

Review on therapeutic potential of nutraceuticals in human health

Moges Demes

Department of Medical Biotechnology, Institute of Biotechnology, University of Gondar
E-mail: demesmoges01@gmail.com

Abstract

Nutraceutical is combining the word "nutrition" and "pharmaceutical." Nutraceuticals are substances that are either foods or parts of foods that have a significant health benefit. Nutraceuticals and nutritional therapy (i.e., nutraceuticals as a complementary therapy that is not only a source of nutrients and energy but may also give therapeutic advantages) have gained in popularity in the prevention and treatment of diseases. Nutraceuticals are produced/developed through both modern and traditional biotechnology methods. Traditional/conventional nutraceuticals contain chemical ingredients (nutrients, herbs, and phytochemicals), probiotic microorganisms, and nutraceutical enzymes, and non-traditional nutraceuticals include (recombinant and fortified nutraceuticals), chemical nature, and mode of action. The nutraceutical revolution entered into a new era of promised medical and health benefits, with the food industry adopting a research-oriented approach similar to that of the pharmaceutical industry. They have played a significant role in the treatment of disorders like obesity, cancer, diabetes, osteoporosis, osteoarthritis, Alzheimer's, cardiovascular, Parkinson's, and COVID 19, etc

Keywords: Health, Nutraceuticals, Pharmaceutical, Therapeutics.

INTRODUCTION

The idea of Nutraceuticals went back 3000 years ago. Hippocrates (460-377 B.C) stated "let food be the medicine and medicine be the food" to predict the link between appropriate foods for health and their therapeutic advantages (Bagchi, 2016). Isolated nutrients, dietary supplements, genetically altered foods, herbal items, and processed foods are the most common nutraceutical items. Modified/unmodified whole foods, unaccompanied plant extracts in a mixture, partially purified, purified, or a combination of diverse phytochemicals are all examples of nutraceuticals (Muredzi, 2013; Siddiqui and Moghadasian, 2020).

Nutraceuticals are natural medically beneficial foods or bioactive phytochemicals that are health-promoting, illness-defeating, rehabilitative, functional foods and beverages that contain specific components (vitamins, lipids, proteins, carbohydrates, minerals, etc.) that have healthful profits (Sharma et al., 2016). In 1989, the term "nutraceutical" was coined by combining the words "nutrition/nutrients" a nourishing dietary component and "pharmaceutical" a medicine or a chemical used as a drug and implying use for illness prevention and/or therapy (Pastor et al., 2021).

Human health, the environment, industry, and the economy are all impacted by eating habits. Obesity, osteoporosis, cancer, and diabetes are just a few examples of the diseases that have emerged as a result of the transformation from developing to developed society. These diseases can occur at any age and are linked to eating habits and preferences. Despite developed countries facing issues such as aging populations, high-energy foods, and unbalanced diets, underdeveloped countries continue to struggle with malnutrition and a lack of healthy foods (Ditu et al., 2018).

The valid classification of a nutraceutical under European Union law is decided, in general, based on its recognized effects on the body. The substance qualifies as a food component if it mainly serves to preserve regular tissues and organs. They will be classified as a medical substance if they have a modifying function on at least one of the body's physiological systems (Swarupananda and Sohini, 2016).

The difference between nutraceuticals and functional food is that the first is made up of bioactive elements derived from natural sources and obtained from various food grids, whereas the latter is defined as any new or processed food that has a healthy impact and prevents diseases in addition

to having a healthy capacity (Chávarri, 2020). Therefore, the objectives of this review are to assess key facts concerning nutraceuticals, their classification, and their possible potential roles in the prevention and treatment of human diseases.

BIOTECHNOLOGY AND NUTRACEUTICALS

Biotechnology and genetic engineering have aided in the development of recombinant nutraceuticals, which are used in the making of resource foods (yogurt and cheese, or the extraction of bioactive components) using enzymatic or fermentation technologies (Srivastava, 2018).

Modern biotechnology, also known as nutraceutical biotechnology, has the promise of generating foods that perform tasks other than those provided by the essential nutrients they contain. Consumers interested in the health advantages of functional foods for the prevention of illness and chronic conditions have been more interested in these functional foods, also known as nutraceuticals (Ghosh, 2012).

