

Neutraceuticals Role in the Alignment of Diseases Linked with Hepatoprotective Remedies

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Abstract

Nutraceutical is a combination of the words “nutrition” and “pharmaceutical.” In general, nutraceuticals are foods or parts of foods that play a substantial role in changing and sustaining proper physiological function in humans. Despite significant breakthroughs in targeted therapy, there are no entirely effective medications for sustaining liver function, assisting in the regeneration of hepatic cells, and providing organ protection without toxicity. The use of some natural medicines, such as plants and fruits, has played an important role in human health care: various scientific

investigations have shown that the presence of phytochemicals has good effects on liver protection. Natural remedies for liver function and other disorders are also included in the review. Investigate the use of nutraceuticals as an alternative treatment for various diseases. In this situation, plant-based natural products (nutraceuticals) play a critical role.

Introduction

Urbanization, industrialisation, stressful schedules, and changing cultures have all had a significant impact on human lifestyles during the previous five decades. These forces have influenced people's eating habits, forcing them to eat quickly, eat pleasant food on the go, eat fast food, and eat junk food. These habits have had a direct impact on our nutritional aspects of food, reducing the quantity and quality of nutrients over time. Immune dysfunctions, metabolic problems, and degenerative diseases have all increased as a result of these changing dietary patterns. People have become more aware of their health in recent years and are worried about health management. Revolutions in medicine, phytomedicine, nutritional science, the food business, and health care have sparked widespread interest among health professionals and the general public in the recent two decades. Nutraceuticals, food products, and phytonutrients have all made significant progress recently. It's a fantastic notion created by pharmaceutical corporations for wellness, disease prevention, and treatment. Ayurvedic therapeutic principles are inextricably linked to a healthy Aahar. Aahar has been used as both food and medicine in the past. Rasayana (Rejuvenation therapy) is a comprehensive concept in Ayurveda that encompasses much more than modern nutraceuticals [1].

Nutraceutical

The term "nutraceutical" initially appeared in a survey conducted in the United Kingdom, Germany, and France, in which consumers ranked food as being more important than exercise or inherited factors in achieving excellent health (2). Stephen De Felice, founder and chairman of the Foundation for Innovation in Medicine (FIM), Cranford, NJ, invented the phrase "nutraceutical" in 1989, combining the words "nutrition" with "pharmaceutical" [3,4]. Nutraceuticals, according to De Felice, are "foods (or parts of foods) that give medicinal or health advantages, including illness prevention and therapy." Nutraceuticals, on the other hand, are defined by Health Canada as "a product derived from foods but offered in the form of pills, powder (potions), or other therapeutic forms not normally associated with foods" [5, 6]. Nutraceuticals can be found in a variety of goods from (a) the food industry, (b) the herbal and dietary supplement sector, (c) the pharmaceutical industry, and (d) the newly integrated pharmaceutical/agribusiness/nutrition conglomerates. It could include isolated nutrients, herbal products, nutritional supplements, and diets, as well as genetically modified "designer" foods and processed foods including cereals, soups, and beverages [7]. Figure 1

