

A Comprehensive Review on Emerging Need for Nutraceuticals

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Abstract:

Nutraceuticals, or "bioceuticals," are alternatives to drugs or medicines that provide numerous health benefits and nutrients for humans and animals. Pharmaceuticals are used for the treatment of various types of diseases, such as cancer, diabetes, anemia, and heart disease, because of the presence of phenolic, flavonoid, and essential oil components. A comprehensive search was conducted across various online databases and search engines, including Scopus, Science Direct, PubMed, Web of Science, and Google Scholar, using specific keywords such as phytochemical compositions, traditional uses, antibacterial, ant proliferative, hypocholesterolemic, insecticidal, cardiovascular, and neurodegenerative diseases. Nutraceuticals play a crucial role in disease prevention and treatment by harnessing the healing power of plant-based materials. The nutraceutical market is a thriving multi-billion-dollar industry projected for rapid growth in the coming decade due to increased consumer awareness and a focus on improved wellness. These diverse food-derived products, including Tulsi, turmeric, papaya, berries, grapes, amaranth leaves, spirulina, and marine sources, are rich in nutrients that aid in preventing ailments such as cardiovascular diseases, gastrointestinal issues, kidney dysfunction, and liver disorders. Notably, nutraceuticals exhibit minimal side effects, are locally available, and are cost-effective, making them accessible to a wider population. With their higher efficacy, nutraceuticals contain physiologically active components that are naturally in foods or added as functional ingredients, contributing to the overall health and well-being of individuals. This review provides concise information and identify various nutraceutical food derivatives and their applications, emphasizing their potential in promoting population health and wellness. Nutraceuticals represent a highly valuable reservoir of bioactive compounds, offering great potential for integration into human food and presenting a promising avenue for managing mild to severe health conditions. Further research and exploration in this field could open new doors for using these beneficial components to improve human health and well-being.

Keywords: *Nutraceuticals, bioactive compound, Cardiovascular, Diabetes, Hypertension*

Introduction

The word "Nutraceuticals" is coined from the two words Nutra (which means the food which provides nourishment) and pharmaceutical (which means medicinal property).[1] Many dietary compounds are present in nutraceuticals, which balance the anabolism and catabolism occurring in the body. [2] In the past three years (2019-2022), COVID-19 has caused a severe health issue to millions of people worldwide, and it has mainly resulted in weakening of the immune system.[3] Nutraceutical industries are one of the few industries that profit from the COVID-19 outbreak. Immunomodulatory supplements have gained popularity over the past year and have had a substantial impact on consumer behavior and purchasing trends. Additionally, preventive healthcare practices such as the use of nutritional supplements will spread after the COVID-19 pandemic. Because of the high incidence of the virus, people have demonstrated a desire for nutritious and healthy items. The market for nutraceuticals is anticipated to expand in the upcoming years due to their high nutritional value and ability to strengthen immunity.[4] The worldwide COVID-19 epidemic has made it possible for nutraceuticals to build a significant position in the global market.[5] Nutraceuticals provide many advantages over medications, including fewer or no side effects, affordability, accessibility, numerous therapeutic effects, and a rise in health value due to bettering human health. Due to their potential nutritional benefits, safety, and medicinal effects, nutraceuticals have recently attracted considerable attention. The US spent 17% and India spent 4% of its total global health expenditures, respectively, according to the World Health Organization's Global Health Expenditure database. Healthcare GDP (WHO Indicators).[6] The tremendous amount of money used for healthcare has impacted both customers' interest in food products with health advantages as well as the research and development departments of numerous multinational corporations. [7] Nutraceuticals are classified as antioxidants, dietary fibers, inorganic vitamins and minerals, phytochemicals, prebiotics, probiotic, and herbs as functional foods based on their chemical makeup. Despite its rapid growth, the nutraceutical business is still in its early stages, given the volume of marketed goods and its contribution to the national GDP.[8] The market for nutraceuticals worldwide reached \$379.061 billion in 2017 and is projected to reach \$734.601 billion by 2026.[9] The nutraceutical and functional food market in India is now valued at US \$ 2.8 billion (2015) and is projected to reach US \$ 8.5 billion by 2022, as per the Associated Chambers of Commerce and Industries of India). The global nutraceutical industry is predicted to increase at a compound annual growth rate (CAGR) of 7.5%, from US \$198.7 billion in 2016 to US \$285.0 billion in 2021. The US market for functional foods that are high in nutraceuticals is worth \$250 billion, compared to \$150 billion for drugs. Approximately 29,000 dietary supplements are available in the US, and approximately 1000 new items enter the market each year, according to a recent report by BCC research. Nutraceutical supplements, meals, and beverages comprise the market. In 2007, the market for nutraceutical foods accounted for the largest share, valued at \$39.9 billion.[10] This is expected to increase by \$56.7 billion in 2013, at a CAGR of 6.9%. The U.S. nutraceutical market is estimated to be worth \$86 billion. Europe and Japan have slightly higher rates. It accounts for roughly 25% of their \$6 billion yearly food sales, or 47% of the Japanese market. The populace uses nutritional supplements.

This succinct analysis emphasizes how nutraceuticals are becoming a more viable option for treating various chronic conditions and managing health.[11] The worldwide demand for nutraceutical vitamin ingredients will reach \$13 billion in 2020, up 6% annually. In India, a considerable portion of the population remains dependent on natural and alternative medications because of imbalances and shortcomings in the country's national medical delivery system.

