



# A REVIEW ON NUTRACEUTICAL USED AS AN ALTERNATIVE TO PHARMACEUTICAL

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## **ABSTRACT**

In the present context, individuals express profound concerns about their well-being due to significant changes in lifestyles, characterized by a surge in working hours and heightened psychological pressures. These shifts have resulted in a notable uptick in the prevalence of severe diseases. Simultaneously, dissatisfaction prevails regarding the costly, high-tech approach to disease treatment and management. Consequently, there is a growing demand for nutraceuticals and phytonutrients, with people increasingly relying on these for diverse therapeutic purposes. Nutraceutical products are acknowledged not only for their positive impacts on health, reducing the risk of cancer, heart diseases, and related conditions, but also for their efficacy in preventing or addressing issues such as hypertension, high cholesterol, excessive weight, osteoporosis, diabetes, arthritis, macular degeneration, cataracts, menopausal symptoms, insomnia, diminished memory and concentration, digestive upsets, and constipation. Nutraceuticals have gained trust in alleviating headaches and migraines induced by stress. Additionally, certain nutraceutical products are promoted as remedies for thinning hair, lack of confidence, poor complexion, varicose veins, alcoholism, depression, and lethargy. This chapter endeavors to categorize various types of nutraceuticals, providing examples and exploring their applications in treating diverse disorders. Furthermore, it delves into the design and development of dosage forms to enhance the delivery of nutraceuticals, outlining both their significance and the challenges associated with implementation.

**Keywords:** Lifestyles; Life-threatening diseases; Disease treatment; Nutraceutical, health

## INTRODUCTION

Nutraceuticals, a term coined by Stephen De Felice in 1989, originates from the fusion of "nutrition" and "pharmaceutical." De Felice defined nutraceutical as a substance, either a food or a part of a food, that confers medical or health benefits, encompassing disease prevention and treatment [1]. However, this terminology isn't widely embraced globally and is often substituted with "dietary supplements" to comply with stringent regulatory requirements. On closer examination, nutraceuticals differ from dietary supplements as they are expected to contribute to disease prevention or treatment rather than merely supplementing the diet. The U.S. FDA does not endorse the term nutraceutical, preferring to categorize such products as food-derived items adding extra value to basic nutritional components. Another misnomer associated with nutraceuticals is "functional foods," defined as foods prepared using "scientific intelligence." However, when these foods aid in preventing or treating diseases beyond anemia, they fall under the category of nutraceuticals. This broad category includes isolated nutrients, plant products, diet supplements, processed cereals/drinks, and genetically modified products [3]. Global lifestyle changes have led to a shift in dietary habits, resulting in lifestyle disorders like obesity and type-2 diabetes. Cardiac dysfunctions such as ischemic heart disease and stroke are prominent causes of mortality worldwide, and nutraceuticals are increasingly recognized as effective in managing these conditions. Nutraceuticals find application in various clinical conditions, including inflammation, immunodeficiency, allergy, arthritis, malignancies, indigestion, depression, sleep disorders, hypertension, and blood cholesterol control [4]. Notably, nutraceuticals often offer more than clinical benefits, making them attractive to consumers. Unlike drugs that undergo rigorous clinical trials before reaching the market, nutraceuticals are exempt from such regulatory processes. This exemption, combined with the global belief in the efficacy and safety of natural products, contributes to the expanding nutraceutical market projected to reach USD 722.49 billion by 2027 with CAGR of over 8%. The nutraceutical market has undergone significant transformations with advancements in technologies like nanotechnology and the development of procedures and instruments for quantitative and qualitative analysis. However, challenges remain, such as indescribable details regarding dosage, drug-nutraceutical interactions, and effects on individuals under specific clinical conditions. Patients often fail to disclose nutraceutical consumption during drug therapy, increasing the risk of interactions that could impact treatment outcomes. Biotechnologists are actively working to enhance the nutritional value of plants and crops to maintain homeostasis. Products marketed as functional foods, dietary supplements, or nutraceuticals may exhibit variability in quality and must undergo stringent analysis to meet proper standards. This overview covers the history, classification, chemistry, regulations, and explores the role of nutraceuticals in drug delivery and therapy.

