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Review Article

Nutritional Supplements: An Overview

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ABSTRACT

There is need for those within the industry to become more vigilant in their use of terminology with increasing consumer awareness as it applies to terms such as nutraceutical, functional, medical and novel foods. Dietary supplements have also been developed to manage a variety of diseases. Recognition of variation in functional food and nutraceutical composition will provide opportunity for the industry to give consumers a variety of new products that can be developed for niche or specialized markets.

Key words: Nutraceuticals and functional foods, Phyto-pharmaceuticals, Pure Extracts.

NUTRITIONAL SUPPLEMENTS

There is need for those within the industry to become more vigilant in their use of terminology with increasing consumer awareness as it applies to terms such as nutraceutical, functional, medical and novel foods. A list of important definitions is included in Table1. In simple terms, nutraceuticals and functional foods are those

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foods or parts of foods that provide health and/or medical benefits to the target consumers, including prevention, protection and treatment of a disease (Belem, 1999). It is important to the development of consumer confidence that functional foods and nutraceuticals are properly categorized. Formal characterization of products provides government and other regulatory agencies with the opportunity to implement controls such as labeling and verification within the industry. While movement in this direction has been taken in some countries (Health Canada, 1998), it is important that those involved in the science and industry be proactive in order to avoid unnecessary conflict and to provide consumers with produce that they can both trust and depend upon.

Categories of nutraceuticals

Nutraceuticals are non-specific biological therapies used to promote wellness, prevent malignant processes and control symptoms. These can be grouped into the following three broad categories[7].

1. Herbs or botanical products as concentrates and extracts - Herbals
2. Substances with established nutritional functions, such as vitamins, minerals, amino acids and fatty acids – Nutrients
3. Reagents derived from other sources (*e.g.* pyruvate, chondroitin sulphate, steroid hormone precursors) serving specific functions, such as sports nutrition, weight-loss supplements and meal replacements – Dietary supplements

1. Herbs or Botanical products as concentrates

There is increasing recognition of the need for scientific evidence to support nutritional and medicinal claims being made within the functional food and nutraceutical industry[8]. In 1997 Clydesdale called for development[9] of an international dialogue on the types of validation required to recognize health claims being made for functional foods and food components. Since then there has been considerable discussion on the need for better characterization of functional foods and food products as well as need for clinical trials demonstrating medicinal claims, and better labeling of products whose active agents may vary considerably in concentration due to genotypic variation, response to environment and/or processing during preparation of a product[8,10]. The health promoting effects of phytochemicals and nutraceuticals and/or functional foods[11] likely are due to a complex mix of biochemical and cellular interactions which together promote overall health of the

Table 1: Important definitions associated with the nutraceutical and functional food Industry

Terminology	Definition
Bioactive compounds	Naturally occurring chemical compounds contained in, or derived from, a plant, animal or marine source, that exerts the desired health/wellness benefit[1].
Functional ingredients	Standardized and characterized preparations, fractions or extracts containing bioactive compounds of varying purity, that are used as ingredients, by manufacturers in the food (human and pet) and fractions or extracts containing bioactive compounds of varying purity, which are used as ingredients by manufacturers in the cosmetics and pharmaceutical sectors[1].
Novel Foods	Products that have never been used as food; foods that result from processes that has not previously been used for food; or, foods that have been modified by genetic manipulation[2].
Functional Foods	A functional food is similar in appearance to. Or may be a conventional food, is consumed as part of a usual diet, and is demonstrated to have physiological benefits and/or reduce the risk of chronic disease beyond the basic nutritional functions[2].
Nutraceuticals	A product isolated and purified from foods that is generally sold in medicinal forms are usually associated with food. A nutraceutical is demonstrated to have a physiological benefit or provide protection against chronic disease[2] (Coined originally by Stephen DeFelice in 1989, founder and chairman of the Foundation for Innovation in Medicine, USA).
Phytochemicals/phyto-nutrients	A nonnutritive bioactive plant substance, such as a flavonoid or carotenoid, considered to have a

	beneficial effect on human health[3].
Dietary Supplements	A product that is intended to supplement the diet that bears or contains on or more of the following dietary ingredients: a vitamin, a mineral, a herb or other botanical, an amino acid, a dietary substance, for use by man to supplement the diet by increasing the total daily intake, or concentrate. Metabolite, constituent, extract. Or combinations of these ingredient; intended for ingestion in pill, capsule, tablet, or liquid form; not represented for use as conventional food or as a sole item of a meal or diet; labelled as dietary supplement; includes products such as approved new drug, certified antibiotics, of licensed biologic that marketed as a dietary supplement or food before approval[6], certification, of license (unless a product is redefined through regulatory government agency).