Biotechnology is used in the manufacture of desired food components. These include traditional fermented foods, as well as providing vitamins, polysaccharides, pigments, glycolipids, enzymes, and improving the safety and functionality of a range of common foodstuffs (Maryam et al., 2017).

Traditional genetic development ("traditional biotechnology") techniques such as classical mutagenesis and conjugation, as well as biotechnological processes, are vital for the improvement of microbial cultures used in food processing (Sundarraaj et al., 2018). Grading biological responses is a barrier in the manufacture of nutraceuticals and the development of biotechnology and/or genetically modified microorganisms, both of which may need to be addressed (Asif and Mohd, 2019).

CLASSIFICATION OF NUTRACEUTICALS

Classification based on food sources

Nutraceuticals are classified as traditional/conventional or no traditional nutraceuticals based on natural food sources (Ruchi, 2017).

Traditional nutraceuticals: Traditional nutraceuticals are manufactured food that has not been altered in any way, and its components are all natural and have the potential to provide health advantages (Srivastava, 2018). Several natural ingredients, such as lycopene in tomatoes, omega-3 fatty acids in salmon, and saponins in soy, are found in a variety of fruits, vegetables, grains, fish, dairy, and meat diets. Tomatoes and salmon are two foods that researchers have shown to provide health advantages beyond basic nutrition (lycopene and omega-3 fatty acids, correspondingly) (Chintale et al., 2013; Prabu et al., 2012).

These classes are usually derived completely from nature,

with no modifications to the original form. Various elements, such as lycopene found in tomatoes, omega-3 fatty acids found in salmon, and saponins found in soy, are available and ingested for a variety of health benefits (Chanda et al., 2019).

Chemical components, probiotic microbes, and nutraceutical enzymes are all examples of classic nutraceuticals.

Chemical constituents include the following classifications:

Nutrients: Strokes, cataracts, osteoporosis, diabetes, heart disease, and cancer can all be treated with nutrients. Minerals derived from plant, animal, and dairy diets are beneficial in the treatment of osteoporosis and anemia. Omega 3-PUFAs, found in flaxseed and salmon, are potent regulators of the inflammatory process, brain function preservation, and cholesterol accumulation reduction.

Herbals: Herbs, often known as botanical foods, are as old as human civilization and provide a wealth of remedies to treat both acute and chronic illnesses. Several nutraceuticals are found in medicinal herbs of important components, providing a whole storage facility of medicine to treat severe and persistent ailments (Khan et al., 2016; Prabu et al., 2012). Some examples are: Parsley (*Petroselinum crispum*) is a diuretic, carminative, and antipyretic herb that includes flavonoids (apiol and psoralen). Willow bark (*Salix nigra*) contains salicin, an anti-inflammatory, analgesic, antipyretic, astringent, and antiarthritic active component. Lavender (*Lavendula Angustifolia*) contains tannins, which aids in the treatment of depression and anxiety (Borkar et al., 2015).

Phytochemicals: Non-nutritive plant compounds with defensive or disease-protective capabilities are known as phytochemicals. They are nonessential nutrients that plants make primarily to protect themselves. Phytochemicals obtained from plants are used in the diet and give health advantages such as Substrate for biochemical reactions, enzymatic reaction cofactors, enzyme inhibitors, enzyme intestinal absorbents that bind to and remove unwanted constituents and enhance the absorption and/or stability of important nutrients by scavenging reactive or harmful molecules. Phytonutrients/phytochemicals are found in a wide range of foods, including whole grains, beans, fruits, vegetables, and herbs. These phytochemicals, alone or in combination, have enormous therapeutic promise in the treatment of a variety of illnesses (Prakash et al., 2012; Patil et al., 2016).

Glucose and insulin regulation are important characteristics of phytochemicals, and there is a promising reconsideration of traditional diabetes treatment. Mushrooms' nourishing, tonic, and restorative powers have long been recognized, as have their therapeutic capabilities such as anticancer, antiviral, and hypolipidemic properties. Lentinan boosts the immune system's ability to fight infections caused by bacteria, fungi, parasites, and viruses, including the AIDS virus (Rajam et al., 2019).

