

## Review

# Nutraceuticals as natural healers: Emerging evidences

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Accepted 12 January, 2009

Various components of foods have clearly established strong links with human health and it is learnt that their deficiencies provoke diseases. The epidemiological evidences and modern research in nutrition during the last few decades have elaborated the molecular level of such interactions of specific food constituents with that of the toxicants generated in the living cells to control and prevent many of the diseases. Edible products possessing such fantastic healing capacity due to the presence of more than 700 non nutrients functional food factor (FFFs) are effective and epochal for health promotion, disease prevention and cure. The natural products releasing such superb active components are known as nutraceutical foods. The bioactive constituents of many foods have been identified during the goal oriented scientific studies and are used frequently in community and clinical nutrition. The protective effects of tocotrienols in flax seed oil, the curcuminoids in turmeric, carotenoids in carrots, flavonoids in fruits/vegetables, omega-3 fatty acids in sea foods, allyl-sulfides in garlic and  $\beta$ -glucans in mushrooms/cereals are few common examples to be cited here. Excess saturated fat is attributed to pose adverse effects on many metabolic processes. However, certain components of fats are now postulated for their clinical manifestations, such as the sphingolipids as inhibitors of carcinogenesis, conjugated linolenic acid (CLA) as immunomodulator, and monounsaturated fatty acids (MUFAs) for control of lipid profile. The nuts, although rich in fat are influential in cholesterol lowering in view of their suitable polyunsaturated fatty acid: saturated fatty acid ratio and excess of the presence of MUFAs. Recent emphasis on fat-replacements to introduce low caloric foods, advances in nutritional immunology, stimulating actions of phytochemicals on neuronal diseases have indicated wide spectrum of applications of functional foods both in daily life and in the industry. Some examples of nutraceutical foods, their chemical diversity and mode of actions are part of presentation which is based on consulting several review articles published since 2005.

**Key words:** Nutraceuticals, nutritional immunity, fatty acids.

## 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 nutraceuticals,

functional or health foods have gained a wide interest during the last few decades (Raskin et al., 2002). 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 chemopreventive benefits of dietary fibers against colon cancer. Nutritional Labeling and Education Act (NLEA) in 1990 has triggered the productivity of processed and semiprocessed nutraceutical foods. The present paper reviews the recent-research in nutraceutical foods and

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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 immuno-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. The research in clinical nutrition has identified many diet ingredients as immune nutrient cocktail such as n-3 PUFA (polyunsaturated fatty acids), glutamine, arginine, sulfur-containing amino acids and nucleotides (Grimble, 2001; Mantzioris et al., 2000). Nutritional support also includes other phytochemicals such as the carotenoids, flavonoids, catechins, curcuminoids, tannins and fibers. Other fatty acids as n-6 FA,  $\gamma$ -linolenic acid (GLA),  $\alpha$ -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 (O'Quin et al., 2000; Thies et al., 2001). The variety of functional foods are getting popularity which has motivated their commercialization in the developed part of the world (Arai et al., 2002), 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. The caloric value of these fat analogs ranges from 0 - 4 kcal/g as compared to that of the fat as 9 kcal/g. Presently, three types of fat replacers are used, that is, fat, carbohydrate or the protein-based-fat substituents (ADA Report, 2005). 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 products (Ang, 2001). 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 (Malkki, 2001). 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. The microparticulated proteins from milk, egg, whey or soy are industrially processed by variety of methods such as the heat induced gelation, aggregation and cross linking which act as suitable fat-replacers (Kulozic et al., 2003). The gel elasticity of  $\beta$ -lactoglobulin from whey isolates has been modified by heat-induced aggregation and thermal fractionation which made the protein isolate as an excellent fat replacer (Orlein et al., 2006). The proteases and transglutaminases have been used for enzymatic modification of certain proteins for inducing fat mimicking properties (Kunst, 2003). 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 less 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" (Heinrich et al., 2005). 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  $\beta$ -

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 (McDevitt et al., 2005). Chew and Park (2004) have reported that both provitamin A carotenoids such as  $\alpha, \beta$ -carotene, zeaxanthin and non provitamin A (NPA) carotenoids such as lutein, canthaxanthin, astaxanthin and lycopene are equally competent to modulate immunofunctions 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 teeth (Wood and Johnson, 2004). The relationship of dietary carotenoids and immuno regulatory activities has been evaluated in various animals such as zebra, song birds, mice and chicken. Lycopene located in low density lipoprotein (LDL) is responsible for preventing against oxidative damage to such proteins/lipids and thereby preventing atherogenesis and carcinogenesis. It is more powerful antioxidant for quenching singlet oxygen than  $\beta$ -carotene or other carotenoids (Rao and Agarwal, 2000).

