REVIEW article

Nutraceuticals: Food-based therapeutics and health benefits

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Abstract: In the modern world, individuals are worried about their health because lifestyles have changed dramatically due to longer workdays and a lot of psychological pressures, which have increased the prevalence of many serious illnesses. Moreover, they disapprove of the costly, high-tech method of disease management and treatment. People have increasingly been interested in using phytonutrients and nutraceuticals for a range of medical applications since a few years ago. In addition to treating or preventing hypertension, high cholesterol, excessive blood sugar, degeneration, cataracts, menopausal symptoms, insomnia, poor memory and concentration, digestive issues, osteoporosis, arthritis, macular degeneration, and constipation, nutraceutical products also reduce the risk of cancer, heart disease, and other related conditions. Micronized food items and other nutraceutical supplements with enhanced health advantages are also produced thanks to nanotechnology. The most recent important discoveries (clinical research) on nutraceuticals that demonstrate their therapeutic effect on a range of diseases have been included in this review article.

Introduction

A new class of natural products named nutraceuticals is upending the link between diet and medicine. The phrase nutraceutical was coined by Stephen De, who combined the words pharmaceutical with nutrition. Felice created the Groundwork for Innovation in Medicine in Cranford, New Jersey, and served as its president in 1989. A food (or part of a diet) that gives pharmacological or well-being uses, together with the suppression and therapy of a disease, is what De Felice defines as a nutraceutical. However, according to Health Canada, a nutraceutical is a product made from food ingredients but synthesized and sold as tablets, capsules, powder, or in another medicinal form that does not typically correspond with foods [1]. Among the many advantages that nutraceuticals have offered are their encouraging outcomes in the management and prevention of complex illnesses [2-5]. To avoid their unchecked usage and adverse effects, nutraceuticals must be administered and prescribed, and their use should be tightly managed [5, 6].

Several researchers have investigated drug compound-based nutraceuticals in an effort to increase both their bioavailability and efficacy. Numerous statins have been used to prevent cardiovascular problems, including in pregnant women, due to their safety and effectiveness. A good therapeutic alternative for preventing diabetes mellitus and hypertensive problems, or as an adjunct to treatment with conventional drugs, maybe nutraceuticals with a well-established effect on pregnancy and an effective safety profile. Potentially successful possibilities for new nutraceuticals include calcium, omega-3 polyunsaturated fatty acids, vitamin D, folic acid, resveratrol, alpha-lipoic acid, zinc, inositol, and probiotic supplements [7]. For patients who are

at risk of elevated statin levels, which further contribute to cardiovascular illnesses, researchers have assessed the nutraceutical linked to the medication ingredient ezetimibe [8]. It has been demonstrated that combining a novel nutraceutical with non-steroidal anti-inflammatory medicines (NSAIDs) may be a viable treatment option for osteoarthritis, increasing the medication's effectiveness and safety for commercial usage [9, 10].

Nutraceuticals including antioxidants, omega-3 fatty acids, plants like algae, aloe vera, seaweed, and wheatgrass, as well as teas and herbs like ginseng and Echinacea, continue to have a strong and expanding market [11, 12]. The nutraceutical business is growing internationally, according to a recent analysis, and it is predicted to reach $340 billion by 2024. Nutraceuticals are expected to increase at a compound annual growth rate (CAGR) of 7.2% between 2016 and 2024. Numerous causes, including an increase in demand for nutraceuticals, public knowledge of the advantages of nutrition, and an incremental rate seen in the healthcare graph, are linked to this increase in the growth of the nutraceuticals-based sector [13, 14]. Over 90.0% of the global nutraceutical industry is currently accounted for by Europe, the United States, and Japan. At a compound annual growth rate (CAGR) of 8.0%, the market is expected to grow from $247 billion in 2019 to $336 billion by 2023. Since the global markets have reached a mature state, nutraceutical companies have turned their attention to developing nations, particularly those in Asia Pacific, including India. In 2017, the Indian market accounted for about 2.0% of the global nutraceutical market. It is predicted to grow at a CAGR of 21.0% to reach $11 billion by 2023. Additionally, it is anticipated that India will account for at least 3.5% of the worldwide market by 2023 [15, 16]. The general public and healthcare professionals now choose nutraceuticals over medications because of their dynamic activity, which combines nutritional and therapeutic properties. A recent review thoroughly examines the use of nutraceuticals in support and preventative therapy, and then it compiles research on patents that have been issued on the subject.

