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## A review on nutraceuticals

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### Abstract

Nutraceuticals, functional foods and dietary supplements are getting universally accepted as people are understanding health and its necessity to lead or fit into this fast life. The other reasons being these products safe compared to medicines, deleterious effects of medicine and mostly health consciousness. The wheel of time having gone a full circle, today the important role of diet in disease prevention is being increasingly realised in current scientific thinking as well that also played a role in triggering the world's belief in this. Therefore Nutraceuticals entirely helps in providing the necessary nutrients and are taken or prescribed based on requirements. The sources might be chemical, herbal extracts, phytoconstituents – traditional or non-traditional type or from minerals.

**Keywords:** Nutraceuticals, phytochemicals, herbals, vitamins, minerals, diet, diseases, functional foods, dietary supplements

### Introduction

Ayurveda places special emphasis on ahara (diet) and anna (food) and believes that healthy nutrition nourishes the mind, body and soul [4]. An ancient Siddha medicine dictum “*Unave marundhu, marundhe unavu*” which means food as medicine, medicine as food, well reinforces the importance of diet for disease free living. Hippocrates (460-377 BC), the well-recognized father of modern medicine, stated "Let food be thy medicine and medicine be thy food", to predict the relationship between appropriate foods and health and their therapeutic benefits. The ancient wisdom of our country seems to be lost in the folds of history with the adoption of modern medical system as the more superior health care provider for most of our populace. The lifestyle patterns, food choices, consumer items has changed a lot which resulted in the abandonment of traditional diet patterns meticulously developed over the ages. The wheel of time having gone a full circle, today the important role of diet in disease prevention is being increasingly realised in current scientific thinking. This is partly triggered by a global pandemic of lifestyle disorders, chiefly linked to excess/improper/reckless eating patterns in addition to other factors such as sedentary lifestyle, industrial age, increasing work, living speed, longer work schedules, and various psychological pressures, which have led to an increased incidence of diabetes, obesity, various cancers and vascular diseases and other stress filled work habits [1].

On one side is the epidemic of obesity–diabetes. On the other side are outbreaks of foodborne illness, food contamination scares, volatile food prices, and “food deserts,” not to mention drought and water shortages, soil depletion, climate change, fishery collapse and other events with significant—albeit less direct—impacts on nutrition and health. Clearly, both food and health systems are under stress [5].

Research activities of nutritionists and food scientists have historically run parallel to those of phytochemists, pharmacognosists and natural product chemists. While vitamins, minerals, amino acids, carbohydrates and lipids are compounds of primary interests to food chemists, natural product chemistry focuses on compounds as potential sources of new pharmaceuticals and other industrial chemicals. An overlap interests of food chemists and pharmacognosist resulted in the recognition that alkaloids, saponins, polyphenolics and other compounds have positive and complex roles in the physiological processes affecting human health. The people have turned their focus on examining food intensively for added physiological benefits which may reduce chronic disease risk or otherwise optimise health [1].

Such a global awakening coupled with an ageing health conscious population, changes in food regulations, numerous technological advances and a marketplace ripe for introduction of health promoting products, coalesced to create a trend for a category of products referred to as health foods, phytomedicines, dietary supplements, nutraceuticals, functional foods, fortified foods and organic foods [1].

**Definitions**

Health foods or functional foods have no universally accepted definition.

**Functional foods:** Functional foods are those whole, fortified, enriched or enhanced foods that provide health benefits beyond provision of essential nutrients such as vitamins and minerals [1].

**Nutraceutical:** Nutraceutical is a term used interchangeably with functional food. It refers to those diet supplements that deliver a concentrated form of a presumed bioactive agent from a food, presented in a non-food matrix and used to enhance health in dosages that exceed those that could be obtained from normal food [1].

**Dietary supplements:** Dietary supplements are defined as any product that is intended to supplement the diet and contains one or more of the following: vitamins, minerals, herbs or other botanicals, amino acids and other dietary substances intended to supplement the diet by increasing the total dietary intake or as any concentrate, metabolite, constituent, extract or combination of these ingredients. The term dietary supplement means products intended for ingestion in a form (tablet, capsule, powder, soft gel, Gel cap and liquid) that is not represented as conventional food or as the sole item of a meal or of diet and that are labelled as dietary supplements [1].

**Categories of nutraceuticals**

These are categorized on the basis of food available in the market.

1. Traditional nutraceuticals
2. Non-Traditional nutraceuticals

**Traditional nutraceuticals**

These are the foods as such without any manipulations or manual changes or chemical changes. The components which are present in these are natural and have some potential which are actively involved in health benefits. Nutraceuticals are grouped on the basis of

**Chemical constituents**

- a) Nutrients: Vitamins, minerals, amino acids, fatty acids
- b) Herbals
- c) Phytochemicals

**Probiotics and prebiotics micro organisms****Nutraceutical enzymes****Chemical constituents****a) Nutrients**

Nutrients are substances that are essential for the maintenance of life and for growth. Most common nutrients used as nutraceuticals are vitamins, minerals, herbals or phytochemicals.

**Health Benefits of Certain Common Nutrients**

**Vitamins:** Vitamins are a group of organic compounds which are essential in very small amounts for the normal functioning of the body. Thirteen vitamins are recognized in human nutrition and these have been classified according to their solubility into two groups:- Fat soluble and Water soluble vitamins [2]

