

**REVIEW ARTICLE**

## **An Overview on Nutraceuticals as Pharmacological Agents**

**Virendra Yadav<sup>1</sup>, Love Sharma<sup>\*2</sup>, Binny Thomas<sup>3</sup>, Moza Al Hail<sup>4</sup>**

Research scholar, Manav Bharti University, Department of Pharmaceutics, Solan, H.P.<sup>1</sup>, India  
Research scholar, National Institute of Pharmaceutical Education and Research, Hajipur, Bihar<sup>2</sup>, India  
Clinical Pharmacist, Indraprastha Apollo Hospitals, New Delhi<sup>3</sup>  
Director of Pharmacy, Department of Pharmacy Practice Hamad Medical Corporation,  
Womens Hospital Doha, Qatar  
Email id: lovesharma62@gmail.com  
Contact no.+918603576020,+919736817441

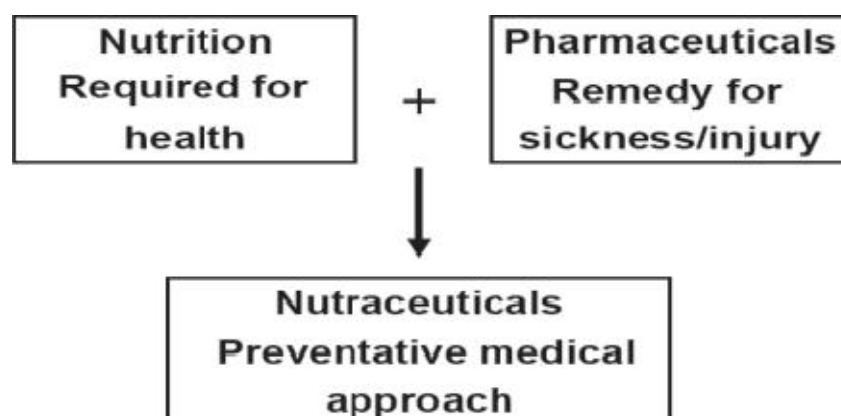
### **ABSTRACT**

*Using food products to promote health and cure disease is renowned. Currently most of the drug molecules available in the formulations were anciently used in their crude form. Dr Stephen De Felice first coins the term nutraceuticals in 1989 to provide medical or health benefits including the prevention and treatment of diseases. This review classified the large number of nutraceuticals available from various sources and its significance uses in the various disease such as Cardiovascular, Obesity, Diabetes, Cancer, Alzheimer, Parkinson, Inflammatory, Allergy. these are cured by herbals nutraceuticals.*

**Key Words:** Nutraceutical, Dietary supplements, disease and treatments.

### **INTRODUCTION**

About 2000 years ago Hippocrates correctly emphasized "Let food be your medicine and medicine be your food". Currently there is an increased global interest due to the recognition that nutraceuticals play a major role in health enhancement. The term "Nutraceutical" was coined by combining the terms "Nutrition" and "Pharmaceutical" in 1989 by Dr Stephen De Felice, Chairman of the Foundation for Innovation in Medicine. Nutraceutical is a marketing term developed for nutritional supplement that is sold with the intent to treat or prevent disease and thus has no regulatory definition. Hence a nutraceutical is any substance that may be considered a food or part of a food and provides medical or health benefits, encompassing, prevention and treatment of diseases. Such products may range from isolated nutrients, dietary supplements and diets to genetically engineered designer foods, herbal products and processed foods such as cereals, soups and beverages. Presently over 470 nutraceutical and functional food products are available with documented health benefits [1-3].



Concept of Nutraceuticals

"Nutraceuticals and functional foods have received considerable interest because of their presumed safety and potential nutritional and therapeutic effects". The nutraceutical and functional food industry is in a unique position to capitalize on consumers' interest. Be it a

multinational pharmaceutical corporation, a nutritional company, a large food multinational or a small vitaminselling firm, all of them recognize the changing trends and are aware of the more health-seeking consumer trend. There is a proliferation of these value-added products aimed at not only keeping oneself healthy but also prevention/treatment of various ailments ranging from heart diseases to cancer. As mentioned earlier functional foods contain larger profit margins than conventional foods (30 to 500 percent higher). The global market size is estimated between 30 and 60 billion US\$, with Japan, US, and Europe occupying the biggest share. By 2010 the nutraceutical demand is forecast to touch \$197 billion [3-5]. There is a lot of confusion regarding the terminologies like nutraceuticals, functional foods, dietary supplements, designer foods, medical foods, pharmafoods, phytochemicals etc. There seems to be thin dividing line in their interchangeable usage by different people on different occasions. Pharmaceuticals may be considered as drugs used mainly to treat diseases, while nutraceuticals are those that are intended to prevent diseases. The above distinction between pharmaceuticals and nutraceuticals is cute, but superficial and erroneous. Pharmaceuticals are substances which have patent protection as a result of expensive testing to conform to the specifications of respective Governments. However, many nutrients may never receive government approval since no one could justify the expense of testing requirements for substances that cannot be protected by patent laws. Both pharmaceuticals and nutrients can cure and prevent disease but only pharmaceuticals have governmental sanction. Many pharmaceuticals have their origin in plants and animals and are no less natural than nutrients. Classic example of nutrients is synthetic vitamins. Nutraceuticals sometimes referred as functional foods, have caused heated debate because they blur the traditional dividing line between food, and medicine. When food is being cooked or prepared using "scientific intelligence" with or without the knowledge of how or why it is being used, then the food is called as "functional food." Thus, functional food provides the body with the required amount of vitamins, fats, proteins, carbohydrates necessary for healthy survival. When functional food aids in the prevention and/or treatment of disease/disorder other than deficiency conditions like anemia it is called a nutraceutical. Thus, a functional food for one consumer can act as a nutraceutical for another. Examples of nutraceuticals include fortified dairy products (milk as such is a nutrient and its product casein is a pharmaceutical) and citrus fruits (orange juice is nutrient and its constituent ascorbic acid is a pharmaceutical) [6,7,8]. A dietary supplement is a product that is intended to supplement the diet that bears or contains one or more ingredients like, vitamin, mineral, herb, amino acid or a concentrate, metabolite, constituent, extract, or combinations of these. 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, inflammatory conditions, cancer and other diseases. The use of nutraceuticals, as an attempt to accomplish desirable therapeutic outcomes with reduced side effects, as compared with other therapeutic agents has met with great monetary success. The preference for the discovery and production of nutraceuticals over pharmaceuticals is well appreciated by the pharmaceutical and biotechnology companies. 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. 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) [10-17].

