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REVIEW ARTICLE

Functional Foods for Replacing Chemical Filled Medicines

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ABSTRACT

Consumers have shifted from an emphasis on satisfying hunger and taste to an emphasis on the use of food to promote their physical and mental health and to reduce the disease risk during the past two decades. People believe that eating the right food i.e. Functional food will increase their life. The change in consumer's attitude towards food is mainly due to increased health care costs, desire to enhance personal health, advances scientific evidence that diet can reduce diseases risk etc. In this review a variety of functional foods are categorized according to this type of evidence supporting their chemical composition, functionality and recommended intakes. Their applications for controlling various diseases without using chemical filled medicines are also discussed. The safety concerns of functional foods are also raised.

Keywords: Functional food, bioactive molecules, functional ingredient, food products, nutrition.

INTRODUCTION

The consumers are offered with many opportunities to improve their diet and reduce their risk of specific disease with the help of functional foods. It is different from natural supplements and traditional health food. As nutraceuticals are the foods which provide nutritional, medical, or health benefits which include their prevention or treatments of disease in the form of pills or powders[1]. Food the basic need for human beings, in the twenty first century is not only consumed to satisfy hunger but also to provide necessary nutrients to humans. Food is also used to prevent diseases and improve physical and mental health of the consumers. In last few decades demand and satisfactory level of consumers have changed considerably. Consumers all over the world believe that food can contribute directly to their health and wellbeing[2]. So number of consumers demanding healthy, nutritious, convention and safe food is steadily increasing. One of the recent changes in the food patterns is the increased interest in functional foods. Annual research conducted by the international food information council between 2002 and 2007 shows that demand for functional food has continued to increase which can be explained by increasing concerns for consuming health products, steady increase as life expectancy and consumers desire to improve quality of their life[3]. Japan was the first country where functional food market was started and popularized; Japan is the largest market for the functional food consumption in the Europe due to rising awareness health among large percentage of elderly people in its population in 1984. Since 1990 over 5500 new types of functional food have been introduced into the market of Japan. In 2001 according to the United States emerged the largest functional food market followed by Europe and Japan[4, 5].

Need for functional food

According to the department of health and human services, five to ten leading cause of death including coronary heart disease, cancer, stroke, diabetes and atherosclerosis are mainly due to the diet[6]. The dietary pattern that has been to these causes of death is characterized as intake of high saturated fat, cholesterol sodium and refined sugars by United States and other developed countries[7]. However food relatively low in fat, whole grams, legumes, fruit and vegetables etc. are linked to diseases risk reduction. The majority of functional

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foods are derived from plants however there are many classes of physiologically active functional foods of animal origin.

Functional foods can be categorized into two classes

Functional foods of plant origin

A number of plant foods have been investigated for their role in diseases prevention and health. Plant foods currently eligible to bear an FDA approved health claim are oat soluble fiber (beta-glucan) soluble fiber from psyllium seed husk, soy protein, a sterol and stanol-ester fortified. Some plant based food which don't have approved health claims but have clinical research supporting their potential health benefits include garlic, nuts, chocolates, cranberries etc.

