THE ROLE OF NUTRACEUTICALS IN DEGENERATIVE DISEASES | PART 1

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The Role of Nutraceuticals in Degenerative Diseases

(Part 1)

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The Role of Nutraceuticals in Degenerative Diseases *(Part 1)*

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FOREWORD

Degenerative diseases, such as cardiovascular disease, respiratory diseases, ophthalmic disease, liver diseases, and neurodegenerative disorders, are among the leading causes of morbidity and mortality worldwide. Despite significant advances in modern medicine, these diseases continue to pose a major challenge to healthcare systems globally. In recent years, there has been growing interest in the potential role of nutraceuticals in the prevention and treatment of degenerative diseases. Nutraceuticals, which include dietary supplements, functional foods, and bioactive compounds, have been shown to possess a range of biological activities that may help to mitigate the risk of degenerative diseases.

The book "**The Role of Nutraceuticals in Degenerative Diseases**" provides a comprehensive overview of the current state of knowledge on the role of nutraceuticals in degenerative diseases. The book brings together contributions from leading experts in the field, who provide insights into the molecular mechanisms underlying the potential health benefits of nutraceuticals, as well as the latest evidence from clinical trials and epidemiological studies.

This book covers a range of topics, including the role of nutraceuticals in the treatment of neurodegenerative diseases, respiratory diseases, and degenerative kidney diseases. Initial chapters were dedicated to the scope and aspects of nutraceuticals and potential nutraceuticals based on in-silico studies.

Throughout the book, the authors provide a critical evaluation of the current evidence, highlighting the potential benefits and limitations of nutraceuticals in the prevention and treatment of degenerative diseases. The editors and the contributors deserve credit for compiling such an informative book that will definitely offer benefits for all readers, students, researchers, academicians, and health care personnel. Hence, this book is an essential resource for all those who are interested in the nutraceutical-based therapy for degenerative diseases. It provides a comprehensive and authoritative overview of the current state of knowledge in this field and highlights the potential for nutraceuticals to play a major role in the prevention and treatment of degenerative diseases in the future.

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PREFACE

This book, “The Role of Nutraceuticals in Degenerative Diseases,” offers scientific information on the significance of nutraceuticals and their potential roles in the management, treatment, and prevention of degenerative diseases. Degenerative diseases are conditions characterized by continuous, deteriorating cell changes that worsen over time, ultimately affecting various vital tissues or organs. The risk factors for degenerative diseases are identified as aging, genetic predisposition, exposure to chemicals and toxins, and viral infections. Other factors like excessive smoking, excessive alcohol consumption, poor diet, either lack of or strenuous physical activity, autoimmune processes, and enduring inflammation may also contribute. Some of the degenerative diseases can be symptomatically relieved, but not always. However, treatments may help improve signs and symptoms, relieve intense pain, and improve the patient's mobility. In this book, we have attempted to cover the degenerative diseases of the respiratory tract, neurodegenerative diseases, and degenerative kidney diseases. A chapter is also based on potential nutraceuticals identified through in-silico studies.

The word "nutraceutical" is a combination of the words "pharmaceuticals" and "nutrition," which encompasses a wide range of bioactive substances found in food. Nutraceuticals are food-derived products with nutritional value that also have therapeutic, disease-prevention, or health-promoting qualities. In today’s era, there is considerable interest in nutraceuticals due to their potential medicinal benefits, safety, and nutritional value. The necessity for a so-called "Healthy Diet" has become apparent to people worldwide as our understanding of how food affects human health has deepened over the past several decades. This book's first chapter covered the fundamentals of nutraceuticals. The health benefits of nutraceuticals in relation to various degenerative diseases are discussed later and will be covered in more detail in the subsequent chapters. The many degenerative diseases are covered in the upcoming chapters, along with nutraceutical therapy methods. Degenerative disease is the outcome of a persistent process involving degenerative cell alterations that harm tissues or organs, causing them to deteriorate more rapidly over time. Toxins, chemicals, viruses, medical problems, heredity, and other factors can all cause degenerative diseases.

The chapter contributors to this book are respected authors and professionals from reputable institutions worldwide. To ensure that even the general public can understand, the chapters are thoughtfully written in simple English. Authors may learn what to eat and why to utilize specific dietary supplements or foods from this book. We hope that this book will be both useful and instructive for all readers. As we welcome your opinions, may the work we put into creating this book illuminate your never-ending pursuit of knowledge.

Finally, we invite readers to share their comments, valuable criticisms, and helpful suggestions for the continuous improvement of the book.

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CHAPTER 1

Introduction to Nutraceuticals: Scope and Various Aspects

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Abstract: Nutraceuticals are substances that are not only utilized for nourishment but also as medications. Nutraceuticals are characterized as compounds that offer protection against certain diseases or have physiological benefits. Nutraceuticals are frequently categorized according to their chemical composition, mechanism of action, and food sources, among other factors. Nutraceuticals have been divided into three categories based on their traditional, non-traditional, and commercial uses. These categories have been further subdivided into fortified, recombinant, phytochemical, herbal, and functional foods, as well as dietary supplements, probiotics, and prebiotics. Different kinds of nutraceuticals have a variety of uses depending on their nature. The definitions and categories of nutraceuticals can overlap due to similarities in chemical composition and methods for providing health benefits. Nutraceuticals come in a variety of forms and are currently gaining a lot of interest due to their safe, potential medicinal, and nutritional benefits. Nutraceuticals are effective in treating a wide range of illnesses, including gastrointestinal problems, cancer, diabetes, allergic reactions, arthritis, cardiovascular diseases, and many inflammatory diseases. The main justification for using these nutraceuticals is their wide range of health benefits, which include improving the nutritional value of our diet, possibly extending lifespan by lowering inflammation and oxidative stress, aiding in the prevention and management of certain medical conditions, and meeting the specific dietary requirements of various populations with few adverse effects. Because of this, nutraceuticals are a vital part of a healthy lifestyle. Therefore, in recent years, the nutraceutical sector has grown drastically.