The increased demand for Indian Ayurvedic treatments has increased the market for formulations containing ashwagandha, haldi, ginger, Tulsi, and other herbs. Due to mounting scientific evidence supporting its role in the prevention of cancer, swine flu, and other diseases, vitamin D will have the fastest increase in demand. The demand for herbal and non-herbal extracts is rising steadily on a global scale.[12] Consumer interest in purportedly functional meals and nutraceuticals has recently increased. Functional foods are said to improve health and wellbeing in addition to their nutritional value and were first popularized in Japan. Similar to this, "bioactives" are dietary components that benefit human health. Nutraceuticals are bioactive substances that are isolated from original foods while retaining their health benefits.[13] They regulate homeostasis functions and boost metabolism in the body, which is required for proper functioning of the organs. It helps in the prevention of osteoarthritis (a degenerative disease), which results in stiffness and swelling in the synovium joint. [14] It is not just a source of tremendous energy but also has several medicinal and therapeutic benefits. The aim of nutritional therapy is to replace the supplementary therapy with nutraceuticals. It improves digestion and has the capability of detoxification and a good dietary fiber. [15] It is not just a source of tremendous energy but also has several medicinal and therapeutic benefits. The aim of nutritional therapy is to replace the supplementary therapy with nutraceuticals. It improves digestion and has the capability of detoxification and a good dietary fiber. [16]

Nutraceuticals are natural biologically active compounds that, apart from playing a nutritional role, promote health and possess curing and prevention features. It contains essential nutrients such as proteins, minerals, carbohydrates, and vitamins. An investigational report confirms that nutraceuticals are effective in treating chronic diseases such as cancer, diabetes, and cardiovascular diseases.[11] The study performed an experiment also called a discrete choice experiment to examine the customers' priorities for the will to pay because while choosing any product, people generally prefer the brand having the least chemicals and more natural or herbal ingredients.[17] According to the international lipid expert panel (LEP), these aids in the prevention of cardiovascular disease and focus on lowering the bad cholesterol that is low-density lipoprotein (LDL). In short, we can say that nutraceuticals are food or products that are obtained from herbal and medicinal plant sources and help in human wellbeing and prevention of chronic diseases such as anemia, calcium deficiency, osteoporosis, psoriasis.[18] To make a clear connection between "nutrients" and "pharmaceuticals," nutraceuticals were created in response to the developing understanding of the health-promoting effects of foods and food ingredients.[19] The word "nutraceutical" and the claims made about the product's qualities have caused some misunderstanding about whether or not nutraceuticals should be classified as medicinal items, even though they are by definition food products.[20] Nutraceuticals have been used to treat all medical conditions, including arthritis, pain management, cold and flu, digestion issues, insomnia, osteoporosis, blood pressure, cholesterol, depression, and diabetes.

The most pressing scientific needs in the field of nutraceuticals are for the standardization of chemicals and/or products, as well as for the proper planning, designing, and conducting of clinical trials to offer the foundation for nutraceutical health claims that have an influence on both consumers and businesses making strategic investments.[21]

Several nutraceuticals offer therapeutic benefits, such as buckwheat seed proteins, which are effective in preventing obesity and constipation by acting similarly to the natural fibers found in the diet. Green tea extract and 5-hydroxytryptophan may promote weight loss. Omega-3 fatty acids may reduce glucose tolerance in people who are predisposed to developing diabetes. Citrus fruit flavonoids appear to act as antioxidants and defend against cancer. Curry's curcumin and soy isoflavones are chemo preventive agents against cancer. Dietary phytosterols can reduce cardiovascular disease morbidity and death.[22] An illustration of the nutraceuticals is shown in **Figure 1**.