Probiotic microorganisms

Probiotics are live bacteria that are given to the host in sufficient quantity to provide a health benefit. They exist in powder, liquid, gel, paste, or granule form, as well as capsule form, and are commonly used to treat gastrointestinal (GI) disorders such as lactose intolerance, acute diarrhea, and antibiotic-related gastrointestinal side effects (Jain, 2020).

Lactobacillus and *Bifidobacterium* species are the most commonly utilized probiotics, however the yeast *S. cerevisiae*, as well as several *E. coli* and *Bacillus* species are also used (Daneshniya et al., 2020). Lactic acid bacteria, such as *Lactobacillus* species, which have been used for thousands of years to preserve food through fermentation, can serve a dual purpose by acting as agents for food fermentation and having the potential to impact health profits (Guarner et al., 2011).

Probiotic treatment has a variety of important effects, including improving intestinal wellbeing through microbiota guidance, relaxing and improving the immune system, delivering and expanding the bioavailability of supplements, reducing the side effects of lactose influence, and decreasing the risk of various illnesses (Nagpal et al., 2012).

Nutraceutical enzymes

Enzymes are essential components of life; without them, our bodies would not function correctly. Anyone suffering from digestive issues such as hypoglycemia, blood sugar abnormalities, or obesity might alleviate their symptoms by adding enzyme supplements to their diet obtained from microbial, plant, and animal sources (Singh and Sinha 2012).

Non-traditional nutraceuticals: Non-traditional nutraceuticals are obtained from agricultural breeding by adding nutrients and/or ingredients, such as calcium-fortified orange juice, vitamin- and mineral-fortified cereals, and folic acid-fortified flour. Agricultural experts have successfully developed strategies to increase a crop's nutritional content (Singh and Sinha 2012). They are further subdivided into recombinant and fortified nutraceuticals (Singh et al., 2018).

Recombinant nutraceuticals: Biotechnology techniques have been successfully employed in a fermentation process to extract enzymes suited for providing critical nutrients at an optimal level in a variety of foods such as cheese and bread (Chanda et al., 2019). Biotechnology assists in the formation of energy-delivering foods such as bread, wine, fermented starch, yogurt, cheese, vinegar, and others. Biotechnology allows for the production of probiotics and the extraction of bioactive components using enzyme/fermentation technologies, as well as genetic engineering (Singh and Sinha 2012).

Fortified nutraceuticals: Fortified nutraceuticals are made by fortifying dietary components and then adding micronutrients (trace elements or vitamins) to the final product (Srivastava, 2018). The process of adding crucial

minor components and nutrients to food to improve the efficiency and nutritional value of the food is known as fortification (Ruchi et al., 2017). In children with diarrhea, respiratory infections, and serious illnesses, prebiotics, and probiotics, preserved milk containing *Bifidobacterium lactis* HN019 are ingested (Sazawal et al., 2010). Persistent bananas could be developed as effective foods to combat iron deficiency caused by malnutrition (Kumar et al., 2011) (Figure 1).

Classification by chemical nature

As shown in Figure 2, nutraceuticals are classified according to their primary and secondary metabolite sources, which include isoprenoid derivatives, phenolic substances, amino acid-based substances, carbohydrates and derivatives, fatty acids and structural lipids, and minerals (Chanda et al., 2019).

Classification by mode of action

To distinguish and evaluate their function and roles, nutraceuticals have been divided into antibacterial, antifungal, antioxidant, anti-inflammatory, and antiobesity groups based on therapeutic properties (Makkar et al., 2020) (Figure 3).

THERAPEUTIC POTENTIAL OF NUTRACEUTICALS IN HUMAN HEALTH

Nutraceuticals in Cardiovascular Diseases (CVD): Heart disorders, such as hypertension (high blood pressure), coronary heart disease (heart attack), and various forms of cerebrovascular disease (stroke), are all associated with cardiovascular diseases (Arora, 2019). Overconsumption of calorie-dense, nutrient-deficient, deeply processed, and easily absorbable meals can result in systemic inflammation, decreased insulin sensitivity, including several metabolic abnormalities, including obesity, hypertension, dyslipidemia, and glucose intolerance (Taiwo et al., 2017).