## LIST OF NUTRIENTS AND THEIR RELEVANCE

Table No.1

S.No.	Nutrients	Health benefit
1	Vitamin A	Antioxidant, essential, for growth and development and in the treatment of certain skin disorders
2	Vitamin E	Antioxidant, helps form blood cells, muscles, lung and nerve tissue, boosts

		the immune system
3	Vitamin K	Essential for blood clotting
4	Vitamin C	Antioxidant for healthy bones, gums, teeth and skin, in wound healing, prevent common cold and attenuate its symptoms
5	Vitamin B1	Helps to convert food in to energy, essential in neurologic functions
6	Vitamin B2	Helps in energy production and other chemical processes in the body, helps maintain healthy eyes, skin and nerve function
7	Vitamin B3	Helps to convert food in to energy and maintain proper brain function
8	Vitamin B6	Produce the genetic material of cells, formation of RBCs, maintenance of central nervous system and synthesize amino acids and metabolism of fats, protein and carbohydrates
9	Folic acid	Produce the genetic materials of cells, in pregnancy for preventing birth defects, RBCs formation, protects against heart disease.
10	Calcium	Bones and teeth and maintaining bone strength important in nerve, muscle and glandular functions
11	Iron	Energy production, carry and transfer oxygen to tissues
12	Magnesium	Healthy nerve and muscle function and bone formation, may help prevent premenstrual syndrome (PMS).
13	Phosphorous	Strong bones and teeth, helps in formation of genetic material, energy production and storage
14	Chromium	With insulin helps to convert carbohydrates and fats into energy
15	Cobalt	Essential component of vitamin B12, but ingested cobalt is metabolized in vivo to form the B12 coenzymes.
16	Copper	Essential for hemoglobin and collagen production, healthy functioning of the heart, energy production, absorption of iron from digestive tract.
17	Iodine	Essential for proper functioning of the thyroid.

### Associated Diseases

- ❖ Cardiovascular agents
- ❖ Antiobese agents
- ❖ Antidiabetics
- ❖ Anticancer agents
- ❖ Immune boosters
- ❖ Chronic inflammatory disorders
- ❖ Degenerative diseases

### Nutraceuticals And Diseases:

**Table No.2**

Types Of Diseases	Nutraceuticals Used
<b>Cardiovascular diseases</b>	Anti-oxidants, Dietary fibres, Omega-3 poly unsaturated fatty acids, Vitamins, minerals for prevention and treatment of CVD. Polyphenol (in grape) prevent and control arterial diseases Flavonoids (in onion, vegetables, grapes, red wine, apples, and cherries) block the ACE and strengthen the tiny capillaries that carry oxygen and essential nutrients to all cells [12].
<b>Diabetes</b>	Ethyl esters of n-3 fatty acids may be beneficial in diabetic patients. Docosahexaenoic acid modulates insulin resistance and is also vital for neurovisual development. Lipoic acid, an antioxidant, for treatment of diabetic neuropathy. Dietary fibers from psyllium have been used for glucose control in diabetic patients and to reduce lipid levels in hyperlipidemia.
<b>Obesity</b>	Herbal stimulants, such as ephedrine, caffeine, ma huang-guarana, chitosan and green tea help in body weight loss. 5-hydroxytryptophan and green tea extract may promote weight loss, while the former decreases appetite, the later increases the energy expenditure. A blend of glucomannan, chitosan, fenugreek, G sylvestre, and vitamin C in the dietary supplement significantly reduced body weight. Conjugated linoleic acid (CLA), capsaicin, Momordica Charantia (MC) possesses potential anti obese properties [14]
<b>Cancer</b>	Flavonoids which block the enzymes that produce estrogen reduce of estrogen-

	induced cancers. prevent prostate/breast cancer a broad range of phyto-pharmaceuticals with a claimed hormonal activity, called "phyto-estrogens" is recommended . Soyfoods source of isoflavones, curcumin from curry and soya isoflavones possess cancer chemopreventive properties. Lycopene concentrates in the skin, testes, adrenal and prostate where it protects against cancer [60].
<b>Anti-inflammatory activities</b>	Curcumin (diferuloylmethane) which is a polyphenol of turmeric possesses anticarcinogenic, antioxidative and anti-inflammatory properties. Top of Form Beet roots, cucumber fruits, spinach leaves, and turmeric rhizomes, were reported to possess anti tumor activity. Gamma linolenic acid (found in green leafy vegetables, nuts, vegetable oils i.e. evening primrose oil, blackcurrant seed oil and hemp seed oil, and from spirulina, cyanobacteria) are used for treating problems with inflammation and auto-immune diseases. Glucosamine and chondroitin sulfate are used against osteoarthritis and regulate gene expression and synthesis of NO and PGE2. Cat's claw has 17 alkaloids, along with glycosides, tannins, flavonoids, sterol fractions, and other compounds and work as potent anti-inflammatory agent.
<b>Alzheimer's disease</b>	$\beta$ -carotene, curcumin, lutein, lycopene, turmerin etc may exert positive effects on specific diseases by neutralizing the negative effects oxidative stress mitochondrial dysfunction, and various forms of neural degeneration
<b>Parkinson's disease</b>	Vitamin E in food may be protective against Parkinson's disease. Creatine modifies Parkinson's disease features as measured by a decline in the clinical signs.

