



REVIEW ARTICLE

PHARMACOGNOSY

MEDICINAL PLANTS DERIVED NUTRACEUTICALS : A RE-EMERGING HEALTH AID**NEHA PANDEY¹ , RAM PRASAD MEENA¹ , SANJAY KUMAR RAI² AND SHASHI PANDEY-RAI^{1*}**

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ABSTRACT

Nutritional therapy and phyto-therapy have emerged as new concepts of health aid in recent years. Strong recommendations for consumption of nutraceuticals from plant origin have become progressively popular to improve health, and to prevent and treat diseases. Nutraceuticals are "naturally derived bioactive compounds that are found in foods, dietary supplements and herbal products, and have health promoting, disease preventing and medicinal properties." Plant derived Nutraceuticals/functional foods have received considerable attention because of their presumed safety and potential nutritional and therapeutic effects. Some popular phyto-nutraceuticals include glucosamine from ginseng, Omega-3 fatty acids from linseed, Epigallocatechin gallate from green tea, lycopene from tomato etc. Majority of the nutraceuticals are claimed to possess multiple therapeutic benefits though substantial evidence is lacking for the benefits as well as unwanted effects. With these trends, improvement of the dietary nutritional values of fruits, vegetables and other crops or enhancement of the bioactive components in folk herbals have become the targets of blooming plant biotechnology industry. The present review has been devoted towards better understanding of the phyto-nutraceuticals from different medicinal plants based on their disease specific indications.

KEY WORDS

Nutraceuticals, Phytotherapy, Functional food, Medicinal plants

INTRODUCTION

Metabolome of the size of about 1.5 to 2 lakh unique molecules together with enzymatic proteome are responsible for the bulk of the functions performed in human body. Most of the diseases of body organs, general vulnerability to infectious diseases and ageing processes, are all related to the deficiencies of one or more of the metabolomic molecules and those that are required for body's functions but are not synthesized by the concerned human organs. Nutraceuticals are these kinds of molecules used singly or in combinations as dietary supplements to complement inborn deficiencies and those that develop with ageing. While some of the

Nutraceuticals serve essentially as therapeutics on patients of specific diseases, bulk of them are useful as health giving food supplements for general population. When a functional food aids in the prevention and/or treatment of disease(s) and/or disorder(s) it is called a nutraceutical. The past decade has witnessed a tremendous resurgence in the interest and use of "Nutraceuticals" (or "functional foods") in which phytochemical constituents can have long-term health promoting or medicinal qualities. Dr Stephen DeFelice¹ coined the term "Nutraceutical" from "Nutrition" and "Pharmaceutical" in 1989 (Figure-1).

Foods as nutraceuticals

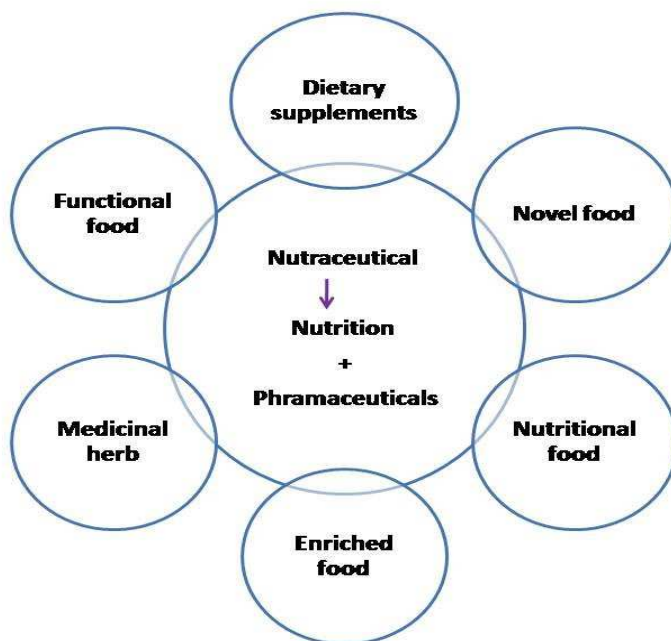


Figure 1
Inter-relationship of various foods as nutraceuticals.



A Nutraceutical is the opposite of "junk food" and according to the World Health Organization, over 80% of the world's population (4.3 billion people) rely upon such traditional plant-based systems of medicine as phytochemicals, nutritional constituents or as functional food^{2,3}. Functional foods are ordinary foods that have components, ingredients, incorporated in them to give them a specific medicinal or physiological benefit other than a purely nutritional effect^{4,5,6}. Although the distinction between medicinal plants and Nutraceuticals can sometimes be vague, a primary characteristic of the latter is that Nutraceuticals have a nutritional role in the diet and the benefits to health may arise from long-term use as foods⁶. The preparations based on them have also been called as functional foods³. The economic production and availability of Nutraceuticals is a highly desirable objective to improve the health of the people of the country, especially that of the poor people⁴. Now, the nutraceuticals related research for improving its quality and quantity is an important area for ongoing biotechnological investigations.

Nutraceuticals are essentially prophylactic or preventive, in contrast to drugs, which are active chemical substances used for pre-protection or to treat an illness⁵. They represent a different approach, one based on nutrition for curing ill health or overall wellness of the whole body, rather than drug based curing of diseases^{6,7,8,9}. Nutraceuticals or functional

foods can be classified on the basis of their natural sources, pharmacological parameters or according to their chemical constitution. The most usual nutraceuticals are Nutrients, herbals, dietary supplements, functional food and natural chemicals derived from different medicinal plants¹⁰.

1. **Nutrients:** Substances with established nutritional functions, such as carbohydrate, proteins, vitamins, minerals, amino acids and fatty acids come under this category. The most commonly known nutrients are antioxidants, vitamins and essential minerals. Antioxidants are substances, which retard or prevent deterioration, damage or destruction caused by oxidation. Fortunately, the body has an army of antioxidants for damage limitation. Antioxidant form an integral part of the nutraceutical market.^{11,12} The Phyto-nutrients are unique substances occur naturally in plants, have been found to hold specific and powerful disease preventing possibilities.^{12,13,14} Both essential and nonessential phyto-nutrients should be considered as bioactive food components based on the specific physiological function they impart, including characterization of their metabolic and physiological functions and associated targets, and biomarkers¹⁵. Fruits and vegetables give us many of the nutrients that we need: vitamins, minerals, dietary fiber, water, and healthful phytochemicals.^{14,15,16} (Figure 2).

2. Natural products as nutraceuticals

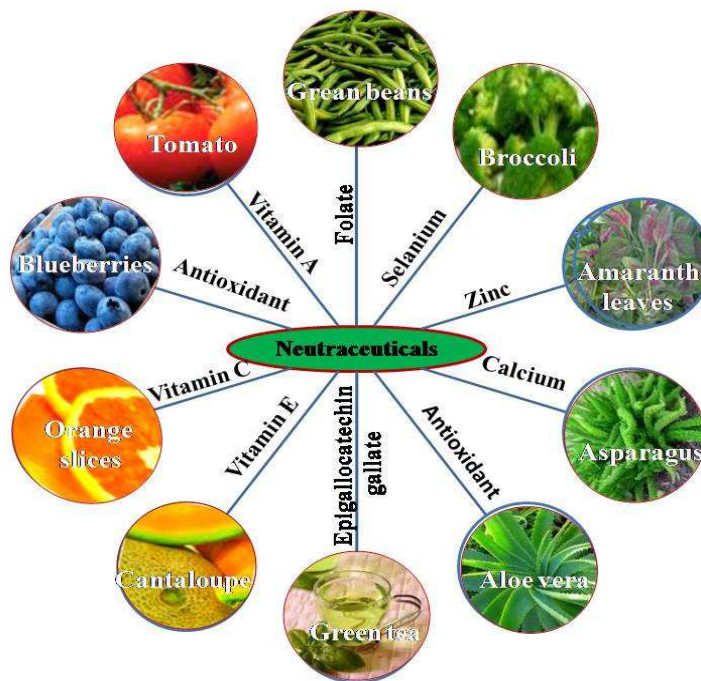


Figure 2
Various natural products as sources of vitamins, minerals and antioxidants.