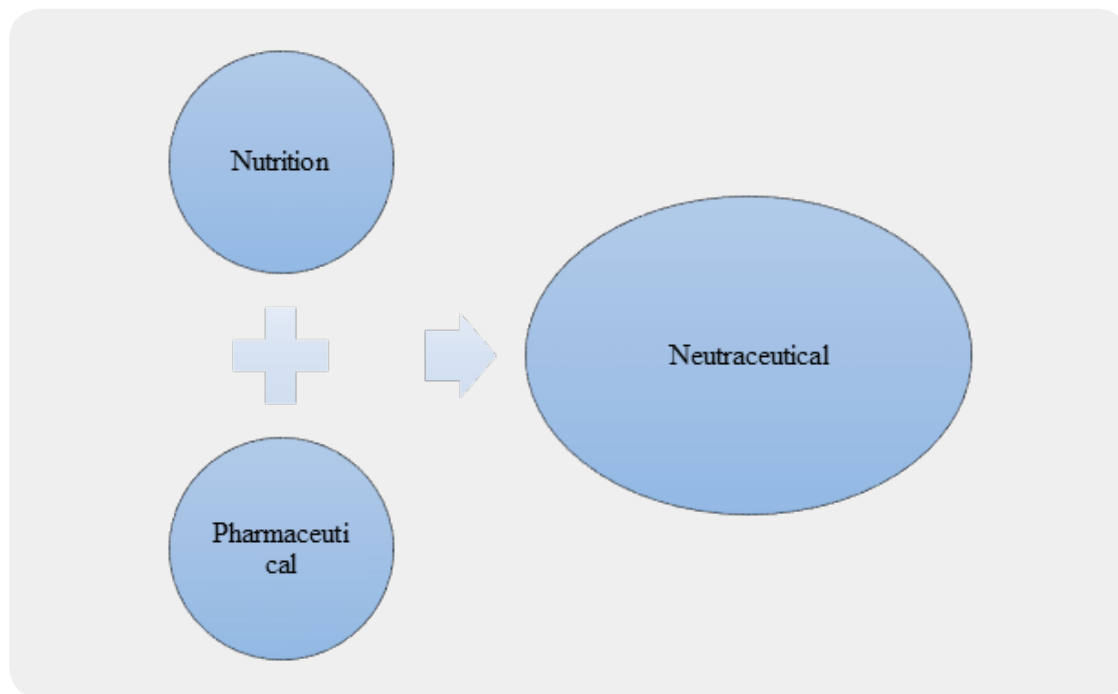


Figure 1: Nutraceutical graphical image

Anti-arthritis, cold and cough, sleeping difficulties, digestion, and the prevention of some malignancies, osteoporosis, blood pressure, cholesterol management, pain relievers, depression, and diabetes are just a few of the therapeutic areas covered by nutraceuticals [2,8]. Herbal/natural goods, dietary supplements, and functional foods are the three primary areas of the nutraceutical industry [9,10]. Herbal/natural products and dietary supplements are the fastest growing segments among these [11].

In this developing nutraceutical industry, research and development is at an all-time high. The most pressing scientific need is for the standardisation of nutraceutical substances or products, as well as the meticulous development and execution of clinical trials to provide the foundation for health claims that will have an influence on both consumers and nutraceutical enterprises.

Different Types of Nutraceuticals

1. Dietary Supplement: A dietary supplement is a product that contains dietary elements derived from food and is meant to complement the diet with additional nutritional value. These can be found in liquid, capsule, pill, or tablet form. It is applicable to the nutraceutical good. Dietary supplements are often sold in tablet form, such as the vitamin B supplement seen above.

A dietary supplement is a product taken by mouth that contains a “dietary element” intended to enhance the diet, according to the Dietary Supplement Health and Education Act (DSHEA) of 1994 in the United States. Vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues and metabolites are examples of “dietary ingredients” in these goods. Dietary supplements can be

extracts or concentrates and come in a variety of formats, including tablets, capsules, liquids, powders etc., [12].

Dietary supplements are not required to be authorised by the US Food and Drug Administration (FDA) before being marketed, but manufacturers must register with the FDA and follow current good manufacturing practises (cGMPs). Dietary supplements may only be marketed to support the structure or function of the body, and may not claim to treat a disease or condition, with the exception of a few well-defined exceptions. They must also include a label that states: These statements have not been evaluated by the Food and Drug Administration. This item is not meant to be used to diagnose, treat, cure, or prevent any illness. The FDA has reviewed and authorised a health claim as an exemption. In some cases, the FDA specifically specifies the exact phrasing that is permitted.

