Nutraceuticals: New Era of Medicine and Healthcare

Manvi Bhatnagar, Shubham K. Soni, Neeraj Patel and Dharmendra Jain*
Department of Pharmaceutical Sciences, Dr. Harisingh Gour University, Sagar, India
Email: dharmjain@gmail.com; Mobile:+91-9425972368

Abstract

The term "nutraceutical" was coined from word "nutrition" and "pharmaceutical" in 1989 by Stephen DeFelice. Nutraceuticals, in broad term, are food or food parts playing an important role in maintaining and modifying normal physiological function that maintains human health. They do not easily fall into the category of food and drug and often fall between these two. Drugs show various side effects and adverse effects due to which consumers are generally switch towards food supplements to improve health. Such products may range from isolated nutrients, dietary supplements and functional foods, herbals products, prebiotics, probiotics, genetically engineered foods and other processed foods including cereals, soups and beverages. The principal reasons for the progressive growth of the nutraceutical market worldwide are the awareness of the population towards their health and eating habits. These nutraceuticals help in preventing some of the major health problems such as obesity, cardiovascular diseases, cancer, diabetes, arthritis, cholesterol etc. Through this review we wish to aware our population towards the essential benefits of nutraceuticals which will lead to the new era of medicine and healthcare.

KEYWORDS: NUTRACEUTICALS, PREBIOTICS, PROBIOTICS, FUNCTIONAL FOOD ETC.

Introduction

Nutraceuticals a portamanteace of the words 'nutrition' and 'Pharmaceuticals', is a food or food products that reportedly provides health and medical benefits including the prevention and treatment of disease (Nicoli et al.,1999).

A nutraceuticals is defined to have physiological benefits or provide protection as well as prevention against chronic disease. Such products are known as isolated nutrients, dietary supplements and specific diets to genetically engineered food, herbal products and processed foods such as cereals, soups and beverage with recent development in cellular level nutraceutical agents. Researchers and medical practitioners are developing templates for integrating and accessing information from clinical studies on complementary and alternative therapies in to responsible medical practices. (Kaur and Kapoor, 2001).

Functional food is a food where a new ingredients has been added to a food and the new product has an additional function (often one related to health promotion or disease prevention) (Dillard and German, 2000). The Indians, Egyptians, Chinese and Sumerians are just a few Civilization that have provided evidence suggesting that food can be effectively used as medicine to treat and prevent disease (Adelaja and Schilling, 1999). Functional food is the generic term for food that has been linked to health benefit. The institute of medicines food and nutrition board (US) has define functional food as 'any food and food ingredients that may provide health benefit behind the traditional nutrition that it contains' (Pandey et al.,

2010). Functional food can be from plant sources or animal sources. The nutraceuticals was coined in the United State and is used to describe food or food components that have the potential to cure specific disease conditions (Maddi et al., 2007; Brower, 1998).

Historically in India multiple laws and regulations prescribed various standards regarding foods, food additives, contaminants, food colors, preservatives and labeling. India has recently passed the food safety and standard Act 2006, modern integrated food law for the regulation of food products including nutraceuticals, dietary supplement and functional food. In India these functional foods can include herbal extract, spices, fruits and nutritionally improved food or food products with edit functional ingredients. The aim of the overview is to focus on the general concept and the health promoting effect of several nutraceuticals that have the potential of being incorporated into foods.

The term ‘nutraceuticals’ was coined from ‘nutrition’ and ‘pharmaceuticals’ by Stephen De Felice founder and chairman of the foundation for innovation in medicine (FIM) in 1989. According to De Felice, nutraceuticals can be defined as ‘a food that provide medical or health benefits, including the prevention and treatment of a disease (Wildman, 2001; Bull, 2000).

Nutraceuticals cover most of the therapeutic areas such as anti arthritis, cold and cough, sleeping disorder, digestion and prevention of certain cancer, osteoporosis, blood pressure, cholesterol control, pain killer, depression and diabetes (Malik, 2008; Dureja et al., 2003).