Almost all fruits and vegetables naturally have essential minerals (Table-1), and that are low in fat and calories with no cholesterol.

Table 1
List of important macro and micro nutrient from fruit and vegetable source

Serial no.	Nutrient	Fruit Sources	Vegetable Sources
1.	Calcium	Blackberries Blackcurrants Dates Grapefruit Mulberries Orange Pomegranate	Amaranth leaves Celery Chinese Broccoli French Beans Okra Spirulina Turnip
2.	Copper	Avocado Blackberries Dates Guava Lychee Mango Pomegranate	Amaranth leaves French Beans Peas Potatoes Pumpkin Spirulina Sweet Potato



3.	Iodine	Fruits grown in iodine-rich soils contain iodine.	Vegetables grown in iodine-rich soils contain iodine.
4	Iron	Blackberries Cherries Dates Figs Grapes Kiwi Lychee Mulberries Pomegranate Strawberry Watermelon	Amaranth leaves French Beans Peas Potatoes Spinach Turnip
5.	Magnesium	Banana Blackberries Blackcurrants Dates Guava Mulberries Pomegranate Raspberries Watermelon	Amaranth leaves Butternut squash French Beans Okra Peas
6.	Manganese	Banana Blackberries Blackcurrants Blueberries Dates Grapefruit Guava Pomegranate Raspberries Strawberry	French Beans Lima Beans Okra Peas Potatoes Sweet Potato
7.	Phosphorus	Avocado Dates Guava Lychee Mulberries Pomegranate	Amaranth leaves Brussels Sprouts Corn French Beans Parsnip Potatoes Pumpkin
8.	Potassium	Bananas Cherries Dates Grapefruit Guava Pomegranate Watermelon	Amaranth leaves Bamboo Shoots French Beans Parsnips Potatoes Pumpkin Sweet Potatoes
9.	Selenium	Bananas Guava	Asparagus French Beans



		Lychee Mango Pomegranate Watermelon	Lima Beans Mushrooms Peas
10.	Sodium	in almost all fresh, whole fruits	Sodium occurs naturally in almost all fresh, whole vegetables
11.	Zinc	Blackberries Dates Pomegranate Raspberries	Asparagus Bamboo Shoots Corn French Beans Okra Peas Potatoes Pumpkin

3. Herbs: The knowledge of herbals has accumulated over thousands of years and today we have many effective means of ensuring health care. Numerous nutraceuticals are present in medicinal herbs as key components^{17,18,19}. A great attention has, now a day's, been given to discover the link between dietary nutrients and disease prevention. Large number of herbs, which had been in use since ancient time, have been shown to play a crucial role in the prevention of disease. In addition to the macro and micro nutrients such as proteins, fats, carbohydrates, vitamins or minerals necessary for normal metabolism, a plant based diet contains numerous nonnutritive phyto-constituents which may also play an

important role in health enhancement^{20,21,22,23}. The Nutraceuticals market comprises two principal segments: Functional Foods and Dietary Supplements. Given in the table 2 is a list of Nutraceutical herbal plants, and the information on specified organs of these plants that serve as source of material that can be used directly or in the form of processed products. The table also mentions the conditions for which the plant materials have proved useful. There is need for domestication and cultivar development for cultivated production of these plants. The post-harvest processing technologies that will allow material to remain active and hygienic also needs to be worked out for a large majority of these plants.

Table: 2
List of some common medicinal plants used as traditional herbal Nutraceutical

No.	Plant species	Common name	Diseases for which used	Form of use
1	<i>Agave americana</i>	Rambans	Antiseptic, diuretic ,	Leaves sap
2	<i>Allium sativum</i>	Garlic	Chemoprevention, cancer, diabetes, arteriosclerosis, lowering cholesterol, respiratory infections	Fresh or dried cloves, capsules, odorless tablets, tinctures, aged garlic extracts
3	<i>Aloe vera</i>	Ghritkumari	First-degree burns, cuts and abrasions, wound healing, anthelmint, antiulcer	Sunscreen, skin creams, lotions, oral intake
4	<i>Avena sativa</i>	Oat straw	Diuresis, cholesterol control, reducing inflammation, itching	Dried herb; capsules, tablets, tinctures
5	<i>Amaranthus</i> spp.	Chaulai	cardiovascular disease	oil from seeds
6	<i>Andrographis paniculata</i>	Kalmegha	Bacillary dysentery, respiratory tract infection	Shoot powder
7	<i>Artemisia annua</i>	Artemisia	Fever, upper respiratory tract infections	Shoot decoction
8	<i>Asparagus</i> spp.	Shatavari	Tonic, astringent	roots
9	<i>Borago officinalis</i>	Bugloss,	Skin care, anti inflammatory, blood purifier.	Herb, Leaves and Flowers
10	<i>Boswellia serrata</i>	Salai guggal	Asthma, anti-arthritis	Gum-resin
11	<i>Bauhinia purpuria</i>	Rakta kanchan	Catarrh, boil, glandular swelling	Roots and leaves
12	<i>Berberis asiatica</i>	Barberry	Roots are used in treating ulcers, urethral discharges, ophthalmia, jaundice, fevers etc fruit is cooling and laxative	Roots and berries
13	<i>Calendula</i> spp	Pot marigold	Anti-inflammatory, may inhibit HIV, anti-bacterial, and anti-tumor. Skin and cancer treatments.	Floweral decoction for wound healing



14	<i>Capsicum annum</i>	Red pepper	Anti-arthritic, anti-oxidant action, stimulant, nutrition, rubefacient, nutrition	Fresh and dried fruit, powder
15	<i>Cassia senna</i>	Senna	Constipation	Dried leaf, /pods
16	<i>Centella asiatica</i>	Gotu kola	Improving memory, sedative, stress reduction, imuno-stimulant, venous insufficiency, wound healing pregnancy-related stretch marks, venous tonic	Herb, powdered, capsules, tablets, tinctures, teas
17	<i>Curcuma longa</i>	Turmeric	Reducing inflammation, indigestion, antioxidant, liver problem	Dried root, whole, powdered
18	<i>Commiphora wightii</i>	Guggal	Cardioprotective, anti-inflammatory, rheumatic diseases	Gum -resin
19	<i>Cymbopogon citratus</i>	Lemon grass	Stomachache, expelling gas	Dried leaf, cut and sifted, tea
20	<i>Echinacea angustifolia, purpurea and pallida</i>	Echinacea	Cold, flu, minor infections, immuno-stimulant	Dried whole herb or root, capsules, expressed juice of fresh flowering plants, flex-tabs, tablets, tinctures
21	<i>Ephedra sinica</i>	Ephedra	Mild anti-asthmatic, nasal congestion, broncho-dilator, fluid retention, obesity	Dried-stems; capsules, tablets, tinctures
22	<i>Echinacea angustifolia</i>	Cone flower	Antibiotic, antiviral and anti allergic used in reducing the common cold.	Whole plant
23	<i>Foeniculum vulgare</i>	Fennel	Stomach bloating, stimulant, digestive spasms, catarrh aphrodisiac, galactagogue	Whole seed, capsules, tinctures
24	<i>Ginkgo biloba</i>	Ginkgo	Age-related memory	Dried leaf, tea