Nutraceuticals as specialized medical products: Dietary meals and supplements used for specific medicinal objectives are considered specialised medical products under the legal foundation. These dietary supplements should be governed by national protocols, typically issued by the Ministry of Agriculture and/or Ministry of Health of different nations worldwide, as well as by regulatory bodies like the European Food Safety Authority and the U.S. Food and Drug Administration [17]. Non-specific biological medicines called nutraceuticals are used to control symptoms, prevent cancer, and enhance well-being. They contribute to the prevention of disease and the promotion of health. **Table 1** provides a summary of the many nutraceuticals used in health promotion [18, 19].

Different types of nutraceuticals: The development of functional meals, clinical trial design, academic training, and nutritional counseling can all benefit from the use of nutraceuticals. Nutraceuticals can be made ahead of time in many cultures. Some of the most reliable techniques for classifying nutraceuticals are based on biological processes, chemical composition, nutrient sources, and other factors [20]. Current and ongoing international research attempts to thoroughly explain the mode of action, safety, and effectiveness of nutraceuticals, which are derived from vegetable or animal diets, by verifying their claimed role using medical fact sources. This special issue explores the impact and perspectives of nutritional supplements on social well-being from a range of perspectives, including effectiveness studies, wellness-related benefits, clinical research, and analytical insights [21]. Dietary fiber, or more specifically the natural products created from it, is the portion of the diet that is absorbed by the intestinal microbiota rather than being broken down by the digestive system's enzymes. Individuals who consume high amounts of nutritional fiber are less likely than those who consume little to no fiber to suffer from heart disease, stroke, high blood pressure, diabetes, obesity, and other gastrointestinal (GI) problems. Additionally, eating more foods high in fiber decreases blood pressure, improves blood sugar regulation in diabetics, promotes regularity, and increases serum lipoprotein levels. Certain soluble fibers have been shown to increase resistance [22]. Humans can take concentrated nutritional formulations known as nutritional supplements in the following forms: liquid, chewable, pills, soft gel, lozenges, powder, and gel caps [23]. A nutritional supplement or diet supplement is any dietary item that

contains at least one of the following nutrients: vitamins, minerals, amino acids, antioxidants, agents that lower stress, blood pressure, and cholesterol, as well as stimulants and antidepressants. For health reasons, these foods are intended to be taken in place of normal meals [24].

Table 1: List of health-promoting nutraceuticals

Nutraceuticals/ Dietary supplements	Nutrients	Health benefits
Water soluble vitamins	Vitamin C	Wound healing, antioxidant
	Vitamin B1	Carbohydrate metabolism, neurological function
	Vitamin B2	Energy metabolism
	Vitamin B3	Brain function
	Vitamin B6	Produce red blood cells, synthesize amino acids, and convert proteins into energy.
	Vitamin B12	Metabolism of fat, protein, and carbohydrate
	Folic acid	Formation of RBCs, formation of the genetic material of cells
Fat-soluble vitamins	Vitamin A	Healthy vision, skin disorder, antioxidant
	Vitamin D	Absorption of calcium, formation of bones and teeth
	Vitamin E	Boost immune system
	Vitamin K	Blood clotting
Minerals	Calcium	Formation of bones and teeth
	Iron	Oxygen transport, energy production
	Magnesium	Healthy nerve and muscle function and bone function
	Phosphorus	Phosphorylation process
	Copper	Heart functioning, iron absorption
	Iodine	Functioning of the thyroid gland
	Zinc	Sperm production, wound healing
Herbal	Aloe vera	Anti-inflammatory, wound healing
	Garlic	Anti-bacterial, anti-fungal
	Ginger	Carminative, anti-emetic
	Ginseng	Energy boosting and adaptogen
	Green tea	Cell-mediated immunity, antioxidant