Categories of Nutraceuticals

The most common way of classifying nutraceuticals can be based on food

source, mechanism of action, chemical nature etc. (Kalia, 2005; Kokate et al., 2002). The food sources used as nutraceuticals are all natural and can be categorized as:

1. Dietary fibre
2. Polyunsaturated fatty acids
3. Probiotics
4. Prebiotics
5. Selenium
6. Antioxidant vitamins
7. Polyphenols
8. Spices

More broadly nutraceuticals can be classified into two groups) (Pandey et al., 2010).

(1) Potential nutraceuticals

(2) Established nutraceuticals

Table 1: Sources and Potential Benefits of Some Nutraceuticals.

Functional Components	Source	Potential benefites
Carotenoids		
α – Carotene/β -carotene	Carrots, Fruits, vegetables	Neutralize free radicals which may cause damage to cells
Lutein	Green vegetables	Reduce the risk of macular degeneration
Lycopene	Tomato products (ketchup, sauces)	A reduce the risk of prostate cancer
Dietary fiber		
Insoluble fiber	Wheat bran	Reduce risk of breast or colon cancer
β -Glucan	Oats, barley	Reduce risk of cardiovascular disease; protect against heart disease and some cancers; lower LDL and total cholesterol
Soluble fiber	Physllium	Reduce risk of cardiovascular disease; protect against hart disease and some cancers; lower LDL and total cholesterol
Fatty acids		
Conjugated linolic acid	Cheese	Improve body composition; decrease risk of certain cancer
Phenolics		
Anthocyanidins	Fruits	Neutralize free radicals; reduce risk of cancer
Catechins	Tea	Neutralize free radicals; reduce risk of cancer
Flavonones	Citrus	Neutralize free radicals; reduce risk of cancer
Flavones	Fruits/vegetables	Neutralize free radicals; reduce risk of cancer
Lignins	Flax, rye, vegetables	Prevention of cancer, renal failure

Tanins	Cranberries, cranberry products, cocoa, chocolate	Improve urinary tract health; reduce risk of CVS disease
Plant sterols		
Stanol ester	Corn, soy, wheat, wood oils	Lower blood cholesterol levels by inhibiting cholesterol absorption
Prebiotics/probiotics		
Frtucto-oligosaccharides	Jerusalem artichokes, shallots, onion powder	Improve quality of intestinal microflora, GIT health
lactobacillus	Yogurt, other dairy	Improve quality of intestinal microflora, GIT health
Soy Phytoestrogens		
Isoflavones; deidzein genistein	Soybeans and soy based foods	Menopause symptoms, such as hot flashes; protect against heart disease and some cancers; lower LDL and total cholesterol
**Source: International Food Information Council.*		

(1) Dietary Fibres

Dietary fibres are the food material or the plant material that is not hydrolysed by enzyme secreted by the digestive tract, digested by microflora in the gut. It mainly includes non starch polysaccharides (NSP) such as cellulose, gum, hemicellulose and pectins, lignins, resistant starch and resistance dextrins. Foods that are rich in soluble fibre include fruits, barley, oats and beans. Chemically dietary fibres means carbohydrate polymer with a degree of polymerization not lower than 3, which are neither digested nor absorbed in the small intestine (Leclere et al., 1994). Based on their water solubility, dietary fibres may be divided into two forms:

(A) Insoluble dietary fibres (IDF), include cellulose, some hemicellulose and lignin which fermented to a limited extent in the colon.

(B) Soluble dietary fibres (SDF)

These include beta glucans, pectins, gums, mucilages and hemicellulose that are fermented in the colon (Cummings 2001).

The soluble components of dietary fibre have the bulking and viscosity producing capability thus retard the gastric emptying of the stomach. This affects the rate of digestion and reuptake of nutrients. Soluble fibres have the ability to selectively lower serum LDL, cholesterol and to improve cellulose tolerance. They also enhance insulin receptor binding. In colon, dietary fibres increase faecal bulk due to increased

faecal bacterial mass caused by soluble fibre fermentation. The fibers also promote the growth of *bifidobacteria* in the gut (Glore et al., 1994).

