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# Dietary Antioxidants and Human Diseases

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**Abstract**

Oxidative stress has been implicated in the development of cancer and various chronic inflammatory and degenerative human diseases of cardiovascular, neurological, respiratory and gastrointestinal origin. Dietary antioxidants intake as part of normal diet or supplements can attenuate free radical induced cel damage and reduce the morbidity and mortality associated with these diseases. In this review, role of dietary antioxidants in common oxidative stress associated human diseases will be discussed.

**Key words**: Oxidative; stress; disease; defense; therapy; protection

## 1. Introduction

Along with the well-known immune defense system, our body has evolved to harbor an antioxidant defense system that functions to maintain the important redox balance. Oxidative stress that plays a major role in pathogenesis of several clinical conditions involving cardiovascular, respiratory & liver diseases, gastrointestinal & neurological disorders, muscle damage, diabetes, and aging (Pizzino et al 2017), is naturally countered by antioxidants. An antioxidant is defined as a substance that inhibits oxidation. For a better understanding, we can state that any substance that has an oxidizable substrate, and when present in low levels, significantly delays or inhibits the oxidation of that substrate, is an antioxidant (Halliwell and Gutteridge 1995). Owing to essential role of antioxidants, these have deemed interesting candidates to be used in therapy for several diseases (Pizzino et al 2017). In the present review, we aim to summarize the available information on the role of dietary antioxidants in several diseases. This will be relevant to understand the protective role of antioxidants and the implications of our dietary habits.

## 2. Types of Antioxidants

The types of antioxidants range from those generated endogenously by the body's own cells to exogenous agents such as dietary supplements (Kurutas 2015). Based on the activity, antioxidants can be categorized as enzymatic or non-enzymatic (Flora 2009). The antioxidant enzymes include catalase, superoxide dismutase, and glutathione peroxidase and glutathione reductase and these enzymes aid in repair or elimination of damaged bio-molecules. Non-enzymatic antioxidants constitute chain breaking antioxidants, and transition metal binding proteins (Nimse and Pal 2015). Chain breaking antioxidants are again of two types, viz., lipid-phase chain breaking antioxidants and aqueous-phase antioxidants. Vitamin E, carotenoids, flavonoids, and Ubiquinol-10, come under lipid-phase chain breaking antioxidants, whereas aqueous-phase chain breaking antioxidants include Vitamin C, uric acid, albumin-bound bilirubin, protein-bound thiol groups and reduced glutathione. Transition metal binding proteins, like, ferritin, ceruloplasmin, lactoferrin, and transferrin, sequester iron and copper and prevent the production

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of free radicals (Nimse and Pal 2015; Pizzino et al 2017).

**3. Sources of dietary antioxidants**

Majority of antioxidants are supplied in diet and contain one or more of polyphenols, lipoic and ascorbic acid, carotenoids, resveratrol, lycopene, quercetine, genstein, ellagic acid, ubiquinone and indole-3 carbinole. Several plant-based polyphenolic antioxidants, proanthocyanidins (PACs) from different fruits, vegetables and edible plants, have come into focus for their antioxidant properties (Huang 2018). Apart from these, spices and culinary herbs, such as, ginger, turmeric and garlic, which are routinely used in our cuisines, have also been regarded as good sources of antioxidants with broad spectrum of health promotion properties (Yashin et al. 2017). For a quick reference, various antioxidants and their sources are presented in the Table 1 and the role of anti-oxidants in different diseased conditions in humans is presented in the Figure 1. It is always good to understand how our dietary habits affect our system. The de-lineation of the molecular mechanisms indirectly re-enforces the age-old maxim, 'You are what you eat'.