Polyphenols present in grape and grape derivatives, cocoa, and tea have been studied for their potential to reduce cardiovascular disease. By altering cellular metabolism, vitamin D, coenzyme Q10, folic acid, omega-3 fatty acids, and polyphenols help to prevent artery disease. Flavonoids found in onion, grape, apples, and cherries inhibit the Angiotensin Converting Enzyme (ACE), lowering blood pressure and reducing the risk of coronary artery disease and myocardial infarction (Swarupananda and Sohini, 2019; Taiwo et al., 2017).

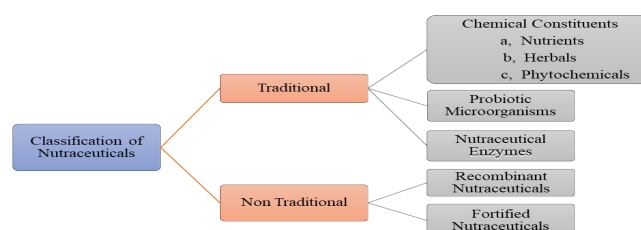


Figure 1. Classification of nutraceuticals based on their sources.

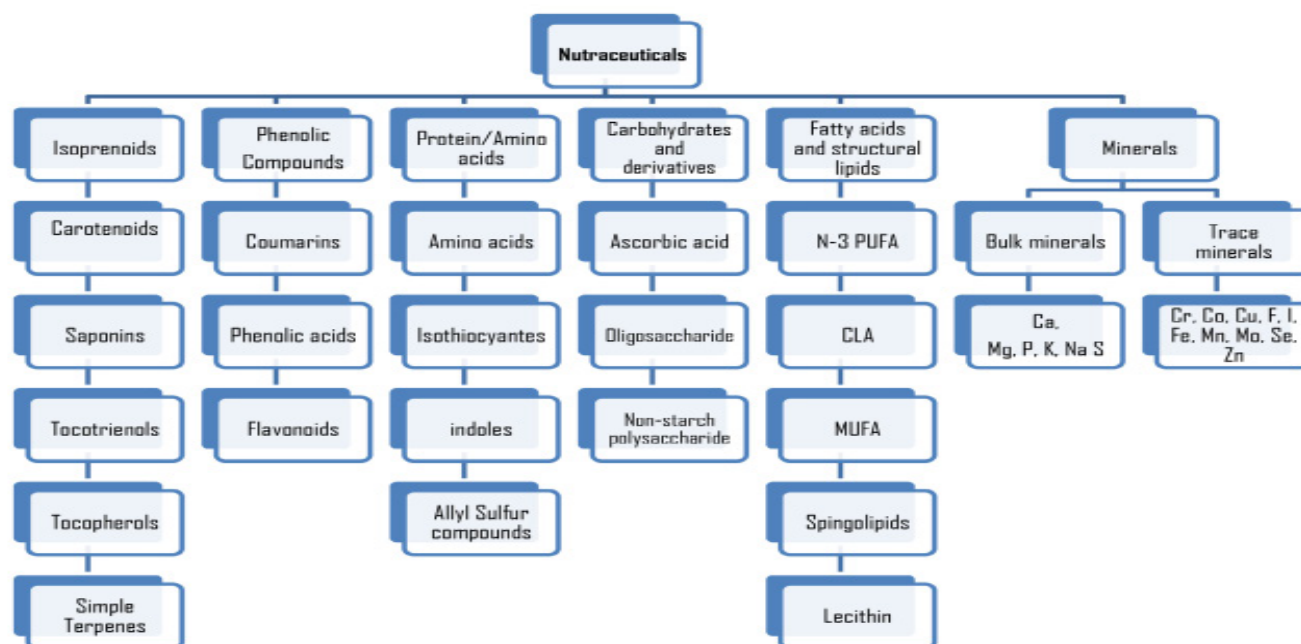


Figure 2. classification of nutraceuticals based on chemical nature.

