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Nutraceuticals: role in metabolic disease, prevention and treatment

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ABSTRACT

Nutraceuticals are products that are also used as medicine other than nutrition. A nutraceutical product may be defined as a substance, which have physiological benefits nor gives protection against chronic diseases. Nutraceuticals may also be used to improve health, delay the aging process, prevent chronic disease, increase life expectancy, or support the structure or function of the body. Nowadays, nutraceuticals has gained considerable interest due to potential nutritional safety and therapeutic effects. Recent studies have shown promising results for those compounds in various complications. Emphasis has been made to present herbal nutraceuticals effective on hard curative disorders related to oxidative stress including allergy, Alzheimer, cardiovascular, cancer, diabetes, and Parkinson's diseases as well as obesity.

Keywords: Nutraceuticals, Metabolic diseases, Probiotics, Prebiotics, Dietary fiber, Antioxidant, Vitamins

1. INTRODUCTION

Over the past several years, nutraceuticals have attracted considerable interest due to their potential nutritional safety and therapeutic effects [1]. These products could have a role in a plethora of biological processes, including antioxidant defenses, cell proliferation, gene

expression, and safeguarding of mitochondrial integrity [1]. Therefore, nutraceuticals may be used to improve health, prevent chronic disease, postpone the aging process, and in turn increase life expectancy, or just support the functions and integrity of the body. These products are said to be a very healthy source for the prevention of life threatening diseases such as diabetes, renal and gastrointestinal disorders, as well as different infections.

A wide range of nutraceutical has been shown to impose crucial roles in immune status and susceptibility to certain disease states. Nutraceuticals also exhibit disease modifying indication related to oxidative stress including allergies, Alzheimer's disease, cardiovascular diseases, cancer, eyes conditions, Parkinson's diseases and obesity [1]. Nutraceuticals is abroad umbrella term that is used to describe any product derived from food sources with extra health benefits in addition to the basic nutritional value found in foods [1].

The definition of nutraceuticals and their related products generally depends on the source. These products can be classified on the basis of their natural sources, pharmacological conditions, as well as chemical constitution of the products. Mostly, nutraceuticals are grouped into four categories that include dietary supplements, functional food, medicinal food, and pharmaceutical [1]. In recent years, a new diet health paradigm is evolving which places more emphasis on the positive aspects of diet. The new lifestyle adopted by people today has changed the basic food habits of the latter [2]. Consumption of junk foods has increased manifold leading to various diseases caused due to malnutrition. Obesity is now recognized as a global issue. Heart disease continues to be a primary cause of death in most of the developing countries worldwide, followed by cancer, osteoporosis, arthritis and many others [2]. Consumers being frustrated with the expensive, high technology, disease treatment approach in the modern medicines are seeking complementary or alternative beneficial products which makes nutraceuticals particularly appealing [2]. Nutraceuticals are the emerging class of natural products that makes the line between drug and food to fade [2].

Although the use of nutraceuticals by people has a long history, only recently scientifically supported nutritional and medical evidence has allowed nutraceutical to emerge as being potentially effective. The nutraceuticals of both plant and animal origin holds exciting opportunities for the food industries in future. Nutraceuticals products can be considered non-specific biological therapies used to promote general well-being, control symptoms and preventing malignant processes. The term "nutraceuticals" combines the two words of nutrient, which is nourishing food component and pharmaceutical, which is a medical drug. The name was coined in 1989 by Stephen DeFelice, founder and chairman of the Founder for Innovation in Medicine, which is an American organization located in Cranford, New Jersey. The philosophy behind nutraceuticals is to focus on prevention, according to the saying by a Greek physician Hippocrate (known as the father of medicine) who said "let food be your medicine". Their role in human nutrition is one of the most important areas of investigation, with wide ranging implications for consumers, healthcare providers, regulators, food producers and distributors [1]. The concept of nutraceuticals arose first in the survey from U.K, Germany and France, where diet was rated higher by the consumers, then exercise or hereditary factors to achieve a good health [3]. According to DeFelice, nutraceuticals can be defined as "a food (or a part of food) that provides medical or health benefits, including the prevention and or treatment of a disease". On the other hand Health Canada defines nutraceuticals as "a product prepared from foods, but sold in the form of pills, or power or in other medicinal form, not usually associated with foods [4]. Nutraceuticals are found in a mosaic of products emerging from:

- a. The food industry
- b. The herbal and dietary supplement market
- c. Pharmaceutical industry
- d. The newly merged pharmaceutical/ agribusiness/ nutrition conglomerates.

It may range from isolated nutrients, herbal products, dietary supplements and diets to genetically engineered “designer” foods and processed products such as cereals, soups and beverages.

1. 1. Benefits of nutraceuticals

Over the past few years, nutraceuticals have become very popular. They are being used as alternative or supplemental treatment along with pharmaceuticals to help prevent and treat a wide range of diseases. Nutraceuticals can play an important role in the body’s various biological processes, which help prevent various diseases and improve overall health and wellbeing. A wide range of nutraceuticals has been shown to impose crucial roles in immune status and susceptibility to certain disease states. Nutraceuticals also exhibit disease-modifying indications related to oxidative stress including allergies, Alzheimer’s disease, cardiovascular diseases, cancer, eye conditions, Parkinson’s diseases and obesity.

1. 1. 1. Prevention the of chronic disease

Nutraceuticals play an important role in preventing the onset of chronic diseases and reduce the complications involved. Evidence suggests that they are used in the prevention of cardiovascular diseases, cancer, diabetes and inflammatory diseases.

1. 1. 2. Improve eye health

Patients with eye disorders and conditions like age related macular degeneration, glaucoma, and visual disorders can benefit from certain nutraceuticals. Nutraceuticals like lutein, zeaxanthin, vitamin C and vitamin E reduces the risk of cataracts.

1. 1. 3. Improve immune function

Immune booster nutraceuticals like green tea, blueberries, amino acids and vitamin D are found to be useful in improving and strengthening immune health and also help to prevent diseases. Herbs and plants extracts like Echinacea and Astragalus help in the development and regeneration of stem cells. The anti-inflammatory effects of garlic can enhance the functioning of the immune system [5].

1. 1. 4. Improve gut health

Many nutraceuticals like probiotics, prebiotics, flavonoids, aloe vera, resveratrol, omega-3 and omega-6 acids can restore and stimulate the growth of good bacteria and reduce the effect of harmful bacteria in the gut.

1. 1. 5. Support reproductive health

Many nutraceuticals play an important role in male and female reproductive health. Nutraceuticals help with male infertility [6] and dysfunction and prevents damage to sperm.

Certain nutraceuticals can influence hormones and are also used to improve fertility, preconception pregnancy outcomes in women, and provide support during menstruation [6].

1. 1. 6. Treat inflammation

Nutraceuticals are showing promising results in the prevention and treatment of inflammation due to the presence of phytochemicals. They can reduce oxidative stress in chronic inflammatory diseases like asthma, osteoarthritis, rheumatoid arthritis, cancer, and autoimmune diseases [7].

2. NUTRACEUTICALS

A wholesome diet with plenty of fruits and vegetables along with the right combination of macronutrients is vital for optimum health. Although in some cases, enough of major nutrients are not always gotten. Not getting enough nutrients can lead to oxidative stress which can lead to other health issues. Research in nutrition is constantly developing with new discoveries and innovative technologies. On such advancement that bridges the gap between nutrition and medicine is nutraceuticals. Nutraceuticals are products gotten from food sources that provides both nutrition and medicinal benefits. Nutraceuticals even include everyday food like prebiotics and probiotics, fortified cereals, processed foods and beverages.

