



A Brief Review on Nutraceuticals and its Application

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Introduction

Stephen L. Defelice, founder and chairman of the Foundation of Innovation Medicine, invented the term in 1989 as a combination of the words nutrition and pharmaceutical. Nutraceuticals are products produced from food resources that are claimed to provide additional health advantages in addition to the fundamental nutritional content present in foods. Depending on the jurisdiction, items may promise to prevent chronic diseases, promote health, slow the aging process, extend life expectancy, or support the structure or function of the body¹. Nutraceuticals are biologically active compounds found in food that have properties similar to both nutrition and medications. Nutraceuticals are natural bioactive or chemical compounds that, in addition to serving as a nutritional supplement, have health-promoting, disease-curing, or preventative qualities. Nutraceuticals are supplements that contain lipids, vitamins, carbohydrates, proteins, minerals, or other essential ingredients. Nutraceuticals have been found to be potential agents in the treatment of a variety of maladies, including cardiovascular disease^{2, 3}, diabetes^{4, 5}, atherosclerosis^{6, 7}, cancer^{8,9} and neurological disorders^{10,11}.

The causes for the trend toward nutraceuticals are as follows¹²⁻¹⁶.

1. A growing proportion of customers are concerned about rising healthcare prices.
2. People who are dissatisfied with pharmaceutical agents for health promotion are turning to nutraceuticals to improve their health and prevent chronic disease.

Abstract

Because of their putative safety, nutraceuticals have sparked tremendous interest. Nutraceuticals are nutritional supplements that are used to improve health, postpone aging, prevent disease and support the healthy functioning of the human body. Nutraceuticals are currently gaining popularity due to their nutritional and medicinal properties. They are classified as dietary supplements or herbal bioactive substances based on their source. Herbal nutraceuticals aid in the maintenance of health and the promotion of optimal health, longevity, and quality of life. Nutraceuticals have demonstrated encouraging results in the treatment of a variety of ailments, including cancer, neurological diseases, cardiovascular disease, and others. The current review provides an overview of several bioactive substances that operate as nutraceuticals (carbohydrates, lipids, edible flowers, alkaloids, medicinal plants, etc.) and their involvement in health benefits. Focus on the need for appropriate diets, health issues associated with failure to adhere to known healthy eating models, development of new nutraceuticals/functional foods/food supplements with novel health benefits, elucidation of mechanisms of action of these products, and to define and understand the analytical, formulation, and regulatory aspects of nutraceuticals. The use of nutraceuticals in the prevention of certain diseases has also been addressed.

Keywords: Nutraceutical, Dietary supplements, Herbal bioactive compounds, Application

3. Health care providers realize that our excessively processed food supply, which is derived from crops farmed with chemical fertilizers, pesticides, herbicides, and frequently genetically engineered seeds, lacks the nutrients required for optimal health.
4. People who believe in prevention rather than cure.
5. People suffering from chronic ailments who have found no relief from allopathic medication.
6. Patients with limited financial resources.

Bioactive Compounds as Nutraceuticals

Bioactive chemicals are found in trace amounts in foods, particularly fruits, vegetables, whole grains, and so on. They have a wide range of therapeutic possibilities and provide numerous health advantages in addition to basic nutritional value. Bioactive chemicals are classified into two types based on their origins: herbal sources and dietary supplements (Table. 1).

Table 1 Bioactive ingredients

Herbal bioactive ingredients	Dietary supplements
Anthraquinones	Carbohydrates
Alkaloids	Proteins
Tannins	Lipids
Carotenoids	Vitamins
Flavonoids	Probiotics
Bitters	Prebiotics
Essential oil	mushroom

Herbal Bioactive Ingredients

Therapeutic Plants Herbs have received a lot of attention over the years because of their diverse array of scents and flavors, which make them useful not only as medicines but also in cooking. Herbal bioactive substances found in herbs, such as carotenoids, coumarins, flavonoids, lignans, phthalates, plant sterols, polyphenols, saponins, sulphides, and terpenoids, are a significant category of nutraceuticals^{17,18}.

