PHYTOCHEMICALS OF NUTRACEUTICAL IMPORTANCE: THEIR ROLE IN HEALTH AND DISEASES

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Summary

Phytochemicals of nutraceuticals importance are bioactive constituents that sustain or promote health and occurs at the intersection of food and pharmaceutical industries. Such substances may range from isolated nutrients, dietary supplements and specific diets to genetically engineered designer foods, herbal products, processed foods and beverages. Phytochemicals are broadly described as polyphenols, flavonoids, isoflavonoids, anthocyanidins, phytoestrogens, terpenoids, carotenoids, limonoids, phytosterols, glucosinolates and fibers. They have tremendous impact on the health care system and may provide medical health benefits including the prevention and/ or treatment of diseases and physiological disorders. Majority of foods, such as whole grains, beans, fruits, vegetables and herbs contain phytochemicals. Amongst these, fruits and vegetables contribute to the significant sources of phytochemicals. These phytochemicals, either alone and/or in combination, have tremendous therapeutic potential in curing various ailments. The respective health benefits are based on science and ethics, for health claims, for functional foods, and presence of certain phytochemicals. They play certain pharmacological effects in human health as antioxidants, antibacterial, antifungal, anti-inflammatory, anti-allergic, antispasmodic, chemopreventive, hepatoprotective, hypolipidemic, neuroprotective, hypotensive, prevent aging, diabetes, osteoporosis, DNA damage, cancer and heart diseases, induce apoptosis, diuretic, CNS stimulant, analgesic, protects from UVB-induced carcinogenesis, prevent, immuno-modulator and carminative.

Key words: Phytochemicals, nutraceuticals, antioxidants, diabetes, cancer and cardiovascular diseases.

Introduction

The term nutraceuticals, coined by Dr. Stephen de Felice**,** is derived from the words "nutrition" and "pharmaceutical", is a food or food product that provides health and medical benefits, including the prevention and treatment of disease (1). Such products may range from isolated nutrients, dietary supplements and specific diets to genetically engineered foods, herbal products, and processed foods such as cereals, soups, and beverages. A nutraceutical is demonstrated to have a physiological benefit or provide protection against chronic disease. Their bioactive ingredients, the phytochemicals, sustain or promote health and occur at the intersection of food and pharmaceutical industries. Such substances may range from isolated nutrients, dietary supplements and specific diets to genetically engineered designer foods, herbal products, processed foods and beverages (2, 3). They play a crucial role in maintaining optimal immune response, such that deficient or excessive intakes can have negative impact on health. 'Nutrigenomics' is the subsequent cutting edge in nutraceutical therapy progressing in the battle against ageing, diseases and sufferings by the availability of genomic information for humans, mice and other organisms. The interface between the nutritional environment and cellular/genetic processes is being referred as nutrigenomics (4). It provides a molecular genetic understanding of phytonutrients that affect health by altering the expression and/or structure of an individual's genetic make-up. This in turn may alter initiation, development and/or progression of specific diseases. The recent notion of **'**customized' or 'personalized' medicine and diet is being comprehensive to the field of nutrition that can be used to delay the onset of disease and to sustain optimum human health (4, 5).

Phytochemicals, are non-nutritive plant chemicals that have either defensive or disease protective properties. They are nonessential nutrients and mainly produced by plants to provide them protection. Dietary intake of phytochemicals may promote health benefits, protecting against chronic degenerative disorders, such as cancer, cardiovascular and neurodegenerative diseases. Majority of foods, such as whole grains, beans, fruits, vegetables and herbs contain phytochemicals (Table 1). Amongst these, fruits and vegetables contribute to the significant sources of phytochemicals. These phytochemicals, either alone and/or in combination, have tremendous therapeutic potential in curing various ailments. Phytochemicals with

nutraceutical properties present in food are of enormous significance due to their beneficial effects on human health since they offer protection against numerous diseases or disorders such as cancers, coronary heart disease, diabetes, high blood pressure, inflammation, microbial, viral and parasitic infections, psychotic diseases, spasmodic conditions, ulcers, etc (Figure 1).