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 documented (Gao et al., 2004). 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 (Ukil et al., 2003). Recently the immuno-nutritional ability of curcumin demonstrating its active role in treatment of the allergic response has been highlighted in a review (Kurup and Barrios, 2008).

## FLAVONOIDS IN IMMUNE RESPONSE

Spencer in 2007, while reviewing the flavonoid's interac-

tions 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 ( $C_6 - C_3 - C_6$ ) 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, isoflavones, flavanones, 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. They are capable to neutralize reactive oxygen species (ROS), to chelate metal ions and to form complexes with bioactive proteins such as the enzymes, especially those involved in generation of free radicals (Majzisova and Kuchta, 2001).

The oxidized LDLs are recognized by macrophages through their accepters and cholesteryl esters, and are then transferred to monocytes/macrophages 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 peroxy-nitrite formation which may affect cellular integrity by reversible oxidation of LDLs. Peroxy-nitrite is formed as a result of the reaction of nitric oxide (NO) and the free radicals. However, flavonoids like silibin inhibit NO reaction with free radicals. The flavonoids also interfere in the conversion of xanthene to uric acid by inhibiting xanthene oxidase (Nijveldt et al., 2001). 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 (Aneja et al., 2004; Mukhtar and Ahmed, 2002). A review has recently been published on nutritional protection ability of flavonoids against oxidative burst and UV induced cellular damage (Saraf et al., 2007).

## 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. Neto (2007)

has reviewed the bioactive phytochemicals from cranberry for its *in vitro* anti-cancer activity. The botanicals are well accepted as complementary medicine in modern medical practices, in view of their synergism, compability and no side effects. 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 transferase (Craig, 1999). Recently new techniques have been introduced to map enzymes that mediate alterations in DNA or its protein conjugates localized in chromatin through its immuno 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 nutraceuticals (Oommen et al., 2005). 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 complications (Wu et al., 2009).

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 (Athar and Bokhari, 2006). The immune modulatory effect of foods at various cellular, subcellular and molecular levels are well studied. Phorbol myristic acid (PMA) ester and zymoson are used for producing respiratory burst *in vitro* study to evaluate the capacity of granulocytes of leukemia for cytotoxic activity for their defense (Lunardi et al., 2006). 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 bioavailability of carotenoids including other soluble nutrients increases through juices (Paterson et al., 2006).

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 longaan are ‘heating’ fruits as they enhance Cox-2 proteins which increase PGE<sub>2</sub> synthesis by the specified macrophages. PGE<sub>2</sub>, 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 (Huang and Wu, 2002). Nowakowska (2007) recently has reviewed the anti-infective and anti-inflammatory activities of chalcones, the major of the flavonoids (with open middle

ring) which are widely distributed among the vegetables and fruits.

## ANTIOXIDATIVE ACTIVITY

The cardioprotective 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 above (Visiole et al., 2006). 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 (Table 1; Chu et al., 2002). The AOA of ginger is reported as 3.76 mmol/100 g against common cereals ranging from 0.04 to 1.15 mmol/100 g, pulses 0.12 – 0.35 mmol/100 g or nuts/seed which generally have less but walnut tops the list with a value of 20.97 mmol/100 g followed by sun-flower seeds as 5.39 mmol/100 g. 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 diseases (Halvorsen et al., 2002).

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 (Chao et al., 2004). However, more re-search is needed to explain the facts. Some of the vitamins are potent antioxidants such as C, E and A or its precursors the  $\beta$ -carotenes, out of these vitamins C is hydrophilic and scavenges variety of ROS which if not interrupted stimulate endothelial dysfunction (Feldman et al., 2001). The impact of adverse function of endothelial cells also includes imbalance secretion of chemicals that regulate vasodilatation. Nitric oxide (NO) is one of these secretory chemicals and its plasma deficiency is linked to

**Table 1.** Bioactivity index (BI), antiproliferative activity score (AA) and antioxidant activity (AOA) of ten vegetables.