Keywords: Dietary supplements, Functional food, Nutraceuticals, Probiotics, Therapeutic effect.

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INTRODUCTION

Nutraceuticals, despite being a modern term, reflect the ancient concept of using food for health benefits. Over 2,000 years ago, Hippocrates, the Greek physician, introduced this concept; he said, "Let food be thy medicine and medicine be thy food." Nutraceuticals are emerging as a promising alternative to traditional medicine, which is helping to preserve the ancient principles of traditional medicine [1]. In 1989, Dr. Stephen L. DeFelice, founder and chairman of the Foundation for Innovation in Medicine in Crawford, New Jersey, introduced the term "nutraceutical." This word merges "nutrition," indicating nourishing food or food components, with "pharmaceutical," referring to medicinal drugs [2, 3].

He defined the term "nutraceutical" as "food or part of food that provides medical or health benefits, including the prevention and/or treatment of a disease" [4]. There is some confusion due to the wide variations in terminology and concepts used across different nations. Nutraceuticals are substances isolated or purified from foods and prepared in pharmaceutical dosage forms to offer medical or health benefits, including disease prevention and treatment, for various chronic conditions. They can be considered as food or part of a food and provide significant physiological advantages [5].

The modern lifestyle of people has led to increased consumption of junk food, resulting in widespread health issues, such as obesity, heart disease, cancer, osteoporosis, polycystic ovary syndrome, and arthritis. Human nutritional security has changed the concept of food from the primitive diets of hunter-gatherers to the self-sustaining practices of farming societies, and this growing trend towards healthier foods offers nutritional benefits and helps in the prevention of various diseases. Natural foods with medicinal qualities have long been consumed in China and India. On the other hand, nations such as Germany, France, and England were among the first to recognize that diet was more important for maintaining general health and well-being than genetics and physical activity [6]. The terms "nutraceutical" and "functional food" have gained significant traction within the health and wellness world. The term "Nutraceutical" is often used in marketing, but does not have a strict, specific definition. "Functional foods," on the other hand, are clearly defined as foods that provide health benefits along with nutrition [5]. Basically, these foods provide more benefits than just essential nutrients. The increasing interest in their potential health advantages has prompted extensive research into their medicinal properties, nutritional content, and safety. As this curiosity continues to grow, the nutraceutical industry finds itself uniquely positioned to highlight the benefits they offer to consumers aiming to improve their health and well-being through dietary choices.

Nutraceuticals, derived from natural sources, are generally considered safe and non-toxic for human consumption. However, they face several challenges, like law harmonization, inconsistent fair trade practices, exposure to chemicals and contaminants, an outdated regulatory system, difficulty in identifying the genuine origin of raw materials, ensuring the quality of isolated compounds, a lack of experimental evidence, misleading advertisements, and possible interactions with other substances. Although various laws and regulations exist to govern nutraceutical products across different countries, many challenges in the development of nutraceuticals are ignored due to a lack of authoritative control [7, 8]. Different regulatory bodies in various countries regulate these products to ensure they meet safety and quality standards, prevent misleading labeling, ensure adherence to regulations, and safeguard consumer health [9]. This chapter comprises the different types, roles, and applications of nutraceuticals.

TYPE OF NUTRACEUTICALS

Currently, there are over 470 nutraceutical products available on the market, out of which many are well-known for their health-beneficial activities [10]. Nutraceuticals can be categorized in various ways, based on how simple it is to understand and use them such as for nutritional guidance, clinical trial design, academic training, or the production of functional foods. Nutraceuticals are frequently categorized according to their chemical composition, mechanism of action, and food sources, among other factors. Nutraceuticals have also been categorized according to how they are used for traditional, non-traditional, and commercial purposes, which have been sub-categorized into fortified, recombinant, phytochemical, herbal, and functional foods, as well as in dietary supplements, probiotics, and prebiotics [6]. Depending on their nature, different types of nutraceuticals have a wide range of applications. Because of similarities in their chemical composition and ways of providing health benefits, the classifications and definitions of nutraceuticals sometimes overlap [11].

Traditional Nutraceuticals

Traditional nutraceuticals are natural foods that contain several natural compounds without making any change to the actual foods that deliver benefits beyond their basic nutrition. Examples include fruits, vegetables, grains, dairy products, and meats, each containing distinct natural components such as lycopene in tomatoes and omega-3 fatty acids in salmon [12], *etc.* They can be further sub-categorized [6, 13, 14] as follows:

CHAPTER 2

Potential Nutraceuticals Based on *In Silico* Studies

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Abstract: The conventional drug discovery approach is time-consuming, costly, and carries significant risks. Recently, *in silico* methods have gained considerable attention due to their advantages in cost efficiency, reduced time requirements, and minimized labor. Many new drugs having much higher potential have been developed successfully using a computational approach. *In silico* approaches have transformed nutraceutical development and optimization, offering expedient and economical methods for identifying bioactive compounds. Derived from natural sources, nutraceuticals show substantial promise in health promotion and disease prevention, particularly for cardiovascular disorders and cancer. This chapter explores the application of *in silico* methodologies, including molecular docking, Quantitative Structure-Activity Relationship (QSAR) modeling, and molecular dynamics simulations in nutraceutical discovery. It emphasizes the effectiveness of computational methods in predicting bioavailability, therapeutic potential, and safety profiles of nutraceuticals prior to experimental validation. Case studies featuring compounds such as curcumin and resveratrol demonstrate successful implementations of these technologies. This chapter also addresses a list of databases for nutraceutical screening and research. The discussion also addresses inherent limitations and challenges, notably the oversimplification of complex biological systems and computational resource constraints. Looking ahead, the chapter outlines future research trajectories, highlighting the increasing significance of personalized nutraceuticals. These advancements, bolstered by progress in artificial intelligence and quantum computing, carry profound implications for public health strategies and outcomes. Thus, computational tools have become crucial in nutraceutical research for designing and optimizing bioactive compounds with enhanced therapeutic potential.

