Review paper

The Nutraceuticals: A Voluminous Torrent in Pharmaceuticals- Coupling Health & Drugs

ABSTRACT

The present review is focused on the nutraceuticals which are present in our surroundings having an excellent impact over the health of humans but are not known for their pharmaceutical use. Nutraceuticals include vitamins, minerals and other dietary supplements, which may be herbs, enzymes, animal extracts etc. Various researchers have proved that nutraceuticals are having an important role in reducing the risk of various diseases such as diabetes, cardiovascular diseases, Parkinson's disease etc. with very few or negligible side effects.

Keywords: ~~Nutrients,~~ Nutraceuticals, Drugs, Dietary supplements, Functional foods.

1. INTRODUCTION

"Let food be your medicine and medicine be your food" this great line said by the great scientist, Hippocrates, is ~~all~~ related ~~with~~ to the chemicals in food having both nutritional and therapeutic values i.e. Nutraceuticals [1].

Nutraceuticals are a heterogenic products category which has a number of synonyms that are used internationally. The term "Nutraceutical" was given by Stephen De Felice who was the founder and chairman of the Foundation for Innovation in Medicine. This term has been part of the industry lexicon for almost a decade [2]. The term "Nutraceutical" is derived from the combination of two words, "nutrient" which means a nourishing food or food component and second "pharmaceutical" which means a medical drug. Nutraceuticals may contain substances that are "natural", intended to treat or prevent a number of diseases, but may not be generally recognized as safe. Hence these are the food products intended for health and medical benefit [3, 4]. It has been proved by research that ~~the~~ nutraceuticals are useful in providing protection from a number of diseases like diabetes, cancer, cardiac disease, hypertension etc., for example, carotenoids and anti-oxidants found in carrots help in ~~avoiding~~ protection against chronic diseases, by preventing free radical damage [5]. Nutraceuticals have become more popular in the modern society due to the belief of reduced ~~negligible~~ chances of adverse effects, being natural, ~~of~~ ~~pharmaceuticals,~~ the ease of self-medication and the positive effects on the aging ~~in~~ population.

2. TYPES OF NUTRACEUTICALS

2.1 Dietary Supplements

Dietary supplements (DS) include herbs, minerals, vitamins, or products obtained from plant sources, animal sources such as yeasts, fungus, algae, seafood and many more,

for example, energy bars, amino acids, and liquid supplements. They are not consumed in large quantities but have the basic objective to provide nutrition. The United States authorities ~~say~~ state that dietary supplements may be regarded as foods, while elsewhere they are classified as drugs or other products [6, 7].

2.2 Functional Foods

Japan introduced the concept of functional food in 1980s, to promote health or reduce the risk of diseases. The functional foods include those food items which are advised to be consumed as part of the normal diet, they contain biologically active constituents offering the potential to enhance health or reduce risk of various diseases. Among these foods are those that contain fatty acids, vitamins, specific minerals or dietary fibers, foods with added biologically active substances such as phytochemicals or other antioxidants and probiotics that have beneficial live cultures [8]. Some examples of functional food products are; milk, cheese and eggs (enriched with omega-3 fatty acids); yogurt enhanced with live active cultures (probiotics); fruit juices and drinks (having antioxidant properties or containing antioxidants); cereals and grains such as wheat, oat, barley (having enriched amounts of dietary fibre); modified fatty acid vegetable oils; ~~and~~ soy, canola and hemp (vegetable proteins) and legumes [9, 10].

~~According~~ In accordance with the established requirement for the functional food in Japan, the functional food should be consumed:

a). In its natural form, rather than a prepared dosage form like capsule, tablet, or powder;
b). Daily, in sufficient quantity; and
c). In the ~~right~~ correct way ~~to~~ such that it can regulate a biological process, in order to prevent or cure a disease [11].

