THE ROLE OF NUTRACEUTICALS IN DEGENERATIVE DISEASES | PART 2

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The Role of Nutraceuticals in Degenerative Diseases

(Part 2)

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FOREWORD

Today's global health landscape is shifting rapidly toward a greater focus on preventative and integrative medicine. This change results from increased incidence rates of chronic degenerative diseases such as cardiovascular diseases, diabetes, arthritis, neurodegenerative diseases, and other similar disorders that continue to place a burden on healthcare systems around the globe, including India's system. The continued rise in the number of incidents will require many novel strategies that extend beyond traditional methods of approaching health care, and will require combining Conventional.

Science with Traditional Practice. Nutraceuticals - compounds that come from nutrient-rich foods - are emerging as valuable partners in health and healing due to their medicinal and therapeutic potentials that are very interesting to the scientific community and that are important in clinical practice, particularly in a country such as India, where the principles of Ayurveda and the traditional dietary culture are inseparable from food and medicine. The book, The Role of Nutraceuticals in Degenerative Diseases, is timely and extensive in its coverage of these topics. It takes a critical view regarding the potential for natural compounds to slow the progression of disease and alleviate suffering from Debilitating conditions. The editors of this volume have chosen the chapters that address a wide variety of disease States and present a Comprehensive and Evidence-Based approach that is a merger between Modern Nutritional Science and Ancient Traditions.

This book provides readers with information about the most common therapeutics that can improve our health and quality of life across different categories of nutraceutical use. The categories are:

1. Cardiovascular Disease- The natural compounds found in many of the products marketed as cardiovascular health support can improve heart health and well-being.

2. Arthritis and Osteoporosis- Nutritional strategies to reduce joint and bone degeneration will assist individuals suffering from these chronic illnesses.

3. Diabetes- Nutraceuticals, specifically as it pertains to glycemic control and chronic diabetes complications' prevention, will improve glycemic management.

4. Ophthalmic Disorders- These types of disorders are often overlooked, but they also represent a growing problem in our society and the health industry.

5. Liver Disorders- Again, these types of disorders are often overlooked, but they also represent a growing problem.

6. Muscle Wasting- The role of nutrition interventions to improve muscle disease management needs further study.

Each chapter contains an enormous amount of information on the mechanisms of action, clinical evidence, and practical applications of each of the products discussed in this book, which makes this book an essential resource for all researchers, clinicians, pharmacists, nutritionists, and students.

This book's editors and contributors deserve credit for producing such an authoritative information source and successfully bridging the divide between traditional Indian medicine's

perspective of food as medicine and traditional science.

Therefore, the book "The Role of Nutraceuticals in Degenerative Diseases" is a true addition to the scientific community and will undoubtedly become a guide for healthcare providers who strive to deliver better care and improve the quality of life as the number of individuals suffering from chronic illness increases.

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PREFACE

The terms "nutrition" and "pharmaceutical" were combined to form the phrase "nutraceutical," which was coined by Dr. Stephen De Felice in 1989. These are foods, or portions of foods, that offer a variety of health advantages, such as disease prevention and/or treatment. Nutraceuticals have numerous benefits, including beneficial results in the prevention and management of complex diseases. Nutraceuticals are beneficial in various therapeutic areas, but their administration and prescription are necessary, and they should be adequately monitored to prevent uncontrolled use and adverse effects. A degenerative disease is a condition where cells, tissues, and organs gradually and irreversibly deteriorate. Over time, this deterioration can cause cell death, impairment, or loss of function. Degenerative diseases are placing a growing economic and social burden on societies, particularly as the world's population increases. Nutraceuticals offer an alternative approach to treating degenerative diseases. In our first volume, we have covered the general introduction to nutraceuticals, degenerative diseases, and potential nutraceuticals based on in silico studies. The first volume also explores the role of nutraceuticals in treating degenerative diseases of the respiratory tract, neurodegenerative diseases, and degenerative kidney diseases.

The second volume of this book, “The Role of Nutraceuticals in Degenerative Diseases,” is a collection of seven chapters that offer scientific information on the significance of nutraceuticals and their potential roles in the management, treatment, and prevention of degenerative diseases, including arthritis, diabetes, cardiovascular diseases, degenerative ophthalmic disease, muscle disease, liver disease, and degenerative osteoporosis. We believe the nutraceutical industry is moving in the right direction. The selected chapters are easily comprehensible and well-illustrated. A broad audience, particularly food scientists, engineers, biotechnologists, biochemists, and industrial companies, as well as any reader interested in learning more about the role of Nutraceuticals in the management of degenerative diseases.

We are grateful to all the authors for their contributions to the completion of this book. We sincerely hope you liked this book, and we'd love to hear your ideas and suggestions for future versions.

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CHAPTER 1

Nutraceuticals in the Management of Cardiovascular Diseases

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Abstract: Nutraceuticals are natural food-derived components that provide additional health benefits and potentially reduce cardiovascular disease (CVD) risk factors, such as hypertension, arrhythmia, myocardial infarction, hypertrophy, and atherosclerosis.

The objective of this book chapter is to explore the underlying mechanisms and provide a thorough assessment of the effects and benefits of nutraceuticals, such as garlic, grapes, ginger, turmeric, onion, blueberry, apple, brassica, tulsi, papaya, spirulina, *etc*.

Dietary habits have an immense effect on cardiovascular health. It has been established that nutraceuticals target various pathways involved in the evolution of CVD and offer a comprehensive approach for treating and preventing CVD. Studies show that consumption of nutraceuticals, such as omega-3 fatty acids, garlic, and dietary fibres in the diet, can improve cardiovascular risk factors, such as hypertension and hyperlipidemia, by reducing blood pressure and lipid profile levels. More specifically, it has been demonstrated that nutraceuticals like grapes, turmeric, and omega-3 fatty acids exhibit anti-inflammatory and anti-oxidation characteristics vital for healthy human blood vessels and arteries. However, these promising results have been achieved through heterogeneous study designs and therefore require further research regarding the applications of nutraceuticals in clinical practice.

In conclusion, nutraceuticals show an attractive emerging field in treating CVD. When combined with traditional therapies, nutraceuticals can play a supportive role by mitigating risk factors while improving treatment outcomes, thereby serving as an essential component of extensive cardiovascular treatment. Future research is needed to better understand the effects and potential of nutraceuticals in improving cardiovascular health.

Keywords: Atherosclerosis, Hypertension, Myocardial infarction, Nutraceuticals, Spirulina, Turmeric.