			loss, fatigue, tinnitus, anti-arthritic, improving microcirculation	
25	<i>Glycyrrhiza glabra</i>	Licorice	Anti-inflammatory, congestion, coughs, stomach or duodenal ulcers	Root powder, capsules, extracts, tablets, tinctures
26	<i>Garcinia cambogia</i>	Garcinia	Weight loss	Extracts of fruit
27	<i>Hypericum perforatum</i>	St.-John's-Wort	Mild to moderate epilepsy, depression, cuts and abrasions	Dried herb, flowering tops for tea, in oil for external use, capsules tablets, tinctures
28	<i>Hibiscus subdariffa</i>	Motherwort	CNS depressant	Calyx powder or decoction
29	<i>Linum usitatissimum</i>	Flaxseed	Constipation, irritable bowel syndrome, source of omega-3-essential fatty acids, cholesterol control, chemoprevention, anti-arthritic	Seed powder, expressed oil of seed
30	<i>Matricaria chamomilla</i>	Chamomile	Sedative, indigestion, insomnia, nausea, inflammation, wound healing	Dried flowers, capsules, cream, salve, tea, tincture, bath products
31	<i>Medicago sativa</i>	Alfalfa	Appetite stimulation, anti-arthritic, nutrition	Dried leaf, capsules, extracts, tablets, tinctures, teas
32	<i>Moringa oleifera</i>	Moringa	Uses include as an antimicrobial, antiviral, hepatoprotective, anticancerous, antiseptic and in treating rheumatism, skin diseases, asthma and venomous bites	tree's bark, roots, fruit, flowers, leaves, seeds, and gum
33	<i>Panax quinquefolius</i> and <i>ginseng</i>	Ginseng	Convalescence, fatigue, diabetes, cholesterol control, improving concentration and well-being, aphrodisiac	Dried root, steamed root, capsules, extracts, tablets, tinctures, teas
34	<i>Plantago ovata</i>	Psyllium	Constipation, lowering	Dried seed, husk,



			cholesterol, type 2 diabetes	capsules
35	<i>Puereria tuberosa</i>	Bilikand	Eases bowel movement, useful in relieving constipation, used in skin diseases	tubers
36	<i>Rosmarinus officinalis</i>	Rosemary	Digestion, rheumatism, stimulating appetite, stimulating circulation	Leaf powdered, tinctures, extracts
37	<i>Phyllanthus emblica</i>	Amla	Stress, diuretic, liver function, anti-ageing, diabetes	Fruit pulp fresh or dry
38	<i>Serenoa repens</i>	Saw palmetto	Benign prostatic hyperplasia, inflammation, impotence	Dried fruit whole, ground, capsules, tablets, tinctures
39	<i>Silybum marianum</i>	Milk thistle	Liver disorders, lactation problems, anti-oxidant	Whole or powdered seed, capsules, tablets, tinctures
40	<i>Swertia chirata</i>	Chirata	Migraine headaches	Fresh or dried whole plant
41	<i>Trigonella foenum-graecum</i>	Fenugreek	Gastritis, excess cholesterol, diabetes, nutrition, skin inflammation	Seed, whole or powdered; capsules, tinctures
42	<i>Urtica dioica</i>	Stinging nettle	Benign prostatic hyperplasia (BPH), diuresis, anemia, osteoarthritis	Dried leaf, dried root; capsules, tablets, tinctures
43	<i>Terminalia chebula</i>	Harar	Antioxidant	Fruit pulp
44	<i>Valeriana officinalis</i>	Valerian	Anxiety, insomnia, hypertension	Root, powder, tea, capsules, tablets, tinctures, extracts
45	<i>Withania somnifera</i>	Ashwagandha	Stress, insomnia, cataract prevention	Root powder, standardized extracts, tinctures
46	<i>Zingiber officinale</i>	Ginger	Indigestion, motion sickness, nausea, anti-oxidant, cholesterol control	Fresh or dried root, capsule, tablets, tinctures

4. **Functional food:** They are consumed as a part of normal diet and are intended to supplement the normal diet. Functional foods

are similar to conventional food or beverage and are consumed as part of a normal diet having physiological benefits. They can also

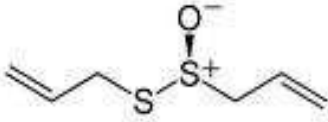
promote growth and developmental processes. They may be used as conventional or fortified foods with bioactive components to reduce disease risk.

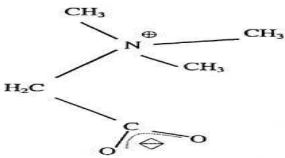
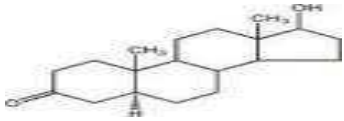
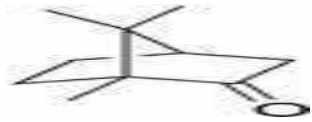
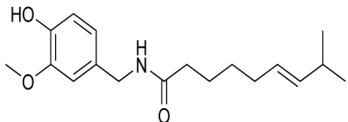
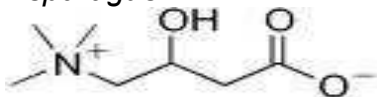
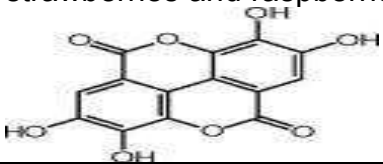
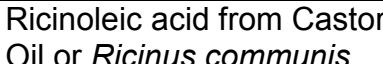
5. Dietary supplements: They are concentrated sources of nutrients or other substances with a nutritional or physiological effect, alone or in combination^{10,11}. Dietary supplements contain all products that can be purchased by the consumer without a prescription. Many potential benefits have been attributed to antioxidant use in the form of dietary intake or supplementation. Antioxidants, in general, may be useful in the prevention of cancer and cerebro-vascular disease^{23,24,25,26}. Dietary supplements are not classified as drugs. The main difference is that they do not have approved therapeutic claims unlike in the case of drugs. Moreover, dietary supplements could either contain vitamins, minerals, herbals, or amino acids, all aimed to add to or supplement the diet of an individual. They are not intended to be taken alone as a substitute to any food or medicine.