**Fat Soluble Vitamins [6]****Table 1:** Fat Soluble Vitamins [6]

Vitamins	Natural Sources	Health Benefits
VIT A - Retinol, Retinal, Retinoic acid	Milk, eggs, liver, in form of carotenes – carrot, beetroot, leafy vegetables	Antioxidant, essential for growth, development and in the treatment of certain skin disorders, responsible to prevent keratin synthesis, Vision.
VIT D -Cholecalciferol (D3)	Sunlight, fortified milk, eggs, liver	Essential for formation of bones and teeth, help the body to absorb and use calcium. Dark skin pigment (melanin) adversely influences the synthesis of cholecalciferol.
VIT E - Tocopherol	Vegetable nut oil, Amla, Almonds, Hazel nuts, Peanuts, Spinach, Broccoli	Membrane antioxidant, protects RBC from haemolysis by oxidizing agents, prevents sterility, preserves and maintains germinal epithelium of gonads, required for proper storage of creatine in skeletal muscle, liver protective from CCl4.
VIT K – Phylloquinone (K1), Menaquinone (K2), Menadione (K3)	K1 - Plant source K2 - Intestinal bacteria of animals K3 – Synthetic form Green leafy vegetables – collards, green leaf lettuce, kale, spinach, swiss chard, turnip greens. Vegetables like broccoli, brussels, sprouts, cabbage	Clotting vitamin - It is required for the carboxylation of glutamic acid and residues of osteocalcin and the matrix <i>Gla</i> ( <i>Gamma carboxy glutamic acid</i> ) protein in bone and nephrocalcin in kidney

**Table 2:** Water Soluble Vitamins [6]

Vitamins	Natural Sources	Health Benefits
VIT C – Ascorbic acid (anti – scurvy factor)	Amla, Citrus fruits, tomatoes, watermelons, berries, green and red peppers, broccoli, potatoes, kiwi, strawberries, cantaloupes	<ul style="list-style-type: none"> <li>• Acts as antioxidant necessary for healthy bones, gums, teeth and skin</li> <li>• Used to prevent and treat the disease scurvy</li> </ul>
VIT B1 – Thiamin (anti-beriberi factor)	Husk of paddy, Sunflower seeds, black beans, green peas, lentils, sweet potatoes, pork, liver, heart, kidney, milk	Helps in carbohydrate metabolism, essential for neurological function
VIT B2 – Riboflavin	Whole grains, green leafy vegetables, organ meats, milk and milk products, eggs, fish	Responsible for energy production, regulation of thyroid activity, prevention of skin diseases and rheumatoid arthritis, helps in

(anti-cheilosis, anti-glossitis, anti – dermatitis factor)		metabolism, maintains good vision, used in the treatment of numbness, multiple sclerosis, Alzheimer’s disease, epilepsy and anxiety.
VIT B3 – Niacin (pellagra preventive factor)	Found in liver, kidney, heart, yeasts, whole grains, peanuts, amino acid tryptophan can supply niacin (60mg of Tryptophan =1mg niacin)	<ul style="list-style-type: none"> <li>• Inhibits lipolysis in the adipose tissue and decreases the circulatory free fatty acids</li> <li>• Triacylglycerol synthesis in the liver decreases</li> <li>• The serum levels of LDL, VLDL and cholesterol are lowered. Hence Niacin is used in the treatment of hyperlipoproteinemia type II B</li> </ul>
VIT B4 – Adenine and Choline <sup>[7]</sup>	<ul style="list-style-type: none"> <li>• Choline is made by the body but only in small quantities. Adenine is an essential purine nucleobases of the nucleic acids RNA and DNA.</li> <li>• Food sources- such as whole grains, vegetables, fruits, raw honey, and any cereal that contain complex carbs.</li> <li>• From several herbs - ginger, blue cohosh, cloves, catnip, <i>Cascara sagrada</i>, capsicum.</li> </ul>	<ul style="list-style-type: none"> <li>• It prevents building up of fats in liver, improves the process of cell formation and cell growth, has an important role for the assimilation of other B-complex vitamins, prevent muscle weakness.</li> <li>• Boosts the immune system to fight off all sorts of infections and diseases.</li> </ul>
VIT B5 – Pantothenic acid	Egg yolk, liver, yeast, kidney, lean meat, skimmed milk, sweet potatoes and molasses	<ul style="list-style-type: none"> <li>• Functions of B5 are exerted through coenzyme A or CoA which is a central molecule involved in all the metabolisms (carbohydrate, lipid and protein)</li> <li>• Aids in synthesis of cholesterol, steroids and fatty acids</li> </ul>
VIT B6 – Pyridoxine	Fish, egg yolk, meat, whole milk, milk powder, whole cereals, legumes and green leafy vegetables, cabbage, corn, wheat, roots and tubers	<ul style="list-style-type: none"> <li>• The synthesis of certain specialized products such as serotonin, histamine, niacin coenzymes from amino acid is dependent on pyridoxine</li> <li>• Pyridoxal phosphate involves in reactions like transamination, decarboxylation, deamination, transsulphuration, condensation etc.</li> <li>• It is required for absorbing amino acids from intestine</li> <li>• Adequate intake of B<sub>6</sub> is useful to prevent hyperoxaluria and urinary stone formation</li> <li>• It is involved in the action of steroidal hormones</li> </ul>
VIT B7 –Biotin (Anti-egg white injury factor, vitamin H)	Liver, kidney, egg yolk, milk, tomatoes, grains	<ul style="list-style-type: none"> <li>• It serves as carrier of CO<sub>2</sub> in carboxylation reactions</li> <li>• Acts as a coenzyme in various metabolic reactions namely in gluconeogenesis and citric acid cycle, fatty acid synthesis, metabolism of propionyl CoA in metabolism of certain amino acids, regulation of cell cycle</li> </ul>
VIT B8 –Inositol <sup>[8]</sup>	Brewer’s yeast, beef liver, pig’s kidney, oat meal, egg whites, nuts like hazel nuts, walnuts, almonds, peanuts, mushrooms, wheat germ, whole meal bread, milk, cheese, butter, yogurt, rice bran and rice germ	<ul style="list-style-type: none"> <li>• Promote the formation of healthy cells, immune system and nervous system, also involves in metabolism of carbs, proteins and fats.</li> <li>• Helps in DNA and RNA synthesis</li> <li>• RBC production</li> <li>• Losing weight</li> <li>• Promotes healthy skin and nails</li> <li>• Promotes healthy hair and prevents premature greying of hair and hairfall</li> <li>• Effectively used in the treatment of psychological disorders like OCD, mood disorders, bulimia, panic attacks, anxiety and depression. Relieves diabetic neuropathy and reduces insomnia</li> </ul>
VIT B9 – Folic acid	Liver, Kidney, whole grains, cereals, fresh leafy vegetables, cauliflower, yeast, eggs	<ul style="list-style-type: none"> <li>• Helps in RBC formation and genetic material of cells</li> <li>• Tetrahydrofolate (THF or FH<sub>4</sub>), the coenzyme of folic acid serves as an acceptor or donor of one carbon units in a variety of reactions involving amino acid and nucleotide metabolism</li> <li>• Folate along with other B vitamins are also vital for nerve function</li> </ul>
VIT B10 – PABA Para Amino Benzoic Acid <sup>[10]</sup>	Green leafy vegetables, whole grains, molasses, eggs, yogurt, wheat germ, mushrooms	<ul style="list-style-type: none"> <li>• Used by the body to promote the growth of beneficial microbes within the bowels</li> <li>• It prevents bacteriostatic properties of certain drugs</li> <li>• Anti-free radical activity</li> <li>• Treats skin diseases like fibrotic disorder</li> <li>• Corrects irritable bowel syndrome, GIT disturbances and various inflammatory reactions</li> <li>• Acts as coenzyme which aids in optimal utilization of proteins by the cells and formation of RBCs</li> <li>• Used in the production of folic acid by the intestinal bacteria</li> </ul>
VIT B11 – Pteryl hepta glutamic acid (Chick growth factor) <sup>[7, 9]</sup>		<ul style="list-style-type: none"> <li>• DNA and RNA synthesis</li> <li>• Cell division</li> <li>• Development of foetus, nervous system</li> <li>• Maintains healthy skin</li> </ul>