Epidemiological and animal studies suggest that the regular consumption of fruits, vegetables and whole grains, reduces the risk of chronic diseases associated with oxidative damage (6-8). Carotenoids, tocopherols, ascorbates, lipoic acids and polyphenols are strong natural antioxidants with free radical scavenging activity. Endogenous antioxidants enzymes like super oxide dismutase (SOD), catalase, glutathione peroxidase, glutathione reductase, minerals like Se, Mn, Cu, Zn, vitamins A, C and E, carotenoids, limonoids and polyphenols exert synergistic actions in scavenging free radicals. Synthetic antioxidants such as butylated hydroxy anisole (BHA) and butylated hydroxy toulene (BHT) play a useful role in food and pharmaceutical industries (9). The natural antioxidant system is mainly classified into two categories namely *in-vitro* and *in-vivo* antioxidants.

The present review summarizes evidence for protective and health-beneficial effects of phytochemicals, which have the potential of being incorporated into foods or food supplements as nutraceuticals, or into pharmaceuticals, and to propose implications of the explosion in information for the future development, discovery and use of phytochemicals as nutraceuticals. A nutraceutical is any non-toxic food extract supplement that has scientifically confirmed health benefits for both disease treatment and prevention.

The protective effects of fruits and vegetables are manifested for cancers of the esophagus, lung, oral cavity, pharynx and stomach, endometrium, pancreas and colon. Among the phytonutrients mentioned as potentially providing the fortification are polyphenols, flavonoids, isoflavonoids, anthocyanidins, phytoestrogens, terpenoids, carotenoids, limonoids, phytosterols, glucosinolates and fibers.

Phytochemicals and Their Health Benefits

Polyphenols: Epidemiological studies provide convincing evidence that diet rich in antioxidants is associated with a lower incidence of

degenerative diseases. The major sources of dietary polyphenols are cereals, legumes (barley, corn, nuts, oats, rice, sorghum, wheat, beans, and pulses), oilseeds (rapeseed, canola, flaxseed and olive seeds), fruits, vegetables and beverages (fruit juices, tea, coffee, cocoa, beer and wine) (6, 8, 10-12). Fruits such as apple, grape, pear, cherry and various berries contain up to 200-300 mg polyphenols per 100g fresh weights.

Table 1: Phytochemicals of nutraceutical importance, their source and health benefits.

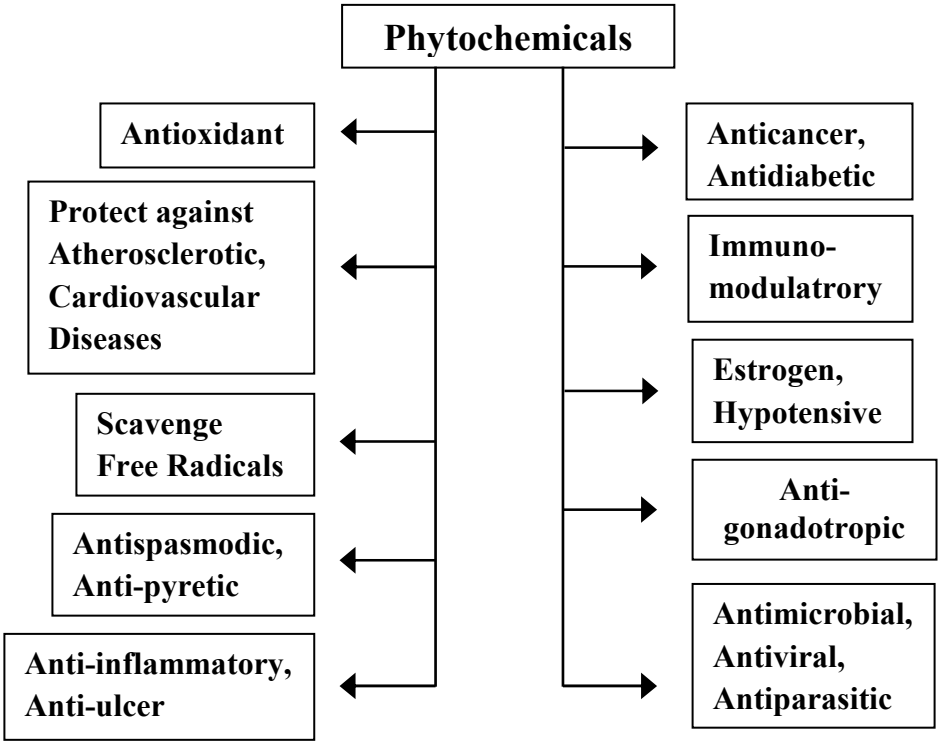
Phytochemicals	Source Plant	Health Benefits
α-linolenicacid (ALA)	Flax seeds	Cancer preventive, reduce risk of coronary heart disease
Allicin	Onion, garlic	Hypolipidemic, antifungal, antibacterial, anticancer, anti-inflammatory, chemopreventive, hepatoprotective, neuroprotective, hypotensive
Anthocyanins	Cherry, red grape, purple corn, raspberry, blackberry, Orange	Antioxidants and pigments, anti-inflammatory, anti-allergic
Apigenin	Apple, artichoke, basil, grape, celery, parsley, nuts, cherry	Chemopreventive, anti-inflammatory, antispasmodic, antioxidant, induce apoptosis, inhibits breast and ovarian cancer
Catechins	Tea	Diuretic, CNS stimulant, antioxidant
Curcumin	Turmeric	Antihypertensive, anti-inflammatory, antioxidant, cancer preventive
Diosgenin	Fenugreek seeds	Hypolipidemic
Ellagic acid	Grapes, strawberry, pecans, cranberry, raspberry, pomegranates,	Antioxidant, anticancer