Keywords: Docking, *In silico*, Modeling, Nutraceuticals, QSAR, Screening.

INTRODUCTION

Nutraceuticals, a fusion of nutrition and pharmaceuticals, are biologically active compounds established to significantly influence optimal health and support

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therapeutic development. Such a term was derived in 1989, given by Dr. Stephen De Felice, in which the two words, nutrition and pharmaceutical, gave their meaning. Nutraceuticals are marketed in various forms, including but not limited to tablets, powders, liquid extracts, and capsules–deriving from functional/ medical foods, dietary supplements, herbal products, processed foods with added nutrients, and isolated nutrients. Offering health benefits and fulfilling dietary requirements beyond basic dietary needs allows them to continue to grow in the market due to their potential to prevent and treat numerous diseases. Nutraceuticals derive from a single or a blend of nutrient-rich foods that exhibit physiological and health benefits [1]. Considering their characteristics and role, they are established as a promising alternative method in healthcare, which is expanding globally, providing lower healthcare costs, and their ability to treat/reduce health conditions, including cardiovascular diseases and cancer, thus increasing life expectancy [2].

Nutraceuticals' recognition stems from their innovative and contemporary method of harnessing the benefits of natural substances. However, its regulation differs globally, posing a major challenge for worldwide marketing. In the United States, dietary supplements are regulated by the FDA under the Dietary Supplement Health and Education Act (DSHEA) of 1994 [3]. However, nutraceuticals do not require FDA approval before marketing, leaving the responsibility of the safeness and efficacy of the product on the manufacturer. While the nutraceutical market has great potential to expand largely, to develop a global best-selling product, companies must strictly follow different regulations in each country. Concerning consumers, their attentiveness towards nutraceuticals depicts their growing consciousness towards their health and alternative ways of prevention and treatment. While the shift to preference for natural resources is evident, consumers must consult healthcare professionals before implementing any new nutraceutical regimen, specifically if they have any existing diseases [1]. Nutraceuticals offer significant potential benefits for health and wellness. However, informed caution and awareness are essential, along with continued research and improved regulatory measures, to maximize their potential while ensuring consumer safety.

In silico evaluations have become increasingly vital in nutraceutical development due to their ability to expedite the discovery and optimization of bioactive compounds. Computational approaches like molecular docking, Quantitative Structure-Activity Relationships (QSAR), Molecular Dynamics Simulations (MDS), Pharmacokinetics-Pharmacodynamics (PK-PD) modeling, and virtual screening enable researchers to predict the efficacy, bioavailability, half-life, and safety of nutraceutical compounds before experimental validation. A notable example is the development of nutraceuticals derived from *Curcuma longa*

(commonly known as turmeric), where molecular docking studies helped identify curcumin's potential as an anti-inflammatory agent by targeting key enzymes like COX-2 [4]. Wu *et al.* [5] conducted docking and MDS to identify bioactive compounds from traditional Chinese medicine, such as *Poria cocos*, that could inhibit the Main protease (Mpro) of SARS-CoV-2, employing network pharmacology to highlight potential anti-COVID-19 compounds and provided experimental insights [5]. Sahu *et al.* demonstrated the utility of *in silico* modeling in recognizing effective nutraceuticals by predicting the molecular interactions and binding affinities of resveratrol with methyl-CpG binding proteins (MBDs), key regulators in cancer-related pathways. The study highlighted that the MBD protein family interacts with other signaling proteins involved in cancer initiation, emphasizing the potential of resveratrol as a therapeutic agent in disrupting these pathways [6].

The objective of this chapter is to provide an inclusive analysis and understanding of the role of *in silico* studies in the development of nutraceuticals. It intends to elucidate the classification, health benefits, and common sources of nutraceuticals, while also exploring the various computational methods and tools necessary in this research. The inclusion of detailed case studies demonstrates the successful application of *in silico* methods in nutraceutical research while integrating the challenges and limitations of this technique. Furthermore, the future perspectives and emerging trends aim to underscore the potential impact of *in silico* technologies on public health and emphasize future research directions in the nutraceutical field.

NUTRACEUTICAL COMPOUNDS: AN OVERVIEW

Classification of Nutraceuticals

The classification of nutraceuticals aids in understanding their diverse nature and roles in public health and disease prevention. Nutraceuticals can be broadly classified based on their origin and intended use. However, their classification and understanding can overlap based on similar functions and chemical constituents. Traditional nutraceuticals are natural foods that have not undergone any modification with known potential to provide benefits beyond basic nutrition [7]. Non-traditional nutraceuticals are artificially designed *via* biotechnology applications, fermentation, or agricultural breeding to improve the quality of nutrition, thus enhancing human health.

1. ***Traditional Nutraceuticals:*** Traditional nutraceuticals are derived directly from natural sources and contain active components beneficial for health promotion and disease prevention. This category encompasses bioactive com-

CHAPTER 3

Degenerative Diseases and Possible Therapeutic Approaches

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Abstract: The progressive and irreversible degradation of cells, tissues, and organs, which aggravate spontaneously over time, is said to be a degenerative disease. Among various cellular and organ systems, degeneration associated with body systems like nervous, cardiovascular, musculoskeletal, ophthalmic, respiratory, hepatocellular, and renal systems is prone to various degenerative disorders. Apart from them, some miscellaneous degenerative diseases like diabetes and arthritis have attracted great concern due to significant health issues globally. Many of these degenerative diseases worsen if genetic and lifestyle management are poorly managed. Excessive alcohol intake, smoking, poor dietary habits, lack of physical activity, and sedentary jobs significantly contributed to most of the deaths related to degenerative conditions. Environmental pollution from industrial waste, chemicals, and solvent exposure, as well as contact with pesticides and heavy metals, may lead to an increased production of reactive oxygen species, causing oxidative stress, DNA damage, and cell death; altogether, they lead to degeneration of cells. Each of the body systems has several degenerative diseases with definite or multiple pathophysiologies. Many of these conditions are incurable and can only be managed to alleviate and improve associated symptoms. Currently, degeneration can be cured, but therapies focus mainly on symptomatic treatment through drugs and herbals, retarding disease progression and improving quality of life. Generally, therapeutic strategies involve regular physical exercise, modification of irregular lifestyle, drug treatment, surgical interventions, biotechnological approaches, and other modern emerging techniques. This chapter summarizes different degenerative diseases, their associated pathophysiological development, and their established as well as proposed therapies.