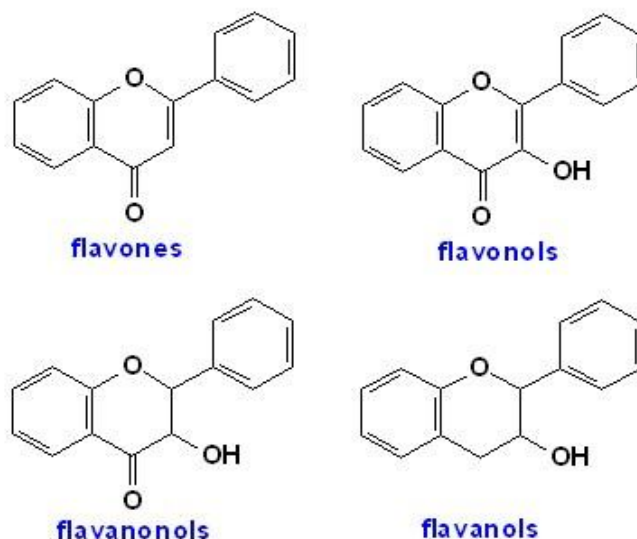
### Cardiovascular diseases

Worldwide, the burdens of chronic diseases like cardiovascular diseases, cancers, diabetes and obesity is rapidly increasing. In 2001, chronic diseases contributed approximately 59% of the 56.5 million total reported deaths in the world and 46% the global burden of disease. 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. In 1999 CVD alone contributed to a third of global deaths and by 2010 it would be the leading cause of death in developing countries. Majority of the CVD are preventable and controllable. It was reported that low intake of fruits and vegetables is associated with a high mortality in cardiovascular disease. 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. It has been demonstrated that the molecules like polyphenols present in grapes and in wine alter cellular metabolism and signaling, which is consistent with reducing arterial disease. Optimal nutrition, nutraceuticals, vitamins, antioxidants, minerals, weight reduction, exercise, cessation of smoking, restriction of alcohol and caffeine plus other lifestyle modifications can prevent, delay the onset, reduce the severity, treat, and control hypertension [20-24]. Nutrients and nutraceuticals with calcium channel blocking activity (thus antihypertensive activity) include  $\alpha$ -Lipoic acid, magnesium, Vitamin B6 (pyridoxine), Vitamin C, Nacetyl cysteine, Hawthorne, Celery,  $\omega$ -3 fatty acids etc. Flavonoids are widely distributed 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 aggregation. Flavonoids also protect the vascular system and strengthen the tiny capillaries that carry oxygen and essential nutrients to all cells. Flavonoids block the enzymes that produce estrogen, thus reducing the risk of estrogen-induced cancers. Polyphenols are simple phenolic molecules to highly polymerized compounds with molecular weights of greater than 30,000Da. Stilbenes, anthocyanins, condensed tannins (proanthocyanidins) in grape and wine, tetrahydro- $\beta$ -carboline, dietary indoleamines,

melatonin, and serotonin, in different plant foods are hypothesized to impart health benefits, associated with Mediterranean dietary style. Hesperidin is a flavanone glycoside which is classified as a citrus bioflavonoid. Sweet oranges (*Citrus sinensis*) and tangelos are the richest dietary sources of hesperidin. The peel and membranous parts of lemons and oranges have the highest hesperidin concentrations. Therefore, orange juice containing pulp is richer in the flavonoid than that without pulp. Hesperidin, in combination with a flavone glycoside called diosmin, is used for the treatment of venous insufficiency and hemorrhoids. Hesperidin, rutin and other flavonoids are reported to possess analgesic and anti-inflammatory activity. Flavonoid intake was significantly inversely associated with mortality from coronary heart disease and the incidence of myocardial infarction. Flavonoids in regularly consumed foods may reduce the risk of death from coronary heart disease in elderly men. Ginger, the rhizome of *Zingiber officinalis*, one of the most widely used species of the ginger family, is a common condiment for various foods and beverages. Ginger has a long history of medicinal use dating back 2500 years. Some pungent constituents present in ginger and other zingiberaceous plants have potent antioxidant and anti-inflammatory activities, and some of them exhibit cancer preventive activity. The anticancer properties of ginger are attributed to the presence of certain pungent vallinoids, viz. 6-gingerol and 6-paradol. Animal studies provide provides sound mechanistic basis for the use of ginger in hypertension and palpitations. Ginger has some antiemetic properties but clinical evidence beyond doubt is only available for pregnancy-related nausea and vomiting. Preclinical safety data do not rule out potential toxicity, especially following ginger consumption over longer periods. Cholesterol has long been implicated as a significant risk factor in cardiovascular disease. Sterols occur in most plant species and are called as phytosterols. Although green and yellow vegetables contain significant amounts, their seeds concentrate the sterols. Phytosterols compete with dietary cholesterol by blocking the uptake as well as facilitating its excretion from the body. Phytosterols in diet have the potential to reduce the morbidity and mortality from cardiovascular disease. *Fagopyrum esculentum* Moench (common buckwheat or sweet buckwheat), originated in Asia. Buckwheat seeds possess proteins, flavonoids, flavones, phytosterols, thiamin-binding proteins etc. Buckwheat proteins are beneficial in constipation and obesity and more importantly lower cholesterol and high blood pressure. Dietary fiber preparation from defatted rice bran has laxative and cholesterol-lowering ability with attendant benefits towards prevention or alleviation of cardiovascular disease, diabetes, diverticulosis and colon cancer. It has been suggested that rice bran is a good fiber source (27%) that can be added to various food products. Milk and eggs are the important animal sources of nutraceuticals like proteins and polyunsaturated fats or essential fatty acids (EFAs). EFAs are required for production and rebuilding of cells, to reduce blood pressure, lower cholesterol and triglycerides, reduce the risk of blood clots, help prevent many diseases including arthritis, arrhythmias, and other cardiovascular diseases. Nutritional value of egg is increased because of added gamma linolenic acid (GLA) which has many benefits, including prevention and management of CVD like hypertension. Fatty acids of the omega-3 series (n-3 fatty acids) present in fish are well established dietary components affecting plasma lipids and the major cardiovascular disorders, such as arrhythmias. Octacosanol is a 28-carbon chain alcohol. This nutraceutical is present in fruit, leaves and skin of many plants and whole grains<sup>30</sup>. It has gastroprotective and lipid lowering effects. Since it has no side effects further studies may be undertaken to prove the claims [25-30].

