

REVIEW ARTICLE

Nutraceuticals: A Review

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Abstract

Around 2500 years ago, “Let food be thy medicine and medicine be thy food” were the words said by Hippocrates. Nutraceuticals are the isolated product obtained from foods, mostly available in medicinal forms and play a vital role in improving health, provides protection against chronic diseases. Nutraceuticals are widely being used rather than medicines because they reduces side-effect and have positive physiological effects on the human body. Nutraceuticals have also been developed for treating a variety of diseases like colon cancer, diabetes and Alzheimer’s disease. Nutraceuticals are derived from various sources such as medicinal plants, marine organisms, vegetables and fruits. In 2006, the Indian government passed Food Safety and Standard Act to regulate the nutraceutical industry. In this review, an attempt has been made to discuss all aspects of Nutraceuticals- Definition, categories, classification, present status, properties with their therapeutic benefits, their use in various diseases, marketed products, application, future and future aspects.

INTRODUCTION

The term 'nutraceutical' was coined by combining the terms 'nutrition' and 'pharmaceutical' by Stephen Defelice MD, founder and chairman for innovation in Medicine, New Jersey, in 1989. According to him, 'nutraceuticals are food or part of a food that provides health benefits and are used for prevention or treatment of a disease'.¹ Hippocrates (460-377 BC), known as the father of modern medicine stated, 'Let food be thy medicine and medicine be thy food' to establish the relationship between appropriate foods for health and their therapeutic benefits.² In human health, nutraceuticals play a major role in treating various diseases like obesity, cardiovascular diseases, cancer, osteoporosis, arthritis, diabetes, cholesterol etc. They help in maintaining our normal physiological functions.³

Categories of Nutraceuticals

1. **Nutrient:** A feed constituent should be available in the form and given at a level that will help support the life of an animal. Some of the feed nutrients are proteins, fats, carbohydrates, minerals and vitamins.
2. **Dietary Supplement:** A product that contains one or more of the following dietary ingredients: vitamin, mineral, herb or other botanical, amino acid (protein) and also includes concentrates, constituents, extracts or metabolites of these compounds.
3. **Nutraceutical:** Any non-toxic food component that has scientifically proven health benefits, including prevention and treatment of disease.
4. **Herbals:** Herbs or botanical products are used as concentrates and extracts that provide various remedies to treat acute and chronic diseases.⁴

Advantages of Nutraceuticals

1. Reduced side effects.
2. Increases health benefits.
3. Provide dietary supplements naturally.
4. Easily available and cheap.
5. It provides food for populations with special needs (eg: nutrient-dense foods for the elderly).¹

Disadvantages of Nutraceuticals

1. **Bioavailability:** Nutraceuticals are being eliminated from the body and do not provide any medicinal benefit with poor bioavailability.
2. **Impact of Placebo Effect:** Consumers may not use nutraceuticals accurately for healing illness, when the body is often able to recover on its own.
3. **Product Quality Issues:** Nutraceuticals from the international market may claim to use organic ingredients, but the lack of regulation may compromise the safety and effectiveness of products.
4. **Safety and Interactions with Other Drugs:** The problem is that many of these products do not provide consumers with proper information about their safety and effectiveness, possible side effects, interaction with prescription medicines or the effect they have on existing medical conditions.⁵

CLASSIFICATION OF NUTRACEUTICALS

The nutraceuticals are classified into different groups, which are described in the Table 1 below: ⁶

Table 1. Classification of nutraceuticals

S.No	Functional Ingredients	Source	Medicinal Use
1.	Carotenoids: Alpha and Beta-carotenoids	Carrots, fruits, vegetables	Neutralize free radicals may cause damage to cells.
2.	Lutein	Green vegetables	Reduce the risk of muscle degeneration.
3.	Lycopene	Tomato products (Ketchup, sauces)	Reduce the risk of prostate cancer.