Garlic

Garlic has been used for thousands of years for a wide variety of medicinal purposes which is attributed mainly to oregano sulphur compounds (e.g.allyclicsulphides, allicin). Garlic contains two types of compounds: Sulphur-containing compounds and Non-sulphur compounds. Sulphur-containing compounds in garlic are soluble in oil or water. Oil-soluble compounds aresulfides, such as diallylsulphide, diallyldisulphide, diallyltrisulphide and allyl methyl trisulphide,ajoene and dithiins. Water-soluble compounds comprise cysteine derivatives, such as S-allyl cysteine, S-allyl mercaptocysteine and S-methyl cysteine and gamma-glutamyl cysteine.Water-soluble compounds are odourless whereas oil-soluble sulphur compounds are odorous. Furthermore, water-soluble compounds are more stable and safer than oil-soluble compounds[9]. Non-sulfur compounds in garlicsuch as allixin and saponins have been found in recent studies to have important contribution to garlic's health benefits[8].Garlic has been found to have a modest blood pressure lowering effectin chemical studies. Anepidemiological data have shown an inverse relationship between consumption of garlic and some cancers mainly that of stomach which may be attributed to the ability of garlic to inhabit the activity of the Helicobacter pylori, the bacteria which is responsible for causing ulcers. The best medical effect of garlic observed is its ability to reduce blood cholesterol but the agency for healthcare resources & quality have concluded that though promising modest short term effect of garlic supplementation on lipid and antithrombotic factors have been shown chemically, but such effects on clinical outcome are not established. Garlic has anticancer effect which has been suggested due to the organ sulfur compounds such as diallyldisulphide and diallyl trisulphidepresent in garlic which act through induction of phase II detoxification enzymes. Garlic has been found to show antibacterial effect. Allicin and other sulphur compounds are believed to be responsible for its antimicrobial properties. Garlic has been observed to be effective against a number of gram-negative, gram-positive, and acid-fast bacteria such as *Staphylococcus*, *Salmonella*, *Vibrio*, *Mycobacteria*, and *Proteus* species[10]. Garlic also showantifungal properties which are attributed to allicin(diallyl-dithiosulfinate), that is produced from the alliinby the garlic enzyme alliinase. A study has shown that antifungal activity of allicin from garlic ismainly against *Candida albicans*[11]. Garlic also has been shown to have antiviral activity,which was attributed in one study to the various contents of garlic in the order: ajoene>allicin>allylmethyl>thiosulfinate>methyl allyl thiosulfinate[12]. The viruse sensitive to garlic extracts are the human*Cytomegalovirus*, *Herpes simplex virus* type 1, *Herpes simplex virus* type 2, influenza B virus, *vaccinia virus,* vesicular stomatitis virus*, Parainfluenza virus type 3,* and *human Rhinovirus* type 2[11].

Nuts

Food high in fat except fatty fish, have not been regarded as heart healthy but variety of nuts like almonds and walnuts when they are part of diet low in saturated fat and cholesterol showed cardiovascular benefits. The best nuts are regarded as with a brown fiber coating like almonds, walnuts, and pecans. Almost all nuts are rich in monounsaturated oils similar to that found in olive oil.Nuts are also the rich sources of magnesium and containabout 150 mg per 1/2 cup serving[13]. The nutritional value of the walnut is due to the seed. Walnut oil largely contains unsaturated fatty acids which include mainly linoleic acid along with lesser amounts of oleic and linolenic acids. Minor constituents

of walnut oil include tocopherols, sphingolipids, sterols, phospholipids, hydrocarbons and volatile compounds. Phenolic compounds present mainly in the seed coat have been found to possess strong antioxidant properties[14]. The residue left after oil extraction is rich in proteins unusually high in arginine, glutamic and aspartic acids. Among vegetable oils, walnut oil has the highest amounts of PUFAs i.e. up to 78% of the total fatty acid content. Clinical trials have established that almonds reduced total cholesterol by 4-12% and LDL cholesterol by 6-15%. Recently trials with walnuts by a life science research revealed decrease in total and LDL cholesterol which lower the risk of CHD[15].

Grape juice

Researches observed that in certain areas of France, where people were avid drinkers of red wine had less heart diseases than other western population even though they had more fat in their diet, in late 1970's.This observation led to a lot of investigations and subsequently it was confirmed that it must be due to the presence of high concentrations of antioxidants of polyphelnolics in red grape skins. A number of studies have shown that moderate consumption of alcoholic beverages like beer, wine etc. reduces the risk of heart diseases. Grape juice also show similar beneficial effects as those of red wine as it is also such in phenolic antioxidant compounds. It has also been found to reduce platelet aggregation.