## **History**

The history of nutraceuticals traces back to ancient times, with Hippocrates (460-370 BC), known as the father of modern medicine, laying the groundwork through his famous statement "Let food be thy medicine and medicine be thy food." He pioneered the concept that specific foods could serve as preventive or therapeutic solutions for diseases, alongside traditional drug treatments. The Roman physician Galen further contributed to this idea by leveraging his professional expertise to design diet regimens aimed at maintaining the health standards of entire populations[5]. The early nineteenth century marked the beginning of nutrition research, spearheaded by François Magendie. His experimental research questioned whether foods lacking nitrogen could still provide essential nutrition, prompting scientists to expand their focus beyond proteins, carbohydrates, fats, and minerals. Nicolai Lunin's experiments with mice supported this hypothesis, revealing that certain components in milk were crucial for nutrition but did not fit into the traditional categories. The discovery of vital nutrients, including vitamins, stemmed from such research findings[6,7]. Throughout history, humanity has relied on natural offerings for managing physiological dysfunctions. Botanicals derived from plants like Vinca Rosea and Taxus brevifolia have been used in cancer management, while Ginseng, a traditional Chinese medicine with a history spanning over 2000 years, is still used in chemotherapy. Ancient healthcare systems, such as Ayurveda, provide evidence of using food for disease prevention and treatment. Egyptians recognized the medicinal value of spices like coriander, fennel, cumin, garlic, and turmeric, considering them as valuable as precious metals like gold. Honey, with its various pharmacological effects, finds mention in the Bible (Old Testament, proverb 24:13) and has been used for wound healing, antibacterial, anti-inflammatory, antifungal, antiviral, and antidiabetic purposes. As scientific knowledge evolved over time, experiences with clinical problems led to dietary alterations becoming remedies. For instance, addressing scurvy among ship crews was achieved through a diet rich in vitamin C, while iodine-rich salt proved effective in preventing goitre. In summary, the development of scientific knowledge over time intelligently modulated food habits for the prevention and treatment of diseases, giving rise to modern-day nutraceuticals.

## **CLASSIFICATION**

The classification of nutraceuticals is essential for understanding their diverse applications. The following categorization is based on their uses:

**Traditional Nutraceuticals:** This category comprises nutraceuticals directly obtained from nature, such as lycopene in tomatoes, omega-3 fatty acids in salmon, or saponins in soy.

Further classifications within traditional nutraceuticals include:

## 1. Chemical Constituents:

- Nutrients: Primary metabolites like amino acids, various vitamins, and fatty acids have well-defined functions in metabolic pathways. Plant and animal products, along with vitamins, offer health benefits and aid in curing diseases related to the heart, kidneys, lungs, etc.

- Herbals: Nutraceuticals combined with herbs have a significant impact on preventing various chronic diseases. For example, salicin present in willow bark (*Salix nigra*) has clinically proven anti-inflammatory, analgesic, antipyretic, astringent, and antiarthritic properties.[11]

- Phytochemicals: Classified based on phytochemicals, flavonoids (a class of secondary metabolites present in most plants) have over 4000 varieties and have been clinically proven to prevent various diseases such as cancer, diabetes, heart diseases, and kidney problems through their antioxidant properties.[12]

## 2. Probiotic Microorganisms:

- Probiotics play a crucial role in maintaining a healthy intestinal flora and creating a friendly environment. For example, the consumption of *Bacillus bulgaricus*. Various probiotic products are available in the market with nutrients to counter pathogens and treat ailments related to the human body[13]

## 3. Nutraceutical Enzymes:

- Enzymes, proteinous in structure, act as biocatalysts, easing metabolic rates and expediting life processes. Enzyme supplements can address medical problems related to the gastrointestinal tract, such as GERD, constipation, diarrhea, or ulcerative colitis. Enzymes may also be a beneficial option for diabetic patients.