Alkaloids

Alkaloids are a unique family of substances that play crucial functions in the biological processes of animals, plants, and microorganisms. It is a heterocyclic chemical molecule with nitrogen that is used in pharmacology, medicine, and ecology¹⁹. Since alkaloids have potent physiological effects when they interact with much cellular and molecular level of organisms, they have been widely used as curative medications in the pharmaceutical industry²⁰. Alkaloids can occasionally be exceedingly harmful in small concentrations and are soluble in organic solvents²¹. In the pharmaceutical business, alkaloids from plants are widely used as anti-malarial (quinine and chloroquine), anti-cancer (vinblastine, vincristine, and taxol), and blood circulation (in the brain) boosting drugs (vincamine)^{22, 23}. The most of us love a cup of black tea or coffee, which include the pharmacologically active alkaloids theophylline and caffeine, respectively, and are essential components of the human diet²⁴. Long pepper (*Piper longum* L.) and pepper (*Piper nigrum* L.), which both contain the alkaloid piperine, are additional often used spices in Indian cuisine as well as many other cuisines²⁵. Capsicum peppers like chili and red pepper (*Capsicum annuum* L.), bird pepper or tabasco (*Capsicum frutescens* L.), Peruvian pepper (*Capsicum bac catum* L.), aji pepper (*Capsicum Chinese* Jacq.), and rocoto pepper (*Capsicum chinense* Jacq.) are some other plants that contain significant amounts of alkaloid (*Capsicum pubescens* Ruizet Pav.). According to research, piperine has significant physiological activity and is not harmful²⁶.

Saponins

Steroid saponins can be obtained from a wide range of plants, microorganisms, and animals²⁷. Aubergines (*Solanum aethiopicum* L.), capsicum peppers (*Capsicum annuum*), ginseng (*Panax ginseng*), and yucca (*Yucca schidigera*) are a few typical medicinal plants that contain saponins²⁸. Saponins are essential for a variety of pharmacological processes, such as hypoglycemic activity, lowering of LDL cholesterol and serum cholesterol, inhibition of cancer cell growth, stimulation of the cell-mediated immune system, antioxidant activity, antifungal activity, neurotrophic and neuroprotective activity, and viricidal effects²⁹.

Tannins

These are a collection of substances that include phenolic and polyphenolic chemicals. They function as astringents in our body by causing tissues to contract and structural proteins in the mucosa and skin to shrink. The prevention of lipid peroxidation, the production of super-oxides, and the completion of free radical scavenging activity are additional roles for tannins³⁰⁻³². Tannins are used to treat ulcerative colitis because they have a number of beneficial health features, including anti-inflammatory, antibacterial, antileishmanial, immunomodulatory, analgesic, anti-lymphocytic, neuroprotective, antidiarrheal, and antihypertensive actions^{33,34}. Legumes with tannin have been utilized as nutritional feed for livestock to protect it against parasites such as gastrointestinal worms³⁵.

Bitters

They are a combination of bitter-tasting chemicals that are present in many herbs. Yarrow (*Achillea mille folium*), chamomile (*Matricaria chamomilla*), horehound (*Marrubium vulgare*), peppermint (*Mentha piperita*), rue (*Ruta*), milk thistle (*Silybum marianum*), and dandelion are among common herbs that contain significant quantities of bitter (*Taraxacum*). Bitter compounds primarily affect the digestive system, which in turn causes the stomach to release digestive enzymes. Additionally, it facilitates the flow of bile from the liver, increasing appetite and facilitating better nutritional absorption from food³⁶. Patients with symptoms like gallbladder issues, liver issues, poor appetite, gastritis, sluggish bowel, and symptoms after the flu are typically advised to take bitters [37]. Other pharmacological advantages of bitters include their ability to treat cancer, to calm the nervous system, and to have antibacterial, antioxidant, anti-inflammatory, and anti-diabetic properties³⁸. Despite their disagreeable taste, the beneficial effects of bitters begin in the mouth itself, therefore oral use is required for the optimum results. Some of the bitters described in Indian Ayurveda are guduchi (*Tinospora cordifolia*), manjista (*Rubia cordifolia*), and neem (*Azadirachta indica*), as well as turmeric (*Curcuma longa*) and *Rubia cordifolia*. Because of their predilection for the liver and spleen, they are widely utilized to treat ailments³⁹.