Nutraceutical is a substance that has a physiological benefit or provides protection from chronic diseases. Nutraceutical can improve health, delay the aging process, prevent chronic diseases, increase life expectancy, or support the structure and functioning of the body. They are also used in the prevention and treatment of mental health issues and disorders. A healthy diet contributes to the health by providing nutrients the body needs to repair itself, grow and function well. When diet does not supply enough of these essential nutrients and vitamins, nutraceuticals can act as a supplement.

2. 1. Types of nutraceuticals

As modern science reveals the importance of a balanced diet, more and more people are beginning to pay attention to what they are eating. Nutrition is an essential factor in all round health and wellness, especially since obesity is now a global issue. For those that do not suffer from those diseases caused by poor nutrition, the most common treatment such as medicine only reduces the symptoms without correcting the true cause, which is the diet.

Nutraceuticals are alternative beneficial products that seek to erase the line between medicine and food. People suffering from poor nutrition often turn to nutraceuticals because they are natural and are designed based on the essentials of a balanced diet. Nutraceuticals are a blend between “nutrition” and pharmaceutical”. Types of nutraceuticals ranges from dietary fiber to prebiotics and probiotics to antioxidants vitamins. In fact, nutraceuticals is one of the most diverse umbrella terms of nutritional medicine since both complex saturated fatty acid and polyphenols as well as basic kitchen cupboard items such as spices can be found in them. Nutraceuticals are broadly classified based on their function, food source and their bioactive components. Most of them fall under two general categories:

- Dietary supplements,
- Functional foods.

2. 1. 1. Dietary supplements

Dietary supplements are those products that contains concentrated bioactive nutrients from a food source processed into a suitable dosage form. These supplements can contain one or more of the following: amino acids, vitamins, herbs and other botanicals, minerals, important metabolites and certain enzymes. Dietary supplements are available in tablets, capsules, powders, and liquids, gummies, energy bars and other suitable form [8].

2. 1. 2. Functional foods

Functional foods are any foods or food ingredients that provides a health benefit other than basic nutrition [8]. The foods under this category includes whole food and fortified, enriched or enhanced foods that can improve health when consumed regularly as a part of varied diet. Functional food and is available as pasta, cereal, whole grains, yogurt, snacks and more [8].

Functional foods can be:

- Traditional Functional Food: These are nutrient rich natural foods that deliver health benefits other than basic nutrition such as omega-3 fatty acids in salmon and lycopene in tomatoes.
- Non-Traditional Functional Foods: These are artificial foods prepared by adding bioactive components to help enhance health and well-being. Examples include fortified nutraceuticals such as juice with added calcium, cereal fortified with iron, flour with added folic acid. Modified functional foods can also include recombinant nutraceuticals, which are energy producing foods such as bread, yogurt, cheese and vinegar produced via biotechnology techniques.

2. 2. Classes of nutraceuticals

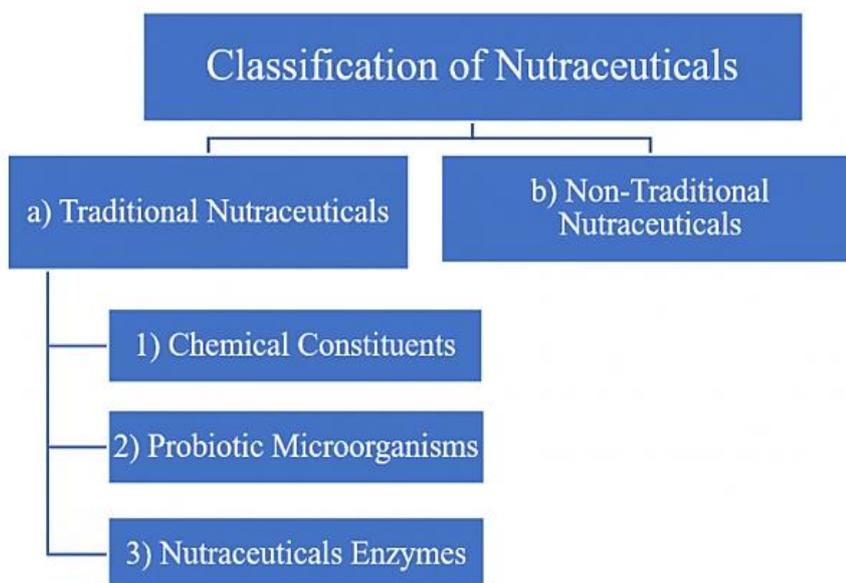


Fig. 1. Classification of Nutraceuticals

Nutraceuticals are classified based on foods available in the market.

- 1) Traditional nutraceutical
- 2) Non-traditional nutraceuticals

2. 2. 1. Traditional nutraceuticals

Traditional nutraceuticals are simply natural with no changes to the food. Food contains several natural components that deliver benefits beyond basic nutrition such as lycopene in tomatoes, omega-3 fatty acids in salmon, or saponins in soy. They are grouped based on Chemical constituents, Probiotic Micro-organism, and Nutraceutical enzymes.

2. 2. 2. Chemical Constituents

Nutrients

Substances such as vitamins, minerals, amino acids, and fatty acids with established nutritional functions. Most vegetables, whole grain cereals, dairy products, fruits and animal products such as meat, poultry contain vitamins and help cure heart diseases, stroke, cataract, osteoporosis, diabetes and cancer. Minerals found in plant, animal, and dairy products are useful in osteoporosis, anemia, and build strong bones, teeth, muscles, improve nerve impulses and heart rhythm. Flaxseed and salmon contain fatty acids omega-3 PUFAS, and are potent controllers of the inflammatory processes, maintenance of brain function, and reduce cholesterol deposition.

Herbals

Nutraceuticals hold a great promise to improve health and prevent chronic diseases with the help of herbals. Some examples are willow bark (*Salix nigra*), having an active component as salicin which is anti-inflammatory, analgesic, antipyretic, astringent, and antiarthritic. Parsley (*Petroselinum crispum*) contains flavonoids (apiol, psoralen) and is diuretic, carminative and antipyretic. Peppermint (*Mentha piperita*) contains menthol as an active component and cures a cold and flu. Lavender (*Lavandula angustifolia*) contain tannin which helps cure depression, hypertension, stress, cold, cough, and asthma. Cranberries (*Vaccinium erythocarpum*) contains proanthocyanidin and are found to be useful in cancer, ulcers, and urinary tract infections.

Phytochemicals

Phytochemicals are one class of nutraceuticals. They are classified based on the chemical name given according to their phytochemical properties. For example Carotenoids (Isoprenoids) found in various fruits, vegetables, and egg yolk, are anti-carcinogenic, boost natural killer immune cells, and protect cornea against UV light. Legumes (chickpeas and soybeans), grains, palm oil contains non-carotenoids, which removes cholesterol and are anti-carcinogenic.

Flavonoid polyphenolics are found in berries, fruits, vegetables, and legumes, which are potent antioxidant, phytoestrogens, prevent breast cancer, prostate cancer, and control diabetes. Non-flavonoid polyphenolics are present in dark grapes, raisins, berries, peanuts. Tumeric roots are strong anti-inflammatory, antioxidant, and effective anti-clotting agents and reduce cholesterol. Phenolic acids, found in blueberries, tomatoes, and bell peppers having antioxidant

activity, reduce mutagenicity of polycyclic aromatic hydrocarbons. Seeds of *Barbarea verna*, broccoli contain isothiocyanates (glucosinolates) and have antitumorigenic activity.

