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Promising Roles of Dietary Antioxidants in the Prevention of Certain Age-Related Diseases

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Abstract: **Free radicals are spontaneously produced by living organisms because of normal cellular metabolism and/or environmental factors. These radicals attack biological macromolecules like proteins, fatty acids, and nucleic acids, causing oxidative damage to tissues and even gene mutation. When there is an overload of free radicals, they cannot gradually be destroyed and thus, are accumulated in the body producing oxidative stress. The latter is closely related to the aging process and the onset of several chronic diseases such as cardiac disorders, diabetes mellitus, neurodegenerative disorders like Alzheimer's and Parkinson's disease and cancer. Dietary antioxidants scavenge the excess free radicals, avoiding oxidative damage of the cell and preventing the onset and progression of many chronic diseases. The common sources of dietary antioxidants Vitamin C (ascorbic acid), Vitamin E (tocopherol), Carotenoids (β-carotene, lycopene and astaxanthin), plant polyphenols present in fruits, vegetables, tea, coffee, red wine, honey and cocoa beans, certain minerals (e.g. zinc, selenium) and selective spices (like turmeric, ginger, peppers etc.). An extensive review of the literature showed that antioxidant rich foods play a beneficial role in the prevention of many diseases. Grape juice, red wine, berries, tomato extract (lycopene), chocolates, cocoa green and black tea etc. are cardiac-friendly foods. They help to reduce blood pressure, improve lipid profile, prevents atherosclerosis. Soybean Isoflavones protect against obesity and co-morbidities. Tocopherol and green tea have certain neuroprotective effects, preventing neuro-degenerative diseases. Dietary polyphenols, vitamin E and C, Selenium, isoflavones reduce the cancer risk. Vitamin C has a potential role in the prevention of hyperuricemia and gout.**

Keywords: **Free radicals, Oxidative stress, Dietary Antioxidants, Foods, Chronic diseases.**

1. INTRODUCTION

Free radicals are chemical species with a single unpaired electron. The unpaired electron is highly reactive as it seeks to pair with another free electron; generating more free radicals. Thus, a chain reaction of free radicals can occur. Most free radicals are reactive oxygen species (ROS), produced by living organisms because of normal cellular metabolism and environmental factors (pollution, cigarette smoke, radiation, medication) [1]. Mitochondria are recognized as the major site for ROS production [2]. Many free radicals attack biological macromolecules such as proteins, fatty acids and nucleic acids, causing oxidative damage to cells or tissues or even resulting in gene mutation [3].

When there is an overload of free radicals, they cannot gradually be destroyed and their accumulation in the body produce oxidative stress. It is an imbalance between the production of reactive oxygen species and antioxidant defense. The study of Anderson, C et. al. (2016) suggested that lower intake of antioxidant nutrients and higher intake of trans fats may be associated with greater oxidative stress among premenopausal women [4]. Oxidative stress is closely related to the aging process. The onset and development of several chronic diseases as well as their complications such as endothelial dysfunction in cardiovascular disease are concomitant with the oxidation of LDL, which are also aggravated by smoking or the appearance of advanced glycosylation end-products in diabetes mellitus. In neurodegenerative disorders such as Alzheimer's disease, neuron plasma membrane malfunction is caused by phospholipids peroxidation, leading to cell death. Cancer develops from genetic mutations resulting from DNA damage [5], [6]. The human body has several mechanisms to counteract oxidative stress by producing antioxidants, which are either naturally produced in situ (endogenous) or externally supplied through foods and/or supplements (exogenous). Antioxidants act as “free radical scavengers” by preventing and repairing damages caused by ROS; and therefore, can enhance the immune defense and lower the risk of disease and cancer [7].

Dietary antioxidants scavenge the excess free radicals, thus avoiding oxidative damage to the cell. Even after a damage, antioxidants reduce the free radical levels preventing further damage thereby alleviating some symptoms caused by oxidative stress [6]. When an antioxidant destroys a free radical, this antioxidant itself becomes oxidized. Therefore, the antioxidant resources must be constantly replenished in the body [5].

Nutrient antioxidants are compounds which cannot be produced in the body and must be provided through foods or supplements. These include vitamin E, vitamin C, carotenoids, trace metals (selenium, manganese, zinc), flavonoids, omega-3 and omega-6 fatty acids, etc. [3].

Phytochemical antioxidants include vitamins (like vitamin-C, E, and K); plant pigments (such as carotenoids, xanthophylls, lycopene, anthocyanins, and phaeophytins); and secondary plant metabolites (like phenolics and polyphenols)[8]. They play a prominent role in the prevention of several age-related disorders. They act as free-radical scavengers, oxidative stress relievers and lipoperoxidation inhibitors [9].

2. COMMON SOURCES OF ANTIOXIDANTS IN THE HUMAN DIET

1. Vitamin C (ascorbic acid): Vitamin C is mainly found in fresh vegetables and fruits. The antioxidant effect of vitamin C is reflected by its reducing capacity. It has a protective role against many diseases caused by oxidative stress, such as cardiovascular disease, cancer and cirrhosis. It can act as a superoxide scavenger in primary hypertension [10].