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INTRODUCTION

Cardiovascular disease (CVD) is one of the most prevalent health problems and is responsible for approximately 17.3 million deaths globally [1]. Many kinds of risk factors associated with CVD are either preventable or manageable. These include obesity, hypertension, high cholesterol, diabetes, metabolic syndrome, smoking, poor diet, and sedentary lifestyle [1, 2]. Nutraceuticals are substances derived from dietary sources that contain bioactive components of natural origin, prevent or manage several diseases, and thus provide potential health benefits. The term “nutraceutical” was coined by S. DeFelice in the early 1980s. Dietary habits vary widely between regions and countries, affecting CVD's prevalence. Improving diet quality could potentially reduce this disease burden. In recent years, people have generally opted for nutraceuticals over synthetic pharmaceuticals because of fewer adverse effects, a lower risk of overdose, minimal chemical alteration, and more holistic benefits. Over the past decade, there has been a rapid increase in the development and availability of nutraceutical products to meet the growing demand for health management remedies [3].

The impact of nutraceuticals on CVD risk is reviewed in this chapter based on the most recent research. A lot of attention is drawn to nutraceuticals such as spirulina, resveratrol, chocolate, quercetin, curcumin, brassica vegetables, berberine, and their roles, as well as the clinical study data that is currently available to support their potential benefits in boosting cardiovascular health.

ARRHYTHMIA

An arrhythmia occurs when a regular rhythmic cycle in the heartbeat is interrupted. This problem can result from irregularities of the electrical signal in the heart, premature contraction, or obstruction in the conduction pathway. Any disruption in the continuous transmission of electrical impulses that control the heartbeat can lead to arrhythmia. Medically, a rapid heart rhythm is termed tachycardia (>100 beats/min) and a slow heart rhythm is termed bradycardia (<60 beats/min), where a normal sinus rhythm is 72 beats/min [4 - 6].

Pathophysiology

The heart comprises modified neuromuscular cells, including the sinoatrial (SA) node and atrioventricular (AV) node. The SA is the heart's primary pacemaker, generating electrical impulses that are transmitted to all atria through depolarization. The AV node delays the generation rate for 0.1 seconds, filling the ventricle with blood. From the AV node, the impulses travel to the Bundle of His and then to the Purkinje fibres, eventually spreading all over the ventricles. This initiates ventricle contraction. Blood reaches the aorta and pulmonary artery,

ensuring normal heart rhythm. When the SA node acts as a pacemaker, the different types of arrhythmias happen [4, 6, 7]. Some types of arrhythmias are described below:

Sinus Arrhythmia

Respiratory sinus arrhythmia occurs due to variations in impulse transmission through the SA node. During inspiration, intrathoracic pressure decreases, increasing lung volume and venous return. It stimulates stretch receptors, which in turn cause the brain to receive vagal afferent impulses. This raises the heart rate, reduces vagal tone, and contracts the vasodilated portion. Expiration increases intrathoracic and lung pressure, causing lung volume reductions and dilation of the vasodilator area, resulting in a decreased heart rate. The electrocardiogram (ECG) shows a moderate heart rate during expiration and a high heart rate during inspiration [6].

Sinus Tachycardia

Abnormal heart rate increases due to SA node stimulation, leading to depolarization and increased heart rate. This leads to decreased cardiac output and angina-like pain, with decreased R-R interval in the ECG [6, 8].

Sinus Bradycardia

Sinus bradycardia is characterized by a heart rate less than 60 beats/min and proper cardiac muscle depolarization that starts at the sinus node. Most patients are asymptomatic, but some may have headaches, dizziness, fatigue, weakness, shortness of breath, chest pain, and low Blood Pressure (BP) [6, 9].

Ectopic Arrhythmia

An irregular heartbeat that results from an electrical impulse coming from an unusual place inside the heart, instead of the heart's typical pacemaker, is known as an ectopic arrhythmia. Sometimes, a few people don’t experience any symptoms, but when it occurs, people may feel a fluttering sensation in the chest, palpitation, a missed heartbeat, *etc*.

Supraventricular Tachycardia

When the atrial muscles and AV node function as pacemakers, they generate impulses, trigger an unexpected attack, and result in tachycardia [10].

CHAPTER 2

Role of Nutraceuticals in the Treatment of Arthritis

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Abstract: Arthritis refers to joint pain, inflammation, or joint disease. It is the most common cause of disability, affecting people of all ages, races, and genders. In most cases, women are more commonly affected, and symptoms may worsen over time. Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by inflammatory arthritis and extra-articular involvement. It typically starts in small peripheral joints, is usually symmetric, and may progress to involve proximal joints if left untreated. Joint inflammation over time can lead to the destruction of the joint, resulting in loss of cartilage and bone erosion. Osteoarthritis (OA) is a chronic autoimmune disease that primarily targets the lining of synovial joints, leading to progressive disability, early mortality, and socioeconomic challenges. The pathogenesis of OA presents a multifaceted landscape, involving diverse etiologies and intricate molecular and cellular mechanisms. OA manifests as functional impairment of the joint, characterized by alterations in joint morphology resulting from the erosion of articular cartilage, the formation of osteophytes, subchondral sclerosis, bone marrow lesions (BMLs), and synovial proliferation. The role of chondroitin sulfate (CS) biosynthesis in OA is highlighted, with altered CS chain length correlating with disease severity. Nutraceuticals have been shown to be effective in the management of both OA and RA by acting as anti-inflammatory agents, primarily through the inhibition of the tumor necrosis factor (TNF) catabolic signaling pathway in chondrocytes. In this chapter, we discuss the effectiveness, safety, and toxicity of nutraceutical products in the treatment of RA and OA.

Keywords: Arthritis, Nutraceuticals, Osteoarthritis, Rheumatoid arthritis.

INTRODUCTION

There are over 100 different types of arthritis and associated disorders. The term “arthritis” refers to joint pain, inflammation, or disease of the joints. The most

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common cause of disability, arthritis, affects people of all ages, races, and genders. The majority of cases occur in women, and while arthritis is not solely age-related, some forms tend to worsen with age. According to the World Health Organisation (WHO), osteoarthritis affected 528 million individuals globally in 2019, representing a 113% increase from 1990. Furthermore, 60% of those with osteoarthritis are women, and about 73% of affected individuals are older than 55 (Fig. **1**).