Chocolate and cocoa powder

Chocolate and cocoa powder have been investigated for their potential beneficial effects on heart health. Flavonols and methylxanthines are the active components of cocoa. Flavonols are polyphenolic compounds in cocoacontain catechin and its derivatives, B2, B3 and C1 procyanidins.These compounds show antioxidant properties[16].The two main methylxanthines in cocoa are caffeine and theobromine. The benefits of chocolate on mood are mainly due to caffeine.Theobromine have benefits on oral health whichled to consider supplementing toothpaste and mouthwash liquids with theobromine. Usmani et al. have described that theobromine is able to suppress cough in both guinea-pigs and humans without the side effects shown by other antitussive drugs, such as codeine[17]. Epidemiological evidence have proposed that theobromine and caffeine improve lung function and produce bronchodilation in asthma patients[18,19] so the patients with asthma and bronchitis may self-administer coffee or cocoa/chocolate to relieve symptoms. Another beneficial effect of methylxanthines on the airways is associated with the apnea of prematurity (AOP).[20-23] A study by Smit et al.[24] has established that the combination of caffeine and theobromine in the proportions found in cocoa has psycho-stimulant effects. The coffee consumption results in the reduction of the incidence of two of the most predominant neurodegenerative diseases: Parkinson's[25] and Alzheimer's[26,27]. The active component acting on the central nervous system is anticipated to be caffeine.It has been observed that people that consume coffee during the middle stages of life are less prone to suffer from neurological diseases when they get older. Chocolate contains flavonoids (procyanidins) which decrease oxidation stress on LDL cholesterol.

Green tea

The most medically relevant components of green tea are the polyphenols, with flavonoids being the most significant[28]. The catechins are the most important flavonoids which make up 80%–90% of the flavonoids, and about 40% of the water-soluble components in green tea[29,30]. The green tea has been found to have a number of potential health benefitsdue to its anti-inflammatory, anti-carcinogenic, antimicrobial and antioxidant properties and benefits in cardiovascular disease and oral health. Studies in animals have shown that consumption of green tea reduces the risk of many types of cancers. Analysis of studies performed using human oral consumption of green tea to assess cancer risk have shown the most consistent and positive results for reduced cancer risk in breast, colorectal, gastric, esophageal, pancreatic, lung, ovarian, and prostate cancers[31]. Studies in Japan have observed that after 12 weeks ofconsuming a green tea extract, the subjects had drops in body fat by 10%, blood pressure by 6.5%, and low-density lipoprotein (LDL) levels by 2.6%, indicating reduced risk of cardiovascular diseases. After two months consuming a green tea extract, diabetic patients have been observed

to have reduced fasting blood glucose levels from 135 to 128.8 mg/dL[32,33].Green tea catechins have been observed to have antioxidant activity through impeding redox sensitive transcription features and pro-oxidant enzymes, scavenging ROS, and inducing anti-oxidant enzymes[30]. One cup of brewed tea has been found to containup to 200mg (-)-epigallocatechin-3-gallets (EGCG), the major polyphenol component of green tea. The studies have described that consumption of green tea catechins lowers total cholesterol and LDL levels and also reduces blood pressure[34]. It has anti-microbial properties and boosts immunity to many infections. Green tea consumption helps to promote oral health due to its anti-inflammatory properties and antimicrobial activity against mouth bacteria such as Streptococcus mutans[28, 35]. Thus prevents the development and progression of period on titis and leads to decreased tooth loss. Even drinking 1–2 cups of tea per day may have some benefits.