	walnuts	
Lycopene	Tomato, tomato products, apricot, papaya, pink guava, watermelon	Lowers risk of prostate cancer and atherosclerosis
Momorbicin	Karela (Bitter gourd)	Antidiabetic
Myristicin	Nutmeg	Hypolipidemic
Piperine	Pepper	Aeromatic, stomachic, analgesic, hepatoprotective
Resveratrol	Red grapes, blueberry, red wine, peanuts	Antioxidant, prevent aging, diabetes, cancer and heart diseases
Silymarin	Milk thistle (*Silybum marianum*)	Protects from UVB-induced carcinogenesis, hepatoprotective
Stigmasterol	Soybean	Anticancer, hypolipidemic, prevention of osteoporosis
Sulforaphane, Glucosinolates	Cruciferous vegetables, cabbage, cauliflower, broccoli sprouts, kale, collards, turnip, radish	Antioxidant, reduce risk of breast and prostate cancer, prevent DNA damage
Ursolic acid	Apple, basil, cranberry, rosemary, lavender, oregano	Anti-inflammatory, antitumor, antimicrobial
Withaferin, Withanolides	*Withania somnifera*	Anticancer, immuno-modulator
Zingiberene	Ginger	Carminative, antibacterial, antifungal, treatment of dizziness

Similarly, a glass of red wine or a cup of coffee or tea contains about 100 mg polyphenols. Their total dietary intake may be about 1g per day, which is about 10 times higher than that of vitamin C and 100 times higher than those of vitamin E and carotenoids (6, 13).The chief constituent of tea polyphenols are flavonols (catechin, epicatechin, catechingallate and epigallocatechingallate), flavanols (quercetin, kaempferol and their glycosides), flavones (vitexin, isovintexin) and phenolic acids (gallic acid, chlorogenic acid). They constitute up to

30% of the dry weight of green leaves and 9-10% of the dry weight of black tea leaves. Ferulic acid is associated with dietary fiber linked with hemi cellulose of the cell wall by means of ester bonds. Caffeic acid in the form of caffeoyl esters and coumaric acids are common in apples, pears, and grapes. Additionally, apples and pears are rich in chlorogenic acid and grapes in gallic acid. Apples contain high levels of quercetin among fruits. Grain-derived products are especially significant in human diet as they have higher concentration of phenolic acids in the outer layers of kernel that constitute the bran. Most of the phenolic acid derivatives are hydrolysable tannins and are usually esterified with glucose. Citrus fruits are major sources of flavonones and hesperidin is found in abundance (120-250 mg/lit) in orange juice.

Figure 1: Some important therapeutic properties of phytochemicals



Quercetin occurs in its glycosylated form as rutin in fruits, vegetables and particularly onions are its rich source (14-16). Anthocyanins are pigments of fruits such as cherries, plums, strawberries, raspberries,

black berries and red currant (Table 1) and their content varies from 0.15 to 4.5 mg/g in fresh berries.