2. 2. 3. Probiotic Microorganism

The scientific interest in probiotics boosted from the work of Metchnikoff to transform the toxic flora of the large intestine into a host-friendly colony of *Bacillus bulgaricus* was found by Hord. Probiotics mean for life and are defined as live microorganisms, which when consumed in adequate amount, confer a health effect on the host. They are friendly bacteria that promote healthy digestion and absorption of some nutrients.

They act to crowd out pathogens, such as yeasts, other bacteria, and viruses that may otherwise cause disease and develop a mutually advantageous symbiosis with the human gastrointestinal tract. They have an antimicrobial effect through modifying the microflora, preventing the microflora, preventing adhesion of pathogens to the intestinal epithelium, competing for nutrients necessary for pathogen survival, producing an antitoxin effect, and reversing some of the consequences of infection on the intestinal epithelium, such as secretory changes and neutrophil migration. Probiotics can cure lactose-intolerance by the production of the specific enzymes (beta-galactosidase) that can hydrolyze the offending lactose into its component sugars.

2. 2. 4. Nutraceutical Enzymes

Enzymes are an essential part of life, without which our bodies would cease to function. Those people who are suffering from medical conditions such as hypoglycemia, blood sugar disorders, digestive problems and obesity, eliminate the symptoms by enzyme supplements to their diet. These enzymes are derived from microbial plants and animal sources.

Table 1. List of nutraceuticals enzymes from microbes, plants, and animals.

Microbial Enzymes/source	Plant Enzymes/ source	Animal Enzymes/ source
Hemicellulase (microorganisms and mushrooms)	Hemicellulase (plant wall)	OxBile (ox)
Amyloglucosidase (ascomycetes)	Alpha-Galactosidase (beans, Brussels, sprouts, broccoli, other vegetables, and whole grains)	Trpsin (pancreatic juice)
Catalase	Pentase (cell wall)	Pancrelipase (pancreatic juice)
Glucoamylase(A.Niger, <i>Saccharomycopsis fibuligera</i>)	Beta-amylase (higher plants)	Chymotrypsin (all classes of vertebrates)
Cellulase (all living cells)	Bromelain (pineapple)	Pepsin (animals, tracheal secretions)
Invertase-Sucrase (yeast)	Biodiatase (soybean)	Lysozyme (saliva, tears, egg white, and many animal fluids)

Lactase-beta-Galactosidase (bacteria)	Glucoamylase(callus and suspension cultures of sugar beets (Beta vulgstris L.) as well as in mature roots)	alpha-Amylase (saliva)
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2. 2. 5. Non-traditional nutraceuticals

Non-traditional nutraceuticals are artificial foods prepared with the help of biotechnology. Food samples contain bioactive component which are engineered to produce products for human-wellness. They are arranged into

- Fortified nutraceuticals
- Recombinant nutraceuticals

2. 2. 5. 1. Fortified nutraceuticals

It constitutes fortified foods from agricultural breeding or added nutrients and/ or ingredients e.g. orange juice fortified with calcium, cereals with added vitamin or minerals, and flour with added folic acid. Some examples are milk fortified with cholecalciferol used in vitamin D deficiency Prebiotics and probiotics fortified milk with Bifid bacterium lactis HN019 used in diarrhea, respiratory infections, and severe illness, in children. Banana fortified using soybean ferritin gene in iron deficiency.

2. 2. 5. 2. Recombinant nutraceuticals

Energy providing foods, such as bread, alcohol, fermented starch, yogurt, cheese, vinegar, and others, are produced with the help of biotechnology. The production of probiotics and the extraction of bioactive components by enzyme/fermentation technologies as well as genetic engineering technology are achieved through biotechnology.

Table 2. Products produced by recombinant microorganisms.

Source	Enzyme	Products
Acetobacter xylinum	Beta-glucuronidase	Kombucha beverage
Escherichai coli K-12	Chymosin	Milk-coagulated products
Fusarium venenatum	Xylanase	Increased bran solubilization
Aspergillus oryzae	Esterase-lipase, Asparticproteinase, Glucoseoxidase, Laccase, Lipase, Pectin, esterase	Alcoholic beverages (Sake, koji)
Saccharomyces	Stilbene synthase and 4 coumaroyl-CoA	
Spirulina Pacifica	Indoleamine 2,3-dioxygenase (IDO)	Resveratrol

2. 3. Categories of nutraceuticals

Nutraceuticals can be arranged in several ways depending on its easy understanding and application, that is, for academic instruction, clinical trial design, functional food development or dietary recommendations. Some of the most common ways of classifying nutraceuticals can be based on food sources, mechanism of action, chemical nature *e.t.c.*, the food sources used as nutraceuticals are all natural and can be categorized as [9].

2. 3. 1. Dietary fiber

Dietary fiber is the food material, more precisely it is the plant material that is not hydrolyzed by enzymes secreted by the digestive tract, but digested by microflora in the gut. Dietary fibres mostly include non-starch polysaccharides such as celluloses, hemicelluloses, gums and pectins, lignin, resistant dextrins and resistant starches. Food rich in soluble fibre include fruits, oats, barley and beans.

Chemically dietary fiber means carbohydrate polymers with a degree of polymerization not lower than 3, which are neither digested nor absorbed in the small intestine. Based on their water solubility, dietary fiber may be divided into two forms;

- Insoluble dietary fiber (IDF), which includes celluloses, some hemicelluloses and lignins which is fermented to a limited extent in the colon.
- Soluble dietary fiber (SDF), which includes beta-glucans, pectins, gums, mucilages and hemicelluloses that are fermented in the colon.

The IDF and SDF are collectively known as non-starch polysaccharides (NSP).

2. 3. 1. 1. Level of dietary fibre in foods

The soluble components of dietary fiber by virtue of their bulking and viscosity producing capabilities, retards the gastric emptying of the stomach [10]. This affects the rate of digestion and the uptake of nutrients and brings a feeling of satiety. Soluble fiber has been shown to lower selectively serum LDL cholesterol and to improve glucose tolerance [11]. They also enhance insulin receptor binding and improve glycaemic response. In colon, dietary fiber increases fecal bulking due to increased water retention, increased transit time and increased fecal bacterial mass caused by soluble fiber fermentation. The fiber also promotes the growth of Bifidobacteria in the gut. Persons consuming generous amounts of dietary fiber, compared to those who have minimal fiber intake, are having low risk of CHR [12], stroke [13], hypertension [14], diabetes [15], obesity [15] and certain gastrointestinal disorders. Again, increase in the intake of high fiber food improves serum lipoprotein values [16], reduces blood pressure level, increases blood glucose control for diabetes, helps in weight loss and promotes regularity [17]. Some potential negative effects of dietary fiber include reduced absorption of vitamins, minerals, proteins and calories. It is recommended that dietary fiber intake for adults generally falls in the range of 20-35 g/day. The recommended dietary fiber intake for children and adults are estimated to be 14 g/1000 kCals.

2. 3. 2. Probiotics

The history of probiotics dates back as far as the first intake of fermented milk, over 2000 years ago. The scientific interest in this area boosted from the work of Metchnikoff (1907) to transform the flora of the large intestine into a host friendly colony of *Bacillus bulgaricus* [18].

A probiotics can be defined as live microbial feed supplement, which when administered in adequate amounts beneficially affects the host animal by improving its intestinal microbial balance [19]. Probiotics are available in various forms as powder form, liquid form, gel or paste or granule forms etc. Specific probiotics are generally used to treat gastrointestinal conditions such as lactose intolerance, acute diarrhea and antibiotic associated gastrointestinal side effect. Probiotics agents possess the properties of non-pathogenic, non-toxic, resistance to gastric acid, adherence to gut epithelial tissues producing antibacterial substances. There are evidences that administration of probiotics decreases the risk of systematic conditions such as allergy, asthma, cancer and many other diseases and infections of the ear, urinary tract [20].