Increase in the intake of high fibre foods improves serum lipoprotein value, lowers blood pressure level, improves blood glucose control for diabetes, maintain weight loss. Certain soluble fibre enhances the immunity in humans (Anderson et al. 2009). Some demerits of dietary fibres include reduced absorption of vitamin, minerals, proteins and calories. It is recommended that dietary fibres intake for adults generally fall in the range of 20 to 25 gram/day. The recommended dietary fibre intake for children and adult are estimated to be 40 gram/1000 kcal (Lairon et al. 2005).

Table 2: Level of dietary fibers in food

S. No.	Product	AOAC (g/100g)*
1	Apples (with skin)	2.0
2	Bananas	1.9
3	Carrots	3.1
4	Baked beans	4.2
5	Cabbag	2.0
6	Wheat bread	2.0
7	Brown bread	4.5
8	Whole meal bread	7.4

* Excludes fructans [Source- AOAC values CRC handbook of dietary fibre in human nutrition]

(2) Polyunsaturated fatty acids (PUFAs)

Polyunsaturated fatty acids are also called ‘essential fatty acids’ as these are crucial to the body function and are introduced externally through the diet. PUFAs have two subdivisions: Omega -3- fatty acids and Omega -6- fatty acids. The major Omega -3- fatty acids are α- linolenic acid (ALA), eicosapentanoic acid (EPA), docosahexaenoic acid (DHA) (Escott-Stump and Mahan, 2000). ALA is the precursor of EPA and DHA. Principal source of ALA are mainly flax seeds, soybeans and red or black currant seeds. Omega -6- fatty acids mainly consist of linolenic acid, γ-linolenic acid and arachidonic acid.

Reports suggest that Omega -3- fatty acids have three major beneficial effects in cardiovascular disease, such as antiarrhythmic, hypolipidemic, and antithrombotic. Recent research show the benefits of Omega-3 oil is another area of health including premature infant health, asthma, bipolar and depressive disorders. Infant formulas nowadays contain DHA along with ARA, which closely mimic the breast milk. FDA recommends a maximum of 3 gram/day intake of EPA and DHA, Omega-3-fatty acids, with not more than 2 gram/day from a dietary supplement (Carlson, 1999).

(3) Probiotics A probiotics can be defined as live microbial feed supplement, which when administered in adequate amount beneficially affect the host animal by improving its intestinal microbial balance (Hord, 2008).

Probiotics generally include the following categories of bacteria:-

A) Lactobacillus such as *lactobacillus acidophilus*, *lactobacillus casei*, *lactobacillus delbrueckii* subspecies *bulgarie bulgaricus*, *lactobacillus brevis* and *lactobacillus cellobiosus* (Suvarna and Boby 2005)
B) Bifidobacteria such as *B. bifidun, B. adotescentis, B. infantis, B. longum, B. thermophilum.*

Probiotics are available in various forms such as powder form, liquid form, gel or paste or granules form, capsule form etc. Specific probiotics are generally used to treat gastrointestinal conditions such as lactose intolerance, acute diarrhoea and antibiotic associated gastrointestinal side effects. Probiotic agents are non-pathogenic, non-toxic resistance to gastric acid, adherence to gut epithelial tissues producing antibacterial substances. These are evidence that administration of probiotics decrease the risk of systemic conditions, such as allergy, cance, asthama and several other infections (Doron et al., 2005).

(4) Prebiotics

Prebiotics are dietary ingredients thatprovides beneficial effectto the host by selectively altering the composition and metabolism of the gut microbiota. These are short chain polysaccharides that have unique chemical structure that are not digested by humans in particular fructose based oligosaccharide that exit naturally in food or are added in the food (Macfarlane et al., 2006; Gibson and Roberfroid, 1995). The prebiotic utilisation generally promotes the *lactobacillus* and *bifidobacterial* growth in the gut, thus helping in metabolism. Vegetable like chicory roots, banana, tomato, alliuns are rich in fructose oligosaccharides.

Some other example of these oligosaccharide are raffinose and stachyose, found in beans and peas (Hord, 2008; Gibson, 1999). The health benefits of the prebiotics include antitumor properties, neutralization of toxins and stimulation of intestinal immune system, to improve lactose tolerance reduction of constipation, blood lipids and blood cholesterol levels. A daily intake of 5 to 20 gram of inulin and oligosaccharides enhance the growth of *bifidobacteria*. Large amount of such oligosaccharides cause diarrhea, abdominal distension and flatulence (Stranges et al., 2006).

