



Health Promoting Properties of Phytochemicals

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ABSTRACT

Phytochemicals are heterogeneous group of bioactive compounds produced by plants, which are extensively researched by scientists for their health-promoting potentials in humans. Unlike vitamins and minerals, phytochemicals are not required for sustaining cell viability, but they play an important role in protecting tissues and cells from the harmful effects of oxidative stress and neuroinflammation-mediated changes. In addition, phytochemicals also stimulate detoxification enzymes, immune and hormonal response in humans who consume colored edible fruits, plants, vegetables, and herbs. Because plant-based foods are complex mixtures of bioactive compounds, information on the potential health effects of individual phytochemicals is linked to information on the health effects of foods that contain those phytochemicals. Examples of phytochemicals include flavonoids, catechins, resveratrol, ginkgo biloba, and sulfur compounds found in garlic. Plants produce phytochemicals and store them in vulnerable regions (the skin, seeds, and leaves) in order to discourage insects and other organisms from eating and killing the plant. In addition, phytochemicals also function in chemical defense against environmental stress and contribute to repair wound healing process in the plant.

Key Words: Phytochemicals; Carotenoids; Human health; Oxidative stress; Chronic diseases; Antioxidants.

INTRODUCTION

The foods providing the health benefits have been the leading trend in human diet and in the food industry since the last decade of the past century. Nutritional research providing clues regarding how foods or their supplements have the ability to optimize health and control diseases have indeed shown a road map to fight against diseases. In view of its medicinal synergy, economical status and no side effects, the nutraceutical, functional or health foods have gained a wide interest during the last few decades¹. International acceptance and recognition of nutraceutical foods in modern global treatment has triggered rapid research on this subject, resulting in a huge volume of literature. Cereal brans were probably the first nutraceutical foods introduced in 1984 claiming the chemo preventive benefits of dietary fibers against colon cancer. Nutritional Labeling and Education Act (NLEA) in 1990 has triggered the productivity of processed and semi processed nutraceutical foods. The present paper reviews the recent-research in nutraceutical foods and nutritional immunity which is an emerging field with promising applications in food industries.

IMMUNO-NUTRITION

Present century is the century of nutraceutical foods rich in bioactive and the immune-modulating components that govern human health. The human defensive mechanism is

based on the immune response which is composed of various cells and is a highly organized, complex and prompt system to perform molecular disintegration of any of the invading organisms. It needs constant supply of nutrients or phytochemicals through diet for its survival and functioning. The immune suppression caused by the inflammatory response against foreign attack is an integral act of immune function. The diet therapy or the supply of active components through diet is essential for recovery from suppression. The studies in human have demonstrated that dietary fat and immune system are closely related. Cholesterol and fatty acids (depending on type of fatty acids) located at the cell membrane regulate microviscosity at membrane level that govern many reactions including enzymatic conversions such as those by the phospholipases and cyclooxygenases. It has been documented that excess fat decreases the immune response and high fat-diet is generally immunosuppressive. Nutritional support also includes other phytochemicals such as the carotenoids, flavonoids, catechins, curcuminoids, tannins and fibers. Other fatty acids as n-6 FA, γ -linolenic acid (GLA), α -linolenic acid (ALA) and conjugated linolenic acid (CLA) are vital for healing of multiple organ failure in critical illness in form of parenteral or enteral nutrition^{2,3}. The variety of functional foods are getting popularity which has motivated their commercialization in the developed part of the world⁴, although natural resources are more abundant in under

developed countries. It seems logical to discuss some of the components of foods identified as immuno nutrients and then their relative presence in food systems which designate the commodities as the immuno-modulating foods such as the vegetables, fruits, nuts, cereals and spices.

FAT-REPLACEMENT AND LOW CALORIES FOODS

The awareness of health benefits of using low fat (reduced calories) foods is increased recently especially among the weight conscious public, however consumer's acceptability of such foods is not at par as their full-fat-counter parts. Presently, three types of fat replacers are used, that is, fat, carbohydrate or the protein –based fat substituents⁵. Carbohydrate based fat substitutes are most widely used group because of their functional behaviors as thickening, bulking, pasting, agents etc. Carbohydrates as gum, pectins, cellulose etc form hydrocolloids and improve viscosity and texture of the products⁶. Starches, modified starches, resistant starches are found to be the good fat replacers. Maltodextrin, dextrin polydextrose, insulin and fibers are also used for the fat replacements^{4,5}. Carbohydrate and protein based fat substitutes are common in variety of foods such as the bakery/meat products, mayonnaise, cheese spread, butter, margarine etc. Proteins, in view of their functional properties as the emulsifying, foaming, gelling and water absorption are competent enough for replacing the fat in variety of food systems. Fat-based-fat replacers are close to the fat, being esters of the fatty acids. These are lipid analogs and are of the two types which differ in their caloric contributions. The first types are low caloric fat consisting of fatty acids of short carbon chain, thus providing fewer calories and the second types consisting of sucrose or some monosaccharides to replace the glycerol back bone for holding the fatty acids. They have the advantage of not being hydrolysed by human lipases and so provide zero calories.

