NANOPHYTOMEDICINE

HARNESSING NATURE AND NANOTECHNOLOGY FOR NEUROLOGICAL AND METABOLIC HEALTH

Editors:
Mandeep Kumar Gupta
Rajnish Srivastava
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Nanophytomedicine: Harnessing Nature and Nanotechnology for Neurological and Metabolic Health

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FOREWORD

Recent years have witnessed the convergence of nanotechnology and phytomedicine, opening unprecedented avenues in healthcare. This book, edited by Dr. Mandeep Kumar Gupta, Dr. Rajnish Srivastava, Dr. Pradeep Singh, Ms. Kanupriya Chauhan, and Mr. Naveen Singh, is dedicated to dynamic synergy and novel perspectives toward solving two major challenges in human health: mental health disorders and metabolic diseases. It eloquently bridges ancient wisdom with cutting-edge science and shows how nanotechnology enhances the efficacy, bioavailability, and precision of natural products. Taking the reader through both the depths of mental health and metabolic affections, it provides a guideline for holistic, sustainable, and effective therapies. The authors bring together a wealth of knowledge, presenting compelling evidence and transformative strategies. As you embark on this journey through nature's remedies and nanotechnological marvels, prepare to witness the future of healthcare—one that prioritizes integration, innovation, and individual well-being. This book is an essential read for researchers, clinicians, and visionaries in healthcare innovation.

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PREFACE

The exponential expansion of nanotechnology and its intersection with conventional plant-derived medicine have portended a new age in therapeutic development. The edited book, NanoPhytomedicine: Unlocking Nature and Nanotechnology for Neurological and Metabolic Health, is a timely and comprehensive exploration of this interdisciplinary frontier. The primary objective of this book is to examine the synergistic potential of phytomedicine and nanotechnology in addressing the increasing global burden of neurological and metabolic disorders—two interrelated areas that continue to challenge modern healthcare systems. In this book, it is demonstrated that nanoformulations are capable of bypassing the limitations of traditional phytotherapy, such as low bioavailability, instability, and targeted delivery limitations, by merging the centuries-long proven efficacy of plant-derived drugs with the precision and effectiveness of nanoscale delivery systems.

This book addresses an overarching theme, from fundamental principles to emerging trends and translational applications of nano-enabled phytotherapeutics. It brings together leading researchers, clinicians, and scientists from across disciplines to contribute novel information, critical reviews, and recent advancements in design, synthesis, characterization, and application of nanophytomedicines. Particular emphasis is placed on their role in governing key molecular processes that are implicated in neurological diseases such as neurodegenerative diseases, depression, anxiety, epilepsy, myasthenia gravis, and stroke, and metabolic diseases such as diabetes, obesity, dyslipidemia, and hepatic disease. Overall, the chapters highlight the importance of pharmacokinetics, nanocarrier systems, green synthesis protocols, and regulatory aspects that are critical to producing safe and effective therapies.

In addition, this book tackles the existing challenges and future directions of applying nanophytomedicine in clinical settings. It examines the neurometabolic disorders of multifactorial etiology and shows how nanophytomedicines exert multifaceted modes of action, providing neuroprotection and regulating metabolic functions. The book further examines the relevance of sustainable and ethical extraction of phytochemicals, as well as the promise of personalized nanophytotherapy. The integration of case studies, preclinical observations, and translational insights adds relevance not only for researchers but also for clinicians, industry experts, and policymakers. Our aspiration is that this collection will spark new research avenues, facilitate interdisciplinary collaboration, and eventually lead towards the creation of useful, safe, and affordable therapeutics to address some of our most urgent health issues today.

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CHAPTER 1

Introduction to NanoPhytomedicine: Pioneering the Future of Natural Drug Delivery

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Abstract: The advent of nanotechnology has enabled the development of innovative, precise, targeted, and effective drug delivery systems. One of the most promising advances is nanophytomedicine, an interdisciplinary science that integrates the medical potential of phytochemicals with the sophisticated delivery features of nanocarriers. This introductory chapter presents a wide-ranging account of nanophytomedicine, following its evolution, constitutive features, and its game-changing potential in natural drug delivery. Targeting the problems of traditional phytomedicine—*e.g.*, low bioavailability, instability, and lack of specificity—it highlights how nanotechnology addresses these challenges with nano-formulations like liposomes, nanoparticles, nano-emulsions, and dendrimers. Particular emphasis is placed on the application of nanophytomedicine in the treatment of neurological and metabolic disorders, where complex pathophysiologies often constrain the effectiveness of conventional therapies. The combination of phytoconstituents with nanocarriers not only improves their stability and solubility but also delivers brain targeting and controlled release, providing a promising approach for metabolic modulation and neuroprotection. Additionally, the chapter also gives an overview of current research trends, regulatory considerations, and the way forward, including the application of green synthesis pathways and personalized nanomedicine. Through bridging the gap between nature and modern science, nanophytomedicine is a revolution in drug delivery that harnesses the understanding of traditional medicine with the precision of nanotechnology. This

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opening chapter establishes the background for the subsequent deliberations in the book and provides insight into the future direction of harnessing nature-based nanomedicine for complex diseases.

Keywords: Bioavailability, Blood-brain barrier, Controlled release, Dendrimers, Drug delivery systems, Liposomes, Metabolic disorders, Metabolic modulation, Nanophytomedicine, Nanocarriers.

INTRODUCTION

Nanophytomedicine: An Overview

Nanophytomedicine is a revolutionary intersection of two strong scientific fields: nanotechnology and phytomedicine. It is a new interdisciplinary science that combines the therapeutic value of bioactive plant-derived compounds (phytochemicals) with the precision and effectiveness of nanoscale drug delivery systems (Fig. **1**) [1]. The idea stems from the need to improve the solubility, stability, bioavailability, and targeted delivery of phytochemicals, most of which are naturally active but constrained by poor pharmacokinetic profiles. Using nanoscale carriers—liposomes, polymeric nanoparticles, solid lipid nanoparticles, dendrimers, and nano-emulsions—nanophytomedicine provides a sophisticated method of drug formulation, maximizing therapeutic effects while reducing side effects [2]. This novel approach not only revitalizes the use of natural products in medicine but also offers a green and biocompatible solution to synthetic drugs in the treatment of complex diseases, particularly those with neurological and metabolic dysregulation [3].

Evolution of Natural Products in Medicine

Natural products have been utilized for therapy since the earliest days of human civilization. All the ancient medicine systems—Ayurveda, Traditional Chinese Medicine, and Unani—were based on the use of herbs and plant-derived substances for disease prevention and treatment [4, 5, 6]. Even in modern pharmaceutical sciences, a major part of drugs either comes directly from nature or is synthetically derived from it. Prominently, phytochemicals like paclitaxel (from *Taxus brevifolia*), artemisinin (from *Artemisia annua*), and metformin (derived from *Galega officinalis*) reflect the significance of plant-derived molecules in modern therapeutics [7]. Yet, despite their tremendous pharmacological potential, phytochemicals frequently encounter challenges of clinical translation because of the limitations such as poor solubility, physicochemical instability in physiological media, high susceptibility to metabolism, and low specificity to targets [8, 9]. These limitations have prevented

phytomedicine from being used on a large scale in mainstream medicine throughout history. The increasing need for management of chronic diseases, especially neurological and metabolic diseases, requires the discovery of safe, effective, and long-term therapies. In this background, the possibility of developing and refining natural products through advanced delivery systems presents a promising area of scientific investigation.

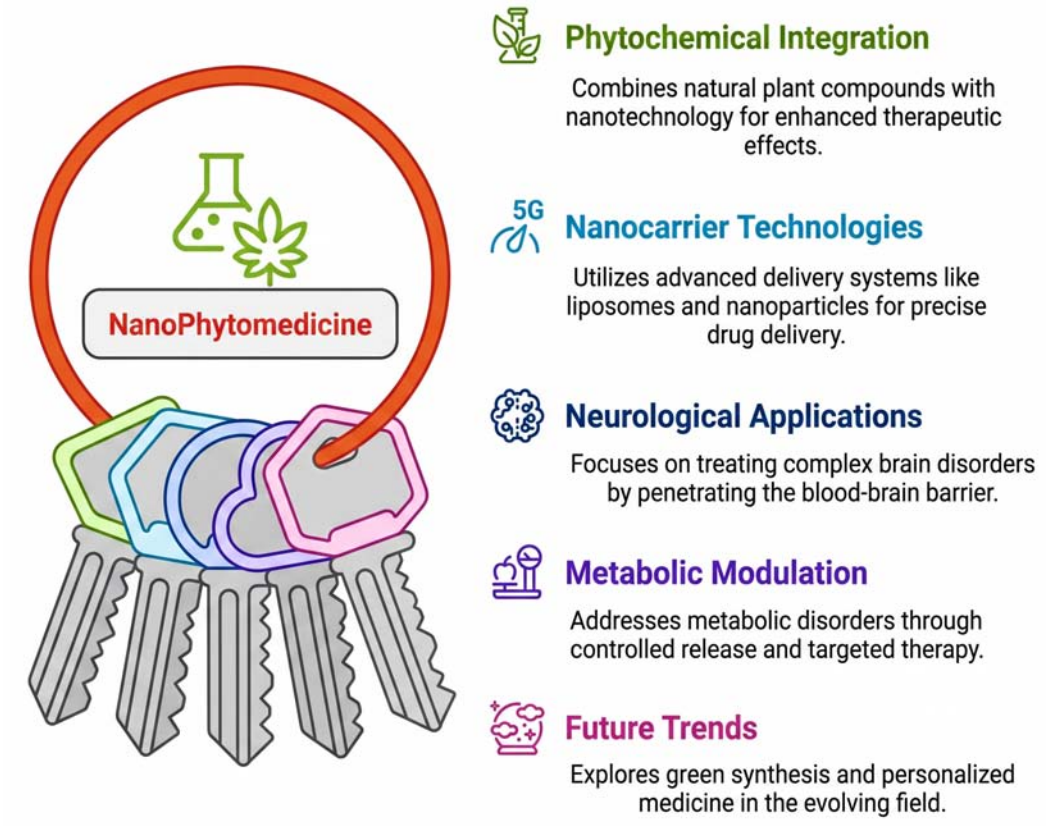

Fig. (1). Revolutionizing medicine with nanophytomedicine.

The Role of Nanotechnology in Modern Therapeutics

Nanotechnology has opened a new chapter in medicine, providing tools and platforms that function at the molecular and cellular levels. Its use in drug delivery has transformed the pharmacological landscape by enabling controlled release, enhanced solubility, increased permeability, and targeted delivery of therapeutic agents [10, 11]. Nanoscale carriers can cross biological barriers, protect drugs against enzymatic cleavage, and selectively target diseased tissue

CHAPTER 2

Nanocarriers for Phytochemical Delivery: Innovative Techniques and Applications

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Abstract: Phytochemicals are plant-derived secondary metabolites that are widely recognized for their significant health benefits and therapeutic potential in the prevention and treatment of various diseases. However, their large molecular size and polar nature present challenges, including their large molecular size, high polarity, and limited bioavailability. These properties restrict their ability to cross biological barriers, such as the blood-brain barrier, the endothelial lining of blood vessels, the gastrointestinal tract, and mucosal layers. Furthermore, phytochemicals are highly vulnerable to enzymatic degradation in the gastrointestinal tract, reducing their stability and efficacy. To address these challenges, advanced drug delivery systems, particularly nanocarriers, have emerged as a transformative approach. Nanocarriers, such as liposomes, dendrimers, micelles, nanoparticles, nano-emulsions, and phytosomes, can encapsulate or conjugate phytochemicals, thus protecting them from enzymatic degradation and enhancing their solubility, stability, and bioavailability. These nanocarriers have the potential to enhance the absorption rate, facilitate targeted delivery, and enable sustained release, ultimately maximizing the therapeutic efficacy of phytochemicals.