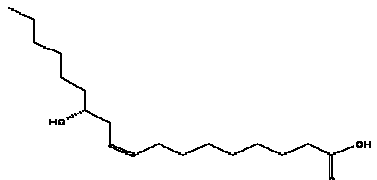
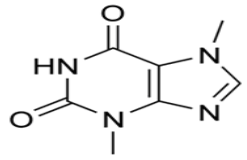
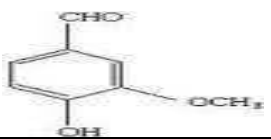
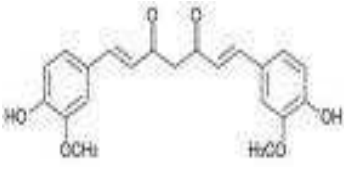
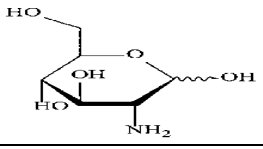
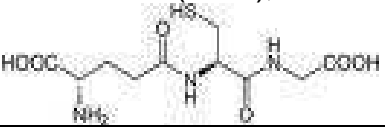
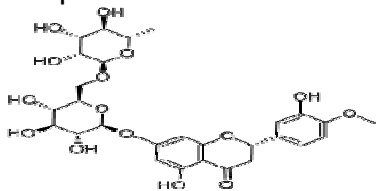
6. Phytochemicals: Phytochemicals are naturally occurring biochemicals that give plants their color, flavor, smell, and texture, which may help prevent diseases^{22,24,26}. They are biologically active natural products such as glucosinolates in cruciferous vegetables, limonoids in citrus fruits, lignans in flaxseed, lycopene in tomatoes, and catechins in tea. They all have specific actions and can be used variously for e.g. as antioxidants and have a positive effect on health^{28,29,30,31}. During 1980s and 1990s, numerous laboratories began studying phytochemicals to "mine" plants for bioactive substances that might be used as medicines or nutraceuticals or for other chemical applications. Many compounds are showing great promise as disease fighters in the body, boosting production or activities of enzymes, which then act by blocking carcinogens, suppressing malignant cells, or interfering with the processes that can cause heart disease and stroke^{30,31,32,33,34}. Systematic classification on the basis of therapeutically important compounds of the Nutraceuticals are responsible for the specific health benefit that can be done as given in Table 3³⁵⁻⁵⁹.

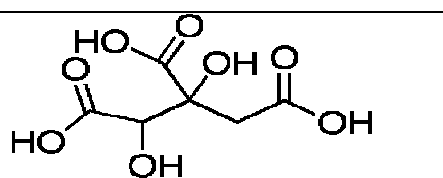
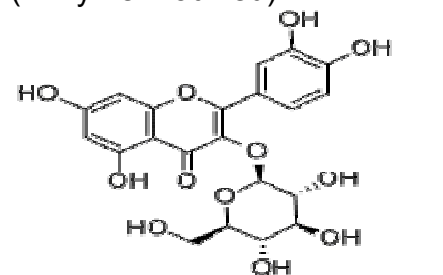
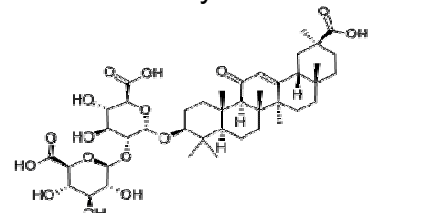
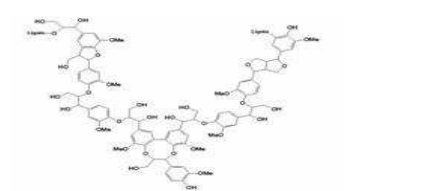
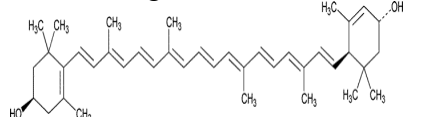
Table 3

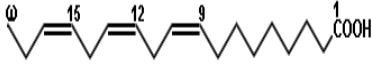
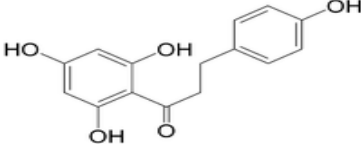
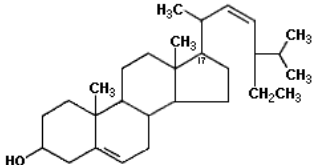
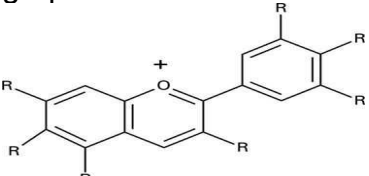
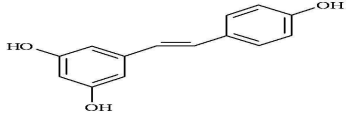
List of some common chemical compounds isolated from plants used as Nutraceuticals.

Serial No.	Chemical compounds/source	Properties	References
1	Allicin from <i>Allium sativum</i> 	It is a powerful antifungal antibacterial. It has been shown to be an antioxidant and has been used to treat arteriosclerosis and serum cholesterol.	Eric Block, 1985 ³⁵
2	Betaine (Trimethyl Glycine) from green leafy vegetables and germinated grains	Reduces toxic buildup of homocysteine.	Pulliainen et al., 2010 ³⁶

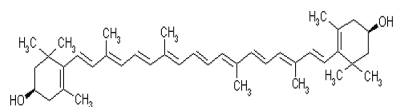
			
3	Bromelain from <i>Ananas sp.</i> 	It is pineapple protease enzyme used to prevent heart disease, reduce the effects of aging, improve the immune system, and to reduce arthritis and inflammation.	Rabelo et al.,2004 ³⁷
4	Camphor from <i>Cinnamomum camphora</i> 	Used as an inhalant to treat cold and flu.	Chen et al ., 2002 ³⁸
5	Capsaicin or trans-8-methyl-N-vanillyl-5 nonenamide from <i>Capsicum annum</i> 	Used for pain relief topically and as a digestive aid when taken internally. It is also seen as a possible antioxidant for the body. It can pose a risk of allergic reactions and the severe damage to the eyes or skin if used in higher doses.	Dray ,1992 ³⁹
6	Carnitine or L-Carnitine from <i>Asparagus</i> 	Responsible for the transportation of long-chain fatty acids groups into the mitochondria..	Steiber et al.,2004 ⁴⁰
7	Ellagic Acid from strawberries and raspberries 	this phytochemical fights cancer in humans.	Vattem and Shetty ,2005 ⁴¹
8	Ricinoleic acid from Castor Oil or <i>Ricinus communis</i> 	Contains ricinoleic acid the active ingredient. Castor oil is used both externally (multiple skin problems) and internally for constipation, upper respiratory problems, and liver	Okui, 1963 ⁴²

		and kidney issues.	
			
9	Chocolate (a mixture of cocoa obtained from <i>Theobroma cacao</i> and vanilla from orchid)	Have positive effects on the heart and blood pressure due to the flavonoids in chocolate. Chocolate also contains a neurotransmitter, serotonin, that acts as an anti-depressant, and other substances, such as theobromine and phenylethylamine. These have a stimulating effect.	Taubert et al., 2007 ⁴³
			
			
10	Curcumin from <i>Curcuma longa</i>	The colorant in turmeric a fraction of which has been shown by studies done at the University of California in Los Angeles to clear brain plaque caused by Alzheimer's disease.	Ram et al., 2000 ⁴⁴
			
11	Plant Glucosamine	Chondroitin and glucosamine are part of normal cartilage and acts as a cushion between the joints.	Mary et al., 1973 ⁴³
			
12	Glutathione (GSH),	A tripeptide, which provides antioxidant properties thereby protecting the cells against damage by free radicals.	Mullineaux, and Creissen, (1996) ⁴⁵
			
13	Hesperitin	Hesperitin is a GRAS ingredient that shows interest as a potential anti-inflammatory.	Chauhan et al., (1978) ⁴⁶
			