2.3 Dietary supplements and Food additives

Dietary supplements provide nutrients that may otherwise not be consumed in sufficient quantities. Generally, dietary supplements ~~are like~~ include vitamins, minerals, fatty acids, fiber or amino acids etc., which according to United State authorities ~~dietary supplements~~ are regarded as foods [12].

Food additives like the dietary supplements, are any substances that are either deliberately added to food to enhance its shelf-life, nutrition, texture, or other quality aspect, or which unintentionally contaminates food (indirect additive) (Figure 1) [13].

Nutrients are the nutritive constituents present in food that a person consumes for his/her survival and growth. Macronutrients provide the bulk energy required for functioning of metabolic system, whereas micronutrients are helpful in providing the necessary co-factors for metabolism. Plenty of these nutrients are available in the environment [14]. Inorganic chemical compounds like water, minerals, and oxygen should also be considered as nutrients [15].

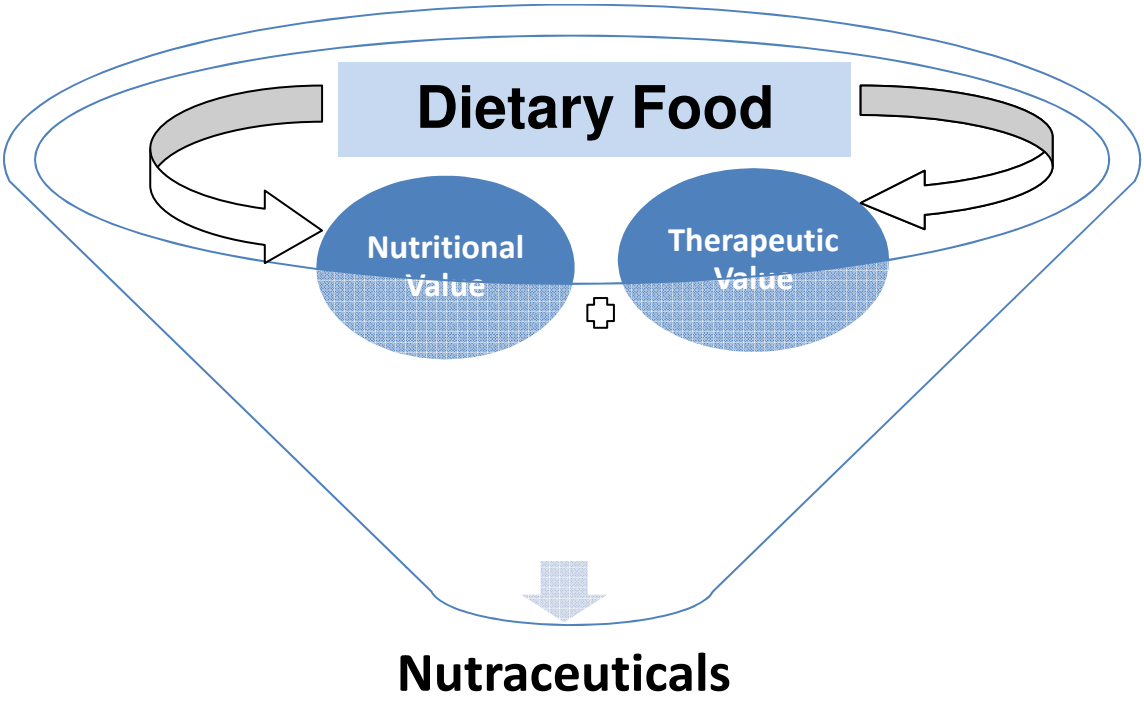

Figure 1: Diagrammatic Representation of Nutraceuticals

2.4 Herbals

In ancient times, a large number of herbs were used to prevent and treat many diseases. A plant containing non-nutritive phytochemicals, provides health benefits if included in diet [16, 17,18]. Nutraceuticals as herbals are big boon to human beings in the aspect of improving their health and to ~~prevent~~ protect them from chronic diseases e.g. willow bark (Salix Nigra) helps as anti-inflammatory, analgesic, anti-arthritic, astringent as well as antipyretic [19].

