled in one review study [1].

This studied divided into several parts introduction, literature review, discussion, and conclusion. In the introductory part, the author gives an overview of bacteriophage and its importance. And in the literature review section, the author talks about the previous study on the importance of bacteriophage. In the discussion section the Phages as delivery systems for vaccinations and application of phase therapy in the healthcare industry.

2. LITERATURE REVIEW

Benjamin K Chan et al. studied Bacteriophages, sometimes referred to as phages, which are bacterial viruses that were first identified about a century ago. Their potential as antibacterial medicines was recognized nearly right on, with the first "phage therapy" studies beginning around 10 years before Fleming discovered penicillin. In this overview, the author talks about phage treatment, which may be used to cure bacterial illnesses in people, pets, and even food. After providing a general review of the subject, humans go into the custom of adding therapeutic phages to cocktail preparations of various viral kinds, which is both experimental as well as, in certain parts of the globe, clinical [2].

Belinda et al. studied multidisciplinary phage therapy in the future.As people learn more about the worldwide health catastrophe brought on by germs that are resistant to most, if not all, antibiotics, our faith in modern medicine is now waning. Soon, we will experience a condition like that of the time when penicillin was discovered, when a little wound like a cut might quickly lead to death if it became infected. "Antimicrobial resistance (AMR) is the beginning of bacteria that are resistant to antibiotics. As a result, governments in several nations have begun programs to understand the molecular but also evolutionary causes of AMR to prevent the spread of resistance and create novel treatments for pathogens that are multidrug-resistant [3].

Richard Adrian Squires studied the quantity and quality of papers addressing bacteriophage treatment have greatly increased during the last 20 years. Some recent publications highlight prospective veterinary uses and expand on good work done in the 1980s. Before phage treatment may be widely used in veterinary settings, several obstacles must be removed, most notably those that pertain to the licensing and registration of phage therapies. One of the most promising strategies for combating the impending antibiotic resistance threat is bacteriophage treatment, but before it is widely used, significant regulatory hurdles must be cleared. Future advances in phage treatment may potentially help treat difficult bacterial illnesses that aren't necessarily drug-resistant to several drugs [4].

Hao-Ming Xu et al. studied potential uses beyond infectious diseases for phage therapy against infectious diseases. Microorganisms found in the intestines include viruses, bacteria, and fungi. They are crucial for preserving human health. Phages make up the majority of these microbes that make up intestine viromes. The viral fraction, which is mostly made up of phages, specifically influences homeostasis by applying selection pressure to the bacterial populations that are present in the intestinal tract. Drug-resistant bacteria are becoming more and more common, and they tend high drug resistance or multidrug resistance due to the widespread utilization and even misuse of antibacterial medications in recent years. As a result, treating severe bacterial infections has also become more challenging.

Gelman et al. studied phage treatment has a bright future in the military. Phage treatment, which involves administering bacteriophages, viruses that particularly target bacteria, as biotherapies, is one of the main strategies. Bacteriophages have been extensively investigated and therapeutically used for over a century in the former Soviet Union and Eastern Europe, where they were discovered to be highly effective at treating a broad range of infectious illnesses while being disregarded in the West until recent years. They also outline the most current, effective therapeutic uses of bacteriophages in various militaries throughout the globe. They think that adding phage treatment to military medicine is a crucial and necessary step in becoming ready for the swiftly approaching post-antibiotic era [5].

Sijia Wu et al. studied To prove a justified need for phage treatments in health care, phage biologists must work to meet regulatory requirements and conduct thorough, rigorous research. However, due to the lack of knowledge about phage biology and the introduction of broad-spectrum antibiotics, phage treatment was given less priority in the West for the treatment of bacterial diseases. These new findings help us understand how to most efficiently employ bacteriophages as potential therapeutic agents [6].

Nannan Wu and Tongyu Zhu studied the high diversity and number of phages in nature provides an opportunity to build an ever-expanding phage library that provides continuous broad-spectrum or poly microbial coverage, in contrast to the restricted treatment options available against AMR bacteria. Phage susceptibility testing can be a quick and economical way to subtype bacteria because of the specificity of phage-host interactions. As a first step in creating ready-to-use phages for patient medicine and environmental sanitation, the library may also provide a database for routine monitoring of nosocomial infections [7].

Mikeljon P. Nikolich studied certain phage cocktail drugs that have been focused on because they are possibly the first bacteriophage products approved for widespread use in Western countries, with potential avenues for the development of bacteriophage therapeutics and the deployment of phage therapies in modern medicine. Bacteriophage therapy, one of the potential antibacterial therapies, has characteristics quite different from those of broad-spectrum antibiotics, the current gold standard of care. They can be used in conjunction with them and often create synergy [8].

Obando Madrigal et al studied the main advantages of using bacteriophage therapy including its high specificity, low risk of damage to the microbiota, ability to self-replicate, synergy with the individual's immune system, ability to be used in conjunction with antibiotics, ability to reach hard-to-reach is included. Organs, activity against biofilms, and lack of reported side effects. Their critics point out that bacteria can become resistant to phages, that they may have genes encoding virulence factors or genetic mutations that confer antibiotic resistance, and that they run the risk of evading an immune response that either clears them or results in anaphylactic reactions and other problems [9].

Kanika Bhargava et al. studied the method through which bacteriophage therapy combats multidrug-resistant infectious illnesses. Phage treatment was mentioned in some case reports as a viable remedy for the new problem of multi-drug resistance. Contrary to antibiotics, bacteriophages have unique characteristics such as host specificity in that they do not harm other commensals. Recent developments in the knowledge of phage immunobiology, whereby phages are repurposed against both bacteria and viruses illnesses, have also given birth to a new perspective [10].

Endersen et al. studied that it is crucial to make efforts to create innovative techniques for limiting microbial contamination in food and the surroundings of food processing. To avoid, treat, and/or eliminate these contaminants in a variety of foods and food processing settings, bacteriophages (phages) and their derivatives have thus emerged as unique, practical, and secure choices. The traditional farm-to-fork context, including areas like primary production, bio sanitation, postharvest processing, or bio-detection, is discussed in terms of current uses or possible future as an antimicrobial. Whole phages, modified phages, as well as their derivatives are all covered in this discussion. To guarantee future bacteriophage use is both safe and productive, the study also raises several security issues [11].

Ben Burrowes et al. studied Phage therapy, also known as the utilization of bacteriophages (phages) to treat bacterial infections, which has a far older history than antibiotics, although antibiotics have been the preferred form of treatment in the West for more than 60 years due

to their effectiveness, low toxicity, and simplicity of manufacture. Antibiotic-resistant bacteria are emerging, while research efforts to find new treatments have significantly decreased. Throughout millions of years, phages have co-evolved with their hosts but have developed defense mechanisms against bacterial defenses such as the development of extracellular biofilm, which significantly lowers the efficacy of traditional antibiotics [12].