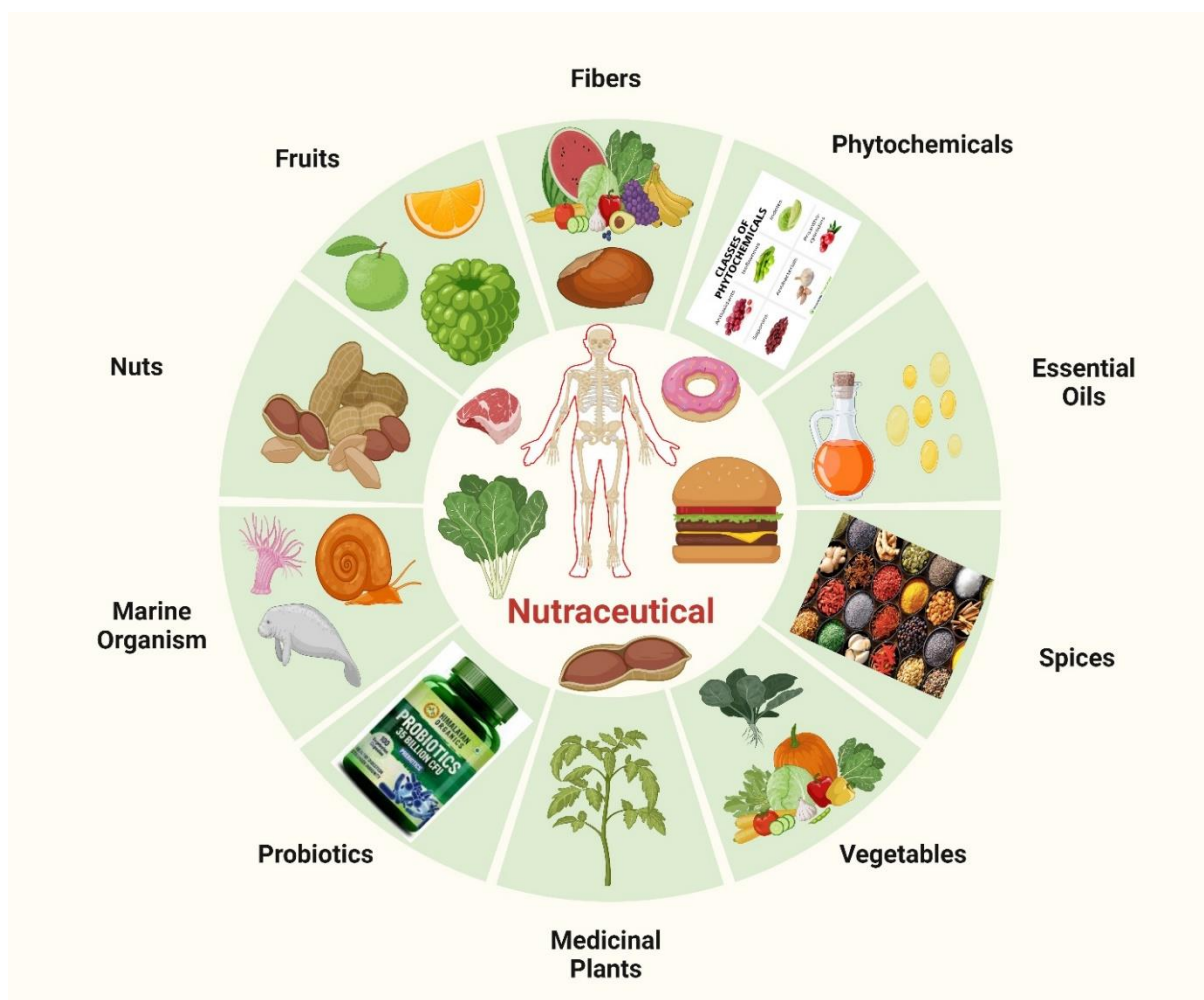


Figure 1: Various source of nutraceuticals. [23]

Rising prevalence of chronic disease

According to the Department of Biotechnology, Ministry of Science & Technology, Government of India, India, being the developing country, has the highest number of people suffering from diabetes in the world. There are around 77 million people suffering from diabetes, and it is expected to rise to 134 million by the year 2045, accounting for one-fourth of all deaths due to cardiovascular diseases. Hypertension is another major problem. The National Health Policy (NHP) of our country aims to reduce premature deaths and various non-communicable diseases by up to one third by the year 2030.[24] Today, healthcare clinicians attend to chronic patients with poor nutritional status. It results from malnutrition, inadequate dietary intake, and unhealthy eating habits. All these factors play a crucial role in the progress and diagnosis of chronic diseases.[25] The link between nutrition and chronic pain seems to be complex and involves certain mechanisms such as glucose metabolism, oxidative stress, and inflammation; therefore, it is essential to manage dietary intake and overall health.[26] We are facing many problems related to the healthcare system, such as healthcare cost i.e. unaffordable by the lower middle class and lower class families, adequate quality, and variation in access and outcomes.[27] Nutraceuticals are considered healthy sources for promoting health and prevent life-threatening disorders such as GIT disorder and diabetes. Kidney and and infections.[28] To reduce the cost of healthcare and provide quality health facilities. Nutraceuticals and functional foods play a crucial role in countering and minimizing diseases and symptomatic disorders associated with lifestyle changes.[29] Nutraceuticals or functional foods contain many essential dietary fibre nutrients that help in maintaining a healthy lifestyle and in the cure of a few diseases. These are beneficial constituents that could be isolated and purified from plant, marine, or animal sources. Predominant clinical studies have shown beneficial effects of various nutraceuticals, including food extracts and phytochemicals that aid in the reduction of inflammation and oxidation, and marine constituents are the source of omega-3 fatty acid.[30]

Shift toward preventive healthcare's

Prevention is always better than cure. Due to the rise in healthcare expenses, prevention is more important now than it was before, Increasing threats of new diseases from different variants (like covid-19) and other recent improvement clinical data collection and disease surveillance have been observed. Prevention mainly focuses on (a) Reducing the number of increasing patients with the help of effective preventive measures, and (b) To providing treatment and decelerating the progression of symptoms and diseases.[31]

Classification of nutraceuticals

Nutraceuticals, a diverse group of bioactive compounds with potential health benefits, can be scientifically classified into several categories based on their chemical composition and biological activities or traditional or non-tradition system as shown in **Figure 2**.