Carotenoids

Carotenoids can be made by bacteria, fungus, algae, and plants. Carotenoids are responsible for the orange, yellow, and red colors that can be seen in fruits, vegetables, and seafood⁴⁰. Animals must obtain carotenoids through dietary intake and metabolize them in order to use them for physiological processes because they are unable to produce them on their own⁴¹. Carotenes have crucial roles in biology as antioxidants, membrane fluidic regulators, and auxiliary light-harvesting components of photosynthetic systems⁴². Apricots (*Prunus armeniaca*) and broccoli are good sources of β -carotene and lutein, while carrots and tomatoes are excellent sources of β -carotene and lycopene, pumpkin (*Cucurbita* spp.) is a good source of β -carotene, β -cryptoxanthin, lutein, and zeaxanthin, and green leafy vegetables offer both lutein and β -carotene. Few carotenoids (about 50 out of the 600 discovered) have provitamin A activity, and the three most significant ones are α -carotene, β -carotene, and β cryptoxanthin^{43,44}. Thus, eating these carotenoids can help us from developing significant eye conditions. Carotenoids serve as antioxidants and improve oxidative stress resistance in all species⁴⁵. They also have anti-cancer properties⁴⁶.

Flavonoids

In nature, flavonoids can be found as glycosides and antioxidants. Vegetables such as broccoli, green pepper, kale, onion, spinach, and tomato; fruits such as orange, grapefruit, apple, and grape; herbs such as *Citrus grandis*, *Hypericum perforatum*, and *Sophora japonica*; and soybeans are major sources of flavonoids⁴⁷. Flavonoids have a protective impact against coronary heart disease in addition to having antiviral, antiallergic, anticholinesterase, anticancer, and antioxidant properties⁴⁸. A variety of products containing flavonoids are either being researched and developed or are already being sold as functional foods and/or dietary supplements. The ADME property of flavonoids in animals has received less attention in published research, which makes it harder to anticipate the biological effects of flavonoids. This restricts the use of them as possible food sources⁴⁹.

Essential oils

The following plant components can be used to make essential oils: buds, bark, fruits, flowers, herbs, leaves, roots, seeds, twigs, and wood⁵⁰. They may be extracted using techniques like solvent or steam extraction since they are a naturally occurring combination of aromatic chemicals. A subcritical water extraction technique has also been used to extract essential oils from *Thymbraspicata* leaf material⁵¹. These volatile oils typically contain a distinctive aroma and are a blend of terpenes, aldehydes, esters, ketones, phenolic chemicals, and aldehydes. Significant levels of terpenoids are found in essential oils, which have antiseptic and antibacterial properties⁵² and stimulate the body's natural defense mechanisms against a number of infectious disorders. It has beneficial effects on and is anti-cancer, anti-inflammatory, and antispasmodic (yarrow and chamomile) on the heart and circulatory system (rosemary, ginger, and thyme)⁵³.

Anthraquinones

A variety of molecules with different biological characteristics are included in anthraquinones⁵⁴. As a result of their stimulation of muscle contraction, they frequently have a laxative effect. Aloe vera (*Aloe barbadensis* Miller), cascara (*Rhamnus purshianus*), dock (*Rumex crispus*), rhubarb (*Rheum palmatum*), and senna are among the numerous plant species that contain high concentrations of anthraquinones (*Senna alexandrina*). Researchers have found that the hydroxyanthraquinone found in aloe vera, aloe-emodin, has the ability to limit the proliferation of a variety of tumor cell lines, including lung cancer cells⁵⁵, hepatoma cells, and leukemia cells⁵⁶. Similar to this, *Rheum rhabarbarum*'s emodin and rhein also have anticancer effects⁵⁷. A particular in-vivo and in-vitro anti-neuroectodermal tumor property of the anticancer drug aloe-emodin has been reported⁵⁸. Aloe's latex contains significant amounts of anti-inflammatory anthraquinones, which are known for their ability to heal and stop pain. Anthraquinone has been found to be produced not just by plants but also by marine life. Two anthraquinones (Lupinacin A and Galvaquinone B) with anti-tumor capabilities were recently found in sea anemone from Easter Island, and a new analysis by a group of researchers in Germany suggested that it might be used as a nutraceutical⁵⁹.