2. 3. 3. Prebiotics

Prebiotics are dietary ingredients that beneficially affect the host by selectively altering the composition or metabolism of the gut microbiota [21]. These are short chain polysaccharides that have unique chemical structures that are not digested by humans; in particular fructose based oligosaccharides that exist naturally in food or are added in the food.

The prebiotics consumption widely promotes the *Lactobacillus* and *Bifidobacteria* growth in the gut, thus helping in metabolism [18]. Vegetables like chicory roots, banana, tomato, alliums are rich in fructo-oligosaccharides. Some other examples of these oligosaccharide are raffinose and stachyose, found in beans and peas. The health benefits of the prebiotics includes improved lactose tolerance, antitumor properties, neutralization of toxins and stimulation of intestine immune system, reduction of constipation, blood lipids and blood cholesterol levels.

3. POLYUNSATURATED FATTY ACIDS (PUFA)

Polyunsaturated fatty acids are also called essential fatty acids as they are crucial to the body's function and are introduced externally through the diet [22]. Polyunsaturated fatty acids have two subdivisions:

- a. Omega-3-(n-3) fatty acids
- b. Omega-6-(n-6) fatty acids

The major omega-3-fatty acids are alpha-linolenic acid (ALA), eicosapentanoic acid (EPA), docosahexanoic acid (DHA). Alpha-linolenic acid is a precursor of eicosapentanoic acid and docosahexanoic acid. Eicosapentanoic acid and docosahexanoic acid are mainly found in fatty fishes such as salmon, herring, trout, blue fin tuna, mackerel and fish oils. Sources of alpha-linolenic acid are flaxseed, canola, soybeans, some nuts e.g. walnuts and red or black current seeds.

Omega-6-polyunsaturated fatty acids mainly consist of linolenic acid, gamma linolenic acid and arachidonic acid. Linolenic acid occurs mainly in vegetable oils e.g. corn, safflower, sunflower and soybeans. Arachidonic acid is found in animal products such as meat, poultry and eggs.

Studies suggests that omega-3-fatty acids have three major effect as cardiovascular diseases anti arrhythmic (preventing and increasing irregularities in the force or rhythm of the heart) [23], hypolipidemic (promoting the reduction of lipid concentration in the serum) [24] and antithrombotic (decreased arteriosclerosis) [25]. Emerging research evidence shows the

benefits of omega-3-oils in other area of health including premature infant health [26], asthma [27], bipolar and depressive disorders [28], dysmenorrhea and diabetes.

4. ANTIOXIDANT VITAMINS

Vitamins like vitamin C, vitamin E and carotenoids are collectively known as antioxidant vitamins. These vitamins act both singly as well as synergistically for the prevention of oxidative reactions leading to several degenerative diseases like cancer, cataracts, cardiovascular disease etc. [29]. These vitamins are abundant in many fruits and vegetables and exert their protective action by free radical scavenging mechanisms. Vitamin E which comprises of tocopherols together with tocotrienols transfer hydrogen atom and scavenge singlet oxygen and other reactive species thus protecting the peroxidation of PUFA within the biological membrane and LDL [30].

Tocotrienols are more mobile within the biological membrane than tocopherols because of the presence of the unsaturated side-chain and hence penetrate tissues with saturated fatty layers, i.e. in brain and liver more efficiently. They have more recycling ability and are a better inhibitor of liver oxidation [31]. Vitamin E and Selenium has a synergistic role against lipid peroxidation. Vitamin C, better known as ascorbic acid donate hydrogen atom to lipid radicals, quenches singlet oxygen radical and removes molecular oxygen. Scavenging of aqueous radicals by the synergistic effect of ascorbic acid along with tocopherol supplementation is a well-known antioxidant mechanism [32]. Carotenoids like lycopene, beta-carotene, lutein, zeaxanthin are known to be the most efficient singlet oxygen quencher in the biological systems without the production of any oxidizing product. Beta-carotene traps peroxy free radicals in tissues are low oxygen concentrations. Hence beta-carotene complements the antioxidants properties of vitamin E.

5. POLYPHENOLS

Polyphenols form a large group of phytochemicals, which are produced by plants as secondary metabolites to protect them from photosynthetic stress, reactive oxygen species. There are approximately 8000 different classes of polyphenols, the most important being flavonols, flavones, flavan-3-ols, flavanones and anthocyanins. The highly branched phenylpropanoid pathway synthesizes majority of polyphenols. The most commonly occurring polyphenols in food include flavonoids and phenolic acids. Dietary polyphenols are of current interest because substantial evidence in vitro have suggested that they can affect numerous cellular processes like gene expression, apoptosis, platelet aggregation, intercellular signaling, that can have anti-carcinogenic and anti-atherogenic implications [33].

These apart polyphenols also possess antioxidant, anti-inflammatory, anti-microbial, cardio-protective activities and play a role in the prevention of neurodegenerative diseases and diabetes mellitus. Polyphenols are mostly acknowledged for their antioxidant activities on the basis of their structural chemistry. Bioavailability of polyphenols is an important factor determining their biological activity. This depends on the chemical properties of polyphenol, conjugation and reconjugation in the intestines, intestinal absorption, and enzymes available for metabolism [34]. It has been found that flavonoids modulate the expression of gamma-

glutamylcysteine synthetase, an important rate limiting enzyme involved in Glutathione being important in redox regulation of transcription factors and enzymes for signal transduction, polyphenol mediated regulation of glutathione significantly alters cellular effects, as detoxification of xenobiotics, glutathionylation of proteins.

The age-old French Paradox refers to the fact that there is a relatively less incidence of coronary heart disease among the French, in spite of the fact that they consume diets relatively rich in saturated fats. This trend was later found to be the result of French's high consumption of red wine. The antioxidant and anti-inflammatory activities of red wine is due to the presence of resveratrol, a triphenolic stilbene present in the black skin of grapes and proanthocyanidines [35]. Moreover, studies have also proved that the oxidative stress induced by alcohol consumption has led to the expression of several cardio-protective oxidative stress-inducible proteins along with HSP 70 (heat shock protein) [36]. Resveratrol is a phytoestrogen receptor agonist and research has suggested that this function may also serve a significant role in cardiovascular benefits.

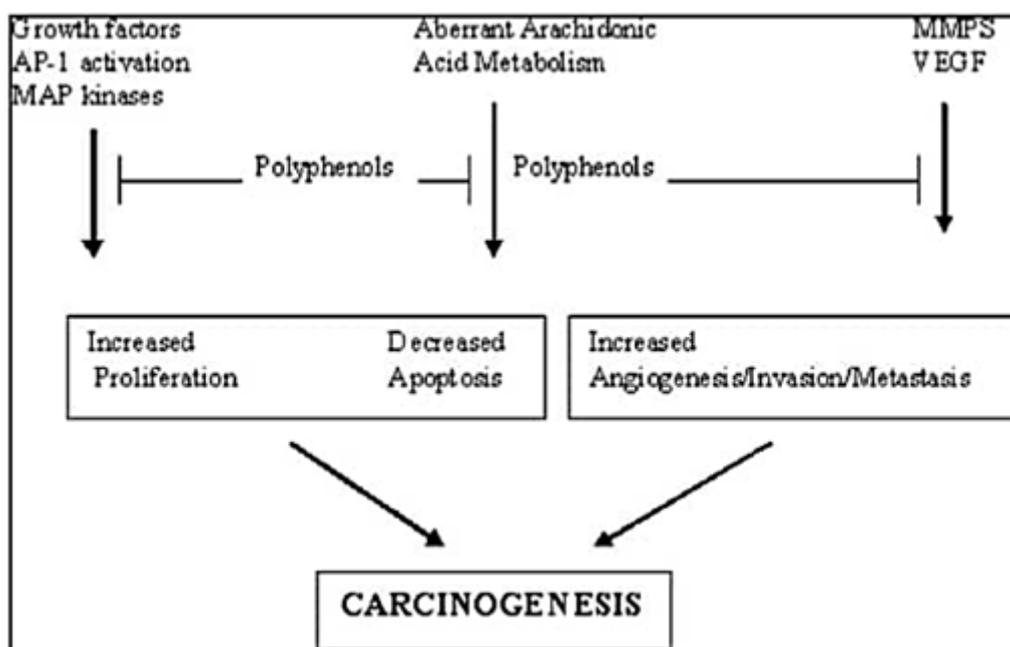


Fig. 2. Mechanistic scheme for prevention of cancer by dietary polyphenols.

