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REVIEW ARTICLE

# Exploring the Evidence: A Systematic Review of Nutraceuticals and its Application

**Moulik Bhattacharyya[1*], Mahanam Brata Paul[1], Goutam Mukhopadhyay[1], Durgesh Ranjan Kar[1], Dipanjan Majumdar[1], Abhijit Mukherjee[1], Saikat Polley[1]and Samar Ghosh[2]**

[1]B.C.D.A. College of Pharmacy and Technology, Madhyamgram Campus, Ghosh Para, Kolkata - 700129, West Bengal, India; moulikbhattacharyya@gmail.com

[2]Calcutta Institute of Pharmaceutical Technology and Allied Health Sciences, Banitabla, Uluberia, Howrah – 711316, West Bengal, India

## Abstract

The core idea of Nutraceuticals is based on the intersection of two words "nutrition" and "pharmaceutical. Nutraceuticals are products of nutrition as well as medicine. Another definition would be a material that offers protection from various diseases or benefits the body physiologically. The nutraceutical field is divided into three sectors dietary supplements, functional foods and herbal/natural products. The most common commercially available nutraceutical products are β-carotene soft gel capsules (β-Carotene), Phytrol (Plant-derived sterols), Revital (Multivitamin and minerals), Yakult (Probiotics) etc. In this review article, neutraceutical products have been classified into various groups according to their sources, chemical nature, application availability etc. Due to their potential health benefits, numerous herbs and plants (also known as nutraceuticals) have been employed traditionally in traditional medical systems including traditional Chinese medicine, Ayurveda and other indigenous practices. In addition to their nutritional value for humans, nutraceuticals are an efficacious treatment and preventive measure for several diseases, includingobesity, diabetes, cancer, heart disease and osteoporosis, as well as other degenerative and chronic illnesses like Alzheimer's and Parkinson's. Nutraceuticals work by modifying signal transduction pathways, maintaining promoting cell proliferation, mitochondrial integrity and activating antioxidant defencesand modifying gene expression linked to cell survival. Nutritional supplements that block the cyclooxygenase pathway and the Angiotensin Converting Enzyme (ACE) include flavonoids, flavonones, flavones, cruciferous vegetables, onions, apples, cherries, blackberriesand berries.

**Keywords:** Antioxidants,Coronary Heart Disease, Dietary FibersNutraceuticals, Flavonoids

## 1. Introduction

The terms "nutrition" and "pharmaceutical" come together to form the fundamental concept of nutraceuticals. However, pharmaceuticals and nutraceuticals differ from one another in various ways. Nutraceuticals are multi-targeted and contain lower quantities of active chemicals than pharmaceuticals, which is the main difference between the two[1]. On the other hand, a pharmaceutical product has a predetermined development path that must be completed before it is released into the market for use by humans. This approach entails the purification of the active chemical compounds, evaluating their solubility, toxicityand pharmacological effects; Formulation development; preclinical studies; and stage I–IV clinical trials. Only after a pharmaceutical molecule has completed each of these steps is it given FDA (Food and Drug Agency) approval for usage in humans. Nutraceuticals have no such restrictions[2]. Toxicity is one further way that medicines and nutraceuticals differ from one another. Because of their natural action, nutraceuticals are generally believed to be safe and free of side effects; nonetheless, any pharmaceutical product, if used without a prescription, has the potential to be hazardous and have negative effects. However, if taken

*Author for correspondence

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in an excessive amount or without taking into account a person's general state of health[3]. Nutraceuticals are products or foods generated from foods that provide health advantages above and beyond those of basic nutrition. They are frequently praised for their ability to improve general well-being, promote healthand prevent or manage diseases. To validate their therapeutic effects, animal studies and research must provide clinical test results to the pharmaceutical development process.But until recently, there was no option to confirm whether a food's ability to prevent disease could be verified when it came to nutrition. However, as the link between lifestyle-related diseases and food composition has been established scientifically, it has recently become a social issue. The health-related properties of nutraceutical products are well known. These include minimising the risk of cancer and heart disease as well as preventing or treating cholesterol, hypertension, osteoporosis, obesity, diabetes, cataracts, menopausal symptoms, insomnia,macular degeneration, poor memory and concentration, digestive upsets and constipation[4].

## 2. Methodology

Scientific information about neutraceuticals and applications was gathered from approximately 100 published papers that were located in several relevant databases. To locate pertinent papers, studies, and investigations, several online scientific databases, including PubMed, SciFinder, Web of Science, Science Direct, Wiley Online, ResearchGate, Google Scholarand Scopus, in addition to other search engines, were combed through until October 2023. To obtain the necessary data on this plant species, search terms including "pharmacological application," "prebiotics," "probiotics" and "nutraceuticals" were employed.