- Nontraditional Nutraceutical ,: This category includes foods enriched with supplements or biotechnologically designed crops to enhance nutrient levels. There are two main types:

### 1. Fortified Nutraceuticals:

- This involves fortification at the agriculture level or the addition of compatible nutrients to main ingredients. Examples include minerals added to cereals, flour fortified with calcium, iron, and folic acid, and milk fortified with cholecalciferol for vitamin D deficiency.[14]

### 2. Recombinant Nutraceuticals:

- This category involves energy-providing foods prepared through genetic engineering. An example is the production of yogurt and cheese.

Class /components	source	Potential benefit
Beta-carotene	Carrots, various fruits	Neutralizes free radicals, which may damage cells; bolsters cellular antioxidant defenses
Lycopene	Tomatoes	May contribute to maintenance of prostate
Mono saturated fatty acids	Tree nuts	May reduce risk of coronary heart disease
Flavonols	Onions, apples, tea, broccoli	Neutralize free radical, which may damage cells;bolster cellular,antioxidation defences
Soy protein	Soybeans and soy-based food	May reduce risk of coronary heart disease
Lactobacilli, bifidobacteria	Yogurt, other dairy and nondairy applications	health and systematic

Fig -1. Classification of Nutraceutical based on chemical groups

## **NUTRACEUTICALS IN DRUG DELIVERY**

In light of the sharp increase in the global nutraceutical market, there is a heightened focus on refining delivery methods for these products. An ideal nutraceutical must exhibit biological activity and efficient absorption within the human body. Given that nutraceuticals are primarily absorbed through oral routes, a central concern revolves around their absorption by the gastrointestinal (GIT) tract and their fate following rapid metabolism. Consequently, the challenges lie in understanding the absorption mechanisms and pharmacokinetics of these products. This challenge has spurred extensive research into delivery approaches, with nanotechnological interventions emerging as the most promising and extensively explored. The nano-scale delivery of mnutraceuticals significantly influences their absorption, distribution, and efficacy enhancements.[16] Examples include delivery systems such as nanoemulsions and nano-micelles, specifically designed to enhance the oral bioavailability of nutraceuticals[17]. Nanocarriers not only amplify absorption and bioavailability but also offer protection against GIT degradation and first-pass metabolism, addressing challenges faced by various nutraceutical products. Ongoing research, including modern drug delivery approaches like nano-sized self-assembled structured liquid (NSSL) technology, aims to further enhance efficacy.

Despite these advancements, the impact on the cost of nutraceuticals remains a crucial factor influencing consumer acceptance and future use. The nutraceutical market is evolving, with ongoing trials and emerging therapies addressing issues related to diseases such as cancer, diabetes, and neurodegenerative conditions[18]. In the forthcoming years, nutraceuticals are poised to make substantial strides in the market .



SI No.	Delivery Approach	Nutraceutical	Intended Effect	Reference
1	Nano-complex	$\beta$ -carotene, folic acid, curcumin and ergocalciferol	Nutraceutical Delivery	[25]
2	Phytosome	Silymarin	Oral delivery	[26]
3	Nutraceutical conjugated gold nanoparticle	Quercetin, Andrographolide	Leishmaniasis	[27,28]
4	Nanospheres and Nanocapsules	Curcumin	Oral delivery	[29]
5	Metal Nanoparticles	Garlic, cayenne pepper	Antibacterial activities	[30]
6	Colloidal nanoparticles	Curcumin	Anticancer oral delivery	[31]
7	Nano hydrogel	Curcumin, Caffeine	Oral delivery	[32]
8	Liposome delivery	Ginseng extract, Curcumin	Oral delivery	[33]
9	Solid Lipid Nanoparticles (SLNs)	$\alpha$ -acid Lipoic acid	Topical Delivery	[34]

Table -1 - Different delivery approaches for Nutraceuticals

## **CONTRIBUTIONS OF NUTRACEUTICALS IN THERAPEUTICS**

Nutraceutical products offer various pharmacological benefits, including anti-aging properties, protection against chronic diseases, maintenance of body homeostasis, prevention of cardiovascular diseases, support for nervous system health, management of metabolic disorders like diabetes, addressing neurodegenerative diseases such as cancer, protein deficiency, ophthalmic conditions, allergic problems, and Parkinsonism [19]. This section of the chapter will provide insights into the contribution of nutraceuticals in managing a range of clinical conditions..