2. Vitamin E (tocopherol): It includes α-tocopherol, β-tocopherol, γ-tocopherol and δ-tocopherol. Vitamin E protects biological membranes and nucleic acids in cells from the free radical attack. Rich sources of Vitamin-E include nuts (such as almonds, walnuts), vegetable oil, kiwi fruits and green vegetables. Vitamin E suppresses tumor growth and reduce the risk of breast cancer [10].

3. Carotenoids (β-carotene, lycopene and astaxanthin): Carotenoids are fat-soluble natural pigment present in dark green, red and yellow fruits. These are polyunsaturated hydrocarbons containing many double bonds. The most common carotenoids are β-carotene, γ-carotene and lycopene in plants, and astaxanthin in animals. Consumption of adequate carotenoids protect from diabetes as well as neurodegenerative, cardiovascular and inflammatory diseases. Astaxanthin have certain anti-aging and anti-inflammatory activities [10].

4. Polyphenols: Polyphenols are natural antioxidants present in fruits, vegetables, tea, coffee, red wine, honey and cocoa beans [10]. Polyphenols play a key role in the prevention and treatment of several diseases, including CVDs, cerebrovascular diseases, Alzheimer’s disease, airway disease, and cancer, with a focus to alleviate the oxidative stress as the causative mechanism in those diseases [11], [12].

Cocoa polyphenols: Cocoa (Theobroma cacao L.) and its products are consumed worldwide. Three groups of polyphenols are mainly present in cocoa beans, namely catechins (37%), anthocyanidins (4%), and proanthocyanidins (58%).

Antioxidant properties of cocoa polyphenols are responsible for many health benefits against cardiovascular diseases, inflammatory processes, and cancer. Cocoa polyphenols induce coronary vasodilatation, increase endothelial NO concentrations to induce vascular relaxation, improve vascular function, and decrease platelet adhesion. They decrease LDL-cholesterol level and its oxidation while increasing HDL-cholesterol, thus preventing arteriosclerosis, coronary heart disease and myocardial infarction. Polyphenols have anti-inflammatory activity, especially against inflammatory bowel disease (IBD), preventing it from evolving into cancer. The phenolics from cocoa also modify the glycemic response and the lipid profile, decreasing platelet function and inflammation along with diastolic and systolic arterial pressures, which, taken together, may reduce the risk of cardiovascular mortality. The phenolics from cocoa may thus protect against diseases in which oxidative stress is implicated as a causal or contributing factor, such as cancer. They also have antiproliferative, antimutagenic, anticariogenic and chemoprotective effects[13]. Cocoa polyphenols can significantly decrease the level of oxidative stress in alcoholic fatty liver [14].

Green tea polyphenols:

The dry matter of green tea infusion releases considerable amounts of active compounds like catechins, mainly of the types epigallocatechin-3-gallate (EGCG), epigallocathechin (EGC), epicatechin-3- gallate (ECG), and epicatechin (EC). Green tea catechins (GTCs), especially EGCG, have been shown to be potent chemopreventive effects [15]. The study of Jian, L et. al. suggested that green tea is protective against prostate cancer [16]. Green tea polyphenols have a protective effect on neurodegenerative diseases such as Alzheimer's disease [17]. They possess potent antioxidative and anti-inflammatory properties that contribute towards good cardiac health [18].

Grape seeds polyphenols:

Grape seeds and red wine contain a large amount of polyphenols. The study of Hokayem, M. et.al. (2013) indicated that grape polyphenols can inhibit the oxidative stress and insulin resistance induced by fructose in type-II diabetic patients at the first phase [19]. Grape seed polyphenols protect against cardiac cell apoptosis via the induction of endogenous antioxidant enzyme like xanthine oxidase [20].

Peach fruits polyphenols:

Polyphenols in peach fruits inhibit the tumor growth and metastasis of breast cancer [21].

5. Flavonoids (flavonoids, isoflavones, xanthones and anthocyanins):

Flavonoids are water-soluble plant pigments, characterized by an aromatic ring structure with one or more hydroxyl groups. They belong to the larger group of plant (poly)phenols. Important dietary sources of flavonoids include onions (flavonols); cocoa (proanthocyanidins); tea, apples, and red wine (flavonols and catechins); citrus fruit (flavanones); berries and cherries (anthocyanidins); and soy (isoflavones) [22].

Flavonoids transform free radicals into inert phenolic radicals after supplying hydrogen to the radicals of lipid compounds. Common flavonoid compounds include flavones, isoflavones, anthocyanins and xanthonoids. Soybean is an extremely useful source of isoflavones. The soybean consumption of Asians is much higher than that of Europeans and Americans. The incidence of prostate cancer in Asia is much lower than that in Europe and USA, suggesting that isoflavone has a preventive effect on prostate cancer [10]. Isoflavones reduces the risk of ovarian and breast cancers [23], [24].

The flavonoids also have some excellent protective effects on the vascular system and the treatment of neurodegenerative diseases. The studies of Xie, H. et.al. (2014) indicated that catechin procyanidin extracted from Ginkgo biloba can inhibit the aggregation of Aβ and disaggregate the formed fiber, suggesting their roles in the treatment of Alzheimer's diseases and other neurodegenerative diseases [25].