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Keywords: Body systems, Degenerative diseases, Pathophysiology, Risk factors, Treatment.

INTRODUCTION

Degenerative diseases, although a broad term, may be defined as a health condition characterized by day-to-day deteriorating features of a patient, leading to a wordless suffering and structural functional worsening of body parts [1]. Degenerative disease may be worsened to the extent that the patient may be unable to move, and this leads to morbidity and mortality [2]. Many of these diseases are associated with normal aging, but they can be worsened if genetic and lifestyle factors are poorly managed. Also, many of these conditions are incurable and can only be managed to alleviate and improve symptoms [3]. Among the many risk factors, aging is at its zenith, especially for degenerative diseases. It is obvious that aging is a cellular-level process that leads to many biological alterations. The intrinsic cause includes DNA damage and loss of the mature cells' ability to divide. Many times, lifestyle poses a great threat to degenerative conditions. For example, excessive alcohol intake, smoking, poor dietary habits, lack of physical activities, and a sedentary job-all significantly contributed to most of the deaths related to degenerative conditions. Moreover, pollution, especially industrial waste, chemicals, and solvent exposure or contact with pesticides, heavy metals may lead to increased production of Reactive Oxygen Species (ROS) and cause oxidative stress, which in turn reduces ATP production, causes DNA damage, and cell death; altogether, they lead to the degeneration of cells. Sometimes, degenerative diseases occur in a specific gene within a family due to epigenetic modifications. It is important to note that the continuous release of certain enzymes and cytokines in cases of chronic inflammation or the accumulation of abnormal proteins may hasten cellular degeneration. Last but not least, the autoimmune process is also related to degenerative diseases. Autoimmune disorders occur when the body's own immune system becomes overactive and attacks its own healthy cells and tissues instead of protecting them. This leads to harm to neurons, joints, synapses, and further tissues, causing progressive degeneration.

DIFFERENT DEGENERATIVE DISEASES

According to the body region, degenerative diseases can be classified into many types, such as neurodegenerative diseases, degenerative respiratory diseases, degenerative kidney diseases, diabetes, degenerative cardiovascular diseases, degenerative ophthalmic diseases, degenerative liver diseases, degenerative muscle diseases , and degenerative spine diseases, among others. They are

explained one by one in detail, covering the pathophysiology and treatment approaches in the following section.

Neurodegenerative Diseases

Worldwide, millions of people are suffering from neurodegenerative disorders. The two most prevalent neurodegenerative disorders are Parkinson's Disease (PD) and Alzheimer's Disease (AD). About 6.5 million Americans aged 65 or older currently have Alzheimer's dementia. This digit could reach 13.8 million by 2060. The Global Burden of Diseases, Injuries, and Risk Factors Study 2019 estimated that more than 8.5 million people worldwide suffer from PD [4]. Progressive malfunction and neuronal loss are hallmarks of neurodegenerative disorders. It happens when nerve cells in the brain or peripheral nervous system gradually stop functioning and eventually die. Neurodegenerative diseases are classified molecularly based on proteins. This highlights the role of protein-processing systems in the pathogenesis. Amyloid-(Aβ), prion protein, tau, a-synuclein, TAR-DNA-binding protein 43 kDa, and fused-in sarcoma protein are the most often implicated proteins in the pathophysiology of neurodegenerative illnesses [5].

Alzheimer's Disease

Alzheimer's Disease (AD) is a progressive, unrelenting, neurodegenerative illness that destroys large portions of the hippocampus and cerebral cortex. It is characterized by a specific age-related cognitive and functional decline that starts and progresses until death and is associated with the degeneration of cholinergic neurons [6]. In the US, AD is thought to be the most prevalent type of neurodegenerative dementia, and minority groups are disproportionately affected by the illness [7]. In AD, synapse loss followed by the atrophy of neurons is seen throughout the cerebral cortex; however, the mid-temporal lobe is severely affected [8]. The accumulation of insoluble forms of Aβ in extracellular spaces and blood vessel walls, as well as the aggregation of the microtubule protein tau in neurofibrillary tangles in neurons, are associated with AD [9].

The Apolipoprotein E4 (APOE4) gene is one of the important genetic risk factors for AD [10]. Environmental risk factors for dementia associated with AD obstruct brain impact assessment for many reasons, as given in Fig. (**1**).

CHAPTER 4

Role of Nutraceuticals in the Prevention and Management of Degenerative Diseases

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Abstract: The class of dietary supplements and natural substances known as "nutraceuticals" presents a potential path for intervention. Degenerative illnesses may become more prevalent in people due to metabolic and systemic disruptions caused by nutritional shortages and imbalances. The primary cause of illness and mortality in both developed and developing countries is degenerative diseases. Degenerative diseases, characterized by a steady decline in organ or tissue function, generate some serious challenges for global healthcare systems. This chapter surveys the current understanding of nutraceuticals concerning degenerative disease, starting with an overview of degenerative diseases and how they affect health, with a special emphasis on how common they are becoming in older populations. Though numerous preclinical and clinical studies have been conducted, these studies are inconclusive due to a lack of toxicological data and small sample sizes. Adequate potential research is required to properly comprehend the underlying mechanisms of action of these nutraceuticals and evaluate their safety, effectiveness, tolerance, dose dependence, and bioavailability in the management of degenerative diseases. Moreover, nutraceuticals are readily accessible, have fewer adverse effects, and offer financial benefits. The high concentration of bioactive substances helps prevent and treat diseases and offers physiological benefits. Herbal nutraceuticals are foods derived from plants, such as their oils, roots, seeds, berries, and flowers. This chapter will aid in understanding the mechanisms by which nutraceuticals function, highlighting their anti-inflammatory and antioxidant properties as well as their capacity to alter cellular pathways implicated in the development of degenerative disease.