Phytochemicals

Phytochemicals are the plant components having bioactivities which are used to get health benefits, but their use always requires to be ~~defended~~ backed up with some scientific rationale for being present in food as potential nutraceutical. Phytochemicals ~~having~~ have following health benefits:

(1) These are used as substrates for biochemical reactions.
(2) These are used as cofactors of enzymatic reactions.
(3) These act as ligands which agonize or antagonize cell surface or intracellular receptors.
(4) These are used as scavengers of various reactive or toxic chemicals.

(5) These are used as compounds to increase the absorption and or improve stability of many essential nutrients.
(6) These work as selective growth factors for gut friendly bacteria.
(7) Fermented phytochemicals are beneficial for non-pathogenic bacteria found in ~~GI~~ gastrointestinal tract.
(8) These are selective inhibitors of deleterious intestinal bacteria. Phytochemicals like terpenoids, phenolics, alkaloids and fiber, are extensively examined and used for their ability to ~~g~~et provide health benefits ~~advantage~~ [20].

2.5 Probiotic/ Prebiotics

Probiotic bacteria are "living microorganisms that taken in tolerable quantity, provide a variety of benefits to host health". These may interact with commensal bacteria to have a direct impact on the host. [21] Metchinkoff was the first person who successfully revamped the toxic flora of the large intestine into a host-sympathetic colony of Bacillus bulgaricus, found by Hord [24, 23]. Hence probiotics are gut friendly bacteria which aid~~s~~ in digestion and absorption of some nutrients. They act by eliminating the disease causing pathogens, like yeasts, other bacteria and viruses which mutually develop advantageous symbiosis within gastrointestinal tract (Table 1) [24]. The Japanese were the first to recognize the value of non-digestible oligosaccharides, and added these in feed of piglets to relieve and prevent ~~from the~~ diarrhoea. It was observed that fructo-oligosaccharides and galacto-oligosaccharides cause an increase in intestinal bifido-bacteria which stimulated their growth in the human gut. Hence a prebiotic is "a selectively fermented ingredient that causes changes in the activity of the gastrointestinal microbiota that ~~are~~ is beneficial for human health" [25]. Some people use lactobacillus for irritable bowel syndrome, Crohn's disease, inflammation of the colon, necrotizing enterocolitis in babies born prematurely, infection with Helicobacter pylori, urinary tract infections, vaginal yeast infections, in prevention of common cold in adults and to prevent respiratory infections in children attending daycare centers. It is also being tested to prevent serious infections in people on ventilators [26-31].

A number of ~~marketed~~ commercial/commercially prepared nutraceuticals are available in market as mentioned in Table 2.

3. PHARMACOLOGICAL USE OF NUTRACEUTICALS

Better life quality is achieved with food items filled with nutrient values and remarkably potent in preventing diseases which may be cancer, diabetes, heart diseases, hypertension etc (Table 3 & Figure 2). Such products may be dietary supplements, food additives, phyto-chemicals, prebiotics, probiotics, genetically modified food, processed food and plant products.

Table 1: Different species of microbes used as Probiotic

S.No.	Genus	Species
1	Lactobacillus	Acidophilus Delbrueckiia Brevis Fermentum Gasseri Johnsonii Paracasei Plantarum Reuteri Rhamnosus Salivarius
2	Bifidobacterium	Adolescentis Animalisb Breve Bifidum Infantis Longum
3	Streptococcus	Thermophilus Salivarius
4	Saccharomyces	Cerevisiae
5	Escherichia	Coli
6	Enterococcus	Faecium
7	Bacillus	Coagulansic Clausii