Keywords: Drug delivery systems, Improved stability, liposomes, Metallic nanoparticles, Molecular stability, Neurotherapeutic, Nanocarriers, Parkinson, Phytochemicals, Phytosomes.

INTRODUCTION

Nowadays, nanocarriers are utilized for encapsulating or conjugating phytochemicals, and their popularity is increasing among researchers due to their potential in targeted drug delivery. Phytochemicals, primarily plant-derived Secondary metabolites have demonstrated substantial health benefits and thera-

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peutic applications. However, their large molecular size and polar nature pose challenges for bypassing barriers such as the blood-brain barrier (BBB), the innermost lining of blood vessels, and the human digestive system. Additionally, these compounds are prone to enzymatic degradation within the digestive system, limiting their bioavailability [1]. Nanocarriers have an important function in the delivery of phytochemicals by increasing the dissolution as well as their bioavailability in the body. These sophisticated systems shield bioactive compounds from premature degradation, allowing them to be released slowly and target the appropriate tissues. By efficiently absorbing and delivering these compounds to the body and minimizing their toxicity, nanocarriers greatly enhance the therapeutic effects of phytochemicals. Their applications in addressing the most significant medical challenges make them useful for curing many diseases [2]. The development of nanotechnology has revolutionized medicine, with one of the most significant advances being more selective treatment in cancer [3]. Cancer deaths are expected to reach 7.6 million annually, with 13.1 million by 2030. Traditional medicine uses phytochemicals to cure cancer, but resistance to multiple drugs may hinder treatment [4]. Cancer remains a leading cause of death globally, with chemotherapy often causing side effects and drug resistance. To improve the efficacy of anti-cancer drugs, researchers are exploring new approaches that combine phytochemicals, or active compounds derived from plants, with chemotherapeutic drugs. Nano drug delivery systems play an important role in delivering these hydrophobic drugs by enhancing their solubility and bioavailability. Results showed that these combination therapies can inhibit cancer cell growth *in vitro* and in preclinical models, suggesting synergistic effects that improve treatment outcomes [5]. Phytochemicals are metabolites with different chemical structures, including glycosides, alkaloids, phenolic acids, saponins, indoles, phytosterols, isothiocyanates, and phytoprostanes/furanes [6]. These have several benefits over conventional drugs, including fewer side effects, the potential to target multiple pathways, and reduced costs. Nano-based drug delivery systems have been studied for cancer and chemopreventive properties, including drug loading efficiency, particle size, drug release, and cell inhibition [7]. Various researchers confirm that the application of phytochemicals in comparison to conventional treatments of cancer has shown better potential when compared to their individual use [8]. Scientists have therefore developed nanotechnology-based drug delivery systems through which phytochemicals can be co-administered with traditional drugs to enhance their efficacy [9]. Polyphenols, terpenes, and tannins have been used for ages to cure infections, wounds, and cancer. Their medicinal benefits are usually limited by poor metabolism and absorption [10]. Nanocarriers are known for their various advantages, such as improved dissolution, greater drug delivery to receptor sites, reduced dosing requirements, fewer side effects, enhanced efficacy, and reduced

drug resistance. Nanocarriers also enhance drug compliance by streamlining dosage regimens. Besides drug delivery, nanocarriers increase the healing of wounds, lower resistance to drugs, and shield drugs from premature degradation, which makes them a very promising agent for therapy based on plants' secondary metabolites [3, 11]. Polysaccharides are derived from nature; as they are inexpensive, biodegradable, and environmentally safe, they are becoming a topic of research for drug delivery *via* the oral route. In the early 2000s, scientists synthesized nanoparticles made from polysaccharides for encapsulating phytochemicals. These nanoparticles protect phytochemicals from degradation, increase their intestinal absorption, and enhance their oral efficacy. Developments in starch-based nanoparticles, alginate, chitosan, dextran, and pectin have further enhanced delivery, concurrent with the effects of phytochemicals [12].

TYPES OF NANOCARRIERS/INNOVATIVE TECHNIQUES IN NANOCARRIER DEVELOPMENT

Nanocarriers have transformed medication delivery by increasing bioavailability, targeting distribution, and controlling the release of therapeutic chemicals. Recent advances in nanocarrier development have resulted in novel approaches that improve their efficiency, stability, and specificity [13]. There are different innovative approaches, *i.e*., lipid-based nanocarriers, inorganic nanocarriers, hybrid nanocarriers, nano-emulsions, nano-capsules, exosome nanocarriers, *etc*.

Polymeric Nanoparticles (PNs)

Polymeric nanoparticles (PNs) are becoming an important choice these days for many researchers owing to their suitability as nanocarriers and different properties, *i.e*., ease of production, better cytocompatibility, and less toxicity (Fig. **1**). Recently, PNs have been utilized *via* incorporation in phytochemicals by using tailored drug delivery systems to manage breast cancer. In this process, chemical constituents are encapsulated or linked by covalent bonds with a polymeric matrix to get the desired therapeutic effect [14]. PNs can be classified into two classes, which are mentioned in Fig. (**2**).

Phytosomes

The word "phyto" is derived from "plant," while "some" is a cell-like structure. Phytosomes are vesicular drug and plant-derived extract delivery systems based on lipids (Fig. **3**). The complexes of phospholipids and phytosubstances resemble miniature cells. If standardized phyto-extracts or individual phytochemicals such as flavonoids, terpenoids, and tannins are incorporated with phospholipids, they give a new drug delivery system that is called phytosomes. Such a system significantly boosts uptake after oral administration, as its lipid nature facilitates

CHAPTER 3

Innovative Approaches to Diabetes Management: Nanophytomedicine as a Therapeutic Strategy

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Abstract: In the current era, diabetes mellitus (DM) is a metabolic disorder that leads to abnormal glucose levels. The current therapy focuses on regulating blood glucose levels *via* the intervention of various pharmacological agents and lifestyle strategies. However, current approaches still have some limitations, possibly related to side effects and sometimes efficacy. This type of limitation creates a scientific gap, which could introduce a significant player to fill the current gaps for treatment. To fill this gap, various phytoconstituents are gaining the spotlight due to their wide ability to treat many disorders such as cancer, Alzheimer's, Parkinson's, diabetes mellitus, chronic wounds, *etc*. To create a more effective formulation, phytochemicals collaborate with nanotechnology, which is further coined as nanophytomedicine. Nanophytomedicine is one of the current approaches, and it uses nanocarriers, dendrimers, and other nanoparticle techniques to deliver herbal bioactive plant molecules for the treatment of DM and other disorders. This technique provides a wide insight into their physiochemical properties by improving their therapeutic efficacy and reducing side effects. There are several techniques, like nano-pumps, smart cells, non-ionized herbal medicine, and nanorobots, that are used by the researchers for target delivery of herbal nanoparticles for the treatment of DM. This chapter will focus on the innovative approaches used by nanophytomedicine for the management of diabetes.

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Keywords: Alkaloids, Diabetes ketoacidosis, Diabetes mellitus, Flavonoids, Gestational diabetes mellitus, Glycosides, Insulin resistance, Liposomes, Maturity onset diabetes of the young, Nanoformulations, Nanoparticles.

INTRODUCTION

Overview of Diabetes Mellitus (DM)

DM is the type of complex metabolic disorder that is detected on the basis of increased glucose concentration within the systemic circulation [1]. Medically, hyperglycemia refers to a raised blood glucose concentration, whereas hypoglycemia refers to the opposite situation, as shown in Fig. (**1**) [2]. Hyperglycemia in diabetes mellitus is a result of either faulty action of insulin or aberrant production from pancreatic beta cells, and occasionally both happen simultaneously. It will show up as chronic and varied lipid, protein, and carbohydrate metabolism [3]. This abnormal metabolism could hamper multiple organs and their vital functioning throughout the body, which leads to a series of abnormal cascade reactions and contributes to the progression of diabetic conditions [4]. Micro- and macrovascular complications result in functional and structural deformities in the vasculature of body systems. Primarily the organ gets damaged and results in dysfunction of the organ system, and if it keeps on progressing, then this situation could worsen and ultimately end with organ system failure, due to which various vital systems get impacted, such as the sensory system, cardiovascular system (CVS), renal system, nervous system (NS), and digestive system [5]. Retinopathy is a type of complication that arises in eyes and leads to blindness; nephropathy is another type of complication associated with the renal system, while hypertension is the type of complication associated with the cardiovascular system, and neuropathy is associated with the nervous system [6]. These all are some major concerns that need to be monitored during diabetes mellitus. The degree of hyperglycemia and the risk for diabetes, retinal vascular disease, diabetic distal neuropathy, and diabetic neuropathy are clearly correlated, according to observational and clinical trial data. According to intervention trials comparing two different glycemic control levels, these diabetic consequences decrease by around 25% to 30% for every 1% decrease in HgbA1c [7]. Additionally, results from the Diabetes Control and Complications Trial indicate that early intensive treatment has long-lasting benefits that last for at least eight years. Early intervention is made possible by early recognition of the problems. The chances of problems may also be decreased by other targeted intervention techniques. These tactics include blood pressure management, renin-angiotensin-aldosterone system (RAAS) modulation for diabetic nephropathy, unloading devices for diabetic neuropathy, and laser photocoagulation for diabetic retinopathy (proliferative retinopathy and clinically significant macular edema)

[8]. Aspirin treatment, hypertension management, and lipid-lowering techniques lessen the prevalence of atherosclerotic vascular disease [9].

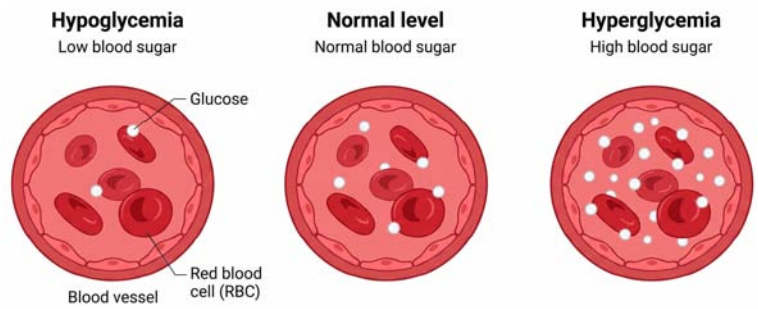

Fig. (1). Blood glucose concentration.

Hyperglycemia is considered a common feature in all variants of diabetes, but there are several other factors that should be accounted for while categorizing the type of diabetes, such as several pathogenic mechanisms, a variety of historical literature on disease progression, and different treatment approaches for different diabetes variants. Initially, in the 5th century, Aretaeus, a physician, used the term "diabetes" to describe the disease as a "melting down of flesh and limbs into urine" [10].