## 3. Current Scenario of Neutraceuticals in the IndianMarket

Functional foods, dietary supplements and herbal/ natural goods are the three primary areas of the nutraceutical industry[5]. By taking into account natural and organic foods ($6.2 billion), functional foods ($13.4 billion), some lesser harmful foods with fewer or no unhealthy ingredients ($23 billion), dietary supplements ($8.9 billion), and a few market standard foods ($28.3 billion). Nutrition Business Journal (NBJ) estimated in 1995 that the nutraceuticals market was worth $80 billion. NBJ started monitoring the expansion of the nutraceuticals sector. According to NBJ, the industry has expanded by 7.1% annually on average since 1995. Sales in the industry reached $91.7 billion in 1997. Dietary supplements and natural/herbal goods were the industry segments with the fastest rate of growth. Dietary supplement sales in the US before the pandemic rose by 5% ($345 million) in the year 2019 over the previous year. In addition, during the first wave of the pandemic, in the six weeks leading up to April 5, 2020, sales increased by 44% ($435 million)[6] (Table 1).

**Table 1.** List of commercially available nutraceuticals

| Products | Category | Application | References |
|---|---|---|---|
| Soft gel capsules of β-carotene (β-Carotene) | Dietary supplement | Antioxidants are beneficial to the eye. | 7 |
| Benecol margarine (Stanol) | Functional food | Reducesabsorption of cholesterol. | 8 |
| Bile salt stimulated lipase (Lipase) | Medical food | For overall well-being and health. | 8 |
| Bimuno (Prebiotic food supplements) | Food supplements and prebiotics | To promote overall health and wellness. | 9, 10 |
| Calcirol D-3 (Vitamins and Calcium) | Food supplements | To fulfil the demand for calcium. | 11 |
| Amiriprash/Chawanprash (Vitamin C and other phytochemicals). | Food supplements | Immunity booster | 11 |
| Children's whole liquid food (Multivitamin) | Dietary supplement | The well-being of children | 12, 13 |

**Table 1.** Continued...

| Products | Category | Application | References |
|---|---|---|---|
| Drops of colloidal silver (colloidal silver) | Supplement | Elimination of single-celled pathogens. | 14 |
| Daflon (Micronized flavonoids from citrus, 90% diosmin and 10% additional) | Medical food | Vasculoprotector in a case ofpersistent vein insufficiency. | 15 |
| Daily formula (Multivitamins and multiminerals) | Dietary supplement | For overall wellness and health. | 12, 13 |
| Drug Axona (Medical food) | Medical food | To improve the metabolism of those suffering from mild to moderate Alzheimer's disease. | 16, 17 |
| Energy shots (Caffeine) | Processed food | Energy drink | 18, 19 |
| Alcohol burner (Extract of *Rhodiola rosea*) | Processed food | Breakdown of alcoholic by-products. | 20 |
| Phytrol (Plant-derived sterols) | Functional food | Lower risk of heart disease. | 8 |
| Green tea (Catechin) | Functional food | Reduced cholesterol, decreased body weightand increased metabolism. | 21, 22 |
| Gluchrom (L-lysine, Vitamin B6, chromium and L-arginine) | Dietary supplement | Regarding athletes' physical prowess. | 23 |
| Joint care and joint aid (methyl sulfonyl methane, glucosamine sulfateand root of ginger) | Medical food | For joint pain | 24 |
| Juven (L-glutamine, Calcium β-hydroxy β-methyl butyrate, L-arginine) | Medical food | For stopping the loss of muscle resulting from AIDS or cancer, for quickening the healing of wounds following surgery or trauma. | 25 |
| Lifoxident (Green tea extract's caffeine, catechins and polyphenols) | Processed food | Antioxidant and for reducing body weight. | 22 |
| Limbrel (flavocoxid) (Plant-derived flavonoids) | Medical food | Prescription diet for long-term osteoarthritis. | 26 |
| Linzee (Ganoderma mushroom extract) | Processed food | Detoxifier | 27 |
| Liquid prenatal vitamins (Multivitamins) | Dietary supplement | For the good health of children. | 12, 13 |
| Natural purified lutein ester (Lipids) | Dietary supplement | Antioxidants | 28 |
| Nestle baby foods (Baby growth nutrients) | Baby food | For proper growth of the baby. | 29 |
| Proteinpremix powder/Proteinex (Proteins) | Dietary supplement | For bodybuilding | 11 |
| Raspberry ketones (Ketones) | Processed food | Hepatoprotective, anti-obesityand metabolism booster. | 30 |
| Revital (Multivitamins and minerals) | Dietary supplement | Increases endurance and acts as an enzyme cofactor. | 31 |
| Sleep Aid Supplement (Melatonin) | Supplement | Regulates sleep and circadian rhythms. | 32 |
| Spirulina (Blue-green algae for vitamins and proteins ) | Dietary supplement | For body growth and stamina. | 33 |
| Vitamin D3 drops (Vitamin D) | Dietary supplement | For optimal well-being of strong bonesand teeth. | 34 |
| Yakult (Probiotics) | Probiotics | For good gastric health. | 35 |