Tomato and tomato products

Tomatoes are a rich source of lycopene, lutein and beta-carotene. Lycopene is a carotenoid that can be synthesized only by plants and not by animals. It is an acyclic isomer of β-carotene, but do nothave vitamin A activity[36,37]. It is a straight chain highly unsaturated hydrocarbon which contains 11 conjugated and two unconjugated doublebonds. Lycopene is the most efficient quencher of free radicals and singlet oxygen species and hence can play an importantrole in the protection from various diseases[38]. Lycopene through itsantioxidant properties may prevent atherogenesis and carcinogenesis by protecting DNA, lipids, low density lipoprotein (LDL) and proteins[39]. The major cause behind atherosclerosis is oxidation of LDL, whichbrings cholesterol into the blood stream leading to ischemic stroke and heart attack[38]. Lycopene results in a rise in LDL receptors hencereduce the cholesterol formation and ultimatelydecreases the risk of cardiovascular disease. It is a major dietary source of lycopene, a carotenoid which is an antioxidant.Its antioxidant properties help to protect lymphocytes from damage caused by NO_2 ((NO from cigarette smoke reacts with oxygen to form NO_2)in cigarette smokers and its ability to quench oxygen radical is twice as high as β- carotene. Tomato and tomato products are being inspected for their role in cancer prevention. An inverse relationship has been shown in a large number of studies between plasma lycopene level and cancer[40]. A comprehensivereview of 75 epidemiologic studies has also observed an inverse relation between tomato consumption and the risk of cancer at a particular site. Cancers of lung,prostate and stomach showed the strongest inverse effects.A 1995 study including more than 47,000 participants, observed that ten serving per week of tomato sauce or tomato juice reduced the risk of prostate cancer by 35%, whereas advanced prostate cancer was reduced by 53%.Only tomato foods were found effective in reducing the risk of prostate canceramong 47 fruits and vegetables, studied. It may be because of theability of lycopene to selectively accumulate in prostate gland where it acts as an antioxidant.Another carotenoidlutein in tomato is being studied mainly for its role in eye health due to its ability to neutralize free radicals which maydamage the eye. The individual who take diet rich in lutein have been found to be less likely to develop age related macular degeneration or cataract, major causes of vision loss. Spinach isalso the good sources of lutein(7.4mg/100mg).

Cranberries

Cranberries have been known for curing urinary tack infections from clinical trials on 153 elderly women. It is attributed to the presence of biologically active component tannins (proanthocyanidins) in cranberry which prevents E.Coli living in the urinary track from adhering to the epithelial cells[41].Cranberry juice contains a high amount of salicylic acid which may help prevent blood clots, reduce swelling and eliminate tumors. Cranberry juice can lower the risk of heartdiseases and helps in supporting cardiovascular health. Cranberries are rich in flavonoids which have antioxidant properties and may reduce the risk of atherosclerosis[42]. According to, Cranberry juice has been found to prevent tooth cavities in a study. It isdue to the presence of Proanthocyanidine, a chemical compound in cranberry which inhibits the harmful bacteria from clinging to the teeth. Proanthocyanidins also inhibit the growth of various cancer cells[43]. Fresh cranberry juice is effective in fighting against infections such as sore throat and colds. Kidney stone formation

is also inhibited due to the high amount of acid components present in cranberry juice. Foods like cranberries, apples and garlic rich in flavonoids, a category that includes anthocyanins, flavonols and proanthocyanidins, help reduce the risk of stomach disorders, including stomach ulcers as these inhibit the growth of a type of bacteria called *Helicobacter pylori* or *H.pylori*responsible for causing peptic ulcers. Cranberries also contain high levels of vitamin-C, which is essential for the body to make collagen, the important component behind the healthy functioning of the tissues. The USDA scientists at the human research center suggest that the age related problems such as memory loss and lack of coordination may be reduced by the phytonutrients and antioxidants present in cranberries.