Occurrence of some of the flavonoids is restricted to a few foodstuffs like the main source of isoflavonoids is soy, which contain ~1mg/g of genistein and daidzein and have received considerable attention due to their suggested role in prevention of cancer and osteoporosis. People who consume traditional diets rich in soy and tea rarely experience breast, uterus and prostate cancer. Although there are a range of potentially antimutagenic fruits, vegetables and cereals but their intake is generally below the level essential to protect from various mutagens (17, 18). Extracts from *Silybum marianum* have been used for centuries in folk medicine for the treatment of liver disorders. Silibinin, the main flavolignan occurring in the flavonoids mixture silymarin of this plant had shown positive effect on liver. Besides being hepatoprotective, silibinin has been extensively evidenced to induce apoptosis, reduce and/or inhibit cell proliferation and tumor angiogenesis in human lung, bladder and prostate cancer models (19-23). Kolaviron from seeds of the *Garcinia kolu* and hispidulin from *Buccuris frimeru* have also been reported as hepatoprotective (7, 24).

Plant polyphenols are secondary metabolites that are broadly distributed in higher plants. Their unique characteristics are: water solubility, intermolecular complexation and antioxidant properties. They are classified as condensed proanthocyanidins, galloyl and hexahydroxydiphenoyl esters and derivatives, or tannins. Polyphenols historically have been considered as anti-nutrients by nutritionists, because some, e.g. tannins, have adverse effects such as decreasing the activities of digestive enzymes, energy, protein and amino acid availabilities, mineral uptake and having other toxic effects. Detection of the antioxidant activities of many polyphenols has reunited opinion toward the health benefits provided by many of these compounds. The most important dietary phenolics are the phenolic acids (including hydroxybenzoic and hydroxycinnamic acids), polyphenols (hydrolysable and condensed tannins) and flavonoids, the latter being the most studied group. Phenols protect plants from oxidative damage. They have also been studied extensively as antioxidant protectants for human beings and play beneficial role in reducing the risk of coronary heart disease, diabetes, hypertension and some types of cancer (25-29).

Flavonoids: These are subclasses of phenols and include the minor flavonoids (flavanones and dihydroflavonols), flavones and flavonols. Among the biological activities of flavonoids are active against free radicals, free radical mediated cellular signaling, inflammation, allergies, platelet aggregation, microbes, ulcers, viruses and tumors and hepatotoxins. Proposed mechanisms by which they provide health benefits, in addition to being direct chemical protectants, involve modulatory effects on a variety of metabolic and signaling enzymes. Flavonoids have been shown to block the angiotensin converting enzyme (ACE) that raises blood pressure; they inhibit cyclooxygenase, which forms prostaglandins; and they block enzymes that produce estrogen. The implications of these in vitro inhibitory actions are that certain flavonoids could prevent platelet aggregation, reducing heart disease and thrombosis; and inhibit estrogen synthase, which binds estrogen to receptors in several tissues, thus decreasing the risk of estrogen related cancers. The major sources of flavonids intake are tea (61%), onions (13%) and apples (10%). There is inverse association between flavonoid intake and coronary heart disease mortality. Flavonoids in regularly consumed foods appeared to reduce the risk of death from coronary heart disease. Whereas flavonoid intake has been associated with reduced risk of death from coronary heart disease some flavonoids have been reported to be mutagenic as well (30).

Luteolin has anti-inflammatory, antimutagenic and antibacterial activities. Apigenin suppressed 12-O-tetradecanoylphorbol-3-acetate (TPA)-mediated tumor promotion of mouse skin, similar to curcumin, a dietary pigmented polyphenol, possibly through suppression of protein kinase C activity and nuclear oncogene expression. Apigenin is antibacterial, anti-inflammatory, diuretic, hypotensive, and also promotes smooth muscle relaxation. Myricetin, a hexahydroxyflavone, exhibits antibacterial activity and has anti-gonadotropic activity, but apparently is not a mutagen. The flavonol kaempferol, which is widely found in the diet, has anti-inflammatory and antibacterial activities and is directly mutagenic. Quercetin, the most common flavonoid in higher plants, seems to contribute to the mutagenicity of kaempferol in the presence of microsomal metabolizing systems. Quercetin inhibits a number of enzymes, inhibits smooth muscle contraction and proliferation of rat lymphocytes. Although it is anti-inflammatory, antibacterial, antiviral and anti-hepatotoxic, it exhibits mutagenic activity and allergenic properties (31). Catechins and gallic acids, major