(5) Selenium

Selenium is an essential trace element that is involved in the defence against the highly reactive oxygen species. Brazil nut are the richest source of selenium. Its deficiency causes serious health effect in human, such as keshan's disease, form of fatal cardiomyopathy that affects young women and child. The most important role of selenium is in the form of antioxidants such as glutathione peroxidase, thioredosin reductase, glutathione peroxidase play a crucial role in protecting cell against oxidative damage from reactive oxygen species (ROS) and reactive nitrogen species (RNS), which includes superoxide, hydrogen peroxide, hydroxyl radicals and nitric oxide.

The antioxidant activity of selenium aids in prevention of cardiovascular disease (Stranges et al., 2006). It maintains the immunity. Recent studies reported that the antioxidant activity of selenoenzymes may prevent the formation of oxidized LDL and hence reduce the occurrence of heart disease, Selenium has the ability to prevent oxidative stress, limiting DNA damage, inducing apoptosis, cell cycle arrest (Tinggi, 2007) A clinical study by Clark and his colleagues revealed that participants who were given 200 µg of yeast based selenium per day for four and half year had a 50% decrease in the cancer death rate compared with the placebo group.

Selenium plays a significant role in impairment of thyroid immunity involving the action of glutathione peroxidase and thioredoxin reductase thereby removing ROS and excess hydrogen peroxide produced by thyrocyte during thyroid hormone synthesis. Recommended dietary allowances for selenium various form 20 µg per day for children to 55 µg per day for adults. The tolerable upper intake level of selenium ranges from 90 µg to 400 µg per day for children and adults respectively (Stranges et al., 2006).

(6) Antioxidant vitamins

Vitamins like vitamin C, vitamin E and carotenoids are collectively known as antioxidant vitamins. These vitamins act both singly as well as synergistically for the prevention of oxidative reaction leading to several degeneration diseases including cancer, cardiovascular diseases, cataract etc. These vitamins are abundant in many fruits and vegetables and exert the protective action by free radical scavenging mechanism. Vitamin E comprises of tocopherol together with tocotrienols transfer hydrogen atom and scavenges singlet oxygen and other reactive species. Tocotrienols are more mobile within the biological membrane than tocopherol because of the presence of the unsaturated side chain and therefore penetrate tissues with saturated fatty layers example in brain and liver more efficiently (Elliot 1999). They have more recycling ability and are a better inhibition of liver oxidation. It was reported that both vitamin E and selenium has a synergistic role in lipid peroxidation.

Vitamin C, also known as ascorbic acid donates hydrogen atom to lipid moiety, quenches singlet oxygen radical and removes molecular oxygen scavenging of aqueous radical by the synergistic effect of ascorbic acid as well as tocopherol is a well-known antioxidant mechanism (Meydani, 2000). Carotenoids, lycopene, beta-carotene, lutien, zeaxanthin are known to be the most efficient singlet oxygen quencher in the biological system without producing any oxidizing product. β-carotene traps peroxy free radical in tissues at low oxygen concentration. Hence β- carotene complements the antioxidant properties of vitamin E (Lee et al., 2004).

(7) Polyphenols

Polyphenols are produced by plants as secondary metabolites to protect them from photosynthesis, stress and reactive oxygen species. There are approximately 8000 different classes of polyphenols, the most important being flavonols, flavones, falavan-3-ols, flavanones and anthocyanins. The most commonly occurring polyphenols includes flavonoids and phenolic acids. Dietary polyphenols are of current interest because substantial evidence *in vitro* have suggested the effective cellular process like expression apoptosis platelet aggregation and carcinogenicity (Dulthie et al, 2003).