- a) **Nutrients:** Vitamins, minerals, amino acids, fatty acids, and antioxidants are examples of dietary constituents.
- b) **Herbals:** With the help of herbals, nutraceuticals has a lot of promise for improving health and preventing chronic diseases. Flax seed oil and powder, for example, are high in omega-3 fatty acids, which are anti-inflammatory, analgesic, antipyretic, astringent, and antiarthritic.
- c) **Phytochemicals:** Phytochemicals are nutraceuticals that are secondary metabolites. These are non-nutritive plant compounds with defence or disease-prevention properties. Polyphenols, isoflavonoids, phytoestrogens, carotenoids, limonoids, phytosterols, glucosinolates and polysaccharides are the most common phytochemicals. Phytochemicals in the diet may provide health benefits, including protection against malignancies, coronary heart disease, diabetes, high blood pressure, inflammation, microbial, viral infections, psychotic diseases, spasmodic conditions, ulcers, osteoporosis, and related disorders.
- d) **Probiotics:** These are live microbial feed supplements that help to improve the microbial balance in the intestine. Lactose intolerance, severe diarrhoea, and antibiotic-associated gastrointestinal adverse effects are all treated with probiotics. They aid in the formation of β -galactosidase, a particular enzyme that hydrolyzes the problematic lactose into its component sugars. The bacteria *Lactobacillus* and *Bifidobacteria* are the most significant probiotics.
- e) **Prebiotics:** Prebiotics are nutraceuticals that aid in the growth of probiotic bacteria. These are dietary substances that have an effect on the host by affecting the composition or metabolism of gut flora specifically. These are short-chain fructo-oligosaccharides with distinct chemical structures that humans are unable to digest. Consumption of prebiotics increases *Lactobacillus* and bacterial growth in the gut, which aids metabolism. It aids in lactose tolerance, detoxification, dyslipidaemia, constipation alleviation, and the treatment of some cancers.
- e) **Nutraceutical Enzymes:** Enzymes are a vital component of the human body that perform a variety of biological tasks. Many symptoms of hypoglycemia, hyperglycemia, digestive issues, and obesity are alleviated by adding enzyme supplements to one's diet. Some others also [1].

2. Functional food/Fortified nutraceutical: Ordinary food with components or substances added for a specific medicinal or physiological advantage rather than just nutritional effect is known as functional food. Japan was the first to establish the notion of functional food in 1991.

Nutraceuticals are functional foods that aid in the prevention or treatment of diseases other than anaemia. It refers to food that has been fortified with additional nutrients or substances. Milk fortified with vitamin D, orange juice enhanced with calcium, cereal flour reinforced with fibre and folic acid are just a few examples. During processing, functional foods are fortified or enriched, and then advertised as giving some value to customers. Additional supplemental nutrients, such as vitamin D, are sometimes added to milk.

Functional foods, according to Health Canada, are “regular foods with components or ingredients added to provide a specific medicinal or physiological advantage other than a simply nutritional one.” All functional foods must meet three criteria: they must be (1) present in their natural state, rather than in the form of a capsule, tablet, or powder; (2) ingested on a daily basis; and (3) regulate a biological process in the hopes of preventing or controlling disease [1].

3. Farmaceuticals/Recombinant Nutraceuticals: Farmaceuticals is a combination of the terms “farm” and “pharmaceutical.” Farmaceuticals is more commonly connected with medical uses of genetically altered crops or animals in agricultural circles. Biotechnology is used to make energy-giving foods including bread, wine, fermented starch, yoghurt, cheese, vinegar, and others. Biotechnology allows for the manufacture of probiotics and the extraction of bioactive components using enzyme/fermentation methods, as well as genetic engineering [1].

4. Medical Food: Medical foods are formulated to be consumed or administered internally under the supervision of a physician, and are intended for the specific dietary management of a specific disease or condition for which distinct nutritional requirements are established by the medical evaluation based on recognised scientific principles. The FDA regulates medicinal foods, and they must be prescribed or overseen by a physician. Supplements for inborn defects of amino acid metabolism, hyperhomocysteinemia, pancreatic exocrine insufficiency, and cachexia in cancer patients, for example.