sources of catechins are grapes, berries, cocoa and green tea. Tea contains considerable amounts of gallic acid esters, such as epicatechin, epicatechingallate and epigallocatechingallate (EGCG). Numerous studies have suggested that these components provide protective benefits by their free radical scavenging ability and their inhibition of eicosanoid synthesis and platelet aggregation. The green tea provides protection against prostate cancer (32). In wines, catechins and procyanidins are involved in the astringency sensation. Catechin is one of the major phenolics in grapes and red wines, and it is considered to be responsible for part of the protective effect of red wine against atherosclerotic cardiovascular disease.

Isoflavonoids: They are another subclass of the phenolic phytonutrients. Soybeans are an unusually concentrated source of isoflavones, including genistein and daidzein, and soy is the major source of dietary isoflavones. The isoflavones of soy have received considerable attention owing to their binding to the estrogen receptor class of compounds, thus representing an activity of a number of phytochemicals termed phytoestrogens. Genistein inhibits the growth of most hormone-dependent and independent cancer cells in vitro, including colonic cancer cells. Isoflavones have received considerable attention as potentially preventing and treating cancer and osteoporosis (33). In mice, dietary soybean components inhibited the growth of experimental prostate cancer and altered tumor biomarkers associated with angiogenesis. Although the epidemiological data suggest that soy potentially decreases the risk of breast and prostate cancer yet the evidence that soy exerts a protective effect against colonic cancer is limited. Exciting mechanistic results that emerged recently showed that the isoflavone genistein from soy selectively bound the beta-estrogen receptor and reduced binding to the alpha-receptor 20-fold.

Anthocyanidins: These are water-soluble flavonoids that are aglycones of anthocyanins. These compounds are among the principal pigments in fruits and flowers (34). The color of these pigments is influenced by pH and metal ion complexes. The flavonoids, anthocyanidins are .antioxidants *in vitro*, and might be expected to have antioxidative and anti-mutagenic properties *in vivo*. They have been found potent antioxidant activity for isolated anthocyanidins (aglycons and glycosides) and complex plant samples in the ferric reducing ability

assay, these compounds did not prevent hydrogen peroxide-induced oxidation of DNA bases in HT29 clone 19A cells.

Phytoestrogens: These are non-steroidal phytochemicals quite similar in structure and function to gonadal estrogen hormone. They offer an alternative therapy for hormone replacement therapy (HRT) with beneficial effects on cardiovascular system and may even alleviate menopausal symptoms. They are potential alternatives to the synthetic selective estrogen receptor modulators (SERMs), which are currently applied in HRT. They have antioxidant effects due to their polyphenolic nature, anti-carcinogenic, modulation of steroid metabolism or of detoxification enzymes, interference with calcium-transport and favorable effects on lipid and lipoprotein profiles (35, 36). On the basis of chemical structure phytoestrogens can be classified as flavonoids, isoflavonoids, coumestans, stilbenes, and lignans. They occur in either plants or their seeds. Soybean is rich in isoflavones, whereas the soy sprout is a potent source of coumestrol, the major coumestan.

Flavonoids have similar structure to estrogen and have the capacity to exert both estrogenic and anti-estrogenic effects and provide possible protection against bone loss and heart diseases. The precursors of these substances are widespread in the plant kingdom, but mainly found in Leguminosae and are especially abundant in soybean and its products, legumes, berries, whole-grains and cereals. They share structural features with estrogen, in the sense that the presence of particular hydroxyl groups that can be positioned in a stereo chemical alignment virtually identical to one of the estrogen. Populations in China, Japan, Taiwan and Korea are estimated to consume high quantities of isoflavones and women of these countries complain fewer incidences of osteoporosis and related health problems, especially hot flushes, cardiovascular diseases, lower incidence of hormone dependent breast and uterine cancer (37-39). The main dietary source of phytoestrogenic stilbenes is resveratrol from red wine and peanuts. Although there are two isomers of resveratrol, *cis* and *trans*, but only the *trans* form has been reported to be estrogenic. It is found only in the skin of red grapes, in green grapes and white wine very low levels of *trans*-resveratrol are found (40). The main dietary sources of coumestans are sprouted legumes such as soy, and alfalfa; however low levels have been reported in brussel sprouts and spinach. Clover and soybean

