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## A review on medicinal importance, pharmacological activity and toxicology of “Nutraceuticals”

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### Abstract

Nutraceutical are substances which are not conventionally predictable nutrients but which have affirmative physiological property on the human body. Innumerable naturally occurring wellbeing-enhancing substances are of plant derivation having a number of physiologically-energetic components that develop awareness for their prospective role in finest health. Nutraceuticals have received substantial interest due to their exploratory protection, impending nutritive and remedial property. They are a substitute for current medicines and in addition, afford healthy living wage. To evade side effects related to medicines, longer anticipation and to amplify the wellbeing, nutraceuticals are being preferred. Nutraceuticals are remedial foods that play a vital role in maintaining welfare, enhancing strength, modulating immunity and thus preventing in addition to treating exact diseases. For that reason, the field of nutraceuticals can be envisioned as one of the omitted blocks in the fitness benefit of a personage. In this review, a challenge has been finished to recapitulate medicinal use of nutraceuticals and their valuable pharmacological effects on human healthiness.

**Keywords:** dietary source, lifestyle, welfare, functional food, nutraceutical

### Introduction

Nutrition is a primary need. A variety of menace factors allied to health result from a disparity in nutrition<sup>[1]</sup>. Mutually, these factors add to more than 40 percent of deaths and 30 percent of the on the whole disease encumber in developing countries. The lifestyle of India's nutrition concerns are three folds-on one hand, is the malnourished populace (380 million) by majority having insufficient purchasing authority to even devour a diet adequate in calories, leave alone acquire satisfactory nutrients<sup>[2]</sup>. In contrast is the vast populace (570 million) that is nourished in calorie ingestion but not in the vocabulary of nutrient intake. Numerous of the factors moving nutrition allied concerns are irretrievable that have led to natural sources of nutrients being inspired in inadequate quantities. For this reason, the necessity of exterior interference that can supplement diet to assist foil nutrition-linked disorders and encourage wellness above the management of sickness has become crucial. About 2000 years ago, Hippocrates exactly emphasized “*Let food be your medicine and medicine be your food*”. Foods include diverse nutritional components among an assortment of health welfares that endeavour an excellent contingency to augment public health and welfare. The medical welfares of foods have been analysed since time primeval<sup>[3]</sup>. Sanitation investigation has shown a bond between the diminution of plant-derived aliment (fruits, vegetables along with whole grains) and a domain of health welfare. Phytochemicals that are existing in the meal have been linked to health welfares are glucosinolates, sulphur comprising a composition of the Alliaceae, terpenoids (carotenoids, monoterpenes, and phytosterols), along with discrete groups of polyphenols (anthocyanins, flavones, isoflavones, stilbenoids, ellagic acid, etc.). This domain of by-products cannot be accurately categorized as ‘food’ and a novel hybrid caption amidst nutrients and pharmaceuticals, accordingly ‘nutraceuticals’, has been forged to title them in 1989 by Stephen DeFelice (Fig. 1 Nutraceutical Terminology), initiator and administrator of infrastructure for alteration in a medicament, an American institution which bucked up medical health<sup>[4, 5, 6]</sup>. It is ascertained “as a food in other words segments of food that bestowed medical or health welfares, inclusive of the cure and therapy of illness”. Nutraceuticals may domain from secluded nutrients, relating to diet supplements, and diets to hereditarily engineered “trendy” food, herbal commodities, and processed products for instance cereals, soups, along with beverages. A nutraceutical is every in noxious food essence supplement that has accurately authenticated health welfares for bo the therapy along with cure of illness<sup>[7]</sup>.

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The hypothesis of nutraceutical was commenced from the inquiry in U.K., Germany along with France and it achieved that nutritional therapy is rated additional extremely by customer followed by implement or genetic factors to achieving a superior welfare. In the U.S. "nutraceutical" was generally used, but no regulative annotation prevailed. Its denotation was altered by health care of Canada which detonated nutraceutical as "a product separated or redeemed from the food, conventionally sold in medicinal profile not accomplice with food and authenticated to have a physiological welfare. It also imparted benefit opposing severe illness"<sup>[8]</sup>.

Functional foods are those that when engrossed habitually endeavour a specific health-welfare effect besides their nutritional resources (i.e., a healthier dignity or a lessened risk of illness) and this outcome must be accurately proven (International Life Science Institute; <http://www.ilsa.org>). Functional foods are alike to conventional foods which are engrossed as part of a customary diet but are acknowledged to augment health status besides leading nutritional activity. As in case of functional foods which incorporate foods that embraces distinct vitamins, minerals, dietary fiber or fatty acids, foods with augmented biologically potent substances suchlike photochemical or another antioxidants along with probiotics. Unmodified whole foods such as fruits along with vegetables epitomize the elementary form of a functional food. As in case of carrots, broccoli and tomatoes would be mediated functional foods for the reason, that they are loaded with physiologically potent substances suchlike lycopene, beta carotene along with sulforaphane. Nutraceuticals are products outgrowth from foods though sold in the medicinal profile of either a tablet, powder, capsule, solution or aromatic which is not commonly affiliated with the food and have manifested physiological welfare or contribute to guarding against severe illness; these are now implicated as "natural health products" in Canada<sup>[9]</sup>. Medical foods are a specific category of therapeutic agents that are intended for the nutritional management of a specific disease. An example of medical foods is formulations intended to manage patients with inborn errors in amino acid metabolism. Newer medical foods are designed to manage hyperhomocysteinemia, pancreatic exocrine insufficiency, metabolic syndrome, obesity, cardiovascular diseases, osteoporosis, diabetes and, among these, hypercholesterolaemia inflammatory conditions, cancer and other diseases. Some popular nutraceuticals include glucosamine (for arthritis), lutein (for macular degeneration), ginseng (for cold), echinacea (anti-immune), folic acid, cod liver oil capsules, etc. The most popular functional food and beverage products include omega-3 eggs, omega-3 enriched yoghurts, calcium enriched orange juice, green tea to mention a few. The aim of this review is to summarize the positive outcome and mechanism of action of some of the most well-known lipid-lowering nutraceuticals on hypercholesterolaemia.