Anthocyanins are naturally occurring, water-soluble, plant pigments having strong antioxidant property. Dark coloured plant foods, ranging from blue to red and orange, such as purple sweet potato, black rice, blueberry, grape, mulberry etc. are useful sources of anthocyanins. They have beneficial effects on the prevention and treatment of cardiovascular diseases, neurodegenerative diseases and cancer. They exert antihypertensive, endothelium protective and anti-atherogenic activities [26], [27].

6. Minerals:

Zinc (Zn) can retard oxidative processes [28]. Zinc supplementation significantly reduces the incidence of infections, oxidative stress biomarkers and inflammatory cytokines in the elderly. Zinc is highly effective in decreasing reactive oxygen species (ROS) [29], [30]. Chronic hyperglycemia in diabetes mellitus favours the manifestation of oxidative stress by increasing the production of ROS and/or reducing the antioxidant defense system activity. Zinc improves the oxidative stress in type 2 diabetic patients by reducing chronic hyperglycemia and improving the activity of antioxidant defense system. It promotes phosphorylation of insulin receptors by enhancing glucose transport into cells [31]. Zinc possess antioxidant and anti-inflammatory properties. The therapeutic roles of zinc in acute infantile diarrhea, acrodermatitis enteropathica, prevention of blindness in patients with age-related macular degeneration, and treatment of common cold with zinc have been reported [32]. Zinc supplementation reduces the duration and severity of diarrhea among preschool-age children [33]. The major food sources of zinc are mainly of animal origins. While oysters are outstanding source of zinc, other sources like beef, meat, poultry, egg yolk are also quite useful. Among plant foods, cocoa wheat germ, dry legumes and peanuts are better sources of zinc compared to leaves, stalks, fruits, or roots [34].

Selenium (Se) is an essential trace element found in vegetables (garlic, onion, grains, nuts, soybean), sea food, meat, liver and yeast. It forms the active site of several antioxidant enzymes including glutathione peroxidase. At low concentration, selenium act as an antioxidant, anti-carcinogenic and immunomodulator agent [5], [35]. It protects against oxidative stress [36]. Selenium has a protective effect against certain cancers. It may enhance the male fertility, decrease the cardiovascular disease mortality and regulate the inflammatory mediators in asthma [37]. Selenium also provide protection from ROS-induced brain cell damage, and the proposed mechanisms mainly invoke the functions of glutathione peroxidases (GPxs) and selenoprotein P [38].

Manganese (Mn) plays a key role in cellular adaptation to oxidative stress. The antioxidant property of Mn help to combat oxidative damage. Manganese superoxide dismutase (MnSOD) is the principal antioxidant enzyme in the mitochondria [39]. Dietary sources of manganese include cereals, nuts, pineapples, beans, mollusks (clams, oysters, mussels), dark chocolate, cinnamon, and tea [40].

7. **SPICES:** Certain spices have good antioxidant properties e.g.,

➢ **Curcumin**, a principal curcuminoid extracted from turmeric, is a potential therapeutic antioxidant against acute hepatotoxicity. It prevents liver injury by suppressing hepatic oxidative stress. It has anti-cancer, anti-inflammatory, anti-obesity, and anti-diabetic properties. Curcumin prevents high fat diet-induced insulin resistance and obesity, attenuating lipogenesis [41], [42]. The study of Liu, H et. al. (2017) suggested that the curcumin intake reduce the risk of coronary heart disease, decreases the oxidative damage and inhibits the myocardium apoptosis[43].

➢ **Ginger phenolics** have been reported for its antioxidant potential and hepatoprotective activity [44]. Myocardial infarction (MI) is an acute condition of necrosis of the myocardium that occurs because of sudden or persistent interruption of blood supply to the demand of myocardium. The cardio-protective effects of ginger are associated with attenuation of hyperlipidemia, suppression of tissue injury markers release and inhibition of myocardial damage biomarkers against alcohol-induced elevation. Ginger-mediated reduction of total cholesterol, LDL and phospholipids, and concurrent increase of HDL concentrations in alcohol-fed rats implies that ginger could primarily contribute to lowering the hyperlipidemia [45].

➢ **Capsaicinoids and capsinoids, alkaloids** primarily found in red hot peppers and sweet peppers, have anti-cancer, anti-inflammatory, antioxidant, and anti-obesity effects. Capsaicinoid consumption increases the energy expenditure and lipid oxidation while reducing appetite and energy intake, thus promoting weight loss [42].

3. ROLE OF ANTIOXIDANTS IN PREVENTING VARIOS LIFESTYLE DISORDERS

CARDIAC DISEASES:

Oxidative stress, associated with atherosclerosis and endothelium-dependent vascular inflammation, plays a key role in the development of CVD [46]. The daily consumption of grape juice reduces the rate of atherosclerotic narrowing of the coronary arteries and incidence of potentially fatal coronary thrombosis [47]. Red wine contains antioxidants (like resveratrol, proanthocyanidine, quarcetin, etc.) which decrease the oxidative stress and reduces the inflammatory atherosclerotic lesion [46]. The study of Erlund, I et. al. (2008) indicated that berry consumption inhibited platelet function (CADP-CT), reduced blood pressure, and increased HDL concentrations [48].