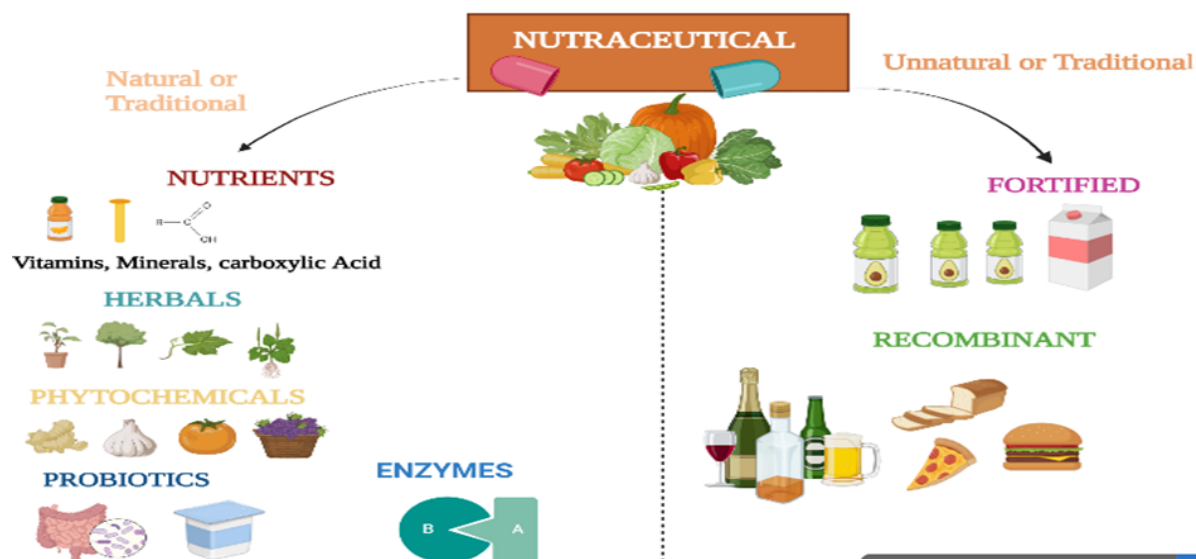


Figure 2: Schematic representation of traditional and non-traditional phytochemicals with specific medicinal properties.[32]

These include vitamins (water-soluble and fat-soluble), essential minerals, amino acids, and proteins, which play crucial roles in metabolism and tissue repair. In addition, nutraceuticals include polyunsaturated fatty acids (PUFAs), such as omega-3 and omega-6, which support cardiovascular health and inflammation regulation. Fiber, probiotics, and prebiotics contribute to gastrointestinal well-being and immune function. Phytochemicals such as flavonoids, polyphenols, carotenoids, and glycosylates exhibit antioxidant, anti-inflammatory, and anticancer properties.[33] Enzymes and coenzymes act as catalysts in biochemical reactions and aid digestion. Furthermore, antioxidants neutralize free radicals, protecting cells from oxidative damage. Marine-derived nutraceuticals offer unique bioactive compounds from aquatic sources. Herbal extracts and botanicals provide various phytochemicals with specific medicinal properties. Lastly, specialty nutraceuticals are tailored formulations designed to target specific health conditions or support specific bodily functions, such as cognitive health or joint support. Expert guidance and empirical research are essential to maximize the benefits of nutraceuticals effectively and safely.[34] Nutraceuticals can be classified on the basis of their phytoconstituents, which are bioactive compounds derived from plants that impart therapeutic and health-promoting effects, as shown in Table 1. These compounds can be grouped into several categories. First, flavonoids, such as quercetin and catechins, are known for their antioxidant and anti-inflammatory properties. Second, polyphenols such as resveratrol and curcumin, which exhibit various health benefits, including cardiovascular and neuroprotective effects. [18] Third, alkaloids such as caffeine and theobromine, which are stimulants found in coffee and cocoa, respectively. In addition, terpenoids such as carotenoids, found in fruits and vegetables, have potent antioxidant properties. Moreover, glycosylates present in cruciferous vegetables have been associated with anticancer effects. Lastly, phytosterols, such as beta-sitosterol, help in reducing cholesterol levels. These phytoconstituents contribute to the diverse array of nutraceuticals that offer promising potential for promoting overall health and well-being. [35]

Table 1: Classification of nutraceuticals on the basis of active phytoconstituents in plants

Category	Phytoconstituents	Plant Source	Health benefits	Citation
Carotenoids	Lycopene	Tomatoes, grapefruit, pink grapefruits	Anti-oxidant, anti-cancer	[³⁶]
	Lutein	Corn, avocado, spinach	Anti-cancer, protects eyes	[³⁷]
	β -carotene, α -carotene, zeaxanthin	Carrots, vegetables, orange	Eye protective, uv-protective, anti-oxidant, anti-cancer	[³⁸]
Dietary fibres	Soluble fibres	Legumes, oats, fruits	Nurtures digestive health, anti-cancer	[³⁹]
	Insoluble fibres	Whole grain, wheat	Colon cancer, nurtures digestive health	[⁴⁰]
Polyphenolic compounds	Flavanones ²³	Citrus fruits	Anti-cancer, anti-oxidant	[²⁴]
	Flavanols	Onions, apples, tea, berries	Anti-cancer, anti-oxidant	[⁴¹]
	Anthocyanins	Blueberries, blackberries	Anti-inflammatory, anti-oxidant, anti-diabetic, regulates blood sugar level	[⁴²]
	Phenolic acids	Berries, legumes	Reduces LDL cholesterol, anti-cancer	[⁴³]
	Resveratrol	Dark grapes, resins, berries	Regulates cholesterol level, increases HDL cholesterol	[⁴⁴]
	Curcumin	Turmeric root	Anti-inflammatory	[⁴⁵]
Fatty acids	Omega-3-fatty acids	Flax seed, salmon	Anti-inflammatory, anti-oxidant, anti-clotting	[³⁰]
	Monosaturated fatty acid	Tress nuts	Cardiovascular disease	[⁴⁶]