Apart from this polyphenols are having antioxidant, anti-inflammatory, antimicrobial, cardioprotective actions. They play an important role in the prevention of neurodegenerative disorders and diabetes mellitus. Polyphenols are mostly known for their antioxidant activity on the basis of their structural chemistry. Polyphenols have been shown to be more effective antioxidents *in vitro* than vitamin E and C on molar basis. Bioavailability of polyphenols is an important factor to determine their biological activity. This depends on the chemical properties of polyphenols, conjugation and reconjugation in the intestine, intestinal absorption and enzyme available for metabolism. It has been found that flavonoids modulate the expression of γ-glutamylcysteinesynthetase, an important rate-limiting enzyme involved in glutathione synthesis. Glutathione being important in redox regulation of transcription factors and enzymes for signal transduction, polyphenol mediated regulation of glutathione significantly alters cellular effects, as

detoxification of xenobiotics, glutathionylation of proteins (Moskaug et al., 2005). It was investigated that red wines strongly inhibit the synthesis of endothelin -1, a vasoactive peptide that is important in the development of coronary atherosclerosis. The antioxidant and anti-inflammatory activity of red wine is due tothe presence of reservatrol, a triphenolic present in the in the black skin of grapes and proanthocyanidins (Corder et al., 2001).

Tea is a rich source of polyphenols, such as catechins, which include (-)-epicatechen, (-) -epigallocatechin, (-)-epicatechen -3-gallate (ECGC), (catechin). Tea also consists of flavonols such as quercetin and myricetin. Tea, mainly consumed in the form of black and green tea has been found to have cancer preventing activity. Several studies suggested that it is effective in inhibition of 4-(methylnitrosamimo) -1-(3-pyridyl)-1-butanone (NNT) induced tumorigensis in mice. Experimental evidence from animal models also suggest that tea plays a significant role in inhibition of carcinogenesis in organ sites in skin, lung, esophedus, stomach, liver, small intestine, pancreas, colon, bladders. Green tea also has been found to be associated with lower risk of CVS diseases through decreased serum cholesterol and triglyceride and provide protection against peroxidation of lipid in kidney (Lambert et al., 2005; Yang et al., 1997).

Legumes are consumed as an alternative source of proteins as they are rich in amino acid like lysine and tryptophan and are cost effective than animal proteins. Studies suggested that in addition to complex carbohydrates, soluble fibers, essential vitamins and metals, legumes also supply the diet with polyphenols, like flavonoids, isoflavones and lignans. Soyabean is the richest source of dietary isoflavones. High intake of polyphenols even from dietary source can result in toxic effects. Flavonoids are reported to induce cleavage in the NLL gene, inhibit enzymes (such as topoisomerase) involved in DNA structure and replication and hence may predispose subjects to infant leukemia. It remain to be determined whether dietary polyphenols modulate cellular glutathione concentration among humans and whether they contribute to regulation of major cellular signaling pathways, which would explain the indisputable fact that fruits and vegetables protect against disease (Yang et al., 2001).

(8) Spices

Spices are esoteric food adjuncts that are used for thousands of years to enhance the sensory quality of food. The quantity and the variety of the spices consumed in the tropical countries are particularly extensive. Tropical import characteristic flavor, aroma and colour to food, stimulating our appetite as well as modify the texture of food. Recent studies reveals that dietary spices in their minute quantities has an immense influence on the human health by their antioxidant, chemo protective, anti-mutagenic, anti-inflammatory, immune modulatory effect on human health by the action of GIT,CVS, respiratory, metabolic, reproductive, neusal and other system (Hendrich et al., 1994).

Most of the spices components are terpenes and other constituents of essential oil. It was found that about 50g of onion and 5-6 cloves of garlic in their raw form are adequate for lowering of cholesterol in human body. Spices and are safe, when used as food but may be toxic, when used as medicine, because of the possibilities of their interaction with other pharmaceutical medication. High doses of onion (500mg/kg) as well causes lung and tissue damage in rats (Rao, 2003). Regular intake of curcuminoids at about 0.5 g reduced blood lipid peroxide level upto about 33% due to their antioxidant activity. The limited states code of federal regulations has considered spices and herbs as (GRAS) i.e generally recognized as safe for human consumption (Hendrich et al., 1994).