Research indicated that low vitamin-C intake increased the risk of cardiovascular diseases. Average daily intake of 100mg vitamin-C could reduce the risk of cardiac ailments among nonsmoking men and women [49]. Results from the Nurses' Health Study (NHS), based on the follow-up of 85,118 women over 16 years also suggested that higher vitamin-C intakes lowered the risk of cardiac ailments [50].

The double-blind, placebo-controlled short-term study of Engelhard, Y.N. et. al. (2006) on the effect of administering tomato extract on the grade-I hypertensive patients showed that tomato extract can effectively reduce the BP of the hypertensive patients [51]. Study of Rissanen, T. et.al. (2000) conclude that low plasma lycopene concentrations are associated with early atherosclerosis, manifested as increased intima-media thickness of the common carotid artery wall, in middle-aged men living in eastern Finland [52]. Several studies indicated that higher blood level of carotenoids is associated with significantly lower measures of carotid artery intima-media thickness [53],[54],[55]&[56].

The flavonoids in cocoa and chocolate are predominately epicatechin based procyanidin oligomers and polymers [57]. They help to maintain good cardiac health by suppressing the platelet function [58]. Several studies indicated that regular intake of tea and flavonoids rich foods decreases the incidence of heart diseases [59], [60].

Several clinical trials have examined the effect of flavonoid-rich foods and beverages on endothelium-dependent vasodilation. The large prospective study, carried out by Li, X. et.al. (2017), indicated that daily tea consumption reduced the risk of ischaemic heart disease (IHD) [61]. Duffy, S.J. et.al. (2001) reported that Short- and long-term consumption of black tea reverses the endothelial vasomotor dysfunction in patients with coronary artery disease [62].

Green tea increases the activity of enzymes implicated in cellular protection against reactive oxygen species: superoxide dismutase in serum and the expression of catalase in the aorta. This action is combined with direct action on ROS by decreasing the plasma nitric oxide concentration. Green tea catechins prevent the atherosclerotic plaque formation and decrease the absorption of both triglycerides and cholesterol [63].

A 6-week cocoa intervention trial in postmenopausal hypercholesterolemic women found improvements in endothelial function with a significant decrease in vascular cell adhesion molecule [64].

OBESITY:

Obesity, a global health problem affecting all age groups, leads to many complications like type-II diabetes, hypertension, cardiovascular disease, dyslipidemia, atherosclerosis, and stroke [65].

A diet rich in antioxidants is found to be inversely related to central adiposity, metabolic and oxidative stress markers as well as risk of ischemic stroke [66]. The study of Suzuki, K. et.al. (2006) indicated that obese women, particularly with high waist circumference, usually have low serum carotenoid levels, and the abdominal fat accumulation is associated with oxidative stress [67]. The study of Nagao, T. et.al. (2009) suggested that green tea (a catechin-rich beverage) help to prevent obesity and improves blood glucose control in patients with type-II diabetes [68].

Isoflavones (genistein, daidzein, and glycitein) are present in legumes, grains, and vegetables. Due to almost similar chemical structure, Soybean Isoflavones can exert estrogen-like effects; and thus, are classified as phytoestrogens and are considered useful towards hormone-dependent cancers (e.g., prostate and breast cancers). Recent evidence suggest soybean Isoflavones also protect against obesity and co-morbidities [42].

NEUROLOGICAL DISORDERS:

Alzheimer's disease (AD) is the most prevalent progressive neurodegenerative disorder, pathologically characterized by deposition of β-amyloid (Aβ) peptides as senile plaques in the brain [17]. It is the most frequent cause of dementia [69]. Aging is the major risk factor for neurodegenerative diseases like Alzheimer's and Parkinson's diseases. Oxidative stress is involved in the pathophysiology of these diseases. Oxidative stress can induce neuronal damages, modulate intracellular signaling, ultimately leading to neuronal death by apoptosis or necrosis. Thus, many antioxidant rich foodstuffs play a beneficial role in reducing the progression of these neurodegenerative diseases [70].

Tocopherol (Vitamin E), a lipid-soluble antioxidant, is essential for the neurological function. It protects the cell membranes from oxidative damage and acts as an anti-inflammatory agent. It is neuroprotective, and it also regulates specific enzymes [71]. Dietary polyphenols have neuroprotective effects through scavenging free radicals and increasing antioxidant capacity [69]. Rezai-Zadeh, K. et.al. reported that green tea epigallocatechin-3-gallate (EGCG) reduces cerebral amyloidosis in Alzheimer transgenic mice. This study suggested that dietary supplementation of EGCG may provide effective prophylaxis for AD [17]. Recently, a study on 1,640 elderly men and women found that those with higher dietary flavonoid intake (>13.6 mg/day) had a better cognitive performance at baseline and experienced a significantly less age-related cognitive decline over a 10-year period than those with a lower flavonoid intake (0-10.4 mg/day) [72].

CANCER:

Epidemiological studies show that a high intake of anti-oxidant-rich foods is inversely related to cancer risk. Selenium and vitamin E reduced the risk of certain cancers, including prostate and colon cancers whereas carotenoids reduce the risk of breast cancer. Experimental studies show that antioxidants, including phytochemicals, selectively kill cancer cells by apoptosis while preventing apoptosis in normal cells, in vitro, and in vivo, and inhibit tumor angiogenesis and metastatic growth [73].