A probiotic is a kind of living microbial feed additive that, when given in moderation, benefits the host animal by balancing the population of bacteria in its intestines. Numerous types of probiotics are available, such as liquid, gel, paste, granules, capsules, powdered prescription, and more. Several probiotic strains are frequently used to treat gastrointestinal (GI) disorders, including lactose intolerance, severe diarrhea, and GI side effects from antibiotics. Probiotics are non-toxic, resistant to stomach acid, and compliant with the gut's epithelial layers, which produce antibacterial substances. Some studies have suggested that taking probiotics may lower the chance of developing systemic disorders like allergies, asthma, malignancies, and different types of ear and urinary tract infections [25]. Elie Metchnikoff, a Nobel laureate from the Pasteur Institute in Paris, enhanced the host's quality of life by successfully transforming the large intestine's hazardous microbiota into a helpful culture of Bacillus bulbaricus. This study found that probiotics had positive effects on human health [26]. To mention a few health benefits, prebiotics have been demonstrated to enhance lactose tolerance, anticancer characteristics, toxin neutralization, blood lipid and cholesterol reduction, constipation, and gut immune system stimulation. When given 5.0-20.0 g of insulin and oligosaccharides each day, Bifidobacterium thrive. Once more, eating a lot of these oligosaccharides results in diarrhea, constipation, and gas. Important treatment considerations include fatigue, irritation, white blotchy nails, gastrointestinal issues, loss of hair follicles, and minor nerve damage [27]. Foods that naturally contain prebiotics include peas, beans, pea shoots, sugar beets, garlic, cilantro, onion, Jerusalem artichokes, wheat, honey, bananas, barley, tomato, rye, soybean, human and animal milk, and, more recently, seaweeds and microalgae. And many more are manufactured artificially from basic elements like lactose, sugar, starch, and plants. The three most well-known at the moment are GOS, FOS, and inulin [28]. Polyunsaturated Fatty Acids (PUFAs) directly regulate systemic and local inflammation that leads to the formation, progression, and instability of plaque. They also reduce blood

pressure, platelet aggregation, and plasma triglycerides. Depending on the location and amount of double bonds, PUFAs regulate a variety of biological functions, including blood pressure, blood coagulation, and the healthy development and operation of the brain and neurological system [29]. In recent years, there has been a notable increase in public interest in the connection between nutrition and health characteristics of particular dietary fats and the effects they have. The impact of acids on human health has been one of the primary topics of interest. Fatty acid chain length, unsaturation level, and omega double bond placement all have an impact on a person's health and nutritional status. The majority of dietary oils and (fats) lipids that come from both plant-based and animal sources are considered fatty acids. The structure, physiology, and metabolism of the body depend on fatty acids, which are the primary constituents of phospholipids, triglycerides, and cholesterol esters [30].

The main objective of research on phytochemicals-natural compounds originating from plants with distinct bio-activities toward mammalian biochemistry and biotransformation is to ascertain their effectiveness. Biological and chemical reactions use them as substrates, enzymatic chemical reactions use them as related components, absorbents, ligands that irritate or agonize intracellular or cell surface receptors, hazardous reactive or toxic chemicals, scavengers of reactive or toxic chemicals, and sequestrants that bind to and remove unwanted substances from the gastrointestinal lining. Alkaloids, phenolic compounds, terpenoids, and fiber are examples of these phytochemicals [31]. Numerous illnesses, such as cancer, heart disease, diabetes mellitus, high blood pressure, inflammation, microbial, viral, and parasite infections, mental health conditions, spasmodic disorders, ulcerated patches, and more, have been demonstrated to be protected by phytochemicals. The use of phytochemicals in animal research, medicinal uses, and in vitro or cultured cells is covered beforehand. Studies about promyelocytic leukemia cell cultures, anti-mutagenic tests, effects on animal pain and inflammation, effects on bacteria, viruses, and parasites, cancer, and in vitro testing of anti-psychotic phytochemicals, among other things. The food and pharmaceutical industries face issues as a result of the rapidly expanding usage of phytochemicals in functional meals and nutraceuticals [32]. Numerous animal research and clinical trials have lately provided empirical evidence for the health-promoting properties of several of these widely used food additives. The antioxidant qualities of the bioactive compounds in spices are extremely important since oxidative stress is a major factor in the development of degenerative diseases like cancer, inflammatory diseases, cardiovascular diseases, and neurological disorders. Spices are a natural and essential part of our daily nutrition, and they also provide our food flavor and taste [33]. Certain spices help with digestion and relieve digestive issues because they have antibacterial properties. They have diuretic, stomachic, carminative, tonic, and antispasmodic qualities. Several of the health benefits of spices have been experimentally confirmed in the last three decades [34]. Anti-inflammatory, anti-atherogenic, anti-lithogenic, gastrointestinal stimulant, cardiovascular protection, and antidiabetic potential Among the many health advantages of spices are their antimutagenic and antioxidant properties, as well as their potential to prevent cancer [35].