Vegetables	BI	AA score	AOA score
Spinach	0.95	1.00	0.90
Red pepper	0.78	0.55	1.00
Broccoli	0.66	0.38	0.94
Cabbage	0.57	0.76	0.38
Carrot	0.45	0	0.91
Yellow onion	0.36	0.42	0.30
Celery	0.05	0	0.11
Potato	0.05	0	0.10
Lettuce	0.03	0	0.06
Cucumber	0.01	0	0.03

From Chu et al. (2002).

many chronic diseases such as cancer, diabetes, obesity, renal disorder and coronary arterial diseases (CAD). However, NO if unchecked interacts with ROS resulting in the formation of pathophysiological intermediates. Dietary and endogenous antioxidants interfere here to control diseases and they quench ROS before their link to NO. 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 (Korantzopoulos and Galaris, 2003).

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 foods (Maisuthisakul et al., 2006).

### 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 LD<sub>50</sub> for mice is

as high as 30 g/kg body weight and a dose of 2 g/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 (Ghazanfari et al., 2002). 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 carcinoma (Kyo et al., 2001). The AGE inhibits platelet aggregation (Allison et al., 2006).

Both the oil and water soluble components from garlic have shown health benefits specially it reduces dementia and CAD (Borek, 2006). The diallyl-trisulfide-rich oil prevents blood coagulation even in diabetes (Chan et al., 2007; Ohaeri and Adoga, 2006) while water extracts are effective on cell cycle and viability of Hep G2 hepatoma cells (De Martino et al., 2006). The beneficial effects of garlic on cardiovascular diseases (CVD) have been reviewed recently (Rahaman and Lowe, 2006) and another review related to its bioactive constituents is also published (Amagase, 2006). Variety of methods of isolating nutraceutical components from garlic have been explored (Kimbaris et al., 2006; Staba and Lash, 2007), and an enzyme-based method for extraction of garlic volatile oil is very recently reported (Sowbhagya et al., 2009).

The cereals are rich source of  $\beta$  glucan which have strong colloidal properties and so are considered as good nutraceutical foods and are used for replacing fat in food as well (Flander et al., 2007; Singh and Mohamed, 2007; Woods and Navder, 2006). The cereal brans, in view of their antioxidant capacity and rheological behavior support the production of whole grain product (Lee and Inglett, 2006; Serpen et al., 2008.). Oats are especially rich in  $\beta$ -glucans, the soluble dietary fibers which have gained special attention for its many health benefits such as lowering serum cholesterol (Lee et al., 2009).  $\beta$ -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 products (Güven et al., 2005). The  $\beta$ -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  $\beta$ -glucan suggests that they prime the immune system by elevating the resistance against invading pathogens (Volman et al., 2008).

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  $\beta$  glucan, however, variety of sugars are involved in formation of such polysaccharides such as the glucose, galactose, mannose, xylose, arabinose, fucose, ribose, glucouronic acid etc. Some of the glycans form conjugates with proteins or peptides that show higher potent antitumor activity (Zhang et al., 2007).

## FOOD SYNERGISM

A remarkable example of synergism of foods is undoubtedly of 'synbiotics' where probiotics (the living organisms promoting health benefits) and prebiotics (the nondigestible part of food responsible for improving the performance of gut microbial flora) are used in combinations. A minireview by Rastall and co-workers (2005) has described the health benefits of probiotics, prebiotics and synbiotics providing an alternative tool for modulating the colonic microbial community.

The hydrophilic and lipophilic vitamins as C and E respectively, benefits each other in the food systems as the vitamin C regenerates the oxidized vitamin E to perform its antioxidant function and then dehydro ascorbic acid behaves as pro-oxidant which has initiated the controversial explanations in prooxidant activity of vitamin C in the presence of transition elements. However, vitamin C is always protective and chemopreventive against diseases. The foods supporting each other for a particular cause must be identified and "top down approach" is applauded for study of such activity or the food synergy, however "bottom up approach" is more suitable in clinical trials where patient is not able to consume the bulk food and only small amount of the isolated active ingredient is provided in form of supplements. Similarly vitamin D and calcium work together and it is known that iron-absorption is increased in pre-

sence of vitamin C. Food synergy is an emerging field in nutraceutical designing of meals, however it needs more input and goal oriented studies to support epidemiological data. Recently a new emerging branch of Nano nutraceutical technology has been included in support of identification of nano quantities of food ingredients in food systems. Nano-nutraceutical bioavailability of food constituents plays important role in diet therapy (Acosta, 2008). The micronutrients play the pivotal role in human nutrition (Chen et al., 2006) and the nanotechnology is especially highly valuable in parenteral nutrition.