14	Hydroxy Citric Acid	Hydroxy Citric Acid found in Garcinia,	Lee and Lee, (2007) ⁴⁷

			
15	<p>Isoquercetin from mangoes and from <i>Rheum nobile</i> (Enzyme Modified)</p> 	<p>Increases blood flow for varicose veins, and possible use for arterial flow as well. Recent studies have shown possibilities in increased brain functions and it might be useful in the treatment of progressive Alzheimer's disease.</p>	<p>Hiroyuki et al., (2003)⁴⁸</p>
16	<p>Licorice or Glycyrrhizic acid</p> 	<p>Licorice has been used as early as Roman and Greek times as a decongestant, anti-inflammatory, to treat stomach ulcers..</p>	<p>Stormer et al.,(1993)⁴⁹</p>
17	<p>Lignan from rye , soybean and brocaoli</p> 	<p>Lignans are one of the two major classes of phytoestrogens. Phytoestrogens are antioxidants and have been viewed as reducing ill effects in the body as cellular destruction, aging, etc.</p>	<p>Prasad et al., (2005)⁵⁰</p>
18	<p>Lutein and Lutein Esters from marigold</p> 	<p>Extracted from marigold seeds, and also found in spinach, rosemary and kale, it is a carotenoid which shows healthful eye benefits.</p>	<p>Berendschot et al., (2000)⁵¹</p>
19	<p>Nattokinase</p>	<p>Natto is fermented soybeans. Nattokinase is the enzyme produced by <i>Bacillus natto</i> used in the fermentation.</p>	<p>Chang et al., (2008)⁵²</p>
20	<p>Olive Oil from <i>Olea europaea</i></p>	<p>Olive oil is high in monounsaturated fat and is a healthy oil in maintaining good cholesterol levels.</p>	<p>Machowetz et al., (2007)⁵³</p>

21	<p>Omega 3 Fatty Acids from <i>Linum usitatissimum</i></p>  <p>Alpha-Linolenic Acid (omega-3)</p>	<p>Among other positive effects (see rest of chart), omega 3 fatty acids have been associated with positive eye health.</p>	<p>Holman , (1998) ⁵⁴</p>
22	<p>Phloretin isolated from apple leaves</p> 	<p>Obtained from the decomposition of phloridzin and used in the treatment of malaria as a quinine replacer. Studies have shown it inhibits protein kinase C and effects the sodium/potassium transfer across membranes.</p>	<p>MacDonald et al., (1952) ⁵⁵</p>
23	<p>Phytosterol obtained from germinated corn</p> 	<p>Chemicals found naturally in foods that have the ability to lower cholesterol absorption in the digestive tract thereby lowering overall cholesterol levels in the bloodstream.</p>	<p>St-Onge et al.,(2003) ⁵⁶</p>
24	<p>Proanthocyanins from grapes</p> 	<p>Help with urinary tract infections by inhibiting adhesion of microorganisms like e. coli to the urinary tract wall.</p>	<p>Busse-Valverde (2011) ⁵⁷</p>
25	<p>Resveratrol especially high in grape skin</p> 	<p>anti-inflammatory, inhibits COX-1 enzyme, blocks adhesion of blood cells to vessel walls shown to reduce skin and breast cancer</p>	<p>Gehm et al., (1997) ⁵⁸</p>
26	<p>Tall oil: Derived phytosterols</p>	<p>Has been seen to reduce arteriosclerosis, and plasma cholesterol in rodents.</p>	<p>Graaf et al.,(2002) ⁵⁹</p>

27. Zeaxanthin



A carotenoid used as an antioxidant. Zeaxanthin is the coloring agent in marigolds and is extracted from them. It is used for eye health and some claim will retard the effect of 'aging eyesight' or Age-Related Macular Degeneration (AMD).

Toyoda,
(2002)³³

Recently, much attention has been given to phytochemicals that possess cancer-preventive properties^{19,31,32}. 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 have anti-cancerous properties by acting as antioxidants. They are found in citrus fruits, soyfoods which are unique dietary source of isoflavones, green tea rich in epigallocatechin gallate and *curcuma longa* rich in curcumin^{18,22,24}. The main soybean isoflavones, genistein, daidzein, biochanin inhibits prostate cancer cell growth. Carotenoids and lycopenes are also important chemicals for human health. Because of the unsaturated nature of lycopene it is considered to be a potent antioxidant and a reactive oxygen species (ROS) quencher. Recently, it was reported that fruits and vegetables containing lycopene exert cancer-protective effect via a decrease in oxidative and other damage to DNA in humans. Among the carotenes, beta carotene is the most active as antioxidants. β - Carotene is the more common form and can be found in yellow, orange, and green leafy fruits and vegetables⁶⁰. These can be carrots, spinach,

lettuce, tomatoes, sweet potatoes, broccoli, cantaloupe, oranges, and winter squash. Another phytochemical Tannins also called proanthocyanidins, detoxify carcinogens and scavenge harmful free radicals. Ellagic acid is a proven anti-carcinogen is used in alternative medicine and to prevent cancer⁴¹. It is present in strawberries, cranberries, walnuts, pecans, pomegranates and the best source is red raspberry seeds.

7. **Prebiotics:** Prebiotics are the substances, which reach to colon in intact form i.e. without getting depleted by the gastric pH and digestive acids. These prebiotics also selectively promote the growth of colonel probiotic bacteria; hence they act as fertilizers for these bacteria. These are collective term for non-digestive but a fermentable dietary carbohydrate that may selectively stimulates growth of certain bacterial groups resident in the colon, such as *Bifidobacteria*, *Lactobacilli* considered to be beneficial for the human host⁶¹. The prebiotic inulin, which is soluble dietary fibers and resistant to digestive enzyme therefore reaches to large intestine or colon essentially intact, where it is fermented by resistant bacteria, *Lactobacilli*⁶².
8. **Probiotics:** It is a substance that contains microorganisms or bacteria that are beneficial to the host organism it can be plant or animal. It is a term commonly used for "Friendly bacteria". Digestive microbes come from



uncooked fruits, vegetables, and fermented products that we eat. There are about 400 different bacteria living in the human GI tract, among them *Lactobacillus acidophilus* is one of the major component of the probiotic fighter⁶³. It enhances the immune system. *Lactobacillus acidophilus* can reduce the incidence of vaginal infections including thrush and bacterial vaginosis. *Bifidobacteria* and *Streptococcus thermophilus* both found in yoghurt can prevent young children suffering from diarrhoea also in treating travelers diarrhoea and rotavirus infection. There are plant based probiotics also available in the market such as Soy-Based Probiotics American Health, Ronkonkoma, NY, has extended its line of probiotic formulas with the introduction of two new Liquid Soy-Based *Acidophilus* supplements. Probiotics only have a transient effect and regular daily intake is needed to bring about health benefits⁶⁴. There are large numbers of benefits of using probiotics as nutraceuticals. Some of these benefits include: enhancing bowel function, prevention of colon cancer, lowering cholesterol, lowering of blood pressure, improving immune function, reducing infections, reducing inflammation, improving mineral absorption, preventing growth of harmful bacteria, fighting off diseases like candida and eczema, and many more. As these "friendly bacteria" are beneficial for humans similarly there are large number of soil bacteria which act as probiotics for plants. They are helpful in promoting the growth, health and yield of crops.

NUTRACEUTICALS AND THEIR CHEMICAL NATURE:

Nutraceuticals is a very broad term which includes a variety of substances/compounds ranging from essential metals, large polymers up to bacteria. Chemical nature of nutraceutical depends upon their structure and function. The chemical characteristics can be

used for grouping nutraceuticals based upon their chemical nature. This approach allows nutraceuticals to be categorized under different molecular/elemental groups and sub groups. For example (1) Amino acid-based substances: aminoacids, ally-S compounds, indole, folate and choline (2) Carbohydrates and derivatives: ascorbic acid, oligosaccharides, nonstarch-polysaccharides (3) Fatty acids and structural lipids: lecithin, fattyacids, oil (4) Isoprenoid derivatives: carotenoids, saponins, tocopherols, simple terpenes (5) Phenolic substances: coumarins, tannins, lignin, anthocyanins, isoflavones, flavones, flavonols (6) Microbes: probiotics, prebiotics(7) Minerals: calcium , selenium, potassium, copper, zinc etc.