More broadly, nutraceuticals can be classified in two groups: [1] Figure 2

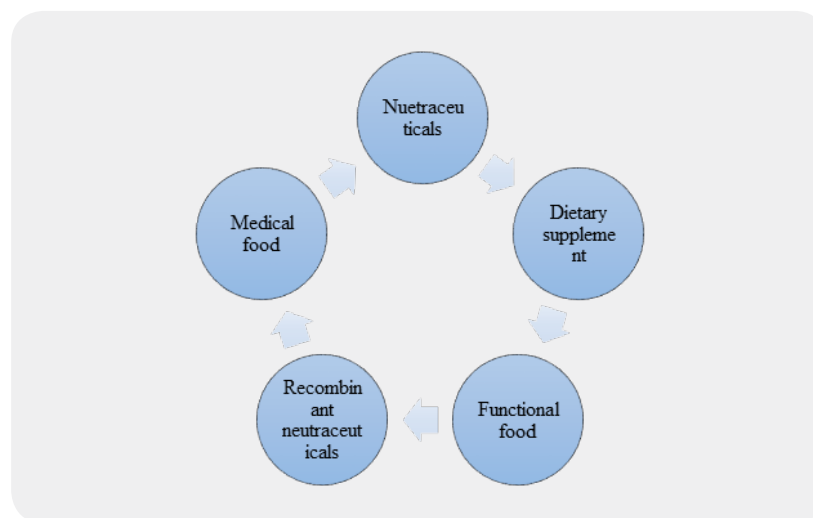


Figure 2: Different types of nutraceutical

1. Potential nutraceuticals
2. Established nutraceuticals

Use of Nutraceuticals in the Treatment of Various Alignments

Rice Bran (Cardiovascular Diseases, Eye Sight)

Rice bran improves cardiovascular health by lowering serum cholesterol levels, lowering the level of (LDL) and increasing the level of (HDL). The higher the ratio, the greater the chance of coronary heart disease. Rice bran is high in the antioxidants Lutein and Zeaxanthin, which help to improve vision and lower the risk of cataracts. Rice bran contains omega-3, omega-6, omega-9, and folic acid, all of which are beneficial to eye health [13].

Corn (Heart Attack, Lung Cancer)

Corn contributes to heart health not only because of its fibre, but also because of the high levels of folate it contains. Corn maintains homocysteine, an intermediate product in the methylation cycle, a key metabolic activity. Homocysteine causes blood vessel damage such as heart attack, stroke, and peripheral vascular disease. It has been calculated that consuming 100 percent of the daily value (DV) of folate will reduce the number of heart attacks by 10% on its own. (13). Cryptoxanthin, a natural carotenoid pigment, is also found in corn. Cryptoxanthin has been shown to lessen the risk of lung cancer by 27% when used on a regular basis [13].

Dietary Polyphenols (Diabetes)

In recent years, there has been emerging evidence that plant-food polyphenols may be distinct nutraceuticals and supplemental treatments for many elements of type 2 diabetes mellitus due to their biological features. Long-term diabetes consequences such as cardiovascular disease, neuropathy, nephropathy, and retinopathy can be prevented by polyphenolic substances [13].

Sorghum (Against Pathogen)

3-deoxyanthocyanidins, which are abundant in the bran of various cultivars, are the principal dietary source for 3-deoxyanthocyanidins [13]. Sorghum's pathogen defence mechanism is based on an active process that results in large amounts of 3-deoxyanthocyanidin phytoalexins accumulating in affected tissues [13,14].

B-Carotene (Cancer)

Vitamin A is mostly obtained from beta-carotene, which contains anti-oxidant qualities, that aid in the prevention of cancer and other disorders. Beta carotene is the most active antioxidant among the carotenes. Lung, colorectal, breast, uterine, and prostate cancers appear to be protected by alpha and beta carotenes, as well as gamma carotene and the non-convertible carotenes lycopene and lutein. The most frequent type of

carotene is B-carotene, which can be found in yellow, orange, and green leafy fruits and vegetables. Carrots, spinach, lettuce, tomatoes, sweet potatoes, broccoli, cantaloupe, oranges, and winter squash are examples of these vegetables [13].

Nutraceuticals (Alzheimer's Disease)

The most common form 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. The numerous Nutraceuticals used to treat Alzheimer's disease are as follows: a) Antioxidants, such as vitamin E and vitamin C, are one type of antioxidant. b) Ginkgo biloba: Ginkgo biloba is one of the most researched herbs in terms of memory, cognition, total brain performance, and, of course, Alzheimer's disease. c) Huperzine alpha: Huperzine alpha, also known as huperzine A, is a plant chemical derived from *Huperzia serrata*, or club moss. It is a sesquiterpene alkaloid that inhibits acetyl cholinesterase in a strong and reversible manner [15].