4.	Dietary fibre, Insoluble fibre	Wheat, Bran	Reduce the risk of breast or colon cancer.
5.	Beta glucan, soluble fibre	Oats, barley, psyllium	Reduce the risk of cardiovascular disease.
6.	Fatty acids: Long chain omega-3 fatty acid DHA/EPA	Salmon and other fish oil	Reduce the risk of cardiovascular diseases, improve mental, visual functions.
7.	Conjugated linoleic acid (CLA)	Cheese, meat products	Improve body composition, decrease risk of certain cancers.
8.	Phenolics: Anthracyanides, Catechins, Flavanones, Lignans	Fruits, Tea, citrus, vegetables, Flax, rye	Prevention of cancer, renal failure.
9.	Tannins	Cranberries, coca, chocolate	Improve urinary tract, reduce risk of cardiovascular diseases.
10.	Plant Sterols: Stanol, ester	Corn, soy, wheat, wood oil	Lower blood cholesterol levels by inhibiting cholesterol absorption.
11.	Prebiotics/Probiotics	Jerusalem, artichokes, shallots, onion powder	Improve quality of intestinal microflora, gastrointestinal health.
12.	Minerals: calcium, selenium, potassium, Zinc, copper	Food	Important constituent of balanced diet.
13.	Soya phytoestrogens: Isoflavones, Daidzein, Genistein	Soyabean and other soy based foods	Protect against heart disease and some cancers, lowers LDL and total cholesterol.

Table 2 lists some common medicinal plants that are used traditionally as nutraceuticals.²⁶⁻²⁷

Table 2. Some common medicinal plants used as nutraceuticals

Plant Species	Common Name	Therapeutic Uses	Form Of Use
<i>Allium sativum</i>	Garlic	Antiseptic, diuretic	Leaves sap
<i>Aloe vera</i>	Ghrit Kumari	First degree burns, cuts and abrasions, antiulcer	Sunscreen, skin lotions
<i>Artemisia annua</i>	Artemisia	Fever, upper respiratory tract infections	Shoot decoction
<i>Borage officinalis</i>	Bugloss	Skin care, anti-inflammatory, blood purifier	Herb, leaves and flowers
<i>Capsicum annum</i>	Red pepper	Anti-arthritis, anti-oxidant action, stimulant	Fresh and dried fruit, powder
<i>Curcuma longa</i>	Turmeric	Reduces inflammation, antioxidant	Dried root, whole powdered
<i>Ephedra sinica</i>	Ephedra	Mild anti-asthmatic, nasal congestion	Dried stems, capsules, tablets, tinctures
<i>Foeniculum vulgare</i>	Fennel	Stomach bloating, stimulant	Whole seed, capsule, tincture
<i>Gingko biloba</i>	Gingko	Age-related memory loss, fatigue, tinnitus	Dried leaf, tea
<i>Glycyrrhiza glabra</i>	Liquorice	Anti-inflammatory, coughs	Root powder, capsules, extract
<i>Silybum maritimum</i>	Milk thistle	Liver disorders, lactation problems, antioxidant	Capsules, tablets, tinctures
<i>Swertia chirata</i>	Chirata	Migraine headaches	Fresh or whole dried plant

The currently available nutraceuticals in market are as follows: ⁷

1. Fortified cereals: contains vitamins and minerals
2. Additional supplements: cod liver oil, garlic etc.
3. Energy drinks and Tablets: Tropicana, Frooti
4. Foods to reduce cholesterol levels: Abcor by Nutri-pharma; claimed to reduce cholesterol by 15-20% in 4 months.
5. Vitamin and Mineral supplement: Vitamin A (Beta-carotene)
6. Probiotics: Yakult; contains 6.5 million lactobacillus casei shirota, which improves gut health.
7. Sports products: Glucon-D (Heinz), Glucose D (Dabur).