CAROTENOIDS AND CURCUMINOIDS

The dietary pattern is changing rapidly world over and plant foods are getting the due importance in view of the information based on epidemiological surveys including that of "Seven Countries Studies"⁷. The putative protective function of carotenoids is associated with its action of scavenging free radicals or as antioxidants that terminates the lipid peroxidation. Carotenoids are exclusive in structure by possessing multiple conjugated double bonds which reduce ROS (reactive oxygen species). The dietary carotenoids as β -carotene, lycopene and luteins circulate in blood in a concentration of 0-8 $\mu\text{mol/L}$ and their carrier molecules are lipoproteins. It has been reported that monocytes present in blood when they come in contact with carotenoids rich lipoprotein (0.2-1.1 nmol/mg of cell) get enriched with carotenoids which alter their functions. The monocytes derived macrophages were inhibited in proliferation by all the three carotenoids and lycopene increased ROS to the same extent as by PMA which indicates self differentiation^{1,8}. Both provitamin A carotenoids such as α , β -carotene, zeaxanthin and non protein A (NPA) carotenoids such as lutein, canthaxanthin, astaxanthin and lycopene are equally competent to modulate immune functions and thus resist the infection. NPA often are more effective like lycopene, the major carotenoid present in serum (50% of the total carotenoids) and other

tissues that modulates hormonal and immune system in the most effective way. It activates the intercellular gap junction communication. An inverse ratio between serum lycopene and inflammatory diseases has been reported specially periodontitis which is a chronic inflammation of teeth².

Curcumin (1, 7-bis (4-hydroxy-3-methoxy phenyl)-1-6-hepatadine-3-5-dione) a member of curcuminoid family represents one of the yellow pigments isolated from turmeric. Turmeric is the dried rhizome of plant *Curcuma longa* and apart from its culinary appeal and common use as the spice, it is well known for its medicinal properties in Egyptian and Indian culture for more than 6000 year ago. Its immunomodulatory properties including anti-oxidant, anti-inflammatory and anti-tumor properties are well documented³. The curcumin reduces nitric oxide (NO) and exerts beneficial effects in experimental colitis; therefore inflammatory bowel diseases (IBD) due to the oxidative and nitrosative stresses are treated by this yellow pigment^{2,7}. Recently the immune-nutritional ability of curcumin demonstrating its active role in treatment of the allergic response has been highlighted in a review⁹.

FLAVONOIDS IN IMMUNE RESPONSE

Spencer in 2007, while reviewing the flavonoid's interactions involved in neuronal signaling has pointed out their ability in protection of neurons against stress-induced injury by suppressing neuroinflammation and enhancing cognitive activity as synaptic plasticity memory.

Flavonoids are the largest class of polyphenols with a common carbon skeleton of diphenyl propane (C6-C3-C6) representing two benzene rings joined through three carbon atoms. More than 4000 flavonoids are identified in fruits, vegetables, nuts, cereals, legumes, spices, tea and coffee. These polyphenolic compounds are further classified into flavonols, flavones, isoflavonones, flavonones, flavanes, flavanols and catechins depending on slight structural variations in the number and positions of –OH groups or the presence of ketonic group in the middle ring. The health benefits of flavonoids are related to their antioxidant capacity apart from their many other interactions.

The oxidized LDLs are recognized by macro-phages through their accepters and cholesteryl esters and are then transferred to monocytes/macro-phages forming foam cells which accumulate in sub endothelial spaces to create atheromatous lesions called atherosclerosis. Flavonoids inhibit the oxidation of LDLs involving variety of mechanisms such as the direct scavenging of ROS and inhibiting peroxynitrite formation which may affect cellular integrity by reversible oxidation of LDLs. Peroxynitrite is formed as a result of the reaction of nitric oxide (NO) and the free radicals. The polyphenols of green tea are found as (-) epicatechin,

(-) epicatechin-3-gallate, (-) epigallocatechin and (-) epigallocatechin-3-gallate while theaflavin and thearubigin are found in black tea, which are able to reduce the risk of cancer, CHD and inflammations^{10,11}. A review has recently been published on nutritional protection ability of flavonoids against oxidative burst and UV induced cellular damage¹².