In the Treatment of Diet-Related Diseases:

Diet-related diseases are on the rise in Western countries, owing to the increased availability of high-calorie foods and a sedentary lifestyle. Obesity, diabetes, atherosclerosis, and neurodegeneration are all important diet-related diseases with low-grade inflammation as a shared pathogenic denominator. Because of their propensity to produce anti-inflammatory responses, functional foods and nutraceuticals may constitute a unique therapeutic approach to prevent or reduce diet-related illness. Intestinal T regulatory cells activation and homeostatic modulation of the gut microbiota, in particular, have the potential to lower low-grade inflammation in diet-related illnesses [15].

Table 1: Nutraceuticals and their uses [13].

	Chemical constituents	Source	Uses
Carotenoids	Lycopene	Guava, papaya, water melon, grape fruit	Reduces cholesterol levels, anti-oxidants, protects against cancer.
	β - Carotene	Vegetables, fruits, oats, Carrots.	Antioxidants, protection of cornea against uv light
	Lutein	Spinach, corn, avocado, egg yolk	Protect eyes against age related muscular degenerations, cataracts, anticancer activity(colon)
	Saponins	Beans like soya beans, chickpeas.	Very effective against colon cancer, reduces cholesterol level.

Polyphenolic Compounds	Flavonones	Citrus fruits	Different types of Anti-oxidant & anti-cancer activity.
	Curcumin	Turmeric root	Strongly anti-inflammatory and strongly anti-oxidant
	Flavonols	Broccoli, tea, Onions, fruits like Apple etc.	Antioxidant activity
Dietary fibre	Soluble fibre	Beans like Legumes, cereals like oats, barley, some fibrous fruits	Maintenance of a healthy digestive tract & have anticancer activity.
	Insoluble fibre	Whole grain foods wheat and corn bran, Nuts, etc.	Maintenance of a healthy digestive tract, and have Anticancer (colon) activity.

Natural Remedies Hepatoprotective Effects

Nopal (Cactus pear) and tuna (Cactus pear fruit) “Opuntia ficus-indica”. Opuntia plants are the most common Cactaceae family members. Because of bioactive substances such as vitamin C and vitamin E, polyphenols, carotenoids, flavonoid (such as kaemferol, quercetin, and isorhamnetin), taurine, and pigments, the fruits of this plant, known as prickly pear fruits, are considered a functional food [16]. These pigments have been found to have beneficial qualities in redox-regulated pathways involved in cellular development and inflammation, and there have been no reported harmful effects in people [17].

They also cause DNA fragmentation in the liver and chromosomal abnormalities in bone marrow cells, as well as increased bcl2 antiapoptotic protein expression and decreased bax expression. The authors also proved that Cactus has an antigenotoxic effect by reducing damage to the genetic material of the liver and bone marrow caused by both toxins during or after treatment with B(a)P or alfa fetoprotein B1 (AFB1), and that Cactus has an antigenotoxic effect by reducing damage to the genetic material of the liver and bone marrow caused by both toxins [18]. Similarly, other researchers have discovered that CCE can block the harmful effects of B(a)P and/or AFB1 by modulating the expression of p53 in a way that causes increases in its related genes, such as bax and bcl2. As a result, the scientific group has determined that the cactus cladode extract is successful in protecting against both carcinogens’ harm, and they have also advised that Opuntia ficus-indica be considered as a plant having hepatoprotective potential [19,20].

Chamomile (Matricaria chamomilla or Chamomilla recutita)

Chamomile (Matricaria chamomilla or Chamomilla recutita) is a diuretic, expectorant, antiseptic, antiphlogistic, febrifuge, sedative, anti-inflammatory, and anticarcinogenic annual herb belonging to the Asteraceae family. Chamomile tea, like black or green tea, has been shown to modulate the function of liver cytochrome P450 sub CYP1A2 [21,22].

Silymarin (*Silybum marianum*)

St. Mary's thistle, also known as *carduus marianus* in southern Europe, and scientifically known as *Silybum marianum*, is a Mediterranean native plant of the Asteraceae family [23,24].

Since 1960, German scientists have investigated the milk thistle fruit chemically, isolating a crude extract containing active chemicals called silymarin, which have hepatoprotective properties. The primary components of silymarin are silybin A, silybin B, isosilybin A, isosilybin B, silychristine A, silychristine B, and silydianine, which were discovered in 1975 [23,25]. The chemical ingredients of silymarin are flavonolignans, which are a mix of flavonoids and lignin structures. [23,26].