		<ul style="list-style-type: none"> <li>Increases the production of breast milk</li> <li>Increases the desire to eat</li> <li>Boosts immunity in children</li> <li>Analgesic</li> <li>Aids in fighting cancer</li> </ul>
VIT B12 – Cyanocobalamin	Liver, kidney, fish eggs, milk, oyster and clams	<ul style="list-style-type: none"> <li>Produce genetic material</li> <li>Helps in formation of red blood cells</li> <li>Maintain central nervous system</li> <li>Synthesis of amino acids</li> </ul>

**Minerals:** These are the inorganic substances that has various functions like maintaining the composition of body fluids, coenzymes, the formation of blood and bone, maintenance of

healthy nerve function and others [3]. Following are the minerals, sources its health benefits and available in the market in brief [6].

**Table 3:** Minerals

Minerals	Health Benefits	Dietary Requirements
Calcium	<ul style="list-style-type: none"> <li>Essential for bone and teeth</li> <li>Nerve transmission and glandular function</li> <li>Helps in blood clotting</li> <li>Muscle contraction</li> </ul>	<ul style="list-style-type: none"> <li>Adult Men and Women – 800mg/day</li> <li>Women during pregnancy, lactation and post menopause – 1.5g/day</li> <li>Children (1 to 18 yrs) - 0.8-1.2g/day</li> <li>Infants (less than one year) – 300-500mg/day</li> </ul>
Iron	<ul style="list-style-type: none"> <li>Helps in energy production</li> <li>Constituent of Haem. Ex: Haemoglobin, Myoglobin, Cytochromes</li> <li>Oxygen transport and biological oxidation</li> </ul>	<ul style="list-style-type: none"> <li>Adult man – 10mg/day</li> <li>Menstruating woman – 18mg/day</li> <li>Pregnant and lactating woman – 40mg/day</li> </ul>
Magnesium	<ul style="list-style-type: none"> <li>Used for healthy neuromuscular function</li> <li>Helpful for bone and teeth formation</li> <li>Acts as co-factor for several enzymes requiring ATP Ex: Hexokinase, Glucokinase, phosphofructokinase, Adenylate cyclase</li> </ul>	<ul style="list-style-type: none"> <li>Adult man – 350mg/day</li> <li>Adult woman – 300mg/day</li> </ul>
Sodium	<ul style="list-style-type: none"> <li>Acid base balance regulation</li> <li>Maintenance of osmotic pressure and fluid balance</li> <li>Normal muscle irritability and cell permeability</li> <li>Intestinal absorption of glucose, galactose and amino acids</li> <li>Initiating and maintaining heart beat</li> </ul>	<ul style="list-style-type: none"> <li>Normal – 5- 10g/day</li> <li>Hypertension (family history) – &lt;5g</li> <li>Hypertension – 1g/day</li> </ul>
Potassium	<ul style="list-style-type: none"> <li>Maintains intracellular osmotic pressure</li> <li>Required for the regulation of acid – base balance and water balance in the cells</li> <li>Transmission of nerve impulse</li> <li>Adequate intracellular concentration of K<sup>+</sup> is necessary for proper biosynthesis of protein by ribosomes</li> <li>Extracellular K<sup>+</sup> influences cardiac muscle activity</li> </ul>	3-4g/day
Chlorine	<ul style="list-style-type: none"> <li>Involved in acid – base equilibrium, fluid balance and osmotic pressure</li> <li>Responsible for the formation of HCl in gastric juice</li> <li>Salivary amylase is activated by chloride</li> <li>Chloride shift</li> </ul>	5 – 10g/day as NaCl
Sulphur	<ul style="list-style-type: none"> <li>Sulphur containing amino acids are very essential for the structural confirmation and biological functions of proteins</li> <li>The vitamins Thiamine, Biotin, lipoic acid and coenzyme of pantothenic acid contain sulphur</li> <li>Heparin, chondroitin sulphate, glutathione, parathionic acid are other sulphur containing compounds</li> </ul>	-
Phosphorous	<ul style="list-style-type: none"> <li>Development of bones and teeth</li> <li>Plays a central role for the formation and utilisation of high energy phosphate compounds. Ex: ATP, GTP, creatine phosphate</li> <li>Phospholipids, phosphoproteins and nucleic acids formation</li> <li>Essential component of several nucleotide co-enzymes. Ex: NAD<sup>+</sup>, NADP<sup>+</sup>, pyridoxal phosphate, ADP, AMP</li> <li>Several proteins and enzymes are activated by phosphorylation</li> <li>Phosphate buffer system is important for the maintenance of pH in the blood (7.4) as well as in cells</li> </ul>	<ul style="list-style-type: none"> <li>Based on the intake of calcium</li> <li>Adult - The ratio of Ca: P of 1:1 is recommended i.e. 800mg/day</li> <li>Infants - 2:1</li> <li>Calcium and phosphates are distributed in the majority of natural foods in 1:1 ratio</li> </ul>
Iodine	Iodine is required for the synthesis of thyroid hormones namely, thyroxine (T <sub>4</sub> ), triiodothyronine (T <sub>3</sub> )	<ul style="list-style-type: none"> <li>Adult: 100-150µg/day</li> <li>Pregnant woman - 200 µg/day</li> </ul>
Fluorine	<ul style="list-style-type: none"> <li>Prevents the formation dental caries</li> <li>Proper development of bones</li> <li>Inhibits activity of certain enzymes</li> </ul>	<ul style="list-style-type: none"> <li>An intake of &lt; 2ppm of fluoride will meet the daily requirement</li> </ul>
Cobalt	<ul style="list-style-type: none"> <li>It is the component of vitamin B12 and B12 coenzymes</li> <li>Administration of cobalt stimulates the production of hormone erythropoietin which promotes erythropoiesis</li> </ul>	-