Macronutrients and Micronutrients ⁸

1. Vitamins: Vitamins are required for the normal metabolism of the human body. The most common vitamins are vitamin A, vitamin C, vitamin D and vitamin E. For example, Golden rice contains high level of vitamin A, the bacterium *Lactobacillus lactis* can synthesize both folate (vitamin B₁) and riboflavin (vitamin B₂), vitamin C is required for cardiovascular and immune cell functions. Vitamin E is required for cardiovascular and Alzheimer's disease.
2. Minerals: Calcium, Iodine, Zinc, Iron, Manganese and Magnesium are required for good human health.
3. Flavanoids: They are also an important part of nutraceuticals and are required in our diet for maintaining the immune system. For example, tomatoes contains high level of flavanols such as quercetin, Kaempferol, glycosides, luteolin, lycopene and luteolin-7-glycoside.
4. Terpenoids: They are the largest class of plant products. Tomato contains terpenoids and good for health because it contains lycopene, b-carotene and lutein.
5. Functional food: When food is being cooked or prepared using scientific intelligence with or without knowledge of how or why it is being used, the food is called functional food.

Estimation of Energy Value

The sample calorific value was determined (in Kcal) by multiplying the percentage crude protein, crude lipid and carbohydrate by the recommended factor (2.44, 8.37 and 3.57 respectively) and used for vegetable analysis.^{8,9}

PRESENT GLOBAL STATUS OF NUTRACEUTICALS

Vitamins and minerals account for 85% of the global market while antioxidants consist about 10%. The herbal extracts constitute about 5% of the market. US is the largest market for the nutraceuticals followed by India and China in the second position. Soy-food has gained popularity because of its antidiarrheal, hypolipidaemic, anticarcinogenic and antiosteoporotic effects. Probiotics are also widely used because it reduces cholesterol, prevents cancer, osteoporosis, allergy and type-2 diabetes.^{10-13,19,21}

The demand for nutraceutical ingredients has increased from 5.8% annually to \$ 15.5 billion. China and India are the fastest growing nutraceutical markets. Herbal and non-herbal extracts are used worldwide and widely used by medical professionals and increased from 6.5% annually to \$1.85 billion in 2010. Nutrients, minerals and vitamins demand reached \$ 9.5 billion in 2010 up to 6.3% annually from 2005. Global demand for nutraceutical vitamin ingredients increased up to 4.6% annually to \$4.2 billion in 2010.¹⁹

Scope and Opportunity of Indian Nutraceutical Market

The Indian nutraceutical market was at \$ 1,480 million in 2011 and can increase to \$ 2,731 million in 2016 according to the reports. According to the reports by business research and consulting Firm Frost and Sullivan, functional foods will be the fastest growing category by 2015. At present, the nutraceuticals is the largest category and constitute for 64% of the nutraceuticals. According to the study, the global nutraceutical market was about \$ 149.5 billion in 2011 along with US, Europe and Japan being the largest markets, accounts for 93% of the global nutraceutical demand.²³

R&D IN NUTRACEUTICALS

Research and development in the field of nutraceuticals is directed towards the following fields: ¹⁴⁻¹⁵

1. To test the safety, potency and purity of products.
2. To develop more effective and means of producing ingredients for use in products.
3. To develop testing methods for ensuring the consistency of the dosage of ingredients included in the company's products.
4. Develop the new products either by combining the existing ingredients used in nutritional supplements or identifying new ingredients that can be used in nutritional supplements.

Some of the pharmaceutical and biotechnological companies which provides major resources for the discovery of nutraceuticals includes Monsanto (St Louis, MO), American Home products (Madison , NJ), DuPont (Wilmington, DE), Abbott Laboratories (Abbott Park, IL), Warner-Lambert (Morris Plains, NJ), Johnson & Johnson (New Brunswick, NJ), Novartis (Basel, Switzerland), Metabolex (Hayward, CA), Genzyme Transgenic, PPL Therapeutics, Interneuron (Lexington, KY). The NREA includes the creation of a Nutraceutical commission (NUCOM) specifically for the discovery of a nutraceutical research and program is held mainly for clinical research.²¹

Table 3 enlists the nutraceuticals that are marketed by different pharmaceutical companies' worldwide.²⁸⁻²⁹