Even though the antioxidant activities of the wines vary over a factor of 2, the ratios of the activities to the total phenol content are approximately the same (about a factor of 10), indicating the direct relationship between the two [37]. The inhibition of COX-2 expression by resveratrol in different cell lines suggest that resveratrol is important in inhibiting carcinogenesis. A diet enriched with red wine solids (solid from 750 ml of red wine per kg diet), which contained catechins, gallic acid, and other polyphenols, delayed the onset of tumors in the HTLV-1 transgenic mouse [34]. Moderate consumption of red wine (400 ml/day) for 2 weeks significantly increases antioxidant status and decreases oxidative stress in the circulation of humans [38].

Tea (*Camellia sinensis*) is a rich source of polyphenols, such as catechins, which include (-)-epicatechin, (-)-epigallocatechin, (-)-epicatechin-3-gallate (ECGC), with ECGC being the major catechin. These apart, tea also constitutes of flavonols like quercetin and myricetin. Tea, mainly consumed in the form of black tea has been found to have cancer-preventing activities. Several studies have suggested that tea is effective in inhibiting 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) induced tumorigenesis in mice.

Administration of black tea preparation to adenoma-bearing mice significantly inhibited tumor cell proliferation and the adenoma to carcinoma [39]. These experiment indicates that tea has a broad inhibitory activity against lung carcinogenesis in organ sites in skin, lung, esophagus, stomach, liver, small intestine, pancreas, colon, bladder, and mammary gland ECGC has been considered by several authors as the active component of green tea and its anti-carcinogenic activity has also been demonstrated [34].

A case control study in Shanghai has reported that frequent consumption of green tea is associated with a lower incidence of oesophageal cancer, especially among nonsmokers and non-alcohol drinkers. On the other hand, in the Netherlands Cohort Study on Diet and Cancer, consumption of black tea was not found to affect the risk for colorectal, stomach, lung, and breast cancers [40]. Such different results on tea and cancer suggest that the amount of tea consumed, lifestyle related factors such as smoking and diet and different etiological factors involved in different populations have an important bearing on the anticancer effect on tea. Green tea has also been found to be associated with lower risk of cardiovascular diseases through decreased serum cholesterol and triglyceride and provides protection against peroxidation of lipids in kidney.

Legumes are consumed worldwide as an alternative source of proteins, since they are rich in amino acids like lysine and tryptophan and they are much cheaper than animal proteins. Studies have revealed that in addition to complex carbohydrate, soluble fibers, essential vitamins and metals, legumes also supply the diet with polyphenols like flavonoids, isoflavones and lignans [41]. Of all legumes, soybeans has received most attention. Soybeans is most significant source of dietary isoflavones.

It has a relatively high concentration of genistein and diadzein, which are generally considered as phytoestrogens. These compounds have been shown to inhibit the growth of most hormones-dependent and independent cancer cells, especially breast, prostate and skin cancer in mouse models. In mice, dietary soybean components inhibited the growth of experimental prostate cancer and altered tumor biomarkers associated with angiogenesis. The protective effect of soy isoflavones against colon cancer is unclear. Bioavailability of genistein is much superior with respect to green tea polyphenols. Recent research has shown that there are several other legume components apart from soy isoflavones, which may be beneficial effects. For instance, kievitone, a potential breast cancer fighting agent is found in hyacinth bean and antimicrobial agents, like agmatine and isovitexin are particularly found in winged bean, but not in common cowpea *Vigna unguiculata* (brown) and underutilized legumes *Cajanus cajan* (brown) and *Sphenostylis sternocarpa* also possess higher antioxidant activity due to their relative higher phenol content. Hence they can play an active role in combating degenerating diseases along with their traditional role of preventing malnutrition.

Although free radical scavenging ability of *C. cajan* (brown), *S. sternocarpa*, and *V. Unguiculata* (brown) were within the same range with the free radical scavenging ability of some commonly consumed green leafy vegetables, it was generally lower than that of fruits and non-leafy vegetables like broccoli and red pepper [41].

The evidence that polyphenols are considered chemopreventive agents because of their antioxidative properties by some authors have been mostly circumstantial and hence more investigations are needed. For more precise information on the role of dietary polyphenols in cancer prevention in humans, reliable biomarkers for the consumption of specific polyphenols are needed, in addition to the use of dietary questionnaires. The association between the consumption of a specific type polyphenol (or food item) and lowered the risk needed to be observed consistently in different studies, before dietary recommendations. High intake of polyphenols even from dietary sources can result in toxic effects.

Flavonoids are reported to induce cleavage in the MLL gene, inhibit enzymes (such as topoisomerases) involved in DNA structure and replication and hence may predispose subjects to infant leukemia [34].

Although the redox potential of most flavonoids radicals are lower than those of superoxide and peroxy radicals, the effectiveness of these radicals in generating lipid peroxidation, DNA adducts, and mutation may still be significant in disease development. Flavonoid supplementation as a general recommendation to increase cellular glutathione concentration may also be troublesome since the active compounds and mechanisms involved in disease preventing effects are still poorly understood. It remains to be determined whether dietary polyphenols modulate cellular glutathione concentrations among humans and whether they contribute to regulation of major cellular signaling pathways, which would explain the indisputable fact that fruits and vegetables protect against disease.

6. SPICES

Spices are esoteric food adjuncts that are used for thousands of years to enhance the sensory quality of foods. The quantity and the variety of the spices consumed in the tropical countries are particularly extensive. The impact characteristic flavor, aroma or piquancy and colour to foods, stimulating our appetite as well as modify the texture of food. Recent research reveals that dietary spices in their minute quantity has an immense influence on the human health by their antioxidative, chemopreventive, anti-mutagenic, anti-inflammatory, immune modulatory effects on cells and a wide range of beneficial effects on human health by the action of gastrointestinal, cardiovascular, respiratory, metabolic, reproductive, neural and other systems [42].

Most of the spices component are terpenes and other constituents of essential oils. They have been found to be effective in different forms. For instance about 50 g of onions and 5-6 cloves of garlic in their raw form are adequate for lowering of cholesterol in human body. Recent studies on lipid profile and blood pressure of moderately hypercholesterolemia subjects showed better beneficial effects of dietary supplement with aged garlic extract relative to the fresh ones [43]. Co-administration of garlic with fish oil had a better beneficial effect on serum lipid and lipoprotein concentrations by providing a combined lowering of total cholesterol, LDL cholesterol and triglyceride concentration.