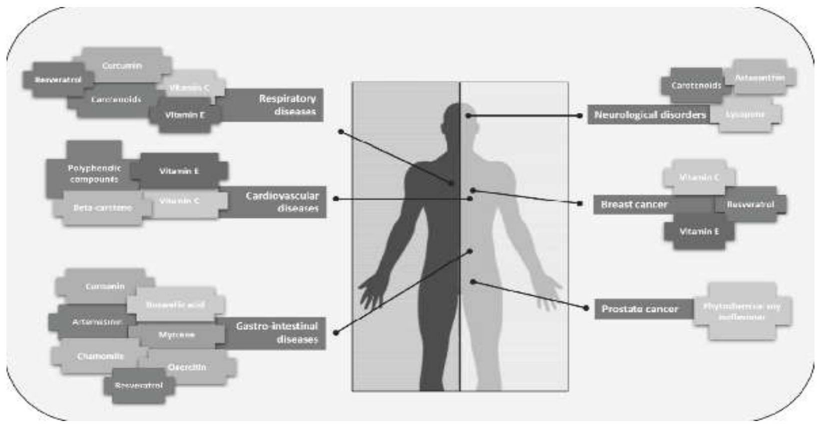


**Figure 1:** Dietary antioxidants linked with different human diseases.

**Table 1. Sources of Natural antioxidants**

| Antioxidants | Common Sources |
|---|---|
| **Beta-carotene** | Carrots, spinach, tomatoes, sweet potatoes, papayas, apricots (Grune et al. 2010) |
| **Vitamin C** | Citrus fruits-orange, lemon, bell pepper, broccoli, kale, strawberries, kiwi, pineapple (Chambial et al. 2013) |
| **Vitamin E** | Cooking oils-sunflower, safflower, olive, cauliflower, sprouts, broccoli, cereal grains, meat, milk, butter, eggs (Grilo et al. 2014; Rizvi et al. 2014) |
| **Flavonoids polyphenol** | Potatoes, tomatoes, lettuce, onions, wheat, dark chocolates, red wine, grapes, black tea (Tsao 2010) |
| Isoflavones, Neoflavonoids and Chalcones | Soybean, red clovers, apple (Tsao et al. 2006, Tsao et al. 2003) |
| Flavones, Flavonols, Flavanones and Flavanonols | Citrus fruits (Kawaii et al. 1999) |
| Proanthocyanidins | Grapes, apple, blue berries (Tsao 2010) |
| Anthocyanidins | Black rice (Anderson et al 2006) |
| Polyphenolic Amides | Oats, chilli pepper (Davis et al 2007; Bratt et al 2003) |
| **Non-flavonoid** | Green tea, blue berries (Tsao 2010) |

| | |
|---|---|
| **polyphenols** | |
| Resveratrol | Grapes, red wines (Salehi et al. 2018) |
| Ellagic acid | Strawberries, raspberries (Abe et al 2012) |
| Lignan | Flaxseed, sesame (Rodríguez -García et al 2019) |
| Curcumin | Turmeric (Stanić 2017) |
| Lycopene | Tomatoes, papaya, watermelon, guava, pink grape-fruit (Emmanouil et al 2016) |
| **Coenzyme Q 10** | Organ meat- heart, liver and kidney, fish, wheat bran (Saini 2011) |

## 4. Role of antioxidants in diseases

### 4.1 *Cancer*

Several observational studies showed that the risk of cancer is inversely related with dietary vegetables and fruits rich in antioxidants (Willett 2010). In most cancer models, tumor dependent immunosuppression promotes evasion of malignant cells via host's anti-tumor immune responses, which can also be modulated by antioxidants. In a mouse experimental model, antioxidants like curcumin were shown to restore tumor-induced depletion of host CD4+/CD8+ T cell proliferation and inhibition of apoptosis of thymocytes and splenocytes (Bhattacharyya 2010). In cases of breast cancer, Resveratrol, a dietary polyphenol inactivates Stat3, prevents generation and function of tumor-evoked regulatory B cells and inhibits lung metastasis of breast cancer(Lee-Chang et al. 2013). Chemotherapy, radiotherapy and immunotherapy are widely used in the management of majority of cancers. After treatment with these modalities, a sizeable number of patients experience adverse effects due to chemotherapy and/ or radiotherapy induced free radical injury to normal cells. Antioxidants like phytochemical soy isoflavones, protects normal cells from radiotherapy induced toxicity in prostate cancers (Raffoul et al. 2007). Dietary antioxidant supplements like Vitamin C and E reduces risk of breast cancer recurrence and overall mortality from breast cancer (Greenlee 2012).

### 4.2 *Cardiovascular Diseases*

After several *in vitro* and *in vivo* studies suggested role of antioxidant vitamins C, E and beta-carotene in preventing or slowing down the progression of atherosclerotic processes (Maeda et al 2000; Devaraj et al 1996; Romanchik et al 1995), large scale clinical trials were conducted. Some experimental studies indicated that antioxidant vitamin supplementation cause reduction in cardiovascular events by preventing endothelial damage and proliferation and production of foam cells (Stephens et al. 1996; Hozawa et al 2007; Wannamethee et al 2006). Polyphenolic compounds are abundant in plants and are readily found in fruit and vegetables. In addition, they are important components of herbs and spices and are likely to be critical ingredients in Chinese medicines. Polyphenolic compounds can directly interact with ROS, block generation of free radicals by inhibiting xanthine oxidase enzyme and chelates iron and copper (Quideau et al. 2011). Polyphenols prevents lipid peroxidation and uptake of oxidized LDL by macrophage (Yamakoshi et al. 1999; Kaplan et al. 2001). Joshipura*et al.* found that intake of green leafy vegetables and a vitamin C rich fruit provides protection against coronary heart diseases (Joshipura et al. 2001) A significant reduction in ischemic stroke, unstable angina, acute myocardial infarction was seen when vitamin E supplements were given to pre -existing coronary heart disease patients (Stephens et al. 1996; Boaz et al. 2000).