In the 5th century BC, Indian physicians consolidated information about the honey-like taste of urine in polyuric patients, which they described as "madhumeha," meaning sweet honey-like urine. The ants and insects get attracted to the sweet urine of polyuric patients [10]. Later, in the 17th century, the word "mellitus" (Latin for "honey") was added. In 1965, WHO classified diabetes for the first time into four stages based on the age of diagnostic criteria: infantile or childhood (0-14 years), young (15-24 years), adult (25-64 years), and elderly (≥65 years) [11]. In addition, WHO recognized other types of diabetes, such as gestational diabetes and juvenile-type diabetes. In 1980, WHO published its first globally acceptable classification system for diabetes, and later it was updated in 1985 [12]. In the 1980 WHO classification, they incorporated two major classes of diabetes: Type I (insulin-dependent diabetes mellitus) and Type II (non-insuli--dependent diabetes mellitus). In the 1985 revision, the words "Type 1" and "Type 2" were omitted, and the classes insulin-dependent diabetes mellitus (IDDM) and non-insulin-dependent diabetes mellitus (NIDDM) were retained, with the addition of two new classes: "malnutrition-related diabetes mellitus (MRDM)" and "gestational diabetes mellitus (GDM)." The same classification as prescribed *via* WHO was reflected in the International Nomenclature of Disease (IND) in 1991 and the International Classification of Disease, tenth revision (ICD-10) in 1992 [13].

CHAPTER 4

Nanophytomedicine in Combating Obesity: Innovations and Insights

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Abstract: Adipocyte development takes place largely as hypertrophy, by which adipocytes increase, combined with hyperplasia, where precursor cells form new adipocytes. Metabolic benefits tend to arise from hyperplasia, whereas hypertrophic expansion carries negative consequences, including metabolic dysfunction, inflammation, insulin resistance, and lipotoxicity. Adipogenesis is significantly controlled by mitochondrial metabolism, which enables PPARγ activation by breaking down branched-chain amino acids (BCAAs) to form acetyl-CoA. The cells adjust their metabolic activities to use the pentose phosphate pathway rather than mitochondrial oxidative phosphorylation to produce more NADPH, which supports lipogenesis. When mitochondrial stress becomes excessive, and ROS are produced, the survival rate of adipocytes declines, and tissue inflammation develops. Dyslipidemia describes obesity by indicators of elevated triglycerides and overproduction of VLDL, leading to excessive amounts of tiny, dense LDL particles. The combined action of cholesteryl ester transfer protein (CETP) and hepatic lipase lowers high-density lipoprotein (HDL) levels, thereby increasing cardiovascular risk. The state of insulin resistance amplifies dyslipidemia by increasing free fatty acid (FFA) flux, which leads to hepatic fat accumulation and impaired lipid filtration. The link between defective adipocytes and mitochondrial stress, combined with dyslipidemia, needs rapid development of particular therapy techniques to tackle obesity-related metabolic disorders. The article focuses on understanding the complex processes that govern adipose tissue growth, mitochondrial function, and lipid regulatory systems, which impact metabolic health and cardiovascular disease risk.

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Keywords: Cardiovascular disease, Herbal medicine, Hypertrophic, Interleukin, Insulin, Inflammation, Microbiota, Nano-phytomedicine, Nanocarriers, Nanotechnology.

INTRODUCTION

The global health epidemic of obesity impacts 640 million individuals globally [1]. The overall number of individuals with weight-related health problems is projected to increase to 167 million by 2025. Global forecasts indicate that obesity rates will escalate after 2035, with over four billion individuals, in addition to four billion more classified as overweight, potentially seeing a two-fold rise in the prevalence of childhood obesity. This epidemic poses significant health risks, including cardiovascular illnesses, diabetes, cancer, and complications from COVID-19, while generating an anticipated yearly economic burden of $4.32 trillion, or roughly 3% of global GDP [2].

Obesity management starts with lifestyle modifications as the initial phase of a tiered strategy. Nutritional initiatives should start with prenatal breastfeeding support, while medical groups advocate calorie regulation and exercise regimens, coupled with behavioral treatment, to address obesity [3]. Lipase inhibitors like orlistat, in conjunction with appetite suppressants, cause efficient weight loss of around 4-5 kg; nevertheless, they can lead to unpleasant effects ranging from gastrointestinal discomfort to psychological disorders and cardiovascular difficulties [4]. Bariatric surgery is the most effective medical intervention as it substantially decreases body weight and improves metabolic health. Bariatric surgery yields exceptional outcomes; nonetheless, some people avoid it because of its complex surgical procedure, high cost, and limited accessibility. Low-income nations, which account for nine of the 10 countries with the fastest-growing obesity rates, lack sufficient healthcare infrastructure [5]. The poor results obtained with current therapies urge scientists to explore plant-derived compounds, termed phytoactives, such as polyphenols, flavonoids, and alkaloids [6]. These natural chemicals promote anti-obesity effects by inhibiting digestive enzyme activity while simultaneously enhancing overall energy expenditure and appetite control, and they also influence how fat cells form and alter the composition of gut flora. The practical translation of photoactive compounds is hindered by their poor bioavailability, which is associated with rapid metabolism and irregular absorption when taken as crude plant extracts or herbal supplements [7].

Researchers developed nano-phytomedicine as a new approach to advance photoactive substances into clinical applications. Researchers use nanocarriers, including liposomes, polymeric nanoparticles, and nanoemulsions, to enhance the

bioavailability of photoactive compounds in pharmaceutical research, as these methods improve chemical integration, minimize enzymatic breakdown, and provide targeted delivery to adipose tissue and the gut microbiota [8]. Studies suggest that the introduction of nanotechnology into pharmaceutical development increases the bioavailability of resveratrol, curcumin, and green tea polyphenols by 2-5 times compared with conventional delivery methods. New technological developments in pharmacokinetics address critical challenges in drug distribution, potentially reducing the amounts of medicine needed while lowering adverse reaction rates [9]. The integration of current medication-delivery technology with traditional botanical insights through nano-phytomedicine offers promising new treatment strategies for obesity-related disorders. The challenge of global health systems in managing obesity, driven by various genetic, environmental, and socioeconomic factors, makes nanotechnology-based plant therapies a promising therapeutic option [10]. The effective deployment of nano-phytomedicine for obesity control involves several hurdles, including substantial clinical trials, regulatory compliance, and cost-effective production procedures. Researchers need to devote future efforts to developing appropriate nanocarrier designs, coupled with delivery optimization, to support thorough safety assessments and ensure the successful implementation of clinical nano-phytomedicine applications [11]. The increased incidence of obesity and accompanying health and economic concerns make nano-phytomedicine a viable future treatment for obesity management. The chapter describes current breakthroughs in nanotechnology by explaining how nanotechnology enhances phytoactive efficiency with translational research solutions. Nano-phytomedicine holds the potential to bridge the gap between traditional natural medicine and modern pharmaceutical technologies, offering enhanced health benefits and contributing to the global reduction of obesity.

Pathophysiology of Obesity

A combination of components, including metabolism, hormones, and inflammatory factors, along with heredity, leads to obesity as a medical disorder. Obesity manifests when cells accumulate excessive fat, leading to several metabolic concerns, including insulin resistance, inflammatory disorders, and lipid abnormalities [12]. Obesity pathophysiology originates from the combination of inadequate adipogenesis, metabolic abnormalities, endocrine disturbances, and inflammatory states and oxidation-related damage that eventually generates metabolic difficulties and heightened cardiovascular dangers [13].

CHAPTER 5

Integrating Nanotechnology and Phytomedicine for Hepatic Disease Treatment

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Abstract: Nanotechnology offers a new strategy for combining plant-based therapy for liver disease. The properties of a nanoscale material, a nanomaterial, are special and may be able to promote and nourish damaged hepatocytes in a less invasive manner than surgery or transplantation, and convert into new tissue in the body. Nano-sized drugs enhance the cure of liver diseases by enhancing drug bioavailability, drug distribution targeting, and drug release control. This is especially critical for resolving issues such as low solubility and rapid degradation of phytochemicals. There are many bioactive compounds in phytomedicine. This type of medicine can shield the liver and prevent inflammation, making it a natural way to fight liver diseases. Liver-specific ligands can be crafted based on the efficacy of the uplift-and attrition effect, with the passive aspect of the targeting principle. Having such a precise way of delivering, one can predict fewer side effects in the body and a higher level of effect, that is to say. An example is fatty liver disease. Nanocarriers loaded with antioxidants have the potential of mitigating oxidative stress. In cirrhosis, anti-fibrotic drugs may prevent hepatic stellate cells from producing too many collagen fibres and other substances to stiffen the liver tissue to the point of ultimately killing a patient.

Keywords: Biocompatible nanocomposites, Cirrhosis nanomedicine, Hepatic regeneration nanoplatforms, Hepatocellular nanodelivery systems, Hepatocellular targeted delivery, Hepatoprotective nanoformulations, Hepatotoxicity nanoamelioration, Herbal nanocarriers, Liver disease nanotherapy, Liver fibrosis nanotherapy, Liver-specific nanotargeting.

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INTRODUCTION

Chronic liver disease (CLD) and its associated complication, cirrhosis, cause approximately 1 million deaths per year. In addition to its clinical effect, CLD causes significant morbidity, damage to health-related quality of life, and costs (Table **1**) [1].

Table 1. Various hepatic diseases, their prevalence, diagnosis, and treatment rate.

Disease/Condition	Total Infections	Annual Deaths	New Infections	Diagnosis Rate	Treatment Rate
Hepatitis B Virus (HBV)	296 million	820,000	1.5 million	10%	2%
Hepatitis C Virus (HCV)	58 million (including 3.2 million children)	300,000	1.5 million	21%	13%
Polaris Observatory Data (Hepatitis-related infections)	316 million	555,000	Not specified	Not specified	Not specified
Global Burden of Disease (GBD) Data (2016)	2.91 million	Not specified	Not specified	10%	8%
Liver Disease (General)	113 million (58.8 million)	500,000	82.5 new cases per 100,000	Not specified	9.4 million treated (2015–2019)
Non-Alcoholic Fatty Liver Disease (NAFLD)	1,235.7 million	1.75–2.18 per 100,000	Not specified	Not specified	Not specified
Alcohol-Related Liver Disease (ALD)	56.8 million	Not specified	1.42 million new infections	2.3%	5%

Even though the development of specific drug delivery systems is a good solution to these issues. Nanotechnology offers a mouth-watering prospect for targeted drug delivery, especially given the liver as the target in this case [2]. The liver, being the primary site of drug breakdown and excretion, has unique anatomy and physiology that facilitate the easy delivery of drugs [3]. Also, targeted to specific liver diseases, nanomaterials can be used to deliver therapeutic agents to specific liver cell populations, including hepatic stellate cells (HSCs) to treat liver fibrosis or hepatocytes to treat Hepatocellular carcinoma with hepatitis B virus (HBV) infection.

Nanotechnology-based drug delivery system that can increase the efficacy of drugs and limit toxicity by targeting the liver and decreasing the exposure of the drug to other organs [4]. Despite improvements in traditional medicine over the last several years, an increasing number of scientists have begun to show interest

in phytomedicine. Most of the recent observations within Europe and the United States have identified that over 65 percent of people with liver disease are currently experimenting with herbal treatment in a matter of a few years [5]. There are molecules that share common therapeutic effects but differ in structure and are derived from different plant species, which can be used as active ingredients in the treatment of various ailments. Many phytochemicals have been reported to possess very strong hepatoprotective effects, including flavonoids, alkaloids, glycosides, and saponins, which are derived from various plant sources. Plants have various compounds that are antioxidants. Somecompounds, including phenolics (including flavonoids and phenolic acids), nitrogen-based compounds (including alkaloids, chlorophyll derivatives, amino acids, and amines), carotenoids, lignans, and terpenes, can prevent the initiation or progression of chain reactions [6].