NEUTRACEUTICAL FOOD TECHNOLOGY:

Nutraceutical food technology or industry places special emphasis on quality control and in this proper inspections are conducted throughout the manufacturing process, including raw material verification, homogeneity testing, weight deviation measurements and package quality sampling^{2,3,4,11,15,65}. Botanicals can be fractionated to produce a natural color fraction, an aroma fraction, an anti-oxidant fraction and/or a flavor fraction. This is important in producing nutraceuticals because unwanted strong flavors in certain botanicals such as garlic and rosemary can be separated from the nutraceutical components. Supercritical fluid technology will allow nutraceutical companies to develop products of standardized concentration of active ingredients, and will simultaneously produce nutraceutical products of much higher concentration (higher yields and purity) and quality (with less creation of artifacts), than possible by conventional chemical engineering unit operations, such as liquid/liquid extraction, distillation, mechanical micronization, liquid and/or gas phase



reactions, etc. Special food preparations are required to meet the needs of children, lactating mothers and elderly people such as nutritious biscuits/laddoos for children, lactating mother. This kind of preparation should be based on the following and suitable additional materials: wheat, gram and soybean flours, Sesamum, Amaranth seeds, spinach leaves, jaggary etc. The molecular diagnostics may play a key role in food safety related to genetically modified foods, food-borne pathogens and novel nutraceuticals^{65,66}. The DNA microarray technology offers a new dimension of strength in molecular diagnostics by permitting the simultaneous analysis of large sets of genes in the food constituents^{67,68,69}.

ROLE OF BIOTECHNOLOGY IN NUTRACEUTICALS DEVELOPMENT:

Biotechnology has a key role to play in this new area of the food industry focused on the major energy-providing foods. More recently, there has been increased interest in biologically active non-nutritive ingredients (or components) from natural products or foods. Major breakthroughs have occurred and enormous progress has been made during the past decade in all aspects of biotechnological nutraceutical development^{15,17}. It has been given high priority by researchers in the production of probiotics and the extraction of bioactive components by enzyme/fermentation technology as well as genetic engineering technology⁵³. Changing values in society, for instance with respect to recombinant DNA, and the growing need to explore all the alternative food sources has made the use of this technique in the production of enzymes and of recombinant microorganisms attractive to the food industry. Some of the benefits include increased enzyme or metabolite production from recombinant microorganisms, improvement of thermostability of these metabolites and enzymes and their ability to tolerate large pH ranges. Genetic engineering has made it possible to isolate

particular genes coding for enzymes or other metabolites of our interest, from organisms of unknown genetics. Using *in vitro* recombination, these genes can be introduced into microorganisms there by getting the desired gene products at a low cost. Genetic engineering methods provide the opportunity to increase gene expression and so affect product yield⁴⁵. For example, it is widely believed that omega-3 fatty acids are beneficial against cardiovascular disease. To-day there are sources of omega-3 fatty acids available to the consumer such as some fish, flax seed and some vegetable oils. Using biotechnology it may be possible in the future to produce a vegetable oil that has ten or twenty times the amount of omega-3 fatty acids compared to present day oils. Such an oil would obviously be very useful to include in the diet of patients prone to heart disease. Conventional plant-breeding methods can also improve nutraceutical quality and production by enhancing both agronomic and medicinal traits. *In vitro* propagation or tissue culture of plants holds tremendous potential for the production of high-quality plant-based medicines. This can be achieved through different methods including micropropagation and somaclonal variant production. Besides these, Nutritional genomics is a recent off-shoot of this genetic revolution in the area of nutraceutical development which includes (1) nutrigenomics: the study of interaction of dietary components with the genome and the resulting proteomic and metabolomic changes; and (2) nutrigenetics: understanding the gene-based differences in response to dietary components and developing nutraceuticals that are most compatible with health based on individual genetic makeup^{15,17}. There are several biotechnology companies involved in investigating and developing nutraceutical products mainly belong to the food (55%) and pharmaceutical (35%) industries through different biotechnological approaches. Developments in plant biotechnology has created a number of results such as various new



cultivars either by traditional crossing or transgenic breeding^{67,68,69}. Super-rice that exhibits high yields has been invented by Chinese scientists, Golden Rice with high levels of the pro-vitamin A carotenoid⁶⁰, beta-carotene, was invented by Swiss and German scientists, and many other crops have been invented with improved agricultural and nutritional traits^{21,67, 70-75}. Thus advances in tissue culture, combined with improvement in genetic engineering, specifically transformation technology, cell culture methodologies for selective metabolite production, has opened new avenues for high volume production of nutraceuticals.

PLANT DERIVED-NUTRACEUTICALS AND MARKET:

The Nutraceutical industry is still in its formative period, and at present, there is no universal agreement or legal definitions of the terms and designations used by this industry sector. According to the widely accepted definition, "A Nutraceutical is any substance that is a food or a part of a food and provides medical or health benefits including the prevention and treatment of disease." Products include isolated nutrients, dietary supplements and processed foods such as cereals, soups, soyfood, and beverages⁷⁶. The Nutraceutical market is becoming more competitive with the entry of pharmaceutical and major food companies into the Nutraceutical arena. Also, many food companies have established their Nutraceutical divisions with a view towards a diversified product line. Pharmaceutical companies have also joined the race by acquiring dietary supplement producers. Recent years have marked the entry of major food and pharmaceutical companies into the Nutraceutical marketplace, including Kellogg, Heinz, M&M, Quaker Oats, Unilever, Cargill, Hormel, Glaxo-SmithKline, Warner-Lambert, Johnson & Johnson and Wyeth. The nutraceuticals market is highly competitive and is driven by several factors such as price, safety, efficacy, packaging and brand loyalty, among

each others^{77,78}. The global Nutraceutical market at the retail level estimated at approximately \$176.7 billion in 2013 with compounded annual growth rate of 7.4%. It is projected to exceed US\$243 billion by 2015, owing to consumer desire for leading a healthy life and increasing scientific evidence supporting health foods. The United States, Europe and Japan dominate the global market, accounting for a combined market share of more than 85%. India being rich in biodiversity can come up as one of the leading countries in the production of plant based nutraceuticals. According to Frost & Sullivan-FICCI, the Indian nutraceuticals market is expected to grow at the rate of 16 percent year-on-year for the next five years, reaching roughly US\$5 billion^{76,79}.

CONCLUSIONS

Plant derived nutraceuticals are of great importance in present system of Medicine and Healthcare. The lack of quality control is a major area of concern for nutraceuticals. The quality of plant material and manufacturing processes used for nutraceuticals are regulated by food laws, which lack the specificity required for botanical drugs. This can have serious consequences. Nutraceutical professionals and regulatory bodies need to play a major role for safety maintenance and advances of nutraceuticals. Future demand of nutraceutical depends upon consumer perception of mankind and the relationship between diet and disease. Although nutraceuticals and functional food have significant role in the promotion and care of human health to prevent diseases, the health professionals, nutritionists, biotechnologists, regulatory toxicologist and nutraceutical industrialist should strategically work together to plan appropriate regulation to provide the ultimate health and therapeutic benefits to mankind with purity, efficacy, and safety.