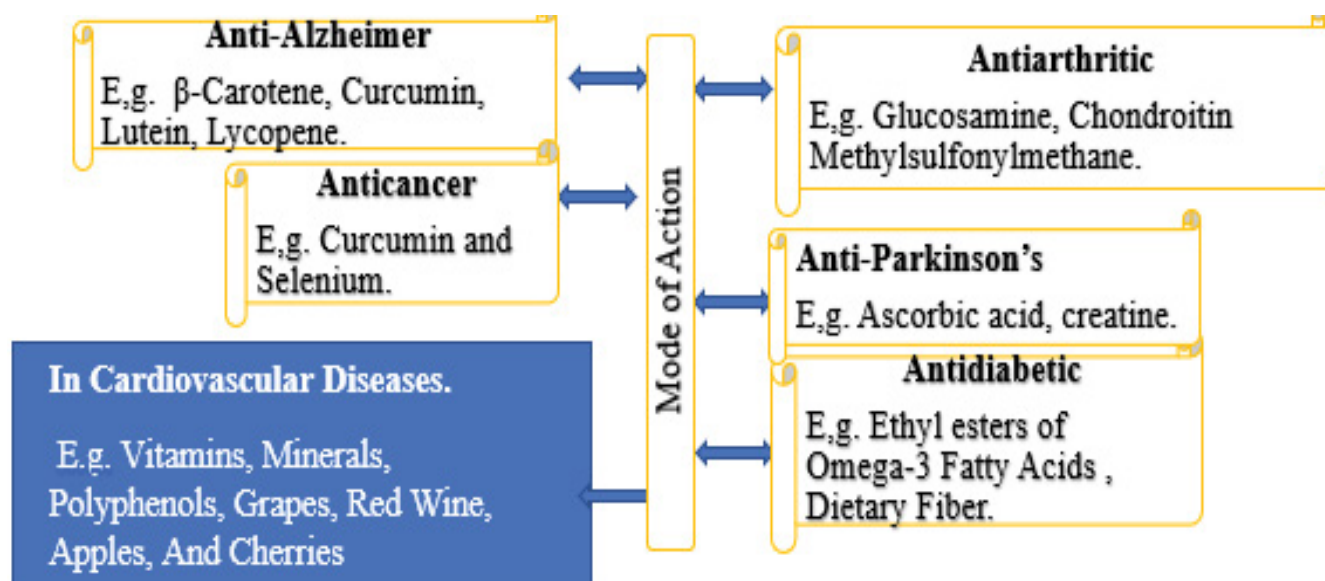


Figure 3. Classification of nutraceuticals based on their mode of action

Flavonoids prevent platelet stickiness and accumulation (by opposing the "suicide" enzyme cyclooxygenase that breaks down prostaglandins), and they also keep the vascular system and support small capillaries that carry oxygen and necessary nutrients to the entire cell (Kumar et al., 2018).

Nutraceuticals in cancer: Cancer is defined as abnormal cell division in any part of the body, and malignant cells can influence our normal cells. Cancer is caused by a combination of complicated elements that develop in a stepwise manner, eventually leading to the uncontrolled spread and proliferation of malignant cells throughout the body, a process known as metastasis. It is one of the most important global health firms, with continuing increases

in revenue and mortality (Golla, 2018; Ghani et al., 2019; Cencic and Chingwaru, 2010).

Oxidative stress and redox waving, in addition to environmental variables, are important in the origin and spread of cancer. Cancer cells' receptivity to therapeutic interventions is also harmed by reactive oxygens (Roy et al., 2019). Chronic inflammation is linked to a higher risk of cancer. Chronic inflammation has also been linked to immunological suppression, which is a cancer risk factor. At the molecular level, free radicals and aldehydes produced by chronic inflammation can promote gene alterations and posttranslational modifications of cancer-related proteins (Gautam et al., 2013).

Natural products or antioxidants (e.g., microbial and plant secondary metabolites) are employed as adjuvants to chemotherapy medications to increase their effectiveness, rather than other pharmaceutical drugs. Ginger, garlic, flaxseed, cabbage, soybeans, fenugreek, green tea, and umbellifers vegetables are examples of foods and herbs with high anticancer activity (Olaiya et al., 2016). Nutraceuticals, especially phytochemicals, play a role in cancer recovery. To date, all widely used cancer medications have come from natural sources. Cancer patients should eat foods that have a low carbohydrate content and a moderate amount of protein, dietary fiber, and fat (Roy et al., 2019).

Nutraceuticals in diabetes mellitus: Diabetes mellitus is a chronic metabolic illness in which the body's ability to utilize carbohydrates is harmed due to an absolute or relative lack of the hormone insulin produced by the β -islets of Langerhans in the pancreas (Khan et al., 2016). Diabetes mellitus is characterized by abnormally high levels of blood glucose, either due to inadequate insulin production or its ineffectiveness (Golla, 2018).