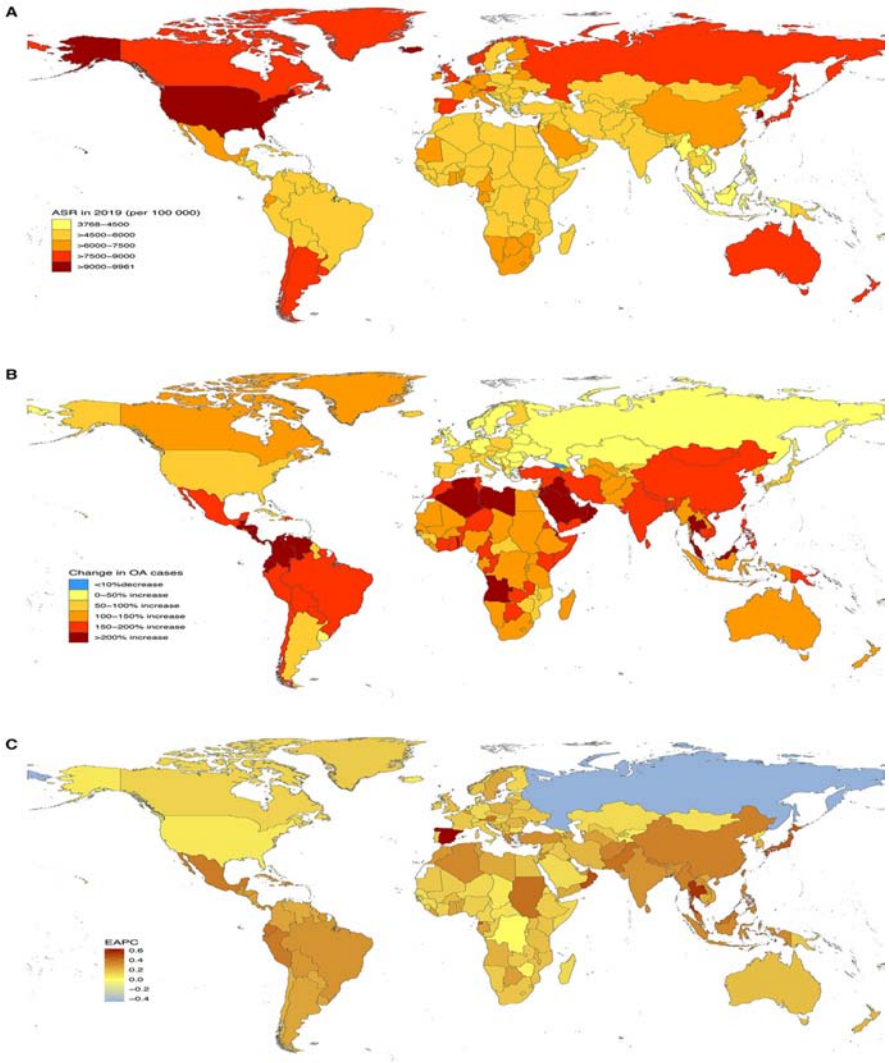

Fig. (1). Prevalence of osteoarthritis (OA) for both sexes combined in 204 countries and territories. **A:** Age-standardized prevalence rate (ASR) of OA in 2019. **B:** Percentage change in prevalent cases of OA between 1990 and 2019. **C:** Estimated annual percentage change (EAPC) of OA from 1990 to 2019 [1].

On the other hand, 18 million people worldwide suffered from rheumatoid arthritis in 2019, as per the WHO (Fig. **2**). Hence, approximately 550 million people are affected by various types of arthritis. The knee is the most commonly affected joint, followed by the hip and the hand [1]. The most common form of arthritis is osteoarthritis (OA). The symptoms of arthritis include pain, swelling, reduced range of motion, and stiffness. In osteoarthritis, an inflammatory joint disease, the main features include subchondral sclerosis, osteophyte formation, alterations in the synovial membrane, and bone enlargement at the joint margins. In contrast, rheumatoid arthritis is characterized by bone loss and synovial inflammation. In both conditions, cartilage may gradually lose its flexibility, eventually wearing down to the point where bone scrapes against bone. In severe cases, cartilage fragments may break off, resulting in intense pain in the muscles adjacent to the affected bone. The progression of these morphological and biochemical changes leads to gradual joint deterioration, reduced mobility and stability, deformity, pain, stiffness, and loss of function. Arthritis is diagnosed through physical examination, radiographic, and microradiographic data. Magnetic resonance imaging (MRI) can reveal joint abnormalities and cartilage degradation, particularly in osteoarthritis [2].

Currently, arthritis has no known cure. The primary goal of treatment is to reduce symptoms such as pain and inflammation while maintaining joint mobility. To achieve this, a variety of pharmaceuticals, nutraceuticals, disease-specific therapies, stem cell treatments, and physiotherapy may be employed. To overcome pain and inflammation, cyclooxygenase (COX)- inhibiting nonsteroidal anti-inflammatory drugs (NSAIDs) have been most commonly used to manage OA. Unfortunately, long-term use of NSAIDs has several adverse effects, such as reduced appetite, vomiting, ulcers, and hepatic as well as renal dysfunction. The American Journal of Medicine revealed in 1998 that NSAIDs resulted in over 100,000 hospital admissions and 16,000 arthritis-related deaths annually in the US.

Alternative treatments for arthritis include weight loss, balanced diet, nutraceuticals, and natural herbs. Nutraceuticals with anti-inflammatory and anti-arthritic properties have gained popularity recently. Nutraceuticals have recently gained popularity as “self-help” treatments among arthritis patients. These include glucosamine, chondroitin, type II collagen, shilajit, 5-Loxin, avocado/soybean unsaponifiables, curcumin, and many others. The effectiveness, safety, and toxicity of nutraceuticals in OA are briefly discussed in this chapter.

CHAPTER 3

Beneficial Effect of Nutraceuticals on Diabetes Mellitus

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Abstract: In recent years, emerging evidence suggests that nutraceuticals, due to their variety and multifaceted therapeutic impacts, may be a distinct and complementary prophylactic option for diabetes and its complications. Several nutraceuticals, including vitamin C, α-lipoic acid, L-carnitine, co-enzyme Q10, and others, have shown anti-diabetic properties over the years. In this chapter, we look at the possible benefits of nutraceuticals against this metabolic disorder and relevant complications. According to several pre-clinical and clinical studies, nutraceuticals can alter the metabolism of lipids and carbohydrates, induce hypoglycaemic effects, reduce insulin resistance and dyslipidaemia, improve lipolysis in adipose tissues, reduce free radical damage, stress-sensitive cascades, and mitigate inflammatory responses. Nutraceuticals can also help in the prevention of chronic diabetic consequences, including cardiovascular complications, nephropathy, CNS ailments, and retinopathy. In summary, the role of nutraceuticals in diabetes treatment is rapidly expanding, with a wide range of bioactive compounds supporting diabetic care through multiple pathways. The advantages of these products include better glycaemic control, enhanced insulin sensitivity, and fewer complications from diabetes. Nutraceuticals are expected to become more significant in the treatment of diabetes as scientific knowledge advances. They offer a holistic approach that empowers people through lifestyle modifications aimed at enhancing long-term health outcomes in addition to supplemental medication therapy. Further research, focusing on clinical utilization, is required to determine nutraceutical supplementation in diabetic patients.