### Overview of nutraceuticals

Our concurrent diets often dearth the balance of nutrients in our bodies craved to nurture optimum health. Nutrition depends upon the entangled interaction of many elements to be effective in nourishing your body (Table 1). Nutraceutical aid to ample the void by subjecting to greater volumes and the befitting balance of vitamins, herbs, along with minerals our systems devoid to perpetuate or improve health. The majority of nutraceuticals are of plant origin. Thus, nutraceuticals are

"pills" that contain concentrated forms of presumed bioactive phytochemicals extracted from the original food item (e.g., genistein from soy). Because of their plant origin, these compounds are considered safe and are popular among consumers. Although there is a renewed interest in identification of synthetic PPAR $\gamma$  modulators for the treatment of type 2 diabetes, developing known dietary components (nutraceuticals) that bind and activate PPAR $\gamma$  with more efficacy and safety, while promoting health benefits has become an absolute necessity<sup>[10]</sup>. The physiological significance of the interactions between dietary lipids and their derivatives with PPARs<sup>[11, 12]</sup>. Dietary fats and oils are major sources of these ligands, which include both n-3 and n-6 lipids and their oxidized counterparts. Elegant structure-function studies have determined the binding efficiency of the dietary lipids with PPARs<sup>[11, 13-14]</sup>. Though dietary lipids similar to synthetic ligands were able to bind to the ligand binding domain and cause conformational changes to activate the receptor, they are considered as weak PPAR $\gamma$  ligands because of their low physiological concentrations. One must keep in mind that most of the studies determining the binding efficiency of the nutraceuticals have been performed in either cell-free or cell based systems. The specificity of the dietary compounds to act as ligands for PPAR $\gamma$  was determined by a lack of response when cells were either pretreated with a known antagonist of PPAR $\gamma$  or with constructs that lacked PPAR ligand binding domain. However, in cell based systems it is conceivable that a metabolite of the parent compound, not the parent compound itself, might be mediating the response through interactions with PPAR $\gamma$ . For example, 13-HODE (oxidized n-6 lipid), a known agonist of PPAR $\gamma$ , could be converted into 13-Ox-HODE prior to interacting with PPAR $\gamma$ .

### Pharmacological Role of Nutraceuticals

Majority of the nutraceuticals do possess multiple therapeutic benefits, however in the present review much effort has been devoted to decentralize them based on their disease specific major indication. Nutraceuticals have been claimed to have a physiological benefit or provide protection against the following diseases (and/or found to act as) such as cardiovascular agents, Anti Obese agents, antidiabetics, Anticancer agents, Immune boosters, Chronic inflammatory disorders and Degenerative diseases.

### Effect of nutraceuticals on CVS

Cardiovascular diseases (CVD) is the name for the group of disorders of the heart and blood vessels and include hypertension (high blood pressure), coronary heart disease (heart attack), cerebrovascular disease (stroke), heart failure, peripheral vascular disease, etc. Many research studies have identified a protective role for a diet rich in fruits and vegetables against CVD. This apart, nutraceuticals in the form of antioxidants, dietary fibers, omega-3 polyunsaturated fatty acids (n-3 PUFAs), vitamins, and minerals are recommended together with physical exercise for prevention and treatment of CVD (Figure 2).

Polyphenols are simple phenolic molecules to highly polymerized compounds with molecular weights of greater than 30,000 Da. Stilbenes, anthocyanins, condensed tannins (proanthocyanidins) present in grapes and in wine alter cellular metabolism and signaling, which is consistent with reducing arterial disease<sup>17</sup>. Nutrients and nutraceuticals with calcium channel blocking activity (thus antihypertensive

activity) include  $\alpha$ -Lipoic acid, magnesium, Vitamin B6 (pyridoxine), Vitamin C, N Acetylcysteine, Hawthorne, Celery,  $\omega$ -3 fatty acids etc.

Flavonoids are present in onion, endives, cruciferous vegetables, black grapes, red wine, grapefruits, apples, cherries and berries. Flavanoids in plants available as flavones (containing the flavonoid apigenin found in chamomile) flavanones (hesperidin-citrus fruits, silybin-milk thistle flavonols (tea, quercetin, kaempferol and rutin grapefruit, rutin buckwheat, ginkgo flavonglycosides-ginkgo) play a major role in curing the cardiovascular diseases. Flavonoids block the angiotensin-converting enzyme (ACE) that raises blood pressure; by blocking the "suicide" enzyme cyclooxygenase that breaks down prostaglandins, they prevent platelet stickiness and hence platelet Hesperidin is a flavanone glycoside and mainly present in sweet oranges (*Citrus sinensis*) and tangelos. Hesperidin, in combination with a flavone glycoside called diosmin, is used for the treatment hemorrhoids and has analgesic and anti-inflammatory activity<sup>18</sup>. Flavonoid intake was significantly inversely associated with mortality from coronary heart disease.

Phytosterols in diet have the potential to reduce the morbidity and mortality from cardiovascular disease<sup>23</sup>. Dietary fiber preparation from defatted rice bran has laxative and cholesterol-lowering ability with attendant benefits towards prevention or alleviation of cardiovascular disease, diabetes and colon cancer. Milk and eggs are the important animal sources of nutraceuticals like proteins and polyunsaturated fats or essential fatty acids (EFAs). EFAs reduce blood pressure, lower cholesterol and triglycerides, reduce the risk of blood clots, help prevent many diseases including arthritis, arrhythmias, and other cardiovascular diseases<sup>26</sup>.