With well-understood mechanisms of action, *Carduus marianus* is one of the most useful herbs for the oral treatment of toxic liver damage. In both acute and chronic liver disorders, silymarin has been utilised as a protective therapy [23,27]. The multiple mechanisms of its protective qualities include suppressing toxin penetration into hepatic cells, raising SOD activity and glutathione tissue levels, preventing lipid peroxidation, and promoting hepatocyte protein synthesis.

Because of the phenolic character of its flavonolignans, silymarin's liver-protective effect can be connected to its antioxidant qualities. It also prevents substances harmful to the liver from accessing hepatocytes by encouraging liver cell regeneration and cell membrane stability [28]. In addition, silymarin has been shown to reduce the risk of getting some malignancies [29]. The molecular targets of silymarin in cancer prevention are specific proteins involved in apoptosis and cell cycle regulation.

The above-mentioned compounds, together with two more related analogues, have been tested for antiproliferative/cytotoxic action against human prostate cancer cell lines in extremely small amounts. The highest strong action has been found in isosilybin B [23,28]. The isolation of six isomers has allowed for a preliminary examination into the structure-activity relationship in the prevention of prostate cancer. Furthermore, Silymarin has inhibited UVA-induced oxidative stress, which can cause skin damage. As a result, topical administration of silymarin could be a useful method for preventing skin cancer [29].

Silymarin's hepatoprotective capabilities, derived from the phenolic character of flavonolignans, could be proved by its antioxidant properties. It also promotes liver cell regeneration and cell membrane stability to prevent liver-toxic substances from entering hepatocytes [30].

Flavonolignans have been demonstrated to have antifibrotic and anti-inflammatory properties [31], owing to their capacity to suppress leukotriene formation.

Blue Green Algae *Spirulina* (*Spirulina maxima*, *Spirulina platensis*, and *Spirulina fusiformis*)

Spirulina is a free-floating blue-green tiny filamentous alga. It is an organism capable of storing a variety of bioactive molecules, including: [32] proteins (60-65% dry weight) containing essential amino acids; [33] polyunsaturated fatty acids (linoleic acid); [34] vitamins (B12 and E); [35] polysaccharides; [5] minerals (Na, K, Ca, Fe, Mn, and Se); and [36] pigments (chlorophyll, c-phyco cyanin, allophycocyanin, b-carotene,

lutein, and zeaxanthin). The concentration of the components varies from species to species, although the phytochemicals c-phycoyanin (12.6 percent in dry spirulina) and significant percentages of dietary zeaxanthin are always present in their biomass [37].

For its biological actions against health disorders, there is a variety of research evidence. In conclusion, antioxidant, anti-inflammatory, hypolipemic, antihypertensive, antidiabetic, antimicrobial, neuroprotective, antianemic, immunostimulant, anticarcinogenic, and hepatoprotective properties were discovered [38-41].

Propolis (bee glue)

Propolis is a natural resinous substance collected by bees from various portions of plants, shoots, and exudates. It has a wide range of biochemical properties, including antioxidant, anti-inflammatory, antibacterial, and antifungal properties [42]. Furthermore, it has the potential to prevent cardiac changes as well as chronic degenerative disorders like diabetes and cancer [43,44].

β -glucans

β -glucans are a type of polysaccharide found in the intermediate layer of the cell wall of yeasts, algae, fungi, and some bacteria, as well as cereals (such barley and oats) [45,46]. Due to their immunological activity, these polysaccharides have recently gained significant economic importance; additionally, numerous studies have demonstrated their antiviral, antiparasitic, antifungal, antimicrobial, antioxidant, antigenotoxic, antitumor, antimutagenic, and anticlastogenic potential [47]. Despite the fact that β -glucans have a variety of therapeutic benefits, research into their hepatoprotective potential has been limited due to the field's novelty [48].

Conclusion

Nutraceuticals have been shown to provide health advantages and the capacity to prevent disease, and should be consumed in accordance with their approved recommended consumption. The existing evidence for several natural treatments' hepatoprotective properties against toxic substances that induce liver damage. Finally, these foods and natural chemicals may provide an alternative to pharmacological therapy choices for liver problems.

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