Keywords: Carbohydrates, Diabetes, Hyperglycaemia, Insulin resistance, Nutraceuticals.

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INTRODUCTION

Diabetes mellitus (DM), a chronic lifestyle-related disorder, is characterized by an abnormally raised blood glucose level. This induction of hyperglycaemia can occur owing to impaired insulin production and/or resistance to the peripheral activity of insulin in insulin-sensitive tissues [1]. Different types of diabetes include type 1 DM (T1DM), type 2 DM (T2DM), gestational diabetes (GDM), and additional specific, less-frequent variants, where T2DM is the most commonly occurring type of diabetes [2].

In developing countries, the number of DM patients is growing at a concerning rate, primarily driven by the escalating prevalence of obesity throughout the lifespan, largely attributed to laziness and poor eating habits. According to Saeedi and colleagues, the global occurrence of diabetes is projected to reach 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045 [3]. Among the continents, Europe has the highest number of T2DM patients [1]. The trend of the prevalence of diabetes underscores the urgent need for effective public health interventions to address lifestyle factors contributing to DM [1].

In T1DM, insulin-producing pancreatic β cells are destroyed, leading to elevated serum glucose levels [4]. Type 2 diabetes mellitus (T2DM) is caused by decreased sensitivity to insulin. In advanced stages of T2DM, a reduction in β-cell mass and function occurs, along with impaired insulin signaling. This progression is also accompanied by altered lipid metabolism and low-grade, chronic inflammation, resulting in tissue damage, fostering diabetes-related complications [5]. Other complications associated with diabetes include angiopathy [6], high blood pressure [7], nephropathy [8, 9], retinopathy [10], neuropathy [11], foot ulcers [12], and weight gain (Fig. **1**) [13]. Oral antidiabetic medications used to address diabetic complications are grouped into sulfonylureas, thiazolidinediones, meglitinides, sodium-glucose co-transporter (SGLT2) inhibitors, α-glucosidase antagonists, dipeptidyl peptidase-4 (DPP4) blockers, biguanides, and incretin-like compounds [14]. Presently available contemporary anti-diabetic medications are mostly synthetic in nature, often accompanied by high costs and a range of potential side effects [5].

Nature-derived products have significantly contributed to the development of novel classes of hypoglycemic agents [5]. Nutraceuticals, primarily derived from naturally occurring foods, possess the potential to prevent various pathological conditions. DM is one of the most commonly occurring lifestyle-related ailments that can be mitigated through different mechanisms with nature-derived nutraceutical products [15]. According to Mabena and co-workers, nutraceuticals are broadly categorized into traditional and non-traditional types [15]. The anti-

diabetic potential of various nutraceuticals, such as vitamin C, α-lipoic acid (ALA), L-carnitine, and coenzyme Q10, has been revealed over the years [16]. Nutraceuticals act through various processes including the activation of nuclear factor erythroid 2-related factor 2 (Nrf2), promoting the transcription of glyoxalase I, inducing mitophagy as well as mitochondrial biogenesis, boosting uncoupling protein 2, inhibiting NAPDH oxidase, recoupling endothelial nitric oxide synthase (eNOS), providing glutathione (GSH) precursors, scavenging membrane oxidants, correcting thiamine deficiency to quell oxidative stress and dicarbonyl stress, thus potentially preventing diabetic complications [17]. In this chapter, various classes of nutraceuticals will be discussed, along with insights into their antidiabetic activity.

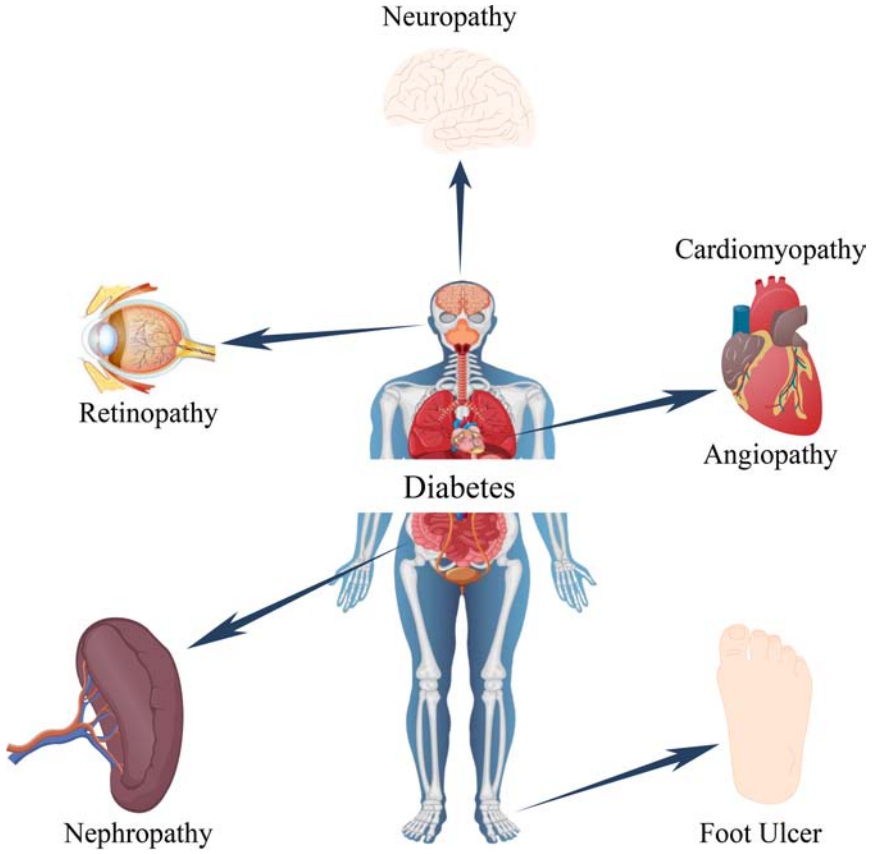

Fig. (1). Various complications related to diabetes.