## CONCLUSION

Some good reviews on nutraceutical foods have recently been published that include legumes in human diet (Duranti et al., 2008; Ofuya and Akhiduc, 2005), emerging health benefits of phytosterols (Trautwein and Demonty, 2007), immunomodulation of dietary  $\beta$ -glucans (Volman et al., 2008), probiotic, prebiotic symbiotic (Rastall et al., 2005), anti-inflammatory activities of chalcones (Nowakowska, 2007), anticancer activity of cranberry (Neto, 2007) chemopreventive nature of flavonoids (Saraf et al., 2007; Spencer, 2007), beneficial effect of garlic on CVD (Rahman and Lowe, 2006) immunonutritional ability in the allergic response (Kurup and Barrios, 2008) and clinical application of flavonoids (Nijveldt et al., 2001). Fermented foods are rich source of bioactive components, Lin and co-workers (2008) have reviewed the therapeutic benefits of fermented rice against CVD. Combined nutraceutical therapy in mitochondrial cytopathies is reviewed by Tarnopolsky (2008). 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 planned future research in the field of nutrition will elaborate desirable interactions in food components which will define new frontiers of healing properties of foods. We simply ignore the fact that composition of foods from even the same group, vary and meal consisting combinations of foods is essential to balance the nutrients. The field of nutraceuticals, if approached through goal oriented research will unveil many beneficial information to be implemented in preventive measures of disorders and clinical practices. 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.

## ACKNOWLEDGMENTS

This review was presented at the International Workshop on "Natural Products, Drugs, Pharmaceuticals and Nutraceuticals for the Benefit of Mankind" held at Karachi, Pakistan during 10 - 19<sup>th</sup> February, 2006 and partly published in the Proceedings by Daya Publishing House, India. Special gratitude is expressed to Prof. Dr. Fakhar Imam, Allama Iqbal Medical College, Lahore, Prof. Dr. Sulman Akhtar, King Edward Medical College, Lahore, Prof. Dr. Zafar Suhail Abbas, Mount Mercy Dental College, Lahore and Brig. Dr. Shahid Javed, Army Medical College, Rawalpindi, Pakistan for their valuable suggestions and helpful criticism on the manuscript. Thanks are also due to unidentified reviewers from USA and Canada for their comments which undoubtedly improved the quality of the manuscript.