3. DISCUSSION

3.1. Phage Treatment:

The therapeutic utilization of bacteriophages for the management of pathogenic bacterial infections is known as viral phage therapy, phage therapy, or phagotherapy. This treatment strategy first appeared at the beginning of the 20th century, but following the Second Globe War, antibiotic usage gradually took its place in the majority of the world. Bacteriophages sometimes referred to as phages, are a kind of virus that infect bacterial cells by attaching to them and injecting their DNA there. The viral genome is produced by the bacterium and interferes with its functionality, stopping bacterial infection. Instead of reproducing, the bacterial cell that is causing the illness creates more phages. When it comes to the bacterial types they are successful against, phages are quite discriminating. Benefits include fewer adverse effects and a lower likelihood of bacterial resistance since bacteriophages are considerably more targeted than antibiotics. They normally pose no threat to the host organism, other helpful bacteria, or the gut microbiota, hence lowering the risk of opportunistic infections. Phage treatment would be anticipated to result in minimal adverse effects, sometimes at higher-than-therapeutic doses, since they have a high therapeutic index. Due to phage replication occurring in vivo (in live cells), a lower effective dosage may be employed [13].

In 1919, shortly after they were discovered, phages were initially employed as therapeutic agents in humans. Phage treatment was first introduced in 1896 when Ernest Hankin discovered its antibacterial activity against Vibrio cholerae, the causative agent of the disease and one of the worst threats faced by mankind. Friedrich Twort proposed in 1915 that a virus (phage) could be responsible for the antibacterial action. , but chose not to pursue his idea; As a result, bacteriophages were identified by Felix d'Herelle in 1917. Phage therapy gained popularity in 1925 after D'Herelle reported treating four different forms of plague with antiplague phages. Later, he traveled and worked in India. On phage treatment of plague at the Haffkine Institute in Bombay (Mumbai). Phage treatment was abandoned in the West in the 1940s as a result of the development of antibiotics, although it continues to be practiced in the former Soviet Union today. In this context, the Eliava Institute in Tbilisi, Georgia, where phage treatment is extensively researched and used, is considered a pioneer [14].

Phage selectivity for target bacteria considerably lowers the harm to the host's natural flora, which is the major benefit of phages. A variety of phages should be utilized, but only after first identifying the bacteria to be targeted. Bacteriophages are self-limiting, which means they need their hosts to be expanding all the time to survive. If the bacterial pathogens they are particular for are not there, they will not be able to do so. Another benefit of phages is their capacity to reproduce at the site of infection. They have fewer or no negative effects and are safe. A further benefit of phages over antibiotics is that if bacteria develop resistance to them, phages will spontaneously adapt to infect the resistant bacteria in question, reducing the likelihood of bacterial escape. Phages may spread fast throughout the body after injection, reaching practically every organ, but the immune system quickly eliminates systemic phages, creating another obstacle to their use as a therapeutic agent. A robust antibody response that would remove the phages more rapidly and prevent their usage for a longer length of time is one of the major concerns with the use of phage treatment in vivo. To prevent secondary

infections, it is essential to ensure that phage preparations are devoid of bacteria or bacterial toxins while making phage stocks. Phage sterilization, however, may render them inactive. Phages may provide bacteria with poisonous characteristics that increase their pathogenicity [15].

3.2. Phage display:

Phage display as a concept was initially proposed in 1985. Phage display is a molecular method for creating polypeptides with distinctive properties. The DNA for the polypeptide is fused with the genes for the phage coat protein, resulting in the expression of the desired protein on the phage particle's surface. Other phages including lambda and T7 are also utilized in the phage display method, but the filamentous phage M13 of E. coli is widely used. The screening or isolation of peptides with high particularity and affinity for target proteins may be done using phage display libraries. These peptides may be employed in medication development as tools for comprehending molecular recognition and reducing receptor mimics. By preventing the interaction of the ligand and the receptor or by acting as an agonist, these peptides may be employed as therapeutic medicines [16]. Additionally, these proteins may be utilized to identify infections and other substances that are thought to pose a risk to the environment. It is possible to improve the enzymatic activity or binding characteristics of proteins by directed evolution. The enzyme's active site is randomly changed, resulting in a rise in enzyme activity. By utilizing phages to show the Fab antibody fragment library primarily on filamentous phage surfaces, the phage display may also be changed. These libraries are used for a variety of scientific purposes, but one of the most crucial ones is the therapy of cocaine addiction, in which phages are delivered nasally before eventually reaching the central nervous system (CNS). The shown antibody binds to the cocaine molecule in the central nervous system and prevents it from acting on the brain. Phage display is an amazing component of biotechnology thanks to the diligent and cutting-edge work of numerous researchers. Phage antibodies have transformed the idea of therapeutic medications and drug design, among other things. Phage display provides a clear explanation for how proteins interact with ligands and evolve throughout molecular evolution [17].

3.3. Typing a phrase:

Phages can be used to type bacterial strains and to identify harmful bacteria because of their selectivity for bacterial cells. The process of accurately identifying microbial strains through the use of sensitivity patterns to certain phages is known as phage typing. If the phage attached to the bacteria is recognized by certain antibodies, the sensitivity of detection will increase. If a plaque (clear area) appears, it means that the phage has grown and destroyed the bacterial cell, making it easier to identify the particular bacterial strain. Several phages are supplied to the lawn for the identification of unknown bacterial strains. The use of phage that can transmit reporter genes, such as lux, or the use of a green fluorescent protein that will express following bacterial infection, are some other techniques that can be used to identify harmful bacteria. Similarly, the fluorescent dye-covalently attached phage can be used to identify some adsorbates. The use of antibodies and peptides that are shown by the phage and will specifically bind to toxins and bacterial pathogens can also be used to identify some of the released components, such as adenylate kinase, followed by specific analysis of the bacteria. . Another method for using phages to identify bacteria is the dual phage technique, which uses phages to look for antibody binding to certain antigens. Pathogenic bacteria can also be found using phage amplification techniques. This method has been most widely used for the identification of Campylobacter species, Mycobacterium tuberculosis, E. coli, Pseudomonas, Salmonella, Listeria and.

3.4. Phage-based targeted gene delivery:

The possible carriers of therapeutic genes are phages. Phage delivery of DNA vaccines, in which the phage coat shields the DNA within from degradation after injection, is comparable to the use of phages for targeted gene delivery. Both, however, are fundamentally distinct. Phages may target certain cell types by displaying foreign proteins on their surfaces, which is a need for effective gene therapy. To show targeting or processing molecules on the surfaces of phages, researchers combine phage display and synthetic covalent conjugation. Targeting sequences like fibroblast growth factor have been utilized to deliver phages to cells with the right receptors. Protein sequences like the adenovirus penton base, which mediates entrance, attachment, and endosomal release, are employed to improve the absorption as well as the endosomal release of phages. The absorption and nuclear targeting of modified phages like lambda have also been improved by the use of the protein transduction domain of the "human immunodeficiency virus" (HIV) that protein and the nuclear localization signal of the simian virus 40 (SV40) T antigen. Integrin binding peptides, which improve binding and uptake, and a DNase II inhibitor, which reduces DNA degradation, are further shown peptides that may help in gene transfer by phages. Phage display libraries have been utilized several times in mice to test the capacity of phages to target certain cells and tissues, and each time phages were discovered in those particular tissues. For example, to identify phages that specifically target the liver, mice were injected with phage display libraries, and phages were then recovered after the livers had been removed. The isolation of phage-displayed peptides that improved mammalian cell cytoplasmic absorption used a similar in vitro technique. Therefore, phages once again demonstrated their versatility by making it feasible to target certain tissues either by randomly scanning phage display libraries or by rational design [18].