Copper	<ul style="list-style-type: none"> <li>Essential constituent of several enzymes</li> <li>For the synthesis of haemoglobin (Cu is a constituent of ALA synthase needed for haem synthesis)</li> <li>Ceruloplasmin involved in conversion of Fe<sup>2+</sup> to Fe<sup>3+</sup> in which form iron (transferrin) is transported in plasma</li> <li>Synthesis of melanin and phospholipids</li> <li>Development of bones and nervous system (myelin) requires copper</li> </ul>	<ul style="list-style-type: none"> <li>Adult – 2-3mg/day</li> <li>Infants and children - 0.5-2 mg/day</li> </ul>
Chromium	<ul style="list-style-type: none"> <li>With insulin, it helps in conversion of carbohydrate and fat into energy</li> <li>Chromodulin protein has chromium which facilitates the binding of insulin to cell receptor sites</li> <li>Lowers total serum cholesterol levels</li> <li>Transports amino acids to cells of heart and liver</li> </ul>	Adult – 10-100mg/day approx.
Selenium	<ul style="list-style-type: none"> <li>Along with Vit E prevents development of hepatic necrosis and muscular dystrophy</li> <li>Maintains structural integrity of biological membranes</li> <li>Acts as antioxidant</li> <li>Helps in functioning of heart</li> <li>Helps in heavy metal poisoning</li> <li>5' deiodinase – a selenium containing enzyme converts T<sub>4</sub> to T<sub>3</sub></li> </ul>	Adult – 50-200mg/day approx.
Zinc	<ul style="list-style-type: none"> <li>Essential component of several enzymes</li> <li>Anti-oxidant</li> <li>The storage and secretion of insulin from β cells of pancreas requires zinc</li> <li>Vit A maintenance</li> <li>Wound healing</li> <li>Enhances cell growth and division</li> <li>Gusten, a zinc containing protein of saliva is important for taste sensation</li> <li>Proper reproduction</li> </ul>	<ul style="list-style-type: none"> <li>Adult – 10-15 mg/day approx.</li> <li>Pregnancy and lactation – increased by about 50%</li> </ul>
Molybdenum	<ul style="list-style-type: none"> <li>It is a constituent of enzymes xanthine oxidase, aldehyde oxidase and sulphite oxidase</li> </ul>	-

**b) Herbals**

The herbs possessing medicinal values to be implicated in treatment and prevention of ailments are been included in the

class. Botanical products may consist of fresh plant used or any part such as dried leaf, fruit, stem, seeds, roots or concentrated extract.

**Table 4:** Herbals

Medicinal Plant	species	Part used	Therapeutic Benefits	Products
Aloe	<i>Aloe barbadensis</i>	Gel, oral intake of juice	Antiulcer, anthelmintic, wound healing	<i>Aloe vera</i> Juice Organic (bare organics), Trifla with <i>Aloe vera</i> juice (Patanjali)
Kalmegh	<i>Andrographis paniculata</i>	Shoot powder	Respiratory tract infection	Karaitu / Kalmegh powder (Naturalmeds), <i>Andrographis capsules</i> (Solaray)
Artemisia	<i>Artemisia annua</i>	Shoot decoction	Anti-malarial	<i>Artemisia annua</i> capsules (Nutricology), <i>Artemisia</i> and Clove drops (Bioray)
Red pepper	<i>Capsicum annua</i>	Fresh and dried fruit powder	Antioxidant, stimulant	<i>Cayenne pepper</i> capsules (bioherba)
Senna	<i>Cassia acutifolia</i>	Dried leaf, pods	Laxative, purgative	Senna, Senna Alexandrina capsules (Solaray)
Turmeric	<i>Curcuma longa</i>	Dried root	Inflammation, indigestion, antioxidant	<i>Turmeric curcumin</i> tablets (Nature Made), <i>Haridra churna</i> – Kasturi turmeric powder (Ancient Living)
Lemon grass	<i>Cymbopogon citratus</i>	Dried leaf	Stomach ache, carminative	Lemon grass essential oil (Aroma Foundry), Lemongrass powder (Siddhi Organics)
Ephedra	<i>Ephedra sinica</i>	Dried stem	Bronchodilator, anti-asthmatic	Ephedren – Advanced thermogenic weight loss compound (NS <sup>+</sup> Laboratories)
Liquorice	<i>Glycyrrhiza glabra</i>	Root powder	Anti-inflammatory, congestion	Licorice root and stolon – system restoration drops (Herb PHARM), DGL Licorice chewable tablets (Nature's Life)
Chamomile	<i>Matricaria chamomilla</i>	Dried flower	Wound healing, indigestion, insomnia	Chamomile flower capsules (Nature's way), Gastritix with chamomile extract capsules (Nature's way), Tulsī – Honey – Chamomile tea bags (Organic India)
Psyllium	<i>Plantago ovata</i>	Dried seed, husk	Laxative	Psyllium Husk capsules (now)
Amla	<i>Phyllanthus emblica</i>	Fruit pulp, dried fruit	Diuretic, anti- ageing, diabetes	AMLA juice (Patanjali), Amla-Shikakai Shampoo (VAADI HERBALS)
Chirata	<i>Swertia chirata</i>	Fresh or dried whole plant	Diabetes, migraine headache	Sage Chirata Capsules