The Future of Nutraceuticals

Increasing awareness about fitness and health, spurred by media coverage are prompting the majority of people to lead healthier lifestyles, exercise more, and eat healthy food. The expanding nutraceuticals market indicates that the end users are seeking minimally processed food with extra nutritional benefits and organoleptic value. This development, in turn leads to expansion in the nutraceuticals markets globally. Its tremendous growth has implications for the food, pharmaceutical, healthcare and agricultural industries.

Many scientists believe that enzymes represent other exiting frontlines in nutraceuticals, (Enzymes have been under employed and they are going to be a hot area in the future). Fermentation technology using microbes to produce new food products also represents potential. Global trends to healthy products cannot be reversed. Companies taking the lead by investing strategically in science, products development, marketing and consumer education, will not go unrewarded.

Conclusion

The nutraceuticals industry is growing at a rate for exceeding expansion in the food and pharmaceutical industry. In tomorrow's market, the most successful nutraceuticals players are likely to be those companies in which functional products are just a part of a broad line of goods satisfying both conventional and health value defense mechanism decrease appreciably with age. These may result in the development of a great many diseases.

Although nutraceuticals have significant promise in the promotion of human health and disease prevention health professional, nutritionists and regulatory toxicologist should strategically works together to plan appropriate regulation to provide the ultimate health and therapeutic benefit to mankind. Long term clinical studies are needed to scientifically validate the nutraceuticals in various medical conditions the interaction of nutraceuticals with food and drugs is another are which should be taken into consideration. Nutraceuticals have proven health benefits and their consumption will keep disease at bay and allow human to maintain an overall good health.

References

[1] Adelaja AO, Schilling BJ. Nutraceutical: blurring the line between food and drugs in the twenty-first century. Mag Food Farm Resour. 1999;14:35–40.

[2] Anderson JW, Baird P, Davis RH Jr, Ferreri S, Knutdson M, Koraym A, Waters V, Williams CL. Health benefits of dietary fibre. Nutr Rev 2009; 67:188–205.

[3] Brower V. Nutraceuticals: poised for a healthy slice of the healthcare market? Nat Biotechnol. 1998;16:728–731.

[4] Buchner HC, Hengstler P, Schindler C, Meier G. N-3 polyunsaturated fatty acids in coronary heart disease—a meta analysis of randomized controlled trials. Am J Med 2002;112:298–304.

[5] Carlson SE. Long-chain polyunsaturated fatty acids and development of human infants. ActaPaediatrSuppl. 1999;88:72–77.

[6] Cummings JH. The effect of dietary fiber on fecal weight and composition. In: Spiller G (ed) Dietary fiber in human nutrition. CRC Press, Boca Raton. 2001; 183–252.

[7] Dillard CJ, German JB. Phytochemicals: nutraceuticals and human health. J Sci Food Agric. 2000;80:1744–1756.

[8] Doron S, Snydman DR, Gorbach SL. Lactobacillus GG: bacteriology and clinical applications. GastroenterolClin North Am. 2005;34:483–498.

[9] Duthie GG, Gardner PT, Kyle JAM. Plant polyphenols: are they the new magic bullet? Proc Nutr Soc. 2003;62:599–603.

[10] Elliot JG. Application of antioxidant vitamins in foods and beverages. Food Technol. 1999;53:46–48.

[11] Escott-Stump E, Mahan LK. Krause's food, nutrition and diet therapy, 10th edn. WB Saunders Company, Philadelphia. 2000;553–559.

[12] Fuller R. Probiotics: the scientific basis. Chapman and Hall, London Gibson GR Dietary modulation of human gut microflora using the prebiotics Oligofructose and Inulin. J Nutr 1999;129:1438S– 1441S.

[13] Gibson GR, Roberfroid MB. Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics. J Nutr. 1995;125:1401–1412.

[14] Gibson GR, Wang X Regulatory effects of bifidobacteria on other colonic bacteria. J ApplBacterio 1994;77:412–420.

[15] Glore SR, Van Treeck D, Knehans A. J Am Dent Assoc. 1994;94:425–436.

[16] Goldbohm RA, Hertog MGL, Brants HAM, van Poppel G, van den Brandt PA. Consumption of black tea and cancer risk: a prospective cohort study. J Natl Cancer Inst. 1996;88:93–100.