NANOTECHNOLOGY IN DRUG DELIVERY

To transport drugs effectively, it is a clever idea to create nanosystems that are designed to move through the environment and bind to receptor sites on target cells, like keys to small, changing locks. Other important areas of research include changes in cell receptors as the disease progresses, the mechanisms and sites of action of drugs, the duration of their presence in the body, the synergies of multiple drugs, the biochemical processes underlying the disease, and the disease's underlying biology. The most important thing is to understand the obstacles drugs face, such as maintaining stability under conditions of changing cellular chemistry [7]. The potency of a drug may be lost due to instability during intracellular existence, inability to reach the target, interference with the chemistry of its delivery molecules, genetic anomalies of cell-surface receptors, hyperactive efflux pumps, altered disease signals, and even simple degradation of the drug; all can undermine its efficacy. An example illustrating this is that when DNA methylation increases in cancer cells, the efficacy of those treatments can be altered by a small amount, as if pushing a lock ajar so that a key cannot fit [8]. This may result in deterioration of the efficacy of most anticancer agents, including doxorubicin and cisplatin. Understanding the process of drug uptake, the intracellular transport, retention, and resistance to degradation is important in enhancing the functionality of encapsulated therapies. The novel opportunities provided by nanotechnology include the possibility of achieving specific control at the atomic, molecular, and supramolecular levels and creating new types of drug delivery systems with exclusive properties. Due to their numerous characteristics, nanocarriers are effective drug delivery systems [9].

The concept of nanotechnology applied to nutraceuticals, however, is new to the industry. Biodegradable nanoparticles can be modified by loading with various

CHAPTER 6

Revolutionizing Dyslipidemia Treatment: The Role of Nanophytomedicine in Lipid Control

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Abstract: One of the major risk factors for stroke, metabolic disorders, and cardiovascular diseases is abnormal lipid levels, also called dyslipidemia. Examples of traditional lipid-lowering drugs are statins, fibrates, and PCSK9 inhibitors. Among their side effects, low patient compliance and inconsistent effectiveness, these drugs often have limitations. Combining phytochemicals with nanotechnology, nanophytomedicine is a novel concept that could resolve these issues. This chapter looks at how nanophytomedicine could control lipids by improving the bioavailability, stability, and targeted delivery of plant-based biologically active components, thereby lowering lipid levels. The chapter opens with a brief overview of dyslipidemia, its pathophysiology, and the issues with current therapies. The next step is to explore the potential of phytochemicals, which have been shown to have lipid-modulating effects but are characterized by low solubility and bioavailability. Different ways to enhance the pharmaceutical efficiency of these phytochemicals, such as nanoparticles, nanotechnology-based liposomes, micelles, and nanoemulsions, have been presented. Preclinical and clinical research that demonstrates the application of nanophytomedicine in personalized therapy and its effectiveness in lipid management has been presented. Formulation development challenges, safety issues, and regulatory

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aspects moving from research to clinical application are also included in this discussion. Nanophytomedicine drives the next generation of dyslipidemia management by combining nanotechnology with natural therapies, resulting in safer, more effective, and patient-centered treatments. This chapter provides a thorough knowledge of its capabilities, challenges, and opportunities for revolutionizing lipid control strategies.

Keywords: Bioactives, Bioavailability, Biocompatibility, Clinical translation, Dyslipidemia, Lipid modulation, Liposomes, Micelles, Nanocarriers, Nanoemulsions.

INTRODUCTION

Understanding Dyslipidemia: Pathophysiology and Health Impact

Dyslipidemia, or abnormal blood lipid levels, is one of the chief contributors to metabolic disorders and cardiovascular diseases (CVD) worldwide. The listed increases are in total cholesterol, HDL-C, low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG). Clinicians and researchers must be aware of the syndrome as it is a major modifiable risk factor for atherosclerosis, coronary artery disease (CAD), and stroke [1, 2]. The pathophysiology of dyslipidemia involves complex interactions among genetic predisposition, metabolic dysregulation, and dietary habits. Primary dyslipidemia can be caused by genetic diseases such as familial hypercholesterolemia (FH), which is a result of mutations in the LDLR, APOB, or PCSK9 genes [3]. Secondary dyslipidemia is the result of lifestyle habits such as drinking too much alcohol and being inactive, as well as the presence of other diseases like diabetes mellitus, obesity, hypothyroidism, and chronic renal disease [4]. Lipid metabolism is regulated in part by the liver, lipid intake, and intestinal absorption. Atherosclerotic plaque and foam cell development are caused by lipid buildup in arterial walls due to dysregulation of these pathways, such as decreased LDL receptor activation or increased VLDL production [2]. Metabolic syndrome-induced insulin resistance exacerbates dyslipidemia by elevating hepatic VLDL secretion and reducing lipoprotein lipase (LPL) activity, thus increasing the level of triglyceride-rich lipoproteins [5]. Dyslipidemia has significant clinical implications and is a leading global cause of morbidity and mortality. Low HDL-C is one factor that affects reverse cholesterol transport (RCT), thereby increasing cardiovascular risk, while elevated LDL-C is a direct causative factor of atherosclerosis. Incidentally, hypertriglyceridemia has a close association with pancreatitis and, when insulin resistance is also present, it leads to non-alcoholic fatty liver disease (NAFLD) [6].

Epidemiological studies evidence the magnitude of the problem of dyslipidemia. The Global Burden of Disease (GBD) study, which estimates that high non-HDL cholesterol accounts for around 4.4 million deaths each year, underlines the importance of early detection and treatment [7]. On top of that, dyslipidemia may also play a role in neurodegenerative diseases such as Alzheimer's, through lipid-mediated oxidative stress and inflammation, as per recent studies [7, 8].

To develop effective therapies, one needs to understand the causes and the impact of dyslipidemia on health. The entire lipid management drug sector has been revolutionized by major pharmacological breakthroughs, including statins, PCSK9 inhibitors, and RNA-based therapies [9].

Current Pharmacological Approaches and Their Limitations

Dyslipidemia is one of the main modifiable risk factors for atherosclerotic cardiovascular disease (ASCVD), and it is still a major worldwide health problem. Different patient populations present a challenge to achieving perfect lipid control, even though there have been significant advances in pharmacotherapy. Through various mechanisms, such as cholesterol synthesis inhibition, promotion of lipoprotein clearance, and modulation of triglyceride metabolism, current therapeutic approaches primarily focus on LDL-C, TG, and HDL-C. Nevertheless, disadvantages such as variable patient responses, adverse effects, and residual cardiovascular risk indicate that we need to evaluate existing therapies [9] thoroughly.

Current Pharmacological Approaches

- **Statins: The First-Line Therapy:** Statins, which inhibit 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, are the cornerstone of treating dyslipidemia. Statins increase LDL receptor expression and improve LDL-C clearance by decreasing hepatic cholesterol production [2]. Statin usage has been shown to significantly reduce ASCVD occurrences in large-scale trials, including the Heart Protection Study and JUPITER [10]. However, 5–15% of people are unable to use statins due to statin intolerance, which might present as myopathy, hepatic dysfunction, or new-onset diabetes [11].
- **Fibrates and Omega-3 Fatty Acids for Hypertriglyceridemia:** By activating peroxisome proliferator-activated receptor-alpha (PPAR-α), fibrates (like fenofibrate) lower TG by 30–50% and slightly raise HDL-C. However, outside of severe hypertriglyceridemia, their cardiovascular advantages are still unknown. Although their effectiveness varies by formulation and is dose-dependent, prescription omega-3 fatty acids (such as icosapent ethyl) lower the incidence of ASCVD in high-risk individuals [12].
- **Ezetimibe and Bile Acid Sequestrants:** As an adjuvant treatment, ezetimibe,

CHAPTER 7

Plant-based Nanotechnology: Innovation in Depression and Anxiety Management

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Abstract: Major depressive disorder and anxiety disorders are prevalent mental disorders that account for substantial worldwide disability and personal suffering. Surprisingly, conventional treatments have unsatisfactory efficacy, severe side effects, or drug resistance and relapse in many patients, which necessitates the development of novel, safe, effective, and durable therapies. Plant-based nanotechnology seems advantageous as it fuses the benefits of plant-derived active compounds and nanotechnology applications. These plant-based nanomaterials, incorporated into nanoparticles and phytochemicals, can easily communicate with molecular biological systems, thus offering a targeted therapeutic approach to treating mental health disorders. This approach may open up new possibilities for increasing the solubility and bioavailability of plant-derived compounds, developing new therapeutic systems for the delivery of antidepressants and anxiolytics, and introducing targeted therapy with fewer or no side effects compared to standard drugs. The antioxidant, anti-inflammatory, and neuroprotective properties of plant-based nanomaterials, being the key depots of depression and anxiety disorders, provide an amplified prospect. However, several limitations have been observed regarding a number of these experimental therapeutics, including safety measures, toxicity, regulatory issues, and a large number of clinical trials to confirm the effectiveness of these therapies. This chapter aims to discuss the application of plant-based nanotechnology in depression and anxiety, the mechanism of action of the treatment, the therapeutic effect, and further research direction.

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Keywords: Antidepressant properties, Anxiety management, Anxiolytic effects, Cognitive function, Depression management, Herbal extracts, Liposomal delivery, Mental health innovation, Nanomedicine, Neuroprotective effects, Plant-based nanotechnology, Phytochemicals, Phytosome technology, Polyphenols, Stress reduction, Targeted drug delivery.

INTRODUCTION

Disturbances in mental health, including depression and anxiety, have now turned into critical global health predicaments. A recent report from the World Health Organization (WHO) shows that over 280 million people in the world suffer from depression, while an estimated 300 million people in the world have been diagnosed with anxiety disorders [1, 2]. Apart from the degradation of quality of life, these conditions cause disability, loss of productivity, and an increase in healthcare costs. Though there have been traditional pharmacological treatment methods like Selective Serotonin Reuptake Inhibitors (SSRIs) and benzodiazepines, some still have disappointing effects with side effects, poor bioavailability, and resistance to drugs. All these have necessitated curiosity in alternative interventions, specifically plant-based compounds, to give better results in the treatment of mental disorders. Different kinds of medicinal plants have been used since ancient times in traditional medical systems such as Ayurveda, Traditional Chinese Medicine (TCM), and other Indigenous practices of healing for understanding mental disorders. Bioactive phytochemicals such as flavonoids, alkaloids, terpenes, and polyphenols have proved to possess neurological and psychotropic promise [3, 4]. To cite a few examples, curcumin (turmeric), Withania somnifera (ashwagandha), CBD from hemp, and polyphenols in green tea. These compounds exert multiple effects, such as anxiety and antidepressant properties, by mechanisms of neurotransmitters, oxidative stress, and inflammation, which are witnessed in several pathways [5, 6].

To enhance the therapeutic efficacy of plant-derived compounds against depression and anxiety, various nanocarrier strategies have been developed to address existing pharmacological challenges. Further research, particularly large-scale clinical trials, is required to determine the efficacy, safety, and best dosing of these novel treatments [7]. Researchers targeting dual-action therapies to enhance the mental aspect from multiple physiological angles may employ nanoparticle formulations aimed simultaneously at the gut as well as the brain. Such a holistic approach could provide specific relief in instances dealing with treatment-resistant depression and anxiety disorders, as mentioned in Table **1** [8].

Table 1. Innovations in plant-based nanoformulations for mental health.