**c) Phytochemicals**

They are classified on the basis of chemical name given according to their phytochemical properties. These are been

reported to have active components which exerts their effect toward metabolism and biochemical reactions in living beings thus provide health benefits.

**Table 5:** Phytochemicals

Phytochemicals	Sources (example)	Chemical Classification	Therapeutic Benefits	Products
Monoterpenoids -Eugenol	<i>Eugenic caryophyllus</i>	Terpenoids	Dental analgesic and dental protection	Eugenol Pure (Densell)
Tetraterpenoids -Beta-carotene	<i>Daucus carota</i> , <i>Beta vulgaris</i>	Terpenoids	Antioxidant acts as provitamin	Beet Root - Beta vulgaris capsules (Nature's way)
Beta-carotene	Carrot, green leafy vegetables	Carotenoids	Acts as antioxidant and provitamin	Beta Carotene soft gels (Adrien Gagnon)
Lycopene	Tomatoes, watermelon, guava, red fleshed papaya, apricots	Carotenoids	Antioxidant	Lycopene soft gels (Biovea), Lycopene plus capsules (AMSEL)
Flavanones -Hesperetin	<i>Citrus limon</i>	Flavonoids	Anti-inflammatory, anti-allergic	Tribulus Formula capsules (pure encapsulation)
Saponin glycosides-Ginseng	<i>Panax ginseng</i>	Glycosides	Fatigue, liver diseases, regulates stress hormones	Panax Ginseng capsules (now), Ginseng powder (Biotrex)
Cyanogeneticglycosides - Bitter almonds	<i>Prunus amygdalus</i>	Glycosides	Anti-cancer	Bitter almond oil (Hashmi)
Isothiocyanate glycoside - mustard seeds	<i>Brassica nigra</i>	Glycosides	Local irritant, decongestant, rubefacient	Full Spectrum Mustard seed capsules (Swanson)
Aldehyde glycoside - vanillin	<i>Vanilla planifolia</i>	Glycoside	Flavouring agent	Vanillin Artificial Flavouring (Castella)
Ellagic Acid	Strawberries Raspberries	Polyphenols and Tannin	Reduces esophageal and colon cancers, Inhibits the formation of DNA adducts, Inhibits phase 1 enzymes and potentiates phase 2 enzymes	Ellagic capsules (Ecological Formulas)
Curcumin	Curcuma species	Non-Flavonoid Polyphenolics	Anti-inflammatory, Anti-oxidant, prevents colon cancer, Anti-clotting agent	Anti-inflammatory advanced Exls (doctors nutra)

**Note:** The above RDA and nutraceutical/dietary supplement products are not constant for all as they vary based on several conditions like age (as specified), body weight, gender (as specified for some), necessity, disease and disorders, etc.. There are products which are used for prevention as well as an additional factor to cure diseases (due to the presence of concentrated form of a presumed bioactive agent responsible for curing).

**Probiotics and prebiotics micro organisms**

**Probiotics:** They are a class of biologically active animal derived components and defined as viable microorganisms that are beneficial to human health. Examples include *Lactobacillus acidophilus* and its other strains being incorporated into functional food products now on the market. Getting probiotics from supplements is popular but can also get from fermented foods <sup>[1]</sup>. Ex: Yogurt, Buttermilk, kefir, sauerkraut, pickles, kombucha, kvass, tempeh, miso.

**Prebiotics:** They are the non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of beneficial bacteria in the colon, thus improving host health <sup>[1]</sup>. Ex: Wheat, Jerusalem artichokes, Onions, Leeks, Jicama, Potatoes(cooked and cooled).

**Synbiotics:** They are the mixture of probiotics and prebiotics that beneficially affect the host by improving the survival and implantation of live microbial dietary supplements in the GIT by selectively stimulating the growth and/or by activating the metabolism of one or a limited number of health promoting bacteria thus improving host welfare <sup>[1]</sup>.

**Nutraceutical Enzymes**

Enzymes are essential part of life without which our body would cease to function. The people who are suffering from medical disorders digestive problems and obesity eliminate the symptoms by enzyme supplements to their diet. These enzymes are derived from microbial plant and animal sources.

**Non-Traditional nutraceuticals**

Boosting of nutritional content by addition of nutrients, dietary components for improvement of quality of nutrition comprise is category of nutraceuticals. Ex. Beta-carotene enriched rice.

**a) Fortified nutraceuticals:** Fortification of food components is the process of addition of micronutrients (essential trace elements and vitamin) to food for enhancing the effectiveness and nutritional value. Ex. Orange juice fortified with calcium cereals with vitamins or minerals

**b) Recombinant nutraceuticals:** It involves in the application of biotechnology and genetic engineering in

the production of energy providing foods Such as yogurt and cheese or extraction of bioactive components by enzymatic or fermentation technology. Gold kiwi fruit is genetically modified for a high level of ascorbic acid, carotenoids and lutein zeaxanthin.