TRADITIONAL NUTRACEUTICALS IN THE MANAGEMENT OF DM

Nutraceuticals obtained from natural sources and used to deliver beneficial roles in human health over time are known as traditional nutraceuticals. These

CHAPTER 4

Role of Nutraceuticals in the Management of Degenerative Ophthalmic Diseases

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Abstract: Nutraceuticals, derived from food sources, offer additional health benefits beyond basic nutrition. Combining "nutrient" and "pharmaceutical," nutraceuticals are increasingly recognized for their potential in managing various diseases, particularly ocular disorders, without the side effects often associated with synthetic pharmaceuticals. These natural compounds contribute to vital biological processes, including antioxidant defence and cellular integrity, thereby enhancing health, preventing chronic diseases, and potentially extending life expectancy. With various forms available, such as pills, powders *etc.*, nutraceuticals are easily accessible and cost-effective. In the realm of neurodegenerative diseases, nutraceuticals can play a significant role in mitigating conditions affecting vision, including age-related macular degeneration (AMD), diabetic retinopathy (DR), and glaucoma. These disorders are often linked to oxidative stress, wherein reactive oxygen species (ROS) contribute to retinal ganglion cell degeneration. Nutraceuticals with antioxidant properties have been shown to reduce ROS levels, thereby offering a protective effect against ocular degeneration. This chapter briefly focuses on the pathophysiology of common degenerative eye diseases and discusses the potential of nutraceuticals in their prevention and management. By enhancing nutritional intake without altering physiological states, nutraceuticals present a compelling alternative to conventional drugs, particularly for age-related vision disorders, promoting overall ocular health and potentially reducing the prevalence of vision impairment in aging populations.

Keywords: Degenerative diseases, Management, Nutraceuticals, Ophthalmic diseases, Pathophysiology.

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INTRODUCTION

A nutraceutical is any product made from food sources that offers additional health advantages beyond the fundamental nutritional value of food. Combining the terms “nutrient,” which describes a healthy food item, and “pharmaceutical,” which describes a medical therapy, result in the term “nutraceutical.” Thus, novel materials in the health sciences may offer a new way to treat different disorders and these are also essential for running the life for a healthy human life.

So, nutraceuticals can have potential roles in the management of many diseases, including eye diseases [1, 2]. Nutraceuticals have garnered much attention in recent years because of their possible benefits in terms of safety and therapy, unlike pharmaceuticals like drug formulations. The drug formulations contain mostly synthetic chemicals, both therapeutic agents (drugs) and auxiliary chemicals (excipients), which may produce side effects or toxicities [3, 4]. Nutraceuticals are beneficial in the management of diseases as they differ from pharmaceuticals in their natural quality. They do not alter any normal physiological condition in our body; rather, they complement the diet with more nutritious values [5].

Nutraceuticals play a crucial role in numerous biological processes, including antioxidant defence, cell proliferation, gene expression, and maintaining mitochondrial integrity, which may be impacted by these products. Nutraceuticals can, therefore, be used to maintain the integrity and functioning of the body as well as enhance health, prevent chronic diseases, delay the aging process, and ultimately lengthen life expectancy. Nutraceuticals like pharmaceuticals are also available in different dosage forms, such as pills, capsules, tablets, powders, *etc*., which resemble pharmaceuticals. They are easily prepared, easy to apply, and provide extensive functionality in humans [6 - 8]. Nutraceuticals are available in various forms in the market based upon their chemical nature, like lipid, protein, carbohydrate, micronutrient; mechanism of action, like metabolic impact, physiologic impact [9 - 11]. Nutraceuticals have a versatile impact on our body, such as an immune system boost by vitamin A, vitamin C [12, 13]; anti-inflammatory properties by carotenoids [14, 15]; cardiovascular system boost by fatty acids [16, 17]; and neurological disorder protectant by phytochemicals [18]. Apart from all these, nutraceuticals have limited side effects, which attracts more people to them as pharmaceutical alternatives [18, 19]. Patient compliance is much higher for nutraceuticals than for pharmaceuticals, also due to their 100% biocompatibility.

Most importantly, nutraceuticals do not change any physiological condition; rather, they work as food supplements to provide important nutrition to our body.

Also, nutraceuticals are easy to manufacture from low cost natural raw materials and cheaply available for people [20]. Another vital point is due to its non-prescription selling practice, people often purchase them for their health benefits, indicating the higher accessibility of nutraceuticals [21].

The progressive degeneration and eventual death of nerve cells in the brain or the peripheral nervous system are the cause of neurodegenerative diseases. Alzheimer's disease and Parkinson's disease are the most well-known, pervasive, and prevalent degenerative disorders among the aged population. However, neurodegenerative processes affect both the retina and the central nervous system (CNS). Amongst the neurodegenerative diseases particularly affecting the normal health of the eye, age-related macular degeneration (AMD), diabetic retinopathy (DR), cataracts, dry eye disease (DED), glaucoma, and presbyopia are commonly prevalent [22]. The primary mechanism underlying retrograde (presynaptic neurons) and anterograde (postsynaptic neurons) trans-synaptic neurodegeneration is the death of retinal ganglion cells. Oxidative stress plays a major pathophysiological role in the ocular degenerative diseases. It has been demonstrated that reactive oxygen species (ROS), whether from internal or external sources, are essential for the survival of ocular tissues [23]. To reduce ROS generation, various nutraceuticals with antioxidant properties have been reported to be beneficial in preventing ocular degenerative diseases [24]. In this chapter, the pathophysiology of the different degenerative ophthalmic diseases is focused on, with the possible nutraceuticals and their role in preventing the occurrence of these ophthalmic diseases.