individual. They suggest that these agents may function: as substrates in metabolic reactions or cofactors of key metabolic enzymes; as ligands that promote or compete with biochemical interactions at the cell surface or with intercellular receptors which can enhance absorption and assimilation of important macro and micro nutrients; and as agents which selectively promote the growth of bacteria with health benefits in the gastrointestinal system and compete with or partially eliminate the growth of harmful bacteria. In addition these agents may act as enzyme inhibitors, absorbents or toxicant scavengers that can associate with and help remove damaging substances or toxins from the body. Major chemical groups now recognized as having potential health promoting effects, at least under some circumstances are the phenolics, flavonoids, alkaloids, carotenoids, pre- and pro-biotics, phytosterols, tannins, fatty acids, terpenoids, saponins, and soluble and insoluble dietary fibres[12,13,14,15]. A list of important phytochemicals (nutraceuticals) commonly promoted and sold in the global market is presented in Table 2 (A & B). While this list seems to expand on a daily basis, considerable more work is required to support claims that often times have been made locally in support of herbal or other traditional medicines but cannot be supported globally due to biological variation in genotype and ecotypic responses[8].

While considerable research may have been done with individual biological isolates, this same research often fails to recognize the vast diversity of biological organisms and consumer products derived from them.

Recognition of variation in functional food and nutraceutical composition will provide opportunity for the industry to give consumers a variety of new products that can be developed for niche or specialized markets. Development of new products with distinctive genetics, ecotypic response and reliable health benefits also could provide local producers with access to more stable and specialized markets similar to those already seen in the coffee and wine marketplace where regionally produced variants of these products have been successfully marketed based on their unique regional attributes. In any case, as scientific studies which reveal new discoveries with potential health benefits are identified by potential consumers and the media, more support, credibility and demand for functional foods and nutraceuticals is being generated. This is resulting in a marketplace with considerable potential for growth and many new opportunities within the industry both internationally and at a regional level.

1.2. Pure Extracts

Pharma Industry prefers extracts in the 'Dry' or 'Soft' form. Often, Extracts with high active content are preferred with the standard BP or USP specification wherever available. Extracts of all Herbs listed in "Herbs and Herbal Powders" may be made available[16]. The following Extracts are the speciality:

Plants

Andrographis panniculata, Nees (Kalmegh).

Piper longum linn (Long Piper, Pippali).

Azadirachta Indica Leave or Seed Kernels (Neem).

Sida Cordifolia Linn (Bala).

Garcinia Combogia (Oat).

Terminalia Belerica Roxb (Behada).

Garcinia Indica (Kokum).

Terminalia Chebula Retz (Harda).

Gymnemasylvestre, r.br. (Gurmar).

Tinospora Cordifolia Mier (Guduchi).

Actives

Azadirachtin (upto 40%)

Hydroxy Citric Acid (upto 75%)
Capsaicin (upto 95%).
Neem Actives (upto 20000 ppm)
Colchicine (upto 99%). Pipperine (upto 99%).
Curcumin (upto 95%). Reserpine (upto 99%).
Gymnemic Acid (upto 70%).
Triacontanol (upto 60%).