3.5. Phages as delivery systems for vaccinations:

As shown in Figure 1, phages have been used as vaccine delivery systems. The vaccination antigens produced on phage particles' surfaces may be employed directly. However, in the case of DNA vaccinations, the sequences required for the manufacture of the vaccine antigen are inserted into the genome of the phage, which subsequently serves as a delivery system for the DNA vaccine. It is possible to create pages with surfaces that show a particular antigenic peptide via phage display. To find new antigens and mimotopes, phage display libraries may be screened with a particular antiserum. Mime types are peptides that, although having a distinct core structure, imitate the antigenic characteristics or secondary structures of protective proteins, lipids, and carbohydrates. To find possible vaccines against certain illnesses, phage display libraries may also be tested against the serum of recovering patients. Whole phage particles with antigenic peptides have sometimes been utilized as vaccinations in animal models.

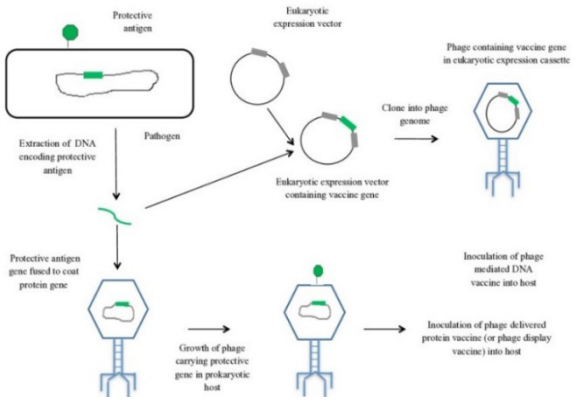


Figure 1: Illustrate the delivery of vaccine via Bacteriophages.

Some chemicals may be chemically attached to the phage surface after development in place of transcriptional fusion to a coat protein, expanding the variety of exhibited antigens. Since phages are thought to be natural immune stimulators, an antigen that is displayed on the phage coat protein would already be readily conjugated with an adjuvant activity, eliminating the need for separate protein purification or subsequent conjugation to a carrier protein before immunization. It has recently been shown that unaltered phages can deliver DNA vaccines more effectively than conventional plasmid DNA immunization. Purified phage particles are administered into the host after the vaccine gene was cloned in a lambda bacteriophage under the direction of a eukaryotic expression cassette. The coat shields DNA from deterioration and, since it behaves like a virus-like particle, directs the vaccine toward the cells that exhibit the antigen. In comparison to the conventional DNA vaccine, the antibody response in mice and rabbits was significantly better. A DNA vaccine encapsulated in phage particles under a eukaryotic promoter and a phage display version of the same antigen located on the phage surface has recently been suggested as potential components of a hybrid phage. A vaccination of this kind would effectively target the cellular and humoral immune systems. By adding certain protein sequences to target particular immune cell types, such as galactose residues that will target galactose-recognizing hepatic receptors in the liver, it may also be extended to the alteration of the phage vaccine's surface. By separating peptides from the phage display libraries, dendritic and Langerhans cells may be targeted in a similar manner.

3.6. Bacteriophage bioprocessing or bacteriophage biocontrol:

Phages may be used as predators of bacterium pests (found close to plants, fungus, or their products). To manage infections of peaches, cabbage, or peppers, phage-mediated biocontrol of plant pathogens has been effectively used against Xanthomonas pruni-related bacterial spots of peaches. Phages have also been used to manage tobacco's Ralstonia solanacearum. They have been used effectively against the tomato-spotting Xanthomonas campestris. Phages may also be used to cure the bacterial blotch on mushrooms that Pseudomonas tolaasii causes. Phages have also been studied as a method of preventing the biofouling of condenser tubes in thermal power plants. Bacteriophages are employed in bioprocessing to lower the bacterial burden in food, often in minimally processed food to prevent cooking-related taste or texture. Fruits and vegetables cannot be further processed to eliminate any infections, thus controlling them is a major problem. Salmonella and Campylobacter growth on chicken skin, Salmonella enteritidis in cheese, and Listeria monocytogenes on meat and fresh-cut fruit may all be controlled using phages, a non-thermal intervention. Phage bioprocessing might be utilized to increase the lifespan of animal products.

3.7. Uses for medicinal bacteriophages:

Phages now possess a wide range of anti-host defenses thanks to co-evolutionary pressures, including modified receptor proteins and hydrolyzing enzymes. Phage cocktails might potentially be employed to guarantee proper coverage of prevalent strains and lower the likelihood of bacterial mutants that are resistant to phages, as shown in Figure 2. One should carefully examine each case and choose the ideal injection route, phage exposure period, dosage, and buffers to avoid immune response problems. Our understanding of the interactions between bacteria and bacteriophages has improved thanks to the development of sequence technology and molecular biology, which has also opened up new opportunities for phage use, such as the creation of genetically modified phages, dual therapies, and phage-derived enzymes. Furthermore, bacteriophages have the potential to be used in a wide range of biotechnological applications, including those in the fields of environmental research, veterinary and human medicine, including food or animal agriculture.

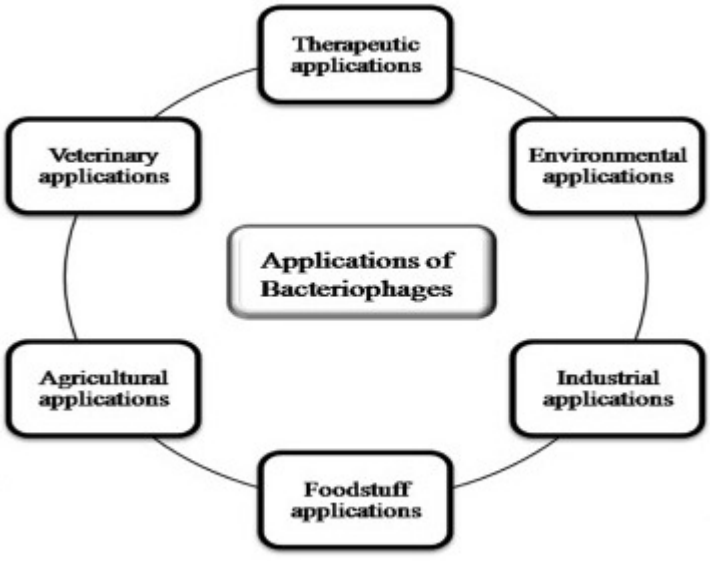


Figure 2: Illustrate the Various Application of Bacteriophages.