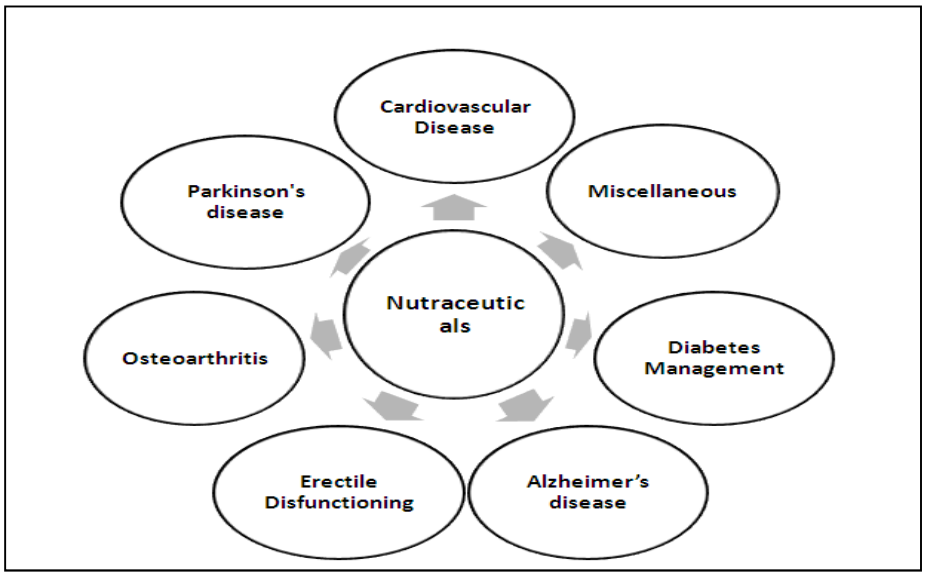

Figure 2: Pharmacological Uses of Nutraceuticals

3.1 In cardiovascular disease

It is not easy to set up a clear impact of nutrition/physical exercise on major cardio vascular diseases because history of cardiovascular diseases is too long [32]. The effect of calcium on hypertension and pre-eclampsia (a condition in pregnancy characterized by high blood pressure, sometimes with fluid retention and proteinuria) is unpredictable as well as ambiguous. It is supposed that high levels of intracellular calcium may increase vascular smooth muscle tone, peripheral vascular resistance, and responsiveness to blood pressure. Treatment with vitamin C and selenium need further study to observe its effect on mortality [33-34].

It has been observed that some nutraceuticals may be useful to prevent the risk of thrombosis in women with thrombophilic gene mutations like viamin E which causes inhibition of platelet aggregation by a protein kinase C-dependent pathway [35-36]. Nutraceuticals like vitamins, minerals, omega-3 poly-unsaturated fatty acids (n-3 PUFAs), dietary fibers and antioxidants, in addition to physical exercise, are recomended to prevent and treat cardio vascular diseases. Researchers have proved that polyphenols found in grapes and in wine are helpful in reducing arterial disease by altering cellular metabolism and signalling [37].

Onion, black grapes, cherries, cruciferous vegetables, grapefruits, red wine, apples and berries are good sources of flavonoids [38] and also available as flavones and flavonols which are beneficial for the treatment of cardiovascular diseases [39-41]. Flavonoids block the angiotensin-converting enzyme, a key moiety that causes a raise in blood pressure [42]. Antioxidant activity of ascorbic acid, alpha-tocopherol, and beta-carotene as has been studied and reviewed [43].

3.2 In the management of diabetes

Various *in-vitro* and *in-vivo* studies (animal) have proved that plant polyphenols including phenolic acids, stilbenes, lignans and flavonoids are effective nutraceuticals in diabetes and ~~in~~ its prevention, although human clinical trials are required to check the efficacy of poly-phenol compounds in treatment of diabetes [44].

Vitamin C (ascorbic acid) is a chain-breaking antioxidant which prevents the propagation of chain reactions that may lead to a reduction in protein glycation. It has been reported that ascorbic acid helps in reducing diabetes-induced sorbitol in animals [16]. Ascorbic acid supplementation (800 mg/day) partially replenishes ascorbic acid levels in patients with type 2 diabetes but endothelial dysfunction or insulin resistance is not effected at all [17].