Dietary Supplements

Probiotics

Probiotics, or helpful microorganisms, which improve human health, are the subject of rising research. When administered in the proper dose, probiotics are a culture of live microorganisms (which can be a single or mixed culture) that have therapeutic benefits for the recipient (FAO and WHO, 2006). Russian immunologist Elie Metchnikoff made observations and hypothesized that the consumption of fermented milk, which contains beneficial *Lactobacillus* bacteria, is the cause of the healthy and long lives of Bulgarian peasants. Probiotics are a result of these observations. Years later, it is evident that bacteria are not just static colonists but rather dynamic, symbiotic co-residents in our bodies⁶⁰. Some modern ailments, such as the increase in inflammatory and allergy disorders, are caused by a decrease in the consumption of helpful microbes as compared to our ancient ancestors⁶¹. *Lactobacillus*, *Bifidobacterium* and *Saccharomyces cerevisiae* are the three bacterial species that are most frequently used to make commercial probiotics. Consuming probiotics has been shown to enhance immune defense against pathogens, suppress auto-immune responses, shorten the duration of infectious diarrhea, increase gastrointestinal tolerance to antibiotics, improve treatment of women with bacterial

vaginosis, lessen symptoms of irritable bowel syndrome, and decrease the incidence of dental caries⁶².

Prebiotics

Prebiotics are food ingredients that, in little amounts, promote the growth of helpful bacteria, whose, when colonized by the host, has a good impact on the health of the host⁶³. Prebiotics can be thought of as food for the different bacterial species that inhabit the inside of humans and are essential to their health and wellbeing. Probiotic bacteria like *Lactobacillus* and *Bifidobacterium* are among the microbes that use prebiotic fiber as a substrate and consume it. In order to ascertain prebiotic fermentation characteristics in a variety of hosts, including humans, prebiotic compounds often undergo a wide range of in-vivo and in-vitro testing. The examined fermentation parameters are often linked to healthy colon function and metabolism^{64, 65}. Numerous food items that contain fermentable fiber are available for human nutrition⁶⁶. A substance's potential to ferment may be the only consideration for selecting it as a prebiotic⁶⁷. Some studies, however, believe that this shouldn't be used as the only criterion because food matrices are diverse and have a variety of metabolic and nutritional advantages⁶⁸. When determining if a substance is a prebiotic, it's also important to consider the fermentation products, which may be advantageous or harmful⁶⁶. The two most popular sources of prebiotics at the moment are resistant starch and fructans.

Proteins

Proteins are key constituents of food as they have organoleptic properties especially texture, tissue building, a valuable source of nutrition, and possess various other health benefits. In order to enhance the development of healthy, novel and safe foods, the use of the plant-derived nutrients is increasing as it is beneficial from both economic and environmental perspectives⁶⁹. Similarly, there is an increasing demand for plant proteins for applications in food matrices to improve the nutritional and health profiles of these food products. One of the modern-day examples is the use of legume proteins as food ingredients that have been traditionally used for derivation of oils and fats. Amongst legumes, Lupin (*Lupinus albus* L.) is the richest source of protein, its protein content is equivalent to soybean, almost 35% of its dry weight⁷⁰. Recently, interest in dietary proteins from seed has emerged around the globe for their nutritional role. They possess various therapeutic activities, such as hypoglycaemic, hypolipidemic, anti-cancer and anti-obesity activities^{71,72}. Therefore, plant proteins possess a vital role in the improvement of human health. Apart from this egg protein, which is considered as an essential source of proteins in a balanced diet, also possesses health benefits, such as anti-cancer, antihypertensive, antimicrobial, antioxidant, immunomodulatory, and protease inhibitor activities⁷³. Protein isolate has been prepared using by-products of waste generated during the milling process of pigeon pea. This protein isolate has been reported as a good source of nutraceuticals and also as an encapsulating material with bioactive properties⁷⁴.