## 4. Classification of Neutraceuticals

### 4.1. Functional Foods

Nutraceuticals consumed as regular food in an unaltered standard form are known as functional foods. These are foods that have been nutrified or fortified to boost their nutritional content without sacrificing their natural flavour and texture[21,28,36]. The two categories of functional foods are fermented foods and processed foods.The microbial treatment of fermented foods modifies their physical shape and achieves the necessary biochemical changes. The microorganisms break down the complex nutrients in the meal into simpler compounds that are easily absorbed by the human body. Additionally, some of these bacteria create vitamin B12, which raises the nutritional value of fermented foods. Fermented milk products such as Acidophilus milk, *lassi*, Yakult, kumiss, filmjolk, junket, kefirand yoghurt are made with Lactic Acid Bacteria (LAB) or both LAB and yeast. Fermented dishes created from grains, legumesand vegetables include *hama-natto*, injera, kimchi, *lao-chao*, *maheu*, *oncom*, pozol, *sauerkraut*, *sufu*and*tef*. Cereals like *prokllada* and flummery contain fermented milk products. The fermented foods *patak*, *pin-dang*, salami, sausage, *tarama* and teewurst are made from meat and fish[37,38].Processed foods that have been processed include regular foods that have been frozen, dried, sliced, pickledand so on to extend their shelf life. It is necessary to keep perishable food items like milk, fruitsand vegetables to meet demand all year long. To be stored safely for an extended length of time, non-perishable goods including grains, millets, pulses, nutsand dry fruits also need to be processedby drying, freezing, smoking, salting, sugaring and pickling[39].

### 4.2. Dietary Fibres

Dietary fibres are edible but indigestible food ingredients. They are not taken up by the intestinal villi; instead, they are partly or completely fermented by bacteria in the large intestine, from which the digested products are taken up and the remaining insoluble undigested materials are expelled as stool. A carbohydrate polymer, dietary fibres are made up of ten or more monosaccharide units, except lignin, which is not a carbohydrate. Based on their chemical makeup, dietary fibres include arabinogalactan, arabinoxylan, β-glucan, cutin, fructose-oligosaccharide, galactomanan, galacto-oligosaccharides, inulin, pectin, polydextrose, resistant maltodextrins, resistant starchand suberin[40]. There are two kinds of dietary fibres: soluble and insoluble[41]. Water-soluble soluble fibres readily ferment in the large intestine to produce gas and physiologically active by-products. They provide viscosity, serve as prebiotics for gut floraand delay the emptying of the stomach, prolonging the sensation of fullness. In addition to being water-insoluble and metabolically inert, insoluble fibres also serve as prebiotics and give faecal matter body weight. They facilitate easy defecation by absorbing water[42,43]. Table 2 lists the many types of dietary fibres, their origins and other significant details.

**Table 2.** List of dietary fibres and their source

| Type of Dietary Fibers | Monomers | Features | Origin | References |
|---|---|---|---|---|
| **Water-insoluble dietary fibers** | | | | |
| **Cellulose** Unbranched and alkali-insoluble | Ten thousand glucose units | main component of a plant's cell wall | All plant | 41, 42 |
| **Chitin** | N-acetylated glucosamine and glucosamine | Natural amino polysaccharides with linear chain | Crabs, lobsters,prawns, shrimps, and mushrooms | 44 |
| **Hemicelluloses** Alkali soluble, branched containing more sugars | 50–200 units of glucuronic and galacturonic acids mixed with pentose and hexose sugars (apart from glucose). | Soluble in water or not | Legumes and cereals | 42 |
| **Lignin** Complex random polymer, non-carbohydrate in nature | Oxygenated phenylpropane units (coniferyl alcohol, paracoumaryl, sinapyl alcohol) | Three-dimensional, Irregular,amorphous and strong branching in phenolic polymers | Pear stones and guava seeds, as well as tough vegetable fibres like ladies' fingers and mature guard, etc. | 42, 45 |