#### **Current status of nutraceuticals in CVD**

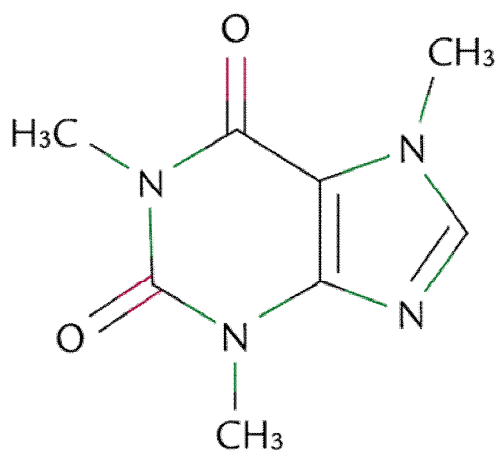
Because of the extremely long history of CVD, the causal relationship of nutrition/physical exercise on major CVD events is still difficult to assess prospectively. The relationship between calcium and risk of hypertension is inconsistent and inconclusive, and the relationship between calcium and risk of pregnancy-induced hypertension and preeclampsia is highly unlikely. Treatment with beta carotene, vitamin A, and vitamin E may increase mortality. The potential roles of vitamin C and selenium on mortality need further study. There are possibilities to develop nutraceuticals to prevent and manage thrombosis risk in women with thrombophilic gene mutations [33].



**Figure no .1: Chemical Structure of Phytochemicals**

### 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 [34-40].



**caffeine**



**Caffeine fruits**

**Figure no.2**

### Current status of nutraceuticals in obesity

A blend of glucomannan, chitosan, fenugreek, G sylvestre, and vitamin C in the dietary supplement significantly reduced body weight and promoted fat loss in obese individuals. Further studies are needed to establish a long term efficacy and adverse effect potential. There is a very high prevalence of obesity globally and hence nutrition and exercise play a key role in its prevention and treatment. Nutraceutical interventions are currently being investigated on a large-scale basis as potential treatments for obesity and weight management. Nutraceuticals like conjugated linoleic acid (CLA), capsaicin, Momordica Charantia (MC) and Psyllium fiber possess potential antiobese properties [32].