## REFERENCES

- Acosta E (2008). Bioavailability of nanoparticles in nutrient and nutraceutical delivery. *Curr. Opin. Colloid. Interface Sci.* 14: 3-15.
- ADA Report (2005). Position of the American Dietetic Association: Fat replacers. *J. Am. Diet. Assoc.* 105: 266-277.
- Allison GL, Lowe GM, Rahman K (2006). Aged garlic extract and its constituents inhibit platelet aggregation through multiple mechanisms. *J. Nutr.* 136(3): 782S-788S
- Amagase H (2006). Clarifying the real bioactive constituents of garlic. *J. Nutr.* 136(3): 716S-725S.
- Aneja R, Hake PW, Burroughs TJ, Denenberg AG, Wong HR, Zingarelli B (2004). Epigallocatechin, a green tea polyphenol, attenuates myocardial ischemia reperfusion injury in rats. *Mol. Med.* 10: 1-6.
- Ang JF (2001). Powdered cellulose and the development of new generation healthier foods. *Cereal Food World* 46: 107-111.
- Arai S, Morinaga Y, Yoshikawa T, Ichiishi E, Kiso Y, Yamazaki M, Morotomi M, Shimizu M, Kuwata T, Kaminogawa S (2002). Recent trends in functional food science and the industry in Japan. *BioSci. Biotechnol. Biochem.* 66: 2017-2029.
- Athar M, Bokhari TZ (2006). Ethnobotany and production constraints of traditional and commonly used vegetables of Pakistan. *J. Vegetable Sci.* 12: 27-38.
- Borek C (2006). Garlic reduces dementia and heart-disease risk. *J. Nutr.* 136(3): 810S-812S.
- Chan K, Yin M, Chao W (2007). Effect of diallyl trisulphide-rich garlic oil on blood coagulation and plasma activity of anticoagulation factors in rats. *Food Chem. Toxicol.* 45: 502-507.
- Chao S, Schreuder M, Young G, Nakaoka K, Moyes L, Oberg C (2004). Pre-clinical study: Antioxidant levels and immuno-modulatory effects of wolfberry juice and other juice mixtures in mice. *J. Am. Nutraceut.* 7: 32-38.
- Chen H, Weiss J, Shahidi F (2006). Nanotechnology in nutraceuticals and functional foods. *Food Technol.* 3: 30-36.
- Chew BP, Park JS (2004). Carotenoid action on the immune response. *J. Nutr.* 134: 257S-261S.
- Chu YF, Sun J, Wu X, Liu RH (2002). Antioxidant and antiproliferative activities of common vegetables. *J. Agric. Food Chem.* 50: 6910-6916.
- Craig WJ (1999). Health promoting properties of common herbs. *Am. J. Clin. Nutr.* 70: 491S-499S
- De Martino A, Filomeni G, Aquilano K, Ciriolo MR, Rotilio G (2006). Effects of water garlic extracts on cell cycle and viability of HepG2 hepatoma cells. *J. Nutr. Biochem.* 17: 742-749.
- Duranti M, Consonni A, Magni C, Sessa F, Scarafoni A (2008). The major proteins of lupin seed: characterization and molecular properties for use as functional and nutraceutical ingredients. *Trends Food Sci. Technol.* 19: 624-633.
- Feldman C, Anderson R, Theron AJ, Steel HC, Rensburg CEJ, Cole PJ, Wilson R (2001). Vitamin E attenuates the injurious effects of bioactive phospholipids on human ciliated epithelium *in vitro*. *Eur. Respir. J.* 18: 122-129.
- Flander L, Salmenkallio-Marttila M, Suortti T, Autio K (2007). Optimization ingredients and baking process for improved whole meal oat bread quality. *LWT Food Sci. Technol.* 40: 860-870.
- Gao X, Kuo J, Jiang H, Deeb D, Liu Y, Divine G, Chapman RA, Dulchavsky SA, Gautam SC (2004). Immuno-modulatory activity of curcumin: suppression of lymphocyte proliferation, development of cell-mediated cytotoxicity and cytokine production *in vitro*. *Biochem. Pharmacol.* 68: 51-61.