Table 2 A: Important phytochemicals (nutraceuticals), their corresponding plant sources and medicinal properties

Phytochemicals: Chemical group	**Plant sources**	**Medicinal Property**
Alkaloids		
Quinine	Cinchona	Anti malarial
Tropane alkaloids	Solanaceous members: Deadly night shade, Datura	In treatment of heart ailments
Morphine	Opium poppy	Antidepressant, pain killer
Ergot alkaloids	Fungus: *Claviceps purpurea*	Abortificient
Vincristine	Periwinkle	Antineoplastic
Vinblastine	Periwinkle	Antineoplastic
Coumarin,	Fenugreek	Hypoglycaemic
Scopoletin	Fenugreek	Hypoglycaemic
Fenugreekine	Fenugreek	Hypoglycaemic
Trigonelliine	Fenugreek	Hypoglycaemic
Carotenoid terpenoids/ Isoprenoids		
α-carotene	Carrots	Antioxidants, anticarcinogenic
β-carotene	Fruits & vegetables	Antioxidants
β-cryptoxanthin	Oranges & tangerines	Antioxidants, anticancer
Lutein	Vegetables (kale, spinach, watercress , parsley)	Reduce risk of macular degeneration, protect against colon cancer

Zeaxanthin	Corn, avocado	Protects eye from macular degeneration and cataracts
Lycopene	Tomatoes, pink grapefruit, watermelon, guava, papaya	Reduces risk of prostrate cancer in males
Non-carotenoid terpenoids		
Perillyl alcohol	Cherries & mints	Anticancer
Saponins	Legumes (Chicks, peas, fenugreek, all pulse crops)	Reduces cholesterol levels in blood
Terpenol	Carrots	Anticancer
Terpene	limonoids Peels and membranes of citrus fruits	Anticarcinogenic
Flavonoid polyphenolics		
Anthocyanins	Stawberries, raspberries, cherries, cranberries, pomegranate, apples, red grapes	Antioxidants
Betacyanins	Beet root	Antioxidant
Catechins	Tea	Antioxidant
Flavonones	Citrus fruits	Antioxidant
Flavones	Fruits & vegetables	Anticancer
Isoflavones	Soybean	Anticancer
Hesperetin	Citrus fruits	Antioxidant
Naringin	Grapefruit	Reduces cholesterol
Rutin	Asparagus, buckwheat & citrus fruits	Protects against cardio vascular ailments
Quercitin	Red onions, buckwheat, red grapes, green tea, apple skins	Anti-sitaminic, antioxidant
Silymarin	Artichoke & milk thistle	Anti-atherosclerotic
Tangeretin	Tangerines	Anticancer
Tannins	Cranberries, pomegranate, cocoa & tea	Reduces blood cholesterol

Table 2 B: Important phytochemicals (nutraceuticals), their corresponding plant sources and medicinal properties		
Phytochemicals: Chemical group	**Plant sources**	**Medicinal Property**
Phenolic acids		
Ellagic acids	Strawberries & raspberries	Prevents colon cancer
Chlorogenic acids	Blueberries, tomatoes, grapes & bell peppers	Antioxidant
p-coumaric acids	Red and green ball peppers, legumes	Antioxidant, anticancer
Phytic acids	Legumes and whole seed grains	Lowers blood glucose
Ferulic acids	Seeds of brown rice, whole wheat and oats, apple, artichoke, orange, peanut & pine apple	Antioxidant, anticancer
Vanillin	Vanilla bean	Antioxidant, anticancer
Cinnamic acid	Cinnamon, balsam tree resins	Antibacterial, antifungal
Hydroxycinnamic acid	Grapes, blueberries & blackberries	Antioxidant, anticancer
Non-flavonoid polyphenolics		
Curcumin	Curcuma	Anti-microbial, anticancer, antioxidant
Resveratrol	Grapes	Anti-inflammatory, anticancer
Lignans	Plant cell walls	Reduces skin cancer
Glucosinolates		
Isothiocyanates	Horseradish, radish & mustard	Anticancer
Phenethyl isothiocyanate	Watercress	Anticancer
Sulforaphene	Broccoli	Anticancer
Indoles	Broccoli	Anticancer
Thiosulfonates	Garlic & onions	reduces blood pressure Anticancer, antimicrobial, and

		blood cholesterol
Anthraquinones		
Senna	Legumes and pulses	Purgative,
Barbaloin	Aloe	Laxative, anti-helminthic
Hypericin	St. John's wort	Analgesic
Capsicum (hot peppers) Capsaicin Anticancer,	antiinflammatory,	antiapoptotic
Piperine	Black peppers, jalapeno peppers	Helps in digestion
Terpenes		
Menthol (Monoterpene)	Plants of mint family	Topical pain reliever & anti-pyretic
Borneol (Monoterpene)	Pine oil	Disinfectant
Santonin (Sesquiterpene)	Wormwood	Photosensitizer
Gossypol (Sesquiterpene)	Cotton	Contraceptive

Oils

Behada Oil. Nirgundi Oil.

