Chapter 3

ROLE OF ANTIOXIDANTS IN HUMAN LIFE

Mrs. Bushaira V

Assistant Professor (Ad hoc), PG Department of Home Science, KAHM Unity Women's College, Manjeri, Kerala-676122, India
E-mail: vbushaira@gmail.com

There is no animal life without oxygen consumption and its conversion to water through mitochondrial electron transport of free radicals, in the course of oxidative phosphorylation and the production of ATP as the ultimate and immediate source of energy. Free radicals may also be formed as nitrogen, carbonyl, chlorine, sulfur and other reactive species. During oxidation electrons or hydrogen are transferred from one molecule to another, the latter serving as an antioxidant. Antioxidants, therefore, can stop the formation of free radicals and the chain reactions, which would otherwise result in cell damage or even death.

Oxidative stress in biological systems is a complex process that is characterized by an imbalance between the production of free radicals (FR) and the ability of the body to eliminate these reactive species through the use of endogenous and exogenous antioxidants. During the metabolic processes, a great variety of reactions take place, where the promoters are the reactive oxygen species (ROS), such as hydrogen peroxide (H_2O_2) and the superoxide radical anion ($O_2^{\bullet-}$), among others. A biological system in the presence of an excess of ROS can present different pathologies, from cardiovascular diseases to the promotion of cancer. Biological systems have antioxidant mechanisms to control damage of enzymatic and non enzymatic natures that allow ROS to be inactivated. The endogenous antioxidants are enzymes, such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase, or non-enzymatic compounds, such as bilirubin and albumin. When an organism is exposed to a high concentration of ROS, the endogenous antioxidant system is compromised and, consequently, it fails to guarantee complete protection of the organism. To compensate this deficit of antioxidants, the body can use exogenous antioxidants supplied through food, nutritional supplements, or pharmaceuticals. Among the most important exogenous antioxidants are phenolic compounds carotenoids and vitamins C and some minerals such as selenium and zinc.

Free radicals are highly reactive compounds, they are chemical species associated with an odd or unpaired electron and can be formed when oxygen interacts with certain molecules. They are neutral, short lived, unstable and highly reactive to pair with the odd electron and finally achieve stable configuration. Once formed these highly reactive radicals can start a chain reaction they are capable of attacking the healthy cells of the body, causing them to lose their structure and function. Cells may function poorly or die if this occurs.

Reactive oxygen species [ROS], sometimes called as active oxygen species, are various forms of activated oxygen, which include free radicals such as superoxide ions O_2^-) and hydroxyl radicals (OH) as well as non-free radical species such as hydrogen peroxide (H_2O_2). These ROS play an important role in degenerative or pathological processes, such as aging, cancers, coronary heart diseases, Alzheimer's disease, neurodegenerative disorders, atherosclerosis, cataracts and inflammations.

ISBN 978-93-5457-774-1

Living organisms have antioxidant defense systems that protects against oxidative damage by removal or repair of damaged molecules. The term 'antioxidant' refers to the activity of numerous vitamins, minerals and phytochemicals which provide protection against the damage caused by ROS.

An antioxidant is a molecule capable of slowing or preventing the oxidation of other molecules. Oxidation is a chemical reaction that transfers electrons from a substance to an oxidizing agent. Oxidation reactions can produce free radicals, which start chain reactions that damage cells. Antioxidants terminate these chain reactions by removing free radical intermediates and inhibit other oxidation reactions by being oxidized themselves.

Oxidative stress has been widely implicated in biomedical sciences during the last 20 years. It significantly participates in the pathophysiology of highly prevalent diseases such as diabetes, hypertension, atherosclerosis, acute renal failure, Alzheimer and Parkinson diseases among others. The metabolism of oxygen by cells generates potentially deleterious reactive oxygen species (ROS). Under normal conditions the rate and magnitude of oxidant formation is balanced by the rate of oxidant elimination. Antioxidants interfere with the oxidative processes by scavenging free radicals, chelating free catalytic metals and by acting as electron donors. The natural antioxidant mechanisms maybe insufficient in variety of conditions and hence dietary intake of antioxidant compounds are important.

