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## Antioxidants: Dietary scavengers in lifestyle diseases

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### Abstract

Many researchers have reviewed the involvement of free radicals in the development of life style diseases like diabetes, cancer, cardiovascular diseases, cataract, ageing, neurodegenerative diseases etc. Antioxidant plays an important role in preventing these degenerative diseases by scavenging free radicals. Antioxidant from exogenous sources are necessary to have as endogenous antioxidant defenses like superoxide dismutases, metal binding protein, H<sub>2</sub>O<sub>2</sub> removing enzymes are inadequate to prevent these diseases. Considering all this, the review article presents the research conducted by various researchers on dietary sources of antioxidants and their benefits in preventing life style diseases.

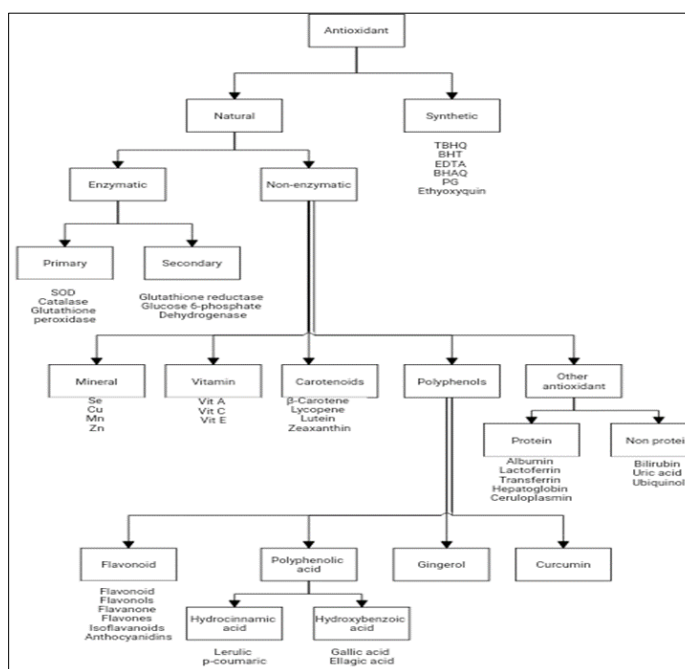
**Keywords:** Antioxidant, degenerative diseases, free radicals, flavonoids, phenolic compounds

### Introduction

Antioxidants are the compounds that can delay, inhibit or prevent the oxidation of biomolecules like lipids, proteins or nucleic acids. A substance that opposes oxidation or inhibits reactions promoted by oxygen or peroxides called antioxidant. Antioxidants may scavenge the free radicals or break the chain reaction due to their redox properties. Antioxidant is “synthetic or natural substances added to products to prevent or delay their deterioration by action of oxygen in air.

### Classification of antioxidants

Antioxidants can be classified into two major types based on their source, i.e., natural and synthetic antioxidants (fig 1). Some antioxidants are produced endogenously which include enzymes, uric acid, bilirubin and enzyme cofactors. Among non-enzymatic antioxidants many are obtained from dietary sources. Non-enzymatic antioxidants can be classified into various classes in which polyphenols present the largest class. Polyphenols consist of phenolic acids and flavonoids. Fig (1) illustrates the classification of antioxidants



**Fig 1:** Classification of antioxidants

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### Sources of antioxidants

Major sources of naturally occurring antioxidants are whole grains <sup>[1]</sup>, fruits <sup>[2]</sup>, vegetables <sup>[3]</sup>, green tea <sup>[4]</sup> and black tea <sup>[5]</sup>, coffee <sup>[6, 7]</sup>, wine <sup>[8]</sup>, beer <sup>[9, 10]</sup> and herbs and spices <sup>[11]</sup>.

### Nutrients as dietary sources of antioxidants

Antioxidant defence system of the body protect cell membrane, lipoprotein, DNA and RNA from the damaging effects of the free radicals. Table 1 depicted nutrient wise source of antioxidants. Some nutrients involve directly in antioxidant activity (Vitamin A, E, C) and other take part as cofactor in enzymatic reaction e.g. cytoplasmic and

mitochondrial superoxide dismutases require copper to catalyze the removal of superoxide radical.

Some antioxidant are synthesized by the cell (endogenous) and other need to be provided by the diet. Ubiquinone is synthesized in the body from the precursor of cholesterol. For this reason it is not classified as vitamin. However, the ability to synthesize ubiquinone is decrease with the age and it have to take from exogenous sources. Melatonin is produced from l-tryptophan which is acquired from protein catabolism. However, high amount of melatonin is needed in sleep disturbance.