### Nutraceuticals Used Based on Diseases

Nowadays, nutraceuticals have received considerable interest due to potential nutritional, safety and therapeutic effects. A market research recently proposed that the worldwide nutraceuticals market is expanding and would reach US \$250 billion by 2019. Nutraceuticals have recently gained importance owing to their multifaceted effects. These food-based approaches are believed to target multiple pathways in a slow but more physiological manner without causing severe adverse effects. Recent studies have shown promising results of these compounds in various pathological complications such as diabetes, atherosclerosis, cardiovascular diseases, cancer, neurological disorders, etc. [13]. Hence they are considered as health promoting sources, preventing life threatening diseases, contemporary uses and most of the times given as “helps to cure” purpose along with medicines.

### Effects on Gastrointestinal system

The possible diseases that occur in GIT are constipation, diarrhoea, irritable bowel syndrome, hemorrhoids, anal fissures, celiac disease, vomiting, Crohn's Disease, Gastroesophageal Reflux Disease (GERD), lactose intolerance, malabsorption syndrome, peptic ulcer disease, ulcerative colitis, perianal abscesses, anal fistulas, perianal infections, diverticular diseases, colitis, colon polyps and cancer.

- Bael (*Aegle marmelos*) tree grows in tropical and subtropical countries. Luvangetin, a pyranocoumarin isolated from the seed of *Aegle marmelos*, has been shown to protect rodents gastric mucosa in multiple model of gastric ulceration through a nonidentified prostaglandin-independent pathway [29]
- Annurca apple (*Malus domestica*, *Mela annurca*) has potential gastroprotective effect of its polyphenolic extract. It is rich in catechin and epicatechin. APE (Apple polyphenolic extracts) counteracted the increased expression both at the mRNA and protein level, of COX-2 and HB-EGF, observed following administration of a damaging dose of aspirin. Interestingly, the gastroprotective effect exerted by APE was not associated to a decrease in gastric acid secretion [29]
- Other herbs that act on GIT are Ginger, Pepper, Turmeric, Coffee, Isapgol, Grapes, Gentian, Fennel, Cumin, Caraway, Dill, Cardamom, Marshmallow, Senna, Cascara, Peppermint, Cinnamon, etc.

### Effects on Cardiovascular system [15, 21]

Cardiovascular disease includes conditions that affect the structures or function of your heart, such as Coronary artery disease (narrowing of the arteries), Heart attack, Abnormal heart rhythms, or arrhythmias, Heart failure, Heart valve disease, Congenital heart disease, Heart muscle disease (cardiomyopathy), Pericardial disease, Aorta disease and Marfan syndrome, Vascular disease (blood vessel disease), etc.. The existing risk factors for Cardiovascular diseases are high blood pressure, abnormal blood cholesterol, tobacco use, Diabetes mellitus, obesity, physical inactivity, unhealthy diets, alcohol use, mental ill health, psychosocial stress, use of certain medications, left ventricular hypertrophy, advance

age, hereditary, gender and ethnicity or race. The possible biomarkers of CVD are Lipoprotein (a), serum homocysteine, coronary artery calcium score, C-reactive protein, Apolipoproteins A-1 and Apo B, carotid intima media thickness, myeloperoxidase, F2-isoprostanes, ankle-brachial index, leucocyte count, fasting blood glucose level, periodontal disease, homocysteine, vitamin-D, lipoprotein phospholipase A2, fibrinogen, brain (B-type) natriuretic peptide and N-terminal, pro B-type natriuretic peptide, markers of renal function [20].

- **Garlic (*Allium sativum*):** Allicin is the active ingredient formed through action of alliinase enzymes on alliin. It decreases intestinal cholesterol absorption, inhibits enzymes of cholesterol synthesis including HMG-CoA reductase [21]
- Green tea and its active ingredient, contains more catechins such as epigallocatechin gallate (EGCG), epicatechin-3-gallate, epigallocatechin and epicatechin reduces gastrointestinal cholesterol absorption by interfering with the emulsification, digestion and micellar solubilization of lipids, upregulates hepatic LDL receptor, stimulates FA synthase and paroxonase, inhibits HMG-CoA reductase, stimulates mitochondrial energy expenditure, and reduces LDL oxidation. They also decrease Apo B lipoprotein secretion from cells, mimics the action of insulin, improves endothelial dysfunction, and decreases body fat. It reduced total serum glucose and LDL-C, TGs and free FAs and increased HDL in diabetic rats, reduced myocardial levels of lipids and improved myocardial function [21]
- **Plant fibres:** Dietary fibres of plant origin are resistant to digestion. They are water soluble and structural. Soluble fibre is found in oats, psyllium, pectin, flaxseed, barley and guar gum. The structural fibres such as cellulose, lignin and wheat bran are insoluble. Fibre rich diets are associated with reduced CHD risk. Soluble fibres physically bind to bile acids during the intraluminal formation of micelles, entrap cholesterol resulting in lowered cholesterol absorption. This leads to increased bile acid synthesis, reduced hepatic cholesterol, upregulated LDL receptors, and increased LDL clearance. They also increase intraluminal viscosity and slow macronutrient absorption and increase satiety leading to lower energy intake. Insoluble fibre does not have any effect on LDL-C unless it replaces foods supplying saturated fats and cholesterol. Ingestion of soluble fibres 2-10 g/day leads to 5-7 percent reduction in LDL-C [21]
- Nuts are a good source of mono- and poly-unsaturated fatty acids, and they also contain dietary fiber, phytosterols, and polyphenols. Almonds, walnuts, hazelnuts, and pistachios have shown reductions in LDL-C. Increased nut consumption is associated with reduced risk of CHD [21]
- Alfalfa (*Medicago sativa*) leaves and sprouts help reduce the blood cholesterol levels and plaque deposits on artery walls
- Turmeric (*Curcuma* sps) lowers blood cholesterol levels by stimulating the production of bile and prevents blood clot formation that can lead to heart attack
- Arjuna (*Terminalia arjuna*), an important Ayurvedic herb, is a coronary vasodilator. It helps to strengthen circulation, maintain tone and health of heart muscle