Flax seeds

The chemical compounds such as polyunsaturated fatty acids (PUFA) of omega-3 family, soluble dietary fibers, lignans, proteins and carbohydrates contained in flaxseeds have specific biological activity and functional properties so are responsible for the health benefits of flax seeds[44]. An analysis of brown Canadian flax have shown an average of 41% fat, 20% protein, 28% total dietary fiber, 7.7% moisture. Flaxseeds contain lipids approximately 30%, α-linolenic acid (ALA) 53%, linoleic acid (LA) 17%, oleic acid 19%, stearic acid 3%, and palmitic acid5%. It has an excellent n-6: n-3 fatty acid ratio of approximately 0.3:1[45]. Hence, the flaxseed may be used as an alternative for supplying omega-3 fatty acid to populations of the world who do not have large access to marine foods, which are the best sources of omega-3 fatty acids[46]. Kaitwash et al. 2010 have reported the antiulcer and anti-secretory properties of flaxseed oil. The increased omega-3 fatty acid intake has been found by numerous studies to help regulate and reduce blood pressure in persons who have been diagnosed with hypertension. Furthermore, a diet such as flax seeds low in saturated fats and rich in monounsaturated and polyunsaturated fats, including omega-3 fatty acids, can reduce risk of heart disease. Flaxseed is rich in essential amino acids required for the synthesis of proteins that play an important role in the maintenance and repair of cells, tissues and organs. Flaxseed contains soluble and insoluble dietary fibers. The insoluble fiber contains mainly cellulose and lignin and the soluble fiber are the mucilage gums[47,48]. Dietary fibers from flaxseed were found to regulate body weight through both hunger suppression and diminished nutrient absorption[49]. Flaxseeds are also a source of many vitamins and minerals such as calcium, magnesium and phosphorus. A fat-soluble vitamin, vitamin E, present in flaxseed in the isomer γ-tocopherol has antioxidant properties and protect cell constituents from the damaging effects of free radicals which otherwise might contribute to cancer development.Besides, vitamin E promotes sodium excretion in the urine which helps in lowering the blood pressure and hence lowers the risk of heart disease, some types of cancer and Alzheimer disease. Flaxseeds are the richest dietary source of lignans which play an important role in the prevention of hormone related cancers, osteoporosisand cardiovascular diseases.Flaxseeds decrease in risk of obesity and dyslipidemia, the risk factors for the development of diabetes and resistance to insulin.However, it also contains few levels of adverse health compounds such as Cadmium, protease inhibitors and cyanogenic compounds which are generally removed by thermal and mechanical processes, including cooking in microwaves, autoclaving and boiling[44].

Citrus fruits and various cruciferous vegetables have been found to show the cancer preventive benefits. Broccoliis highly marketed due to the potential cancer preventive action of itsphysiologically active component, sulforaphane which has been found to be a powerful inducer of detoxifying enzymes in the liver. Such enzymes inactivate toxicsubstance and hence accelerate their elimination from body.

Functional foods of animal origin

The omega-3 fatty acids are the physiologically active component derived from animal products mainly found in fatty fish such as salmon, tuna, sardines, herring and mackerel[50]. The two most intensely investigated omega-3 fatty acids are docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). DHA is essential component of the phospholipids of cellular membranes,especially of the brain and retina of the eye and essential for their normal functioning. FDA has allowed the use of DHA and arachidonic acid for full term infants[51].

The omega-3 fatty acid has been found to have major health benefit in heart health as it reduces mortality due to myocardial infarction and sudden death in patients with CHD[52]. But the consumption of Omega-3 fatty acids should be controlled up to maximum of 2g per day of EPA and DHA because its high levels may cause the higher risk of hemorrhagic stroke, raised levels of LDL cholesterol, increased bleeding timesand lessens glycemic control among people with diabetes, formation of biologically active oxidation products due to oxidation of omega-3 fatty acids[53].

Probiotics are another biologically active animal derived components studied in recent years. It is found that a wide variety of microorganisms contribute to human health.Probiotics are commonly known as microbial food supplements having beneficial effects on the consumers. Most probiotics are the lactic acid-producing bacteria and are generally consumed in the form of yogurt, fermented milks or other fermented foods[54]. Some of the benefits consuming foods containing lactic acid bacteria are: (a) improvement of intestinal tract health; (b) boosting the immune system; (c) reducing risk of some cancersand (d) decreasing symptoms of lactose intolerance, lessening the occurrence of allergy in vulnerable individuals. The probiotics may result in these benefits byadjusting gut pH, annoying pathogens through formation of antimicrobial compounds, competing with pathogen for binding and receptor sites as well as for available nutrients and growth factors and producing lactase enzyme[55].

Safety measures

We have seen with evidence that certain functional food can play an important role in health promotion and disease prevention but safety concerns have been raised recently due to the haphazard addition of botanicals to foods, some of which may be harmful to some consumers. The Issue of interaction of herb with drug has caught growing attention. In United Stated some consumer groups have asked the FDA to stop the sale of some functional food in the market. General accounting office (GAO) has made following recommendations regarding the safety of functional foods.

i. Develop and communicate regulation to industries to document the safety of new dietary supplements.
ii. Develop and communicate regulations to the industry on the safety related information mandatory on the labels for functional foods.
iii. Develop and augment system to record and analyse reports of health problems associated with functional foods.