**Table 2.** Continued...

| | | | | |
|---|---|---|---|---|
| **Resistant starch** (RS) | D-Glucose | In the colon, fermentation, resistant to hydrolysis by amylase | High amylose corn and wheat, barley, bananas and legumes etc. | [46] |
| **Water-soluble dietary fibers** | | | | |
| **Xanthan gum and Gums** | Isolated polysaccharides like, galactomannan, arabinogalactan, and glycoproteins | Secreted due to injury at wounded sites by secretor cells | Xanthomonas tamarindo, guar, karaya, tragacanth, locust bean, and acacia | [42, 47] |
| **Arabinoxylan and Mucilage** | Natural metabolitesformed intracellularly | Produce slimy mass with water, prevent desiccation of endosperm | Senna, Linseed, psyllium, aloe, marshmallow, slippery elm | [47] |
| β-Glucans Branched and smaller than cellulose | Glucose | principal ingredient in barley and oats | Oats, bran, barley, whole grains and wheat | [41] |
| **Alginate, agar and carrageenan** Unbranched polysaccharides | Mannuronic acid and Guluronic acid | Dietary fibres with high viscosity | Algae | [48] |
| **Inulin** | heterogeneous combination of fructose polymers | Does not digest in the small intestine and ferments in the colon | Asparagus, onions, wheat, garlic and chicory root | [49] |
| **Pectin** Branched fibre | 300–1000 D-galacturonic acid and rhamnose units | found in fruit and vegetable cell walls and intracellular tissues | Peels of vegetables and fruits | [41, 42] |

## 4.3 Substances with Established Nutritional Functions

### *4.3.1 Vitamins*

Vitamins are low molecular weight chemicals that are essential to life in trace amounts for essential metabolic processes. Certain illness symptoms may result from a deficiency in certain chemicals. Microorganisms and plants provided the vitamins that animals needed. Water-soluble vitamins (like B and C) and fat-soluble vitamins (like A, D, and E) are the two categories of vitamins. Genetically modified food, herbal medicines, biofortified cropsand processed foods are examples of nutraceuticals. To improve immunity and prevent, or treat specific ailments, nutraceuticals offer more than just a simple diet. The origins and biological activities of some vitamins and substances that resemble vitamins are included in the following (Table 3)[1,11,50,51].

### *4.3.2 Minerals*

Minerals are inorganic substances that the body cannot create; they must come from food. They are naturally present in both soil and water. Plants absorb a significant amount of minerals from their surroundings, and these minerals are frequently passed to animals at higher levels of the food chain. Deficiency in these essential minerals often leads to death. Minerals are necessary parts of the organism. They are necessary for the human body's important biomolecules to function and be synthesised. Although minerals don't give the body energy, they are necessary for the maintenance of normal metabolic processes. Zn, Mn, Mg, Cl, Co, Fe, Mg, Na, K, P, I, Ca and other minerals are essential elements for human health[52]. Table 4 describes various minerals with their sources and health benefits.

### *4.3.3 Polyunsaturated Fatty Acids*

Due to differences in the location of the first double C-bound, Polyunsaturated Fatty Acids (PUFAs) are classified into two groups: omega-3 (n-3) and omega-6 (n-6) PUFA. Because they are necessary for maintaining physiological integrity and cannot be produced by the

**Table 3.** List of vitamins and their source and health benefits

| Vitamins | Types | Source | Health Benefits |
|---|---|---|---|
| Fat-soluble vitamins | Vitamins A | Cheese, liver, fish liver oil, butter carrots | Antioxidants are essential for normal growth and development as well as the maintenance of healthy skin, eyes, and mucous membranes. They may also be used to treat certain skin disorders and prevent or manage some types of cancer. |
| | Vitamins D | Fish liver oil, egg yolk, milk, butter | Helps the body absorb and use calcium, which is necessary for the development of bones and teeth. |
| | Vitamins E | Wheat germ oil, cotton seed oil, peanut oil | Promotes the immune system, blood cells, muscles, lungs, and nerve tissue |
| | Vitamins K | Cabbage, cauliflower, tomatoes | Need for blood clotting |
| Water soluble vitamins | Vitamins C | Citrus fruits, amla, green chillies | Help in wound healing, improves bone, gum, tooth, and skin health, and may help minimise the symptoms of the common cold. |
| | Vitamins $B_1$ | Cereals, pulses | Helps in converting food into energy and is crucial for neurological processes |
| | Vitamins $B_2$ | Nuts, yeast | Enhances the body's energy production and other chemical processes, as well as maintaining healthy neuron, eye, and skin functions. |
| | Vitamins $B_3$ | Liver, meat, yeast | Helps in maintaining healthy brain function and converting food into energy. |
| | Vitamins $B_5$ | Yeast, egg, milk | Helps produce fatty acids, cholesterol, and steroids, all of which are essential for the intraneuronal production of acetylcholine. |
| | Vitamins $B_6$ | Banana, tomato juice | Helps in the production of essential proteins and the conversion of protein into energy |
| | Vitamins $B_{12}$ | cheese, meat, fish, crab, oysters, and fortified cereals | Contributes to the synthesis of amino acids, the metabolism of lipids, proteins, and carbohydrates, the creation of red blood cells, the maintenance of the central nervous system, and the formation of genetic material in cells. |
| | Folic acid | Green vegetables | Necessary for the creation of cellular genetic material, vital during the first three months of pregnancy to prevent birth defects, aids in the development of red blood cells, and shields against heart disease. |
| Vitamin like compounds | Biotin | | Necessary for many metabolic processes |
| | L-Carnitine | | Fatty acid oxidation, encouragement of certain organic acid excretion, and acceleration of oxidative phosphorylation |
| | Choline | | Treatment for fatty liver and irregular fat metabolism with the lipotropic drug |
| | Vitamine F | | Involved in the synthesis of different hydroxy fatty acids, prostaglandins, and leukotrienes as well as the appropriate development of different membranes |
| | Inositol | | The transport of amino acids and the movement of sodium and potassium both require the lipotropic substance. |
| | Taurine | | Helps in the function of the retina's photoreceptors, bile acid conjugation, the antioxidant activity of white blood cells, platelet aggregation, CNS neuromodulation, cardiac contraction, and sperm motility. |