Antioxidant compounds in food play an important role as a health protecting factor. Plant sourced food antioxidants like vitamin C, vitamin E, carotenes, phenolic acids, phytate and phytoestrogens have been recognized as having the potential to reduce disease risk. Most of the antioxidant compounds in a typical diet are derived from plant sources and belong to various classes of compounds with a wide variety of physical and chemical properties. Some compounds such as gallates which has strong antioxidant activity, while others such as the mono-phenols are weak antioxidants. The main characteristic of an antioxidant is its ability to trap free radicals.

Most plant-derived foods have a range of antioxidant compounds which include vitamin C (at lower exposures), vitamin E (tocopherols and tocotrienols), polyphenols, carotenoids and ubiquinols. Flavonoids promote antioxidant activity, cellular health and normal tissue growth and renewal throughout the body. They also work with vitamin C to reduce oxidative stress for the water based portion of the cell and may slow down some of the effects of aging. There are more than 4,000 unique flavonoids and they are most effective when several types are consumed together. Food sources include: cranberries, kale, beets, berries, red and black grapes, oranges, lemons, grapefruits, and green tea.

Antioxidant capacity is required both extra and intracellular (in cytosol, nucleus and mitochondria) for the homeostasis of oxidant status. Physical activity increases the oxidant load, and, if regular, progressively increases the body's ability to respond to such a load. Pro-oxidant foods are principally those with excessive metals such as manganese, iron, or copper or when vitamin C (ascorbic acid) exceeds that usually obtainable from food by way of supplements.

Antioxidants are often added to foods to prevent the radical chain reactions of oxidation, and they act by inhibiting the initiation and propagation step leading to the termination of the reaction and delay the oxidation process. Due to safety concerns of synthetic compounds, food industries have focused on finding natural antioxidants to replace synthetic compounds. In addition, there is growing trend in consumer preferences for natural antioxidants, all of which has given more impetus to explore natural sources of antioxidants.

ISBN 978-93-5457-774-1

Synthetic antioxidant like butylated hydroxyl toluene (BHT), butylated hydroxyl anisole (BHA), propylgallate (PG) and *tert*-butyl-hydroquinone (TBHQ) are known to ameliorate oxidative damages but they have been restricted due to their carcinogenic and harmful effect on the lungs and liver. Therefore, investigations of antioxidants are focused on naturally occurring substances, especially plant phytochemicals. There are two major groups of antioxidants in living cells: enzymatic antioxidants and non-enzymatic antioxidants. These groups are divided into several subgroups. The enzymatic antioxidants are divided into primary and secondary enzymatic defenses.

The primary defense is composed of three important enzymes that prevent the formation of and neutralize free radicals: glutathione peroxidase, which donates two electrons to reduce peroxides by forming selenols and also eliminates peroxides as potential substrates for the Fenton reaction; catalase, which turns hydrogen peroxide into water and molecular oxygen—one of the most important and efficient antioxidants known today, when just one molecule of catalase converts 6 billion molecules of hydrogen peroxide; and lastly, superoxide dismutase, which converts superoxide anions into hydrogen peroxide as a substrate for subsequent catalase action.

The secondary enzymatic defense includes glutathione reductase and glucose-6-phosphate dehydrogenase. Glutathione reductase reduces glutathione (antioxidant) from it's oxidized to its reduced form, and by this recycling, to continue neutralizing more free radicals. Glucose-6-phosphate regenerates NADPH, which creates a reducing environment. These two enzymes support the primary enzymatic defense antioxidants and do not neutralize free radicals directly.

HEALTH BENEFITS OF ANTIOXIDANTS

The human body has a complex system of natural enzymatic and non-enzymatic antioxidant defenses which counteract the harmful effects of free radicals and other oxidants. Protection against free radicals can be enhanced by ample intakes of dietary antioxidants, of which the best studied are vitamin E, vitamin C and carotenoids. Substantial evidence indicates that foods containing antioxidants and possibly in particular the antioxidant nutrients may be of major importance in disease prevention. Efforts should be made to ensure optimum intakes of foods containing these important molecules. There is a need for improvement in the quality of the diet, especially with respect to increased consumption of fruits and vegetables. However, other strategies, including optimization of food processing, selective fortification of foods and the use of safe nutritional supplements, may also need to be considered. All three of the major antioxidant nutrients — vitamin E, vitamin C and ß-carotene — are safe even at relatively high levels of intake. There is, however, a growing consensus among scientists that a combination of antioxidants, rather than single entities, may be more effective over the long term.