ROLE OF VEGETABLES AND FRUITS IN IMMUNE SYSTEM

The phytochemicals especially polyphenolic compounds as catechins from tea and resveratrol in lipid rich extracts have sparked potential interest in chemopreventive agents that

have been isolated and identified in apple, citrus fruits, guava, berries etc. The oxidative cellular damage has been inhibited in low density lipoproteins (LDLs) and other oxygen species. The bioactive phytochemicals from cranberry for its *in vitro* anti-cancer activity. Some of the phytochemicals are unique in controlling a variety of disorders through antinitrosation, inhibiting DNA adducts and biosynthesis and facilitating the activity of protective enzymes as glutathione transferase¹³. Recently new techniques have been introduced to map enzymes that mediate alterations in DNA or its protein conjugates localized in chromatin through its immune precipitation and DNA microarrays. These tools will provide the excellent opportunities to identify the bioactive components in foods such as folate, biotin, niacin, catechins and flavonoids acting as anticancer nutraceuticals¹⁴. The extract from guava (*Psidium guajava* L.) leaves is strongly protective against complications in diabetes because it prevents the protein glycation. Hyperglycemia provides the opportunity for protein-carbohydrate interactions to generate early and advanced glycation end products (AGEs) responsible for diabetic complications¹⁵.

The vegetables consumed individually or in mixed form are known for their protective role in chronic diseases as they are able to minimize ROS and other inflammatory biomarkers^{2,4}. The immune modulatory effect of foods at various cellular, subcellular and molecular levels are well studied. Phorbol myristate acid (PMA) ester and zymosan are used for producing respiratory burst *in vitro* study to evaluate the capacity of granulocytes of leukemia for cytotoxic activity for their defense¹⁶.

The plasma carotenoid concentration was found to be increased by regular intake of fruit and vegetable in the form of liquid diet such as soup or other beverages which were effective in reducing homocysteine in blood. The old concept of "heating" and "cooling foods" shows some scientific connotations and fruits/vegetables consisting of a large amount of water are diuretic or "cooling" while cereals, fats and oils consisting less water are antiuretic or "heating". This may not always be true as litchi and longan are 'heating' fruits as they enhance Cox-2 proteins which increase PGE2 synthesis by the specified macrophages PGE2, an inter and intra-cellular messenger is a major prostaglandin and is pro-inflammatory compound produced in response to cytokines and lipopolysaccharides (LPS) acting as important intrinsic and extrinsic factors respectively to activate Cox-2 present in macrophages^{7,17}.

ANTIOXIDANT ACTIVITY

The cardio protective properties of local food nutraceuticals such as wild artichoke and thyme increase nitric oxide (NO) production by stimulating endothelial cells. They control vascular functions by scavenging ROS especially HOCL which promote cardiovascular damage. HOCL oxidizes apoB which is taken up by macrophages; also HOCL present in LDL is responsible for loss of tryptophan and lysine in apoB that may be replaced by the plant extracts mentioned above¹⁸.

In general, vegetables are rated high in possessing antioxidant activity (AOA) which is a strong tool to detoxify ROS and to control the respiratory burst. However, a single component is hardly identified and a limited amount of phytochemicals are related to fight the infections.

The phenolic antioxidant index (PAI) and bioactivity index (BI) have been introduced to help consumers for the selection of appropriate vegetables with high health benefits. The BI is half of the sum of total AOA score and anti-proliferative activity score (AAS) against liver cancer cells. The BI for other diseases will be different and similarly may be determined for other vegetables. Dietary plants vary widely in their antioxidant contents (AOC) and a difference of 0-1000 times may be expected, however AOC is a reliable yard stick to evaluate the healing power of the edible plants against certain diseases¹⁹.

Berries are known as a rich source of AOC and facilitate the immune response as mice receiving the wolf-berry in the parenteral nutrition form, were found to have the increased spleen weight. Generally increase in number of macrophages in blood is not a healthy sign but their large number in phagocytic cell is a strong defense in view of the fact that they are predominant in spleen phagocytes^{1,20}. However, more research is needed to explain the facts. Some of the vitamins are potent antioxidants such as C, E and A or its precursors the β -carotenes, out of these vitamins C is hydrophilic and scavenges variety of ROS which if not interrupted stimulate endothelial dysfunction²¹. The impact of adverse function of endothelial cells also includes imbalance secretion of chemicals that regulate vasodilation. Nitric oxide (NO) is one of these secretory chemicals and its plasma deficiency is linked to many chronic diseases such as cancer, diabetes, obesity, renal disorder and coronary arterial diseases (CAD). The vitamin C is an excellent antioxidant and neutralizes ROS if ingested in sufficient dose as in case of chronic diseases, has been reported to improve the inflammatory endothelium dependent vasodilation^{3,22}.