Carbohydrates

It is the most widely distributed nutritional class, and it plays an important role in the human body. Carbohydrate molecules in the dietary matrix range from complicated to tiny. According to dietary standards, carbohydrates should account for at least 5% of total calories ingested in a balanced diet⁷⁵. Carbohydrates help with human physiology and metabolic activity. It aids in the prevention of a number of chronic diseases, including cancer, cardiovascular disease, diabetes,

obesity, and gastrointestinal disorders. Starchy carbs are an important source of energy and help keep the digestive tract healthy. Untapped research potential exists in the application of bioactive carbohydrates in functional meals⁷⁶. Inulin (fructans), fructose, as well as other oligosaccharides, for example, promote the growth rate measures how fast of health-promoting bacteria such as Bifidobacteria, which can limit the proliferation of potentially hazardous anaerobic microbes in the gut and act as immunomodulators⁷⁷. Chitosan and chitin have been used as functional dietary additives, with possible anti-obesity activity⁷⁸. According to study conducted, consuming carbs together with a suitable amount of protein has a good impact on the gut bacteria count, which has numerous benefits in humans⁷⁹. As a result, the utilization of carbohydrates as a nutraceutical offers great promise for human health.

Lipids

Lipids are a broad category of compounds that share the trait of being soluble in organic solvents but insoluble in water. Initially, it was assumed that consuming dietary fats causes weight gain and other health concerns. Recent technologies, however, combine the beneficial effects of fatty acids with triacylglycerol molecules to increase the nutritional value of lipids. Structured fats play an obvious function in lowering the caloric value of the diet to which they are added, as well as providing certain medical benefits. The link between lipid nutrition and stereospecific fatty acid position suggests that acidolysis could be used to improve the nutrition profiles of triacylglycerols. Because of such advantages of lipid isolation, more research is required for cost-effective lipid manufacturing. According to one investigation, kelp is an alternate source of nutraceuticals⁸⁰. Take Control®, Bece Proactiv, and Flora Proactiv by Unilever, CookSmart® by Procter & Gamble, Danacol® by Danone, and others⁸¹ are some of the prominent nutraceuticals on the market that include large levels of phytosterols, phytosterols, and their fatty acid esters. Aside from these items, new study indicates that flaxseed is a good source of lipids and could be used as a nutraceutical. It is projected that eating flaxseed reduces the chance of cancer and cardiovascular disease, relaxes artery smooth muscles, and lowers cholesterol levels⁸².

Vitamins

Due to their anti-oxidant properties, vitamins can be used as nutraceuticals and play a significant part in maintaining human health. These nutraceutical items may be helpful to people on special diets and smokers who are prone to vitamin deficiencies. Lack of food intake, poor body absorption, and insufficient use are causes of vitamin insufficiency. As their nutrient profiles contain adequate concentrations of the B complex vitamins (B1, B2, and B12), vitamins with antioxidant properties (such as vitamin C and E), provitamins A and E, and carotenoids, seaweeds are a rich source of vitamins⁸³. It has a beneficial effect on lung and cervical malignancies and aids in the decrease of cases of death brought on by cerebrovascular illnesses⁸⁴.

Red algae are a rich source of vitamin B12, which is typically insufficiently prevalent in vegan diets (*Porphyra* sp.). People who consume vitamin C-rich diets often have a lower chance of acquiring stomach cancer than patients who consume regular diets⁸⁵. According to a study, the combination of Shilajit and B-complex vitamins is effective in preventing Alzheimer's disease⁸⁶. For the treatment of dry eye symptoms, it is advantageous to employ oral supplementation of nutraceuticals containing vitamins, minerals, omega-3 fatty acids, and antioxidants⁸⁷. As a result, vitamins have a lot of

potential, and adding them to the diet as a nutraceutical is good for people's health.

Mushrooms

Humans have recently exploited mushrooms for both culinary and medicinal purposes. Its applications have grown to include cosmeceuticals, nutraceuticals, and medicines. Around 2000 of the approximately 12000 diverse species of mushrooms are suitable for human consumption⁸⁸. Around 35 different species are commercially produced throughout the world (*Agaricus bisporus* is the most common species⁴¹, while 200 different wild species are used for therapeutic purposes⁸⁹. Fruiting bodies contain between 50 and 65 percent carbohydrates and 20 to 30 grams of unsaturated fatty acids per kilogram of dry mass⁹⁰. In addition to polysaccharides (β -glucans), peptides, minerals, unsaturated fatty acids, dietary fiber, terpenes, glycoproteins, alcohols, and antioxidants, edible mushrooms also contain other active ingredients⁹¹. Because ergothioneine, selenium, vitamin B1 and vitamin D2 are highly bioavailable when consumed, mushrooms are regarded as great functional foods. Mushrooms are pharmaceutically significant for boosting the immune system to treat and prevent life-threatening disorders such cerebral stroke, cancer, heart disease, and hypertension because they contain unique biologically active compounds. The antibacterial, anti-diabetic, anti-tumor, anti-fungal, anti-inflammatory, antithrombotic, antiviral, and hypolipidemic effects of mushrooms are among their other qualities^{92,93}.