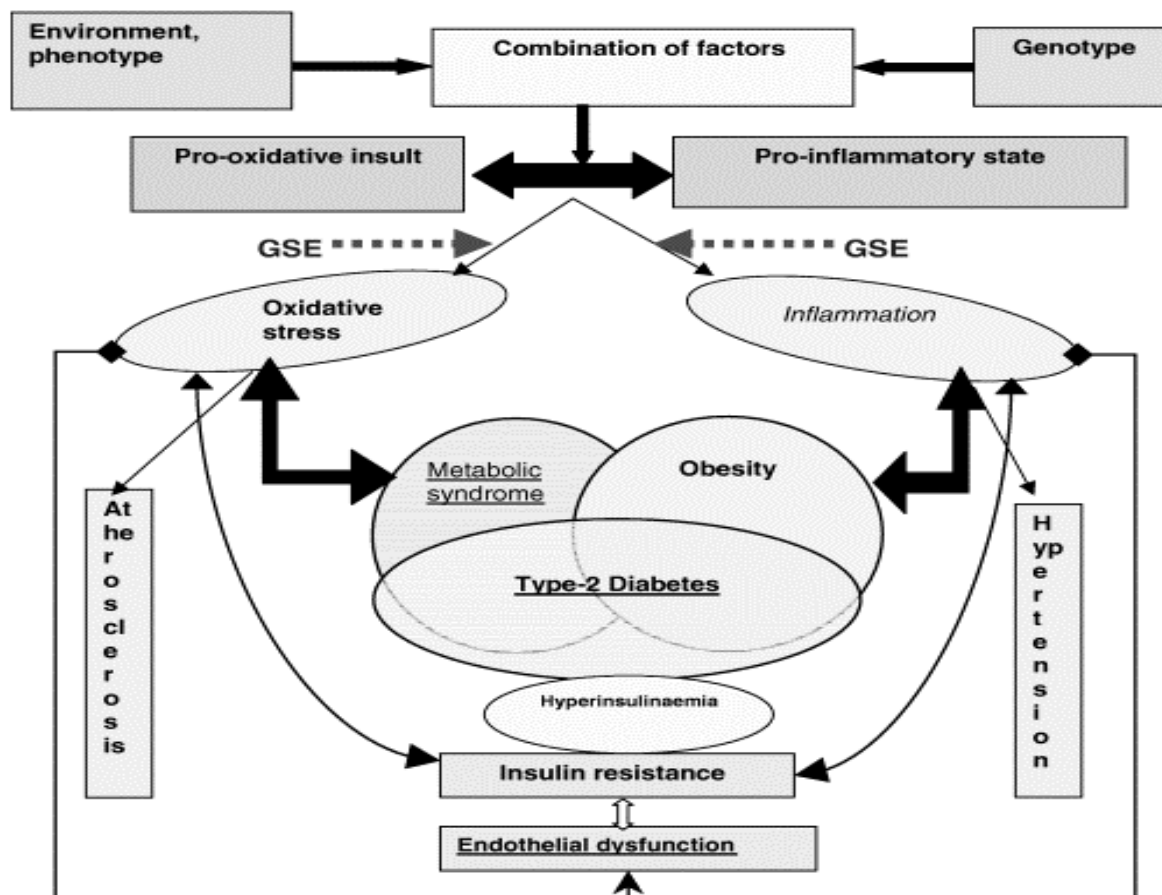


Figure no.3

### 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. Gestational diabetes occurs in pregnancy [45]. Globally the total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2003 [46]. 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 [47]. 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>. Docosa-hexaenoic acid modulates insulin resistance and is also vital for neurovisual 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.

### Cancer

In the year 2000 malignant tumors were responsible for 12 per cent of the nearly 56 million deaths worldwide from all causes. According to the World Cancer Report the cancer rates there would be 15 million new cases in the year 2020 i.e. a rise in 50%. 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. 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. 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 immune 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. Recently, attention has been on phytochemicals that possess cancer-preventive properties. Besides chemopreventive components in vegetables and fruits, some phytochemicals derived from herbs and spices also have potential anticarcinogenic and antimutagenic activities, among other beneficial health effect. A broad range of phyto-pharmaceuticals with a claimed hormonal activity, called "phyto-estrogens" is recommended for prevention of prostate/breast cancer. Flavonoids found in citrus fruit appear to protect against cancer by acting as antioxidants. Soyfoods are a unique dietary source of isoflavones, the polyphenolic phytochemicals exemplified by epigallocatechin gallate from tea, curcumin from curry and soya isoflavones possess cancer chemopreventive properties. The main soybean isoflavones, genistein, daidzein, biochanin inhibits prostate cancer cell growth. 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. Lycopene prevents cancer, cardiovascular disease, and gastrointestinal tract. It concentrates in the skin, testes, adrenal and prostate where it protects against cancer. 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. Lycopene is one of the major carotenoids in western diets and is found almost exclusively in tomatoes, water melon, guava, pink grapefruit and papaya. 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<sup>68</sup> 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. They are also present in spinach, tomatoes, potatoes, alfalfa and clover. Commercial saponins are extracted mainly from *Yucca schidigera* and *Quillaja saponaria*. 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. Tannins also called proanthocyanidins, detoxify carcinogens and scavenge harmful free radicals. 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 anticarcinogen is used in alternative medicine and to prevent cancer. 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. Naturally occurring phenolic acid derivatives are reported to possess potential anticancer properties. Phenolics such as ferulic, caffeic, gallic acids and curcumin are reported to possess anticancer activity. 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. 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. Bio transformation products of glucosinolates include isothiocyanates, dithiolthiones and sulforaphane. They block the enzymes that promote tumor growth, particularly in the breast, liver, colon, lung, stomach and esophagus. The sulfur compounds, in garlic were found to kill bacteria and parasites, boost the immune system and reduce atherogenesis and platelet stickiness. All members of the cruciferous family broccoli, cauliflower, cabbage, bok choy, Brussels sprouts, collards, cress, kale, kohlrabi, mustard contains a group of closely related sulfur compounds known as glucosinolates. Sulforaphane rich in broccoli is a potent phase II enzyme inducer. It produces D-glucarolactone, a significant inhibitor of breast cancer. Sulforaphane is an antioxidant and stimulator of natural detoxifying enzymes. Sulforaphane has been reported to reduce the risk of breast cancer and prostate cancer. Thiosulfonates an organosulfur phytochemical is present in garlic and onions (*Allium cepa*). 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. 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. 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. Non-prescription antioxidants and other nutrients (patients using beta-carotene, vitamins A, vitamin C and vitamin E, selenium, cysteine, B vitamins, vitamin D<sub>3</sub>, vitamin K<sub>3</sub> and glutathione as single agents or in combination.) do not interfere with therapeutic modalities for cancer.

#### **Current status of nutraceuticals in cancer**

Approximately 20-30% of Americans consume multivitamin supplements daily, indicating high public interest in the prevention of cancer and other chronic diseases through a nutrition-based approach. Because epidemiologic studies generally evaluate foods rather than specific bioactive food components, a systematic approach to determining how combinations of vitamins and minerals may interact to ameliorate cancer risk is necessary to further our understanding of the potential benefits and risks of supplement use. Increasing consumption of vegetables and fruits elevates the levels of antioxidative components, for example, selenium, vitamin E, vitamin C,

lycopene, cysteine-glutathione and various phytochemicals. These detrimental processes of heme catalysis of oxidative damage hypothesized here are not well recognized. More investigative studies in this field to be done large scale clinical trials suggest that some agents such as selenium, lycopene, soy, green tea, vitamins D and E, anti-inflammatory and inhibitors of 5 $\alpha$ -reductase are effective in preventing prostate cancer. In order to demonstrate clinical benefit with the minimum adverse effects. Appropriate selection of agent, trial design and end points is critical in selecting the most promising regimens to accomplish these goals.