Isothiocyanates	Sulforaphane	Cauliflower, broccoli, cabbage	Anti-oxidant, aids detoxification	[⁴⁷]
Phenols	Caffeic acid & ferulic acid	Apples, pears, citrus fruits, vegetables	Anti-oxidant, eye protective, cardiovascular disease	[⁴⁸]
Plants stanols/sterols	Stanol/sterol esters	Fortified table, spreads, stanol, ester dietary	Coronary heart disease	[⁴⁹]
Tocotrienol (isoprenoids)	-	Grains, palm oil	Anti-cancer, Cardiovascular disease	[⁵⁰]
Saponins	-	Chickpeas, soyabeans	Regulates cholesterol level, anti-cancer	[⁵¹]
Probiotics/prebiotics, Lactobacilli, Bifidobacterium		Yogurt, other dairy and non-dairy applications	Improves GIT health & boosts immunity	[⁵²]
Alkaloids	Quinine	Chinchona	Anti-malarial	[⁵³]
	Tropane alkaloids Tropane alkaloids	Solanaceous members, deadly night shade	Effective in Heart disease	[¹¹]
	Morphine	Opium poppy	Analgesic, anti-depressant	[⁵⁴]
	Ergot alkaloids	Fungus	Abortive agents	[⁵⁵]
	Vincristine & vinblastine	Periwinkle	Anti-cancer	[⁵⁶]
	Coumarin, scopoletin & trigonelline	Fenugreek	Hypoglycaemic	[⁵⁷]
	Non-carotenoid terpenoids	Peryllyl alcohol	Cherries and mint	Anti-cancer
Saponins		Chickpeas, fenugreek	Regulates blood cholesterol	[⁵⁹]
Terpinol		Pulses	Anti-cancer	[⁶⁰]
Terpene		Limonoids	Anti-oxidant	[⁶¹]
Anthraquinones	Senna	Legumes and pulses	Purgatives	[⁶²]

	Barbaloin	Aloe	Laxative, effective against helminths	[⁶³]
	Hypericin	St. John warts	Analgesic	[⁶⁴]
	Capsaicin	Hot peppers	Anti-inflammatory, anti-cancer, slows down apoptosis	[⁶⁵]
	Piperine	Black peppers, jalapeno peppers	Aids in digestion	[⁶⁶]
Terpenes	Menthol	Mint family	Anti-pyretic, analgesic	[⁶⁷]
	Borneol	Pine oil	Disinfectant	[⁶⁸]
	Santonin	Wormwood	Photosensitizer	[⁶⁹]

Evidence-based Nutraceutical Practice

Clinical trials:

Clinical evidence on the drug or product for specific patients is the basis for clinical decisions made by healthcare professionals using a method known as "evidence-based practice." Evidence-based medicine combines professional judgment with observations, research from the scientific community, and the viewpoint of the patient. Benefits: Evidence-based practice has several advantages.[70] Evidence-based practice can be used to provide effective patient care, which ultimately leads to better patient outcomes. EBP strongly endorses individualized treatment plans. This strategy also enhances the professionals’ ability to provide patients with higher-quality care. EBP enables healthcare professionals to stay current on emerging trends and techniques. [71]

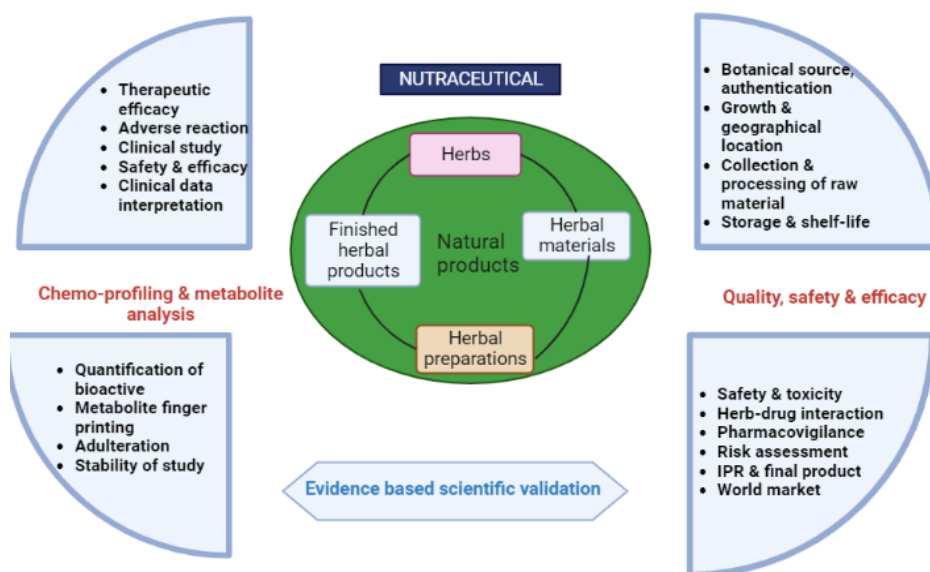


Figure 3: Evidence-based scientific evaluations. [72]

Implementing it may be hampered by an abrupt switch from evidence-based nutraceutical practice to conventional medical practice⁷². New implementation may face challenges from management or coworkers. Given that a patient may be managed by more than a single health professional, obtaining support from teammates may be difficult. Lack of time to inform all healthcare workers about evidence-based practice. [73]