sprouts are reported to have its highest concentration (Table 2). The term lignan is used for a diverse class of phenylpropanoid dimers and oligomers. Secoisolariciresinol and matairesinol are two lignan dimers which are not estrogenic by themselves, but readily convert to the mammalian lignans, enterodiol and enterolactone, respectively, which are estrogenic. These are of great interest because of their estrogenic, anticarcinogenic, antiviral, antifungal and antioxidant activities (41).

Table 2: Phytoesterogen contents (μg/g) of some commonly used foods.

Sources	**Isoflavones**	**Sources**	**Resveratrol**	**Sources**	**Lignans**
Soy	610-2440	Wine	0.32-15.35	Flaxseed	348-1140
Ground-nut	3.5-8.4	Peanut butter	0.02-0.98	Lentils	19.6
Green Tea	2.34	Peanuts	0.03-0.073	Carrot	29.3
Black gram	6.4-12.6	Green grapes	0.02-0.32	Cabbage	18.6
Red gram	2-5.6	Black grapes	0.95-1.87	Cauli-flower	16.2
Lentil	0.23-0.4	Raisins	0.003-0.01	Onion	10.3

The phytolignans are found in high amounts in flaxseed, asparagus, whole grains, vegetables, and tea. Fruits also have their low levels with the exception of strawberries and cranberries (Table 2). In humans, after consumption of plants rich in isoflavones and lignans, enzymatic metabolic conversions occur in the gut, by micro flora and the mammalian lignans are readily absorbed (42).

Terpenoids: The terpenes, also known as isoprenoids, are the largest class of phytonutrients in green foods, and grains. Their importance to plants relates to their necessity to fix carbon through photosynthetic reactions using photosensitizing pigments. Animals have evolved to utilize these compounds for hormonal and growth regulatory functions (vitamin A) and, as it is now being understood, the presence of these molecules in animal tissues also provides a measure of protection from certain diseases, especially those related to chronic damage and growth dysregulation. Terpenes have a unique antioxidant activity in their

interaction with free radicals. They react with free radicals by partitioning themselves into fatty membranes by virtue of their long carbon side chain. The most studied terpene antioxidants are the tocotrienols and tocopherols. They are found naturally in whole grains and have effects on cancer cells. The tocotrienols are effective apoptotic inducers for human breast cancer cells. The impact of a diet of fruits, vegetables and grains on reduction of cancer risk may be explained by the actions of terpenes *in vivo* (12, 31, 43).

Carotenoids: They are highly pigmented, yellow, orange and red, are present in fruits and vegetables, and when consumed by birds are incorporated into the yolk of eggs. Carotenoids comprise two types of molecules, carotenes and xanthophylls. Carotenes are tissue specific in their biological activity and beta-carotene has vitamin A activity. Beta-carotene, lycopene and lutein, protect against uterine, prostate, breast, colorectal and lung cancers. They may also protect against risk of digestive tract cancer. The xanthophyll types of carotenoids offer protection to other antioxidants, and they may exhibit tissue specific protection. Zeaxanthin, cryoptoxanthin and astaxanthin are members of the xanthophyll group (18, 44).

Limonoids: These are terpenes present in citrus fruit. They provide chemotherapeutic activity by inhibiting Phase I enzymes and inducing Phase II detoxification enzymes in the liver. D-Limonene, the commonest monocyclic monoterpene, found within orange peel oil, inhibits pancreatic carcinogenesis induced in experimental models and also provides protection to lung tissue (18, 44).