It has been estimated that 30–40% of all cancers can be prevented by lifestyle and dietary measures alone. Obesity, nutrient sparse foods such as concentrated sugars and refined flour products that contribute to impaired glucose metabolism (which leads to diabetes), low fiber intake, consumption of red meat, and imbalance of omega 3 and omega 6 fats all contribute to excess cancer risk. Intake of flax seed, especially its lignan fraction, and abundant portions of fruits and vegetables lower cancer risk. Allium and cruciferous vegetables are especially beneficial, with broccoli sprouts being the densest source of sulforophane [74].

Protective elements in a cancer prevention diet include selenium, folic acid, vitamin B-12, vitamin D, chlorophyll, and antioxidants such as the carotenoids (α-carotene, β-carotene, lycopene, lutein, cryptoxanthin). Such a diet would be conducive to preventing cancer and would favor recovery from cancer as well (74). Diet high in total antioxidant capacity is inversely associated with pancreatic cancer risk [75].

The Swedish Mammography Cohort study on 59,036 women (40-76 years) who were overweight and/or had a high intake of linoleic acid (more than 6g/day), suggested that high intake of ascorbic acid rich foods is inversely related to breast cancer [76].

Many observational studies have found increased dietary vitamin C intake to be associated with decreased risk of stomach cancer, and laboratory experiments indicate that vitamin C inhibits the formation of carcinogenic compounds in the stomach [77], [78].

The study of Chen, M. et.al. (2014) suggested that soy isoflavone intake could lower the risk of breast cancer for both pre- and post-menopausal women in Asian countries [79].

GOUT:

The 20 year-long study of Choi, H.K. (2009) on 1317 gout patients suggested that higher vitamin C intake is independently associated with a lower risk of gout [80]. The population-based study of Gao, X. et.al. (2008) on 1387 men without hypertension and with body mass index less than 30 indicated that vitamin C intake is inversely associated with serum uric acid concentrations [81]. These findings support a potential role of vitamin C in the prevention of hyperuricemia and gout.

4. CONCLUSION

Free radicals are produced in our body throughout the life by normal cellular metabolism, which is further increased due to the exposure to pollution, cigarette smoke, radiation and medication. They attack biological macromolecules such as proteins, fatty acids and nucleic acids, causing oxidative damage to cells or tissues or even resulting in gene mutation. Excess production of free radicals in the body leads to oxidative stress, which is closely related to the aging process and the onset of several chronic diseases such as cardiac disorders, diabetes mellitus, neurodegenerative disorders like Alzheimer’s and Parkinson's disease and cancer.

Dietary antioxidants include ascorbic acid, tocopherol, carotenoids (β-carotene, lycopene and astaxanthin), plant polyphenols present in fruits, vegetables, tea, coffee, red wine, honey as well as cocoa beans and certain minerals (e.g. zinc, selenium) and selective spices (like turmeric, ginger, peppers etc.). They scavenge the excess free radicals, avoiding oxidative damage of the cell and preventing the onset and progression of many chronic diseases.

Antioxidant rich foods, particularly grape juice, red wine, berries, tomato extract (lycopene), chocolates, cocoa green and black tea etc. are cardiac-friendly foods. They help to reduce blood pressure, improve lipid profile, prevents atherosclerosis. Dietary antioxidants are found to be inversely associated with central adiposity. Soybean Isoflavones protect against obesity and co-morbidities. Tocopherol and green tea have certain neuroprotective effects, preventing neuro-degenerative diseases. Dietary polyphenols, vitamin-E and vitamin-C, Selenium, isoflavins reduces the cancer risk. Vitamin-C has a potential role in the prevention of hyperuricemia and gout.

Regular intake of antioxidant rich diet helps to prevent many age-related diseases like cardiac ailments, Neurodegenerative diseases, many types of cancers, gout etc. Hence the diet of adults, particularly middle-aged and elderly people should be well balanced containing a high amount of antioxidants, to retard the ageing process and reduce the occurrence of age related diseases.

REFERENCES

[1] Gemma, C, Vila, J, Bachstetter, A, & Bickford, PC. (2007). Chapter 15: Oxidative Stress and the Aging Brain: From Theory to Prevention. In: Brain Aging: Models, Methods, and Mechanisms. Boca Raton (FL): CRC Press/Taylor & Francis, 2007.

[2] Lenaz G. (2012). Mitochondria and reactive oxygen species. Which role in physiology and pathology? In: Advances in Mitochondrial Medicine. Advances in Experimental Medicine and Biology. Vol 942, 93-136. Springer, Dordrecht, 2012.

[3] Gupta RK, Patel AK, Shah N et al (2014). Oxidative Stress and Antioxidants in Disease and Cancer: A Review. Asian Pacific Journal of Cancer Prevention, 15(11): 4405-4409.

[4] Anderson C Milne GL Sandler DP et al (2016). Oxidative stress in relation to diet and physical activity among premenopausal women. The British journal of nutrition, 116(8):1416–1424.

[5] Pham-Huy,LA He,H Pham-Huy,C. (2008). Free Radicals, Antioxidants in Disease and Health. International journal of biomedical science, 4(2):89–96.

[6] Urquiza-Martínez MV, & Navarro BF. (2016). Antioxidant Capacity of Food. Free Radicals and Antioxidants, 6(1):1-12.