Application of Nutraceuticals

For more than 20 years, researchers have been attempting to link phytochemicals with potential health advantages. Research shows that consuming fruits and vegetables lowers the incidence of esophageal, stomach, lung, endometrial, oral cavity, pancreatic, pharyngeal, and colon disorders⁹⁴. The main phytochemicals that play a role in disease prevention are allium compounds; beta carotene, dietary fibers, flavonoids, folic acid, D-limonene, dithiolthiones, indole-3-carbinol, inositol hexaphosphate, iso flavones, isothiocyanates, lutein, lycopene, phytosterols, selenium, saponin Heart and blood vessel problems are referred to as cardiovascular diseases (CVD). Low intake of fruits and vegetables is associated with increased risk of CVD⁹⁵. Numerous studies have documented the beneficial effects of a diet high in fruits and vegetables on the prevention of CVD. For the prevention and treatment of CVD, nutraceuticals in the form of minerals, vitamins, dietary fibers, antioxidants, and omega-3 polyunsaturated fatty acids are recommended together with physical activity. The likelihood of vascular disease is decreased by polyphenols because they alter cellular communication and metabolism⁹⁶. Additionally, flavonoids are crucial for preventing CVD. They prevent platelet aggregation by inhibiting angiotensin-converting enzyme and cyclooxygenase enzymes⁹⁷. One of the main public health issues nowadays is cancer. Carotenoids have antioxidant properties and are helpful in preventing cancer. Lycopene and other carotenoids like it provide a protective role against cancer⁹⁸. By reducing oxidative stress and DNA damage, lycopene-rich fruits and vegetables have an anti-cancer impact⁹⁹. Tomatoes, pink grapefruit, guava, water melon, and papaya all contain lycopene. Apples contain pectin, a soluble fiber that has been shown to be protective against prostate cancer by preventing cancer cells from sticking to healthy cells in the body. Natural phenolic substances with anticancer properties include gallic acids, curcumin, ferulic acid, and caffeic acid⁹⁷. An extract of *Curcuma longa* called curcumin has been found to have anti-inflammatory, anti-oxidative, and anti-carcinogenic properties. Obesity is a global health issue that is linked to a number of serious illnesses,

including cancer, congestive heart failure, hypertension, angina pectoris, hyperlipidemia, osteoarthritis, respiratory issues, and renal vein thrombosis. The eating of high-fat foods is one of the key contributors to obesity. The potential of nutraceuticals to help manage obesity is now being studied. Nutraceuticals with putative anti-obesity benefits include capsaicin conjugated linoleic acid, Momordica charantia, Citrus aurantium, and psyllium fiber^{97, 100}. Herbal stimulants that help with weight loss include ephedrine, caffeine, chitosan, and green tea.

Conclusion

Nutraceuticals are a different source of all-natural treatments that not only treat but also prevent a wide range of fatal illnesses. They are in demand because they are more affordable and accessible than prescription medications. Long-term study is necessary to understand the function that nutraceuticals play in health and how diseases are treated. It is also necessary to conduct more study on how nutraceuticals affect disease activity and pathogenesis. It is necessary to conduct research on how bioactive compounds interact with other food components and how this interacts with their ability to act as drugs. In addition, depending on the type and quantity of bioactive compounds added to the food products, sensory qualities such as look, body, flavor, color, and texture may also be impacted. This will have an impact on how well the product functions as a whole. The microbial instability of these functional elements when they are incorporated into the food matrix is another obstacle that needs to be overcome. To boost the acceptability of these products in the global market, clinical studies must be conducted more quickly, precisely, and uniformly.

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