## **NUTRACEUTICAL IN ALLERGIC DISORDERS**

Allergy ,a common disorder, arises from hypersensitivity in the human immune system. Clinical management is challenging as many causes of allergies are either unknown or difficult to trace. Allergic reactions can range from mild irritation to severe ones, such as acute respiratory distress, leading to various physiological changes in the

body [26]. Allergic conditions are often linked to hematological changes, including an increase in white blood cell and basophil count. Quercetin, a plant-derived bioactive compound, is frequently employed in nutraceuticals for allergy management due to its impact on low-density lipoprotein [27]. Eucalyptus essential oil, derived from the eucalyptus plant, is another plant extract commonly used in nutraceuticals for allergy management [28].

## **NUTRACEUTICAL IN CARDIOVASCULAR DISEASE**

Cardiovascular issues rank as the leading global causes of mortality, as reported by the World Health Organization. Manifesting in various forms such as cardiac failure, vesicular blockage, hypertension, and stroke, these conditions may lead to death or necessitate urgent interventions like angioplasty and bypass surgery. Approximately 50% of cardiovascular diseases can be averted through proper nutrition, including vitamins, antioxidants, omega-3 fatty acids, dietary fiber, and minerals. Physical exercise is also recommended for managing cardiovascular health. Flavonoid compounds, prevalent in fruits and vegetables, are designed as natural agents for addressing cardiovascular problems. These compounds inhibit specific enzymes and processes, reducing cardiovascular risks [25]. Substances like melatonin, serotonin, dietary indoleamines, and tannis are explored as natural elements to minimize cardiovascular risk. Omega-3 fatty acids, found in fish oil, are utilized as supplements to lower lipid and bad cholesterol levels in the treatment of cardiac arrhythmia. Consumer acceptance of these natural approaches in heart disease management is linked to the belief that they pose no residual side effects.

## **NUTRACEUTICAL USED IN CANCER THERAPY**

The complexity in current cancer treatment primarily stems from the side effects of conventional therapies and the emergence of drug resistance. A global survey projected 15 million new cancer cases in 2020, indicating a 50% increase in cancer incidence. Traditional cancer treatments include chemotherapy, radiation therapy, and surgery, but adopting a healthy lifestyle with an antioxidant-rich diet is considered a preventive measure against cancer. Natural compounds and plant extracts in nutraceuticals are promising candidates to address the limitations of conventional treatments, offering fewer side effects and compounds that may overcome resistance. Recent research highlights the potency of carotenoids like lycopene in various cancers, making them key components in nutraceutical formulations. Plant extracts rich in biochanin, flavonoids, tannins, and bioactive compounds such as curcumin and gallic acid exhibit remarkable effectiveness against diverse cancers. Nutraceuticals containing  $\beta$ -carotene and docosahexaenoic acid are found to be active in prostate cancers due to their free radical scavenging activity. Regular consumption of fruits provides the body with diverse nutraceuticals like cysteine, Vitamin C, Vitamin E, and lycopene, offering protection against different types of cancer. Some biotransformed products from glucosinolates demonstrate efficacy against colon, lung, breast, and liver cancers. Ongoing clinical trials are

exploring the potential of specific nutraceuticals, including lycopene, green tea, and Vitamins D and E, in managing prostate cancer.