Health practitioners working in remote locations may have difficulties because of inadequate access to the resources needed for evidence-based practices.[74] A shortage of facilities to find supporting data for the practice of nutraceuticals. Obstacles to the use of evidence-based nutraceuticals can arise from a lack of collaboration. Accessing research on nutrition to support practice is difficult. Lack of time can make it difficult to learn about or conduct research on the nutraceutical industry.[75] To produce relevant clinical data, numerous clinical studies are required. When extensive studies are conducted, the product's safety and tolerability are well recognized. The therapeutic value and utility of the drug must be adequately established to win over the public and medical community. For nutraceutical items, the pharmacodynamics information is obvious, but there is no information available regarding how the substance is removed or metabolized within the body or any other pharmacokinetic information. To learn more about the pharmacokinetics of nutraceuticals, more clinical trials must be conducted and more clinical data must be produced.[76] The ideal dosage for nutraceuticals has not yet been determined. For all medical conditions and populations, most dose is prepared standard. The most common dose types for nutraceuticals are oral and topical. Novel formulations are not being generated because there is less information available about the efficacy and stability of various dosage forms. The most effective way to raise awareness of nutraceuticals among the wider population is through marketing, but without sufficient proof and clinical data to back it up, this can be difficult to do.[77]

Disease-specific studies

Nutraceuticals, commonly referred to as nutritious foods or nutraceuticals, are food-derived products that offer additional health advantages over and beyond their fundamental nutritional content. Despite not being medications, they are frequently advertised as food additives and may be useful in treating some ailments. Several instances of disease-specific nutraceuticals are provided below:

Neurological diseases: The most prevalent type of dementia is Alzheimer's disease (AD), also known as senile dementia of the Alzheimer type (SDAT), primary degenerative dementia of the Alzheimer's type (PDDAT), or simply Alzheimer's. [70] Neurodegenerative conditions such as Alzheimer's disease (AD) and Parkinson's disease (PD) are largely caused by oxidative stress. Numerous studies have linked a significant intake of dietary antioxidants with a decreased risk of AD, which is crucial because preventing disease is far simpler than treating it. It is currently being investigated whether vitamin E actually decreases the course of AD. The results revealed that individuals undergoing permutation therapy degenerated at a markedly lower rate.

Alpha-lipoic acid is a strong antioxidant that helps the brain ingestion and metabolism of glucose. In a 337-day open research, Hager et al. provided 600 mg of ALA every day to 9 individuals with AD and associated dementia who were previously on typical acetylcholinesterase inhibitors. The AD and MMSE assessment scale scores of individuals who received ALA exhibited a stabilization of cognitive function, according to the results.[78] Parkinson's disease is a brain ailment that often manifests in mid to late adulthood and is caused by nerve injury in certain parts of the brain that results in rigidity of muscles, shaking, and problems walking [100]. According to Canadian experts, dietary vitamin E may offer protection against Parkinson's disease. A decrease in the clinical indicators suggested that creatine altered the characteristics of Parkinson's disease. To understand glutathione's impact on the nervous system and its antioxidant potential, researchers have also researched it.[79]

Cardiovascular diseases: Heart and blood vessel illnesses collectively known as cardiovascular diseases (CVD) include hypertension (elevated blood pressure), coronary heart disease (heart attack), peripheral vascular disease, cerebrovascular disease (stroke), and heart failure. In 1999, CVD accounted for one-third of all fatalities worldwide, and by 2010, it would have surpassed all other causes of mortality in emerging nations. For the prevention and treatment of CVD, nutraceuticals such as antioxidants, dietary fiber, omega-3 polyunsaturated fatty acids (n-3 PUFAs), vitamins and minerals are advised in addition to physical activity. It has been established that chemicals found in grapes and wine, such as polyphenols, change cellular signaling and metabolism, which is linked with a decrease in artery disease.[80] By inhibiting the "suicide" enzyme cyclooxygenase, which ruptures prostaglandins, flavonoids prevent blood pressure-raising angiotensin-converting enzyme (ACE) and platelet stickiness and aggregation. The tiny vessels that deliver oxygen and vital vitamins and minerals to all cells are strengthened by flavonoids, which also safeguard the vascular system. In hypertension, the blood pushes against the artery walls with such force that it can ultimately result in health issues, including heart disease. Pomegranate juice, grape seed extract, hesperidin, and melatonin have been found to lower blood pressure. Natural compounds known to lower the risk of stroke and facilitate smooth heart functions are called flavonoids. The carotenoid family member lycopene lowers blood pressure and oxidative stress. Garlic consumption lowers blood pressure and is helpful in treating individuals taking medication.[81]

Obesity: An energy imbalance occurs when consumption of energy exceeds energy expenditure, resulting in obesity. Modifying one or both of the elements of energy balance is necessary to combat obesity, whether through prevention or treatment. Thus, diet intake, consumption of energy, and energy storage are three different areas of the energy equilibrium systems that can be targeted by weight control strategies (including a functional diet strategy).

Diabetes: Diabetes is a long-term metabolic illness in which the cell of the islets of Langerhans in the pancreas, which naturally produces the hormone insulin, is completely or partially deficient. As a result, the body is unable to use carbohydrates. Isoflavones, which are phytoestrogen with properties comparable to those of human estrogen, have been used by people all over the world. Consumption of green tea and cinnamon tea can benefit diabetics. Psyllium-derived dietary fibers have been used to lower lipid concentrations in hyperlipidemia and manage blood sugar in diabetic individuals.[80]