CONCLUSION

To gain success in functional food market all forms of functional foods that are involved in food industry should discover consumer awareness, safeguards and the motives as to why consumers pick these products as part of their daily diet. Any health benefit shown due to a particular functional food should be based on rigorous studies of safety and efficacy. Persons choosing a particular functional food must first consult their doctor in order to avoid any side effects due to interaction of functional foods with other dietary foods and medicines a person is already taking for some ailment. Interaction of functional foods with other dietary foods and their adverse interactions with medicines must be properly and noticeably communicated to the consumers. Functional foods can be most effective to promote good health and reduce disease risk if combined with exercise, maintenance of healthy body weight, positivity, stress reductions etc.

REFERENCES

1. International food information council, functional foods: Attitudinal research; 2002
2. International market bureau, “consumer trend: functional foods2009
3. Mallet and I.Rowlan,”functional foods at the frontier between food and pharma” current opinion in biotechnology, Vol-14, pp 367-370
4. K.Menard,”market and marketing of functional foods in theEurope, “Journal of food engineering Vol.56, PP 181-188, 2003.
5. Verbeke, W (2006) functional food willingness to compromise taste for health. Food quality and preference, 17:126-131.
6. Williams, P. (July 2005) consumer understanding and use of health claims for foods, Nutrition Reviews 63(7): 256-264.
7. Department of health andhumanservices U.S food and drug administration (1997) food labeling health claims Oats and Coronary heart disease fed. Register 62:3584-3601.
8. Garlic effects on cardiovascular risks and diseaseprotective effects against cancer www.ahrq.gov/clinic/epcsums/garlicsum.htmJuly30,2002.