- Ghazanfari T, Hassan ZM, Ebrhimi M (2002). Immuno-modulatory activity of a protein isolated from garlic extract on delayed type hypersensitivity. *Int. Immunol. Pharmacol.* 2: 1541-1549.
- Grimble RF (2001). Symposium on "Evidence-based nutrition" Nutritional modulation of immune function. *Proc. Nutr. Soc.* 60: 389-397.
- Güven M, Yasar K, Karaca OB, Hayaloglu AA (2005). The effect of inulin as a fat replacer on the quality of set-type low-fat yogurt manufacture. *Int. J. Dairy Technol.* 58: 180.
- Halvorsen BL, Holte K, Myhrstad MCW, Barikmo I, Hvattum E, Remberg SF, Wold AB, Haffner K, Baugerød H, Andersen LF, Moskaug JO, Jacobs DR, Blomhoff R (2002). A systematic screening of total antioxidants in dietary plants. *J. Nutr.* 132: 461-471.
- Heinrich M, Leonti M, Nebel S, Peschel W (2005). Local Food - Nutraceuticals An example of a multidisciplinary research project on local knowledge. *J. Physiol. Pharmacol.* 56(1): 5-22.
- Huang CJ, Wu MC (2002). Differential effects of foods traditionally regarded as heating and cooling on prostaglandin E production by a macrophage cell line. *J. Biomed. Sci.* 9: 596-606
- Kimbaris CA, Siatis GN, Daferera JD, Tarantilis AP, Pappas SC, Polission GM (2006). Comparison of distillation and ultrasound-assisted extraction methods for the isolation of sensitive aroma compounds from garlic (*Allium sativum*). *Ultrasonic Sonochem.* 13: 54-60.
- Korantzopoulos P, Galaris D (2003). The protective role of vitamin C on endothelial dysfunction. *J. Clin. Basic Cardiol.* 6: 3-6.
- Kunst T (2003). Protein modification to optimize functionality. Protein hydrolyzates, In: Whitaker JR, Voragen AG, Wong DWS (eds.), *Handbook of Food Enzymology*, Marcel Dekker, New York, pp. 221-236.
- Kulozik U, Tolkach A, Bulca S, Hinrichs J (2003). The role of processing and matrix design in development and control of microstructure in dairy food production - a survey. *Int. Dairy J.* 13: 621-630.
- Kurup VP, Barrios CS (2008). Immuno-modulatory effects of curcumin in allergy. *Mole. Nutr. Food Res.* 52: 1031-1039.
- Kyo E, Uda N, Kasuga S, Itakura Y (2001). Immuno-modulatory effects of aged garlic extract. *J. Nutr.* 131: 1075-1079.
- Lee S, Inglett GE (2006). Rheological and physical evaluation of jet-cooked oat bran in low calorie cookies. *Int. J. Food Sci. Technol.* 41: 553-559.
- Lee S, Inglett GE, Palmquist D, Warner K (2009). Flavor and texture attributes of foods containing  $\beta$ -glucan-rich hydrocolloids from oats. *LWT - Food Sci. Technol.* 42: 350-357.
- Lin YL, Wang TH, Lee MH, Su NW (2008). Biologically active components and nutraceuticals in the *Monascus*-fermented rice. *Appl. Microbiol. Biotechnol.* 77: 965-973.
- Lunardi F, Lima JHC, Assreuy J (2006). Comparative study of respiratory burst induced by phorbol ester and zymosan in human granulocytes. *Clin. Biochem.* 39: 78-85.
- Maisuthisakul P, Pongsawatmanit R, Gordon MH (2006). Antioxidant properties of Teaw (*Cratogeomys formosum* Dyer) extract in soybean oil and emulsions. *J. Agric. Food Chem.* 54: 2719-2725.
- Majzisova G, Kuchta M (2001). Dietary flavonoids and risk of coronary heart disease. *Physiol. Res.* 50: 529-535
- Malkki Y (2001). Physical properties of dietary fibers as keys to physiological functions. *Cereal Food World* 46: 196-199.
- Mantzioris E, Cleland LC, Gibson RA, Neumann MA, Demasi M, James