Table 3. List of marketed nutraceuticals

Marketed Nutraceutical	Category	Ingredients	Manufacturer
Omega Woman	Immune supplement	Antioxidants, vitamins	Wassen, Surrey
ROX®	Energy drink	Taurine, caffeine	ROX America, SA
Proteinex®	Protein supplement	Predigested proteins, vitamins, minerals and carbohydrates	Pfizer Limited
Calcitriol D-3®	Calcium supplement	Calcium and minerals	Cadilla Healthcare Limited
Betafactor® capsules	Immune supplement	Beta-glucan	Ameriden® International INC.
Red Bull®	Energy drink	Taurine, caffeine	Austrian Red Bull Gmbh
5-Hour energy	Energy drink	Taurine, caffeine	Living essentials, USA
Pediasure®	Nutritional supplement	Protein, vitamins	Abbott Nutrition
Revital®	Daily health supplement	Vitamins and minerals	Ranbaxy Lab Ltd

NUTRACEUTICALS AND THEIR THERAPEUTIC BENEFITS

Important nutraceuticals and their health benefits are enlisted in Table 4.¹³

Table 4. Therapeutic benefits of some important nutraceuticals

Name of Nutraceutical	Therapeutic Benefits
Natural Lycopene	Reducing risk of prostate and cervical cancers.
Natural purified Lutein Esters	Dietary supplement.
Garlic	Cholesterol lowering and prevention of cardiovascular diseases.
Green Tea	Prevention of cardiac diseases, cancer prevention and weight management.
Gymnema, Mamordica	Diabetic control.
Glucosamine	Arthritis treatment.
Gingko biloba	Allergy relief.
Digestive enzymes	Digestive support.

Ginseng

Immunomodulator.

CEREALS: FROM STAPLE FOOD TO NUTRACEUTICALS

Many cereals, which are used as staple food in different countries of the world, have different nutraceutical properties.¹⁶ Some of the cereals and their nutraceutical properties are described below:¹⁶⁻¹⁷

1. Rice: Rice is an important source of energy, hypoallergenic, easily digested, providing protein with high nutritional quality. The rice Kernel consists 20% hull, 8-12% of bran and embryo and 70-72% endosperm or milled rice. The rice grain contain 5% bran, of which 12-18.5% is oil. Rice bran lowers the cholesterol levels in the blood, lowers the level of LDL and increases HDL level and used in treatment of cardiovascular disease. Rice bran also contains phosphorous, potassium, magnesium, calcium and manganese. Metabolic antioxidants are also present which controls body weight. The essential fatty acids, omega-3, omega-6 and omega-9 improves eye health.
2. Barley: It is the worldwide used traditional food grain and used for malt and beer production. The active component in barley is β -glucan. β -glucan reduces the risk of coronary heart disease, diabetes and heart related problems.
3. Wheat: It is used as a food ingredient, the fraction of the grain is used for enhancing health and prevention of chronic diseases. The FDA permits foods that contain at least 51% whole grains by weight to display a health claim stating consumption is linked to lower heart disease and certain cancers.
4. Millet: It is highly nutritious, least allergenic rich in B vitamins, especially niacin, B6 and folic acid, calcium, iron, potassium, magnesium and Zinc. The seeds are also rich in phytochemicals and Phytic acid which helps in lowering cholesterol and Phytate, which is associated with reduced cancer.
5. Buckwheat: It has nutritional benefits, easily digestible. Buckwheat is higher in iron and the minerals present in it play an important role in the prevention of hypertension and anaemia (Udesky, 1992).
6. Milk: Milk provides nutritive elements, biologically active substances to both neonates and adults. It also contains biologically active peptides. Several bioactive peptides are used in the treatment of diarrhea, hypertension, thrombosis, dental diseases and immunodeficiency.