Cancer was not prevented by beta-carotene, alphatocopherol, retinol, retinyl palmitate, N-acetylcysteine, or isotretinoin in smokers. Ongoing trials may help define new avenues for chemoprevention. The concept of chemoprevention in lung cancer is still in its infancy, but in the future it may have a significant impact on the incidence and mortality of lung cancer. Several studies have demonstrated the improvement in quality of life and the value of complementary medicine as an adjuvant to chemotherapy or radiotherapy. Complimentary therapy might serve as a valuable and useful supportive measure for prostate cancer patients. Majority of the studies indicate a preventive role of nutraceuticals in cancer, however more elaborate randomized double blind studies are needed [56-60].

### **Immune boosters and anti-inflammatory agents**

#### **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 pillida, 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, colon-rectal, 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, Sadenosylmethionine, 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 dihomogamma 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

from OA and other joint disorders may reduce physical activity in individuals experiencing this 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 gastroprotective 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 helenien is used for the treatment of visual disorders. Zea xanthin 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, turmerin 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[6].

#### **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 [5].

### **MISCELLANEOUS**

In our modern society women can be over-fed, but undernourished which can lead to nutrient deficiencies with adverse impact on the pregnancy outcome. Good quality nutritional supplements (combinations rather than isolated single nutrients) can play a valuable role in the health of the pregnant mother and the baby though emphasis must always be on eating a good diet. There is also insufficient evidence to identify adverse effects and to say that excess multiple-micronutrient supplementation during pregnancy is harmful to the mother or the fetus. Angiogenesis is an enzymatic process involved in almost all classes of enzymes. It is a process that is generally down regulated in healthy individuals. Antiangiogenic compounds are selective against newly formed blood vessels while sparing existing ones may not lead to side effects even after prolonged exposure. Available indirect evidences suggest that antiangiogenic compounds may prevent diseases involving degenerative process like, arthritis, multiple sclerosis, Alzheimer's, Parkinson's, osteoporosis, diabetes and cancer. Many inhibitors of angiogenesis are being isolated from functional foods [30]. Naturally occurring bioactive compounds are speculated to be potentially effective and safe anti-angiogenic compounds. Such compounds include catechins, flavins, Curcumin, Isoflavones, Resveratrol, proanthocyanidins, flavonoids, Saponins, terpenes, Chitin, chitosan, Vitamins B<sub>3</sub>, Vitamin D<sub>3</sub>, Fatty acids, peptides and amino acids (alpha 2-macroglobulin, arginine, phenylalanine etc. Psyllium, a dietary fiber is valuable in the management of irritable bowel syndrome, inflammatory bowel disease-ulcerative colitis, colon cancer, constipation. *Moringa oleifera* Lam (Moringaceae) has an impressive range of medicinal uses with high nutritional value. Different parts of this plant contain a profile of important minerals, and are a

good source of protein, vitamins, beta-carotene, amino acids and various phenolics. It provides a rich and rare combination of zeatin, QR, beta-sitosterol, caffeoylquinic acid and kaempferol. With water purifying powers and high nutritional value. Various parts of this plant such as the leaves, roots, seed, bark, fruit, flowers and immature pods act as cardiac and circulatory stimulants, possess antitumor, antipyretic, antiepileptic, anti-inflammatory, antiulcer, antispasmodic, diuretic, antihypertensive, cholesterol lowering, antioxidant, antidiabetic, hepatoprotective, antibacterial and antifungal activities, and are being employed for the treatment of different ailments in the indigenous system of medicine, particularly in Asia[10-16].

## CONCLUSION

Nutraceuticals are currently receiving recognition as being beneficial in coronary heart disease, obesity, diabetes, cancer, osteoporosis and other chronic and degenerative diseases such as Parkinson's and Alzheimer's diseases. Evidences indicate that the mechanistic actions of natural compounds involve a wide array of biological processes, including activation of antioxidant defenses, signal transduction pathways, cell survival-associated gene expression, cell proliferation and differentiation and preservation of mitochondrial integrity. It appears that these properties play a crucial role in the protection against the pathologies of numerous age-related or chronic diseases. It is very imperative that the nutrients found in many foods, fruits and vegetables are responsible for the well documented health benefits. For example, lutein and zeaxanthin prevent cataracts and macular degeneration; beta-carotene and lycopene protect the skin from ultraviolet radiation damage; lutein and lycopene may benefit cardiovascular health, and lycopene may help prevent prostate cancer. Because of these and other marked health benefits of these, it must be taken regularly and to reduce the risk factors like high cholesterol, high blood pressure and diabetes. Some of the most popular nutraceutical products marketed today are botanicals such as St. John's wort, echinacea, ginkgo biloba, saw palmetto, and ginseng. Many industries manufacture and market the nutraceuticals, where the side effects (especially consumed in large quantities) of these nutraceuticals not reported or often unproven. In order to have scientific knowledge about the nutraceuticals, publics should be educated, where recommended daily doses of these nutraceuticals should be known by each consumer. With the rapidly increasing interest in the nutraceutical revolution, we need to establish a vibrant nutraceutical research community which is absolutely necessary to convert the majority of potential nutraceuticals to established ones thereby truly delivering their enormous benefits to all of us. The list of nutraceuticals being studied is changing continually and reflects ongoing research, market developments and consumer interest.