### 4.3 *Neurological Disorders*

Oxidative stress induced cell damage, impaired damaged DNA repair and mitochondrial dysfunction are well established factors in the development of neurodegenerative disorders like Alzheimer's disease, Parkinson's disease, Huntington's disease and familial amyotrophic lateral sclerosis (Kim et al. 2015; Federico et al. 2012).In addition, increase in protein aggregates activates microglia cells and leads to sustained neuroinflammation (Masgrau et al 2017).Microglia releases several cytokines and chemokines which aggravates oxidative stress and results in neuronal damage(Frank-Cannon et al. 2009). Dietary antioxidants have the potential to prevent, delay, or ameliorate these disorders. In vitro and animal model studies support the potential beneficial role of various dietary antioxidant compounds in neurodegenerative diseases. In murine models of Alzheimer's disease, dietary lycopene administration attenuates mitochondrial oxidative damage, inhibits pro-inflammatory cytokines in brain and suppress protein aggregation (Prakash and Kumar 2014; Katayama et al 2011).

In Parkinson's disease, lycopene-rich tomato powder intake prevented decline in striatal dopamine neurotransmission and degeneration of nigral dopaminergic neurons in rodent models (Suganuma et al 2002; Di Matteo et al 2009). Similarly, lycopene showed protection against Huntington's disease induced by 3-nitropropionic acid in rodent models (Prakash and Kumar 2009). Also, lycopene treatment was shown to be effective in in cultured cell models of Alzheimer's disease and Parkinson's disease (Qu et al. 2011; Yi et al. 2013). Dietary carotenoids like fucoxanthin, astaxanthin, and crocetin were found to be protective against Alzheimer's disease (Xiang et al. 2017; Lobos et al. 2016; Tiribuzi et al. 2017). Astaxanthin inhibits oxidative stress and provides neuroprotection in Parkinson's disease and familial amyotrophic lateral sclerosis (Ye et al. 2013; Isonaka et al. 2011).

### 4.4 *Gastro-intestinal Diseases*

Irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD), which includes Crohn's disease and ulcerative colitis are associated with oxidative stress (Balmus et al. 2016; Mete et al. 2013). Several studies suggested role of dietary antioxidants in CD, UC and IBS. Curcumin, derived from Curcuma longa plant, found to be useful in ulcerative colitis when combined with mesalamine drug in a random double-blind controlled study (Lang et al. 2015). Other dietary antioxidants, like, boswellic acids (Gerhardt et al 2001), artemesinin, myrcene (Krebs et al 2010), *T. wilfordii* (Zhu et al 2015), and fish oil (Feagan et al 2008), found to be beneficial in Crohn's disease. Also, Chamomile (Langhorst et al 2014), and fish oil (Barbosa et al 2003) improved the oxidative stress in Ulcerative colitis. Liver is the principal detoxifying organ. It metabolizes various compounds that produce reactive oxygen species. Oxidative stress as a result of environmental pollution, drug overdose, alcohol intake and high calorie intake leads to liver diseases (Jadeja et al. 2017). Curcumin and Quercetin has demonstrated hepatoprotective actions on acute and chronic liver injury (Wang et al 2012; Reyes-Gordillo et al 2007; Hernández-Ortega et al. 2012). Resveratrol protects against alcohol-induced lipid peroxidation in animal models (Kasdallah-Grissa et al. 2006).

### 4.5 *Respiratory Diseases*

Vitamin E, vitamin C, beta-carotene, polyphenols, catechins, flavonol and flavone have been speculated to have therapeutic effects in Chronic Obstructive Pulmonary Disease (COPD) patients (Grievink et al. 1998; Santus et al. 2005). Elevated levels of dietary antioxidants lead to lower prevalence of chronic bronchitis and dyspnea (Rautalahti et al. 1997). An increase of Vitamin C levels by 20 mmol / L was associated with a 13% reduction in the risk of COPD (Sargeant et al. 2000). Resveratrol and curcumin inhibit inflammatory response seen in COPD (Kode et al 2008; Biswas et al 2005). Recently, a cross-sectional study in Korean population, revealed that dietary antioxidant like carotene, vitamin A and C intake was beneficial in male smokers with COPD (Hong et al 2018). Oxidative stress might exacerbate asthma by increasing airway inflammation, and responsiveness (Fitzpatrick et al 2009). Several studies suggested an association between low vitamin E intake and increased severity of bronchial asthma (Nurmatov et al 2011; Pearson et al 2004). Vitamin C intake aided recovery in exercise induced asthma (Kurti et al 2016). Carotenoids consumption was found to reduce airway inflammation (Lovett-Racke et al 2002) and associated with low prevalence of asthma in women (Romieu et al. 2006).

## 5. Conclusion

Oxidative stress occurs from the imbalance between free radical production and antioxidant defenses. Oxidative stress is involved in various diseases such as cancer, cardiovascular, respiratory, gastrointestinal and neurological disorders. Dietary antioxidants are widely reported to exert a protective effect in cells and animal models.Therefore, further research should focus on disease specific, molecular target oriented dietary antioxidants.

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## AUTHOR DECLARATIONS

The authors declare that they have no conflict of interest for this piece of work. JS conceived the

the review article, collected information, prepared the rough draft, proof-read and revised the manuscript, constructed the table and provided final approval for submission of the manuscript. RR provided substantial intellectual input for different sub-sections, created the figure, proof-read and revised the manuscript and approved the final version of the article.

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