Innovation	Description	Potential Benefits	Refs.
Nano-encapsulation of Herbal Extracts	Encapsulation of plant-based compounds (e.g., curcumin, ashwagandha) in nanoparticles.	Enhanced bioavailability, prolonged release, improved absorption.	[9]
Lipid-based Nanocarriers	Use of liposomes and phytosomes for delivering plant-derived anxiolytics.	Improved brain penetration and targeted delivery.	[10]
Polymeric Nanoparticles	Encapsulation of flavonoids (e.g., quercetin) in biodegradable polymers.	Controlled drug release, reduced toxicity.	[10]
Nano-emulsions	Formulation of essential oils (e.g., lavender, chamomile) into nano-sized emulsions.	Faster onset of action, enhanced solubility.	[11]
Nanoparticle-assisted Neurotransmitter Modulation	Use of plant-derived nanoparticles to regulate serotonin and dopamine levels.	Non-invasive therapy reduces dependency on synthetic drugs.	[12]

Plant-based Nanotechnology: Concept and Mechanism

This kind of nanotechnology mostly involves the use of different kinds of plant extracts in the synthesis of nanoparticles, using phytochemicals and other derived compounds from plants [13]. Synthesis of nanoparticles through plants can be called the green, sustainable alternative to chemical and physical methods typically used [14].

Rationale of Plant-based Technology

Plant-derived compounds such as curcumin, quercetin, resveratrol, ashwagandha, ginsenosides, and crocin exhibit notable antidepressant and anxiolytic properties through multiple mechanisms. They modulate monoaminergic neurotransmission, enhance neurotrophic signaling, attenuate oxidative stress, and suppress neuroinflammatory responses. However, many of these molecules have hydrophobic structures, undergo rapid metabolism, and display minimal Blood-Brain Barrier (BBB) penetration. Nanotechnology-based carriers—including liposomes, Solid Lipid Nanoparticles (SLNs), Nanostructured Lipid Carriers (NLCs), polymeric nanoparticles, and phytosomes—address these challenges by increasing solubility, prolonging circulation time, and enabling targeted delivery (Figure 1). Furthermore, the green synthesis of nanoparticles using plant extracts or phytochemicals themselves provides an environmentally sustainable and biocompatible alternative to conventional nanomaterial fabrication.

CHAPTER 8

Innovative Therapies for Neurodegeneration: The Role of Nanophytomedicine

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Abstract: The hallmarks of neurodegenerative diseases, including Huntington's, Parkinson's, and Alzheimer's, include progressive loss of neurons and compromised cognitive and physical abilities. Effective treatment approaches are still elusive despite tremendous progress because of the intricate pathophysiology of these conditions. Nano Phytomedicine, which combines nanotechnology with bioactive substances obtained from plants, has become a viable way to get beyond the drawbacks of traditional treatments. By improving bioavailability, focusing on specific targets, and overcoming biological barriers such as the blood-brain barrier, nanocarriers can minimize systemic toxicity by delivering phytochemicals directly to the areas of damaged neurons. This chapter examines the novel ways that nano-phytomedicine can be used to treat inflammation, oxidative stress, and protein development in the creation of nanocarriers that include phytochemicals like quercetin, resveratrol, and curcumin, including liposomes, polymeric nanoparticles, and dendrimers. Additionally, clinical and preclinical research that highlights the potential for therapy and difficulties in bringing these innovative systems to clinical settings are examined in this chapter. In order to battle neurodegenerative diseases and improve patient results and standard of life, Nano Phytomedicine provides a revolutionary avenue for the development of safe, effective, and targeted medicines through the integration of interdisciplinary techniques.

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INTRODUCTION

A variety of diseases known as neurodegenerative disorders are characterized by a progressive loss of neuronal structure and function, which results in impairments in behavior, motor function, and cognition [1]. Alzheimer's Disease (AD) is the most common type, which is characterized by amyloid-beta plaque accumulation and tau tangles, which lead to cognitive impairment and memory loss. The development of Lewy bodies and the death of dopaminergic neurons cause bradykinesia, stiffness, and tremors, which are the primary symptoms of Parkinson's Disease (PD). Genetic abnormalities leading to abnormal protein aggregation cause Huntington's Disease (HD), which manifests as emotional instability, uncontrollable movements, and cognitive impairment [2]. Motor neuron degeneration, which causes progressive muscle weakness and eventually respiratory failure, is a hallmark of ALS. The hallmark of Multiple Sclerosis (MS) is an immune-mediated attack on the central nervous system that causes demyelination and neurological deficits. While genetic defects affecting cerebellar neurons cause loss of motor coordination in spinocerebellar ataxias (SCAs), tau or TDP-43 protein deposits in frontotemporal dementia (FTD) induce personality changes and linguistic difficulties. Excitotoxicity, neuroinflammation, mitochondrial dysfunction, oxidative and nitrosative stress, and protein aggregation are among the basic mechanisms underlying these diseases [3]. Because many disorders share common pathogenic pathways, understanding the molecular mechanisms behind them is essential to developing targeted treatment approaches that will reduce their devastation [4].

Problems With Modern Therapeutic Strategies

Despite advances in our understanding of the underlying causes of neurodegenerative disorders, several challenges remain in developing and implementing effective treatment plans [5]. The creation of treatments that alter disease is severely hampered by the intricacy of these conditions [6].

Limited Understanding of Disease Mechanisms

Neurodegenerative diseases are associated with a number of pathogenic processes, such as neuroinflammation, protein aggregation, excitotoxicity, oxidative stress, and mitochondrial failure. The interaction between these elements is currently unclear, making the design of tailored treatments difficult [7].

Blood-Brain Barrier (BBB) Penetration

This barrier has prevented several potential therapeutic medications from passing through, which has limited the central nervous system's (CNS) bioavailability. Creating delivery systems that can efficiently target brain tissues is difficult [8].

Lack of Disease-modifying Therapies

Acetylcholinesterase inhibitors and NMDA receptor antagonists, for instance, are medications used to treat Alzheimer's disease that only temporarily alleviate symptoms; they do not treat the underlying neurodegeneration [9].

Heterogeneity of Neurodegenerative Disorders

The start, course, and response to therapy of diseases vary greatly among patients. This diversity makes it more difficult to create standardized treatment plans and emphasizes the necessity of personalized medical tactics [10].

Ineffective Targeting of Protein Aggregates

Clinical trials have largely failed due to the ineffectiveness or adverse side effects of treatment techniques that attempt to eliminate dangerous protein clumps, such as amyloid-beta in Alzheimer's disease or alpha-synuclein in Parkinson's disease [11].

Chronic Neuroinflammation

The results of anti-inflammatory therapy have been inconsistent, even though inflammation is a major factor in neurodegeneration. Because inflammation has both beneficial and detrimental properties, finding effective anti-inflammatory medications is challenging [12].

Addressing these problems requires a multipronged approach that includes developing advanced drug delivery systems, improving our understanding of the mechanisms behind disease, using personalized medicine techniques, and integrating cutting-edge technologies like gene therapy and nanomedicine. These challenges must be overcome to develop effective disease-modifying therapies for neurodegenerative illnesses [13].

Nanomedicine's Rise to Prominence as a Novel Therapeutic Strategy

The use of nanomedicine has revolutionized the treatment of neurodegenerative illnesses by addressing many of the shortcomings of traditional therapy approaches. This innovative sector delivers more accuracy, greater bioavailability,

CHAPTER 9

Nanophytomedicine in Epilepsy: Unlocking Nature's Potential for Seizure Control

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Abstract: Epilepsy, a chronic neurological disorder affecting millions worldwide, demands innovative treatment approaches. This abstract explores the emerging field of nanophytomedicine as a promising avenue for seizure control. Nanophytomedicine integrates the therapeutic capabilities of plant-based medicines with nanotechnology, providing improved bioavailability, targeted drug delivery, and reduced adverse effects. We review recent advancements in developing nanoformulations of phytochemicals with anticonvulsant properties, highlighting their mechanisms of action and efficacy in preclinical and clinical studies. The integration of nanotechnology with traditional herbal remedies has shown remarkable potential in improving drug delivery across the blood-brain barrier, increasing the therapeutic index, and minimizing adverse effects associated with conventional antiepileptic drugs. Additionally, we examine the obstacles and prospects in translating nanophytomedicine studies into clinical use, highlighting the necessity for standardized and quality-assured herbal extract formulation and nanoparticle production. This review underscores the importance of nanophytomedicine as a novel, nature-inspired approach to epilepsy treatment, potentially revolutionizing seizure management and improving the quality of life for individuals with epilepsy.

Keywords: Anticonvulsant, Bioavailability, Blood-brain barrier, Drug delivery, Epilepsy, Herbal medicine, Liposomes, Nanocarriers, Nanomedicine, Nanoparticles, Nanopharmacology, Nanophytomedicine, Natural compounds, Neuroprotection, Oxidative stress, Phytochemicals, Polymeric nanoparticles, Seizure control, Solid lipid nanoparticles, Targeted therapy.

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INTRODUCTION

Epilepsy is a recurrent neurological disorder characterized by recurring seizures with no clear triggers [1]. Epilepsy is a type of neurological condition that involves unexpected and recurring disturbances of normal brain activity, known as seizures. Unpredictable, recurrent disruptions of normal brain function are known as epileptic seizures. More than 50 years ago, the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE) characterized epilepsy as a neurological disorder characterized by recurrent epileptic seizures, resulting in neurobiological, psychological, cognitive, and social ramifications. In terms of mechanics, an epileptic seizure is described as "a condition generated through an inappropriate, uncontrolled neuronal discharge inside the central nervous system". Some types of epilepsy that are inherited are caused by mutations in genes that encode voltage- and ligand-gated ion channel subunits. Generalized epilepsy and infantile seizure syndromes are caused by changes in Na+, K+, and Cl- channels in voltage-gated ion channels [2, 3]. Patient survey results suggested that epilepsy affects 4 to 10 individuals per 1,000 members of the population and is a prevalent neurological illness among demographic groups [4, 5]. Research indicates that epilepsy impacts 50 to 60 individuals per 100,000 annually [4, 6], whereas seizures affect 8% of the population at some stage in their lives [7]. Patients with epilepsy exhibit heightened prevalence of many medical and psychological problems, alongside increased healthcare utilization and elevated mortality rates relative to the general population [8, 9]. Individuals with recurrent seizures exhibit a decreased quality of life (QoL) [8], accompanied by diminished work prospects and productivity levels [10]. Hospital admissions due to epileptic seizures account for 1% of all hospital cases, but 3% of emergency department patients encounter these incidents. Individuals with epilepsy have annual healthcare costs beyond US$11,000, along with other expenses exceeding US$3,000 [11]. Enhancements in supplementary investigations, such as EEG, magnetic resonance imaging, and genetic testing, address the diagnostic and therapeutic challenges of epilepsy, while they do not fully resolve them [12]. The diagnosis and treatment plan selection processes for epilepsy are essentially reliant on medical histories and clinical follow-up procedures [13].

Medical research indicates that India has 55 million individuals with epilepsy, compared to 20 million in the USA and 3 million in the UK. Medical institutions in the United States indicate an annual incidence of newly identified seizures in 120 individuals per 100,000 population [14]. At least 8% of the general population experiences a single seizure while remaining clear of epilepsy. The probability of an individual experiencing a further unprovoked seizure within five years after their initial episode ranges from 23% to 80%. Epilepsy affects 44

individuals per 100,000 annually when age variables are standardized for assessment. Annually, around 125,000 new epilepsy cases are reported, with thirty percent arising before the age of 18. Medical authorities presently acknowledge the prevalence of epilepsy among senior people. Medical data reveal that over 10 percent of senior long-term care residents are currently administered six or more antiepileptic medicines (AEDs) for the management of their diseases. The research indicates that epilepsy results in over 1,000 deaths per year in the United Kingdom, predominantly due to seizures; yet, 42 percent of these deaths are deemed preventable [15].