[7] Valko M, Rhodes CJ, Moncol J et al (2006). Free radicals, metals and antioxidants in oxidative stress-induced cancer. Chemico-biological interactions, 160(1):1-40.

[8] Bors W, & Michel C. (2002). Chemistry of the antioxidant effect of polyphenols. Annals of the New York Academy of Sciences, 957:57-69.

[9] Scalbert A, Johnson IT, Saltmarsh M. (2005). Polyphenols: antioxidants and beyond. The American journal of clinical nutrition, 81:215S-217S.

[10] Li S, Chen G, Zhang C et al (2014). Research progress of natural antioxidants in foods for the treatment of diseases. Food Science and Human Wellness, 3(3-4):110–116.

[11] Choi DY, Lee YJ, Hong JT et al (2012). Antioxidant properties of natural polyphenols and their therapeutic potentials for Alzheimer's disease. Brain research bulletin, 87(2-3):144-53.

[12] Wood LG, Wark PA, & Garg ML. (2010). Antioxidant and anti-inflammatory effects of resveratrol in airway disease. Antioxidants & redox signaling, 13(10):1535-48.

[13] Andújar I, Recio MC, Giner RM et al (2012). Cocoa Polyphenols and Their Potential Benefits for Human Health. Oxidative Medicine and Cellular Longevity, 2012, 1-23.

[14] Suzuki K, Nakagawa K, Miyazawa T et al. (2013). Oxidative stress during development of alcoholic fatty liver: Therapeutic potential of cacao Polyphenol. Bioscience, Biotechnology, and Biochemistry, 77(8):1792-1794.

[15] Bettuzzi S, Brausi M, Rizzi F et al (2006). Chemoprevention of human prostate cancer by oral administration of green tea catechins in volunteers with high-grade prostate intraepithelial neoplasia: A preliminary report from a one-year proof-of-principle study. Cancer Research, 66(2):1234-1240.

[16] Jian L, Xie LP, Lee AH et al (2003). Protective effect of green tea against prostate cancer: A case-control study in southeast China. International journal of cancer, 108(1):130–135.

[17] Rezai-Zadeh K, Shytle D, Sun N et. al. (2005). Green tea epigallocatechin-3-gallate (EGCG) modulates amyloid precursor protein cleavage and reduces cerebral amyloidosis in Alzheimer transgenic mice. The Journal of Neuroscience, 25(38):8807-8814.

[18] Bornhoeft J, Castaneda D, Nemoseck T et al (2012). The protective effects of green tea polyphenols: lipid profile, inflammation, and antioxidant capacity in rats fed an atherogenic diet and dextran sodium sulfate. Journal of medicinal food, 15(8):726-32.

[19] Hokayem M, Blond E, Vidal H et. al. (2013). Grape polyphenols prevent fructose-induced oxidative stress and insulin resistance in first-degree relatives of type 2 diabetic patients. Diabetes Care, 36(6):1454–1461.

[20] Du Y, Guo H, & Lou H. (2007). Grape seed polyphenols protect cardiac cells from apoptosis via induction of endogenous antioxidant enzymes. Journal of Agriculture Food Cheistry, 55(5):1695–1701.

[21] Noratto GD, Porter W, Byrne D et al (2014). Polyphenolics from peach (Prunus persica var. Rich Lady) inhibit tumor growth and metastasis of MDA-MB-435 breast cancer cells in vivo. The Journal of Nutritional Biochemistry, 25(7):796–800.

[22] Geleijnse JM & Hollman PC (2008). Flavonoids and cardiovascular health: which compounds, what mechanisms? The American Journal of Clinical Nutrition, 88(1):12-13.

[23] Wada K, Nakamura K, Tamai Y et. al. (2013). Soy isoflavone intake and breast cancer risk in Japan: From the Takayama study. International Journal of Cancer, 133:952–960.

[24] Lee AH, Su D, Pasalich M et al (2014). Soy and isoflavone intake associated with reduced risk of ovarian cancer in southern Chinese women. Nutrition research, 34(4):302-7.

[25] Xie H, Wang JR, Yau LF et.al. (2014). Catechins and procyanidins of Ginkgo biloba show potent activities towards the inhibition of β-amyloid peptide aggregation and destabilization of preformed fibrils. Molecules, 19(4):5119-34.

[26] Pascual-Teresa SD (2014). Molecular mechanisms involved in the cardiovascular and neuroprotective effects of anthocyanins. Archives of Biochemistry and Biophysics, 559:68-74.

[27] Zafra-Stone S, Yasmin T, Bagchi M et al (2007). Berry anthocyanins as novel antioxidants in human health and disease prevention. Molecular nutrition & food research, 51(6):675-83.

[28] Powell SR (2000). The Antioxidant Properties of Zinc. The Journal of Nutrition, 130(5):1447S-1454S.

[29] Prasad AS, Beck FW, Bao B et.al. (2007). Zinc supplementation decreases incidence of infections in the elderly: effect of zinc on generation of cytokines and oxidative stress. The American journal of clinical nutrition, 85(3):837-44.

[30] Prasad AS (2014). Zinc is an Antioxidant and Anti-Inflammatory Agent: Its Role in Human Health. Frontiers in Nutrition, 1(14):1-10.