Phytosterols: These are another important terpene subclass. Two sterol molecules that are synthesized by plants are beta-sitosterol and its glycoside. In animals, these two molecules exhibit anti-inflammatory, anti-neoplastic, anti-pyretic and immuno-modulating activity. Phytosterols were reported to block inflammatory enzymes, for example by modifying the prostaglandin pathways in a way that protected platelets. Phytosterols compete with cholesterol in the intestine for uptake, and aid in the elimination of cholesterol from the body. Saturated phytosterols appear to be more effective than unsaturated compounds in decreasing cholesterol concentrations in the body. Their actions reduce serum or plasma total cholesterol and low-density lipoprotein (LDL) cholesterol. Competition with cholesterol for

absorption from the intestine is not unexpected as the structure of plant sterols is similar to that of cholesterol. In mammals, concentrations of plasma phytosterol are low because of their poor absorption from the intestine and their faster excretion from liver, and metabolism to bile acids, compared with cholesterol (17).

Glucosinolates: They are present in cruciferous vegetables, are activators of liver detoxification enzymes. Consumption of cruciferous vegetables offers a phytochemical strategy for providing protection against carcinogenesis, mutagenesis and other forms of toxicity of electrophiles and reactive forms of oxygen. The sprouts of certain crucifers, including broccoli and cauliflower, contain higher amounts of glucoraphanin (the glucosinolate of sulforaphane) than do the corresponding mature plants. Crucifer sprouts may protect against the risk of cancer more effectively than the same quantity of mature vegetables of the same variety (45, 46). The mechanism of the protective effects is thought to involve the modulation of carcinogen metabolism by the induction of Phase 2 detoxification enzymes and inhibition of Phase 1 carcinogen-activating enzymes, thereby possibly influencing several processes related to chemical carcinogenesis, e.g. the metabolism, DNA binding and mutagenic activity of promutagens. A reducing effect on tumor formation has been shown in rats and mice, and studies carried out in humans using high but realistic human consumption amounts of indoles and brassica vegetables have shown putative positive effects on health. Indole-3-carbinol is a glucosinolate metabolite that inhibits organ-site carcinogenesis in rodent models. Its preventive effect on human mammary carcinogenesis may be due in part to its ability to regulate cell cycle progression, increase the formation of anti-proliferative estradiol metabolite and induce cellular apoptosis (17, 45, 46).

Fibers: Although dietary meat and fat intake have a positive relation to the incidence of colon cancer, dietary fiber has been associated with alterations of the colonic environment that protect against colorectal diseases. Fiber may also provide protection by increasing fecal bulk, which dilutes the increased colonic bile acid concentrations that occur with a high-fat diet. Short chain fatty acids, including butyric acid, and dietary sugar beet fiber also suppress cholesterol synthesis in a rat liver and intestine model. Different dietary fibers have markedly diverse cancer protective effects, and that the differences may be related to the

differential bacterial fermentation of fiber in the colon to short-chain fatty acids, especially butyric acid. Butyric acid induces growth arrest, differentiation and apoptosis of colonic epithelial cells and tumor cells in vitro. Butyric acid in the colon also appears to influence the ongoing process of apoptosis within the mucosa. The potential for fermentation of fiber to butyric acid and its derivatives is of substantial interest. Its enrichment through food products, such as fiber and starch, may emerge as a molecular-based strategy that provides significant health benefits (13, 17).

Role of Phytochemicals in Health and Diseases

The rapid growths of apparent health foods, now frequently defined by the industry as nutraceuticals, have enormously impacted the consumers. They are now expending billions of dollars each year for the purchase of health-related foods and supplements. The respective health benefits are based on science and ethics, for health claims for functional foods, and presence of certain phytochemicals (Figure 1). They are constituents of plants and have certain pharmacological and/or physiological effects in the ethnomedical treatment of various disorders. Traditionally, natural plant products have been the source for the search for new drugs, by pharmaceutical companies. Phytochemicals play important role in human health as antioxidants, antibacterial, antifungal, anti-inflammatory, anti-allergic, antispasmodic, chemopreventive, hepatoprotective, hypolipidemic, neuroprotective, hypotensive, prevent aging, diabetes, osteoporosis, cancer and heart diseases, induce apoptosis, diuretic, CNS stimulant, analgesic, protects from UVB-induced carcinogenesis, immuno-modulator and carminative (13, 17, 31).