EYE AND VISION

The eye is an extraordinary organ that captures and focuses light, converting it into chemical and electrical signals sent to the brain, where they are interpreted as visual images. It comprises the body's only two clear tissues; one is directly involved in vision, include the cornea and lens, which focus light onto the retina's central foveal area (macula). The retina then transforms the light into signals transmitted *via* the optic nerve to the brain. Supporting tissues, like the aqueous humor, nourish the lens. The retina and brain together form the CNS, which is responsible for our sense of sight [25]. The eye uses a focusing lens to project an inverted image onto a dense array of light-sensitive receptors, which convert light patterns into electrical impulses that the brain can interpret. Vision begins in the retinas, which are brain outgrowths containing rods and cones; rods detect shades of gray in low light, while cones detect color in daylight. There is no color vision at the borders of the retina because there are few cones there. Images from the right half of each retina are processed on the left side of the brain, and *vice versa*, because the optic nerve fibers from the inner and outer halves of the retinas cross

CHAPTER 5

Beneficial Effect of Nutraceuticals on Liver Diseases

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Abstract: Nutraceuticals are employed to improve health, offering physiological benefits alongside their nutritional value. Nutraceuticals can support the normal functioning of the human body, prevent certain diseases, and slow down the aging process. The edible nature, absence of adverse effects, and excellent *in vivo* compatibility have made nutraceuticals an excellent alternative to available marketed dosage forms. Recently, liver disorders have emerged as one of the major issues due to an unhealthy lifestyle. The over-consumption of medicines can also affect the healthy liver. Nutraceuticals can be an alternative and effective option for preventing and managing liver diseases. Several nutraceuticals are reported to be effective against different liver disorders, including hepatitis, non-alcoholic fatty liver disease, alcoholic fatty liver disease, liver cirrhosis, hepatocellular carcinoma, *etc.* The most commonly applied nutraceuticals in the treatment of several liver disorders include silymarin, Omega-3 fatty acids, curcumin, liquorice root, vitamin E, berberine, ginseng, beetroot, and probiotics. These nutraceuticals have shown considerable efficacy in the therapy of various liver diseases. The beneficial effects of nutraceuticals can surely encourage their use in the prevention and therapy of hepatic disorders. However, further randomized controlled studies are required to establish the direct effect of nutraceuticals on liver diseases with histological changes. This chapter provides a detailed insight into various liver disorders, including their pathogenesis and diagnosis. Additionally, it describes various nutraceuticals, along with their sources and the beneficial effects they have on several liver diseases.

Keywords: Hepatitis, Hepatocellular carcinoma, Liver cirrhosis, Liver diseases, Non-alcoholic fatty liver disease, Nutraceuticals.

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INTRODUCTION

Nutraceuticals emerged as a potent bridge between nutrition and pharmaceuticals in the constantly evolving health sector. Nutraceutical refers to edibles or edible-derived consumables that combine the terms nutrition and pharmaceuticals. These include edible consumables that provide health and therapeutic benefits, including the prevention and treatment of illnesses [1]. Nutraceuticals have their roots in ancient civilizations, including China, India, and Greece. These cultures utilized traditional herbal medicines and natural chemicals to enhance overall health and treat health issues.

Nevertheless, nutraceuticals have become increasingly popular in recent years due to breakthroughs in scientific research, consumer demand, and the acknowledgment of the limitations of traditional pharmaceutical methods [2]. One of the significant reasons for the rise of nutraceuticals is the growing understanding of the drawbacks of existing medications. While many of the existing medications were made to address specific ailments or symptoms, most have several negative impacts and numerous potential long-term adverse effects. In contrast, nutraceuticals are regarded as more natural and authentic, offering the possibility of addressing the underlying causes of health problems and providing a more comprehensive approach to well-being [3]. The diverse range of nutraceutical goods includes vitamins, minerals, herbs, probiotics, omega-3 fatty acids, antioxidants, and a wide variety of other bioactive components derived from natural sources. These nutraceuticals are thought to have multiple health benefits. These include reducing the risk of developing chronic diseases, boosting the immune system, enhancing brain function, and promoting overall well-being [4]. A key benefit of nutraceuticals is that they can simultaneously impact multiple aspects of health. For instance, a nutraceutical product containing a combination of antioxidants, substances with anti-inflammatory properties, and immune-boosting nutrients can be used to target various health concerns, including cardiovascular health, cognitive function, and the prevention of different diseases [5].

The regulatory environment regarding nutraceuticals varies between countries and regions, reflecting the ongoing debate and changing perception of their classification and safety. Some countries consider nutraceuticals a separate category, meaning they must be labelled and sold according to particular guidelines. At the same time, in certain jurisdictions, they can be regulated as dietary supplements or even pharmaceutical products, depending on the intended purpose and composition [6]. The global nutraceuticals industry has experienced rapid expansion in recent years, despite facing regulatory challenges. This growth is attributed to the increasing demand for natural and authentic health treatments.

In addition, the current surge is fuelled by the growing incidence of chronic diseases, the ageing population, and the heightened interest in preventive medicine [7]. As the nutraceutical industry expands, scientists and healthcare professionals are working to achieve a more thorough scientific understanding of how these substances function as therapeutic agents. This can be achieved through clinical trials, research into synergies among the various components of nutraceuticals, and the development of new nutraceutical treatments tailored to patient-specific characteristics, such as genetic factors and behavior [8].

Nutraceuticals represent a highly promising and rapidly growing area that unites the expertise of nutrition and medicine. The potential use of natural chemicals presents an opportunity to address various health conditions, maintain individuals in good health, and serve as a valuable addition to traditional medical treatment. Over time, nutraceuticals have become increasingly critical to healthcare as scientific knowledge and legal basis advance [9].

The term "nutraceutical," a fusion of "nutrition" and "pharmaceutical," is deeply rooted in the rich tradition of humanity. Using natural chemicals and food-based products for curative and preventive care has been a long-standing practice in well-developed traditional health systems [10]. In ancient China, herbal treatments and traditional Chinese medicine have been used for thousands of years. Traditional Chinese Medicine (TCM) practitioners understand the connections between diet, lifestyle, and overall health. They utilized various natural chemicals, including herbs and substances derived from both natural and animal sources, for the treatment of various disease conditions [11]. A similar approach was practised by the Ayurvedic school of medicine in ancient India, which also stressed the importance of balanced nutrition and the use of natural products, including spices, herbs, and plant extracts, for maintaining health and preventing and treating diseases. The Ayurvedic approach to wellness is centred on restoring balance and harmony within the body, mind, and spirit [12]. The ancient Greeks also significantly contributed to studying the therapeutic effects of food and natural chemicals. Hippocrates, commonly referred to as the "father of medicine," famously declared, "Let food be thy medicine and medicine be thy food," underlining the underlying connection between nutrition and health [13]. As civilizations progressed, the knowledge of implementing natural cures and food-derived substances strengthened health, including the application of specific preparations such as plant serums or dressings. Over the centuries and millennia, one can observe a cross-flow of expertise and practices acquired and utilized in different cultures and by various schools. This fundamentally reshaped the environment and laid the primary framework that would later give rise to what people would call nutraceuticals nearly 25 centuries later. An earlier mention of the term "nutra" dates back to the late 20th century [14]. As individuals became