9. Agarwal K.C. Therapeutic actions of garlic constituents. Med. Res. Rev. 1996;16:111–124.
10. Tariq HA, Kandil O, Elkadi A, Carter J. Garlic revisited: therapeutic for the major diseases of our times. J Natl Med Assoc. 1988;80:439–445.
11. Ankri S, Mirelman D. Antimicrobial properties of allicin from garlic. Microbes Infect. 1999;2:125–129.
12. Weber ND, Andersen DO, North JA, Murray BK, Lawson LD, Hughes BG. In vitro virucidal effects of Allium sativum (garlic) extract and compounds. Planta Med. 1992;58:417–423
13. Spiller, G.A. Jenkins, D.A Bosello,O Gates, J-E cragen, L.N Bruce B(1998)Nuts and plasma lipids: J.Am.Cell Nutr. 11:126-130
14. Crews C, Hough P, Godward J, Brereton P, Lees M, Guiet S, et al, Study of the main constituents of some authentic walnut oils. J Agric Food Chem 53:4853–4860 (2005).
15. Zhang Z, Liao L, Moore J, Wu T and Wang Z, Antioxidant phenolic compounds from walnut kernels (Juglansregia L). Food Chem 113:160–165 (2009).
16. Andújar, I.; Recio, M.C.; Giner, R.M.; Ríos, J.L. Cocoa polyphenols and their potential benefits for human health. Oxid. Med. Cell. Longev. 2012, 2012, doi:10.1155/2012/906252.
17. Usmani, O.S.; Belvisi, M.G.; Patel, H.J.; Crispino, N.; Birrell, M.A.; Korbonits, M.; Korbonits, D.; Barnes, P.J. Theobromine inhibits sensory nerve activation and cough. FASEB J. 2005, 19, 231–233.
18. Bara, A.I.; Barley, E.A. Caffeine for asthma. Cochrane Database Syst. Rev. 2001,doi:10.1002/14651858. CD001112.
19. Simons, F.E.; Becker, A.B.; Simons, K.J.; Gillespie, C.A. The bronchodilator effect and pharmacokinetics of theobromine in young patients with asthma. J. Allergy Clin. Immunol. 1985, 76, 703–707. Nutrients 2013, 5 4172
20. Pagano, R.; Negri, E.; Decarli, A.; La Vecchia, C. Coffee drinking and prevalence of bronchial asthma. Chest 1988, 94, 386–389.
21. Zhao, J.; Gonzalez, F.; Mu, D. Apnea of prematurity: From cause to treatment. Eur. J. Pediatr. 2011, 170, 1097–1105.
22. Aranda, J.V.; Beharry, K.; Valencia, G.B.; Natarajan, G.; Davis, J. Caffeine impact on neonatal morbidities. J. Matern. Fetal Neonatal Med. 2010, 23, 20–23
23. Henderson-Smart, D.J.; Steer, P.A. Caffeine versus theophylline for apnea in preterm infants. Cochrane Database Syst. Rev. 2010, doi:10.1002/14651858. CD000273.
24. Smit, H.J.; Gaffan, E.A.; Rogers, P.J. Methylxanthines are the psycho-pharmacologically active constituents of chocolate. Psychopharmacology 2004, 176, 412–419.
25. Costa, J.; Lunet, N.; Santos, C.; Santos, J.; Vaz-Carneiro, A. Caffeine exposure and the risk of Parkinson's disease: A systematic review and meta-analysis of observational studies J. Alzheimer's Dis. 2010, 20, S221–S238.
26. Maia, L.; de Mendonca, A. Does caffeine intake protect from Alzheimer's disease? Eur. J. Neurol. 2002, 9, 377–382.
27. Eskelinen, M.H.; Ngandu, T.; Tuomilehto, J.; Soininen, H.; Kivipelto, M. Midlife coffee and teadrinking and the risk of late-life dementia: A population-based CAIDE study. J. Alzheimer's Dis.2009, 16, 85–91
28. Gupta, D.A.; Bhaskar, D.J.; Gupta, R.K.; Karim, B.; Jain, A.; Dalai, D.R. Green tea: A review on its natural anti-oxidant therapy and cariostatic benefits. Biol. Sci. Pharm. Res. 2014, 2, 8–12
29. Wang, Y.; Ho, C.T. Polyphenolic chemistry of tea and coffee: A century of progress. J. Agric. Food Chem. 2009, 57, 8109–8114. [CrossRef] [PubMed]
30. Babu, P.V.; Liu, D. Green tea catechins and cardiovascular health: An update. Curr. Med. Chem. 2008, 15, 1840–1850
31. Boehm, K.; Borelli, F.; Ernst, E.; Habacher, G.; Hung, S.K.; Milazzo, S.; Hornebar, M. Green tea (Camellia sinensis) for the prevention of cancer. Cochrane Database Syst. Rev. 2009, 3. [CrossRef]
32. Nagao, T.; Hase, T.; Tokimitsu, I. A green tea extract high in catechins reduces body fat and cardiovascularrisks in humans. Obesity (Silver Spring) 2007, 15, 1473–1483. [CrossRef] [PubMed]
33. Fukino, Y.; Shimbo, M.; Aoki, N.; Okubo, T.; Iso, H. Randomized controlled trial for an effect of green tea consumption on insulin resistance and inflammation markers. J. Nutr. Sci. Vitaminol. (Tokyo) 2005, 51, 335–342. [CrossRef] [PubMed]
34. Tian, C.; Huang, Q.; Yang, L.; Légaré, S.; Angileri, F.; Yang, H. Green tea consumption is associated with reduced incident CHD and improved CHD-related biomarkers in the Dongfeng-Tongji cohort. Sci. Rep. 2016, 6, 24353. [CrossRef] [PubMed]
35. Awadalla, H.I.; Ragab, M.H.; Bassuoni, M.W.; Fayed, M.T.; Abbas, M.O. A pilot study of the role of green tea use on oral health. Int. J. Dent. Hyg. 2011, 9, 110–116. [CrossRef] [PubMed]
36. Rao A, Agarwal S. Role of lycopene as antioxidant carotenoid in the prevention of chronic diseases: a review. Nutr Res 1999;19:305-23.
37. Clinton, S.K (1998) Lycopene: Chemistry biology and implications for human health and diseasesNutr. Rev. 56:35-51
38. Di Mascio P, Kaiser S, Sies H. Lycopene as the most efficient biological carotenoid singlet oxygen quencher. Arch BiochemBiophys 1989;274:532-8.
39. Rao A, Agarwal S. Bioavailability and in vivo antioxidant properties of lycopene from tomato products and their possible role in the prevention of cancer. Nutr Cancer 1998;31:199-203.
40. Schmitz HH, Poor CL, Wellman R, Erdman Jr JW. Concentrations of selected carotenoids and vitamin A in human liver, kidney and lung tissue. J Nutr 1991;121:1613-21.
41. Afshar K, Stothers L, Scott H, MacNeily AE. Cranberry juice for the prevention of pediatric urinary tract infection: a randomized controlled trial. J Urol. 2012;188:1584-7.
42. McKay DL, Blumberg JB. Cranberries (Vacciniummacrocarpon) and cardiovascular disease risk factors.Nutr Rev. 2007;65:490-502.