Keywords: Cellular pathways, Degenerative diseases, Dose, Nutraceutical, Supplement.

INTRODUCTION

Everything that can be categorized as food or a food component with health or medical benefits, such as disease prevention and treatment, is referred to as a

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nutraceutical. Nutraceuticals can include anything from food regimens and dietary supplements, separated nutrients from processed goods, genetically modified "designer" foods, and herbal products. The impact of functional foods and nutraceuticals on health has gained popularity in the scientific field in recent years.

The aging population, the increasing prevalence of chronic diseases, and growing consumer awareness of health and well-being are the main factors driving the rapid expansion of the worldwide nutraceutical industry [1, 2]. Nutraceuticals have received a lot of interest in recent years because of their safety and potential therapeutic value. A paradigm shift from pharmaceuticals to nutraceuticals indicates a new era in the healthcare sector [3].

Nutraceuticals are related to nutritional supplements like pharmaceutical products and are generally marketed Over The Counter (OTC). Over-the-counter medications are those that are marketed without a doctor's prescription [4]. The scientific idea of a customized diet, which is now a component of leading a healthy life, depends on nutraceuticals. Although plants and extracts may have chemical and health-promoting properties, their nutritional and nutraceutical value is highly prized. The FDA categorizes over-the-counter medications into two groups, namely OTC monograph drugs and new OTC drugs. The US FDA OTC monograph deals with approved active ingredients, doses, and labeling requirements under which an OTC drug is approved to be safe and effective. On the other hand, new OTC drugs needed approval through the NDA (New Drug Application) or ANDA (Abbreviated New Drug Application) process [5]. Healthcare providers should be aware of the ingredients in over-the-counter medications and nutraceuticals and recommend ones that include the fewest possible combinations of the safest substances at a single dosage. Insufficient understanding of over-the-counter drugs can result in negative drug responses and treatment program noncompliance. In some other cases, it can be wiser to use a prescription drug that has been studied more thoroughly than to risk the unknowns that come with many over-the-counter medications.

Customers are more conscious not only of the critical relationship between nutrition and health but also of the role of nutrition in preventing degenerative illnesses like diabetes, heart disease, Alzheimer's, autoimmune disorders, *etc*. Degenerative diseases are characterized by the progressive deterioration of tissues and organ structure and function. Degenerative illnesses may precede other illnesses, such as those that affect the respiratory system, nervous system, kidneys, heart, eyes, liver, muscles, *etc*. A lung disease called Chronic Obstructive Pulmonary Disease (COPD) is brought on by aging or neuromuscular disorders, which are examples of degenerative ailments. Degenerative disorders can

potentially lead to kidney ailments such as nephrosclerosis and Chronic Kidney Disease (CKD). Degenerative alterations in blood arteries can lead to cardiovascular illnesses, such as heart failure and atherosclerosis. Degenerative illnesses can also lead to other conditions, such as diabetes, ocular diseases, muscle diseases including sarcopenia and muscular dystrophy, liver diseases like cirrhosis, and liver diseases like non-alcoholic fatty liver disease [6].

WHAT ARE NUTRACEUTICALS?

Nutraceuticals are food ingredients that possess bioactive molecules with high nutritional value and physiological effects that favor human health. Nutraceuticals cover vitamins, herbal goods, dietary supplements, and genetically engineered foods [7]. The high content of bioactive compounds provides physiological benefits and aids in preventing and treating illnesses. Foods made from plant sources, including their oils, roots, seeds, berries, and flowers, are known as herbal nutraceuticals, which improve well-being and treat both acute and chronic illnesses. Many ancient cultures strongly believed that herbs could be used for both medicinal and dietary purposes [8]. Nutraceuticals frequently exhibit distinct chemical effects that are not found in systematic medicines. Certain naturally occurring compounds derived from food have antidepressant qualities that can combat certain Neurodegenerative Illnesses (NDDs). These substances, referred to as "nutraceuticals," have a variety of biochemical and metabolic effects, and a wealth of research has demonstrated their neuroprotective qualities. Nutraceuticals, functional foods, dietary modifications, and nutritional supplements are effective ways to alter or avoid the natural course of non-diagnostic diseases [9]. Nutraceuticals are essential for regulating energy metabolism and signaling pathways that govern neuroinflammation and neurotransmission. Additionally, it is known that they activate neurotrophic factors to control synaptic plasticity and avert neurodegenerative illnesses. It has been demonstrated that certain nutraceuticals, including vitamins, polyphenols, stilbene, creatine, carnitine, coenzyme Q10, unsaturated fatty acids, and phytoestrogens, can reduce neuroinflammation and lower the risk of neurodegeneration [10].

Often classified under alternative medicine, nutraceuticals, and dietary supplements include vitamin and mineral supplements, herbs, essential oils, enzymes, homeopathic remedies, and similar products (except tobacco derivatives). Many of these categories are now, to varying degrees, making their way into mainstream medicine. Americans use these products extensively; an estimated 55% of American adults take a dietary supplement every month, and 35% take a multivitamin or multimineral supplement annually. Nutraceuticals, which include herbal products, functional foods, and dietary supplements, are

CHAPTER 5

Beneficial Effect of Nutraceuticals on Respiratory Diseases

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Abstract: Respiratory diseases encompass a range of conditions affecting the lungs and airways, including acute infections (*e.g*., bacterial and viral pneumonia) and chronic diseases (*e.g*., chronic obstructive pulmonary disease, asthma, pulmonary fibrosis, and lung cancer). They also impose significant socio-economic burdens. A number of reasons, including virus outbreaks, the emergence of drug-resistant pathogens, air pollution, smoking, and low immunization rates, have designated respiratory ailments as one of the leading causes of mortality worldwide. Various prevention and control strategies have been adopted to reduce the burden of respiratory illnesses. Among them, nutraceuticals, also known as functional foods, have emerged as one of the most effective choices for supporting respiratory health. Nutraceuticals, including polyunsaturated fatty acids, vitamins, dietary fibers, minerals, and polyphenolic compounds with anti-inflammatory, antioxidant, and immune-modulating properties, have shown promise in managing respiratory diseases by reducing airway inflammation and oxidative stress to improve lung function and disease symptoms. As supplemental therapies, they also maximize the benefits of traditional pharmaceutical treatments while reducing their side effects. Although nutraceuticals appear promising, further studies are needed to determine their optimal formulations and dosing regimens for achieving prolonged benefits. To guarantee the safety and effectiveness of nutraceutical products, standardization and regulatory control are also essential. This chapter first briefly outlines major respiratory illnesses affecting human health. Then, it discusses the functions of promising nutraceuticals in sustaining respiratory health, followed by a highlight of the challenges and considerations associated with their usage.