## REFERENCES

1. Brower V. (2000). Nutraceuticals: poised for a healthy slice of the healthcare market? *Nat Biotechnol.* 19, 16:pp 728-731.
2. Zeisel SH. (1999). Regulation of Nutraceuticals Science. , 285: pp185-186.
3. Eskin N.A. M and Tamir S. (2006). Dictionary of Nutraceuticals and Functional Foods, CRC Press, Boca Raton, USA.
4. Benkouider C. (2005). Functional Foods and Nutraceuticals. 2005, 44: pp 8-11.
5. Kalra EK. (2003). *AAPS PharmSci.* , 5:pp 1208-1212.
6. Nelson NJ. (1999). Purple carrots, margarine laced with wood pulp? Nutraceuticals move into the supermarket. *J Natl Cancer Inst.*,91: pp 755-757.
7. Whitman M. (2001). Understanding the perceived need for complementary and alternative nutraceuticals: lifestyle issues. *Clin J Oncol Nurs.* 5: pp 190-194.
8. Rissanen TH, Voutilainen S, Virtanen JK, Venho B, Vanharanta M, Mursu J and Salonen JT. (2003). Low Intake of Fruits, Berries and Vegetables Is Associated with Excess Mortality in Men: the Kuopio Ischaemic Heart Disease Risk Factor (KIHD) Study. *J Nutr.* 133:pp 199-204.
9. Temple WJ and Gladwin KK. (2003). Fruits, vegetables, and the. Prevention of cancer: Research challenges. *Nutrition.*,19: pp 467-470.
10. Hu FB and Willett WC. (2002). Optimal diets for prevention of coronary heart disease. *JAMA*, 288:pp 2569-2578
11. German JB and Walzem RL. (2000). The health benefits of wine. *Annual Review of Nutrition.*,20: pp 561-593. *Research J. Pharm. and Tech.* 1(4): Oct-Dec. 2008,pp 338.
12. Houston MC. (2005). Nutraceuticals, Vitamins, Antioxidants, and Minerals in the Prevention and Treatment of Hypertension. *Progress in Cardiovascular Diseases.*, 47: pp 396-449.
13. Hollman PCH, (1996). Hertog MGL and Katan MB. Analysis and health effects of flavonoids, *Food Chem.*, 57:pp 43-46.
14. Majoa, DD, Guardiaa ML, Tripolia E, Giammancoa S and Finotti E. (2005). Flavonoids as Inhibitors of Lipid Peroxidation in Membranes. *Food Research Int.*, 38: pp 1161-1166.