### Effect of nutraceuticals on obesity

Obesity defined as an unhealthy amount of body fat is a well-established risk factor for many disorders like angina pectoris, congestive heart failure, hypertension, hyperlipidemia, respiratory disorders, renal vein thrombosis, osteoarthritis, cancer, reduced fertility etc. Obesity is now a global public health problem, with about 315 million people are estimated to fall into the WHO defined obesity categories. One of the primary causes this rapid rise in obesity rates is the increased availability of high-fat, energy dense foods. Excessive consumption of energy-rich foods (snacks, processed foods and drinks) can encourage weight gain, which calls for a limit in the consumption of saturated and Trans fats apart from sugars and salt in the diet. Caloric restriction and increased physical activity has been shown to be only moderately successful in managing obesity. Thus many health care practitioners and obese individuals are seeking the help of pharmaceuticals and nutraceuticals to treat obesity. A tolerable and effective nutraceutical that can increase energy expenditure and/or decrease caloric intake is desirable for body weight reduction. Herbal stimulants, such as ephedrine, caffeine, ma huang-guarana, chitosan and green tea have proved effective in facilitating body weight loss. However, their use is controversial due to their ability to cause undesired effects. Buckwheat seed proteins have beneficial role in obesity and constipation acting similar to natural fibers present in food. 5-hydroxytryptophan and green tea extract may promote weight loss, while the former decreases appetite, the later increases the energy expenditure<sup>[34-40]</sup>.

### Effect of nutraceuticals on Diabetes

Diabetes mellitus is characterized by abnormally high levels of blood glucose, either due to insufficient insulin production, or due to its ineffectiveness. The most common forms of diabetes are type I diabetes (5%), an autoimmune disorder, and type II diabetes (95%), which is associated with obesity (Figure 3). Gestational diabetes occurs in pregnancy<sup>[45]</sup>. Globally the total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2003<sup>[46]</sup>. Diabetes, like most chronic health conditions, not only places substantial economic burdens on society as a whole but also imposes considerable economic burdens on individual patients and their families. In US alone an estimated the expenditures for health care for people with diabetes totaled \$85.7 (11.9% of total health care expenditures) in 1992<sup>[47]</sup>. Diet therapy is the cornerstone for the management of gestational diabetes mellitus. Although there is widespread use of herbal dietary supplements that are believed to benefit type 2 diabetes mellitus, few have been proven to do so in properly designed randomized trials. Isoflavones are phytoestrogens; they have a structural/functional similarity to human estrogen and have been consumed by humans worldwide. Of all phytoestrogens, soy isoflavones have been studied most. A high isoflavone intake (20-100 mg/day) is associated with lower incidence and mortality rate of type II diabetes, heart disease, osteoporosis and certain cancers<sup>48</sup>. Omega-3 fatty acids have been suggested to reduce glucose tolerance in patients predisposed to diabetes. For the synthesis of the long chain n-3 fatty acids, insulin is required; the heart may thus be particularly susceptible to their depletion in diabetes. Ethyl esters of n-3 fatty acids may be potential beneficial in diabetic patients<sup>49</sup>. Docosahexaenoic acid modulates insulin resistance and is also vital for neuro visual development. This is especially important in women with gestational diabetes mellitus which foster the recommendation for essential fatty acids during pregnancy. Lipoic acid is a universal antioxidant, now used in Germany for the treatment of diabetic neuropathy. It is possible that lipoic acid may be more effective as a long-term dietary supplement aimed at the prophylactic protection of diabetics from complications. Dietary fibers from psyllium have been used extensively both as pharmacological supplements, food ingredients, in processed food to aid weight reduction, for glucose control in diabetic patients and to reduce lipid levels in hyperlipidemia. Good magnesium status reduces diabetes risk and improves insulin sensitivity, chromium picolinate, calcium and vitamin D appear to promote insulin sensitivity and improve glycemic control in some diabetics, extracts of bitter melon and of cinnamon have the potential to treat and possibly prevent diabetes. However it has been suggested that nutraceuticals with meaningful doses of combinations may substantially prevent and presumably could be marketed legally.

In Figure 3 beneficial effects of polyphenols on management of blood glucose in diabetes are summarized. The hypoglycaemic effects of polyphenols are mainly attributed to reduce intestinal absorption of dietary carbohydrate, modulation of the enzymes involved in glucose metabolism, improvement of  $\beta$ -cell function and insulin action, stimulation of insulin secretion, and the antioxidative and anti-inflammatory properties of these components<sup>[25, 26, 27]</sup>.

### Effect of nutraceuticals on Cancer

Cancer has emerged as a major public health problem in developing countries, matching the industrialized nations. A

healthy lifestyle and diet can help in preventing cancer 54, 55. People who consume large amount of lutein-rich foods such as chicken eggs, spinach, tomatoes, oranges and leafy greens experienced the lowest incidence of colon cancer 56.

Chronic inflammation is associated with a high cancer risk. At the molecular level, free radicals and aldehydes, produced during chronic inflammation, can induce deleterious gene mutation and posttranslational modifications of key cancer-related proteins. Chronic inflammation is also associated with immuno suppression, which is a risk factor for cancer. Ginseng as an example of an anti-inflammatory molecule that targets many of the key players in the inflammation-to cancer sequence 57.

Phytochemicals derived from herbs and spices also have potential anticarcinogenic, antimutagenic activities, are and hormonal activity, called "phyto-estrogens", for prevention of prostate/breast cancer 58.

Flavonoids found in citrus fruit appear to protect against cancer by acting as antioxidants 59. Soyfoods are a unique dietary source of isoflavones, the polyphenolic phytochemicals exemplified by epigallocatechin gallate from tea 60, curcumin from curry and soya isoflavones possess cancer chemopreventive properties 61. The main soybean isoflavones, genistein, daidzein, biochanin inhibits prostate cancer cell growth 62, 63.