**Table 4.** List of minerals and their health benefits

| Minerals and Trace Elements | Sources | Health benefits |
|---|---|---|
| Calcium | Milk, cheese, dairy products, green leafy vegetables, sardines, beans | Important for the development of bones and teeth and functions of nerves, muscles and glands. |
| Iron | Liver, red meat, kidney beans, nuts, dried fruits | Vital for the synthesis of energy and the delivery of oxygen to tissues. |
| Magnesium | Pumpkin seed, almonds, spinach, cashew, peanut | Crucial for bone development, muscle and nerve function, and potential prevention of premenstrual syndrome (PMS). |
| Phosphorous | Dairy products, red meat, poultry, seafood, legumes, and nuts | Essential for the formation of bones, teeth and genetic materials and the production of energy and its storage |
| Chromium | Mussels, Shellfish, Broccoli, yeast, meat, grape juice, nuts | Converts carbohydrates and fats into energy with the help of insulin |
| Cobalt | Fish, nuts, green leafy vegetables, cereals | Important for the formation of Vitamin B12 and its coenzymes. |
| Copper | Oysters, whole grains, beans, nuts, potatoes, kidneys, liver, dark leafy vegetables, prunes, black pepper, yeast | Important for the production of haemoglobin, collagen and energy, the functioning of the heart and absorption of iron from g.i.t. |
| Iodine | Seaweed, sea fishes, iodised table salt, eggs, shrimp | Essential for the functioning of the thyroid gland. |
| Selenium | Brazil nuts, seafoods, liver, kidney, eggs | Antioxidant, important for the functioning of heart muscle. |
| Zinc | Oysters, shellfish, meat, legumes, nuts, eggs, whole grains | Important for the reproduction of cells, wound healing, production of sperm and testosterone and for the development of children. |

body, two PUFAs linoleic acid and linolenic acid are referred to as essential fatty acids and must be received through diet[4].

## 4.4 Probiotics

When taken in sufficient amounts, probiotics are collections of microorganisms that offer the host several health advantages. Probiotics work through many processes, such as the release of antimicrobials, the reduction of antitoxic effects, the prevention of pathogen attachment to the intestinal epithelium, competition for nutrients and spaceand the improvement of conditions following pathogen-caused infection. Elie Metchnikoff, a Nobel laureate from the Pasteur Institute in Paris, researched the benefits of probiotics for humans. He was able to change the harmful microbiota in the large intestine into a host-friendly colony of *Bacillus bulgaricus*, which improved the host's health[53]. He disclosed that the beneficial bacteria included in probiotics suppress harmful and pathogenic germs from the digestive system, which would otherwise infect the host and cause illness. Because yoghurt contains probiotics, he hypothesised that Bulgarian peasants who consume it in their diet live longer than those who do not. Probiotics aid in food digestion and break down complex nutrients into simpler ones that the human gut can easily absorb. The management of lactose intolerance is an exemplary case of probiotic-induced nutritional change. Table 5 lists the most popular bacteria found in probiotic meals[54-56].

## 4.5 Prebiotics

Prebiotics are insoluble dietary fibres that are fermented by gut bacteria in the large intestine after being undigested in the small intestine. Probiotic bacteria, particularly bifidobacteria, eat prebiotics. Foods high in insoluble fibre, like chicory, onions, garlicand Jerusalem artichokes, naturally contain them. To guarantee that the body has an adequate amount of probiotic bacteria, a combination of probiotics and prebiotics is known as "synbiotics"[57,58].