Spices and herbs are in most cases harmless, when used as foods, but may exhibit toxicity, when used as medicine, because of their relative higher dose administered, or rather due to the possibilities of their interactions with other pharmaceutical medications [44]. Again report says that excessive consumption of garlic (4 ml/kg for raw garlic juice of 100 mg/kg for garlic oil) lead to adverse effects on health such as anemia, weight loss, heart, liver, kidney toxicity [45]

and other dermatological problems [46]. High doses of onions (500 mg/kg) as well causes lung and tissue damage in rats [47]. Fenugreek seeds (25-50g), garlic (5-6 cloves), onions (50 g) and turmeric powder (1 pinch) in the daily diet of diabetes. Regular intake of curcuminoids at about 0.5 g reduces blood lipid peroxide level up to about 33% due to their antioxidant activity.

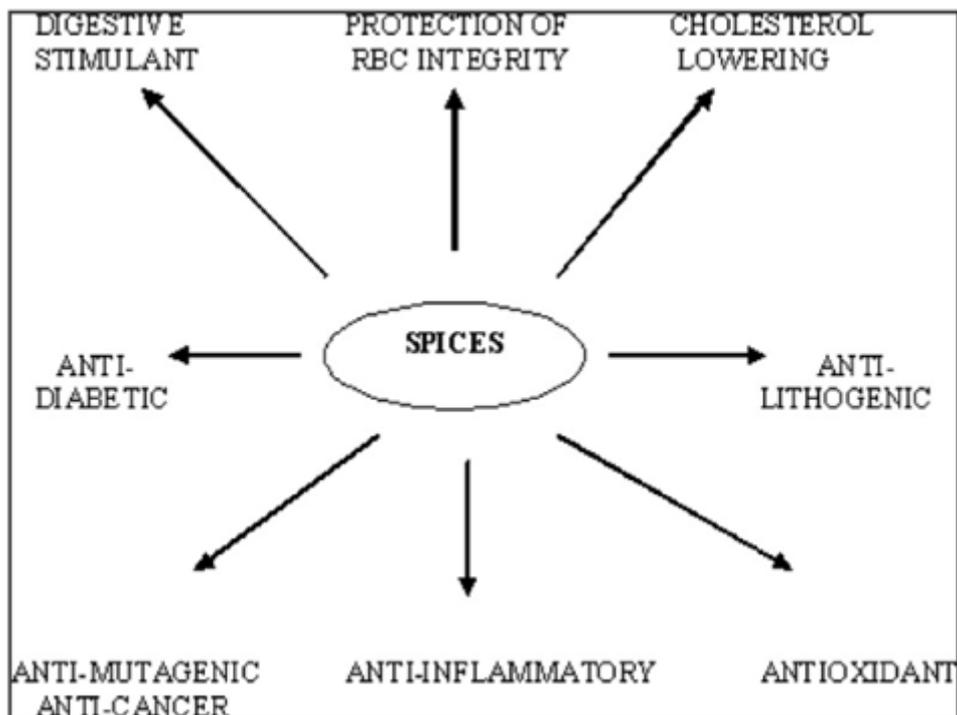


Fig. 3. Health benefits of spices

Table 3. Potential health benefit of spice.

POTENTIAL HEALTH BENEFITS	SPICES
Lowering of blood cholesterol	Garlic, Fenugreek, Onions and Tumeric
Prevention and dissolution of cholesterol gallstones	Curcumin and Capsaicin
Hypoglycemic potential	Garlic, Fenugreek, Onions and Tumeric
Antioxidant effects	Tumeric/Curcumin, Capsaicin
Anti inflammatory and anti arthritic effects	Tumeric/Curcumin, Capsaicin
Digestive stimulant action	Piperine, Ginger, Mint, Onions, Tumeric
Antimicrobial	Tumeric/Curcumin, Garlic

6. 1. Relationship between functional food and nutraceuticals

6. 1. 1. Differences between Functional Food and Nutraceuticals

Functional foods refer to the foods with ingredient which gives that food-health-promoting properties over and above its usual nutritional value while nutraceuticals refer to the foodstuff (as a fortified food or a dietary supplement) held to provide health or medical benefits in addition to its basic nutritional value.

The main difference between functional foods and nutraceuticals is that the functional foods naturally contain bioactive compounds found in foods while nutraceuticals are the bioactive compounds found in fortified food, dietary supplements or herbal products.

Another difference between functional foods and nutraceuticals is their origins. Functional foods are natural which nutraceuticals include traditional nutrients. The bioactive compounds in functional foods are different from the traditional nutrients while nutraceuticals include traditional nutrients.

Grapes, strawberries, and apples are examples of functional foods while beta-carotene, lycopene, resveratrol, and ferulic acids are examples of nutraceuticals.

6. 1. 2. Similarities between Functional Food and Nutraceuticals

- Functional foods and nutraceuticals are two types of compounds with related functions.
- Therefore, their names are used interchangeably.
- They both have health promoting, disease-preventing or medicinal properties.

7. METABOLIC DISEASES

Metabolic diseases are genetic conditions that results in metabolism problems. Most people with inherited metabolic disorders have a defective gene that results in an enzyme deficiency. There are hundreds of different genetic metabolic diseases, and their symptoms, treatments, and prognoses vary widely.

Metabolism refers to all the chemical reactions taking place in the body to convert or use energy. A few major example of metabolism includes:

- Breaking down the carbohydrates, proteins, and fats in the food to release energy.
- Transforming excess nitrogen into waste products excreted in urine.
- Breaking down or converting chemicals into other substances and transporting them inside cells.

Metabolism is an organized but chaotic chemical assembly line. Raw materials, half-finished products, and waste materials are constantly being used, produced, transported and excreted. The “workers” on the assembly line are enzymes and other protein that make chemical reaction happen.

7. 1. Types of metabolic diseases

Hundreds of inherited metabolic disorders have been identified, and new ones continue to be discovered. Some of the more common and important genetic metabolic disorders include:

- **Lysosomal storage disorders:** Lysosomes are spaces inside cells that breakdown waste products of metabolism. Various enzyme deficiencies inside lysosomes can result in build-up of toxic substances, causing metabolic disorders including:
 - **Hurler syndrome:** (abnormal bone structure and developmental delay).
 - **Niemann-Pick disease:** (babies develop liver enlargement, difficulty feeding, and nerve damage).
 - **Tay-Sachs disease:** (progressive weakness in a month-old child, progressing to severe nerve damage; the child usually lives only until age 4 or 5).
 - **Gaucher disease:** (bone pain, enlarged liver, and low platelet counts, often mild, in children or adults).
 - **Fabry disease:** (pain in the extremities in childhood, with kidney and heart disease and strokes in adulthood; only males are affected).
 - **Krabbe disease:** (progressive nerve damage, developmental delay in young children; occasionally adults are affected).
- **Galactosemia:** Impaired breakdown of the sugar galactose leads to jaundice, vomiting and liver enlargement after breast or formula feeding by a newborn.
- **Maple syrup urine disease:** Deficiency of an enzyme called BCKD causes buildup of amino acid in the body. Nerve damage results, and the urine smells like syrup.
- **Phenylketonuria (PKU):** Deficiency of the enzyme PAH results in high levels of phenylalanine in the blood. Intellectual disability results if the condition is not recognized.
- **Glycogen storage disease:** Problems with sugars to store lead to low blood sugar levels, muscle pain, and weakness.
- **Mitochondrial disorders:** Problems inside mitochondria, the powerhouse of cells, lead to muscle damage.
- **Friedreich ataxia:** Problems related to protein called frataxin cause nerve damage and often heart problems. Inability to walk usually results by young adulthood.
- **Peroxisomal disorders:** Similar to lysosomes, peroxisomes are tiny spaces filled with enzymes inside cells. Poor enzyme function inside peroxisomes can lead to buildup of toxic products of metabolism. Peroxisomal disorders include:
 - **Zellweger syndrome:** (abnormal facial features, enlarged liver, and nerve damage in infants).
 - **Adreno leukodystrophy:** (symptoms of nerve damage can develop in childhood or early adulthood depending on the form.)
- **Metal metabolism disorders:** Levels of trace metals in blood are controlled by special proteins. Metabolic disorders can result in protein malfunction and toxic accumulation of metal in the body.
- **Wilson disease:** (toxic copper levels accumulate in the liver, brain, and other organs)
- **Hemochromatosis:** (the intestines absorb excessive iron, which builds up in the liver, pancreas, joints, and heart, causing damage)
- **Organic acidemias:** methyl malonic acidemia and propionic acidemia.
- **Urea cycle disorder:** ornithine transcarbamylase deficiency and citrullinemia.