- MJ (2000). Biochemical effects of a diet containing foods enriched with n-3 fatty acids. *Am. J. Clin. Nutr.* 72: 42-48.
- McDevitt TM, Tchao R, Harrison EH, Morel DW (2005). Carotenoids normally present in serum inhibit proliferation and induce differentiation of a human monocytes/macrophage cell line (U937). *J. Nutr.* 135: 160-164.
- Mukhtar H, Ahmed N (2000). Tea polyphenols: prevention of cancer and optimizing health. *Am. J. Clin. Nutr.* 71: 1698S-1702S.
- Nijveldt RJ, Nood E, Hoorn DEC, Boelens PG, Norren K, Leeuwen PAM (2001). Flavonoids: a review of probable mechanism of action and potential applications. *Am. J. Clin. Nutr.* 74: 418-425.
- Neto CC (2007). Cranberry and its phytochemicals: A Review of *in vitro* anticancer studies. *J. Nutr.* 186-193.
- Nowakowska Z (2007). A review of anti-infective and anti-inflammatory chalcones. *Eur. J. Med. Chem.* 42: 125-137.
- Ofuya ZM, Akhidue V (2005). The role of pulses in human nutrition: a review. *J. Appl. Sci. Environ. Manage.* 9: 99-104.
- Ohaeri OC, Adoga GI (2006). Anticoagulant modulation of blood cells and platelet reactivity by garlic oil in experimental diabetes mellitus. *Biosci. Rep.* 26: 1-6.
- Oommen AM, Griffin JB, Sarath G, Zemleni J (2005). Roles for nutrients in epigenetic events. *J. Nutr. Biochem.* 16: 74-77.
- O'Quinn PR, Nelssen JL, Goodband RD, Tokach MD (2000). Conjugated linoleic acid. *Anim. Health Res. Rev.* 1: 35-46.
- Orlien V, Pedersen HB, Knudsen C, Skibsted LH (2006). Wey protein isolate as functional ingredient in high-pressure induced milk gels. *Milchwissenschaft.* 61: 3-6.
- Paterson E, Gordon MH, Niwat C, George TW, Parr L, Waroonphan S, Lovegrove JA (2006). Supplementation with fruit and vegetable soups and beverages increases plasma carotenoid concentrations but does not alter markers of oxidative stress or cardiovascular risk factors. *J. Nutr.* 136: 2849-2855.
- Rahaman K, Lowe GM (2006). Garlic and cardiovascular disease a critical review. *J. Nutr.* 136(3): 736S-740S.
- Rao AV, Agarwal S (2000). Role of antioxidant lycopene in cancer and heart diseases. *J. Am. Coll. Nutr.* 19: 563-569.
- Raskin I, Ribnicky DM, Komarnytsky S, Ilic N, Poulev A, Borisjuk N, Brinker A, Moreno DA, Ripoll C, Yakoby N, O'Neal JM, Cornwell T, Pastor I, Fridlender B (2002). Plants and human health in the twenty-first century. *Trends Biotechnol.* 20: 522-531.
- Rastall RA, Gibson GR, Gill HS, Guarner F, Klaenhammer TR, Pot B, Reid G, Rowland IR, Sanders ME (2005). Modulation of the microbial ecology of the human colon by probiotics, prebiotics and synbiotics to enhance human health: An overview of enabling science and potential applications. *FEMS Microbiol. Ecol.* 52: 145-152.
- Saraf S, Ashwat MS, Saraf S (2007). Flavonoids: a nutritional protection against oxidative and UV induced cellular damages. *Pharmacog. Rev.* 1: 30-40.
- Serpen A, Gökmen V, Pellegrini N, Fogliano V (2008). Direct measurement of the total antioxidant capacity of cereal products. *J. Cereal Sci.* 48: 816-820.
- Singh M, Mohamed A (2007). Influence of gluten-soy protein blends on the quality of reduced carbohydrates coolies. *LWT Food Sci. Technol.* 40: 353-360.
- Sowbhagya HB, Purnima KT, Florence SP, Rao AGA, Srinivas P (2009). Evaluation of enzyme-assisted extraction on quality of garlic volatile oil. *Food Chem.* 113: 1234-1238.
- Spencer JPE (2007). The interactions of flavonoids within neuronal signaling pathways. *Genes Nutr.* 3: 257-274.
- Staba EJ, Lash L (2007). A commentary on the effects of garlic extraction and formulation on product composition. *J. Nutr.* 1118S-1119S.
- Tarnopolsky MA (2008). The mitochondrial cocktail: Rationale for combined nutraceutical therapy in mitochondrial cytopathies. *Adv. Drug Deliv. Rev.* 60: 1561-1567.
- Thies F, Nebe-von-Caron G, Powell JR, Yaqoob P, Newsholme EA, Calder PC (2001). Dietary supplementation with eicosapentaenoic acid, but not with other long-chain n-3 or n-6 polyunsaturated fatty acids, decreases natural killer cell activity in healthy subjects aged > 55 years. *Am. J. Clin. Nutr.* 73: 539-548.
- Trautwein EA, Demonty I (2007). Phytosterols: natural compounds with established and emerging health benefits. *OCL* 14: 259-265.
- Ukil A, Maity S, Karmakar S, Datta N, Vedasiromoni JR, Das PK (2003). Curcumin, the major component of food flavor turmeric, reduces mucosal injury in trinitrobenzene sulphonic acid-induced colitis. *Br. J. Pharmacol.* 139: 209-218.
- Volman JJ, Ramakers JD, Plat J (2008). Dietary modulation of immune function by  $\beta$ -glucans. *Physiol. Behavior* 94: 276-284.
- Visioli F, Bogani P, Grande S, Detopoulou V, Manios Y, Galli C (2006). Local food and cardioprotection: the role of phytochemicals. *Forum Nutr. Basel, Karger* 59: 116-129.
- Wood E, Navder KP (2006). Effect of C-Trim as a fat replacer on the physical textural and sensory properties of chocolate chip cookies. *J. Am. Diet. Assoc.* 106(1): A55.
- Wood N, Johnson RB (2004). The relationship between tomato intake and congestive heart failure risk in periodontitis subjects. *J. Clin. Periodontol.* 31: 574-580.
- Wu JW, Hsieh CL, Wang HY, Chen HY (2009). Inhibitory effects of guava (*Psidium guajava* L.) leaf extracts and its active compounds on the glycation process of protein. *Food Chem.* 113: 78-84.
- Zhang M, Cui SW, Cheung PCK, Wang Q (2007). Antitumor polysaccharides from mushrooms: a review on their isolation process, structural characteristics and antitumor activity. *Trends Food Sci. Technol.* 18: 4-19.