### Effects on Nervous system

Nutraceuticals here are given to non-pathological conditions or to improve the physiology of the nerves as well. Nervous disorders or diseases can be originated either from central or peripheral nervous system. Disorders of the nervous system may involve the following:

1. Vascular disorders, such as stroke, Transient Ischemic Attack (TIA), subarachnoid hemorrhage, subdural hemorrhage and hematoma, and extradural hemorrhage
  2. Infections, such as meningitis, encephalitis, polio, and epidural abscess
  3. Structural disorders, such as brain or spinal cord injury, Bell's palsy, cervical spondylosis, carpal tunnel syndrome, brain or spinal cord tumors, peripheral neuropathy, and Guillain-Barré syndrome
  4. Functional disorders, such as headache, epilepsy, dizziness, and neuralgia
  5. Degeneration, such as Parkinson disease, multiple sclerosis, amyotrophic lateral sclerosis (ALS), Huntington chorea, and Alzheimer disease
- *Rosmarinus officinalis* (Rosemary) has the natural COX-2 inhibitors namely: Apigenin, carvacrol, eugenol, oleanolic acid, thymol and ursolic acid. It has the capability of preventing Alzheimer's disease
  - Galantamine, a tertiary phenanthrene alkaloid occurs naturally in Daffodil (*Narcissus tazetta*), Snowdrop (*Galanthus nivalis*) and the Snowflake (*Leucojum aestivum*). The drug also belongs to a class of cholinesterase inhibitors and is capable of stimulating nicotinic receptors which further enhance cognition and memory [30]
  - Sulforaphane is a compound within isothiocyanate group of organosulphur compounds present in broccoli, brussels, sprouts and other cruciferous vegetables. Several studies have reported neuroprotective effects of sulforaphane in animal models of both acute and chronic neurodegenerative conditions. It has been reported to protect cultured neurons against oxidative stress and dopaminergic neurons against mitochondrial toxins [30]
  - Naphthodianthrones such as hypericin and pseudohypericin are present in *Hypericum perforatum*. Evidences show hypericin and pseudohypericin have antidepressant action. Inhibition of monoamine oxidase is one mechanism by which some antidepressants operate to increase levels of neurotransmitters such as serotonin, norepinephrine, or dopamine. This constituent blocks synaptic re-uptake of serotonin, dopamine, and norepinephrine leading to the elevation of their synaptic concentration [30]
  - Other known neuroprotective herbs are Brahmi, Centella, Eucalyptus, Ginseng, *Terminalia chebula*, Valerian, Ashwagandha, Shankapushpi, *Ginkgo biloba*, *Magnolia officinalis*, Ginger, Liquorice, *Piper methysticum*, etc..

### Effects on Liver

Various physiological processes and functions, such as metabolism, secretion (i.e. bile), synthesis (i.e. albumin, coagulation factors), lipid and glycogen storage are modulated by the liver. It is able to eliminate endogenous (waste metabolites) and/or exogenous (toxic compounds) materials via fecal and/or urinary ways [16]. The term hepatic disease means the damage to cells, tissues, structure, or liver function, and this harm can be caused by biological causes (bacteria, virus, and parasites), and autoimmune diseases (immune

hepatitis, primary biliary cirrhosis), or by the action of different chemicals, such as some drugs [elevated dosage of paracetamol (PCM) and antitubercular medicines], toxic compounds [carbon tetrachloride (CCl<sub>4</sub>), thioacetamide, dimethyl nitrosamine (DMN), D-galactosamine/lipopolysaccharide (GalN/LPS)] and unquestionably, high uptake of alcohol [16].

- The grapefruit (*Citrus paradisi*) of Rutaceae has a biologically active flavonoid, Naringenin which is proved to have anti fibrinogenic and hepatoprotective effect. It renewed natural protein levels in serum, albumin and hepatic malondialdehyde levels. A study showed that naringenin was able to significantly reduce the levels of serum ALAT and ASAT, gamma-glutamyl transpeptidase (GGT), thiobarbituric acid-reactive substances (TBARS) tissue, conjugated dienes, lipid hydroperoxides, protein carbonyl content, bilirubin, ALP, lactate dehydrogenase (LDH), and phase I enzymes; it also increases the action of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GRx), glutathione-S-transferase (GST), alcohol dehydrogenase (ADH), and aldehyde dehydrogenase (ALDH), as well as the vitamins C and E levels in tissues, and phase II enzymes in rats
- Grapes (*Vitis vinifera*) rich in resveratrol plies a shielding effect by controlling chronic ethanol intoxication and by lowering the harm caused by hepatocarcinogens, like azoxymethane (AOM)
- Chamomile tea (*Matricaria chamomilla* or *Chamomilla recutita*) of Asteraceae has the capability of modulating the action of hepatic cytochrome P450 sub CYP1A2 [16].
- Silymarin from *Silybum marianum* (St. Mary's thistle or *Carduus marianus*) of Asteraceae has been used as a protective treatment in acute and chronic liver diseases. Suppressing toxin penetration into hepatic cells, increasing SOD activity and the glutathione tissue level, inhibiting lipid peroxidation and enhancing hepatocyte protein synthesis are the many mechanisms of its protective capacities [16].
- *Opuntia ficus indica* (Cactus pear fruit) fruits of which are known as prickly pear fruits, are considered a functional food and their bioactive compounds, like vitamin C and vitamin E, polyphenols, carotenoids, flavonoid (for instance, kaempferol, quercetin, and isorhamnetin), taurine, and pigments induce fragmentation of the DNA in the liver and chromosomal aberrations in bone marrow cells, amplify the expression of the bcl2 antiapoptotic proteins, and reduce the expression of bax. It was proved to have antigenotoxic effect through the reduction of the damage to the genetic material of the liver and to the bone marrow [16]

### Effects on Immune system

Good nutrition strengthens immunity and it is required to protect the body from infections of all sorts. To prevent or cure, the nutraceuticals play a major role as well like enhancing natural killer cell function, macrophage activity, production of tumor necrosis factor, neutralizing oncogenes (cancer promoting substances), re-differentiation of cancer cells (transforming cancer cells to normal cells through re-establishment of cell cycle controls), inducing programmed cell death (apoptosis).