Carotenoids are a group of phytochemicals that are responsible for different colors of the foods. Recent interest in carotenoids has focused on the role of lycopene in human health. Because of the unsaturated nature of lycopene it is considered to be a potent antioxidant and a singlet oxygen quencher 64. Lycopene prevents cancer, cardiovascular disease, and gastrointestinal tract. It concentrates in the skin, testes, adrenal and prostate where it protects against cancer 65. The linkage between carotenoids and retinoids and the prevention of cancer coronary artery diseases, and advanced age-related macular degeneration heightened the importance of value-added fruits in human diet. Recently, it was reported that lycopene containing fruits and vegetables exert cancer-protective effect via a decrease in oxidative and other damage to DNA in humans 66. Lycopene is one of the major carotenoids in western diets and is found almost exclusively in tomatoes, water melon, guava, pink grapefruit and papaya 67. Beta-carotene, the important precursor of vitamin A has anti-oxidant properties and help in preventing cancer and other diseases. Among the carotenes, beta carotene is the most active as antioxidants. Alpha carotene possesses 50% to 54% of the antioxidant activity of beta carotene, whereas epsilon carotene has 42% to 50% of the antioxidant activity. Alpha and beta carotenes, along with gamma carotene and the carotenes lycopene and lutein 68 which do not convert to vitamin A, seem to offer protection against lung, colorectal, breast, uterine and prostate cancers.  $\beta$ - Carotene is the more common form and can be found in yellow, orange, and green leafy fruits and vegetables. These can be carrots, spinach, lettuce, tomatoes, sweet potatoes, broccoli, cantaloupe, oranges, and winter squash.

Saponins are reported to possess antitumor and antimutagenic activities and can lower the risk of human cancers, by preventing cancer cells from growing. Saponins are phytochemicals which can be found in peas, soybeans, and some herbs with names indicating foaming properties such as soapwort, soapbark and soapberry. The non-sugar part of saponins has also a direct antioxidant activity, which may result in other benefits such as reduced risk of cancer and

heart diseases 69.

Tannins also called proanthocyanidins, detoxify carcinogens and scavenge harmful free radicals 70. Tannins in cranberries also protect against urinary tract infections. It is present in blackberries, blueberries, cranberries, grapes, lentils, tea and wine. Ellagic acid is a proven anti-carcinogen 71 is used in alternative medicine and to prevent cancer 72. It is present in strawberries, cranberries, walnuts, pecans, pomegranates and the best source, red raspberry seeds. Pectin is a soluble fiber found in apples. A new form of citrus pectin called modified citrus pectin (MCP) has been shown to prevent prostate cancer metastasis by inhibiting the cancer cells from adhering to other cells in the body. Several studies have also shown pectin to have positive influences in decreasing serum cholesterol levels, without effecting serum triglyceride levels. Pectin also has the ability to reduce the rise of blood sugar when combined with meal 73.

Naturally occurring phenolic acid derivatives are reported to possess potential anticancer properties 74, 75. Phenolics such as ferulic, caffeic, gallic acids and curcumin are reported to possess anticancer activity 76. Glucosinolates are found in cruciferous vegetables including the *Brassica* crops-Brussels sprouts, broccoli, cauliflower, cabbage, watercress, oilseed rape, and mustard and are powerful activators of liver detoxification enzymes 77. Glucosinolates and their hydrolysis products, including indoles and isothiocyanates, and high intake of cruciferous vegetables has been associated with lower risk of lung and colorectal cancer they also regulate white blood cells and cytokines. White blood cells are the scavengers of the immune system and cytokines act as "messengers," coordinating the activities of all immune cells. The sulfur compounds, in garlic were found to kill bacteria and parasites, boost the immune system and reduce atherogenesis and platelet stickiness. Onions are rich in two chemical groups that have perceived benefits to human health, which include anticarcinogenic properties, antiplatelet activity, antithrombotic activity, antiasthmatic and antibiotic effects 79. Curcumin (diferuloylmethane) is a polyphenol derived from the plant *Curcuma longa*, commonly called turmeric. Curcumin, an active yellow pigment of turmeric reported to possesses anticarcinogenic, antioxidative and anti-inflammatory properties 80-82. The anticancer potential of curcumin stems from its ability to suppress proliferation of a wide variety of tumor cells. Top of Form Beet roots, cucumber fruits, spinach leaves, and turmeric rhizomes, were reported to possess anti tumor activity 83. Non-prescription antioxidants and other nutrients (patients using beta-carotene; vitamins A, C, and E; selenium; cysteine; B vitamins; vitamin D3; vitamin K3; and glutathione as single agents or in combination.) do not interfere with therapeutic modalities for cancer 84.

## **Effect of nutraceuticals an inflammatory disorders and immune boosters**

### **Immune boosters**

Various nutrients in the diet play a crucial role in maintaining an optimal immune response, on the organism's immune status and susceptibility to a variety of disease conditions. a broad range of phytopharmaceuticals with a claimed hormonal activity, called phyto-estrogens, is recommended for prevention of various diseases related to a disturbed hormonal balance. In this respect, there is a renewed interest in soy isoflavones (genistein, daidzein, biochanin) as potential superior alternatives to the synthetic selective estrogen