7. 2. Causes of metabolic diseases

In most metabolic disorders, a single enzyme is either not produced by the body at all or is produced in a form that doesn't work. The missing enzyme is like an absentee worker on the assembly line. Depending on that enzyme's job, its absence means toxic chemicals may build up, or an essential product may not be produced.

The code or blueprint to produce an enzyme is usually contained on a pair of genes. Most people with metabolic disorders inherit two defective copies of genes—one from each parent. Both parents are the “carrier” of the bad gene, meaning they carry one defective copy and one normal copy. In the parents, the normal gene copy compensates for the bad copy. Their enzyme levels are usually adequate, so they have no symptoms of a genetic metabolic disorder. However, the child who inherits two defective gene copies cannot produce enough effective enzyme and develops the genetic metabolic disorder. This form of genetic transmission is called autosomal recessive inheritance.

The original cause of most genetic metabolic disorders is a gene mutation that occurred many, many generation ago. The gene mutation is passed along through the generation, ensuring its prevention. Each inherited metabolic disorder is quite rare in the general population. Considered all together, inherited metabolic disorders may affect about 1 in 1,000 to 2,500 newborns. In the certain ethnic populations, such as Ashkenazi Jews (Jews of central and eastern European ancestry), the rate of inherited metabolic disorders is higher.

7. 3. Symptoms of metabolic diseases

The symptoms of genetic metabolic disorders vary widely depending on the metabolism problem present. Some symptoms of metabolic diseases include:

- Lethargy
- Poor appetite
- Abdominal pain
- Vomiting
- Weight loss
- Jaundice
- Failure to gain weight or grow
- Developmental delay
- Seizures
- Coma
- Abdominal odor of urine, breath, sweat, or saliva

The symptoms may come on suddenly or progress slowly. Symptoms may be brought on by foods, medication, dehydration, minor illnesses, or other factors. Symptoms appear within a few weeks after birth in many conditions.

8. ROLES AND TREATMENT OF NUTRACEUTICALS IN METABOLIC DISEASES

Metabolic disease such as diabetes mellitus, obesity are rapidly increasing in the westernized world because of poor lifestyle habits favoring fat and sucrose enriched meals and

low physical activity or sedentariness. Medical nutritional therapy is an integral component of diabetes mellitus, obesity and metabolic syndrome management. Pharmacological intervention is taken into consideration when diet associated physical exercise and healthy lifestyle is insufficient to control blood glucose, body weight and metabolic profile. In contrast, pharmacological intervention for obesity still remains a controversial issue because of the only modest long term efficacy and concern about safety. Obesity is the major underlined reason for metabolic syndrome. The worldwide incidence of obesity has been rapidly increasing in the last two decades. According to WHO report, obesity has been classified as a growing epidemic, and if immediate action is not taken, millions of people will suffer from serious weight related disorders. Obesity counts a higher major health problem and common chronic disease. In health surveys conducted in the United States in 2005, 24.2% of men and 23.5% of women or over one-fifth of the respondents were classified as obese [48].

Obesity mainly arises when there is an imbalance between energy intake, principally stored as triglycerides (food consumption), and energy expenditure (basal metabolic rate and biochemical processes). The excess energy is primarily stored in adipose tissue in the form of triglycerides. When adipose tissue, liver, and other organs predisposes the individual to the development of metabolic changes that increase overall morbidity risks [49]. Hence, the recent recognition of metabolic syndrome and its influence on health has led the researchers to consider the potential drug-food or nutrient drug interaction here since nutrition therapy and pharmacological intervention are the major component in managing metabolic syndrome. An interaction is said to take place when the effects of one drug are changed by the presence of another food, drug, and drink or by some environmental chemical agents. Interaction between food and drugs may inadvertently reduce or increase the effect of drugs, resulting in therapeutic failure (i.e. hyperglycemia in case of diabetes mellitus) or increase adverse effect (i.e. hyperglycemia in case of diabetes mellitus). The conventional clinically relevant food-drug interactions are caused by food induced changes in the bioavailability of drugs. Thus, in the field of metabolic disorders where nutrition plays a major role in the overall treatment, the potential influence of food and nutrient intake on drug therapeutic effect may be crucial.

A potential nutraceutical can only become an established one after sufficient data on its medicinal and the clinical aspects are obtained. Pharmacokinetic interferences often occur as a result of change in drug metabolism. Cytochrome- P450 (CYP-450) system oxidizes a broad spectrum of drugs by a number of metabolic processes that can be enhanced or reduced by various drugs (known as inducers or inhibitors). Other factors involve age, sex, patient and administration.

8. 1. Curcumin

Curcumin [1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5dione] being an active component of tumeric is responsible for the yellow colour and is known to possess multiple pharmacological effects. It is used in the treatment for a wide variety of inflammatory ailments, including obesity and other metabolic diseases. Curcumin is the principal curcuminoid of the popular Indian spice tumeric, which belongs to the family Zingiberaceae. The yellowish compound, curcumin, is known to possess multiple pharmacological effects [50].

Obesity comes with one of the major component and that is inflammation. The chronic and subclinical inflammation is recognized, as being part in the development of diabetes, and obesity-related atherosclerosis. Adipose tissue is an important initiator of inflammatory response, and which is involved in energy regulation and homeostasis.

8. 1. 1. Mechanism of Action

Curcumin interacts directly with cyclooxygenase-2 (COX-2), DNA polymerase, Lipoxygenase (LOX), glycogen synthase kinase-3b (GSK-3b), and cytokines (TNF- α). It interacts indirectly with several transcription factors, activator protein1 (AP-1), β -catenin, signal transducer and activator of transcription (STAT) proteins and peroxisome proliferator-activated receptor c (PPARc) (Europharmas Curcumin Superior in Absorption). Adipose tissue is not simply a storage depot for excess calories but it also actively secretes fatty acids and a variety of polypeptides. The adipose tissue consists of adipocytes, immune cells and pre-adipocytes. They secrete leptin, adiponectin and other inflammatory cytokines such as TNF, interleukins 1,6 (Iyer chronic inflammation).

8. 1. 2. Safety and Efficacy

Various clinical trials (phase 1 and phase 2) dealing with curcumin safety has shown that curcumin is safe and is well tolerated. Doses (500-1200mg/day) were administered in capsules form by patients and safety was assessed. Few developed adverse reactions such as diarrhea, headache, skin rashes and yellow stool. Curcumin has also been reported to inhibit the activity of drug metabolizing enzymes such as CYP-450, glutathione S-transferase, UDP-glucuronosyltransferase [51]. The major obstacle for the clinical development of curcumin is its poor absorption, rapid excretion, and low systematic bioavailability which suggest that the therapeutic potential of oral curcumin is limited.