[17] Hendrich S, Lee K-W, Xu X, Wang HJ, Murphy PA. Defining food components as new nutrients. J Nutr. 1994;124:1789s–1792s.

[18] Hord NG. Eukaryotic microbiotic crosstalk: potential mechanisms for for health benefits of prebiotics and probiotics. Annu Rev Nutr. 2008;28:215–23.

[19] John B. Natural compounds in cancer therapy. Oregon Medical Press, Princeton Kabara JJ (1991) Phenols and chelators. In: Russell NJ, Gould GW (eds) Food preservatives. Glasgow & London, Blackie. 2001;200–214.

[20] Kalia AN. Textbook of Industrial Pharmacognocy. CBS publisher and distributor, New Delhi. 2005;204–208.

[21] Kaur C, Kapoor HC. Antioxidants in fruits and vegetables-the millenium's health. Int J Food Sci Technol 2001;36:703–725.

[22] Kokate CK, Purohit AP, Gokhale SB. Nutraceutical and Cosmaceutical. Pharmacognosy. 21st edition, Pune, India: Nirali Prakashan, 2002;542–549.

[23] Lairon D, Arnault N, Bertrais S, Planells R, Clero E, Hercberg S, Boutron-Ruault MC. Dietary fiber intake and risk factors for cardiovascular disease in French adults. Am J Clin Nutr.2005;82:1185–1194.

[24] Lee J, Koo N, Min DB. Reactive oxygen species, aging and antioxidative nutraceuticals. CRFSFS. 2004;3:21–33

[25] Macfarlane S, Macfarlane GT, Cummings JH. Review article: prebiotics in the gastrointestinal tract. Aliment PharmacolTher. 2006;24:701–714

[26] Malik A. The potentials of Nutraceuticals. Pharmainfo.net 6 Metchinkoff E. The prolongation of life. Putmans Sons, New York.2008;151–183.

[27] Meydani M. Effect of functional food ingredients: vitamin E modulation of cardiovascular diseases and immune status in the elderly. Am J Clin Nutr. 2000;71:1665S–1668S.

[28] Micallef M, Lexis L, Lewandowski P. Red wine consumption increases antioxidant status and decreases oxidative stress in the circulation of both young and old humans. Nutrition J. 2007;6:27–34.

[29] Nicoli MC, Anese M, Parpinel M (1999) Influence of processing on the antioxidant properties of fruits and vegetables. Trends Food Sci Technol.1999;10:94–100.

[30] Oboh G. Antioxidant properties of some commonly consumed and underutilized tropical legumes. Nutrition Business Journal. Eur Food Res Technol. 2006;224:61–65.

[31] Pandey M, Verma RK, Saraf SA. Nutraceuticals: new era of medicine and health. Asian J Pharm Clin Res. 2010;3:11–15.

[32] Rishi RK. Nutraceuticals: borderline between food and drug? Pharma Rev. 2006;51–53.

[33] Sahu SC. Dual role of organosulfur compounds in foods: a review. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev 2002;20:61–76.

[34] Stranges S, Marshall JR, Trevisan M, Natarajan R, Donahue RP, Combs GF, Farinaro E, Clark CL, Reid ME. Effects of selenium supplementation on cardiovascular disease incidence and mortality: secondary analyses in a randomized clinical trial. Am J Epidemiol. 2006;163:694–699.

[35] Suvarna VC, Boby VU. Probiotics in human health: a current assessment. Curr Sci. 2005;88:1744–1748.

[36] Tinggi U (2007) Selenium: its role as antioxidant in human health. Environ Health Prev Med 13:102–108

[37] Yang G, Wang ZY, Kim S, Liao J, Seril DN, Chen X, Smith TJ, Yang CS. Characterization of early pulmonary hyperproliferation and tumor progression and their inhibition by black tea in a 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanoneinduced lung tumorigenesis model with A/J mice. Cancer Res 1994;57:1889–1894.

[38] Yang CS, Landau JM, Huang MT, Newmark HL. Inhibition of carcinogenesis by dietary polyphenolic compounds. Annu Rev Nutr. 2001;21:381–406.