receptor modulators (SERMs), which are currently applied in hormone replacement therapy. Phytochemicals integrate hormonal ligand activities and interfere with signaling cascades, their therapeutic use may not be restricted to hormonal ailments only but may have applications in cancer chemoprevention and/or certain inflammatory disorders as well. Nutraceuticals that belong to the category of immune boosters and/or anti-viral agents are useful to improve immune function and accelerate wound-healing. They include extracts from the coneflowers, or herbs of the genus Echinacea, such as Echinacea purpurea, Echinacea angustifolia, Echinacea pallida, and mixtures thereof; extracts from herbs of the genus Sambuca, such as elderberries; and Goldenseal extracts. The coneflowers in particular are a popular herbal remedy used in the central United States, an area to which they are indigenous. The extract derived from the roots contains varying amounts of unsaturated alkyl ketones or isobutylamides. Goldenseal is an immune booster with antibiotic activity, and includes compounds like berberine and hydrastine, which stimulate bile secretion and constrict peripheral blood vessels respectively. Astragalus membranaceus, Astragalus mongholicus, and other herbs of the genus Astragalus are also effective immune boosters in either their natural or processed forms. Astragalus stimulates development and transformation of stem cells in the marrow and lymph tissue to active immune cells. The effect of plant and bacteria on systemic immune and intestinal epithelial cell function has led to new credence for the use of probiotics and nutraceuticals in the clinical setting. The probiotics have been found to effective in conditions like in infectious diarrhea in children and recurrent Clostridium difficile induced infections. Evidence is being acquired for the use of probiotics in other gastrointestinal infections, irritable bowel syndrome and inflammatory bowel disease. The dietary approach to allergy has evolved to include active stimulation of the immature immune system in order to support the establishment of tolerance. Supplementation with probiotics may provide maturational signals for the lymphoid tissue and improve the balance of pro- and anti-inflammatory cytokines. Enteral polymeric feeding is effective in Crohn's disease. Dietary nucleotides may improve growth and immunity, optimize maturation, recovery and function of rapidly dividing tissue. Usage of probiotics (live viable microbial organisms) in the treatment of specific diseases has evolved into an extremely valuable option. The ability to reduce antibiotic use, the apparently very high index of safety, and the public's positive perception about "natural" or alternative therapies. These products manipulated the intestinal microflora to maintain the normal balance between pathogenic and non-pathogenic bacteria. Therapeutic effects of most commercial preparations are unsubstantiated. Certain probiotics will be effective in the treatment or prevention of certain conditions. Lactobacillus GG has been shown to be effective in the treatment or prevention of a number of problems including acute diarrhea in children, travelers' diarrhea in adults, Crohn's disease, and reduction of the incidence of antibiotic associated diarrhea in infants. Most probiotic preparations are comprised of one or more lactic acid bacteria (LAB). Within this group, strains of Lactobacillus, Bifidobacterium sp. And occasionally Streptococcus are most commonly used. A supplementary use of oral digestive enzymes and probiotics is also an anticancer dietary measure towards decreasing the incidence of breast, colorectal, prostate and bronchogenic cancer.

### Inflammatory disorders

Inflammation is the response of body tissues to injury or irritation, characterized by pain and swelling and redness and heat. Arthritis is a general term that describes inflammation in joints. Some types of arthritis associated with inflammation include- rheumatoid arthritis shoulder tendinitis or bursitis gouty arthritis and polymyalgia rheumatica. Micronutrients for which preliminary evidence of benefit exists include vitamin C and vitamin D. In addition, numerous nutraceuticals that may influence osteoarthritis pathophysiology, including glucosamine, chondroitin, S-Adenosylmethionine, ginger and avocado/soybean unsaponifiables, have been tested in clinical trials. These products are safe and well tolerated, but interpretation of the collective results is hampered by heterogeneity of the studies and inconsistent results. Cat's claw is a potent anti-inflammatory agent. The two known species of cat's claw are Uncaria guianensis, used traditionally for wound healing, and Uncaria tomentosa, which has numerous medicinal uses and is most commonly found in supplements. Cat's claw is a rich source of phytochemicals: alkaloids, along with glycosides, tannins, flavonoids, sterol fractions, and other compounds. Scientists previously attributed the efficacy of cat's claw to compounds called oxindole alkaloids; more recently, however water-soluble cat's claw extracts that do not contain significant amounts of alkaloids were found to possess strong antioxidant and anti-inflammatory effects are independent of their alkaloid content. Resveratrol is present in the fruits of bilberry (*Vaccinium myrtillus*), the lowbush "wild" blueberry (*Vaccinium angustifolium*), the rabbiteye blueberry (*Vaccinium ashei* Reade), and the highbush blueberry (*Vaccinium corymbosum*). Although blueberries and bilberries were found to contain resveratrol, the level of this chemoprotective compound in these fruits was <10% that reported for grapes. Resveratrol shows the strongest sirtuin-like deacetylase action of any known phytochemical. Sirtuins have been shown to extend the lifespan of yeast and fruit flies. It acts as an anti-inflammatory agent, antifungal and inhibits cyclooxygenase-1 enzyme. Other beneficial health effects include anti-cancer, antiviral, neuroprotective, anti-aging and life prolonging effects. The omega-3 and omega-6 series play a significant role in health and disease by generating potent modulatory molecules for inflammatory responses, including eicosanoids (prostaglandins, and leukotrienes), and cytokines (interleukins) and affecting the gene expression of various bioactive molecules. Gamma linolenic acid (GLA, all cis 6, 9, 12-Octadecatrienoic acid, C18:3, n-6), is produced in the body from linoleic acid (all cis 6, 9-octadecadienoic acid), an essential fatty acid of omega-6 series by the enzyme delta-6-desaturase. Preformed GLA is present in trace amounts in green leafy vegetables, nuts, vegetable oils, such as evening primrose (*Oenothera biennis*) oil, blackcurrant seed oil, borage oil and hemp seed oil, and from spirulina, cyanobacteria. It is a nutraceutical used for treating problems with inflammation and auto-immune diseases. The most significant source of GLA for infants is breast milk. GLA is further metabolized to dihomo gamma linolenic acid (DGLA) which undergoes oxidative metabolism by cyclooxygenases and lipoxygenases to produce anti-inflammatory eicosanoids. Phytoconstituent gentianine present in Gentian root is an effective anti-inflammatory agent. Anti-inflammatory herbal nutraceuticals and anti-inflammatory nutraceutical compounds derived from plants or herbs may also be used as anti-inflammatory agents. These include bromelain, a

proteolytic enzyme found in pineapple; teas and extracts of stinging nettle; turmeric, extracts of turmeric, or curcumin, a yellow pigment isolated from turmeric [48, 53, 54, 55].