~~N.~~ Bunyapraphatsara *et al* (1996) observed a combined effect of Aloe vera juice with glibenclamide in diabetic patients and concluded that glibenclamide alone did not show any effect while Aloe vera juice showed significant reduction in fasting blood glucose level and triglycerides within two weeks and four weeks respectively. Aloe vera, however, did not show any effect on level of cholesterol, but was found to be effective in the treatment of diabetes [45]. Acacia is non-starch polysaccharides which is not digested in the intestine, but generate short chain fatty acids in large bowel that produce extensive biological effects. Philips ~~AO~~ *et al* (2011) conducted study over the extract of Acacia Arabica and confirmed the anti-diabetic e ffect of acacia resulted by increasing the insulin release [46]. Hou *et al* (2003) demonstrated significant hypoglycemic effects of Acacia Arabica powder in healthy rabbits, whereas no significant decrease in blood sugar was observed in the alloxan-induced diabetic rabbits was observed [47]. Wadood *et al* concluded that Acacia arabica initiates the release of insulin from pancreatic beta cells of normal rabbits [48]. Antidiabetic activity of glycerrhiza in non-insulin dependent diabetic model was observed by Takii [49].

High intake of isoflavone (20–100 mg/day) is helpful in lowering of rate of mortality in diabetes of type 2, osteoporosis, cardiac disease and certain cancers [50]. Docosahexaenoic acid is vital for neuro-visual development which helps in modulating insulin resistance and nurture the advocacy for essential fatty acids in pregnancy in women with gestational diabetes mellitus [51].

Omega-3 fatty acids helps in reducing blood glucose tolerance in patients predisposed to diabetes. Insulin is needed to synthesize long chain n-3 fatty acids; thus heart may be victim to their depletion in case of diabetes. Hence it is concluded that ethyl esters of n-3 fatty acids may be advantageous in diabetic patients [52]. Lipoic acid is a well-known antioxidant, and in Germany being used to cure diabetic neuropathy. Lipoic acid; as a long-term dietary supplement is aimed at the prophylactic protection of diabetics from complications [53]. α-Lipoic acid enhances insulin sensitivity by approximately 18–20% in patients suffering from type 2 diabetes [54]. Clinical trial studies on α-lipoic acid reported advantageous in the treatment of diabetic neuropathy [55].

Dietary fibers obtained from psyllium have been used to reduce weight and lipid levels in hyperlipidemia as dietary supplement [56]. Intake of Chromium supplements may be helpful to enhance sensitivity to insulin and boost glucose tolerance in type II diabetic patient [48]. Magnesium-rich diet intake may reduce risk of diabetes by improving in insulin sensitivity [57]. Diabetes management is supported by one of the nutraceuticals Biotin which increase insulin production and stimulates liver glucokinase activity, thus improves the uptake of glucose in muscle cells [58-60]. Pharmacological effect of epinephrine can be inhibited by Azadirachta Indica which results in enhanced utilization of peripheral glucose [61-62] and reduce hypo-glycaemic activity without change in the serum cortisol level [63-64].

Kernels of Eugenia jambolana (*Syzygium cumini)* are useful in diabetes management; their aqueous/alcoholic extract shows hypoglycemic effect [65]. Green Tulsi (*Ocimum sanctum*) leaves extract also reduces blood sugar significantly by cortisol inhibiting potency as proved in both normal and alloxan induced diabetic rats [66-67].

3.3 In Parkinson's disease

Latif S *et al* concluded that diet enriched with vitamin E may decreases the chances of Parkinson's disease [68] while Brower V reported that creatine is helpful in management of Parkinson's disease by decreasing the clinical symptoms [69].

Antioxidant vitamin supplements such as tocopherol, ascorbic acid and beta-carotene are the abundantly occurring nutraceuticals. As per various earlier literature vitamin E supplements are becoming popular in treatment of Parkinson's disease, whereas epidemiological studies reported that vitamins C and E rich diets are associated with decreased risk of Parkinson's disease [70-71].