Keywords: Antioxidant, Anti-inflammatory, Asthma, COPD, Dietary fibers, Fatty acids, Lung, Minerals, Nutraceuticals, Pathogens, Pharmaceutical, Pneumonia, Pollutions, Polyphenols, Pulmonary fibrosis, Respiratory diseases, Smoking, Supplements, Virus, Vitamins.

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INTRODUCTION

In the third edition of "Global Impact in Respiratory Disease," the significance of retaining respiratory health has been reaffirmed [1]. The pulmonary system is an important and intricate part of the human body that is responsible for the operation of both respiratory and non-respiratory processes, like controlling venous return during physical activities and promoting effective fibrinolysis for dissolving blood clots [2]. Despite the complex design of the pulmonary system, which is crucial for human survival, the lungs are inherently vulnerable to injury and infection due to their constant exposure to chemicals, contaminants, and airborne pathogens during the process of gaseous exchange. According to the latest global epidemiology data on the COVID-19 pandemic from the World Health Organization (WHO), it has already resulted in over 700 million infections and more than 7 million fatalities [3]. Other respiratory diseases, including Chronic Obstructive Pulmonary Disease (COPD), pneumonia, and lung cancer, are also significant causes of global morbidity and mortality. COPD alone stands as one of the top three causes of global mortality, claiming the lives of approximately 3.2 million individuals annually. Pneumonia is responsible for the leading cause of death among children and the elderly populations, and lung cancer causes the most deaths among all types of cancers [1]. With the emergence of drug-resistant pathogens, climate change, and air pollution, the respiratory system will continue to face challenges, and therefore, it is important to maintain good respiratory health.

Nutraceuticals, a term derived from "nutrition" and "pharmaceuticals," are bioactive compounds or substances derived from natural food sources that provide health benefits beyond basic nutrition [4]. They are often considered to be a bridge between food and medicine. Nutraceuticals can be classified into various categories based on their composition and mechanisms of action. These categories include vitamins, minerals, amino acids, fatty acids, fiber, prebiotics, probiotics, herbal extracts, and phytochemicals. Each category encompasses a diverse range of compounds with distinct physiological functions and potential therapeutic effects [5]. The classification of nutraceuticals facilitates a deeper understanding of their distinct roles in promoting health and preventing or managing various diseases. Furthermore, it provides a framework for research, regulation, and clinical application of these compounds in the field of nutrition and healthcare. Emerging evidence highlights their significance and importance in lung disease management [6, 7]. In this chapter, we will first provide a brief introduction on major respiratory diseases that affect human health. Then, nutraceuticals reported to be beneficial for respiratory health will be discussed in detail. Lastly, we will highlight the prospects and challenges in developing nutraceuticals as the next generation therapeutics for respiratory health.

OVERVIEW OF MAJOR RESPIRATORY DISEASES

Different types of lung diseases can result in several complications associated with their pathogenesis and etiology. Inflammation in the respiratory tract is a hallmark of many persistent respiratory conditions, including allergic rhinitis, asthma, COPD, and lung fibrosis, which are largely associated with different types of stimulants (Fig. **1**). Asthma is a chronic inflammatory airway disease characterized by bronchoconstriction, excessive mucus, and long-term airway remodeling. In 2019, it affected 262 million people and caused 455,000 deaths globally [8]. Risk factors include pollutants, allergen exposure, family history, and smoking. During attacks, allergens triggered Th2 lymphocytes and mast cells, which released cytokines and spasmogens. This subsequently caused bronchoconstriction and inflammation, leading to epithelial damage and muscle hypertrophy [9]. COPD, characterized by chronic bronchitis, bronchiolitis, and emphysema, leads to shortness of breath and reduces forced expiratory volume in one second (FEV_1) [10]. In 2020, COPD affected 480 million people, projected to reach 600 million by 2050 [13]. Its pathogenesis involves inflammation, protease imbalance, and oxidative stress. Inflammatory mediators, such as LTB4, IL-8, and TGF-β, attract immune cells, leading to inflammation and fibrosis [11]. The overproduced proteases and elevated oxidative stress (mitochondrial reactive oxygen species, ROS) also damage lung tissues [12]. Idiopathic Pulmonary Fibrosis (IPF) is another chronic lung disease with a prevalence of 50 per 100,000 [14]. Its pathogenesis involves three stages: predisposition (genetic mutations, environmental exposure, and aging), initiation (TGF-β activation, fibrocyte recruitment, epithelial-to-mesenchymal transition, and unfolded protein response activation), and progression (fibroblast differentiation, matrix deposition, remodeling, and profibrotic changes) [14].