REFERENCES

1. DeFelice SL. FIM, Rationale and Proposed Guidelines for the Nutraceutical Research & Education Act NREA, Foundation for Innovation in Medicine. Available at: <http://www.fimdefelice.org/archives/arc.research.html>, November 10 (2002).
2. Allen LV., Nutritional products, *In: Covington TR, Berardi RR, Young LL, Kendall SC, Hickey MJ, editors. Handbook of Nonprescription Drugs. Washington DC: American Pharmaceutical Association (1997).*
3. Kasbia GS., Functional foods and nutraceuticals in the management of obesity. *Nutrition and Food Science*, 35 : 344-351,(2005)
4. Brower V., Nutraceuticals: poised for a healthy slice of the healthcare market? *Nat Biotechnol.*, 16 : 728-731(1998).
5. Elizabeth AC., Over-the-counter products: nonprescription medications, nutraceuticals, and herbal agents. *Clin Obstet Gynecol.*, 45(1):89-98 (2002) .
6. Whitman M., Understanding the perceived need for complementary and alternative nutraceuticals: lifestyle issues. *Clin J Oncol Nurs.*, 5:190-194 (2001).
7. Adom KK, Liu RH. Antioxidant activity of grains. *J Agric Food Chem.*, 50: 6182-6187 (2002).
8. Alasalvar C, Shahidi F, Quantick P. Food and health applications of marine nutraceuticals: a review. *In: Alasalvar C, Taylor D, editors. Seafoods-Quality, technology and nutraceutical applications. New York: Springer-Verlag. (2002) PP 175-204.*
9. Halliwell B., Antioxidants in human health and disease. *Ann Rev Nutr*, 16: 33-50 (1996).
10. Bickford PC, Tan J, Shytle RD, Sanberg CD, El-Badri N, Sanberg PR., Nutraceuticals synergistically promote proliferation of human stem cells. *Stem Cells Dev.*, 15:118-23 (2006).
11. Devi V.K. and Rehman F., Nutraceutical antioxidants-An overview, *Indian journal of pharmaceutical education*,.36 (1):3-8 (2002).
12. Sagar B.P.S., Zafar R., Tyagi K., Kumar V., Kumar S. and Panwar R., 'Antioxidants', *The Indian Pharmacist*, 29-35 (2004) .
13. Frasher P.D. Phytosterols as functional food components and nutraceuticals, *Phytochemistry*, .67: 212-214 (2006) .
14. Nordvisk E, Salomonsson AC, Aman P., Distribution of insoluble bound phenolic acids in barley grains. *J Sci Food Agric*, 35: 657-661 (1984).
15. Tucker G., Nutritional enhancement of plants. *Current Opinion in Biotechnology*, 14: 221-225 (2003).
16. Sirtori C R and Galli C., Fatty acids and the Omega3. *Biomedecine and Pharmacotherapy*. 56: 397-406 (2002).
17. Ravi Subbiah M. T., Nutrigenetics and nutraceuticals: the next wave riding on personalized medicine. *Translational Research*. 149: 55-61 (2007).
18. Inti M and Faoro F., Grape phytochemicals: a bouquet of old and new nutraceuticals for human health *Medical Hypotheses.*, 67: 833-838 (2006) .
19. Shukla Y and Singh M., Cancer preventive properties of ginger: a brief review. *Food and Chemical Toxicology*, 45: 683-690 (2007).
20. Hamid AA and Luan YS., Functional properties of dietary fiber prepared from defatted rice bran. *Food Chemistry*, 68: 15-19 (2000).
21. Mermel VI., Old paths new directions: use of functional foods in the treatment of obesity. *Trends in Food Science and*



- Technology, 15: 532-540 (2004).
22. Dulloo AG, Duret C and Rohrer D., Efficacy of a green tea extract rich in catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans. *Am J Clin Nutr.*, 70: 1040-1045 (1999).
 23. Bell SJ and Goodrick GK., A Functional Food Product for the Management of Weight Critical Reviews in Food Science and Nutrition, 42: 163-178 (2002).
 24. Brouns F., Soya isoflavones: a new and promising ingredient for the health foods sector. *Food Research International*, 35: 187-193 (2002).
 25. Sirtori CR and Galli C., Fatty acids and the Omega 3. *Biomedicine and Pharmacotherapy*, 56: 397-406 (2002).
 26. Bland JS., Phytonutrition, phytotherapy, and phytopharmacology. *Altern Ther Health Med.*, 2:73-76 (1996) .
 27. Berger MM, Shenkin A., Vitamins and trace elements: Practical aspects of supplementation. *Nutrition*, 22:952-55 (2006).
 28. Bagchi D., Nutraceuticals and functional foods regulations in the United States and around the world. *Toxicol*, 221:1-3 (2006).
 29. Ramaa CS, Shirode AR, Mundada AS, and Kadam VJ., Nutra-ceuticals-an emerging era in the treatment and prevention of cardiovascular diseases. *Curr Pharm Biotechnol*, 7:15-23(2006). .
 30. Whitman M., Understanding the perceived need for complementary and alternative nutraceuticals: lifestyle issues. *Clin J Oncol Nurs*, 5: 190-94 (2001).
 31. Burney PG, Comstock GW, Morris JS., Serologic precursors of cancer: serum micronutrients and the subsequent risk of pancreatic cancer. *Am J Clin Nutr*, 49:895-900 (1989).
 32. Clark LC, Combs Jr GF, Turnbull BW, Slate EH, Chalker DK, Chow J., Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin. A randomized controlled trial. Nutritional Prevention of Cancer Study Group. *JAMA*, 276:1957-63 (1996).
 33. Toyoda Y, Thomson LR, Effect of dietary zeaxanthin on tissue distribution of zeaxanthin and lutein in quail. *Invest Ophthalmol Vis Sci.*, 43(4):1210-21 (2002).
 34. Weststrate, J. A. & Meijer, G. W. Plant sterol-enriched margarines and reduction of plasma total- and LDL-cholesterol concentrations in normocholesterolaemic and mildly hypercholesterolaemic subjects. *Eur. J. Clin. Nutr.*, 52:334-343(1998)
 35. Eric Block, The chemistry of garlic and onions. *Scientific American* , 252 : 114–9 (1985).
 36. Pulliainen, K., Nevalainen, H., Vakevainen, H., Jutila, K. and Gummer, C. L., An analytical method for the determination of betaine (trimethylglycine) from hair. *International Journal of Cosmetic Science*, 32: 135–138 (2010).
 37. Rabelo, A. P. B.; Tambourgi, E. B. and Pessoa Jr., A., Bromelain partitioning in two-phase aqueous systems containing PEO-PPO-PEO block copolymers. *Journal of Chromatography B*, 807(1), 61-68(2004).
 38. Chen, P.F., Chang, S.T., Wu, H.H., Antimite activity of essential oils and their components from *Cinnamomum osmophloeum*. *Quart. J.Chin. For.* 35, 397–404 (2002).
 39. Dray A., Mechanism of action of capsaicin-like molecules on sensory neurons. *Life Sci.*, 51 (23): 1759–65 (1992).
 40. Steiber A, Kerner J, Hoppel C., Carnitine: a nutritional, biosynthetic, and functional perspective. *Mol. Aspects Med.* 25 (5-6): 455–73 (2004).
 41. Vattem D. A. and K. Shetty, Biological Function of Ellagic Acid: A Review. *Journal of Food Biochemistry* 29 (3): 234–266 (2005).