**Table 5.** List of commonly used microbes in probiotic foods

| Name of microbes | Use in probiotic foods |
|---|---|
| ***Lactobacillus*** | |
| *L. acidophilus* | Produces lactocidin and acidophilin, which inhibit the growth of bacteria such as *S. aureus, Salmonella, E. coli, C. albicans*, and others while boosting immunity. |
| *L. bulgaricus* | Produces lactic acid, which enables other species to coexist peacefully. |
| *L. casei* | Soothes bowel movement and improves immunity. |
| *L. lactis biovar diacetylactis* | Minimises glucose intolerance supports leaky gut and keeps the gut environment normal. |
| *L. paracasei* | Prevents teeth cavities and reduces the impact of environmental sensitivities. |
| *L. Plantarum* | Produces antibiotic lactogen and antiviral amino acid L-lysine, enhances calcium absorption and blocks the creation of the pathogen through nitric oxide production. |
| *L. reuteri* | Supports the digestive system, and helps to maintain oral health and immunity. |
| *L. rhamnosus* | Protects the small intestine and helps in lactose intolerance. |
| *L. salivarius* | Crucial for maintaining dental health and combating undesirable oral bacteria. |
| ***Bifidobacterium*** | |
| *B. bifidum* | Produces lactic and acetic acids, which alter pH levels. It also increases the absorption of calcium, iron, zinc and magnesium. |
| *B. breve* | Improves digestion and maintains colon health while the host is using antibiotics. |
| *B. infantis* | Enhances cytokines production and boosts the immune system. |
| *B. lactis* | Neutralises the effects of the wheat protein gliadin, which causes leaky gut syndrome and gluten sensitivity by damaging intestinal linings. |
| *B. longum* | Stops the growth of infections and lowers the incidence of nausea and gastrointestinal issues when using antibiotics. |
| **Others** | |
| *Bacillus coagulans* | Improves the secretion of gastric juices, stomach motility, the absorption of calcium, iron, and phosphorus, and helps with lactose intolerance. |
| *Pediococcus acidilactici* | Prevents rotting of undigested food in the gut. |
| *Saccharomyces boulardii* | supply of the B complex and vitamin B. |
| *Streptococcus salivarius K12, S. salivarius M18* | They generate BLIS, or bacteriocin-like inhibitory substances, which stop the growth of harmful bacteria in the mouth. |
| *Streptococcus thermophilus* | Helps in lactose intolerance. |

One kind of prebiotic cannot sustain the growth of all probiotics since different probiotic microbes require different kinds of food for their growth. Fructooligosaccharides, galactooligosaccharides, inulin starch, lactuloseand lafinose are examples of common prebiotics[53,54].

## 4.6 Polyphenols

Phytochemicals known as polyphenols, are found naturally in plant-based foods such as fruits, vegetables, whole grains, cereal, legumes, tea, coffee, wineand cocoa. These substances are the plants' secondary metabolites and serve as protection from oxidants, pathogensand UV light. Depending on the number of phenol rings and the structural components that connect these rings, they can be divided into a variety of groups. The two main classes of phenolic acids are derivatives of hydroxybenzoic acid, such as gallic acid, protocatechuic acidand p-hydroxybenzoic acid and hydroxycinnamic acid derivatives, such as caffeic acid, chlorogenic acid, coumaric acid, ferulic acidand sinapic acid. Phenolic acids make up about one-third of the polyphenolic compounds found in diet. Foods high in phenolic compounds include apples, berries, cherries, chicory, coffee, kiwisand pears[59].

### 4.7 Spices

Spices are aromatic plant materials that are used in food flavouring more than nutritional value. For millennia, people have utilised spices for their possible health benefits as well as to add flavour to meals. Bioactive substances with antibacterial, anti-inflammatory, antioxidantand other advantageous qualities can be found in several spices. These spices have the potential to improve overall wellness and health when used daily and in sensible quantities. Here are some examples of spices commonly recognised for their potential nutraceutical properties[60, 61].

## 5. Development of Neutraceuticals

Nutraceutical development is a complex procedure that combines the fields of pharmaceuticals and nutrition. Nutraceuticals are foods or dietary ingredients that offer health advantages over those found in regular diets. They can be applied to several issues, including illness prevention and treatment, health enhancement, and well-being promotion. We have excluded products that lack clinical proof based on precise extracts and where traditional usage predominates over verified dietary or medicinal application[62]. The market for mushrooms and β-glucans is enormous[63], but there are many different product sources, and turmeric has received so much attention nowadays. Research and Development (R and D) playsa major role in developing nutraceuticalproducts. The gap between nutrition and pharmaceuticals, fulfilled by R and D in the nutraceutical industry includes scientific study and innovation. The primary functions of research and development are to ascertain the safety, potencyand purity of samples; to guarantee and confirm the consistency of ingredient dosage to create more effective and efficient processes for producing ingredients for use in goods; combine pre-existing components to produce the new items[64].

## 6. Application of Neutraceuticals in Various Diseases

Numerous illnesses, such as constipation, depression, indigestion, irregular blood pressure, colds, and coughs, have been reported to respond well to nutraceuticals. These days, osteoporosis, diabetes, obesity, cancer, coronary heart disease and other degenerative and chronic illnesses like Parkinson's and Alzheimer's are treated with nutraceuticals. Nutraceuticals work by activating antioxidant defences, promoting cell division and proliferation, altering signal transduction pathways, regulating gene expression linked to cell survival, and maintaining mitochondrial integrity. ACE and the cyclooxygenase pathway are inhibited by nutraceuticals such as flavones, flavonoids, flavanones, cruciferous vegetables, quercetin in onions, cherries, blackberries, apples, berries, and other antioxidant vitamins and minerals[65]. This may reduce the risk of cardiovascular disorders. Allicin reduces blood pressure and cholesterol. Flavonoid groups keep the tiny capillaries healthy[66]. Strong antioxidant and anti-inflammatory properties of ginger are suggested in the management of hypertension and palpitations.