15. Cook NC and Samman S. (1996). Flavonoids - Chemistry, metabolism, cardioprotective effects, and dietary sources. *J. Nutritional Biochem.*, 7:pp 66-76.
16. Hollman PCH, Feskens EJ and Katan MB. (1999). Tea flavonols in cardiovascular disease and cancer epidemiology. *Proc Soc Exper. Biol. Med.*, 220:pp 198-202.
17. Inti M and Faoro F. (2006). Grape phytochemicals: a bouquet of old and new nutraceuticals for human health *Medical Hypotheses.*, 67:pp 833-838.
18. Garg A, Garg S, Zaneveld LJD and Singla AK. (2001). Chemistry and pharmacology of the citrus bioflavonoid hesperidin. *Phytother Res.*, 15:pp 655-669.
19. Hertog M G L, Feskens E J M, Kromhout D, Hertog M G L, Hollman P C H and Katan MB. (1993). Dietary antioxidant flavonoids and risk of coronary heart disease. *The Lancet.*, 342: pp 1007-1021.
20. Shukla Y and Singh M. (2007). Cancer preventive properties of ginger: a brief review. *Food and Chemical Toxicology.* 45:pp 683-690.
21. Ghayur MN, Gilani, AH Afridi MB and Houghton PJ. (2005). Cardiovascular effects of ginger. *Vascular Pharmacology.*, 43:pp 234-241.
22. Chrubasik S, Pittler M H, Roufogalis B D. (2005). Zingiberis rhizoma: a comprehensive review on the ginger effect and efficacy profiles. *Phytomedicine.* 12: pp 684- 701.
23. Dutta P C, (2003). Phytosterols as functional food components and nutraceuticals, Marcel Dekker, Edinburgh.
24. Si-quan L and Zhang, Q H. (2001). Advances in the development of functional foods from buckwheat. *Critical reviews in food science and nutrition.* 41: pp 451-464.
25. Hamid AA and Luan YS. (2000). Functional properties of dietary fiber prepared from defatted rice bran. *Food Chemistry.* 68:pp 15-19.
26. Gita C. (2004). Functional Food Attributes of n-3 Polyunsaturated and Conjugated Linoleic Acid Enriched Chicken Eggs. *Current Topics in Nutraceutical Research.* 2: pp 113-121.
27. Tucker G (2003). Nutritional enhancement of plants. *Current Opinion in Biotechnology.* 14: pp 221-225.
28. Sirtori C R and Galli C (2002). Fatty acids and the Omega 3. *Biomedecine and Pharmacotherapy.* 56:pp 397-406.
29. Sidhu KS (2003). Health benefits and potential risks related to consumption of fish or fish oil. *Regul Toxicol Pharmacol.* 38: pp 336-344.
30. Kato S, Karino K, Hasegawa J, Nagasaki A, Eguchi M and Ichinose T. (1995). Octacosanol affects lipid metabolism in rats fed on a high fat diet. *Br J Nut.* 73:pp 433-442.
31. Rapport L and Lockwood B (2000). Nutraceuticals. *The Pharmaceutical Journal.* 265:pp 170- 171.
32. Ignarro L J, Balestrieri M L and Napoli C. (2007). Nutrition, physical activity, and cardiovascular disease: an update. *Cardiovascular Research.*, 73:pp 326-340.
33. Trumbo PR and Ellwood KC. Supplemental calcium and risk reduction of hypertension, *Nutr Rev.* 2007, 65: pp 78-87.
34. Bjelakovic G, Nikolova D, Gluud LL, Simonetti RG and Gluud C. (2007). Mortality in randomized trials of antioxidant supplements for primary and secondary prevention: systematic review and meta-analysis. *JAMA.* 297: pp 842- 857.
35. Ravi Subbiah M T (2000). Nutrigenetics and nutraceuticals: the next wave riding on personalized medicine. *Translational Research.* 149:pp 55-61.
36. Caterson ID and Gill TP. (2002). Obesity: epidemiology and possible prevention. *Best Pract Res Clin Endocrinol Metab.* 16: pp 595-610.
37. Mermel VI. (2004). Old paths new directions: use of functional foods in the treatment of obesity. *Trends in Food Science and Technology.* 15: pp 532-540.
38. Daly PA, Khrieger DR and Dulloo AG. (1993). Ephedrine, caffeine and aspirin: safety and efficacy for treatment of human obesity. *Int J Obes Relat Metab Disord.* 17: pp 73-78.
39. Boozer CN, Nasser JA and Heymsfield SB (2001). An herbal supplement containing Ma Huang-Guarana for weight loss: a randomized, double-blind trial. *Int J Obes Relat Metab Disord.* 25:pp 316-324.
40. Dulloo AG, Duret C and Rohrer D. (1999). Efficacy of a green tea extracts rich in catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans. *Am J Clin Nutr.* 70: pp 1040-1045.
41. Schiller RN, Barranger E, Schauss AG and Nichols E. (2001). Life style management of Obesity. *JAMA.* 4:pp 34-41.
42. Bell SJ and Goodrick GK. (2002). A Functional Food Product for the Management of Weight. *Critical Reviews in Food Science and Nutrition.* 42: pp 163-178.
43. Woodgate DE and Conquer JA. (2003). Prevalence of self-treatment with complementary products and therapies for weight loss: A randomized, cross-sectional Study in Overweight and Obese Patients in Colombia. *Current Therapeutic Research.* 64: pp 248-262.
44. Kasbia GS. (2005). Functional foods and nutraceuticals in the management of obesity. *Nutrition and Food Science.*, 35:pp 344-351.
45. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus Diabetes Care. Alexandria, Virginia, USA, 2003.
46. Wild S, Roglic G, Green A, Sicree R and King H. (2004). Global prevalence of diabetes: estimates for 2000 and projections for 2030. *Diabetes Care.*, 27, pp 1047.
47. Rubin RJ, Altman WM and Mendelson DNJ. (1994). The endocrinology of vasoactive peptides: synthesis to function. *Clin Endocrinol Metab.* 78:pp 6-10.
48. Brouns F. (2002). Soya isoflavones: a new and promising ingredient for the health foods sector. *Food Research International.* 35:pp 187-193.
49. Sirtori CR and Galli C (2002). Fatty acids and the Omega 3. *Biomedecine and Pharmacotherapy.*, 56:pp 397-406.
50. Thomas B, Ghebremeskel K, Lowy C, Crawford M and Bridget Offley-Shore R N (2006). Nutrient intake of women with and without gestational diabetes with a specific focus on fatty acids. *Nutrition.* 22: pp 230-236.

**Yadav et al**

51. Coleman MD, Eason RC and Bailey CJ. (2001). The therapeutic use of lipoic acid in diabetes: a current perspective *Environmental Toxicology and Pharmacology*. 10: pp 167-172.
52. Baljit S. (2007). Psyllium as therapeutic and drug delivery agent. *Int. J.Pharmaceutics*. 2007, 334 pp 1-14.
53. McCarty M F. (2005). Toward practical prevention of type 2 diabetes. *Medical Hypotheses*.2005,64: pp 151-158.
54. WHO release (2003b) Available at <http://www.who.int/mediacentre/news/releases/2003/pr27en/> downloaded on 9 April 2007.
55. Willis M S and Wians FH. (2003). The role of nutrition in preventing prostate cancer. *Clin Chim Acta*. 330:pp 57-83.
56. Nkondjock A and Ghadirian P. (2004). Dietary carotenoids and risk of colon cancer: a case- control study. *Int J Cancer*., 110: pp 110-116
57. Hofseth LJ and Wargovich MJ. (2007). Inflammation, Cancer, and Targets of Ginseng. *J Nutr.* ,137: pp 183-185.
58. Limer JL and Speirs V (2004). Phyto-oestrogens and breast cancer chemoprevention. *Breast Cancer Res*. 2004, 6: pp 119-127.
59. Frydoonfar HR, McGrath DR and Spigelman AD (2003). The variable effect on proliferation of a colon cancer cell line by the citrus fruit flavonoid Naringenin. *Colorectal Dis*. 2003,5: pp 149- 152.
60. Mandel S, Packer L, Youdim MBH and Weinreb O (2005). Proceedings from the Third Int. Conf. Mechanism of Action of Nutraceuticals. *J. Nutritional Biochem*. 16 pp 513-520.