- Rosemary – The highly aromatic needlelike leaves of rosemary contain substances that increase circulation, improve digestion and are anti-inflammatory. In animal



studies an extract made from rosemary leaves was shown to have powerful and measurable antioxidant and anti-inflammatory effects. In a clinical study, the rosemary capsules were protecting the cells from oxidative damage and lowered the inflammatory markers in the cells. It also has immune boosting properties [28]

- Boneset (*Eupatorium perfoliatum*) contain antiviral properties and strengthens the immune system by enhancing the secretion of interferons. Interferons belong to large class of proteins called cytokines. They interfere with viral replication by protecting cells from virus infections. Other studies have found that they are effective against minor viral and bacterial infections by stimulating the white blood cells [28].
- There are many immune boosting herbs namely Aloe, Amla, Ginger, Barberry, Astragalus, Ashwagandha, Camu camu, Cordyceps, Echinacea, Elderberry, Golden Seal, Hibiscus flower, Noni, Graviola, Turmeric, etc.....

### Cancer and Nutraceuticals

Current cancer treatments such as chemotherapy, radiotherapy and surgery induce unintended side effects compromising also health and well-being of patients. Emerging studies suggest that some plant based agents may impact cellular and molecular processes underlying tumour progression. Cancer is basically a disease of uncontrolled cell division. Cells have many different mechanisms to restrict cell division, repair DNA damage, and prevent the development of cancer. Because of this, it's thought that cancer develops in a multi-step process, in which multiple mechanisms must fail before a critical mass is reached and cells become cancerous [25]. ALK gene, Alpha fetoprotein, Beta-2-microglobulin, beta-human chorionic gonadotropin, BRCA1 and BRCA2, C-kit/CD117, Calcitonin, Circulating tumor cells of epithelial origin, Lactate dehydrogenase etc. are some of the tumour markers [26].

- Grape seed proanthocyanidins inhibit colon cancer induced angiogenesis through suppressing the expression of growth factors such as vascular endothelial growth factor (VEGF) and angiopoietin-1. They are widely consumed dietary supplements that have antitumor activity. The mechanisms of their action were related to inhibiting the expression of both VEGF and Ang1 through scavenging reactive oxygen species [27].
- Dandelion (*Taraxacum officinale*) leaves have long been used by Chinese medicine and Ayurvedic practitioners to treat abscesses, water retention, tumors, and cysts. In a study, it selectively reduced the metabolic activity of aggressive colon cancer cells, blocked the growth of breast cancer cells and the invasions of prostate cancer cells [27].
- Saffron (*Crocus sativus*) contains a carotenoid compound called crocetin. Studies explain the antitumor effect of saffron in skin is related to increase in the levels of carotene and vitamin A in the serum. It was suggested that saffron carotenoids possessed provitamin activity according to the hypothesis that the action of carotenoids was dependent upon its conversion to retinal (Vitamin A), because most of the evidence supporting the anticancer effects of carotenoids were referred to  $\beta$ -carotene. Scientists detected significant inhibition in the synthesis of nucleic acids, and suggested that dimethyl-crocetin could disrupt DNA-protein interactions (e.g. topoisomerases II) important for cellular DNA synthesis – for leukaemia [27]

### Obesity and Nutraceuticals

Obesity is a risk factor to number of other diseases like sleep apnea, asthma and other respiratory disorders, diabetes, high blood pressure, atherosclerosis, angina pectoris, hyperlipidaemia, congestive heart failure, fatty liver disease, renal vein thrombosis, reduced fertility, osteoarthritis and cancer. Possible targets of nutraceuticals to reduce obesity can be centrally acting serotonin/noradrenaline reuptake inhibitor that mainly increases satiety, can induce thermogenesis to facilitate energy expenditure, increasing HDL cholesterol, inhibiting pancreatic lipase that reduces fat absorption by partially blocking the hydrolysis of dietary triglycerides, etc.. [13, 22]

- Curcumin (active component of turmeric) interacts directly with cyclooxygenase-2 (COX-2), DNA polymerase, lipoxygenase (LOX), glycogen synthase kinase3b (GSK-3b), and cytokines (TNF- $\alpha$ ). It interacts indirectly with several transcription factors, activator protein 1 (AP-1), b-catenin, signal transducer and activator of transcription (STAT) proteins, and peroxisome proliferator-activated receptor c (PPARc). 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. These factors are critically involved in obesity-induced insulin resistance and chronic inflammation [23]
- *Lagenaria siceraria* (bottle gourd) reduces total cholesterol, triglycerides (TG) and low density lipoproteins (LDL) levels, improvement in high density cholesterol levels (HDL) and decrease in fasting glucose [23]
- *Vigna mungo* (black gram or black lentil) direct favourable action on  $\alpha$  amylase protein inhibitors has been considered for its potential use in prevention of obesity and weight loss [23]
- *Garcinia cambogia* [(–)-Hydroxycitric acid (HCA)] - HCA is a potent inhibitor of adenosine triphosphate-citrate lyase, a catalyst for the conversion process of citrate to acetyl-coenzyme A, which plays a key role in fatty acid, cholesterol and triglycerides synthesis. The crude extract or constituents from the plant also exerts hypolipidaemic, antidiabetic, anti-inflammatory, anticancer, anthelmintic, anticholinesterase and hepatoprotective activities [24]

### Conclusion

Herbs have variety of constituents that has different functions and acts as a wholesome diet. There are many plants having various therapeutic uses that can be introduced in nutraceuticals selecting the best form ensuring its quality, safety, stability, efficacy and toxicity (possibly) status. Nutraceuticals are the combination of several sources in one form that ensures the complete health of healthy as well as the unhealthy. The current race of the world needs such health ensuring products and the market of nutraceuticals with other health foods is on a rise. A large shift of people's interest to such products from taking medicine can be observed in the recent scenario.

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