Cancer

Cancer is the end point of a multistep process involving a sequence of events that occur over a period of years or even decades. Antioxidant nutrients and the foods that contain them may have important protective effects in the prevention of human cancer. The evidence for a beneficial effect of fruits and vegetables is over- whelming. The evidence for protective effects from individual antioxidant nutrients is less definitive, and therefore other constituents of a diet may also play an important role.

DNA damage is considered to be one of the most important contributors to cancer. Much of this damage is oxidative in nature. A marker of mutagenic DNA damage would be

ISBN 978-93-5457-774-1

useful in the estimation of cancer risk of various populations and in monitoring the effects of chemoprevention. Much of this damage is oxidative in nature. If a cell containing damaged DNA divides before its DNA can be repaired, the result is a permanent genetic alteration, the first step in carcinogenesis. Cells that divide rapidly are more susceptible to carcinogenesis than slowly dividing cells because there is less opportunity for DNA repair before cell division.

Oxidants and antioxidants may also play a role in the later stages of cancer development. There is increasing evidence that oxidative processes contribute to the promotion stage of carcinogenesis, although the mechanisms for this are not well understood. Antioxidants may be able to cause the regression of premalignant lesions or inhibit their development into cancer. Preliminary studies have indicated that some antioxidants, particularly ß-carotene, may be of benefit in the treatment of precancerous conditions such as oral leukoplakia (which may be a precursor of oral cancer). Some antioxidant nutrients may protect against cancer through mechanisms other than their antioxidant properties. For example, carotenoids may both enhance immune function and increase gap functional communication (a type of interaction between cells that inhibits cell proliferation); both of these actions may be relevant to cancer prevention.

Cardiovascular disease

Oxidation may play a role in cardiovascular disease in two ways, one involving the long-term development of atherosclerosis and the other involving the immediate damage that occurs during a heart attack or stroke. Antioxidants may help counteract both of these processes.

The role of free radicals in heart attacks has been assessed in experimental model systems. Free radicals have been found to accumulate in isolated heart muscle that has been subjected to a temporary interruption of blood flow. In some experimental models, treatments that inhibit the accumulation of free radicals have been shown to reduce the severity of damage to the heart muscle. In one human study, pretreatment with vitamin C was apparently of benefit to patients who underwent long periods of cardiac arrest during cardiopulmonary bypass surgery. The release of enzymes associated with ischemia was strikingly decreased in those patients who received vitamin C, indicating a reduction in cell damage. High intakes of antioxidants with reduced risks of cardiovascular diseases. The evidence is strongest for vitamin E, limited but promising for ß-carotene, and inconsistent for vitamin C.

Eye diseases

Age-related diseases of the eye are major health problems around the world. In technologically developed countries, the treatment of cataracts is one of the largest contributors to total health care costs for the elderly. In less developed countries, where treatment is often unavailable, cataracts are a major cause of blindness in older adults. World-wide, approximately 50 million people are blind from cataracts.

Cataracts occur when transparent material in the lens of the eye becomes opaque. Much of the material in the lens consists of extremely long-lived proteins, which can become damaged over the decades of a human lifetime. Since there is no direct blood supply to the lens, nutrients enter and waste products are removed by a simple diffusion process which is slow and inefficient. Oxidation, induced primarily by exposure to light, is believed to be a major cause of damage to the proteins of the lens. When these proteins become oxidized, they clump together and precipitate, causing portions of the lens to become cloudy.

ISBN 978-93-5457-774-1

The eye has defense systems which protect the lens from oxidative damage. Antioxidants and antioxidant enzymes inactivate harmful free radicals and proteases (enzymes which break down proteins) selectively remove damaged proteins from the lens. However, these defense systems cannot always keep pace with oxidative damage. As a result, oxidized proteins may accumulate. As people age, the defense systems grow less effective, and damage to lens proteins may become irreversible. High intakes or blood levels of antioxidant nutrients will reduce the rates of cataract. All three of the major dietary antioxidants — vitamin C, vitamin E and carotenoids — have been associated with decreased cataract risk.

Age-related macular degeneration

Excessive exposure to light and the resulting production of oxidants contribute to the causation of age- related maculopathy. In particular, exposure to blue light has been implicated in this disorder. If blue light is involved, carotenoids might be protective, since they can absorb blue light.