Black Pepper Oil. Nutmegh Oil.

Chaulmoogra Oil. Turmeric Oil.

Malakanguni Oil. Vavding Oil.

Neem Oil. Vekhand Oil.

Oleoresins

Black Pepper Oleoresin. Nutmegh Oleoresin.

Capsicum Oleoresin. Paprika Oleoresin.

Fenugreek Oleoresin. Turmeric Oleoresin.

Product Concepts

Anti Obesity Powder Immuno Boosters.

Aphrodisiacal Extracts. Pure Herb Capsules.

Herbal Candies.

2. Substances with established nutritional functions

The most commonly known nutrients are antioxidant, water and fat-soluble vitamins. Many potential benefits have been attributed to antioxidant use in the form of dietary intake or supplementation[17-21]. Antioxidants, in general, may be useful in the prevention of cancer and cerebrovascular disease[17]. High dietary intake of vitamin E may prevent Parkinson's disease[18]. Agus *et al.,* determined that the oxidized form of vitamin C, dehydroascorbic acid, readily crosses the blood brain barrier[19]. These findings have implications for increasing the uptake of antioxidants in the central nervous system; thus, some feel that this has the potential for improving the treatment of Alzheimer's disease. Jialal and Fuller found that the combination of vitamin E, C and beta carotene has been useful in reducing low density lipoprotein oxidation and subsequent atherosclerosis[20]. Vitamin supplement is associated with increased antibody titre response to both hepatitis B and tetanus vaccines as a result of macrophage and T cell stimulation[21]. Those genetically predisposed to pancreatic cancer have low serum levels of selenium; thus, it is assumed that supplementation with selenium may help to prevent this condition[22,23]. Those suffering from asthma and skin cancer have also been evaluated with selenium for its potential use, although results have been inconclusive[24]. Zinc is an essential component of more than hundred enzymes involving digestion, metabolism and wound healing. L-arginine is a semi-essential amino acid that is a substrate for nitric oxide production. Ceremuzynski *et al.* demonstrated that supplementation of L-arginine improved exercise capacity in patients, who had angina[25]. A list of common nutrients with their health benefits is given in Table 3 (A & B).

3. Reagents derived from other sources:

Dietary supplements have also been developed to manage a variety of diseases. The two nutraceuticals namely glucosamine sulfate and chondroitin sulfate are effective and safer to alleviate symptoms of osteoarthritis[26] whereas Deal and Moskowitz emphasized that glucosamine sulfate and chondroitin sulfate are not FDA-evaluated or recommended for treatment of osteoarthritis[27]. Immune milk products are promising examples of health promoting nutraceuticals[28]. Numerous casein and whey protein derived angiotensin-I-converting enzyme inhibitory peptides/hydrolysates have been identified. These peptides/hydrolysates may be classified as nutraceuticals due to their ability to provide health benefits[29]. Buckwheat has been used and will be

better used as an important raw material for functional food production. Buckwheat proteins have unique amino acid composition with special biological activities of cholesterol-lowering effects, antihypertension effects and improving constipationand obesity by acting similar to dietary fiber and interrupting the *in vivo* metabolism. The trypsin inhibitor isolated from buckwheat seeds are heat stable and can cause poor digestion if they are not suitably cooked before consumption. The buckwheat seeds may also contain some allergenic proteins, which induces allergy. Buckwheat flour can improve diabetes, obesity, hypertension and constipation[30].

Dehydroepiendrosteron (DHEA) and melatonin is used as nutritional supplements. Dehydroepiendrosteron is precursor secreted by the adrenal cortex and lesser extent by the central nervous system; it is readily converted to androstendione, testosterone and androsterone.In peripheral tissues, aromatase converts DHEA to estradiol. In the plasma, DHEA is converted to DHEA sulfate (DHEAS). Although no specific physiologic function has been attributed to DHEA or DHEAS, the relationship between endogenous level and various diseases have been widely researched. Exogenous DHEA supplementation has been advocated for variety of indication including relief of age disorder, promotion of weight loss, reduction of heart disease risk, prevention of variety of cancers, Alzheimer disease, treatment of HIV infection/AIDS and in diabetes.