Historical records indicate that pharmacological intervention for seizures commenced in 1912 when Alfred Hauptmann of Poland discovered the anticonvulsant properties of phenobarbital. Phenobarbital is the leading antiepileptic medication for seizure management due to its continuous application since its inception in 1912. Epilepsy was first effectively treated with phenytoin in 1940, succeeded by ethosuximide in 1958, carbamazepine (CBZ) in 1974, and sodium valproate (VPA) in 1978. Since the mid-1990s, physicians have primarily utilized these medications as components of the initial generation of antiepileptic drugs (AEDs). Medical experts introduced vigabatrin in 1989, followed by lamotrigine in 1990 and further antiepileptic drugs during that decade and the early years of the new millennium. These medications were part of the second generation of antiepileptic medicines (AEDs) that offered clinical effectiveness with less toxicity. The latest antiepileptic medications include vigabatrin (1989), lamotrigine (1990), oxcarbazepine (1990), gabapentin (1993), felbamate (1993), topiramate (1995), tiagabine (1998), zonisamide (2000), and the AEDs lacosamide (2008), eslicarbazepine (2009), and perampanel (2012). These are the pharmaceuticals that emerged subsequent to the second generation. In November 2019, the FDA sanctioned cenobamate for the treatment of partial-onset seizures in adults. In 2022, the FDA sanctioned ganaxolone from Marinus Pharmaceuticals for the treatment of epileptic seizures in children and adolescents with cyclin-dependent kinase-like 5 (CDKL5) deficient disorder [16]. Subsequent examination encompasses three pharmacological candidates: CGP46381 [17], SGS-742, and cannabidivarin (CBDV) [18]. Over thirty distinct pharmaceuticals have received FDA approval as therapeutic options for the treatment of epilepsy. Despite significant developments in drugs, conventional antiseizure drugs (ASMs) have several drawbacks and difficulties. These include possible long-term hazards such as organ poisoning and concerns with bone health, as well as adverse effects like drowsiness, light-headedness, and cognitive impairment. Finding the proper drug frequently requires trial and error, and while ASMs are beneficial for many, they do not function for around 30% of people. Long-term usage can be difficult because of side effects and pregnancy concerns, while drug interactions and the requirement for frequent dosage changes add complication. Another issue is

CHAPTER 10

Nanophytomedicine for Myasthenia Gravis: Natural Approaches to Autoimmune Modulation

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Abstract: Myasthenia gravis (MG) is a rare, chronic autoimmune disorder caused by autoantibodies that target receptors on the postsynaptic membrane of the neuromuscular junction. Recent data indicates that ferroptosis and mitochondrial damage may be involved in the pathophysiology of MG, in addition to immunological dysfunction. Medicinal plant-based phytotherapy has great capabilities for treatingvarious types of illnesses. Herbal medications are crucial to the health sector because of their medicinal ingredients, which provide a high safety profile with few adverse effects. Many medicinal plants are useful resources in pharmaceutical research and development because they have anticancer, antioxidant, and gene-protective properties. Nonetheless, MG might benefit from the application of nanodrug delivery systems that include immunomodulatory medications, antioxidants, or ferroptosis inhibitors. Furthermore, nanoparticles are appropriate delivery methods for a variety of pharmacological agents, including RNA and drugs with lower water solubility and bioavailability, because they are sufficiently biocompatible and degradable. Because of its exceptional adaptability and biocompatibility, nanomedicine has become a ground-breaking method of treating a variety of diseases. However, little is known about its potential to treat Myasthenia Gravis (MG). This chapter provides a comprehensive analysis of various herbal-based nanoplatforms that may be used for targeted MG treatment in an effort to bridge this gap. By possibly controlling immunological dysfunction and restoring mitochondrial integrity, these innovative formulations provide a novel therapeutic approach to enhance illness management.

Keywords: Acetylcholine receptors, Blood brain barrier, Clinical manifestation, Conventional treatment, Dendrimers, Diagnostic approaches, Future scope, Herbal metabolites, Immune modulation, Marine therapeutics, Myasthenia gravis, Nanoemulsion, Nanotechnology, Neuromuscular Junction, Pathogenesis, Physiology, Plants, Symptoms, The central nervous systems, Therapeutical applications.

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INTRODUCTION

Myasthenia gravis (MG), a long-term autoimmune disease affecting the neuromuscular system, results in intermittent muscle weakness and fatigue in different body parts. Usually, it disrupts nerve-muscle transmission, impacting voluntary muscles and making it challenging to move, breathe, and carry out other essential functions [1]. Autoantibodies against the acetylcholine receptors (AChRs) at the junction of muscle fibers and post-synaptic motor nerve ends lead to the development of this disorder. It disrupts the normal synaptic transmission in muscles and nerves.

Myasthenia Gravis can manifest in a variety of ways, from mild ocular symptoms to widespread muscle weakness that can interfere with day-to-day activities [2]. In order to enable coordinated movements, nerve signals are sent to muscle fibers *via* the neuromuscular junction, a specialized synapse found between muscle fibers and motor neurons. Acetylcholine (ACh) is released from presynaptic neurons inside the synaptic cleft during this neurotransmitter release process [3]. After that, the acetylcholine molecule binds to the nicotinic receptor located on the muscle cell membrane. This activation of the receptor allows the sodium ions to penetrate the cell, which, in return, causes the muscle cell to contract. In order to maintain controlled signal transmission, acetylcholinesterase (AChE) rapidly degrades ACh during the neurotransmitter recycling process [4]. Myasthenia gravis affects 1 in 5,000 persons globally and is more common in males over 50 and women under 40. The management of symptoms has been enhanced by developments in immunotherapy, targeted biological treatments, and clinical diagnostics. But it is still incurable, necessitating ongoing disease surveillance [5].

Pathophysiology of Myasthenia Gravis

The neuromuscular junction (NMJ) is responsible for signal transmission from motor neurons to skeletal muscles, enabling coordinated voluntary movements. In Myasthenia Gravis, this mechanism is impaired due to autoimmune-mediated destruction of AChRs (Fig. **1**) [6].

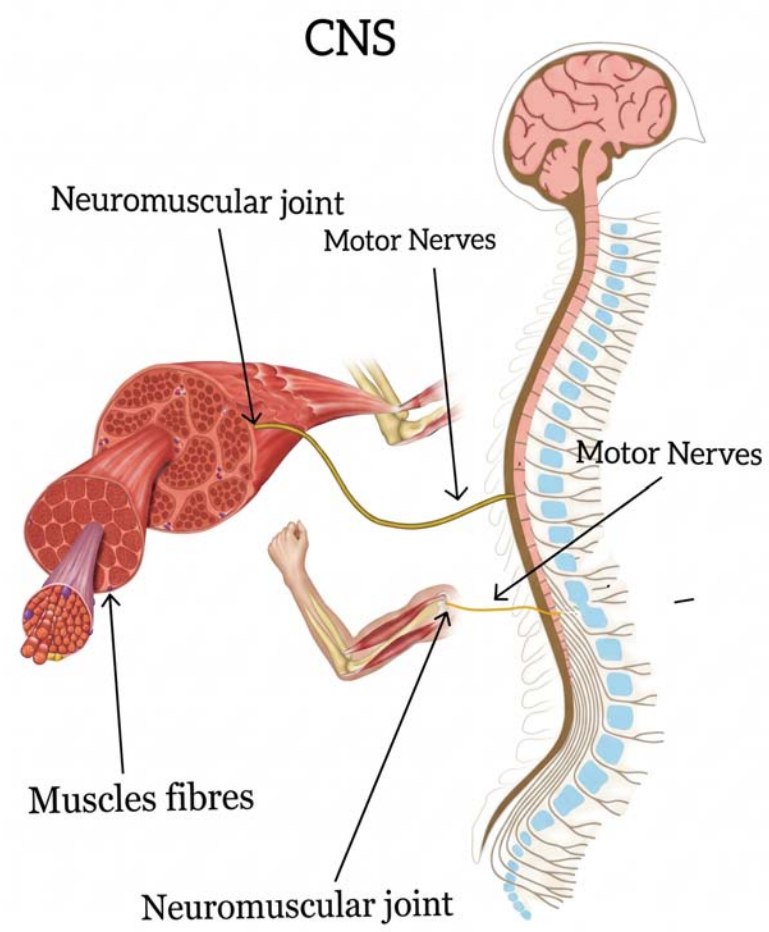

Fig. (1). Representation highlighting the central nervous system communication with skeletal muscles *via* motor nerves, enabling voluntary movement and muscle control, illustrating their role in transmitting neural signals for muscle movement.

In healthy individuals, neuromuscular transmission happens in the NMJ, where the impulses from nerves provide a trigger to release the ACh from presynaptic motor neurons into the synaptic cleft. Released Ach from neurons binds with nAChRs on the postsynaptic membrane of muscle fibers, which causes the release of an action potential that results in contraction of muscles [7]. In MG, autoantibodies attack the neuromuscular junction, which causes impairment of synaptic signals transmission and progressive weakness of the muscle. The mechanisms include three pathways: autoantibody-mediated receptor blockade, complement-mediated destruction of AchRs, and thymic dysfunction and autoimmune activation (Fig. **2**) [8].

CHAPTER 11

Targeting Stroke With Nanophytomedicine: Innovations in Neuroprotection and Repair

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Abstract: Stroke, or cerebral infarction, is a multifactorial (both vascular and neurologic etiologies) complex neurological disorder resulting caused by occlusion of blood vessels, resulting in altered cerebral blood flow, and is devoid of a cure to date. It is the second leading cause of death and the leading cause of disability worldwide, affecting over 500,000 people each year in the United States. Its complex pathophysiology poses significant challenges for comprehension and appropriate disease management. Despite improvements in stroke care, difficulties such as side effects, resistance to treatment, and the costs associated with therapy reduce both the efficacy of treatment and accessibility. Moreover, low bioavailability, poor blood-brain barrier penetration, and rapid elimination are also the barriers that prevent stroke from being effectively treated with current drug treatments. In essence, there is an urgent need to find more effective treatment methods for stroke. Accordingly, nanophytomedicine provides a prospective method and a new opportunity for stroke therapy because of its special characteristics. A number of nanocarrier systems, such as liposomes, nanoemulsions, nanoparticles, polymeric micelles, quantum dots, and dendrimers, are preferred because they are highly stable, biocompatible, and can promote drug absorption. By these properties, therapeutic efficacy, toxicity, and pharmacokinetic potential are increased. Thus, the targeted therapy of nanophytomedicine could selectively act on diseased nerve tissues and regions, control drug release, improve its bioavailability at the site of cerebral infarction, and reduce drug resistance so as to attain the ideal therapeutic effects with a lower dose of drugs. According to the currently available scientific evidence, this chapter provides an overview of stroke, highlighting the advantages of nanophytomedicine compared to

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conventional therapies, various approaches in development and uses of nanophytomedicine, as well as the usage and delivery of drug systems based on nanoparticles with extracted active principles and their mechanisms.