Neutraceutical development: The process of developing nutraceuticals is intricate and blends the domains of nutrition and medicine. Foods or dietary components known as nutraceuticals have health benefits over those included in conventional diets. They can be used to address a number of problems, such as promoting well-being, improving health, and preventing and treating illness. Products with no clinical evidence based on exact extracts and where traditional use outweighs confirmed nutritional or therapeutic use have been disqualified [36]. The market for β-glucans and mushrooms is huge [37], but there are several product sources, and turmeric is gaining a lot of attention these days. The development of nutritional products heavily relies on research and development. R&D in the nutraceutical sector bridges the gap between pharmaceuticals and nutrition through scientific research and innovation. Finding the safety, potency, and purity of samples; ensuring and validating the consistency of ingredient dosage to establish more effective and efficient processes for producing

ingredients for use in goods; and combining pre-existing components to create new items are the main goals of research and development [38].

Utilizing neutraceuticals for a number of diseases: Nutraceuticals are effective in treating a wide range of conditions, including colds, coughs, indigestion, depression, constipation, and abnormal blood pressure. Nutraceuticals are being used to treat a variety of chronic and degenerative diseases, including Parkinson's and Alzheimer's, as well as osteoporosis, diabetes, obesity, cancer, and coronary heart disease. Activating antioxidant defenses, encouraging cell division and proliferation, modifying signal transduction pathways, controlling gene expression associated with cell survival, and preserving mitochondrial integrity are all ways that nutraceuticals function. Nutraceuticals such as flavones, flavonoids, flavanones, cruciferous vegetables, quercetin in onions, cherries, blackberries, apples, berries, and other antioxidant vitamins and minerals block ACE and the cyclooxygenase pathway [39]. This could lower the chance of cardiovascular diseases. Allicin lowers cholesterol and blood pressure. The small capillaries are kept healthy by flavonoid groups [40]. Ginger is recommended for the treatment of palpitations and hypertension due to its potent anti-inflammatory and antioxidant qualities.

Cancer: Herbal nutraceuticals have properties that stop mutations and cancer [41]. Carotenoids, which include lycopene and beta carotene from orange and yellow fruits, are antioxidants that quench oxygen, lessen oxidative stress, and help prevent cancer. Nutraceuticals regulate factors that break down DNA in cells and restrict DNA transcription in tumors. Cruciferous vegetables suppress the enzymes responsible for lung and colon cancer, preventing the development of tumors. Herbal nutraceuticals can change how cancer spreads meta-statically.

Cardiovascular disease: By encouraging the formation of endothelium Nitric Oxide (NO), reducing vascular inflammation, and stopping platelets from aggregating, RES (3,4,5-trihydroxy-trans-stilbene), an antioxidant found in grape skin, can lower blood pressure [42]. Through the pathways of adenosine monophosphate activated protein kinase, sirtuins (SIRT-1), and nuclear erythroid factor (Nrf2), it reduces vascular smooth cell contractility by inhibiting Ang-II and increases NO availability by increasing endothelial NO synthetase (eNOS) activity [43]. Cocoa lowers insulin resistance and systemic inflammation via increasing plasma's antioxidant capacity, protecting the vascular endothelium, and increasing the bioavailability of NO due to its oligomeric procyanidin content [44, 45]. Through vasodilatation, greater NO release (caused by higher eNOS expression), decreased ACE impact, balancing of K+ channel activation, and release of intracellular Ca++ channels, the vegetable alkaloid berberine can reduce hypertension [46].