### Osteoarthritis

Osteoarthritis (OA) a debilitating joint disorder is the most common form of arthritis in the United States, where it affects an estimated 21 million people. In 2004, the direct and indirect health care costs associated with all forms of arthritis were approximately 86 billion dollars. Joint discomfort condition, resulting in energy imbalance and weight gain. Increased weight can exacerbate existing problems, through additional stress on joints. Glucosamine (GLN) and chondroitin sulfate (CS) are widely used to alleviate symptoms of OA. These nutraceuticals have both nutrient and pharmaceutical properties and seem to regulate gene expression and synthesis of NO and PGE2, providing a plausible explanation for their anti-inflammatory activities.

### Allergy

Allergy is a condition in which the body has an exaggerated response to either a drug or food. Quercetin (QR) belongs to a group of polyphenolic substances known as flavonoids. QR is a member of the class of flavonoids called flavonols. It is widely distributed in the plant kingdom in rinds and barks. Especially rich sources of QR include onions, red wine and green tea. QR is a natural antihistamine and opposes the actions of the histamine in the body. Histamines are responsible for allergic and inflammatory reactions. It can help reduce the inflammation that results from hay fever, bursitis, gout, arthritis, and asthma. QR inhibits some inflammatory enzymes, such as lipid peroxidases, and decreases leukotriene formation. QR has anti-inflammatory, antiviral, immunomodulatory, anticancer and gastro protective activities. QR blocks an enzyme that leads to accumulation of sorbitol, which has been linked to nerve, eye, and kidney damage in those with diabetes. QR also possesses potent antioxidant properties. It protects LDL cholesterol from becoming damaged. QR prevents damage to blood vessels by certain forms of cholesterol and other chemicals produced by the body. LDL cholesterol is an underlying cause of heart disease. QR also works as an antioxidant by scavenging damaging particles in the body known as free radicals. People with diabetes are at higher risk of blood vessel damage from free radicals [50, 54].

### Degenerative diseases

#### Macular degeneration

The prevalence and effects of age-related macular degeneration (AMD) are increasing dramatically as the proportion of elderly in our population continues to rise. A combination of vitamin C, vitamin E, beta-carotene, and zinc (with cupric oxide) is recommended for AMD. Healthy lifestyle with a diet containing foods rich in antioxidants, like lutein and zeaxanthin, n-3 fatty acids appears beneficial for AMD. Herbs or herbal extracts, such as garlic, (which contain allicin), green tea (containing catechins and bioflavonoids such as QR, hesperidin, rutin) are effective antioxidants. Bioactive components of food which are of special interest include the Vitamins E and C, polyphenols, carotenoids-mainly lycopene and  $\beta$ -carotene, and coenzyme Q10 possess antioxidant properties. High content of polyphenolic flavonoids in nutraceuticals and functional foods had been ascribed to possess antioxidant/radical scavenging activity.

Antioxidant therapy is supposed to be effective in the early stages of atherosclerosis by preventing LDL oxidation and the oxidative lesion of endothelium. Astaxanthin is an important naturally occurring molecule and the most abundant carotenoid in the marine world. It can be found in many of our favorite seafood such as salmon, trout, seabream and shrimps. Natural astaxanthin is produced from *Haematococcus pluvialis* microalgae. Unlike  $\beta$ -carotene, astaxanthin has no pro-vitamin A activity. It has a number of essential biological functions in aquatic animals such as protecting against oxidation process, protecting against UV light effects, immune response and pigmentation. It is also a very potent anti-oxidant and it has ten times more powerful antioxidant activity than any other carotenoids. For more than ten years, astaxanthin's role in enhancing the immune system and preventing oxidative stress has been the subject of international research. It offers powerful protection for the eyes and prevents macular degeneration. Prevents heart disease due to oxidative damage, boosts immune system function, protects the nervous system from degenerative diseases like Alzheimer's disease. It is used in drug delivery for medicines that are insoluble in water. *In vivo* antioxidant activity of carotenoids from green microalgae (*Dunaliella salina*) was reported [48-53].

### Vision improving agents

Lutein is one of the carotenoids, found in many fruits and vegetables including mangoes, corn, sweet potatoes, carrots, squash, tomatoes and dark, leafy greens such as kale, collards and bok choy. Lutein dipalmitate is found in the plant *Helenium autumnale*. Lutein also known as helenium is used for the treatment of visual disorders. Zeaxanthin is used in traditional Chinese medicine mainly for the treatment of visual disorders. Food sources of Zeaxanthin, include corn, egg yolks and green vegetables and fruits, such as broccoli, green beans, green peas, brussel sprouts, cabbage, kale, collard greens, spinach, lettuce, kiwi and honeydew. Lutein and Zeaxanthin are also found in nettles, algae and the petals of many yellow flowers. In green vegetables, fruits and egg yolk, lutein and zeaxanthin exist in non-esterified forms. They also occur in plants in the form of mono-or diesters of fatty acids. A new source of these carotenoids, a crystalline lutein product, is an extract from the marigold flower (*Tagetes erecta*) that contains approximately 86% by weight of the carotenoids lutein and Zeaxanthin.

### Alzheimer's disease

Alzheimer's disease (AD) is characterized by progressive dementia with memory loss as the major clinical manifestation. In 1996, approximately 4 million people in the United States were clinically diagnosed with AD; which is expected to triple in the next 50 years [34]. Women are more affected than men at a ratio of almost 2:1 due in part to the larger population of women who are over 70. Several lines of evidence strongly suggest that oxidative stress is etiologically related to a number of neurodegenerative disorders including Alzheimer's disease. Nutraceutical antioxidants like  $\beta$ -Carotene, curcumin, lutein, lycopene, turmeric etc. may exert positive effects on specific diseases by neutralizing the negative effects oxidative stress, mitochondrial dysfunction, and various forms of neural degeneration. A great deal of research has pointed to deleterious roles of metal ions in the development of Alzheimer's disease, by the augmentation of oxidative stress by metal ion. The growing trend in



nutraceutical intake is in part a result of the belief that they postpone the development of dementias such as Alzheimer's disease. However, pathogenic events centered on metal ions are expected to be aggravated by frequent nutraceutical intake<sup>[6]</sup>.