**Table 1:** Nutrients as dietary sources of antioxidants

Compound Name	Natural Source
Vitamin E	Cereals, cereal products, oil seeds, nuts, broccoli, cooking oil, brussels sprouts, cauliflower
Vitamin C	Citrus fruits, guava, tomatoes, goose berry, sprouted pulses.
Carotenoids	Green leafy vegetables, ripe yellow fruits and vegetables like papaya, musk melon, mango, pumpkin, carrots
Flavonoids	Potatoes, tomatoes, lettuce, onions, wheat, concord grapes, black tea, red wine, chocolates, apple, grapes, peaches, pears
Polyamines	Oranges, soy sauce, grapefruit juice, soybean, green peas, corn, shell fish, chicken liver, pumpkin
Melatonin	Fish, egg, milk, cereals, mushrooms, nuts, germinated legumes
Phytoestrogen	Soyabean, flax seeds, sesame seeds, fenugreek, oats, barley, nuts and oil seeds, apple, carrot
Ubiquinone	Wheat bran, organ meat, oily fish (such as salmon and tuna)
Copper	Oysters, liver, mushroom, nuts, chocolate
Lipoic acid	Spinach, broccoli, yams, potatoes, yeast, tomatoes, Brussels sprouts, carrot, beets, rice bran, organ meat.
Various allyl sulphides	Garlic, onion, leeks
Selenium	Brazil nuts, Whole grains, Seafood
Folate	Fortified cereal and breads, avocado, Salmon, Green leafy vegetables.
Isothiocyanataes	Cauliflower, cabbage, brocholi, horse raddish

### Natural antioxidants from cereals and legumes

Whole grain cereals contain high amount of bioactive components <sup>[12, 13]</sup>. Zilic *et al.*, (2011) <sup>[14]</sup> reported that hull-less barley and oats have high content of total free phenols, flavnoids and flavan-3-ols and tocopherols respectively. [Table 1]. Sreeramulu *et al.*, (2009) <sup>[15]</sup> concluded that total phenolic content contributes significantly to the antioxidant activity of Indian cereals and millets. Cereals exhibited free radical scavenging activities, ferric reducing power, ability for inhibition of lipid peroxidation and total phenolic contents <sup>[16]</sup>. A variety of studies have reported the antioxidant activities of many legumes, such as green gram, red kidney beans, chickpea, red lentil, soybean, moth bean (Gujral *et al.*, 2013) <sup>[17]</sup> pinto bean, cow pea, baby lima bean, lentil, small red bean, black kidney bean, navy bean <sup>[18]</sup> horse gram, common bean <sup>[19]</sup>, soybean and cowpea sprouts <sup>[20]</sup>.

### Natural antioxidants from nuts and oilseeds

Sreeramulu and Raghunath, (2011) <sup>[21]</sup> reported high amount and moderate amount of antioxidants and phenolic content in arecanut and mustard seed respectively [Table 1]. Sunflower and safflower seeds have moderate amount of antioxidants. Carlsen *et al.*, (2011) <sup>[22]</sup> reported walnuts, pecans, chestnuts, peanuts, pistachios and sunflower seeds are very rich in total antioxidants whereas hazelnuts, almonds, Brazil nuts, macadamias, pine kernels, cashew nuts, flax seeds, poppy seeds and sesame seeds contain significant amount of total antioxidant. Arcan and Yemenicioglu, (2009) <sup>[23]</sup> also found high amount of antioxidants and phenolic contents in fress nuts (hazelnuts, walnut and pistachios) [Table 1]. Pumpkin seed extract has been reported to have anticancer, antimutagenic, and antioxidant activities <sup>[24]</sup>.

### Natural antioxidants from milk and animal food

According to Grazyna, *et al.*, (2017) <sup>[25]</sup> milk contain lipophilic (conjugated linoleic acid,  $\alpha$ -tocopherol,  $\beta$ -carotene,

vitamins A and D<sub>3</sub>, coenzyme Q<sub>10</sub>, phospholipids) and hydrophilic antioxidants (proteins, peptides, vitamins, minerals and trace elements). However meat, fish and other foods from the animal kingdom are comparatively low in antioxidants <sup>[26]</sup>.

### Natural antioxidants from sugar and jaggery

Jaggery and brown sugar have different phenolic acid and antioxidant activity <sup>[27]</sup>. Dark and black strap molasses have the highest antioxidant activity while maple syrup, brown sugar and honey have intermediate antioxidant capacity. Refined sugar, corn syrup and agave nectar contain minimal antioxidant activity <sup>[28]</sup>.