8. 2. Lagenaria siceraria

Lagenaria siceraria also known as bottle gourd belonging to the family Cucurbitaceae is extensively grown in India and other tropical and sub-tropical regions of the world. Bottle gourd has certain potent nutraceutical and therapeutic functions and they include phyto-constituents, minerals, vitamins, fiber etc. L. siceraria is reported to exhibit cardioprotective, antihyperlipidemic, analgesic, anti-inflammatory, immunomodulatory and hepatoprotective functions in human [52]. Drinking one or two glasses of raw bottle gourd juice in the morning on an empty stomach is one popular practice in India to deal with obesity associated disorders.

8. 2. 1. Mechanism of Action

A study shows that L. siceraria reduces total cholesterol, triglycerides (TG) and low density lipoproteins (LDL) levels. This study involves fifty subjects in the age group of 40-60 years and participating subjects were asked to consume freshly prepared L. siceraria juice for about 90 days in an empty stomach. Daily attendance was recorded and sustained during the study period. During the study periods, the parameters such as kidney functioning, body weight and BMI were measured and monitored. At the end of the study, feedback and viewpoints of participating subjects were recorded. Hence, the results showed that there are an improvement in high density cholesterol level (HDL) and a reduction in low density cholesterol levels [53]. Kidney functioning evaluation showed that there was a decrease in urea with a considerable improvement in the uric acid level [54].

8. 3. Trigonella foenum-graecum

Fenugreek (*Trigonella foenum-graecum* L. Leguminosae) is one of the oldest medicinal plants mostly used as spice. It is known to originate in India and Northern Africa. This herb is

known to have diverse medicinal uses. It includes wound healing, bust enhancement, as an aphrodisiac and promote of lactation weaning mothers. A number of important chemicals with medicinal values has been found in fenugreek seeds and leaves (Fenugreek uses and properties). Fenugreek seed is an important source of steroidal sapogenins such as diosgenin which are used extensively by pharmaceutical and nutraceuticals industries. Diosgenin is used as a raw precursor for the production of steroidal drugs and hormones such as testosterone, glucocorticoids and progesterone.

8. 3. 1. Mechanism of Action

In human studies, the mechanism of action in the reduction of the plasma glucose and increase insulin receptors remains unclear. Fenugreek seeds also lower serum TGs, total cholesterol and LDL cholesterol. These effects are mainly because of constituent's sapogenins, which increase cholesterol excretion enzyme [55].

8. 3. 2. Safety/ Adverse Effects

Fenugreek is generally considered safe and is well tolerated, but there certain side effects associated with the same. Caution in using fenugreek is warranted in patients known to be allergic to it or who are allergic to chicken peas because of cross reactivity. The known side effects include dizziness, transient diarrhea, and flatulence. Blood glucose level needs to be checked during the beginning of supplementation [56].

8. 3. 3. Potential Drug Interaction

Toxicological evaluation of 60 diabetic patients who took powdered fenugreek seeds at a dose of 25 g/day for 24 weeks disclosed no clinical hepatic or renal toxicity and no haematological abnormalities. Fenugreek being rich in fiber can interfere with the absorption of oral medications in the gut because of its mucilaginous and highly viscous nature [57].

8. 4. Emblica officinalis

Emblica officinalis also known as Amla belong to the family Euphobiaceae is the most important medicinal plant in India medicines. It is extremely nutritious and is a chief dietary source of vitamin C, amino acids and minerals. Entire parts of the plant are used for medicinal purposes, particularly the fruit. The fruit is known to treat ailments such as fever and cold.

8. 4. 1. Mechanism of Action

Increased level of lipids such as cholesterol and triacylglyceride in serum as well as in liver is significantly decreased by the administration of *E. officinalis*. Peroxisome proliferator-activated receptors (PPAR α) regulate the transcriptions of gene involved in lipid and cholesterol metabolism. The oral administration of *E. officinalis* significantly increases the hepatic PPAR protein level [58].

8. 5. Murraya koenigii

The leaves of *Murraya koenigii* are widely used as spice for flavoring food and as such it appears to be without any side effects and toxicity. *Murraya koenigii* belongs to the family of Rutaceae [59]. According to ayurveda, various parts of plants have been used in folk medicines

for the treatment of hypertension, hepatitis, rheumatism, cough, hysteria, skin eruptions and poisonous bites. The stems are very popular for cleaning teeth and gums [60].

8. 5. 1. Mechanism of Action

The anti-diabetic effect of *Murraya koenigii* is due to the increase in hepatic glycogen concentration and decrease in concentration of glycogen phosphorylase and gluconeogenic enzymes. It exhibits antioxidant activity. It is also known to induce apoptosis in human myeloid cancer cells and also a time dependent anti-proliferative in acute lymphoid and chronic myeloid leukemic cell lines. It is an inhibitor of lipoxygenase.

8. 6. Vigna mungo

Vigna mungo is also known as black gram or black lentil. Grain legumes are the important source of food proteins. The leguminosae are the most important family in Dicotyledonae. These grams are the richest source of proteins and amino acids for human as well as animal nutrition [61].

- 1) **Cardiovascular disease:** the frequent intake along with a saturated fat poor diet can help in controlling the lipid homeostatis and consequently reduce the risk of CVD. The legume high fiber content, low glycemic index and the presence of minor components such as phytosterols, saponins, oligosaccharides etc. are considered the main responsible agents for this property.
- 2) **Diabetes:** because of low glycemic index and high content of indigestible fibers, dry legumes are claimed to maintain glycemic control in diabetes individuals. Moreover, black grams also help to prevent insulin resistance which represent Type 2 diabetes.
- 3) **Overall weight and obesity:** despite their content of lipids, starch and protein, dry legumes help in maintaining a regular body weight, and is because of their satiety effects, thus limiting overall food daily intake.

8. 6. 1. Mechanism of Action (in weight control and obesity)

Various studies suggest that proteins are more satiating than carbohydrates or fats. In this respect, an increased gram protein intake may have weight loss benefits, and it also has credits to the lower extent of kidney workload of plant proteins. A specific direct action of black gram on an amylase protein inhibitors has been considered for its potential use in prevention of obesity and weight loss.

8. 7. Marketed preparations

Marketed preparation of the above mentioned spices, herbs, etc. are available in the market in the form of tablets, capsules, powder etc.

9. SUMMARY AND CONCLUSION

With this changing lifestyle, individuals are more prone to disorders such as diabetes, hypertension and obesity etc. These disorders are known to be silent killers. In order to prevent the wide spread of these disorder, researchers have understood the importance of nutraceuticals

and their benefits on health. The potential nutraceuticals should be evaluated further to study their mechanism responsible for the beneficial effect in metabolic syndrome.

Nutraceuticals are important bioactive, chemical compound that have health promoting, disease preventing, and medicinal properties and are also referred as phytochemicals. As nutraceuticals blur the line between food and drugs, it is often difficult to distinguish between nutrients, food additives, drugs and nutraceuticals. Nutraceuticals have the advantage over medicines since they avoid side effects, and are naturally dietary supplements.

Nutraceuticals on the basis of their natural source, chemical grouping, and categories, fall into three key terms, nutrients, dietary fiber, dietary supplements, and herbals. Also, unfortunately, nutraceuticals sometimes find themselves in the same regulatory category as common food: standardization of dose and method of delivery to improve efficacy and health benefits could overcome this. The nutraceutical industry is growing at a very far rate exceeding expansion in the food and pharmaceutical industries.

Future demand of nutraceutical depends on the consumer perception of the relationship between diet and disease. The interaction of nutraceuticals with food and drugs is another area which should be taken into consideration. The effect of different processing methods on the biological availability and effectiveness of nutraceuticals remains uncertain. As like drugs, there should be strict regulatory controls for nutraceuticals.

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