Capsaicin, the pungent ingredient present in red pepper and ginger, has anti-carcinogenic and anti-mutagenic effects. In humans, curcumin, another polyphenolic phytochemical, acts as an anti-inflammatory and cancer preventive drug. Tumor volumes in mice treated with genistein, dietary soy phytochemical concentrate, at 1%, or dietary soy protein isolate were decreased 40, 48 or 37%, respectively as compared with the controls. Genistein (5,7,4'-trihydroxyisoflavone) is one of two major isoflavonoids in soy. In human breast cancer cells in culture, genistein has anti-proliferative effects on mitogen-stimulated growth

(47, 48). Soy isoflavonoid conjugates have chemopreventive activity in carcinogen induced rat models of breast cancer.

Osteoporosis is related to multiple factors including aging, hormone deficiency and diet. Most of the studies suggest that phytoestrogens are somewhat effective in maintaining bone mineral density (BMD) in postmenopausal women and to alleviate the osteoporosis and associated disorders. Evidence from several human studies demonstrates that certain dietary phytoestrogens can produce estrogenic effects in the postmenopausal women, including estrogen-like effects on vaginal cytology and reductions in hot flushes. In postmenopausal women, cardiovascular diseases (CVDs) are one of the leading causes of death in United States and Europe. Isoflavonoids or soy products/soy protein and flaxseed have the ability to lower total and LDL cholesterols and raise HDL cholesterol resulting in reduced risk of CVDs. There is evidence to support the hypothesis that phytoestrogen consumption contributes to the lower incidence of CVDs in Asian countries and in vegetarians and that they may also be cardio protective (35, 49, 50).

A large number of epidemiological studies had shown that people who consume high amounts of isoflavonoids (phytoestrogens) in their diets have lower incidences of various types of cancers including breast, prostate and colon cancer. A high plasma concentration of the mammalian lignan, enterolactone, is correlated with a reduced risk of breast cancer. Similar correlations have also been found between dietary intakes of isoflavonoids and lignans and thyroid, ovarian, and breast cancers in pre- and postmenopausal women. The incidence of hormone dependent tumors is lower in Asia and Eastern Europe where consumption of phytoestrogens is higher than western countries and amongst vegetarians. Breast, ovarian, prostate, and colon cancer show a negative correlation with phytoestrogen intake when compared with mortality rates due to cancer. The epidemiological, animal, and cell-line data suggest that phytoestrogens may play a protective role against the development of prostate and breast cancer. It has been reported that increased consumption of beans, lentils and peas, tomatoes, and dried fruits was associated with significantly decreased prostate cancer risk (35, 49, 50).

Diets rich in phytonutrients may supply a variety of phytoestrogens such as isoflavones, resveratrol, lignans etc, capable of producing a

range of pharmacological effects. In females, life is affected by a variety of estrogen-related conditions such as osteoporosis, cognitive and cardiovascular decline, increased risk of breast cancer and other symptoms that decrease the overall quality of life. Phytoestrogens appear to have physiological effects in humans, with the most supportive data being related to the effects of soy protein supplements on lipids and lipoproteins and on vascular function. Therefore, postmenopausal women who have the greatest breast cancer risk should be encouraged to increase their phytoestrogen intake (35, 49, 50).

Conclusions

The use medicinal plants by indigenous people to treat different ailments has a long history, very recently the scientific data supported nutritional and medical importance of phytonutrients/phytochemicals for the prevention and treatment of several diseases. The `novel' nutraceuticals of plant origin may evolve to be considered a vital aspect of dietary disease-preventive food components. Careful studies are necessary on the various phytochemicals for their roles in the prevention of chronic degenerative diseases. The resurgence of interest in these compounds will eventually lead to needed information on structure-function relationships.

The ever-widening choice of food ingredients makes it possible for food designers to provide food choices that meet the public's expressed desire for healthy food. Other aspects of determining the role of phytochemicals in functional foods include consumer attitudes, any competitive advantage for manufacturers producing functional foods and identification of those areas of research needed to produce foods with the desired health effects. The future of nutraceuticals of both plant and animal origin holds exciting opportunities for the food industry to create novel food products. The food industry will need to persuade investors of the potential for monetary rewards to be gained by investing in the value of nutraceuticals, and it will need to market the products so as to capture the interest of and, perhaps most important, to please the tastes of consumers.

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