Phenolic antioxidants, although a complex but powerful system, act by donating a phenolic hydrogen to produce an antioxidant radical that is stabilized by delocalizing the participating electron/ or intramolecular hydrogen bonding or by further oxidation. Teaw leaves (*Cratoxylum formosum* Dyer) is an indigenous Thai vegetable consisting large quantity of chlorogenic acid responsible for high AOA, that is extractable in soy oil and its emulsions is used to produce nutraceutical foods²³.

MISCELLANEOUS NUTRACEUTICAL FOODS

The spices and nuts both play distinct role in human nutrition and are counted as potent nutraceuticals. Clove, cumin seeds, turmeric, onion, garlic, fennel, fenugreek, nutmeg and mace have shown effective healing properties. Garlic consisting of a variety of sulfur compounds is reported to decrease LDL by controlling the aortic stiffness and to increase HDL. Allicin and ajoene, the major sulfur components of garlic are identified to inhibit inducible nitric oxide synthase (iNOS) by reducing the protein and mRNA and thus to promote vasodilation. Garlic with strong immunopotentiating capacity enhances the natural killer (NK) activity and proliferation of T- lymphocytes and has augmented the response of delayed type hypersensitivity (DTH). The toxic effects of garlic are quite low and LD50 for mice is as high as 30 g/kg body weight and a dose of 2g/kg BW is declared safe, however even this quantity is much more than the daily human consumption in countries where spices are largely used. A glycoprotein of 14 kDa is linked to immunomodulatory action in addition to sulfur compounds. The aged garlic extract (AGE) with 15% solids

and 0.1% S-allylcysteine is a promising immune modifier with homeostasis balance, and particularly in case of controlled Sarcoma-180 and lung carcinoma²⁴. The AGE inhibits platelet aggregation^{18,25}.

Both the oil and water soluble components from garlic have shown health benefits specially it reduces dementia and CAD. The diallyl-trisulfide oil prevents blood coagulation even in diabetes²⁶ while water extracts are effective on cell cycle and viability of Hep G2 hepatoma cells^{3,16}. The beneficial effects of garlic on cardiovascular diseases (CVD) have been reviewed recently and another review related to its bioactive constituents is also published⁵. Variety of methods of isolating nutraceutical components from garlic have been explored^{1,20} and an enzyme-based method for extraction of garlic volatile oil is very recently reported¹⁸.

The cereals are rich source of β -glucan which have strong colloidal properties and so are considered as good nutraceutical foods and are used for replacing fat in food as well^{12,16,17}. The cereal brans, in view of their antioxidant capacity and rheological behavior support the production of whole grain product²². Oats are especially rich in β -glucans, the soluble dietary fibers which have gained special attention for its many health benefits such as lowering serum cholesterol²⁷. β -glucans present in cereal brans are attributed to the good water retention capacity, gelling ability and hydrocolloid-forming properties that have triggered their use as fat-replacers. Variety of dietary fibers as gums, pectins, celluloses, hemicelluloses, tannins, phytates etc have been used as substitutes of fat. Inulin has successfully replaced fat in dairy products²¹. The β -glucans, a family of diversified structure found in the cell wall of yeast, fungi, bacteria and cereal brans modulate immune system by enhancing leucocytic activity that is responsible for enhancing body defensive mechanism. A recent review article on β -glucan suggests that they prime the immune system by elevating the resistance against invading pathogens²⁸.

Mushroom's polysaccharides have been focused for their antitumor activity during the past few decades and the chemical diversity of these glycans ranges from homopolymers to highly complex heteropolymers. The most widely studied antitumor glycopolymer is the well known 1-3- β glucan, however, variety of sugars are involved in formation of such polysaccharides such as the glucose, galactose, mannose, xylose, arabinose, fucose, ribose, glucuronic acid etc. Some of the glycans form conjugates with proteins or peptides that show higher potent antitumor activity^{14,29}.

CONCLUSION

Some good reviews on phytochemical foods have recently been published that include legumes in human diet, emerging health benefits of phytosterols, immunomodulation of dietary β -glucans, probiotic, prebiotic symbiotic, anti-inflammatory activities of chalcones, anticancer activity of cranberry chemopreventive nature of flavonoids, beneficial effect of garlic on CVD immunonutritional ability in the allergic response and clinical application of flavonoids. Fermented foods are rich source of bioactive components, the therapeutic benefits of fermented rice against CVD. Combined nutraceutical therapy in mitochondrial cytopathies. It is well documented now that lack of nutraceuticals in our every day diet leads to variety of diseases. The present age is facing stress,

pollution, hyperactivity and tension, where nutraceutical foods may play beneficial role in prevention and cure of diseases. The health promoting foods are promising for the economical growth of the country and nutritious foods of low cost may be processed for global utilization. Nutraceutical and beyond is the future of tropical countries to achieve the optimal productivity from their natural resources. The future of nutraceutical foods is bright for developing countries as they have rich sources of raw materials, economically available human resources and the large local consumption.

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