Acute respiratory infections (pneumonia) can be caused by various pathogens, including SARS-CoV-2, influenza, respiratory syncytial virus, and other seasonal viruses and bacteria. Community-acquired Pneumonia (CAP) alone claims 3 million lives annually worldwide [15]. Bacteria typically colonize the mucosal surface of the upper respiratory tract; however, they can also invade the lower respiratory tract when inhaled, resulting in lung inflammation [16]. The inhaled bacteria can evade mucus entrapment and inhibit mucociliary clearance through specific proteins, triggering inflammatory responses *via* Pattern Recognition Receptors (PRRs) and pathways like Nuclear Factor kappa-B (NF-κB) and Mitogen-activated Protein Kinase (MAPK), resulting in persistent lung inflammation [17, 18]. Viral infections, caused by influenza viruses, hijack host cell machinery for replication. They attach to alveolar epithelial cells *via* haemagglutinin binding to α2,6-linked sialic acids, leading to fusion and release of viral RNA into the host cell [19]. The antiviral defense of the host involves

CHAPTER 6

The Role of Nutraceuticals in the Treatment of Neurodegenerative Diseases

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Abstract: Primarily characterized by impairment of neurons, neurological disorders stand as one of the most significant challenges to be treated in the global healthcare sector. As the focus shifts towards embracing healthier choices, the demand for nutraceuticals is rapidly rising, particularly for their contribution to neurological disorders, over the past decade, due to their potential to bear lesser or no side effects in contrast to increased therapeutic activity. Neurons, being the functional unit of the brain, are particularly susceptible to any effect on the electrical impulses in the nervous system, which can result in neurological degeneration, whether acquired, congenital, or induced by injury. Neurodegenerative diseases are characterized by neuronal dysfunction or even death of neurons that can affect both the central and peripheral nervous systems. The understanding of the pathophysiology and underlying mechanisms of the main neurodegenerative disorders like Alzheimer's and Parkinson's disease is indispensable, while rendering the right treatment is intricate and grim to address. While numerous drugs are currently approved for treating neurodegenerative disorders, the majority of them alleviate associated symptoms rather than addressing the underlying condition. Neuro-nutraceuticals, which are natural plant compounds combining dietary and pharmaceutical properties, play a crucial role. They aim to enhance cerebral blood flow and contribute to illness prevention and management, which can be commonly found in food, herbal remedies, and nutritional supplements. When considering the neuroprotective and neuromodulatory properties of neuro-nutraceuticals, it is hypothesized that these herbs offer a safer alternative compared to single-target medicines, promoting holistic improvements in brain health with minimal adverse effects. Recently, there has been a significant worldwide increase in the availability and use of nutraceutical products designed to address neurodegenerative diseases. This growth is driven by factors such as relatively lax regulatory oversight and the promotion of these products as safe and effective alternatives to traditional pharmaceuticals. The increasing demand for dietary supplements focused on improving

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brain health is substantial and poised to create a larger market in the foreseeable future, exerting an influence on both individual well-being and the global economy.

Keywords: Blood-brain barrier, Clinical trials, Market value, Neurodegenerative diseases, Nutraceuticals.

INTRODUCTION

Recently, there has been a growing trend towards healthier food options, driven not only by their nutritional and sensory benefits but also by their positive impact on mental and physical well-being, the regulation of nutritional balance, disease prevention, and more [1]. Moreover, the word 'Nutraceuticals' has been coined by combining 'nutrition' and 'pharmaceuticals. Nutraceuticals are derived from food sources and are promoted for their medicinal or health-enhancing properties. Another common name, 'functional food', on the other hand, refers to food that has been altered or enriched with specific components to offer health benefits beyond basic nutrition. Both functional foods and nutraceuticals aim to deliver various health benefits, including lowering the risk of chronic diseases, augmenting immune function, and improving cognitive function [2], provided they are taken regularly in adequate quantities for a long duration.

According to the American Nutraceutical Association, a nutraceutical is described as a food or related product that possesses health-enhancing properties [3]. Apart from imparting nutritional value, these products offer their medicinal benefits, providing physiological advantages and protection against chronic diseases [4]. Nutraceuticals can be categorized according to various criteria, such as their origin, chemical makeup, mechanism of action, and health advantages [5]. They offer the benefits of isolated nutrients, vitamins, minerals, probiotics, and genetically modified food, as well as natural food and supplements with anti-inflammatory and antioxidant properties [6]. These products are utilized to delay aging, enhance bodily functions, improve health conditions, prevent chronic diseases, and increase longevity (Fig. **1**) [7]. Additionally, nutraceuticals have been found to enhance the therapeutic effects of certain medications by augmenting various biological pathways, such as the reuptake of monoamines, leading to significant neurobiological effects [8].

Neurodegeneration involves the gradual loss of both structural and functional elements within neurons, often leading to deformities like AD (AD), Parkinson's disease (PD), Brain Trauma (BT), Multiple Sclerosis (MS), Huntington's disease (HD), spinocerebellar ataxias (SCA), Prion Disease (PrD), Progressive Supra-nuclear Palsy (PSP), and Amyotrophic Lateral Sclerosis (ALS). The neurological consequences of neurodegeneration can profoundly affect the physical and mental

well-being of individuals. The human brain utilizes approximately 20% of the total oxygen consumed, with a significant portion consisting of easily peroxidizable polyunsaturated fatty acids, leading to the generation of substantial amounts of ROS, referred to as "oxidative stress," a condition linked to chronic diseases that result in cell death. This imbalance is particularly prevalent in conditions characterized by elevated and sustained ROS production and diminished levels of antioxidant defenses, as observed in various pathologies and during the natural aging process [9]. Neurodegenerative diseases present a formidable challenge as they involve the progressive deterioration of nerve cells, primarily within the brain. This category encompasses a spectrum of conditions such as AD, PD, dementia with Lewy bodies, vascular dementia, Huntington's disease, frontotemporal dementia, progressive supranuclear palsy, motor neurone disease, and Creutzfeldt-Jakob disease. Unfortunately, these diseases currently lack curative treatments, making management and care exceptionally challenging [10]. These diseases are complex conditions with multifactorial causes, and the exact etiology may vary depending on the specific disease. Common factors and mechanisms associated with the development and progression of neurodegenerative diseases include mitochondrial dysfunction, genetic factors, protein misfolding and aggregation, chronic brain inflammation, age, and environmental factors. Neurological diseases, thus, represent significant healthcare challenges globally.

Fig. (1). Probable Neurodegenerative Diseases, either born or acquired, that can be lessened with specific nutraceuticals.