CHAPTER 6

Role of Nutraceuticals in the Treatment of Degenerative Muscle Diseases

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Abstract: Degenerative muscle diseases are commonly known as neuromuscular disorders where degeneration and progressive weakness are observed in the muscles due to genetic disorders or mutations. Degenerative muscle diseases are caused by a variety of factors, including autoimmune disorders, genetic mutations, metabolic abnormalities, and environmental influences. Among the genetic factors, Duchenne muscular dystrophy, Becker muscular dystrophy, and spinal muscular atrophy are commonly observed, which mostly affect humans of all age groups. Autoimmune responses cause rare inflammatory diseases, polymyositis and dermatomyositis, causing muscle weakness and a distinctive skin rash. There is currently no approved cure for degenerative muscle diseases. Still, treatments such as a combination of corticosteroids and immunosuppressive drugs, physical therapy, and other supportive approaches are commonly used to help muscle function, strength, manage complicated symptoms, and improve quality of life. However, the clinical trial of several drugs (rimeporide and alendronate for Duchenne muscular dystrophy) has been going on. Nutraceuticals, naturally present in food, are dietary supplements that are thought to provide both nutrition and medicinal benefits. Although nutraceuticals cannot correct the genetic abnormalities underlying muscular dystrophy, they can provide additional benefits like maintenance of bone health, muscle hypertrophy, protection against muscle damage, and reduction in inflammation and oxidative stress in muscle tissues. Some nutraceuticals used in neuromuscular disorders are omega-3 fatty acids, vitamins C, D, and E, amino acid derivatives, *etc*. Nutraceuticals and their supplements can regenerate, repair, and remodel the injured tissue by increasing and improving the growth of muscle tissue. The chapter focuses on the current scenario of the different types of degenerative muscle diseases and the role of nutrients in these types of diseases.

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Keywords: Degenerative muscle diseases, Duchenne muscular dystrophy, Dermatomyositis, Mitochondrial myopathies, Nutraceuticals, Polymyositis.

INTRODUCTION

The term “degeneration” refers to transitioning from a higher to a lower form and declining moral, physical, or mental attributes [1]. In the eighteenth century, the term “degeneration” was coined to describe the diversity within the human species. A nineteenth-century theory concerning human degeneration began to be connected to progressively horrific incidents both before and during World War II. The term “degeneration,” used to describe the deterioration of cells and structures, fell out of use in genetics and psychiatry after World War II [1, 2]. Recently, degenerative muscle diseases have garnered increasing attention from researchers due to their severity and the challenges involved in finding effective treatments. Besides neurodegenerative diseases, muscle degeneration is widely affecting children and adults [3]. A group of conditions affecting the genetics of the skeletal muscle system came to be known as degenerative muscle diseases [4]. One of the primary causes of degenerative muscle disease is a mutation. Mutations causing substitutions or rearrangements in the mt-DNA can cause inherited disorders affecting the skeletal muscle, heart, brain, kidneys, endocrine system, and hematological functions [3, 4]. Furthermore, several genetic abnormalities, including cycles of muscle necrosis, regeneration, increasing muscle weakness, and degradation, are believed to play a significant role in the pathophysiology of degenerative muscle disease [5]. Though there are currently few treatments available for degenerative muscle diseases, numerous trials have been carried out to date to prevent and block the development of these degenerative muscular diseases. To avoid this degeneration of muscles, consuming food components, plant extracts, and phytochemicals has recently gained interest as a potential therapy option [6]. The entire range of foods with health-promoting and disease-preventing qualities enhanced with certain nutrients, such as vitamins, minerals, herbs, phytochemicals, and probiotics, which are known as functional foods and nutraceuticals. It is possible to obtain nutraceuticals from microbial, animal, and plant sources, including aquatic environments [7]. Researchers have examined the impact of nutraceuticals on muscle degeneration by tracking the molecular processes related to protein turnover, mitochondrial function, and myogenesis [6, 8]. This chapter explores various types of degenerative muscle diseases, their progression, available treatments, and the effects of nutraceuticals on muscle degeneration, providing insight into the underlying molecular pathways.

PATHOPHYSIOLOGY OF DEGENERATIVE MUSCLE DISEASES

Configuration of Skeletal Muscle and its Function

Myofibers are the fundamental building blocks of voluntary skeletal muscle. Long, multinucleate cells produce myofibers. Basically, myofibers form when singly nucleated myoblasts fuse together to create myofibers during development and regeneration (Fig. **1**). The endomysial sheath, a connective tissue, surrounds individual myofibers. In contrast, the epimysial connective tissue encases groups of myofibers [3]. At myotendinous junctions, the ends of myofibers produce a specialized attachment for bone insertion that is very force-resistant. Sarcomere chains that run parallel to the length of each myofiber are seen in the highly organized cytoplasm of each myofiber. Each sarcomere has boundaries defined by electron-dense Z bands, and each sarcomere is made up of thick and thin filaments that consist of myosin and actin, respectively [9]. The basement membrane, originally called the extracellular matrix (ECM) layer, envelops myofibers and comprises an external reticular lamina and an internal basal lamina [10]. Moreover, the sarcolemma, which is a specialised plasma membrane, also surrounds myofibers and converts impulses from the motor neurons and other external stimuli into muscle fibres. Together, the sarcolemma and basal lamina form a close alliance that creates a safe niche for satellite cells, which are muscle-regenerating cells. Primarily, these satellite cells are referred to as unipotent adult stem cells, which activate to initiate differentiation and proliferation in response to significant muscle injury [9]. This process produces myoblasts, which can fuse with leftover myofibers or one another to reconstruct the muscle. Furthermore, these satellite cells possess a strong self-renewal capability, which guarantees their survival within the muscle and maintains the muscle's ability to heal after damage [3, 5].