3.7.1. Environmental science:

Antibiotic resistance genes are spread among bacteria in the environment as a consequence of the large amounts of trash and antibiotics that are discharged into the environment by home, commercial, and agricultural activities. Due to its entry into the food chain, it has increased the danger from soil to people and jeopardizes the effectiveness of antimicrobials in preventing pathogenic illnesses. Phage treatment might be used to prevent bacterial diseases in the environment, according to scientists. After 63 days of incubation, biochar and polyvalent phage showed favorable synergistic effects for the dispersal of antimicrobial-resistant strains in the soil lettuce system. Phage application greatly slowed down the spread of antibiotic-resistant genes in the soil as well as the prevalence of drug-resistant bacteria (such as E. coli and P. aeruginosa). To reduce sludge and effluent emissions into the environment, researchers from all over the globe are attempting to use phage-based strategies to eradicate pathogens in wastewater treatment [19].

3.7.2. Animal agriculture for food:

Due to the emergence of infections that are resistant to antibiotics, bacteriophage treatment is now attracting a lot of attention as a new strategy. All around the globe, they are utilized with success in agriculture. To prevent agricultural illnesses, the Food and Drug Administration (FDA) has authorized the use of certain phages on crops. Phages were employed to effectively cure the bacterial blight on soybeans brought on by bacteria that were resistant to antibiotics. Phage applications to avoid bacterial infections from different crops, such as onions and citrus, have been shown in several papers. Phage cocktails in the food processing sectors have also received FDA approval. Phage preparations are approved as antibacterial food additives for ready-to-eat beef and poultry products.

3.8. Future Possibility:

Phage therapy is currently difficult to use for acute systemic infections such as septicemia or meningitis because these diseases require immediate and parenteral treatment. To do this, specialized, purified bacteriophages that can be readily potentiated will be necessary.

Governments, academic institutions, and commercial businesses are needed to fund global phage treatment research activities. An example of this is the German collaboration Phage4Cure, which aims to assess the effectiveness, safety, and tolerability of an inhaled phage cocktail for the treatment of persistent P. aeruginosa infections.

Each step of the process will be prepared following GMP guidelines to produce the finished product which meets the norms of western regulatory bodies and is the first phase treatment authorized for use in the inhalation of patients. served as a template for the manufacture of phages for therapeutic use in Germany with bronchiectasis and perhaps with additional diseases. To create more phage banks to improve access to them for use in clinical trials or palliative therapy, and to research topics such as pharmacokinetics or pharmacodynamics, phage-antibiotic interactions, as well as the potential formation of immune responses, among other things important.

4. CONCLUSION

The information provided above provides a glimpse of the broad spectrum of uses for phages in biotechnology and medicine. Phage uses include anything from illness detection by phage type and prevention (phage vaccination) to treatment (phage therapy). The possibility exists that phages may benefit humans in a variety of ways. It would be simple to cure a range of bacterial diseases that are now resistant to the most recent generations of antibiotics by creating a cock tail of phages. When a phage can lyse a bacterial cell, it may be utilized alone to treat a bacterial infection. In addition, since phages are so adaptable, we could employ the antibodies to fight the bacteria that had been visible on the phage surface. Similar to how a DNA or phage display vaccination may deliver a protective antigen. Therefore, a combination of genetically altered phages would be more beneficial in solving all of these issues. Phages have also proved effective in treating bacterial infections in plants and fruits as well as the issue of food deterioration.It covers difficulties with effectiveness and safety as well as immunological reactions to phages that have been delivered. It's also important to address the optimization of phage growth and purification methods. It is thought that these creatures (phages), which are abundantly prevalent in the biosphere, might provide answers to several concerns that people are now grappling with due to the quick advancements in the domains of molecular biology and biotechnology. The major objective of this investigation into the potential applications of bacteriophage treatment in healthcare. This research will be aware of bacteriophage use in the healthcare sector in the future.

REFERENCES:

[1] J. B. Doub *et al.*, “Salvage Bacteriophage Therapy for a Chronic MRSA Prosthetic Joint Infection,” *Antibiotics*, vol. 9, no. 5, p. 241, May 2020, doi: 10.3390/antibiotics9050241.

[2] B. K. Chan, S. T. Abedon, and C. Loc-Carrillo, “Phage cocktails and the future of phage therapy.,” *Future Microbiol.*, vol. 8, no. 6, pp. 769–83, Jun. 2013, doi: 10.2217/fmb.13.47.

[3] B. Loh and S. Leptihn, “A Call For a Multidisciplinary Future of Phage Therapy to Combat Multi-drug Resistant Bacterial Infections,” *Infect. Microbes Dis.*, vol. 2, no. 1, pp. 1–2, Mar. 2020, doi: 10.1097/IM9.0000000000000018.

[4] R. A. Squires, “Bacteriophage therapy for challenging bacterial infections: achievements, limitations and prospects for future clinical use by veterinary dermatologists,” *Vet. Dermatol.*, vol. 32, no. 6, p. 587, Dec. 2021, doi: 10.1111/vde.12958.

[5] D. Gelman, A. Eisenkraft, N. Chanishvili, D. Nachman, S. Coppenhagem Glazer, and R. Hazan, “The history and promising future of phage therapy in the military service,” *J. Trauma Acute Care Surg.*, vol. 85, no. 1S, pp. S18–S26, Jul. 2018, doi: 10.1097/TA.0000000000001809.

[6] S. Wu, E. Zachary, K. Wells, and C. Loc--Carrillo, “Phage Therapy: Future Inquiries,” *Postdoc J.*, Jun. 2013, doi: 10.14304/SURYA.JPR.V1N6.3.

[7] N. Wu and T. Zhu, "Potential of Therapeutic Bacteriophages in Nosocomial Infection Management," *Front. Microbiol.*, vol. 12, Jan. 2021, doi: 10.3389/fmicb.2021.638094.

[8] M. P. Nikolich and A. A. Filippov, "Bacteriophage Therapy: Developments and Directions," *Antibiotics*, vol. 9, no. 3, p. 135, Mar. 2020, doi: 10.3390/antibiotics9030135.

[9] L. Obando Madrigal, A. R. Rodríguez, and J. P. Castro Ruiz, "An in depth analysis of bacteriophage therapy in the medical field: advantages, limitations and future challenges," *J. Anesth. Crit. Care Open Access*, vol. 13, no. 4, pp. 145–148, Jul. 2021, doi: 10.15406/jaccoa.2021.13.00486.

[10] K. Bhargava, G. Nath, A. Bhargava, G. K. Aseri, and N. Jain, "Phage therapeutics: from promises to practices and prospectives," *Appl. Microbiol. Biotechnol.*, vol. 105, no. 24, pp. 9047–9067, Dec. 2021, doi: 10.1007/s00253-021-11695-z.