### 6.1 Cardiovascular Diseases

Resveratrol (3,4,5-trihydroxy-trans-stilbene) (RES), a type of antioxidant present in grape skin, can reduce blood pressure by promoting the production of endothelial Nitric Oxide (NO), suppressing vascular inflammationand preventing platelets from aggregating[67,68]. It works through the Adenosine Monophosphate Activated Protein Kinase (AMPK), Sirtuins (SIRT-1)and Nuclear Erythroid Factor (Nrf2) pathways, which are linked to enhanced NO availability through elevated Endothelial NO Synthetase (eNOS) activity and decreased vascular smooth cell contractility through Ang-II inhibition[69-72]. Because cocoa contains oligomeric procyanidins, it protects the vascular endothelium, increases the bioavailability of NO, and reduces insulin resistance and systemic inflammation by boosting the antioxidant capacity of plasma[73,74]. Through vascular compliance and elastic resistance, quercetin helps to maintain blood pressure levels. It can also lower autonomic nervous system activity[75-79]. Moreover, it can control the overall blood volume by downregulating Epithelial Sodium Channel (ENaC) gene expression, which lowers the volume of bodily fluids[80]. The regulation of transepithelial chloride secretion by quercetin-induced activation of Sodium Potassium Chloride Co Transporter 1 (NKCC1) results in a decrease in ENaC mRNA expression, which in turn causes a decrease in ENaC-related Na+-reabsorption, resulting in a decrease in blood volume and body fluids and a subsequent drop in blood pressure[81,82]. It has

been shown that curcumin, a yellow-orange pigment present in fruits and vegetables, reduces the expression of Angiotensin II Type 1 Receptor AT1R in arteries and acetylates GATA 4[83,84], and can mitigate hypertension brought on after nephrectomy by upregulating Nrf2 expression[85]. Vegetable alkaloid berberine can alleviate hypertension through vasodilatation through enhanced NO release (due to increased expression of eNOS), decreased ACE impact, balance of K+ channel activation, and release of intracellular Ca++ channels[86-89].

## 6.2 Cancer

Herbal nutraceuticals offer qualities that prevent cancer and mutation[90]. Antioxidants such as carotenoids such as beta carotene from orange and yellow fruits and lycopene are oxygen quenchers, reduce oxidative stress and are useful for cancer. Nutraceuticals limit DNA transcription in tumours and control factors that degrade DNA in cells. Cruciferous vegetables prevent tumour formation by inhibiting the enzymes that cause colorectal and lung cancer. Herbal nutraceuticals can alter the metastatic spread of cancer.

## 6.3 Diabetes

The treatment of diabetic neuropathy, nephropathy, and retinopathy involves the use of universal antioxidants such as lipoic acid and catechins, as well as spices like fenugreek and cinnamon. Insulin sensitivity is increased by calcium, magnesium, chromiumand vitamin D. Insulin-resistant patients' high plasma glucose is decreased with caffeineic acid. Insulin resistance is decreased along with fasting and postprandial glucose levels by green tea and epicatechin 3 gallate. Pomegranate and bitter melon control metabolism and move blood glucose into cells[28].

## 6.4 Obesity

Excellent anti-obesity qualities can be found in nutraceuticals such as psyllium, conjugated linoleic acidand capsaicin. Weight loss is aided by chitosan, vitamin C, fenugreek, caffeine, black grammes, green tea, bottle guard curcumin, etc. They decrease Low-Density Lipoprotein (LDL) and total cholesterol and release cytokines and leptin like IL-1 and IL-6[91].

## 6.5 Osteoarthritis

Nutraceuticals such as chondroitin sulfate, diacerin, glucosamine, oxaceprol, curcumin, banana, pomegranate, ginger, green tea, avocado, willow bark, boswellia, tipi, soybean etc are used to reduce complications in osteoarthritis. They play a significant part in controlling how genes are expressed. Antioxidants aid in the treatment of joint degradation, pain, and inflammation. Using olive oil also helps to reduce knee pain, stiffness and swelling[92].

## 6.6 Oral Diseases

Odonto nutraceuticals are high in polyphenols, proanthocyanidin sand flavonoids. Examples of these include green tea, grape extract, and cocoa seed extracts. *Aloe vera* gel helps lessen oral lichen planus pain and cure mucosal wounds. Probiotics can help prevent periodontitis, halitosis, dental cavities, malodor, gingivitisand other conditions[93].