Process of Muscle Degeneration

Typically, muscle damage is characterized by myofiber necrosis and subsequent regeneration. In this process, only a fragment of a single myofiber may be involved. Necrosis is linked to membrane disruption and cytoplasmic protein leakage, including creatine kinase (CK) and lactate dehydrogenase, which can function as serum indicators of muscle injury. Fig. (**2**) shows the three different phases of muscle from degeneration or destruction, repair, and remodelling. Sometimes, overlap is observed in these phases. Myofiber necrosis is initiated during the degeneration or destruction phase, where the myofiber sarcolemma is disrupted and damaged due to an influx of extracellular calcium, an increase in myofiber permeability, and the activation of calcium-dependent proteases. The first inflammatory cell, neutrophils, is recruited into the damaged muscle within

CHAPTER 7

Role of Nutraceuticals in the Treatment of Degenerative Osteoporosis or Disc Disease

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Abstract: Degenerative disc disease (DDD) is a common condition affecting the intervertebral disc and vertebral bodies, particularly in the lumbar spine, and it is often diagnosed in early to middle age. Osteoblasts and osteoclasts play a crucial role in bone remodeling, which preserves metabolic balance and skeletal integrity. After the old or injured bone has been reabsorbed, new bone material is deposited. Osteocytes regulate bone formation, collagen breakdown, hormonal signals, mechanical strain, and remodeling site and timing. A reduction in bone density may result from imbalances. Commonly, it is associated with various factors, such as genetics, obesity, diabetes, smoking, physical strain, discogenic pain, and gene polymorphisms. Modern medical technologies can help identify encouraging variables to prevent DDD. However, many people do not receive early diagnosis and treatment. Hence, understanding the underlying cellular mechanisms of the inflammatory response can significantly enhance the prevention and treatment of DDD. Additionally, lifestyle modifications like maintaining a healthy diet, exercising regularly, quitting smoking and alcohol, and monitoring DDD-promoting variables can help reduce its incidence. As a consequence of their anti-inflammatory and antioxidant qualities, phytoconstituents produced from plants have drawn interest for their possible therapeutic function in DDD. The significance and utilization of nutraceuticals, pharmaceuticals, and supplements to enhance bone health in DDD patients are highlighted in this chapter.

Keywords: Anulus fibrosus, Degenerative disc disease, Flavonoids, Interleukins (IL), MAPK pathways, Nutraceuticals, Polyphenols, Supplements, Tumor necrosis factor (TNF–α).

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INTRODUCTION

Degenerative Disc Disease

Sciatica, or sciatic nerve pain, is a neurological discomfort that originates in the back and radiates down the leg and hip, as described for the first time by Domenico Cotugno in 1764 [1]. Schmorl and Andrea further addressed herniations and degenerations and created the contemporary concept of the intervertebral disc [2, 3]. In 1933, Mixter and Barr eventually established the disc's significance in the pathophysiology of lumbosciatic pain and nerve dysfunction. Regardless of gender, degenerative disc disease (DDD) is a frequent problem in early to middle age, and it gets worse with age. Degenerative diseases of the intervertebral disc and accompanying vertebral bodies are more common in the lumbar spine [4]. Degeneration and discogenic pain are connected to several disorders. Largely, DDD is caused by physical and biomechanical stresses on the lumbar spine.

Role of Intervertebral Disc Components

The intervertebral disc is an inflatable padding that serves as a hinge, ligament, and shock absorber between the vertebrae in the spine. When functioning decorously, it transfers force to the lower vertebrae, acting as a closed hydraulic system, where the “vicious circle” starts to break [5, 6].

The anulus fibrosus (AF) and nucleus pulposus (NP) are the two primary components of the intervertebral disc. The constituents include water, type II collagen, chondrocyte-like cells, and proteoglycan. NP, which is the innermost portion, can withstand severe pressure. AF, due to its increased fibrousness and collagen content, serves as the capsule of the nucleus. As they are avascular, the nucleus and anulus rely on molecular diffusion from blood vessels to get oxygen and nutrients and remove metabolic waste [7, 8].

As degeneration can result from a reduction in the nutritional supply, this idea is essential for understanding the architecture and pathophysiology of the disc. Chondrocytes produce matrix metalloproteinases (MMP) to ensure matrix turnover. Matrix production is aided by growth factors, including insulin-like growth factor, transforming growth factor, and basic fibroblast growth factor. Matrix degradation is controlled by metalloproteinase tissue inhibitors. To maintain the equilibrium between production and breakdown, as well as to reduce matrix synthesis and increase MMP activity, macrophages utilize cytokines, including interferons (IFNs), tumor necrosis factor-α (TNF-α), and interleukin-1 (IL-1) [9]. By stimulating nitric oxide production and inducible nitric oxide synthetase, which breaks down matrix components and prevents matrix formation,

TNF-α and IL-1 enhance inflammation [10, 11]. Superoxide, which is secreted by macrophages, has the ability to break down proteoglycans and hyaluronic acid, resulting in deaggregation and halting chondrocyte growth [11]. However, when the pH falls, matrix synthesis progesses more slowly [12].

Factors Influencing Degenerative Disc Diseases

Degenerative disc disease (DDD) is a common aging condition, with only 5-10% experiencing chronic back pain. Age-related trends show a low prevalence under 30 years old, increasing significantly between 30 to 50 years old, with 30-50% showing some disc degeneration on imaging. In people aged 50 to 70 years, 70-90% show evidence, and in people over 70 years, nearly 100% show some signs on imaging [13 - 15].

DDD and its contributing factors in normal aging-related degeneration of the lumbar intervertebral disc occur before degenerative conditions of the lumbar disc, such as lumbar disc herniation and lumbar spinal canal stenosis. Heredity is a significant risk factor for DDD in several investigations. Some people may acquire DDD earlier than others if they have particular gene polymorphisms. A study reports on genetic factors that contribute to the degenerative process of the intervertebral disc, with certain polymorphisms defining its integrity. Mutations in genes coding for matrix molecules alter matrix morphology, affecting disc function and biochemical processes. Degradation enzymes and inflammatory cytokines are influenced by these polymorphisms [16 - 21]. A cohort study in South Africa by Megan Collins and Brendon Pearce reveals such a genetic polymorphism associated with mitochondrial dysfunction and disc degeneration. However, more study on population-specific variations and personalized therapy is needed [22]. Moreover, acquired factors like obesity, diabetes, smoking, physical loading, and bone mineral density have also been associated with DDD [23].

Advanced technology in medical science may assist in the identification of promoting factors as preventive measures in DDD. For example, a study report on lumbosacral arteries, atherosclerosis, and obstruction of the abdominal aorta demonstrates how inadequate blood flow and nourishment to the lumbar intervertebral disc may be a factor in lumbar degenerative disorders. Suspected risk factors for DDD include cardiovascular conditions like diabetes, obesity, and smoking.

DDD prevalence varies globally due to lifestyle, healthcare access, and demographics. Low- and middle-income countries have four times more cases than high-income countries. Nutritional interventions that will assist and ensure food security can be guided by monitoring the diversity and quality of diets. The

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