[11] L. Endersen, J. O'Mahony, C. Hill, R. P. Ross, O. McAuliffe, and A. Coffey, "Phage Therapy in the Food Industry," *Annu. Rev. Food Sci. Technol.*, vol. 5, no. 1, pp. 327–349, Feb. 2014, doi: 10.1146/annurev-food-030713-092415.

[12] B. Burrowes, D. R. Harper, J. Anderson, M. McConville, and M. C. Enright, "Bacteriophage therapy: potential uses in the control of antibiotic-resistant pathogens," *Expert Rev. Anti. Infect. Ther.*, vol. 9, no. 9, pp. 775–785, Sep. 2011, doi: 10.1586/eri.11.90.

[13] A. Kakasis and G. Panitsa, "Bacteriophage therapy as an alternative treatment for human infections. A comprehensive review," *Int. J. Antimicrob. Agents*, vol. 53, no. 1, pp. 16–21, Jan. 2019, doi: 10.1016/j.ijantimicag.2018.09.004.

[14] M. Ye *et al.*, "A review of bacteriophage therapy for pathogenic bacteria inactivation in the soil environment," *Environ. Int.*, vol. 129, pp. 488–496, Aug. 2019, doi: 10.1016/j.envint.2019.05.062.

[15] X. Wittebole, S. De Roock, and S. M. Opal, "A historical overview of bacteriophage therapy as an alternative to antibiotics for the treatment of bacterial pathogens," *Virulence*, vol. 5, no. 1, pp. 226–235, Jan. 2014, doi: 10.4161/viru.25991.

[16] J. B. Doub, "Bacteriophage therapy for clinical biofilm infections: Parameters that influence treatment protocols and current treatment approaches," *Antibiotics*, 2020, doi: 10.3390/antibiotics9110799.

[17] O. W. Barber, I. M. Miramontes, M. Jain, E. A. Ozer, and E. M. Hartmann, "The Future of Bacteriophage Therapy Will Promote Antimicrobial Susceptibility," *mSystems*, 2021, doi: 10.1128/msystems.00218-21.

[18] M. Kwiatek, S. Parasion, and A. Nakonieczna, "Therapeutic bacteriophages as a rescue treatment for drug□resistant infections – an in vivo studies overview," *J. Appl. Microbiol.*, vol. 128, no. 4, pp. 985–1002, Apr. 2020, doi: 10.1111/jam.14535.

[19] G. Verbeken *et al.*, "Access to bacteriophage therapy: discouraging experiences from the human cell and tissue legal framework," *FEMS Microbiol. Lett.*, vol. 363, no. 4, p. fnv241, Feb. 2016, doi: 10.1093/femsle/fnv241.

CHAPTER 24

ASSESSMENT OF PHARMACOLOGICAL ACTIVITIES OF POLYPHENOL COMPOUNDS

Upendra Sharma U S, Assistant Professor, Department of Life Science,
School of Sciences, B-II, Jain (Deemed to be University),JC Road, Bangalore-560027.,
Email Id- upendra.sharma@jainuniversity.ac.in

ABSTRACT: Polyphenols, which are produced by plants and are regarded as highly useful nutrients in human diet, are produced by them. Depending on the variety of their chemical structures, they are divided into numerous classes. Flavonoids, stilbenes, phenolic acids, and lignans are only a few of the many sub-classes of the polyphenols, a broad collection of bioactive phytochemicals. Although specific deficiency disorders are not caused by a lack of polyphenols, appropriate consumption of polyphenols may have health advantages, particularly in the case of chronic conditions. Polyphenols may be found in abundance in tea, cocoa, berries, fruits, and vegetables. The present review aims at providing a comprehensive approach on the health benefits and pharmacological activities of polyphenolic compounds of different natural sources. The findings of the study revealed that polyphenol compounds have the ability to manage different conditions with cardioprotective, neuroprotective, anti-microbial and anti-diabetic activity with diverse mechanism of action.

KEYWORDS: Polyphenol, Pharmacological, Plants, Quercetin.

1. INTRODUCTION

Plant foods, such as fruits and vegetables, serve a critical role in human health by providing calories and other necessary elements for the body. Over the last 16 years, there has been an increase in research on plant secondary metabolites, and these substances are now being seriously studied for their potential to enhance human health. In addition to being a significant source of active medicines, these phytochemicals are considered to be crucial in helping plants adapt to their environment. The function of primary metabolites in fundamental life processes including growth and development, respiration, storage, and reproduction has been described by modern chemistry and biology for about 200 years.

In plants, polyphenols are among the most prevalent families of secondary metabolites. They are notably important in green vegetables, fruits, berries, tea, and other drinks, and a variety of health-promoting actions have been linked to them. Regarding their biosynthesis, chemical composition, and pharmacological effects, they are also among the most extensively researched natural compounds. A variety of polyphenols, including anthocyanins, coumarins, carotenoids, flavonoids, and xanthones, have been identified as potential anti-inflammatory, anticancer, antidiabetic, antihyperlipidemic, antioxidant, and neuroprotective agents. The isolation, characterisation, and assessment of polyphenol bioactivity have been the subject of an increasing number of articles in recent years (Figure 1).

In the last ten years, polyphenols have drawn more and more attention from scientists and food producers. The primary drivers of this interest are the growing understanding of polyphenols' antioxidant properties, their abundance in our diet, and their potential for use in the prevention of a wide range of conditions brought on by oxidative stress, including cancer, cardiovascular disease, and neurodegenerative diseases.Recent decades have seen an increase in interest in nutrition related to polyphenols, chemical substances that are widely present in plants. A increasing amount of evidence suggests that eating polyphenols may have a significant impact on health by controlling things like metabolism, weight, chronic illness, and cell proliferation. Although their short- and long-term health impacts have not yet been

thoroughly described, there are already over 8,000 polyphenols known to exist. Numerous polyphenols contain antioxidant and anti-inflammatory characteristics, according to research on animals, people, and epidemiology, which may help prevent or treat diseases including obesity, cancer, and cardiovascular disease. Overconsumption, however, has raised concerns from some, particularly when compounds are ingested alone rather as as part of a dietary matrix.