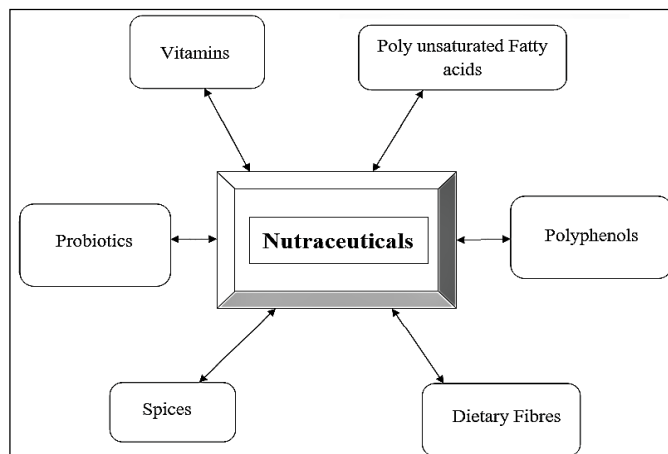
**Parkinson's disease**

Parkinson's disease is a brain disorder that results from nerve damage in certain regions of the brain causing muscle rigidity, shaking, and difficult walking, usually occurring in mid to late adult life. Canadian researchers indicated that vitamin E in food may be protective against Parkinson's disease. Creatine appeared to modify Parkinson's disease features as measured by a decline in the clinical signs. Researchers have also studied glutathione to determine its effect on nerve and its power as an antioxidant. The appropriate long-term dosing, side-effects and the most effective method of administration are not yet clear. Nutritional supplements have shown some promising results in preliminary studies, it is important to remember that there is not sufficient scientific data to recommend them for Parkinson's disease at present. The patients should be cautioned that over the-counter medications do have side effects and interactions with other drugs and are also expensive<sup>[5]</sup>.

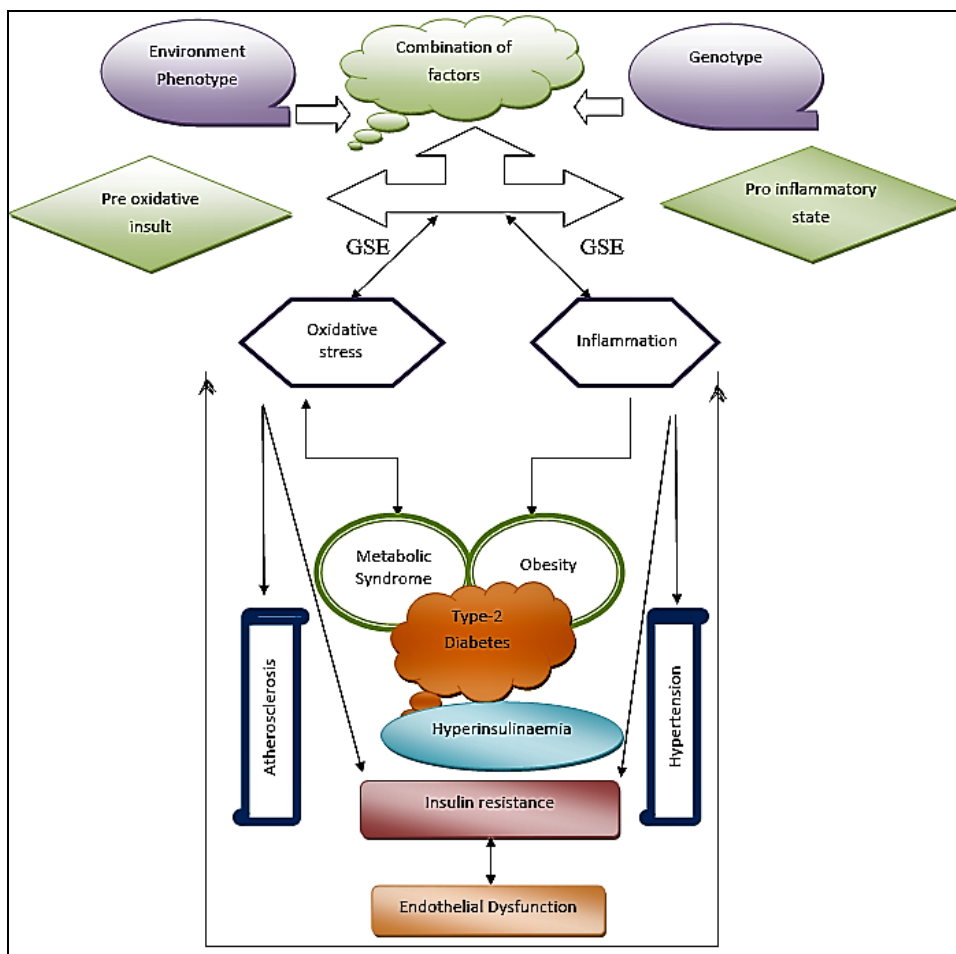
**Toxicology of Nutraceuticals**

Nutraceuticals are increasingly being used as nutritional supplements in treatment of diseases. Due to the plant origin of these supplements they are considered safe for human consumption. However, the levels of the active substance consumed vary when taken as a whole food, as compared to a nutritional supplement<sup>[65, 66]</sup>. Very few studies have reported