3.4 In Alzheimer's disease

Literatures have been reported that fulvic acid, an active principle of Shilajit is highly effective against brain disorders exclusively and in combination with vitamin B complex. [72] Patients suffering from Alzheimer's disease treated with donepezil and vitamin E found effective although future study was suggested to check and compare additive as well as individual effect. [73] Wettstein A. *et al* reported that mild to moderate Alzheimer's dementia could be treated with metrifonate, donepezil, rivastigmine which are second-generation cholinesterase inhibitors [74].

Hager *et al* found stable cognitive function especially in those patients who were administered with 600 mg Alpha-lipoic acid along with acetyl-cholinesterase inhibitors, in comparison to those patient who only received therapy of of standard acetyl-cholinesterase inhibitors since last 337 days [75]. Huperzine-alpha is a plant alkaloid derived from club moss plant (*Huperzia serrata*)**,** which is a member or the *Lycopodium* species. Huperzine-alpha is in phase III clinical trial in the USA and is available as a dietary supplement [76]. The meta-analysis of Huperzine A reported here highlights that this treatment has certain significant improvement for patients with Alzheimer's disease

and Vascular Dementia, and longer durations may result in better efficacy for patients with Alzheimer's disease [77].

Literature survey supports that Lipoic acid also helps to improves potential of mitochondrial membrane, memory loss due to ageing and brain ailments as well as in patient suffering from Parkinson´s and Alzheimer's disease [78].

3.5 In Erectile Disfunctioning

L-arginine in combination with pycnogenol, a product obtained from the pine bark (*Pinus pinaster),* is found safe and effective in mild to moderate erectile dysfunction in Japanese patients [79]. When Patients suffering from moderate to severe ED and dyslipidemia were kept on Niacin rich diet, significant improvement was observed in patients [80].

Kaempferia Parviflora Wall. Ex. Baker (KP), which is a Thai plant with name, Kra-Chai-Dum and rhizomes of which are used as a traditional medicine to alleviate male impotency, improve male libido, as energizer, control blood pressure and also reduce stomachache. Study reveals that KP is a potential nutraceutical compound effective in male erectile dysfunction caused due to ageing [81].

3.6 Osteoarthritis

Chondroitin sulfate and Glucosamine both are commonly used to alleviate/reduce the symptoms of osteoarthritis. Chondroitin sulfate and Glucosamine both act as nutraceuticals and possible mechanism of their anti- inflammatory activity may be due to synthesis of NO and PGE2 [82]. Capsaicin reduces pain and stiffness and increases joint functioning by acting as agonist for transient receptor potential lvanilloid 1 (pain receptor) [82]. Boswellia serrata relieved joint pain, reduced joint swelling, and stiffness by inhibiting TNF-α-induced MMP-3 expression and protected against IL-1β-induced chondrocyte death [83-85]. Capsaicin reduces pain and stiffness to increased joint function by agonising transient receptor potential vanilloid 1 (pain receptor) while prolonged exposure of capsaicin leads to desensitization of this pain pathway [86-87].

Cat's claw reduces osteoarthritis associated pain by Inhibiting lipo-polysaccharide induced PGE2 production and activation of TNF-α. Avocado/soybean unsaponifiables reduced pain in osteoarthritis patients and reduces NSAID consumption by suppressing TNF-α, IL-1β, COX-2, and iNOS in LPS-activated chondrocytes [88-89]. Collagen hydrolysates alleviate osteoarthritis related pain by stimulating regeneration of type II collagen and by increasing biosynthesis of proteoglycans [90].

.4. Nutraceuticals tailoring genes- Nutragenomics or Nutrigenomics? Which is correct?