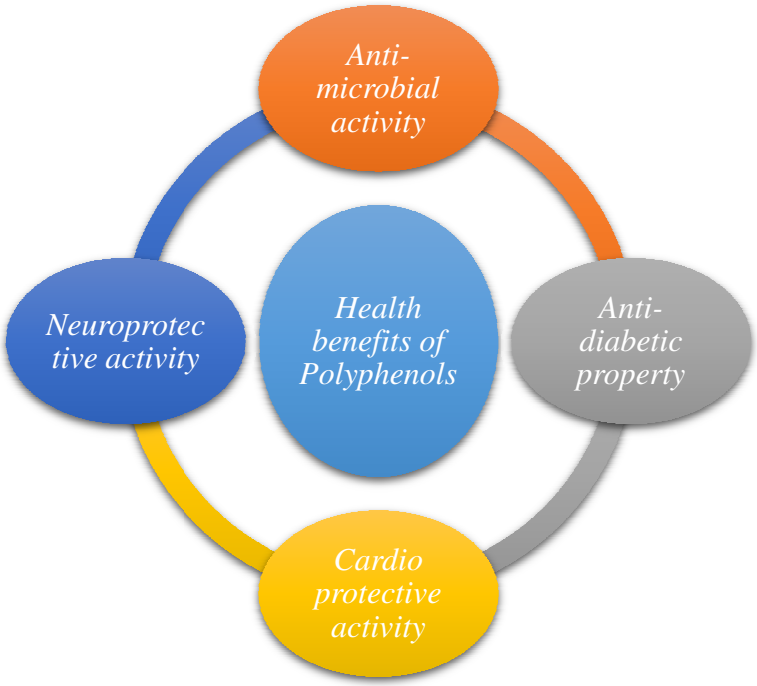


Figure 1: Health benefits of Polyphenols

2. LITERATURE REVIEW

2.1.Anti-microbial activity

Macelignan, a compound derived from nutmeg (Myrisica fragrans Houtt.), has been shown by Yanti et al. to have anti-biofilm action towards oral bacteria such as S. sanguinis, S. mutans, and Actinomyces viscosus. This investigation showed that macelignan action at 10 g/mL for a 30 min period of exposure may eliminate more than 50% of each individual oral biofilm generated by S. sanguinis, S. mutans, and A. viscosus at the plateau accumulation phase (24 h)[1].

In a research by Beatriz A. Cano-Avendao et al., catechin-like polyphenols derived from tea were shown to effectively suppress the hepatitis C, Zika, and Chikungunya viruses. Additionally, they have shown promise as SARS-CoV-2 preventative and therapeutic agents. On a number of microorganisms, including Escherichia coli and Salmonella typhimurium, epicatechin isolated from the hawthorn tree demonstrated antiviral activity. The key nutritional advantage of include these organic ingredients in diets is that they help avoid a number of diseases [2].

The database was also utilised to investigate sick enzymes and therapeutic targets in the dengue processes of Homo sapiens, and Rani et al. employed a variety of tools to investigate the anti-dengue capability of the chosen polyphenols. Following molecular docking, all of the investigated polyphenols had outstanding docking values and impressive hydrogen - bonding interactions with the dengue protein.

J. W. Betts et al. examined 15 *P. aeruginosa clinical MDR strains*. These bacteria, that are impervious to aztreonam, become vulnerable to the antibiotic and the polyphenol when used together, proving their synergistic effects both in vitro and in vivo. Additionally, EGCG may bring aztreonam's antibacterial activity down to levels below the sensitivity cutoff set by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for P. aeruginosa. Additionally, there was evidence of synergy among EGCG and cefotaxime, a third-generation cephalosporin [3].

In a different study, three methanol extract plant extracts—Scutellaria drummondii, Nothoscordum bivalve, P. laevigata, Marrubium vulgare, O. ficus-indica, and G. microcephala—that contain polyphenolic compounds like tannins and flavonoids were chosen for phytochemical analysis. The other six extracts were Sphaeralcea ambigua, Sophora secundiflora, P. laevigata was the extract with the greatest results when it came to killing the enterobacteria under test. However, no studied microbial agent was active against N. bivalve bulb [4].

2.2. Cardio protective activity

In H9c2 rat cardiomyocytes injured by ischemia/reperfusion, Chen et al. examined the cardioprotective effects of quercetin (1 mM). The researchers found that administration with 1 mM quercetin and 5 mM H2O2 resulted in a weaker enzymatic reaction than treatments with 5 mM H2O2, which caused phosphotyrosine to respond strongly. Additionally, Src kinase and focal adhesion kinase were tyrosine phosphorylated less often when quercetin was consumed (FAK). Quercetin plus H2O2 treated cells displayed greater closed regions than H2O2 alone, according to the wound-healing assay[5].

Bees pollen polyphenols have been shown to preserve cardiac arteries in vivo investigations conducted by Rzepecka-Stojko et al. They greatly lower and/or totally prevent atherosclerosis, as well as degenerative and hepatic steatosis changes brought on by a high-fat diet [6].

When Serban et al. reviewed 7 randomised controlled studies, they found that quercetin flavonol had positive benefits on high blood pressure (BP). Both systolic and diastolic blood pressure were shown to be reduced by quercetin administration, according to the results, to be -3.04 and -2.63 mmHg, respectively [7].

2.3.Anti-diabetic property

Flavonoid-rich grape seed preparations effectively reduced the markers of inflammatory response, glycemia, and oxidative stress in the events of obese T2D people with high cardiovascular disease risk in a double-blind, 4-week, randomised, placebo-controlled experiment including 32 T2D patients [8].

Masataka Kusunoki et al. demonstrated that administration of BS alone seemed to have no influence on blood glucose or lipid levels, but then that administration of fenofibrate alone but fenofibrate in conjunction with BS decreased dramatically fasting serum triglyceride (TG) levels of their subjects. The % reduction in serum TG level following combined administering was also considerably higher than in the subjects who were given fenofibrate alone [9].

During a research by Ong et al. When 250 mg/kg of chlorogenic acid was administered intraperitoneally to db/db mice, a considerable drop in fasting blood sugar was seen 10 minutes later. The effect remained for an additional 30 minutes following the glucose challenge. In addition, CGA induced and boosted 2DG transporters in soleus muscle that

were both basal and insulin-mediated. The effects of CGA on glucose transport in L6 myotubes were dose- and time-dependent [10].

An investigation by Jin Ji et al. The sugarcane extract's high content of polyphenols and antioxidant components is supported by quantitative analytical investigations. The Caco-2 cells and dysfunctional beta-cell models used in subsequent cellular studies provided evidence that the polyphenol-rich sugarcane decoction could help prevent glucose as well as fructose absorption in intestinal cells and restore insulin production in dysfunctional -cells—essential tasks in the treatment of diabetic conditions [11].

2.4.Neurogenerative diseases

The diabetic rat model was used by Tian et al. to assess the impact of oral administration of RSV on cognitive functions since cognitive deficits are closely associated to a number of disorders, including diabetes. The findings demonstrated that RSV considerably enhanced learning and memory in addition to a notable decrease in oxidative stress and the production of TNF- and IL-1 in the hippocampus [12].

According to Vioricaetal et al., the SCFA combination increased transepithelial resistance and decreased paracellular permeability to control gut barrier function. Sodium butyrate intraperitoneal administration prevented blood-brain barrier (BBB) damage in a rat model of acute focal cerebral ischemia [13].

2.5. Microbiota

Green TPs were shown to be an efficient way to counteract the decline in microbial diversity brought on by HFD, according to studies by Wang et al. on the effects of green TPs on the colonic microflora of C57BL/6J mice that are similar to human flora. It was also shown that supplementing with oolong TPs may greatly improve the variety of faecal microflora and lower the faecal microorganism/Bacteroides ratio by reversing the HFD-induced Firmicutes/Bacteroides ratio. The relative abundance of negative bacilli and Clostridium spp. dramatically reduced, whereas that of Bacillus spp. [14].