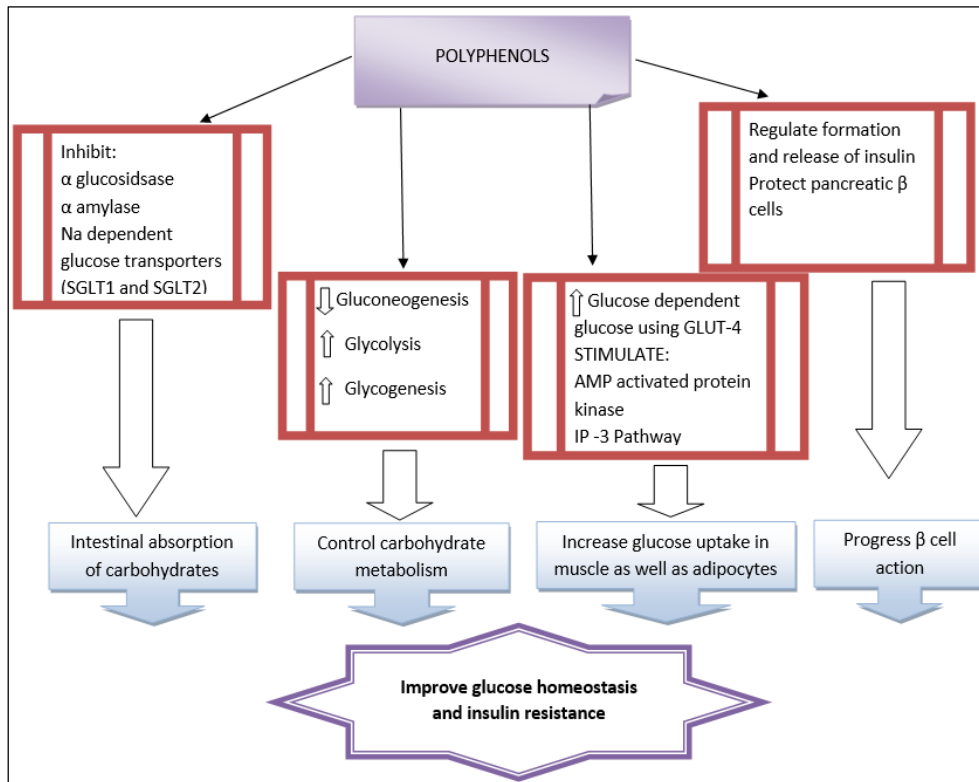
on long-term effects of nutrition supplements in humans. High consumption of lipids is associated with high risk of cardiovascular disease, diabetes, obesity, and cancer<sup>[67, 68]</sup>. Higher consumption of flavonoid supplements can alter the physiological levels of iron, vitamins, and other nutrients<sup>[66]</sup>. Flavonoids also interact with cytochrome P450 enzymes thus altering pharmacodynamics and pharmacokinetics of various drugs<sup>[69-71]</sup>. Similar to reports on TZDs, some of the flavonoids such as genistein have been associated with increased cancer risk<sup>[72-75]</sup>. Therefore, unless safety profiles of these nutraceutical supplements in humans are available, caution should be used in their long term use as PPAR modulators.



**Fig 1:** Importance of nutraceuticals in various diseases



**Fig 2:** Link between obesity, diabetes and hypertension



**Fig 3:** Role of polyphenols in curing diabetes

**Table 1:** Nutrients and its importance in the body

S. No.	Nutrients	Role In Improving Health
•	Vitamin A	➤ Antioxidant ➤ Growth and development ➤ Treat skin disorders.
•	Vitamin E	➤ Antioxidant ➤ Boost up the immune system.
•	Vitamin K	➤ Blood clotting.
•	Vitamin C	➤ Antioxidant ➤ Role in prevention of cold
•	Vitamin B1	➤ Change food in form of energy ➤ Vital in neurologic functions.
•	Vitamin B2	➤ Aids in energy production ➤ Helps in maintaining in good health our eyes, skin as well as nerve function.
•	Vitamin B3	➤ Maintaining brain functions
•	Vitamin B6	➤ Fabricate the genetic material of cells ➤ Formation of Erythrocytes ➤ produce amino acids and role in metabolism of fats, protein as well as carbohydrates.
•	Folic Acid	➤ Fabricate the genetic material of cells ➤ Formation of Erythrocytes ➤ Protects against heart disease.
•	Calcium	➤ Maintaining Bones and teeth
•	Iron	➤ Transmit and transfer oxygen to tissues.
•	Magnesium	➤ Healthy nerve, muscle function as well as bone formation ➤ Aids in preventing premenstrual syndrome (PMS).
•	Phosphorus	➤ Strong bones and teeth ➤ Energy production and storage.
•	Chromium	➤ With insulin helps to alter carbohydrates and fats in form of energy.
•	Cobalt	➤ Essential constituent of vitamin B12
•	Copper	➤ Essential for hemoglobin as well as collagen production ➤ Absorption of iron from digestive tract
•	Iodine	➤ Essential for accurate functioning of thyroid gland

**Conclusion**

Mounting confirmations hold up the surveillance that functional foods enclose physiologically dynamic constituents, whichever from plant or else animal resources, may augment health. Nutraceuticals, as well as functional

foods, can supply capital to concentrate on the ever-increasing load on the health care organization by endorsing health through thwarting more willingly than management. Health-cognizant consumers are progressively more looking for functional foods in an endeavor to manage their personal



health as well as well-being. The ground of functional foods, conversely, is in its immaturity. Asserts about health profits of functional foods must be supported by sound methodical criterion<sup>[26]</sup>. A numeral of features obscure the founding of a sturdy technical organization; on the other hand, these features take account of the intricacy of the food material, consequences on the food, compensatory metabolic alterations that may take place with dietary amends, and, be deficient in surrogate markers of ailment improvement. In addition, it is complicated to categorize apposite bioactive materials and ascertain their task in fighting or curative a variety of diseases. An extra investigation is obligatory to authenticate the impending health advantages of those foods for which the diet-health interactions are not adequately logically authenticated. As a final point, those foods whose health profits are sustained by adequate logical writing have an immense prospective to be a progressively more imperative constituent of a hale and hearty standard of living and to be advantageous to the community and the food diligence.

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