## **NUTRACEUTICAL IN MANAGEMENT OF DIABETES**

Diabetes, a prevalent metabolic disease, ranks among the top ten causes of mortality globally, according to the World Health Organization. Obesity is a major contributor, with over 50% of worldwide cases associated with lifestyle changes, particularly in type 2 diabetes. Conventional medications for diabetes often come with diverse adverse effects, creating a demand for alternative approaches[24]. Herbal medicines and dietary supplements are gaining attention in preclinical trials for diabetes management. Phytoestrogen, such as genistein, demonstrates efficacy in treating type 2 diabetes and contributes to a significant reduction in mortality rates. Omega-3 fatty acids and ethyl esters of n-3 fatty acids are also utilized in diabetes management. Nutraceuticals containing lipoic acid and dietary fiber like psyllium are integrated to address diabetic neuropathy, hyperlipidemia, and blood sugar control. Various medicinal plants are reported to exhibit activity in controlling type 2 diabetes. As research progresses, these alternative approaches offer potential benefits in the comprehensive management of diabetes.

## **NUTRACEUTICAL IN ALZHEIMER'S DISEASE**

Alzheimer's is a neurodegenerative disease affecting over 26 million people worldwide, typically starting with mild cognitive impairment and progressing to Alzheimer's, often leading to death. Primarily occurring in individuals aged 60 and above, it remains incurable to date. Scientific reports suggest that women are more susceptible to this disease than men, possibly linked to stress-related factors. Certain nutraceutical products like  $\beta$ -carotene, lycopene, curcumin, and lutein show promise in Alzheimer's management. Research indicates that extracts from plants such as *Lavandula* and *Zizyphus jujube* may be beneficial in treating Alzheimer's by contributing to memory enhancement. Ongoing studies explore the potential of natural compounds in addressing the challenges posed by Alzheimer's disease.

## **NUTRACEUTICAL IN OPHTHALMIC DISORDERS**

Age-Related Macular Degeneration (AMD) poses the risk of severe complications, including blindness, which can be mitigated through the use of vitamins and compounds such as lutein, n-3 fatty acids, and zeaxanthin. Polyphenolic compounds, carotenoids, and certain marine-derived substances are potent antioxidants that can prevent AMD. Astaxanthin, a carotenoid present in sea animals like shrimp, salmon, and sea bream, exhibits significant activity in addressing ophthalmic issues, deriving its efficacy from marine sources. Lutein, another carotenoid found in foods like sweet potatoes, carrots, mangoes, and corn, is known for its role in preventing visual disturbances associated with AMD. Incorporating these compounds into one's diet may contribute to the prevention of age-related macular degeneration.



## **THE FUTURE OF NUTRACEUTICAL**

A significant portion of global attention in healthcare is directed toward maintaining proper health, where nutraceuticals play a crucial role. Heightened awareness of adverse effects associated with pharmaceutical drugs has led to increased interest in nutraceuticals, offering diverse benefits from vitamins to plant-based compounds. Nutraceuticals are gaining popularity for addressing complex clinical conditions such as cancer, diabetes, and cardiovascular diseases, with high consumer acceptance attributed to lower health risks compared to synthetic drugs.[30] Consumers are increasingly interested in various nutraceuticals to relieve stress, enhance energy, improve mental alertness, and manage metabolic disorders. To stay competitive in the global market, nutraceutical companies focus on innovation, utilizing advertising through print and web media to attract a wider customer base. Leading countries like the U.S.A, Germany, China, and the U.K. are investing significantly in nutraceutical research, foreseeing substantial growth in the future, particularly in addressing critical issues like antibiotic resistance.

## **Conclusion**

While the common myth suggests that age is just a number, the reality is that our body's defense mechanism weakens with age, increasing the risk of various degenerative diseases and age-related disorders. Nutraceutical products, comprising natural ingredients, have emerged as preventive measures against these conditions. Ongoing research focuses on the efficacy of nutraceuticals in treatment and natural therapies. The market for nutraceuticals has seen significant success due to their proven effectiveness against various diseases, leading to a high demand for these natural products. The nutraceutical industry is rapidly growing in both the food and pharmaceutical sectors. The market is expanding worldwide with a gradual increase in dietary supplements, food products, and beverages incorporating nutraceutical components. The future development of nutraceutical products holds great promise in combating deadly diseases, contributing to overall health and well-being. Despite existing gaps in the understanding of nutraceuticals, there is a need for a shift in mindset toward adopting a healthier lifestyle and dietary choices, fostering the concept of "Health for All."

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