3. METHODOLOGY

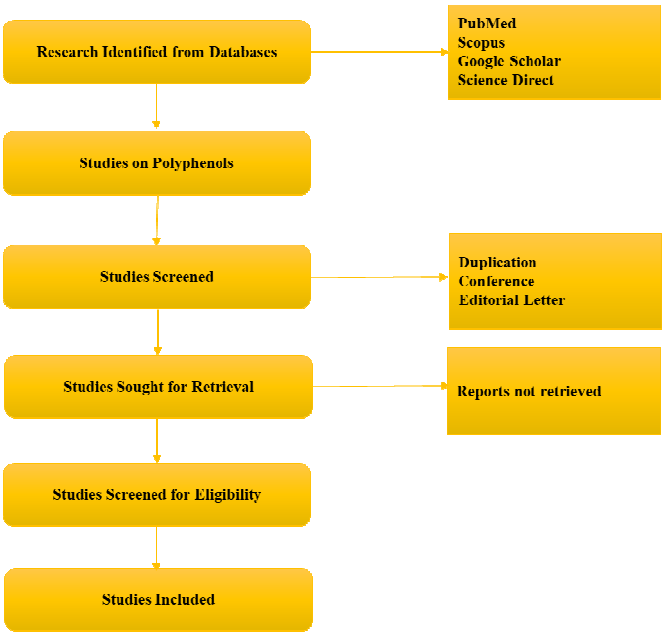


Figure 2: Methodology utilised to conduct the review research.

Google Scholar, PubMed, Science Direct, Scopus, and Research Gate were used to conduct the electronic database search for this review research. A search method was used to get the relevant information using a combination of keywords. Records were excluded if they had unextractable data, inadequate information, or duplicate research. In order to find any pertinent records that may have been overlooked, manual retrieval of the studies was also done. Figure 2 below depicts the methodology utilised to conduct the review research.

4. DISCUSSION

Natural products that include dietary polyphenols have emerged as a promising class of prospective agents in health promotion, backed by their structure and the findings of molecular investigations. When it comes to the stimulation of the autophagic flow, polyphenols may have positive effects on a variety of molecular targets.The human food has the largest quantity of PCs, and flavonoids in particular, as has previously been mentioned. The most common phytochemicals found in the diet of humans include genistein, quercetin, kaempferol, daidzein, lutelin, apigenin, myricetin, and biochanin A. The overall concentration of PCs in the human diet may vary greatly, despite the fact that these substances are naturally present in plants. For instance, the amount of quercetin in the edible parts of fruits and vegetables is less than 10 mg/kg. For kaempferol, this ranges from 5 to 17 mg/kg.

Given that numerous techniques are utilised to prepare and process food, it is possible that the concentration of PCs in food is reduced by these techniques. Plant-based meals' overall PC content is significantly impacted by cooking, frying, and freezing. Simply eating foods high in polyphenols is insufficient; additional processes, such as glucuronidation, sulfation, methylation, and metabolism to other phenolic compounds (PCs), may alter the bioavailability of PCs in the body. The utilisation of contemporary techniques for producing foods high in polyphenols and the recommended dosages of these substances in the diet should thus get further attention from the food industry. PCs have been identified as the best therapeutic target on the market by several in vitro and in vivo investigations, however using these drugs has a number of drawbacks.

One of the most crucial things to consider is how much PCs should be used to attain their health advantages and whether or not PCs have negative impacts on people. The answer to these questions may help future study on PCs. Quercetin, for instance, may be a beneficial substance for treating a variety of ailments, but when added to mice's long-term diet, it also shortens their life expectancy. To improve basic research on PC, it is essential to take into account a number of important factors, including the use of molecular modelling to predict interactions, large-scale screens for toxic or other common effects, affinity-based methods to identify drug-interacting proteins, and a better synthesis of the available data, including legislation to encourage the release of clinical trial results and tracking voluntary supplement consumption.

There is still more research to be done to determine if this class of drugs will likely have a favourable effect on health and to determine whether they may be used to treat slowly worsening neurodegenerative disorders. Eating foods rich in poly-phenols has the ability to prevent or slow down age-related decreases in cognitive function as well as minimise neurodegeneration because of their many biological roles. Humans have yet to fully benefit from the therapeutic and pharmacological potential of these natural substances in clinical settings.

Effectiveness in RCT is also necessary to support the mostly consistent results from epidemiological and mechanistic studies. Despite the dearth of effectiveness information and

the ambiguity of their effects in vivo, studies into the absorption and metabolism of various polyphenols in humans reveal that most polyphenols are metabolised through similar routes, most notably via their bacterial metabolism in the large intestine. Thus, investigations on the bioavailability and bioactivity of smaller polar polyphenols for the brain should be prioritised in the development of dietary polyphenols for applications in neurodegenerative diseases. Thus, caution would be advised in going ahead until complete randomised controlled clinical trials have been carried out before determining empirically if polyphenols and/or their metabolites are useful in treating patients with dementia and other neurodegenerative illnesses.

It is crucial to comprehend how polyphenols interact with other food components, such as proteins or dietary fibres, since food preparation might result in complicated chemical reactions. PCs have been proved in several studies to be beneficial to human health, and it is essential to incorporate them in diets at the recommended dosages. The ingestion of these phytochemicals should be viewed with notable caution since, although being powerful antioxidants, PCs also exhibit pro-oxidant (oxygen radical producing) action.

Apples, chocolate, coffee, tea, and other foods high in polyphenols have been linked to a number of health advantages, including a reduced risk of developing type 2 diabetes and cardiovascular disease. Blood pressure, endothelial function, glucose metabolism, inflammation, oxidative stress indicators, platelet function, cholesterol, and indirect effects mediated by contact with the gut flora are just a few examples of possible processes.

Epidemiologic research encompassing various dietary patterns and consumption of certain classes of foods provide for a fraction of the data demonstrating the function of polyphenols in cardiovascular health.

In order to properly understand the results of observational research, a number of things must be taken into account. For instance, a decrease in the intake of potentially harmful meals derived from animals may balance out an increase in the consumption of foods high in polyphenols from plants, and this decrease may help explain any association between the consumption of polyphenols and enhanced function. In research where participants self-report their food intake, the memory accuracy, variances in portion size, and possible variations in the polyphenol content of related foods all significantly limit the assessment of polyphenol consumption's accuracy and may conceal any association.

When polyphenols were first discovered, it was believed that their direct antioxidant properties were their main mode of action. As a result of these chemicals' inability to reach concentrations high enough to have a noticeable impact on the scavenging of free radicals in the majority of tissues, these effects are no longer thought to be as important in vivo. Nevertheless, a number of additional potential biochemical and molecular mechanisms have been discovered. These include a wide range of effects on intra- and intercellular signalling pathways, such as controlling nuclear transcription factors and fat metabolism, as well as modifying the synthesis of inflammatory mediators like tumour necrosis factor-a, interleukin (IL)-1, and IL-6.