## 6.7 Alzheimer's Disease

Alzheimer's disease is also known as senile dementia. It seems that antioxidants slow down the disease's progression. Utilising their antioxidant properties, nutrients such as beta carotene, lycopene, curcumin, luteinand lavandula can prevent brain damage caused by oxidative stress. These substances can postpone the onset of dementia[94].

## 6.8 Parkinson's Disease

Polyphenols from plants, soybeans and other phytoestrogens, stilbenes and unsaturated fatty acids are found effective against Parkinson's disease[95]. *Brahmi* is a naturally occurring brain tonic that enhances hormone release, blood circulation in the brain, mental calm, relaxationand memory. It helps in migraine, insomnia, headache, anxiety, depression and brain cell rejuvenation.

## 6.9 Eye Disorders

It has been discovered that nutraceuticals can help with age-related macular degeneration. Antioxidant-producing substances such as lutein, Docosahehexaeonic Acid (DHA), vitamin E, carotenoids, green tea, flavonoidsand coenzyme Q10 can help prevent cataracts and presbyopia. Retinitis pigmentosa can benefit from the following: vitamin C, vitamin E, carotenoids, flavonoids, caffeine, and pyruvate[96]. Rice bran, fruits, and vegetables are rich sources of lutein and zeaxanthin, which improve

vision and lower the chance of developing cataracts. Additionally supporting eye health are rice bran's folic acid, omega 3, 6, 9and essential fatty acids.

### 6.10 Stress Management

Adaptogens are naturally occurring bioactive molecules that can stop cellular damage caused by stress. They gradually improve emotional functioning, which aids in recovering from trying circumstances. Good adaptogens like ginseng and ashwagandha stimulate the synthesis of heat-shock protein 70 (HSP-70), which suppresses stress. Herbal nutraceuticals also lessen anxiety and depression, stabilise physiological systems and enhance sleep, secondary memory, homeostasisand tolerance to external stress[97].

## 7. Drawbacks of Nutraceuticals

Nutrients have certain drawbacks. Because they are mostly foods and not drugs, their mechanism of action is relatively slow. Second, there are regional variations in the content, quantityand source of each ingredient; there are no stringent laws governing food quality. Therefore, the health benefits associated with a given nutrient can vary greatly[1]. Third, due to poor bioavailability, the benefits of nutrients can be reduced or completely lost. Patients with multiple illnesses that require treatment often self-prescribe nutritional supplements. At the same time, they are not aware of drug interactions that can have harmful effects in addition to reducing the effectiveness of dietary supplements. Improperly or excessively used nutrients can have mild, moderate or severe side effects. Therefore, it is important to understand the toxicity, bioavailability and side effect profile of nutrients before using them[98, 99].

## 8. The Future of Nutraceuticals

Consumers are moving towards a healthier lifestyle as a result of increased media attention to fitness and health issues.This tendency is driving the rise of the global nutraceutical industry. Increasing rates of obesity, high blood pressure, diabetesand cholesterol, as well as rising healthcare expenses, are also propelling the market's expansion. Healthier products are increasingly becomingpopular. Enzymes are considered by many researchers as a promising area of nutritional research. The use of microbes in fermentation techniques for the preparation of new foods is also promising. However, the business is being held back by contaminated ingredients and raw materials, a lack of awareness among the population, and ambiguous regulatory rules. It is anticipated that the global market for nutraceuticals will develop at a Compound Annual Growth Rate (CAGR) of 7.6% by 2026 when it is expected to reach $734.60 billion[64]. By the end of 2025, the Indian nutraceutical marketwhich is predicted to growwill be valued at $18 billion. The introduction of 100% Foreign Direct Investment (FDI) in the nutritional supplement industry has resulted in a notable surge in foreign investments. It seems likely that the country's developing food industry will have a significant impact on the healthcare system in the coming years[100].

## 9. Conclusion

Thus we can conclude that nutraceutical development is a complex procedure that combines the fields of pharmaceuticals and nutrition. Nutraceuticals are foods or dietary ingredients that offer health advantages over those found in regular diets. They can be applied to several issues, including illness prevention and treatment, health enhancement, and well-being promotion. The study has excluded products that lack clinical proof based on precise extracts and where traditional usage predominates over verified dietary or medicinal applications. The market for mushrooms and β-glucans is enormous, but there are many different product sources. Turmeric has also received much attention in recent times. Research and Development (RandD) plays a huge role in developing nutraceuticalproducts. The gap between nutrition and pharmaceuticals, fulfilled by RandD in the nutraceutical industry includes scientific study and innovation. Major roles in RandD are to determine the safety, purity and potency of samples; to ensure and verify the consistency of ingredient dose to develop more efficient and effective methods of generating ingredients for usage in products, create new products by blending pre-existing components.

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