42. Okui S, Uchiyama M, Mizugaki M., Metabolism of hydroxy fatty acids. II. Intermediates of the oxidative breakdown of ricinoleic acid by genus *Candida*. *J. Biochem.* 54: 536–540 (1963).
43. Taubert, Dirk; Renate Roesen, Clara Lehmann, Norma Jung, Edgar Schömig, "Effects of Low Habitual Cocoa Intake on Blood Pressure and Bioactive Nitric Oxide". *The Journal of the American Medical Association* 298 (1): 49–60 (2007).
44. Ram S. Mohan, Andrew M. Anderson, and Matthew S. Mitchell. "Isolation of Curcumin from Tumeric" *Journal of Chemical Education* 77 (3): 359-360 (2000).
45. Mullineaux, P., and Creissen, G., Opportunities for the genetic manipulation of antioxidants in plant foods. *Biochem. Soc. Trans.* 24:829-835(1996).
46. Chauhan J.S., S.K. Srivastava and M. Sultan, Hesperetin 7-rhamnoside from *Cordia obliqua*. *Phytochemistry*, 17, (2), 334-335(1978).
47. Lee, K. H., and Lee, B. M., Evaluation of the genotoxicity of (–)-hydroxycitric acid (HCA-SX) isolated from *Garcinia cambogia*. *J. Toxicol. Environ. Health*, 70 (5):388–392 (2007).
48. Hiroyuki S., Yoshinori H., Satoshi N., Hitoshi A., Kazuki K., Simultaneous determination of all polyphenols in vegetables, fruits, and teas *Journal of Agricultural and Food Chemistry* 51, (3): 571-581(2003).
49. Stormer, FC; Reistad R, Alexander J., Glycyrrhizic acid in liquorice - evaluation of health hazard. *Food Chem Toxicol* 31 (4): 303–12 (1993).
50. Prasad K., Hypocholesterolemic and antiatherosclerotic effect of flax lignan complex isolated from flaxseed. *Atherosclerosis*.179:269–275(2005).
51. Berendschot TT, Goldbohm RA, Klöpping WA, van de Kraats J, van Norel J, van Norren D ,Influence of lutein supplementation on macular pigment, assessed with two objective techniques. *Invest. Ophthalmol. Vis. Sci.*, 41 (11): 3322–6 (2000)..
52. Chang YY, Liu JS, Lai SL, Wu HS, Lan MY., Cerebellar hemorrhage provoked by combined use of nattokinase and aspirin in a patient with cerebral microbleeds". *Intern. Med.* 47 (5): 467–9 (2008).
53. Machowetz, A., Poulsen, H.E., Gruendel, S., Weimann, A., Fitz, M., Marrugat, J., Effect of olive oils on biomarkers of oxidative DNA stress in Northern and Southern Europeans. *FASEB J.*, 21: 45-52 (2007).
54. Holman RT., The slow discovery of the importance of omega 3 essential fatty acids in human health". *J. Nutr.*, 128 (2): 427S–433S (1998).
55. MacDonald, R. E. and Bishop, C. J., Phloretin: An antibacterial substance obtained from apple leaves. *Canadian Journal of Botany*, 30: 486-89 (1952).
56. St-Onge, Marie-Pierre; Lamarche, Benoit; Mauger, Jean-Francois; Jones, Peter J. H; Marie-Pierre St-Onge, Benoit Lamarche, Jean-Francois Mauger, Peter J. H. Jones. Consumption of a Functional Oil Rich in Phytosterols and Medium-Chain Triglyceride Oil Improves Plasma Lipid profiles in Men. *Journal of Nutrition*, 133 (6): 1815–1820 (2003).
57. Naiara B-Valverde, Encarna G-Plaza, Jose M. L-Roca, Rocio G-Muoz, and Ana B. Bautista-Ortn, The Extraction of Anthocyanins and Proanthocyanidins from Grapes to Wine during Fermentative Maceration Is Affected by the Enological Technique. *J. Agric. Food Chem.*, 59 (10), 5450–5455 (2011).
58. Gehm BD, McAndrews JM, Chien PY and Jameson JL, Resveratrol, a polyphenolic compound found in grapes and wine, is an agonist for the estrogen receptor". *Proceedings of the National Academy of*



- Sciences of the United States of America, 94 (25): 14138–43 (1997).
59. De Graaf J, De Sauvage Nolting PR, Van Dam M, Belsey EM, Kastelein JJ, Haydn Pritchard P and Stalenhoef AF, Consumption of tall oil-derived phytosterols in a chocolate matrix significantly decreases plasma total and low-density lipoprotein-cholesterol levels. *Br J Nutr.* (5):479-88 (2002).
60. Ye X, Al-Babili S, and Kloti A, Engineering the provitamin A (beta-carotene) biosynthetic pathway into (carotenoid-free) rice endosperm. *Science*, 287:303-5 (2000).
61. Gibson GR, Roberfroid MB. Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics. *J Nutr.*, 125(6):1401-12 (1995).
62. Peppelenbosch MP, Ferreira CV. Immunology of pre- and probiotic supplementation. *Br J Nutr* 101:2-4 (2009).
63. Hamilton-Miller, Professor J. M. T.; G. R. Gibson, W. Bruck. "Some insights into the derivation and early uses of the word 'probiotic'". *British Journal of Nutrition*, 90: 845(2003).
64. Hamilton-Miller JM The role of probiotics in the treatment and prevention of *Helicobacter pylori* infection. *International Journal of Antimicrobial Agents* 22 (4): 360–6 (2003).
65. Wildman, Robert E. C., ed. *Handbook of Nutraceuticals and Functional Foods* (1st ed.). CRC Series in Modern Nutrition. ISBN 0-8493-8734-5 (2001).
66. Zeisel SH. Regulation of "Nutraceuticals." *Science*, 285:185-186 (1999).
67. Ernst E. Functional foods, nutraceuticals, designer foods: innocent fad or counterproductive marketing ploy. *Eur J Clin Pharmacol* 57:353-5 (2001).
68. Hathcock J. Dietary supplements: How they are used and regulated. *J.Nutrition*, 131:1114-7 (2001).
69. Andlauer W, Furst P., Nutraceuticals: a piece of history, present status and outlook. *Food Research International* 35:171-6 (2002).
70. Thomas B, Ghebremeskel K, Lowy C, Crawford M and Bridget Offley-Shore R N Nutrient intake of women with and without gestational diabetes with a specific focus on fatty acids. *Nutrition*, 22: 230-236 (2006).
71. Grusak MA, DellaPenna D. Improving the nutrient composition of plants to enhance human nutrition and health. *Annu Rev Plant Physiol Plant Mol Biol*, 50:133-61(1999).
72. Baima, S., Plant genomics and plant breeding: at the root of human nutrition and health. *Curr Top Nutra Res*, 3(2): 95-112 (2005).
73. Acharya, S.N., J.E. Thomas and S.K. Basu, Methods for the improvement of plant medicinal properties, with particular reference to fenugreek (*Trigonella foenum-graecum* L.), In: *Advances in Medicinal Plant Research* (2007) pp: 491-512.
74. Belem, M.A.F., Application of biotechnology in the product development of nutraceuticals in Canada. *Trends Food Sci & Technol*, 10(3): 101-106 (1999).
75. Schilter B, Andersson C, Anton R, et al. Guidance for the safety assessment of botanicals and botanical preparations for use in food and food supplements. *Food Chem Toxicol* 41:1625- 49 (2003).
76. Ahmad, M.F., Ashraf S.A., Ahmad F.A., Ansari J.K., and Siddiquee M.R.A., Nutraceutical markets and its regulation., *Am. J. Food Technol.*, 6, 342-347 (2011).
77. Kroes R, Walker R. Safety issues of botanicals and botanical preparations in functional foods. *Toxicol* 198:213-220 (2004).
78. Taylor CL. Regulatory frameworks for functional foods and dietary supplements. *Nutr Rev.*, 62 : 55-9 (2004).
79. Kaushik D., Kaushik N., Nutraceuticals Regulation In India, *Pharma info.net*, 7:45-46 (2009).