Keywords: Anti-inflammatory, Bioavailability, Blood-brain barrier, Cerebral blood flow, Cytokines, Drug release, Glutamate release, Ischemic stroke, Mortality, Mitochondrial dysfunction, Neurological disorder, Natural product nanophytomedicine, Nanocarrier, Nanoparticles, Oxidative stress, Polymers, Reperfusion, Stability, Therapeutic efficacy.

INTRODUCTION

Cerebral infarction, or stroke, is a complex central nervous system disorder caused by the multi-factor induction of vascular occlusion resulting in perturbed cerebral perfusion and irreparable damage to neurons, with no clear cure [1]. Symptoms of stroke are based on the volume and site of brain injury, and may include paresis, sensory abnormalities, weakness, nausea, aphasia (language disorder), dysarthria (speech disorder), and visual disturbances [2]. Motor deficits, cognitive impairments, and an incidence of epilepsy [3, 4] are reported in up to 80% of stroke survivors. The implications of these deficits are overwhelmingly negative with regard to normal daily-life activities, independence, and health [5, 6]. The etiology of stroke, which can be classified as ischemic or hemorrhagic, is primarily caused by embolism, thrombosis, hypoperfusion, and vasculopathies like atrial fibrillation and atherosclerosis that often cause catastrophic consequences [7, 8]. Ischemic stroke is an acute cerebrovascular event caused by an impaired cerebral blood circulation, leading to irreversible infarction in the core and potentially salvageable damage in the penumbra, for which only marginal therapeutic strategies are available [9]. According to the most recent statistics from the American Heart Association (AHA), Ischemic stroke, which is caused by the blockage of a blood vessel that supplies blood to the brain, represents nearly 87% of total cases. On the other hand, hemorrhagic strokes are caused by arterial bursting or leaking and account for almost 15% of all strokes [10, 11].

GLOBAL BURDEN

Throughout the world, stroke is the second leading cause of death and the third leading contributor to disability, resulting in approximately 5.5 million deaths every year and posing a significant burden on disability (12.8% in developing countries and 8.7% worldwide) [12, 13]. Stroke is responsible for 10–14% of all cases in young adults (<50 years), and about 50% of survivors are left with disabilities, leading to significant morbidity [13 - 15]. Stroke among adults (20–44

years of age) has increased from 17 per 100,000 in 1993 to 28 per 100,000 in the United States. Donkor *et al*. (2018) have estimated in their projections that the global stroke burden will be 23 million cases by 2030, leading to 7.8 million deaths due to strokes [16, 17].

RISK FACTOR

Oxidative stress is a vital mechanism in the pathogenesis of ischemic stroke and has been linked to established influencing factors, such as diabetes, obesity, smoking cigarettes, hypertension, and dyslipidemia. Although known stroke risk factors in early adult life are similar to those in the general population, other contributors, like patent foramen ovale (PFO), migraine headache, oral contraceptive usage, pregnancy, and recreational drug use, also contribute. Conventional cerebrovascular pathogenic factors, such as atrial fibrillation and physical inactivity, continue to be the major factors for stroke incidence and progression [18].

PATHOPHYSIOLOGY OF STROKE

The vasculature of the human brain has developed to sustain cerebral perfusion through the major extracranial and intracranial arteries, with the assistance of the Circle of Willis for flow redistribution and intercommunication between deep brain structures. This distinctive anatomy guarantees an uninterrupted perfusion to vital areas of the brain. Stroke in young patients has been associated with several underlying pathophysiologies, such as atherogenic, cardioembolic, arterial dissection, or thrombotic. The most common subtype, atherothrombotic stroke, is caused by atherosclerosis, which leads to the narrowing or hardening of medium and large arteries. On the other hand, cardioembolic stroke, which is usually more severe, results in larger emboli and thus causes increased damage and worse outcomes. Ischemic stroke is characterized by blockage of cerebral arteries *via* a cardiac embolus, artery-to-artery embolism, causing reduced perfusion to the brain [19]. Ischemic injury happens due to the resultant break in vascular supply and is associated with acute neurological deficits and functional decline. At the molecular level, blood supply depletion in the brain causes a deprivation of oxygen and glucose in the vascular field, resulting in decreased ATP [adenosine triphosphate] production and disruption of cellular balance. As a result, depletion of ATP compromises ion transport processes, leading to membrane depolarization and stimulation of voltage-dependent Ca^{2+}, Na^{+}, and K^{+} channels. Thereby, it leads to an overload of Ca^{2+} and Na^{+} influx and a loss of K^{+} efflux, which induces glutamate release, followed by the induction of excitotoxicity. Furthermore, increased intracellular Ca^{2+} also activates proteases and lipases, leading to the generation of radicals that damage important cell

CHAPTER 12

Gut-Brain Axis and Nanophytomedicine: Unlocking the Potential for Comprehensive Treatment

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Abstract: The gut-brain axis (GBA) establishes a complex system that enables communication between the gastrointestinal system and the central nervous system. The gut microbiota and their metabolites control brain activity, human behavior, and immune responses, thus showing that GBA modulation plays a critical role in treating brain disorders. The new therapeutic method of nanophytomedicine combines plant-based compounds with nanotechnology to improve the brain delivery of bioactive plant chemicals through better availability and stability management. The research examines how GBA interacts with nanophytomedicine through its assessment of how microbial products determine neurotransmitter balance, immune response, and neural communication throughout the GBA. The research demonstrates how nanophytomedicine enables better phytochemical delivery systems, which result in better treatment results for Alzheimer's disease, Parkinson's disease, depression, and anxiety because standard methods usually do not meet treatment needs. The chapter examines how nanophytomedicine research faces translational research problems, which include issues with scalability and biocompatibility, as well as the need to meet regulatory requirements. The research determines how nanophytomedicine enhances GBA modulation through current developments and future research paths, creating new treatment possibilities for neurological disorders while enhancing brain function.

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Keywords: Alzheimer's disease, Anxiety, Bioavailability, Clinical study, Depression, Drug delivery, Ethics, Gut-brain axis, Gut microbiome, Immune modulation, Microbial metabolites, Nanophytomedicine, Nanotechnology, Neurology, Parkinson's disease, Pharmacokinetics, Phytochemical, Preclinical study, Regulatory, Translational research.

INTRODUCTION

Overview of the Gut-Brain Axis (GBA)

The gut-brain axis (GBA) represents a bidirectional communication network that connects the central nervous system (CNS) with the gastrointestinal (GI) tract through neural, endocrine, immune, and metabolic pathways. This interaction plays a crucial role in brain development, function, and aging because it affects cognitive abilities, memory retention, and emotional reactions to stimuli [1, 2]. The vagus nerve serves as a major conduit for signals between the gut and the brain, while neurotransmitters such as serotonin and dopamine enable the enteric nervous system (ENS) to interact with the CNS [2]. The gut microbiota, which exists as a complex ecosystem of microorganisms in the gastrointestinal tract, provide bioactive metabolites that influence brain function through its various metabolic processes [2, 3].

The GBA system functions beyond its digestive functions because it uses both neural and hormonal mechanisms to maintain balance within the body. The ENS, which people commonly call the "second brain", contains a vast system of neurons that control peristalsis and secretion and nutrient absorption without needing CNS control, but they maintain continuous contact with the CNS [4]. Gastrointestinal hormones such as ghrelin and leptin impact how people control their appetite, which affects their energy usage, thereby showing that the GBA system helps people maintain their metabolic equilibrium [3, 5]. The gut microbiota produces short-chain fatty acids (SCFAs), including acetate and butyrate, which perform two key functions for the body: reducing inflammation and maintaining intestinal mucosal health [6].

The gut microbiota influences human body metabolism, brain development, and immune system function. Microbial colonization of infants begins when their genetic makeup interacts with their surrounding environment, including their food intake, antibiotic use, and contact with various microorganisms [7]. The adult human body maintains a stable microbiota, but external factors, including stress, dietary changes, and infections, can disrupt it, leading to changes in brain function and behavior [6, 8]. Research in germ-free mice shows that mammals without a microbiome experience major alterations in neurotransmitters, including

serotonin, brain-derived neurotrophic factors, and tryptophan metabolism, resulting in changes in cognitive abilities, social behavior, and anxiety levels [9].

Disruptions in the GBA system, which result from gut dysbiosis, have been connected to multiple neurological and psychiatric disorders, which include Alzheimer's disease, Parkinson's disease, and depression [1, 3, 8]. Dysbiosis occurs when microbial populations become unbalanced, which leads to immune system activation and inflammation, resulting in neuroinflammation and changes to neurotransmission pathways [8]. The composition of gut microbiota changes in response to stress-related disorders, which include anxiety and depression, thus proving the gut-brain axis link between these two mental health conditions [8]. The research demonstrates that changes in the gut microbiota affect the body's response to stress and anxiety behavior and the activation of the hypothalamic-pituitary-adrenal system, providing evidence that the gut-brain axis can serve as a treatment target for neuropsychiatric disorders [10, 11].

The gut-brain axis functions as a biochemical pathway that comprises brain, immune, and metabolic pathways, creating a complex bidirectional communication system [2, 4]. The gut microbiome shows essential importance in mediating the effects, while the neuroinflammatory response, cognitive impairment, and mood disorders result from disturbances in this biological system [1, 9]. The gut microbiota produces neurotransmitters, regulates immune systems, and controls whole-body inflammation, which together determine the state of neurological health [3]. The study of gut microbiota patterns and their functions in brain development will lead to new methods for preventing and treating neurological disorders, which will create new possibilities for microbiome-based medical treatments [6, 7].

Role of the Gut Microbiome in Neurological Health

The gut microbiome functions as a crucial body system that interacts with GBA pathways to control brain activity and human behavior [12, 13]. The gut microbial system maintains two-way communication with the central nervous system through its neural, endocrine, immune, and metabolic pathways that track microbial activities [14]. Early-life delivery methods, maternal dietary choices, breastfeeding practices, and antibiotic usage create permanent changes that determine intestinal microbial composition and diversity and control neurological development [15].

Recent studies show that gut microbiota produce neurotransmitters, as specific bacterial strains produce γ-aminobutyric acid (GABA), serotonin, and dopamine, which serve as important mood and cognitive control mechanisms [16, 17]. Dysbiosis, an imbalance in microbial composition, has been implicated in

CHAPTER 13

Nanophytomedicine in the 21st Century: Ethical Dilemmas, Regulatory Hurdles, and Clinical Innovations

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Abstract: The 21st century has seen tremendous advancements in nanotechnology and phytomedicine, giving rise to a whole new discipline called nanophytomedicine that promises tremendous potential as an integrated modality for changing the management of serious morbidities involving complex neurological and metabolic health conditions. The chapter covers the intricate ethical triggers that accompany nanophytomedicine—the patient-safety-related, equity-in-access-related, and informed-consent-in-clinical-practice-related ones. It examines the pricier and far-reaching structural barriers that hinder a seamless transition from research to practice and gives evidence of the great necessity for generic protocols, a robust risk assessment framework, and harmonized global regulatory policy. The current chapter includes transformational clinical advancements in the form of nanopharmaceutical products that demonstrate improved bioavailability, as well as therapies that exhibit reduced side effects and improved behavioral efficacy. With regard to innovation, this chapter, as a precursor of ethical perspectives in regulation and clinical advancements, helpsdevelop a holistic introduction to nanophytomedicine within a health paradigm that urges responsible innovation, justice, and technology access.

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Keywords: Bioavailability, Biomarker, Blood-brain barrier, Clinical innovations, Data security, Disease, Ethical dilemmas, Patient, Metabolic health, Nanophytomedicine, Nanotechnology, Nanocarrier, Neurological health, Pharmaceutical industries, Phytomedicine, Privacy, Regulatory agencies, Regulatory hurdles, Targeted therapy, Treatment.