NUTRACEUTICALS AND DISEASES

Nutraceuticals are used for cardiovascular diseases, diabetes and metabolic syndrome. Metabolic syndrome includes a variety of risk factors which includes cardiovascular disease and type 2 diabetes. Both metabolic syndrome and diabetes causes inflammation, altered oxidative status, platelet activation. The compounds such as vitamins like vitamin C and E, vitamin D, flavanoids omega-3 fatty acid, minerals such as chromium, magnesium, phytoestrogens and dietary fibres are used for treating metabolic syndrome and diabetes.⁹⁻¹⁸

Cactus pear is another important nutraceutical with lot of health benefits. Majority of vitamins are found in cactus pear. Carotenes and vitamin E found in this plant, have antioxidant properties by which they improve the stability of fatty oil. Ascorbic acid is the major vitamin found in cactus pear. The fruit pulp contains high amount of minerals especially calcium, potassium and magnesium. The seeds are rich in minerals and sulphur amino acids. A total calorific value of 50 Kcal is obtained and directly absorbed so, high glucose concentrations in cactus fruits are available for brain and nerve cells.¹²

Sesame is an extremely beneficial medicine and helps in lowering cholesterol, controlling blood pressure, dermatological disease management and many areas.¹⁵ Sesame contains variety of nutrients such as proteins, carbohydrates, antioxidants, lignans, tocopherols and other micronutrients. It is having properties like anticancer, antioxidative, antiimmunoregulation and antihypersensitivity.

The main by-product of the banana processing industry is the peel. According to the National Cancer Standard Institute, banana peel extract is classified as non-toxic to normal human cells. Among the three varieties of banana, Yelakkibal banana peel have high protein, ether and calcium content and he have also studied the antioxidant activity in banana peel and have found that unripe banana peel showed high antioxidant activity as increasing the polarity, the extracts exhibited stronger antioxidant activity. Banana peel is also rich in pectin which is 19-22%. Standardized and developed jellies are found to be more

nutritive, beneficial for health and better than tablets or pills. As it was proved non-toxic so, it can be used as a natural source of antioxidants and enzyme to cure diseases.²²

Different diseases in which nutraceuticals have been reported to provide benefits include:

1. Cardiovascular diseases: The nutraceuticals used are antioxidants, dietary fibres, omega-3 fatty acids, flavanoids, polyphenols and 25 g of soya foods are used in the prevention of cardiovascular diseases.
2. Diabetes: Lipoic acid, an antioxidant is used for treatment of diabetic neuropathy, dietary fibres from psyllium have been used for glucose control in diabetic patients.
3. Obesity: Herbal stimulants, caffeine ephedrine and green tea helps for reduction in body weight, a mixture of glucomannan, chitosan, fenugreek and vitamin C in dietary supplement significantly reduced body weight.
4. Cancer: Phytoestrogens is recommended to prevent prostate/breast cancer, lycopene concentrates in the skin, testes, adrenal and prostate protects against cancer, saponins contains antitumor and antimutagenic activities.
5. Anti-inflammatory activities: Cucurmin which is a polyphenol of turmeric have anticarcinogenic, antioxidative and anti-inflammatory properties.
6. Vision improving agents: Lutein (found in tomatoes, carrots, leafy vegetables) is used for the treatment of visual disorders.
7. Osteoarthritis: Glucosamine (GLN) and chondroitin sulphate (CS) is used for treatment of osteoarthritis.
8. Alzheimer's disease: β -carotene, cucurmin, lutein, lycopene, turmeric is used for the treatment of Alzheimer's diseases.

Nutraceuticals for Cardiovascular Diseases

The major reason for the spread of mortality and morbidity is cardiovascular disease (CVD) all over the world. According to WHO, 17.3 million people died from CVDs in 2008, out of which 7.3 million people died due to coronary heart disease and 6.2 million were due to stroke.¹¹⁻¹² The following nutraceuticals have beneficial effects in the therapy of CVD:

1. Coenzyme Q10 (Ubiquinone): Researches have found that intake of CQ10 was used to reduce statin induced myopathy.
2. Cucurmin: olszanecki et al. 2005, had found that cucurmin contains anticarcinogenic, antiinflammatory, antioxidative, antiinfectious and hypocholesterolemic activities.
3. Flavanoids: They block the angiotensin-converting factor (ACE) that increases blood pressure, by blocking enzyme cyclooxygenase that breaks down prostaglandins and prevent platelet aggregation. Flavanoids are found in plants such as flavanones, Kaempferol and rutin buckwheat are used for the treatment of cardiovascular diseases.
4. Garlic: Houston et al. 2009; had found that garlic reduces blood pressure, platelet inhibition, reduction in oxidized LDL and coronary artery calcification.
5. Green Tea: Tokunaga et al. 2002 had found that green tea and its active ingredient E gallate (EGCG) reduces cholesterol levels which ultimately causes reduction in atherosclerotic CVD.
6. Nuts: Kris-Etherton et al 2001; had found that of 28 g of unsalted nuts daily, reduces the risk of CVD.
7. Soy Proteins: Welty et al 2007, had found that 25 g of soyprotein causes 9.9% reduction in systolic and diastolic BP in hypertensive patients.

Nutraceuticals Used In Diabetes

The following nutraceuticals have beneficial effects in the therapy of diabetes:²⁰

1. Coffee berry: It contains antioxidant and other phytonutrients known as polyphenols i.e chlorogenic acid and caffeic acid. Its mode of action is that it reduces the gene expression of key enzymes involved in glucose production from glycogen stored in liver, chlorogenic acid decreases the intestinal absorption rate of glucose.

2. Cinnamon: It contains water soluble polyphenol called MHCP (methylhydroxy chalcone polymer). Its mode of action is up regulated the expression of genes involved in activating the cell membrane's insulin receptors, thus increasing glucose uptake and lowering blood glucose levels.
3. Aloe vera: It contains water-soluble polysaccharide Glucomannan. Its mode of action is insulin sensitizing glucose lowering activities.
4. Optunia: It contains very high soluble fibres and pectin. Its mode of action is that it recovers glycemic control and improves insulin sensitivity.
5. Gymnema sylvestre: It contains glycosides, a peptide gurmarin, several amino acid derivatives and water soluble acidic division called GS4. Its mode of action is that it increases glucose uptake utilization, increased insulin secretion and β -cell number.

Nutraceuticals in Hypertension

The following nutraceuticals are used in hypertension therapy: ²⁴

1. Sodium: The average sodium intake is 5000 mg per day and the minimum requirement for Na⁺ is 500 mg per day. Na⁺ is required in our diet together with other nutrients for controlling BP and decreasing cardiovascular disease.
2. Potassium: The average K⁺ intake is 45 mEq per day. High potassium intake reduces cardiovascular disease and BP.
3. Magnesium: Magnesium competes with Na⁺ for binding sites on vascular smooth muscle and acts like a calcium channel blocker, increases PGE and helps in reducing BP.
4. Fats: omega-3 fatty acids are found in fish oil, flax seed, flax oil and nuts. Omega-3 fatty acids reduces BP and DHA is very effective in reducing BP and heart rate (HR).
5. Vitamin C: It is an antioxidant, reduces BP, diuretic effect, increases NO and PGI₂ levels, reduces thrombosis, decreases TXA₂ and reduces lipids (decreases TCs, LDLs, TGs and HDLs)

FUTURE ASPECTS

The increasing nutraceutical market indicates that end users are seeking minimal processed food with extra nutritional benefits. This development have expanded worldwide. Many scientists believe that enzymes represent another exciting frontier in nutraceuticals, use of nutraceuticals in sports application is appealing, carotenoids will play a crucial role in nutraceutical product development, Lycopene offers tremendous nutraceutical opportunities and also used in the field of sports medicine for athletes so they can recuperate quickly when injured.³⁰

CONCLUSION

Nutraceuticals provide all the important substances that should be present in a healthy diet for humans. Nutraceuticals provide energy and nutrient supplements to body, which are required for maintaining good health. Nutraceutical industry is growing at a much faster rate in both food and pharmaceutical industry. Nutraceutical and functional food plays an important role in the promotion and care of human health to prevent diseases. The use of nutraceuticals is a key to obtain therapeutic outcomes with reduced side effects.

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DECLARATION OF INTEREST

It is hereby declared that this paper does not have any conflict of interest.

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