Nutraceuticals and a wide range of bioactive components, such as phenolic compounds, sulfur compounds, herbs, and natural antioxidants, are all involved in glucose metabolism and may help to prevent the development of diabetes and other complications. Some dietary supplements, such as L-carnitine-lipoic acid, omega-3 fatty acids, berberine, chromium, soy, and phytoestrogens, are currently available in markets and are widely prescribed by clinicians (Roy et al., 2019).

Nutraceuticals in obesity: Obesity develops as a result of excessive consumption of high-fat and energy-dense foods, which leads to the formation of fatty plaques on the inside surface of arteries, which restrict blood flow to various sections of the body. Angina pectoris, heart attack, cardiac arrest, transient ischemic attacks, and stroke can all be caused by a lack of blood supply in certain organs (Rajasekaran, 2017).

It is characterized by an excess of body fat; however, the threshold value that defines what amount of body fat is "unhealthy" is unclear, and the ability to reliably degree body fat mass necessitates specialized equipment that is not readily available in most clinical settings. Following that, body mass index (BMI) records are used to define people as "normal weight" (BMI 18.5-24.9 kg/m²), "overweight" (BMI 25-29.9 kg/m²), or "obesity" (BMI 30 kg/m²), which stratifies health risk based on the link between weight and height (Berthoud and Klein 2017).

Fortified margarine (Plant sterol and stanol esters), oolong tea (catechins), green tea (Organosulfur compounds), garlic (Organosulfur compounds), Psyllium (Soluble fiber), and soybean (protein) are all beneficial in the treatment and prevention of obesity. These functional foods remove excess fat from the body by a variety of processes, including inhibiting pancreatic lipase, increasing thermogenesis,

limiting adipocyte differentiation, improving lipid metabolism, and decreasing hunger (Emmanuel et al., 2020).

Nutraceuticals in Alzheimer's disease: Alzheimer's disease is the most common form of dementia and a degenerative neurological illness. This sickness has no cure and will ultimately kill everyone (Sachdeva et al., 2020). Necrobiosis in Alzheimer's disease results from the mass of beta-amyloid protein fragments forming solid plaques that affect the ability of acetylcholine to affect synaptic communication and initiate inflammatory progression and variations in the chemical nature of the specific proteins and also leads to necrobiosis in Alzheimer's disease wherein neuron's microtubules couples with other tubules creating neurofibrillary tangles that cause tubule (Josmi et al., 2019; Khan et al., 2016; Makkar et al., 2020).

β -carotene, curcumin, lutein, lycopene, and turmeric have antidisease Alzheimer's properties by neutralizing the negative effects of oxidative stress, mitochondrial malfunction, and neuronal degeneration (Verma and Mishra, 2016).

Nutraceuticals in osteoporosis: Low bone mass, thinning bone tissue, and disruption of bone microarchitecture are all symptoms of osteoporosis. Many factors that influence low bone mass are divided into two categories: those that cannot be changed and those that can. Gender, age, body size, and race are unchangeable, whereas hormonal status, lifestyle factors such as food, smoking, and alcohol consumption patterns, and physical activity levels can be changed (Rajput et al., 2018).

Nutraceuticals such as herbs, minerals, and dairy products are increasingly being utilized to combat this condition. Calcirol D-3 is a popularly marketed nutraceutical product that contains calcium and vitamins to aid in the treatment of osteoporosis. Probiotics are effective in alleviating osteoporosis symptoms and lowering osteoporosis risk (Arora and Singh, 2019).

Nutraceuticals in osteoarthritis: Osteoarthritis is characterized by articular cartilage loss, synovial membrane inflammation, and subchondral bone resorption. It is the most well-known form of arthritis, afflicting millions of individuals all over the world. When the protecting cartilage on the extremities of the bones breaks down over time, it causes this condition. It can cause pain in any joint in the body. It most usually affects the joints of the hands, knees, hips, and spine. Although there is no cure for osteoarthritis, there are therapies that can help with pain relief and joint mobility. (Ganapathy and Bhunia 2016; Akhtar and Haqqi 2012).