Anti-inflammatory: This is the body's response to damage or irritation and is characterized by pain, swelling, redness, and heat. Rheumatoid arthritis, for instance. Many researchers have undertaken numerous studies on the anti-inflammatory benefits of fish oil, primrose oil, curcumin, fenugreek, licorice, coriander, tomato, and carrot. Changes in oxidative stress (malondialdehyde), inflammatory biomarkers (erythrocyte sedimentation rate [ESR], C-reactive protein [CRP], seromucous, fibrinogen, tumor necrosis factor [TNF], prostaglandin E2]), and antioxidant status (total antioxidant capacity, vitamin C, vitamin E, retinol, beta-carotene]) were observed during these studies. According to studies, most nutraceuticals have favorable effects on chronic inflammatory disorders, which may be because they contain a combination of the aforementioned phytochemicals.[82]

Synergistic and Combinational Therapies

The improvement of specific functionalities when other chemicals are present is known as the synergistic effect. Numerous nutraceutical component combinations have been shown to have enhanced therapeutic effects, including powerful antioxidant, anti-inflammatory, anti-obesity, anti-cancer, and cardioprotective effects. The following are explanations of the applications that have received the most recent media attention:

Anti-inflammatory effect: By bringing leukocytes to the damaged area, inflammation is essential for pathological processes such as wound healing and infection prevention. It also controls the physiology of many disorders. However, the inflammatory reaction frequently tends to harm healthy cells. According to reports, malignant diseases are closely associated with chronic inflammation [57]. According to several studies, nutraceutical components combined with one another have anti-inflammatory properties.

For instance, the synergistic actions of curcumin and quercetin decrease the formation of inflammatory agents such as leukotrienes and prostaglandins because both substances are known to inhibit the emission of nitric oxide by macrophages and the production of reactive oxygen species. According to earlier research, quercetin suppresses histamine release, lipoxygenase, phospholipase A2, and cyclooxygenase activities, whereas curcumin lowers edema in rat paws because of its powerful anti-inflammatory effect. In contrast to their separate effects, a combined therapy for acute inflammation in rats showed larger results, with a several-fold decrease in oxidative stress, inhibition of tumor necrosis factor-alpha (TNF-alpha) release, and increase in heme oxygenase-1 mRNA expression.[83]

Cardioprotective effect: It is desirable to use efficient and secure alternative treatment procedures for controlling lipid and glucose levels because of the long-term exposure to therapeutic medications for the management of cardiovascular risk factors, including dyslipidemia and hyperglycemia. By utilizing different molecular mechanisms of action and targets, effectively lowering plasma cholesterol concentrations and broadening the range of modulating action toward additional targets in addition to cholesterol⁶⁴, nutraceuticals can achieve pronounced synergistic effects. According to studies, the synergistic effects of nutraceuticals produce advantageous effects on cardiovascular diseases. Ibrahim Fouad (2020) outlined how coenzyme Q10 and omega-3 work in concert to provide cardioprotective benefits in rats with hypercholesterolemia.

In contrast to the control groups, the combination therapy dramatically increased the serum levels of creatine kinase while also inhibiting oxidative stress. The antioxidant abilities of both chemicals may have contributed to the cardioprotective effect by lowering lipid peroxide levels and inducing an increase in NO and GSH concentrations in heart tissue.[84]

Anticancer effect: Nutraceuticals work together more effectively than they do separately to cure cancer thanks to their synergistic effects. The synergistic advantages of various nutraceutical combinations for treating various forms of cancer. Hepa 1-6 hepatocellular carcinoma cells, which exhibit significant anticancer effects from polyphenols along with dosage and time-varying relationships, respond well to the combined effects of curcumin and resveratrol. Using Hoechst 33258 staining, Hepa 1–6 cells were treated with polyphenols alone and in combination to induce apoptosis. In the curcumin and resveratrol combination, [93] morphological alterations, including nuclear shrinkage, resulting in cell apoptosis were more pronounced. The combination of curcumin and resveratrol (3 μ M each) synergistically causes apoptosis in MCF-10ATr (cigarette smoke-induced breast cancer epithelial cells) via an increase in the Bax/Bcl-xL ratio and p21Waf/Cip1 level and a decrease in intermediates of the Hedgehog–Gli cascade both in vitro and in vivo, with an almost 10-fold reduction in the IC50 compared with individual compounds.

Anti-diabetic effect: Nutraceutical synergism-based treatment is a new field with promising results for the treatment of diabetes and its consequences. Curcumin's antidiabetic action can be improved when coupled with piperine and quercetin. This triple combination reduces plasma glucose, cholesterol, and triglycerides, increases low-density lipoproteins (LDL), and improves body weight in streptozotocin (STZ) and nicotinamide-induced diabetic rats better than curcumin alone. Curcumin bioavailability is enhanced in the presence of piperine and quercetin.[85]

Future Prospects and Challenges

The term "nutraceuticals," referring to products derived from food sources with health benefits beyond basic nutrition, has gained significant popularity in recent years. The nutraceutical sector presents both promising opportunities and challenging obstacles for the future.[86] Growing consumer demand arises from a rising interest in natural health-enhancing options and a more health-conscious population, fostering a sizable market for nutraceuticals. Advancements in research and technology, particularly in understanding the medicinal properties of various food compounds and improving extraction, formulation, and delivery methods, drive innovation and expand product offerings. Personalized nutrition is anticipated to become more popular with advanced genetic testing and data analysis, allowing tailored nutraceuticals to cater to individuals' unique health needs and genetic makeup, enhancing their efficacy. Combining nutraceutical constituents in synergistic ways or integrating them with traditional medicines offers the potential for better health outcomes and comprehensive treatment options for specific illnesses. [87] Regulatory support is expected to provide a conducive environment for the nutraceutical industry's growth, ensuring safety, effectiveness, and accurate labeling of products through clear standards and regulations.