[31] Cruz KJC, Oliveira ARSD, Marreiro DDN (2015). Antioxidant role of zinc in diabetes mellitus. World Journal of Diabetes, 6(2):333–337.

[32] Prasad AS (2008). Zinc in human health: effect of Zinc on immune cells. Molecular Medicine, 14(5-6):353–357.

[33] Sazawal S, Black RE, Bhan MK et al (1995). Zinc supplementation in young children with acute diarrhea in India. The New England Journal of Medicine, 333(13):839-844.

[34] Murphy EW, Willis BW, Watt BK (1975). Provisional tables on the zinc content of foods. Journal of the American Dietetic Association, 66(4):345-55.

[35] Sen S & Chakraborty R (2011). Chapter 1: The Role of Antioxidants in Human Health. In Oxidative Stress: Diagnostics, Prevention and Therapy. Washington, DC: ACS Symposium Series 1083/ Oxford University Press, Inc, 2011

[36] Tinggi U. (2008). Selenium: its role as antioxidant in human health. Environmental Health and Preventive Medicine, 13(2):102–108.

[37] Brown KM & Arthur JR (2001). Selenium, selenoproteins and human health: a review. Public health nutrition, 4(2):593-9.

[38] Chen J & Berry MJ (2003). Selenium and selenoproteins in the brain and brain diseases. Journal of Neurochemistry, 86(1):1-12.

[39] Aguirre JD & Culotta VC (2012). Battles with Iron: Manganese in oxidative stress protection. The Journal of Biological Chemistry, 287(17):13541–13548.

[40] Price CT, Langford JR, Liporace FA (2012). Essential nutrients for bone health and a review of their availability in the average North American diet. The Open Orthopaedics Journal, 6:143-149.

[41] Lee GH, Lee HY, Choi MK et al (2017). Protective effect of Curcuma longa L. extract on CCl4-induced acute hepatic stress. Biomed Central research notes, 10(17):1-9.

[42] Savini I, Catani MV, Evangelista D et al (2013). Obesity-associated oxidative stress: Strategies finalized to improve redox state. International Journal of Molecular Sciences, 14(5):10497–10538.

[43] Liu H, Wang C, Qiao Z et al (2017). Protective effect of curcumin against myocardium injury in ischemia reperfusion rats. Pharmaceutical Biology, 55(1):1144-1148.

[44] AVV, KRR, Kurrey NK et al (2017). Protective effects of phenolics rich extract of ginger against Aflatoxin B1-induced oxidative stress and hepatotoxicity. Biomedicine & pharmacotherapy, 91:415-424.

[45] Subbaiah GV, Mallikarjuna K, Shanmugam B et al (2017). Ginger treatment ameliorates alcohol-induced myocardial damage by suppression of hyperlipidemia and cardiac biomarkers in rats. Pharmacognosy Magazine, 13(1):S69–S75.

[46] Saleem TSM & Basha D (2010). Red wine: A drink to your heart. Journal of Cardiovascular Disease Research, 1(4):171–176.

[47] Osman HE, Maalej N, Shanmuganayagam D et al (1998). Grape juice but not orange or grapefruit juice inhibits platelet activity in dogs and monkeys (Macaca fascularis). The Journal of Nutrition, 128(12):2307-2312.

[48] Erlund I, Koli R, Alfthan G et.al. (2008). Favorable effects of berry consumption on platelet function, blood pressure, and HDL cholesterol. The American Journal of Clinical Nutrition, 87(2):323-331.

[49] Carr AC & Frei B (1999). Toward a new recommended dietary allowance for vitamin C based on antioxidant and health effects in humans. The American Journal of Clinical Nutrition, 69(6):1086-107.

[50] Osganian SK, Stampfer MJ, Rimm E et al (2003). Vitamin C and risk of coronary heart disease in women. Journal of the American College of Cardiology, 42(2):246-52.

[51] Engelhard YN, Gazer B, Paran E. (2006). Natural antioxidants from tomato extract reduce blood pressure in patients with grade-1 hypertension: a double-blind, placebo-controlled pilot study. American heart journal, 151(1), 100.e1–100.e6.

[52] Rissanen T, Voutilainen S, Nyyssönen K (2000). Low plasma lycopene concentration is associated with increased intima-media thickness of the carotid artery wall. Arteriosclerosis, thrombosis, and vascular biology, 20(12):2677-81.

[53] Rissanen TH, Voutilainen S, Nyyssönen K et al (2003). Serum lycopene concentrations and carotid atherosclerosis: the Kuopio ischaemic heart disease risk factor study. The American Journal of Clinical Nutrition, 77(1):133-8.

[54] Dwyer JH, Paul-Labrador MJ, Fan J et al (2004). Progression of carotid intima-media thickness and plasma antioxidants: the Los Angeles sterosclerosis study. Arteriosclerosis, thrombosis, and vascular biology, 24(2):313-9.

[55] D'Odorico A, Martines D, Kiechl S et al (2000). High plasma levels of alpha- and beta-carotene are associated with a lower risk of atherosclerosis: results from the Bruneck study. Atherosclerosis, 153(1):231-9.