CHAPTER 7

The Role of Nutraceuticals in the Management of Degenerative Kidney Diseases

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Abstract: Degenerative kidney diseases, including chronic kidney disease, diabetic nephropathy, and hypertensive nephropathy, represent significant global health challenges affecting millions worldwide. While conventional treatments remain essential, their limitations and side effects have sparked growing interest in complementary therapeutic approaches. This chapter comprehensively examines the role of nutraceuticals in managing degenerative kidney diseases, synthesizing evidence from both preclinical and clinical studies. Various nutraceuticals, including polyphenols (such as curcumin and resveratrol), omega-3 fatty acids, probiotics, and vitamin D, have demonstrated promising results in modulating key pathological pathways. Preclinical studies have revealed their ability to reduce oxidative stress, inflammation, and metabolic dysregulation, while clinical trials have shown improvements in kidney function markers and associated comorbidities. The chapter examines the mechanisms of action, comparing nutraceutical interventions with conventional treatments and assessing their market value within the expanding global nutraceuticals industry. Despite encouraging results, challenges remain, including standardization issues, limited large-scale clinical evidence, and potential drug interactions. The integration of nutraceuticals into conventional treatment regimens holds promise for improving patient outcomes, particularly in managing inflammation and oxidative stress associated with kidney disease progression. Future research requires larger clinical trials and enhanced quality control measures to establish evidence-based guidelines for the use of nutraceuticals in degenerative kidney diseases. This review offers healthcare professionals and researchers valuable insights into the potential of nutraceuticals as complementary therapeutic options in the management of kidney disease.

Keywords: Chronic kidney disease, Diabetic nephropathy, Hypertensive nephropathy, Metabolic dysregulation, Nutraceuticals, Omega-3 fatty acids, Polyphenols.

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INTRODUCTION

Degenerative kidney diseases are a group of chronic and progressive conditions that lead to the gradual deterioration of kidney structure and function. The destruction and impairment of nephrons characterizes these disorders, the functional units of the kidneys, resulting in a decline in glomerular filtration rate and the accumulation of waste products in the body [1]. The most common types include chronic kidney disease (CKD), diabetic nephropathy, and hypertensive nephropathy. These conditions are major public health concerns, as they are associated with an increased risk of cardiovascular events, end-stage renal disease, and premature mortality [2, 3].

CKD often develops slowly over many years and may not cause any noticeable symptoms until the later stages of the disease. Early symptoms can include foamy urine, frequent urination, and fatigue. CKD affects over 10% of the global population, amounting to more than 800 million individuals worldwide. The condition is more prevalent in older individuals, women, racial minorities, and those with underlying conditions such as diabetes or hypertension. In the United States alone, nearly 808,000 people are living with end-stage renal disease (ESRD), with 69% receiving dialysis and 31% having undergone a kidney transplant [4, 5].

Traditionally, the treatment of degenerative kidney disorders has involved a combination of medicinal therapy, lifestyle modifications, and, in severe cases, renal replacement therapies like dialysis or kidney transplantation. Medical interventions often focus on managing the primary underlying illnesses, such as diabetes and hypertension, which are significant contributing factors to the progression of kidney disease [6].

However, conventional therapy for chronic kidney disease has several significant limitations. Current treatments are often inadequate in halting disease progression, leading many patients to reach the advanced stage of renal disease, known as ESRD. Factors such as inadequate patient education and poor adherence to medications, including ACE inhibitors and ARBs, contribute to the underutilization of effective therapies [7].

Furthermore, current treatment approaches for CKD have not adequately addressed the metabolic imbalances associated with the disease, including acidosis, hyperphosphatemia, and vitamin D deficiency. Insufficient attention has been given to the underlying disease-causing pathways, and the process of transitioning to ESRD treatment, including dialysis or transplantation, remains a major challenge [8, 9].

These drawbacks of traditional therapies, including undesirable side effects and less-than-ideal effectiveness, have led to an increasing interest in the use of nutraceuticals as a supplementary method to control and manage degenerative kidney disorders. Nutraceuticals are dietary items, extracts, or derivatives that are natural, non-toxic, and include bioactive chemical compounds, such as herbs, vitamins, amino acids, minerals, and enzymes. These food-derived products with potential health benefits have garnered attention for their capacity to regulate metabolic pathways associated with the development of degenerative kidney disorders, including inflammation, oxidative stress, and metabolic abnormalities [10, 11].

The bioactive chemicals present in nutraceuticals, such as omega-3 fatty acids, curcumin, resveratrol, probiotics, and coenzyme Q10, have shown promise in reducing the course of chronic kidney disease by virtue of their antioxidant, anti-inflammatory, and anti-fibrotic capabilities. Preclinical and clinical research have investigated the use of nutraceuticals as supplementary treatments or independent interventions, aiming to enhance patient outcomes and mitigate the impact of chronic and debilitating kidney disorders [11 - 13].

Integrating nutraceuticals into treatment plans for chronic kidney disease may improve kidney health and slow the progression of the disease, potentially in combination with traditional medications and lifestyle modifications.

This chapter provides a brief overview of the growing importance of nutraceuticals in the treatment of chronic kidney disease. This analysis will encompass the mechanisms by which nutraceuticals can regulate inflammation, oxidative stress, and metabolic dysregulation, as demonstrated by both preclinical and clinical research. The objective of this chapter is to demonstrate the use of nutraceuticals as complementary or independent therapies that have the potential to improve patient outcomes and reduce the burden of chronic kidney disease.

OVERVIEW OF DEGENERATIVE KIDNEY DISEASES

Chronic Kidney Disease (CKD)

CKD is a progressive and irreversible condition characterized by the gradual deterioration of kidney structure and function over time. It is defined by the presence of kidney damage, evidenced by structural or functional abnormalities, or by a decreased glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2 for at least 3 months, regardless of the underlying cause.

CKD is categorized into five distinct stages based on the severity of renal impairment and the level of kidney function. Stage 1 is characterized by a normal

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