### Natural antioxidants from spices and herbs

Most of the spices and herbs have high antioxidant contents. Although spices and herbs contribute little weight on the dinner plate, they may still be important contributors to our antioxidant intake <sup>[26]</sup>. Green tea consists of essential oil, tannin, caffeine, vitamin, pigment, pheophytin and pheophorbide and reported to have antioxidant activity <sup>[29]</sup>. Singhal *et al.*, (2017) <sup>[30]</sup> found high antioxidant activity in spices (rai, fennel, ajwain and kalonji).

### Natural antioxidants from fruits and vegetables

The main sources of flavonoids are vegetables and fruits <sup>[31]</sup>. The most of fruits are rich source of vitamin C, carotenoids and polyphenolic compounds [Table 1] <sup>[32, 33]</sup>. Apple has been reported to possess strong antioxidant activity; inhibit cancer cell proliferation, decrease lipid oxidation, and lower cholesterol <sup>[34]</sup>. Pink grape fruit <sup>[35]</sup> beet root <sup>[36]</sup> avocado <sup>[37]</sup> have high amount of antioxidant. Moreover, there are some new and unique antioxidants that have been discovered in spinach. NAO is an aqueous spinach-leaf extract that contains derivatives of flavonoids and p-coumaric acid <sup>[38]</sup>. Table 1 depicted nutrient wise source of antioxidants.

### Antioxidants as scavengers in diseases prevention

Free radicals and reactive oxygen species (ROS) are regularly and continuously produced as byproducts of normal cellular metabolism in aerobics as well as by pollution, radiation, smoking and stress [39]. Being unstable and reactive, free radicals possess the ability to damage essential bio molecules (lipid, DNA and protein) in the form of tissue injury and cell death; if they exceed a certain limit. Free radicals are responsible for causing a large number of diseases including cancer [40, 41], cardiovascular diseases [42, 43], neural disorders [44, 45], alzheimer's disease [46, 47], parkinson's disease [48, 49], liver disease [50, 51], ulcer-ative colitis [52, 53], aging [54, 55], skin diseases [56] and rheumatoid arthritis [57]. Harmful effects of free radicals can be avoided by their regular removal from the body. To meet the purpose, there is a built-in natural antioxidative defense system (enzymatic and non-enzymatic) in the human body, which continuously and proportionally neutralizes free radicals by scavenging [58]. Consumption of food rich in antioxidant may not only reduce oxidative damage but also provide protection against oxidative stress-related disorders [59]. Additional supplements of antioxidants are not needed until we are having good diet. But certain conditions such as aging, prolonged illness, stress, poor diet increase demand of antioxidants.

The main role of antioxidants is to liquidate the uncontrolled production of reactive oxygen species (ROS) that is being linked to pathogenesis of cardiovascular disease (CVD), malignancy, diabetes type 2, mechanism of infection, fibrogenesis and some neurological disorders [60]. Under certain conditions both water soluble antioxidants (e.g. vitamin C and urate) and the lipid soluble antioxidant tocopherol [Table 1] promote or even induce peroxidation [61]. Epidemiological studies and associated meta-analyses strongly suggest that long term consumption of diets rich in plant polyphenols offer protection against development of cancers, cardiovascular diseases, diabetes, osteoporosis and neurodegenerative diseases [62]. García-Lafuente *et al.*, (2009) [63] studied the anti-inflammatory activity of flavonoids [Table 1] and the implications of these effects on the protection against cancer and cardiovascular disease.

Eugenol component of clove oil exhibits *in vivo* anti-inflammatory action in lipopolysaccharide-induced lung injury [64]. Jayameena *et al.*, (2018) [65] found rutin, a dietary flavonoid (buckwheat, apricots, cherries, grapes) beneficial in treatment of different conditions and ailments such as inflammation, cancer, diabetes, hypertension, hypercholesterolemia, inflammatory bowel disease and other neurological disease. Resveratrol, a natural antioxidant first obtained from white hellebore, has been found to be tremendously useful in treatment of various diseases like inflammation, cancer, diabetes and cardiovascular and neurological disorders [66].

### Cardiovascular diseases

Higher dietary intake of antioxidant is associated with a reduced risk for stroke, especially among men [67]. Antioxidants have the capacities of preventing cardiovascular diseases include atherosclerosis, coronary heart disease, arterial hypertension, and heart failure [68]. Pruthi *et al.*, (2001) [69] observed 37 percent reduction in CVD after intervention of 100IU/day vitamin E. Kritharides *et al.*, (2002) [70] also reported significant reduction in risk of CVD as well as mortality due to CVD. Significant increase in elasticity of large and small artery was observed in patients with multiple

cardiovascular risk factors after antioxidant supplementation by Shargorodsky *et al.*, (2010) [71].