INTRODUCTION

The integration of phytomedicine and nanotechnology has resulted in the evolution of nanophytomedicine, a new frontier that taps the therapeutic action of bioactive phytochemicals at the nanoscale. With increased solubility, bioavailability, and delivery at the targeted site of phytochemicals, nano-based formulations offer a revolutionary approach to disease treatment [1, 2]. This innovation is most significant in neurological and metabolic disorders, where therapeutic pharmacological interventions are generally limited by inefficient penetration across the blood-brain barrier, pharmacokinetic instability, and systemic toxicity. Nano-phytomedicine has the potential to overcome these limitations, optimize therapeutic effectiveness, and reduce side effects and toxicity, thus transforming the healthcare horizon [3].

Despite its huge potential, a major setback to the mass-scale application of nanophytomedicine involves regulatory and ethical issues. The ethical issues fall into three major areas: consent, equality, the environment, and the dual-use potential of nanotechnologies. It is also hindered by a lack of specific regulatory frameworks for nanophytomedicine, which in turn creates challenges in its approval and developmental processes. The current regulatory agencies, such as FDA, EMA, CDSCO, and TGA, evaluate nanopharmaceuticals according to conventional norms, which leads to confusion in the approval and evaluation of this nanomedical platform. They effectively address the ethical and regulatory issues of this emergent therapeutics platform in order for it to reach humanity in a safe and efficient manner [5, 6, 7]. Furthermore, the recent emerging clinical advances in the area of nanophytomedicine have demonstrated a promising potential in the treatment of various neurological disorders like Alzheimer's disease, Parkinson's disease, and stroke. Also, there are many emerging potential areas in the treatment of different kinds of metabolic disorders like diabetes, obesity, and metabolic syndromes. By virtue of recent advances in the development of nanoparticle drug carriers like liposomes, polymeric nanoparticles, and dendrimers, it has become possible to employ targeted drug delivery through different pathways. At the same time, the combined potential of AI drug development and precision medicine is driving the development of new kinds of nanodrug therapy based on the different characteristics of patients. As

such, nsanophytomedicine is likely to revolutionize the treatment paradigms in the future [11].

ETHICAL DILEMMAS IN NANOPHYTOMEDICINE

The application of nanotechnology in phytomedicine poses significant ethical concerns, especially regarding informed consent [12]. Due to the complexity and uncertain risks and benefits of nanomats, patients will never be able to comprehend the issues involved and give consent for nano-treatment [13]. Traditional consent strategies are inadequate, and advanced education strategies are required to enable patients and research participants to make truly informed decisions. Furthermore, variation in health literacy and access to information further adds to the process and raises questions regarding whether consent is voluntary and informed [14]. With nanophytomedicine moving forward, the ethical guidelines also need to keep pace with these challenges and provide openness, patient choice, and access to novel therapy in a balanced manner. Patient comprehension of nanomedical therapy is one of the major ethical concerns of nanophytomedicine [15]. As nanotechnology and phytomedicine are extremely sophisticated, it may be challenging for patients to realize how such kinds of treatments work, what are the risks involved, and what their long-term effects will be. Informed consent is particularly challenging in non-scientifically literate or access-restricted populations to clear, unbiased information, as shown in Fig. **1** [16]. Furthermore, the novelty of nanophytomedicine results in the lack of long-term safety information being typically available, adding another source of uncertainty for healthcare providers and patients. To address this challenge, effective communication strategies, patient education initiatives, and open regulatory systems need to be established to facilitate ethical decision-making and informed involvement in nanophytomedicine therapy [13].

Informed Consent in Nanotechnology-Based Therapies

On an ethical basis, informed consent is extremely difficult to obtain in the case of nanotechnology-based therapy due to its intrinsic complexity. The fact is that nanomedicine operates at the molecular and atomic level, normally through novel mechanisms of action, novel drug delivery, and pharmacokinetic features that are extremely difficult for patients to understand [17]. It is important to understand that patients need to be educated about such innovative therapy through simple and intelligible communication, yet they cannot be informed sufficiently through traditional informed consent designs about the full range of benefits and risks involved. Being transparent is very important, as the long-term effects of some nanomaterials used in therapy have yet to be evaluated and, as such, bring questions of safety, toxicity, and accidental biological interaction to the attention

CHAPTER 14

Recent Trends, Innovations, and Implications of Nanophytomedicine in the Pharmaceutical Industry

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Abstract: Nanophytomedicine is an interdisciplinary domain that can utilize nanotechnology for the improved delivery of phytomedicines. Plant-based bioactive medicines are often associated with poor pharmacokinetics and can be efficaciously administered using certain nanocarriers to achieve the desired bioavailability. Nanocarrier-based phytomedicines are currently being developed to improve pharmacokinetics and pharmacodynamics for better bioavailability. Improved bioavailability of nanomaterials is entirely dependent on their smaller size, which provides a large surface area for enhanced absorption across the plasma membrane, along with better solubility and chemical stability in systemic circulation. Personalized treatment using nanophytomedicine is one of the upcoming advancements that can provide a better therapeutic window and be achieved through the incorporation of artificial intelligence databases to overcome the existing challenges related to cancer, neurodegenerative disorders, and chronic inflammatory diseases. The proposed chapter explores the possibilities for addressing the above-mentioned challenges through the implementation of nanophytomedicine-based research and development.

Keywords: Antibacterials, Antimicrobials, Bioimaging, Biosensors, Cancer, Electrospinning, Hydrogels, Nanophytomedicines, Nanotechnology, Nanoparticles.

INTRODUCTION

Nanotechnology has been widely used as an affordable and game-changing option. Products in which different types of nanomaterials are used—such as medical equipment, food processing equipment, desktops, beauty products, and coverings—have seen a strong growth in the global market. This is mainly

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because technology is developed through collaborative efforts across multidisciplinary fields such as robotics, electronics, and medicine [1]. On the other hand, this method is utilized in manufacturing equipment for aeronautical and space research, including Mars exploration.

The prefix "nano" generally denotes a small size, typically in the range of 1 to 100 nm. The glucose molecule is the smallest at 1 nanometer, and the herpes virus is the largest at 100 nm. Because of their small size, they can easily be manipulated in any laboratory condition. The importance of nanotechnology in the phytomedicine field—hence the term nano phytomedicine"—is the focus of this article [2]. Across the globe, natural products have been utilized to treat and prevent a range of diseases. These products, from various plant species, have been the most researched source for the formulation of new drugs. Currently, the most extensively studied compounds are those possessing anti-infectious and anti-cancer activities. Certain drugs are popular worldwide. Examples of natural compounds with numerous medicinal uses include morphine, which is analgesic in nature; erythromycin, with antibiotic activity; cyclosporine, an immunosuppressive agent; and artemisinin, used against malaria [2]. Extensive research in nanotechnology allows the production of herbal medications and phytopharmaceuticals known as nanophytomedicine. It can be used in biological research and medicine delivery. In other words, it combines the concepts of nanotechnology and phytotherapy to address the challenges of poor solubility, stability, and targeted delivery of plant-based bioactive compounds. The formulation of different dosage forms that consist of a variety of nanomaterials, such as nanocapsules, nanogels, herbal nanoparticles, nanotablets, nanopaste, nanopowder, and nanoemulsions, provides several advantages for Ayurvedic therapeutics in nanophytomedicine research. These advantages include better solubility, better bioavailability, decreased toxicity, favorable pharmacological characteristics, and enhanced stability. These preparations are designed to offer protection from fast chemical degradation and to enhance the capability for extended administration [3]. Thus, nanophytomedicines may have a significant role to play in modern medical practice.

SCOPE

Pharmaceutical Application

Improved Drug Delivery: Bioavailability and therapeutic efficacy have been increased by the incorporation of plant-based chemicals like nanophytomedicines. Targeted therapy cuts down systemic adverse effects by precise administration of medications to specified areas (such as tumors or inflammatory tissues).

Controlled Release Systems: Active compounds can be released gradually and under control using nanosystems like polymeric nanoparticles and liposomes [3].

Cancer Therapy

Anti-Cancer Potential: Nanoformulations improve the physicochemical properties, like solubility and stability, of certain plant-derived chemicals that exhibit anticancer activity, such as resveratrol and curcumin.

Overcoming Drug Resistance: Nanocarriers can target cancer cells' drug resistance mechanisms.

Chronic Disease Management

Diabetes: To enhance bioavailability and bioactivity, bionanopharmaceuticals have been developed using phytomedicines, including flavonoids, which can be utilized for glucose metabolism [3].

Neurodegenerative Disorders: Nanophytomedicines are targeted to enhance the delivery of neuroprotective and antioxidant formulations and are highly applicable to AD and PD.

Therapeutic Foods and Nutrients

Enhanced Bioavailability: In functional meals, nanocarriers improve the uptake of bioactive and plant-derived nutrients.

Therapeutic Benefits: Designed to provide specific health advantages, such as improved cardiovascular or mental function.

Historical Evolution of Phytomedicine and Nanotechnology

The ancestry of phytomedicine may be traced back to the Paleolithic era, some 60,000 years ago. Nonetheless, written records from the Sumerians, who created plant inventories, trace back almost 5000 years [4]. Herbal therapy is the most widely used method worldwide and has been employed to manage wellness since prehistoric times. Ayurvedic, Chinese, Tibetan, and Unani medicines are the four traditional medical systems used worldwide, and they are all found in the Hindu Kush Himalayas, which today include Afghanistan, Bangladesh, Bhutan, China, India, Nepal, and Pakistan. In addition to a few other countries, Ayurveda is an old and popular practice in India and Sri Lanka. The ancient Vedic text known as the Atharvaveda was composed in 1200 BC, and the Charak Samhita and Sushrut Samhita, which were composed between 1000 and 500 BC, have comprehensive descriptions of over 700 medicinal plants [5].

SUBJECT INDEX

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Dr. Mandeep Kumar Gupta is an author specializing in pharmacy education and course development and dedicated to creating comprehensive and engaging content for students pursuing undergraduate and postgraduate courses in pharmacy as per the course curriculum given by the Pharmacy Council of India, New Delhi. He has done M. Pharm. (Pharmaceutical Chemistry) and Ph.D. in Pharmacy and transitioned into the professional realm, where he has the privilege of working as a Associate Professor at Amity Institute of Pharmacy, Amity University Uttar Pradesh Lucknow Campus, Uttar Pradesh, India. He is also a lifetime member of the Association of Pharmaceutical Teachers of India (APTI). He has 15 years of academic experience and has authored over 20 research papers in international and national journals, edited 5 books for national and international publishers, authored more than 20 book chapters, served as reviewer for more than 10 reputed journals, participated in 15 faculty development programs, and attended more than 60 international and national conferences.

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Mr. Naveen Singh is a dedicated researcher currently working on a DST-SERB funded project investigating PFAS contamination in river and drinking water sources and its implications for human health. His research interests encompass toxicology, neuropharmacology, diabetic neuropathy, and environmental health, with a particular focus on toxicology and human risk assessment. He is also actively engaged in molecular docking, network pharmacology, and in vivo experimental studies to understand disease mechanisms and therapeutic interventions. Currently pursuing his doctoral research, he is particularly focused on unraveling the neurotoxic effects of PFAS and other emerging contaminants. He is a lifetime member of the Association of Pharmaceutical Teachers of India (APTI), demonstrating his continued commitment to academic and scientific advancement.