Plant extracts used to treat problems of the eyes associated with ageing have drawn increased attention in recent years. Numerous carotenoids, including lutein, zeaxanthin, and mezoxanthin, as well as polyphenols such anthocyanins, Ginkgo biloba, quercetin, and resveratrol, have shown important therapeutic and preventative advantages against the aforementioned illnesses. The involved mechanisms in these findings include reducing reactive oxygen species production, blocking the pathways of tumour necrosis factor and vascular endothelial growth factor, suppressing p53-dependent apoptosis, and reducing the

production of inflammatory markers like interleukin-8 (IL-8), IL-6, IL-1a, and endothelial leucocyte adhesion molecule-1. Furthermore, studies into the processes by which these substances function and their impact on molecular signalling point to potential synergistic interactions between substances from the two groups with complementing antioxidant and anti-inflammatory effects. Carotenoids' antioxidant activity has increased as a result of bacterial carotenoids and a few phenolic chemicals. The absorption of lutein, on the other hand, was reduced when lutein was combined with certain polyphenols. It may be possible to maximise the antioxidant effects of phytochemicals by combining antioxidant substances with complimentary action mechanisms.

According to studies on the synergistic interactions between carotenoids and polyphenols, there are a number of proinflammatory pathways that may be inhibited by combining carotenoids and polyphenols in certain ways. The inhibition of several carotenoids (lycopene, lutein, and beta-carotene) on the production of inflammatory mediators like NO, TNF-alpha, and PGE2 has recently been shown to be produced (synergistically) by these polyphenols of curcumin and carnosic acid.

5. CONLUSION

The specific mechanism of action by which these substances comprise extra and intracellular locations under normal and pathological circumstances should be further established and clarified in future studies. The adoption of these drugs for use in clinical practise would be aided by understanding the mechanisms underlying their actions. Although epidemiological and in vitro/in vivo studies have demonstrated the positive effects of plant-based diets or phytochemicals on lowering the risk of chronic diseases, much more mechanistic and clinical evidence is needed to categorise a given phytochemical as an inhibitor of a given cellular pathway or to identify the plant-derived active compound with a given therapeutic property. The best dosages, delivery methods, and precise mechanisms of action should also be identified by researchers as they further explore the phytochemicals' toxicological features.

REFERENCES:

[1] V. S. Nikitina, L. Y. Kuz'mina, A. I. Melent'ev, and G. V. Shendel', "Antibacterial activity of polyphenolic compounds isolated from plants of Geraniaceae and Rosaceae families," *Appl. Biochem. Microbiol.*, vol. 43, no. 6, pp. 629–634, Nov. 2007, doi: 10.1134/S0003683807060117.

[2] B. A. Cano-Avendaño, J. C. Carmona-Hernandez, R. E. Rodriguez, G. Taborda-Ocampo, and C. H. González-Correa, "Chemical properties of polyphenols: a reviewfocusedonanti-inflammatory and anti-viral medical application," *Biomedicine*, vol. 41, no. 1, pp. 3–8, Apr. 2021, doi: 10.51248/.v41i1.524.

[3] J. W. Betts *et al.*, "Restoring the activity of the antibiotic aztreonam using the polyphenol epigallocatechin gallate (EGCG) against multidrug-resistant clinical isolates of Pseudomonas aeruginosa," *J. Med. Microbiol.*, 2019, doi: 10.1099/JMM.0.001060.

[4] E. Sánchez, C. Rivas Morales, S. Castillo, C. Leos-Rivas, L. García-Becerra, and D. M. Ortiz Martínez, "Antibacterial and Antibiofilm Activity of Methanolic Plant Extracts against Nosocomial Microorganisms," *Evidence-Based Complement. Altern. Med.*, vol. 2016, pp. 1–8, 2016, doi: 10.1155/2016/1572697.

[5] Y.-W. Chen *et al.*, "Cardioprotective Effects of Quercetin in Cardiomyocyte under Ischemia/Reperfusion Injury," *Evidence-Based Complement. Altern. Med.*, vol. 2013, pp. 1–16, 2013, doi: 10.1155/2013/364519.

[6] A. Rzepecka-Stojko *et al.*, "Protective Effect of Polyphenol-Rich Extract from Bee Pollen in a High-Fat Diet.," *Molecules*, vol. 23, no. 4, p. 805, Mar. 2018, doi: 10.3390/molecules23040805.

[7] M. Serban *et al.*, "Effects of Quercetin on Blood Pressure: A Systematic Review and Meta□Analysis of Randomized Controlled Trials," *J. Am. Heart Assoc.*, vol. 5, no. 7, Jul. 2016, doi: 10.1161/JAHA.115.002713.

[8] P. Kar, D. Laight, H. K. Rooprai, K. M. Shaw, and M. Cummings, "Effects of grape seed extract in Type 2 diabetic subjects at high cardiovascular risk: A double blind randomized placebo controlled trial examining metabolic markers, vascular tone, inflammation, oxidative stress and insulin sensitivity," *Diabet. Med.*, 2009, doi: 10.1111/j.1464-5491.2009.02727.x.

[9] M. Kusunoki, D. Sato, K. Tsutsumi, H. Tsutsui, T. Nakamura, and Y. Oshida, "Black Soybean Extract Improves Lipid Profiles in Fenofibrate-Treated Type 2 Diabetics with Postprandial Hyperlipidemia," *J. Med. Food*, vol. 18, no. 6, pp. 615–618, Jun. 2015, doi: 10.1089/jmf.2014.3234.

[10] K. W. Ong, A. Hsu, and B. K. H. Tan, "Chlorogenic Acid Stimulates Glucose Transport in Skeletal Muscle via AMPK Activation: A Contributor to the Beneficial Effects of Coffee on Diabetes," *PLoS One*, vol. 7, no. 3, p. e32718, Mar. 2012, doi: 10.1371/journal.pone.0032718.

[11] J. Ji, X. Yang, M. Flavel, Z. P. I. Shields, and B. Kitchen, "Antioxidant and Anti-Diabetic Functions of a Polyphenol-Rich Sugarcane Extract," *J. Am. Coll. Nutr.*, 2019, doi: 10.1080/07315724.2019.1587323.

[12] X. Tian *et al.*, "Resveratrol limits diabetes-associated cognitive decline in rats by preventing oxidative stress and inflammation and modulating hippocampal structural synaptic plasticity," *Brain Res.*, vol. 1650, pp. 1–9, Nov. 2016, doi: 10.1016/j.brainres.2016.08.032.

[13] S. Pryde, "The microbiology of butyrate formation in the human colon," *FEMS Microbiol. Lett.*, vol. 217, no. 2, pp. 133–139, Dec. 2002, doi: 10.1016/S0378-1097(02)01106-0.

[14] L. Wang *et al.*, "Green Tea Polyphenols Modulate Colonic Microbiota Diversity and Lipid Metabolism in High-Fat Diet Treated HFA Mice," *J. Food Sci.*, 2018, doi: 10.1111/1750-3841.14058.