Nutrigenomics is an emerging field to know interactions between food and genes, due to manipulated diet [91]. Nutrigenomics is the study of the use of functional genomic tools to probe a biological system followed by a nutritional stimulus to understand how nutritional molecules may affect metabolic pathways and homeostatic control [92].

Study of effect of nutrigenomics also becomes necessary to find out the effect of foods on factors that may interact with particular genes to increase risk of diseases like diabetes mellitus, obesity, cardiovascular diseases etc. [93]. Hence it is a vast field ~~to~~ that describes the impact of food on genes of human being and requires that a lot of studies be done.

Conclusion

In the present scenario nutraceuticals have become more popular in modern society and became important due to increasing applications of Nutraceuticals which serves as a part of growing pharmaceutical industry. Modern society now is being aware ~~about~~ of the food products that are beneficial ~~for~~ to them in the aspects of health and nutrition owing to very few or no side effects. ~~Nutraceuticals are being used to treat fatal diseases like cancer, diabetes, cardiovascular diseases; as well as Parkinson's disease, osteoarthritis etc.~~ Poor conclusions. Suggestion: Nutraceuticals thus appear to be the way forward to prevent, control and possibly cure chronic diseases in the most natural, safe and easily affordable manner.

Table 2: List of Marketed Nutraceuticals

Products	Category	Contents	Manufacturer
Alamin SE	Protein supplement	L-Arginine & other Protein	Albert David Ltd., India
Albumen Care	Protein supplement	L-arginine, multivitamins & minerals	B.V. Bio-Corp Pvt. Ltd., India
Arginine	Protein Supplement	L-argnine, proantho- cyanidis	Manikind Pharma Pvt. Ltd, India
Appetite Intercept™	Appetite suppressant	Caffeine, tyrosine and Phenylalanine	Natrol, Chatsworth, CA, USA
Betafactor™	Immune supplement	Beta glycan	Ameridan Inernational Inc. USA
Brainspeed Memory®	Brain Health supplement	Vitamin and minerals	Natrol, Chatsworth, CA, USA
Biovinca™	Neurotonic	Vinpocetine	Cyvex nutrition, Irvine, USA
Coral calcium	Calcium supplement	Calcium and trace minerals	Nature's answer, Hauppauge, NY, USA
Calcirol D-3®	Calcium supplement	Calcium and vitamins	Cadilla healthcare, India
Chaser™	Hangover supplement	Activated calcium carbonate, and vegetable carbon	Living essentials, Walled lake MI, USA
GRD®	Nutritional supplement	Proteins, vitamins, minerals and carbohydrates	Zydus Cadila Ltd. Ahmedabad, India
Weight smart™	Nutritional supplement	Vitamins and trace elements	Bayer corporation, Morristown, NL, USA
Yakult	Probiotic dairy product	Skimmed milk, *Lactobacilli casai Shirota*	Danone india Ltd. India
ImmunAge	Fermented papaya Preparation	Papaya, yeast, dextrose	Osato laboratory Inc. USA
Glowelle®	Beauty drink	Antioxidants, vitamins and fruit extracts	Nestle, India
HiOwna	Nutriional supplement	Protein, multivitamins, minerals and antioxidant	Himalaya herbal ltd, India
PediaSure®	Nutritional supplement	Protein, multivitamins and antioxidant	Abbott India ltd, India
Revital®	Health suppliment	Ginseng, vitamin and minerals	Ranbaxy, India
Proteinex®	Protein supplement	Predigested proteins, vitamins, minerals and carbohydrates	Pfizer Ltd., Mumbai, India
Rox® Glucon-D Glucose-D	Energy drink	Taurine, caffeine and glucuronolactone Glucose	Rox America, Spartanburg, SA, USA Dabur
Omega woman	Immune supplement	Antioxidants, vitamins and. phytochemicals (*eg.* Lycopene, and resveratrol)	Wassen, Surrey, U.K
Mushroom optimizer™	Immune supplement	Mushrooms polysaccharides and Folic acid	Jarrow formulas, Los Angeles,CA, USA
Proplus®	Nutritional supplement	Soy proteins	Campbell soup company, Camden, NJ, USA
Snapple-aday™	Meal replacement beverage	Vitamins and minerals	Snapple beverage group, White Plains, NY, USA
WelLife®	Amino acid supplement	Granulated-L-glutamine	Daesang America Inc., Hackensach, NJ, USA
Olivenol™	Dietary supplement	Natural antioxidant, Hydroxytyrosol	Cre Agri, Hayward, CA, USA
Threptin®	Diskettes Protein supplements	Proteins and vitamin B	Raptakos, Brett & Co. Ltd., Mumbai, India
Red bull®	Energy drink	Taurine, Caffeine,	Austrian red bull GmbH