### Cancer

Various bioactivities of phenolic compounds are responsible for their chemopreventive properties (e.g., antioxidant, anticarcinogenic, or antimutagenic and anti-inflammatory effects) and also contribute to their inducing apoptosis by arresting cell cycle, regulating carcinogen metabolism [72]. Prevention of cancer risk against oxidative damage was observed in lower doses of retinol palmitate and/or ascorbic acid [73]. High dietary quercetin (buckwheat) and apigenin (parsley, onions, oranges) have been reported to be inversely related to the risk of noncardia gastric adenocarcinoma [74], colon cancer [75] and rectal cancer [76] respectively. Chemopreventive effects of anthocyanidins (found in wine and fruit juice) and isoflavonoids have been found in esophageal adenocarcinoma, gastric cancer [77] and esophageal squamous cell carcinoma [78]. Dietary intake of total flavonoids, anthocyanidins, flavanones, flavonols, flavones and flavan-3-ol monomers [Table 1] have been reported to reduce the risk of esophageal cancer [79, 80], head and neck cancer [81], gastric cancer [82, 83, 84] and lung cancer [85]. Rossi *et al.*, 2010 [86] and Hernández-Ramírez *et al.*, (2009) [87] suggest that higher intake of cinnamic acids (pears, mangos and beans), secoisolariciresinol (beans, carrots and squash), coumestrol (legumes) and proanthocyanidins (pine bark and grape seeds) reduce gastric cancer risk through inhibition of endogenous nitrosation. The intake of flavonols, flavones and flavanones [Table 1] is associated with a decreased risk of breast cancer among post-menopausal women [88, 89], menopausal women [90] and ovarian cancer [91].

### Diabetes

Higher intakes of total flavonoids and subclasses (anthocyanidins, flavan-3-ols, flavonols, and isoflavones) [Table 1] are associated with lower risk of T2DM [92, 93]. Antioxidants such as N-acetylcysteine, vitamin C, and  $\alpha$ -lipoic acid are effective in reducing diabetic complications [94]. Intake of alpha-tocopherol, gamma-tocopherol, delta-tocopherol, and beta-tocotrienol were inversely related to a risk of type-2 diabetes [95, 96]. Brusell *et al.*, (1999) [97] reported that vitamin E supplementation help in normalizing retinal blood flow and creatinine clearance in patients with type 1 diabetes and high-dose ascorbic acid supplementation have a beneficial effect in NIDDM subjects on both glycemic control and blood lipids.

### Dementia, depression and Alzheimer disease

Higher intake of foods rich in vitamin E may modestly reduce long-term risk of dementia and Alzheimer diseases [98, 99]. Higher flavonoid intakes may be associated with lower depression risk, particularly among older women [100]. High intake of lycopene or lutein and zeaxanthin rich food has observed important for reducing the dementia and AD mortality risk [101, 102]. Mullan *et al.*, (2017) [103] observed significantly lower level of  $\alpha$ -Tocopherol and all six carotenoids in patients with AD compared with cognitively intact control. Wang *et al.*, (2008) [104] also reported lutein, beta-carotene and beta-cryptoxanthin slow the rate of cognitive decline.

### Age related macular degeneration

Arslen *et al.*, 2018 [105] reported that high dietary intake of carotenoids, vitamins C and E [Table 1], zinc, and omega-3 reduce the risk of developing age-related macular degeneration in people aged >50 years. Johnson (2010) [106]

observed decreased AMD risk with increased intakes of lutein/zeaxanthin, B vitamins, zinc and docosahexaenoic acid.

### Parkinson disease

Intake of some flavonoids may reduce parkinson disease risk, particularly in men <sup>[107]</sup>. Dietary vitamin E and  $\beta$ -carotene [Table 1] may have a neuroprotective effect attenuating the risk of PD <sup>[108, 109, 110, 111]</sup>. Zhang *et al.*, (2002) <sup>[112]</sup> observed moderate amounts of vitamin E may reduce risk of PD, but this benefit may be lost with higher intakes. Kim *et al.*, (2016) <sup>[113]</sup> reported decreases in serum  $\alpha$ -carotene,  $\beta$ -carotene and lycopene associated with the pathogenesis as well as progression of PD.

### Conclusion

Free radicals have been reported in the etiology of large number of lifestyle diseases like diabetes, cancer, hypertension, atherosclerosis etc. Antioxidants mainly from natural dietary sources such as enzymes tocopherol, carotenoids, ascorbic acid, polyphenols etc. have great potential in prevention of these life threatening diseases by scavenging free radicals. Antioxidants are ubiquitous in commonly consumed food products and are easily available. A number of synthetic antioxidants are available in the market but natural dietary sources possess no side effects so it is recommended to switch on to natural dietary sources.

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