[56] Iribarren C, Folsom AR, Jr JDR et al (1997). Association of serum vitamin levels, LDL susceptibility to oxidation, and autoantibodies against MDA-LDL with carotid atherosclerosis. A case-control study. The ARIC study investigators. Atherosclerosis risk in communities. Arteriosclerosis, thrombosis, and vascular biology, 17(6):1171-7.

[57] Porter LJ, Maa Z, Chanb BG (1991). Cacao procyanidins: major flavanoids and identification of some minor metabolites. Phytochemistry, 30(5):1657-1663.

[58] Rein D, Paglieroni TG., Wun T, et al (2000). Cocoa inhibits platelet activation and function. The American Journal of Clinical Nutrition, 72(1):30-35.

[59] Geleijnse JM, Launer LJ, Kuip DAMVD et al (2002). Inverse association of tea and flavonoid intakes with incident myocardial infarction: the Rotterdam Study. The American Journal of Clinical Nutrition, 75(5):880-886.

[60] Hertog MG, Feskens EJ, Hollman PC et al. (1993). Dietary antioxidant flavonoids and risk of coronary heart disease: the Zutphen Elderly Study. Lancet, 342(8878):1007-11.

[61] Li X, Yu C, Guo Y et.al. (2017). Tea consumption and risk of ischaemic heart disease. Cardiac risk factors and prevention, 1-7.

[62] Duffy SJ, Keaney JF, Holbrook M et al (2001). Short- and llong-term black tea consumption reverses endothelial dysfunction in patients with coronary artery disease. Circulation, 104(2):151-6.

[63] Khan N & Mukhtar H (2013). Tea and health: Studies in humans. Current pharmaceutical design, 19(34):6141–6147.

[64] Wang-Polagruto JF, Villablanca AC, Polagruto JA et al (2006). Chronic consumption of flavanol-rich cocoa improves endothelial function and decreases vascular cell adhesion molecule in hypercholesterolemic postmenopausal women. Journal of Cardiovascular Pharmacology, 47:S177-S186.

[65] Hassan HA & El-Gharib NE (2015). Obesity and clinical riskiness relationship: Therapeutic management by dietary antioxidant supplementation--A review. Applied biochemistry and biotechnology, 176(3):647-69.

[66] Hermsdorff HH, Puchau B, Volp AC et al (2011). Dietary total antioxidant capacity is inversely related to central adiposity as well as to metabolic and oxidative stress markers in healthy young adults. Nutrition & Metabolism, 8(59):1-8.

[67] Suzuki K, Inoue T, Hioki R, Ochiai J et.al. (2006). Association of abdominal obesity with decreased serum levels of carotenoids in a healthy Japanese population. Clinical nutrition, 25(5):780-9.

[68] Nagao T, Meguro S, Hase T et al (2009). A catechin-rich beverage improves obesity and blood glucose control in patients with type 2 diabetes. Obesity, 17(2):310-7.

[69] Choi DY, Lee YJ, Hong JT et al. (2012). Antioxidant properties of natural polyphenols and their therapeutic potentials for Alzheimer's disease. Brain research bulletin, 87(2-3):144-53.

[70] Ramassamy C (2006). Emerging role of polyphenolic compounds in the treatment of neurodegenerative diseases: a review of their intracellular targets. European journal of pharmacology, 545(1):51-64.

[71] Imounan F, Bouslam N, Aasfara J et al (2012). Vitamin E in ataxia and neurodegenerative diseases: A review. World Journal of Neuroscience, 2(4):217-222.

[72] Letenneur L, Proust-Lima C, Gouge AL et al (2007). Flavonoid intake and cognitive decline over a 10-year period. American journal of epidemiology, 165(12):1364-71.

[73] Borek C (2004). Dietary antioxidants and human cancer. Integrative Cancer Therapies, 3(4):333-341.

[74] Donaldson, M.S. (2004). Nutrition and cancer: A review of the evidence for an anti-cancer diet. Nutrition Journal, 3(19):1-21.

[75] Lucas AL, Bosetti C, Boffetta P et.al. (2016). Dietary total antioxidant capacity and pancreatic cancer risk: An Italian case–control study. British Journal of Cancer, 115:102–107.

[76] Michels KB, Holmberg L, Bergkvist L et al (2001). Dietary antioxidant vitamins, retinol, and breast cancer incidence in a cohort of Swedish women. International journal of cancer, 91(4):563–567.

[77] Tsugane S, & Sasazuki S (2007). Diet and the risk of gastric cancer: review of epidemiological evidence. Gastric Cancer, 10(2):75-83.

[78] Liu C, & Russell RM (2008). Nutrition and gastric cancer risk: an update. Nutrition reviews, 66(5):237-49.

[79] Chen M, Rao Y, Zheng Y et al (2014). Association between soy isoflavone intake and breast cancer risk for pre- and post-menopausal women: a meta-analysis of epidemiological studies. PloS one, 9(2):e89288.

[80] Choi HK, Gao X & Curhan G. (2009). Vitamin C intake and the risk of gout in men: a prospective study. Archives of internal medicine, 169(5):502-7.

[81] Gao X, Curhan G, Forman JP et al. (2008). Vitamin C intake and serum uric acid concentration in men. The Journal of rheumatology, 35(9):1853-8.