		Glucuronolactone, b- group vitamins	

Table 3: Detailed Review on Various Nutraceuticals

Types of Nutraceuticals	Sources	Active Constituents	Applications
Dietary Fibre	Whole grain foods wheat and corn bran, nuts	Insoluble Fibre	Reduce chances of colon or breast cancer (anticancer) [94, 95], maintain health of digestive tract [96]
	Oats, barley	Beta-Glucan	Reduce risk of cardiovascular disease, lower down Low Density Lipids and total cholesterol [97,98]
	Beans e.g. Legumes, oats, barley and some fibrous fruits	Soluble Fibre	Anticancer (Colon Cancer), Digestive [99.100]
Fatty Acids	Salmon and other fish oils	Long chain omega-3 Fatty Acids-DHA/EPA	Reduce risk of CVD, Improve mental, visual functions[101-103]
	Cheese, meat products	Conjugated Linoleic Acid	Improving of body composition, Decreases chances of certain cancers[104-106]
	Fruits	Anthocyanidins	Antioxidant ; reduce risk of cancer[87-109]
	Green Tea	Catechins	Antitumor [110]
Phenolics	Citrus	Flavonoids	Antioxidative activity, Prevention of coronary heart disease, hepato-protective, Effective in inflammation and cancer [111]
	Cocoa, Chocolate, Cranberries & cranberry	Tannins	Anti-microbial, Reduce risk of cardiovascular disease [112]
	Corn, soy, wheat, wood oils	Plant Sterols, Stanol ester	Lower blood cholesterol levels by inhibiting cholesterol absorption [113]
	Tomatoes	Lycopene	Antioxidant, protect against prostate cancer [114]
Carotenoids	Corn, various fruits, egg yolk, spinach	Lutin	Antioxidant, Muscle regeneration, anti cancer activity, protect eyes against age related muscular degenerations, cataract [115, 116]
	Carrots, various fruits (Guava, papaya, Water melon etc) and vegetables (tomatoes etc).	Beta carotene	Antioxidant, protection of cornea against UV light.
	Soya beans	Saponins	Effective against colon cancer, reduces cholesterol level [117]
Probiotics/ Prebiotics	Curd	Lactobacillus	Antibacterial, acute diarrhea [118]
	Whole grains, onions, combination of Pro & Prebiotics	Fructo–oligosaccharides	Improve GI health, restore gut flora [119]
	Grains	Tocotrienols and tocopherols	The growth of diverse tumors cell lines was suppressed via initiation of apoptosis and concomitant arrest of cells in the G1 phase of the cell cycle [120]
Phytochemical	Cereal grain, dairy & egg products and plants oil	Phytosterols	Exhibitantioxidant, anti-inflammatory, anti-neoplastic, anti-pyretic & immune-modulating activity, decrease cholesterol [121-123]
	Various plants, whole grain	Phenolic constituents	Antioxidants, Anti-hyperglycemic, and anti hypertensive [124]
	Grapes, berries, cocoa, green tea, acacia spp.	Catechin & gallic acids	Antioxidants, Antiradical property, cyto-protective.[125, 126]

	Soybeans	Isoflavonoids	Treating cancers & attenuates bone loss [127, 128]

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