Alzheimer's disease: Another name for Alzheimer's disease is senile dementia. It appears that antioxidants decrease the progression of the illness. By utilizing their antioxidant qualities, nutrients like lutein, beta carotene, lycopene, curcumin, and lavandula can stop oxidative stress-induced brain damage. These drugs can delay dementia's onset [2, 47].

Diabetes: Universal antioxidants like lipoic acid and catechins, together with spices like fenugreek and cinnamon, are used to treat diabetic neuropathy, nephropathy, and retinopathy. Vitamin D, calcium, magnesium, and chromium all promote insulin sensitivity. Caffeineic acid lowers elevated plasma glucose in insulin-resistant individuals. Green tea and epicatechin 3 gallate lower fasting and postprandial glucose levels as well as insulin resistance. Bitter melon and pomegranates regulate metabolism and transport blood sugar into cells [48].

Obesity: Nutraceuticals including psyllium, conjugated linoleic acid, and capsaicin have excellent anti-obesity properties. Chitosan, vitamin C, fenugreek, caffeine, black grams, green tea, bottle guard curcumin, and other substances help people lose weight. They release leptin and cytokines like IL-1 and IL-6 and lower total cholesterol and low-density lipoprotein [3, 49].

Osteoarthritis: To lessen osteoarthritis complications, nutraceuticals such as chondroitin sulfate, diacerin, glucosamine, oxaceprol, curcumin, banana, pomegranate, ginger, green tea, avocado, willow bark, boswellia, tipi, soybean, etc. are utilized. They have a major impact in regulating the expression of genes. Antioxidants can cure inflammation, discomfort, and joint deterioration. Additionally, applying olive oil reduces knee pain, stiffness, and swelling [50].

Eye disorders: Nutraceuticals have been found to be effective in treating age-related macular degeneration. Cataracts and presbyopia can be avoided with the use of antioxidant-producing compounds like lutein, docosahexaenoic acid (DHA), vitamin E, carotenoids, green tea, flavonoids, and coenzyme Q10. Vitamins C and E, carotenoids, flavonoids, caffeine, and pyruvate are all beneficial for retinal pigmentosa [51]. Rich sources of lutein and zeaxanthin, which enhance eyesight and reduce the risk of cataract development, include rice bran, fruits, and vegetables. The folic acid, omega 3, 6, 9, and essential fatty acids found in rice bran also promote eye health.

Stress management: Adaptogens are bioactive compounds that occur naturally and can prevent stress-induced cellular damage. They help people recover from difficult situations by progressively enhancing emotional functioning. Good adaptogens that reduce stress include ginseng and ashwagandha, which promote the production of heat-shock protein 70 (HSP-70). Additionally, herbal nutraceuticals stabilize physiological systems, improve sleep, secondary memory, homeostasis, and stress tolerance, and reduce anxiety and sadness [52, 53].

Conclusion: Nutraceuticals are a potentially expanding industry that, works in both nutrition and medical therapy to provide comprehensive medical support. They may be used as dietary supplements, to prevent disorders including cardiovascular disease, to support and treat different kinds of cancer, and for other medical purposes. Therefore, the potential success of nutrients that affect individuals in healthcare is now widely understood and perceived by the nutritional businesses. Currently, pharmaceuticals are thought to be the realm of medical treatment. Better medical care and health benefits result from the use of newer technologies, such as genetically modified food, nutraceuticals based on nanotechnology, etc., which further prolonged the growth in the nutraceuticals revenue market. The enhanced safety and possible benefits of recently created nutraceutical products, according to scientific research, will encourage further investments in more advanced technologies like nutrigenomics, convergent approaches, diverse imaging technologies, and their uses in healthcare and nutrition development.

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