43. Mohammed Abdul MI, Jiang X, Williams KM, Day RO, Roufogalis BD, Liauw WS, Xu Neto CC. Cranberry and blueberry: evidence for protective effects against cancer and vascular diseases. MolNutr Food Res. 2007;51:652-64. Review.
44. Rubilar M, Gutierrez C, Verdugo M, Shene C, Sineiro J. Flaxseed as a source of functional Ingredients. J Soil Sci Plant Nutr.2010; 10: 373-377.
45. Simopoulos AP. The importance of the ratio of omega-6/omega-3 essential fatty acids. See comment in PubMed Commons below Biomed Pharmacother. 2002; 56: 365-379.
46. El-Beltagi HS, Salama ZA, El-Hariri DM. Evaluation of fatty acids profile and the content of some secondary metabolites in seeds of different flax cultivars (LinumUsitatissimum L.). General Applied Plant Physiology.2007; 33: 187-202.
47. Qian KY, Cui SW, Goff HD. Flaxseed gum from flaxseed hulls: Extraction, fractionation, and characterization. Food Hydrocolloids.2012; 28: 275-283.
48. Cui W, Kenaschuk E, Mazza G. Influence of genotype on chemical composition and rheological properties of flaxseed gums. Food Hydrocolloids.1996; 10: 221-227.
49. Kristensen M, Jensen MG, Aarestrup J, Petersen KE, Søndergaard L, Mikkelsen MS, et al. Flaxseed dietary fibers lower cholesterol and increase fecal fat excretion, but magnitude of effect depend on food type. See comment in PubMed Commons below NutrMetab (Lond). 2012; 9: 8.
50. Bouwens M, van de Rest O, Dellschaft N, Bromhaar MG, de Groot LC, Geleijnse JM, Muller M, Afman LA. Fish-oil supplementation induces antiinflammatory gene expression profiles in human blood mononuclear cells. Am J ClinNutr. 2009;90:415–24.
51. Micallef MA, Garg ML. Anti-inflammatory and cardioprotective effects of n-3 polyunsaturated fatty acids and plant sterols in hyperlipidemicindividuals. Atherosclerosis. 2009;204:476–82.
52. Ebrahimi M, Ghayour-Mobarhan M, Rezaiean S, Hoseini M, ParizadeSM, Farhoudi F, Hosseininezhad SJ, Tavallaei S, Vejdani A, AzimiNezhadM, et al. Omega-3 fatty acid supplements improve the cardiovascular risk profile of subjects with metabolic syndrome, including markers of inflammation and auto-immunity. ActaCardiol. 2009;64: 321–7.
53. Kris-Etherton PM, Harris WS, Appel LJ. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease.Circulation.2002; 106:2747–57.
54. De Vuyst, L. and Vandamme, E.J. (1994) Antimicrobial potential of lactic acid bacteria.In Bacteriocins of Lactic Acid Bacteria ed. De Vuyst, L. and Vandamme, E.L. pp. 91–142. Glasgow, UK: Blackie Academic and Professional.
55. Dodd, H.M. and Gasson, M.J. (1994) Bacteriocins of Lactic Acid Bacteria. In Genetics and Biotechnology of Lactic acid Bacteria ed. Gasson, M.J. and de Vos, W.M. pp. 211–251. Glasgow, UK: Blackie Academic and Professional. D