Chondroitin Sulfate (CS) and Glucosamine (GLN), also known as 2-amino-2-deoxy-d-glucose (C₆H₁₃NO₅), are widely utilized to alleviate the symptoms of osteoarthritis. MSM (Methyl Sulfonyl Methane) is a synergistic combination

of glucosamine and chondroitin that is used to treat osteoarthritis and joint problems (Gautam et al., 2013). Glucosamine (GLN) is an amino monosaccharide that is found in the exoskeletons of crustaceans and mushrooms. It is a component of glycosaminoglycan (GAG) chains. GAG is made up of two sugars that alternate: glucuronic acid and acetyl-d-galactosamine sulfate (Adamo et al., 2020).

Nutraceuticals in Parkinson's disease: It is a neurodegenerative disease characterized by a shortage of dopaminergic neurons in the substantia nigra, resulting in striatal dopamine exhaustion (Mythri et al., 2015). Numerous nutraceuticals have been proven to provide neuroprotection in animal settings and may be useful as alternatives to synthetic pharmacological molecules such as L-Dopa, which has a long list of negative side effects. Iron chelation, modulation of cell signaling pathways, Reactive Oxygen Species (ROS)/free radical scavenging, anti-inflammation, anti-apoptosis, and mitochondrial homeostasis are some of the mechanisms by which they work, although several nutraceuticals essentially work through a slew of unthinking pathways rather than a single mechanism (Hang et al., 2016). Plant polyphenols, stilbenes, soybeans, and other phytoestrogens, as well as vitamins C, D, E, coenzyme Q10, and unsaturated fatty acids, have been shown to protect against Parkinson's disease progression (Dutta et al., 2018).

Nutraceuticals in COVID-19: SARS-CoV-2 has affected global health and economic well-being since its emergence in early 2020. The virus infection was initially reported in Wuhan by the World Health Organization's (WHO) regional office in China on December 31, 2019, and the infection was declared an epidemic on March 11, 2020 (Savant et al., 2021). SARS-CoV-2, also known as COVID-19, is a coronavirus with high pathogenicity. It is a single-stranded positive-sense RNA virus, which means its RNA can be immediately translated into viral proteins in infected cells. Fever, gastrointestinal problems, and memory loss are just a few of the symptoms that SARS-CoV-2 infection can cause (Akula et al., 2020).

The current COVID-19 virus has increased the demand for immune-boosting foods, vitamins, and nutraceuticals. Food bioactive and nutraceuticals have been suggested as an alternative therapy for COVID-19 disease based on their anti-inflammatory properties as well as their capacity to inhibit virus activity (e.g., SARS-CoV, MERS-CoV, and SARS-CoV-2) by disrupting their protein envelopes (Pandhi and Gupta, 2021).

functional foods containing various functional components such as vitamins (A, B, C, and D), minerals (selenium, zinc, and iron), and polyphenolic compounds (quercetin, resveratrol, catechins, and anthocyanins) can act as natural therapeutic agents against SARS-CoV-2 or preventive therapy for COVID-19 patients, in addition to enhancing the body's immunity to fight COVID-19 infection (Hamid et al., 2021).

CONCLUSION AND FUTURE PERSPECTIVE

There is a long history of nutraceutical use in the treatment of illness, and these chemicals have a position in current and future medicine. However, additional research is needed to ensure the items' safety, enhanced quality, purity, efficiency, health-promoting, and disease-curing effects, as well as a greater awareness of the various methods that go into item development. When taking supplements, extreme caution is very essential. As a result, there is a need for basic discussion and studies on the benefits, suggested, daily consumption, and potential side effects of supplement use. After that, we can replace the ancient proverb "an apple day keeps the doctor away" with "nutraceutical day may keep the doctor away." Nutraceuticals will be promoted in the future to promote healthy health. When ingested as part of a well-balanced and healthy diet, it has been demonstrated to be beneficial for its intended purpose. Anticipation and treatment with nutraceuticals are now considered by public health authorities to be effective functional foods for maintaining health and combating nutritionally induced acute and chronic diseases, as well as for improving quality of life. Because nutraceuticals play such an important role in the promotion and care of human health and disease prevention, health experts, nutritionists, biotechnologists, and industrialists should collaborate strategically to develop regulations that will ensure high-quality health care.

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