[88] However, challenges persist, such as limited scientific validation for efficacy and safety claims, intellectual property issues surrounding well-known natural compounds, difficulties in marketing and educating consumers about nutraceutical advantages and risks, and ensuring affordability and accessibility of these products, especially from uncommon or exotic sources. Overcoming these challenges and capitalizing on opportunities will require continuous research, stakeholder collaboration, regulatory support, and ethical marketing practices to unlock the vast potential of the nutraceutical sector in promoting health and well-being. [89 90 91]

Safety Considerations in Nutraceuticals

Varieties of nutraceuticals are available in the market; most of them are safe for human consumption, but some may produce adverse reactions in humans. Safety considerations in nutraceuticals are of utmost importance to ensure consumer well-being. Here are some key safety considerations in nutraceuticals:

Quality control: Nutraceuticals derived from natural sources may be susceptible to contamination with toxins, heavy metals, or microbial pathogens. Manufacturers should implement rigorous testing procedures to monitor and minimize the presence of such contaminants, ensuring the safety of the final product. [92] Plant derived nutraceuticals have alkaloids that react with proteins, producing abnormal cell functioning and necrosis and, in some cases, have the potential to cause cancer. [93] Stringent quality control measures are crucial to ensure that nutraceutical products are safe for consumption. Manufacturers should adhere to Good Manufacturing Practices (GMP) and conduct regular quality checks to ensure consistency, purity, and absence of contaminants or adulterants. [94]

Interaction of nutraceuticals with other substances or drugs: Nutraceuticals often include herbs or botanical extracts, which can interact with prescription medications. Some herbs may interfere with the metabolism or action of certain drugs, leading to adverse effects or reduced efficacy. It is important for individuals taking medications to consult healthcare professionals to identify potential herb– drug interactions before using nutraceutical products.[95] Ginseng increases the activity of certain drugs because it is a P-glycoprotein pump inhibitor. [96]

Processing of Nutraceuticals: Nutraceutical formulations may contain excipients (inactive ingredients) such as fillers, binders, or coatings. Some individuals may have sensitivities or allergies to certain excipients. Manufacturers should disclose the complete list of ingredients, including excipients, on product labels to enable consumers to make informed choices.[97] Nutraceutical products should be packaged in materials that ensure the preservation of their quality and safety. Proper packaging helps protect against contamination, oxidation, moisture, and light exposure, which can degrade the product and compromise its safety and efficacy.[98] Nutraceutical manufacturers should ensure consistency in the composition and quality of their products across different batches. This helps maintain the safety and efficacy of the nutraceuticals and prevents any variations that may impact consumer health.[99]

Regulatory Status of Nutraceuticals: Compliance with relevant regulations and guidelines is vital for ensuring the safety of nutraceuticals. Regulatory bodies, such as the United States The Food and Drug Administration (FDA) or the European Food Safety Authority (EFSA) establish safety standards, ingredient approvals, and labeling requirements to protect consumers. Manufacturers and regulatory agencies should establish mechanisms for monitoring and reporting adverse events associated with nutraceutical use. This facilitates the identification of potential safety issues, enabling prompt action to protect consumers. Nutraceutical manufacturers may consider obtaining certifications such as ISO 22000 (Food Safety Management System) or NSF International's Good Manufacturing Practices (GMP) to demonstrate their commitment to safety and quality. Compliance with international standards can provide consumers with additional assurance regarding the safety of products.[100]

Conclusion

Future therapeutic advancements are expected to greatly benefit from the use of nutraceuticals. Community health authorities view nutraceutical prevention and treatment as a potent instrument for preserving health and combating nutritionally induced chronic and acute disorders, thereby ensuring the best possible health, endurance, and quality of life. In this comprehensive review, we have delved into the emerging need for nutraceuticals, a field that is gaining prominence considering the rising prevalence of chronic diseases and the global shift toward preventive healthcare. The classification of nutraceuticals spans dietary supplements, functional foods, and beverages, each of which plays a crucial role in supporting health beyond basic nutrition. Examining the mechanisms of action of nutraceuticals, we explored their anticancer, antioxidant, and anti-inflammatory activities, shedding light on their potential therapeutic applications. Clinical trial evidence forms a cornerstone in substantiating the efficacy of nutraceuticals. Through a rigorous analysis of various trials and studies, we have observed compelling evidence supporting the use of nutraceuticals in addressing conditions such as hypertension and diabetes. The principles of evidence-based nutraceutical practice, outlined in a systematic five-step approach, underscore the importance of scientific rigor and clinical validation in guiding nutraceutical interventions. Highlighting the significance of nutraceuticals in the context of chronic diseases, our review underscores their pivotal role in preventive healthcare. With an aging population and growing awareness among consumers, the demand for natural and personalized nutraceutical solutions is escalating. Technological advances further contribute to the field by facilitating innovative delivery systems that enhance bioavailability and efficacy. As we look into the future, nutraceuticals hold promising prospects in supporting healthy aging and addressing a spectrum of health concerns. However, challenges such as regulatory complexities and the need for robust clinical evidence persist. Navigating these challenges requires concerted efforts from researchers, policymakers, and industry stakeholders. In this comprehensive review, we synthesize the current state of nutraceutical research, emphasizing its relevance in the context of chronic disease management and preventive healthcare. The convergence of scientific evidence, technological innovation, and burgeoning consumer awareness sets the stage for the continued evolution of nutraceuticals as integral components of health and wellness strategies.

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