Melatonin is a serotonin derivative produced by the pineal gland and some other tissues, is believed to be responsible for regulating sleep wake cycles.

Table 3 A. Common nutrients and their associated health benefits

Nutrients	Health benefits
Fat Soluble Vitamins	
Vitamin A	Antioxidant, essential, for growth and development, maintains healthy vision, skin and mucous membranes, may aid in the prevention and treatment of certain cancers and in the treatment of certain skin disorders.
Vitamin D	Essential for formation of bones and teeth, helps the body absorb and use calcium
Vitamin E	Antioxidant, helps form blood cells, muscles, lung and nerve tissue, boosts the immune system

Vitamin K	Essential for blood clotting
Water Soluble Vitamins	
Vitamin C	Antioxidant, necessary for healthy bones, gums, teeth and skin, helps in wound healing, may prevent common cold and attenuate its symptoms
Vitamin B1	Helps to convert food in to energy, essential in neurologic functions
Vitamin B2	Helps in energy production and other chemical processes in the body, helps maintain healthy eyes, skin and nerve function
Vitamin B3	Helps to convert food in to energy and maintain proper brain function
Vitamin B6	Helps to produce essential proteins and convert protein in to energy
Vitamin B12	Helps to produce the genetic material of cells, helps with formation of red blood cells, maintenance of central nervous system and synthesize amino acids and is involved in metabolism of fats, protein and carbohydrates
Folic acid	Necessary to produce the genetic materials of cells, essential in first three months of pregnancy for preventing birth defects, helps in red blood cell formation, protects against heart disease
Pantothenic acid	Aids in synthesis of cholesterol, steroids and fatty acids, crucial for intraneuronal synthesis of acetylcholine

Minerals	
Calcium	Essential for building bones and teeth and maintaining bone strength, important in nerve, muscle and glanddular functions
Iron	Helps in energy production, helps to carry and transfer oxygen to tissues
Magnesium	Essential for healthy nerve and muscle function and bone formation, may help prevent premenstrual syndrome (PMS)
Phosphorous	Essential for building strong bones and teeth, helps in formation of genetic material, energy production and storage

Table 3 B. Common nutrients and their associated health benefits

Nutrients	**Health benefits**
Trace elements	
Chromium	With insulin helps to convert carbohydrates and fats into energy
Cobalt	Essential component of vitamin B12, but ingested cobalt is metabolized *in vivo* to form the B12 coenzymes
Copper	Essential for hemoglobin and collagen production, healthy functioning of the heart, energy production, absorption of iron from digestive tract
Iodine	Essential for proper functioning of the thyroid
Selenium	Antioxidant, essential for healthy functioning of the heart

	muscle
Zinc	Essential for cell reproduction, normal growth and development in children, wound healing, production of sperm and testosterone
Vitamin like compounds	
Biotin	Required for various metabolic functions
L- Carnitine	Oxidation of fatty acids, promotion of certain organic acid excretion and enhancement of the rate of oxidative phosphorylation
Choline	Lipotropic agent used to treat fatty liver and disturbed fat metabolism
Vitamin F	Involved in proper development of various membranes and synthesis of prostaglandins, leukotrienes and various hydroxy fatty acids
Inositol	Lipotropic agent necessary for amino acid transport and movement of potassium and sodium
Taurine	Aids in retinal photoreceptor activity, bile acid conjugation, white blood cell antioxidant activity, CNS neuromodulation, platelet aggregation, cardiac contractility, sperm motility, growth and insulin activity

Melatonin release coincides with darkness; it typically begins around 9 Pm and last until about 4 Am. Melatonin release is suppressed by day light. Melatonin has also been studied for a various functions, including contraception, protection against endogenous oxidants, prevention of aging, and treatment of depression, HIV

infection, and a variety of cancers. Currently, melatonin is most often administered to induce sleep and to prevent Jet lag[31].

CONCLUSION

Nutritional supplements have proved their significance from ancient period. Majority of substances are being used are innocuous in nature thereby reinforcing the natural well being of human body. These may benefit the human in healthy as well as diseased conditions.

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