The vitamin A in foods actually consists of carotenoids precursors of the vitamin rather than preformed vitamin A (retinol).Age-related maculopathy found markedly reduced risks in individuals with high blood carotenoid levels. Significant associations were detected for the sum of all carotenoids and for four of five individual carotenoids (ß-carotene, α-carotene, cryptoxanthin and lutein/zeaxanthin, but not lycopene). Vitamin C and vitamin E did not show significant effects.

Neurological disorders

Oxidation may play a role in the causation of several disorders of the brain and nervous system. There f o re, it has been hypothesized that antioxidants might be helpful in ameliorating the symptoms or in slowing the progression of some neurological disorders. Studies have shown beneficial effects of vitamin E supplementation in decreasing the severity of tardive dyskinesia; others have not found an effect. Tardive dyskinesia is a disorder involving involuntary movement. It occurs as a side effect of long-term treatment with certain antipsychotic drugs.

Sperm damage, birth defects and childhood cancer

The children of fathers who smoke cigarettes have increased rates of congenital malformations and childhood cancer. These problems may be related, at least in part, to increased oxidative damage to sperm cells caused by oxidants in cigarette smoke. Cigarette smoking is associated with reduced sperm count and poor sperm quality; it is also associated with decreased blood vitamin C levels. Vitamin C supplementation has been shown to improve sperm quality in heavy smokers. Ample intakes of vitamin C have also been shown to reduce oxidative damage to sperm DNA. Further studies are needed to determine whether improved antioxidant status, particularly with respect to vitamin C, is of benefit in reducing infertility and germ-line mutations in men who smoke cigarettes or who are exposed to oxidative stress from other causes.

Exercise-induced oxidative stress

Because exercise leads to increased oxygen consumption, it causes an increase in the production of oxygen-initiated free radicals. Some studies have reported that antioxidant supplementation reduces evidence of exercise-induced muscle damage. Antioxidants may also play a role in reducing muscle soreness after overexertion. However, it is unclear whether antioxidants can directly enhance physical performance.

ISBN 978-93-5457-774-1

Inflammatory disorders

Free radicals and oxidative stress may play a role in inflammatory diseases. Rheumatoid arthritis is one example. The products of free radical reactions have been detected in the blood and joints of patients with this disease. Other lines of evidence also suggest the involvement of oxidative stress in rheumatoid arthritis and in other inflammatory diseases such as glomerulonephritis.

Decrease in immune function

Several aspects of immune function show a marked decline with increasing age. Preliminary studies in elderly people have indicated that this decline can be partly offset by dietary antioxidant supplementation. The age-associated decrease in cell-mediated immunity may be due to a decreased level of small-molecular-weight antioxidants and decreased activity of antioxidant enzymes.

Rheumatoid arthritis

Rheumatoid arthritis is an autoimmune disease characterized by chronic inflammation of the joints and tissues around the joints with infiltration of macrophages and activated T cells. The pathogenesis of this disease is due to the generation of ROS and RNS at the site of inflammation. Oxidative damage and inflammation in various rheumatic diseases were proved by increased levels of isoprostanes and prostaglandins in serum and synovial fluid compared to controls.

Antioxidants are absolutely critical for maintaining optimal cellular and systemic health and well-being. Naturally there is a dynamic balance between the amount of free radicals produced in the body and antioxidants to scavenge or quench them to protect the body against deleterious effects.The amount of antioxidant principles present under normal physiological conditions may be insufficient to neutralize free radicals generated. Therefore, it is obvious to enrich our diet with antioxidants to protect against harmful diseases. Hence there has been an increased interest in the food industry and in preventive medicine in the development of "Natural antioxidants" from plant materials. The possible toxicity of synthetic antioxidants has resulted in decreased use of these compounds in foods for human consumption. As a consequence of this and due to the appeal of natural products to consumers, numerous studies have been carried out in order to identify naturally occurring compounds which possess antioxidant activities such as phenolic phytochemicals.

REFERENCES

1. Baedia A, Tleyjeh IM, Cerhan JR, Sood AK, (2008) Efficacy of antioxidant supplementation in reducing primary cancer incidence and mortality: systematic review and meta-analysis. Review. Mayo Clin Proc.; 83:23-34.
2. Bahorun T, Soobrattee MA, Luximon-Ramma V, Aruoma OI (2006). Free radicals and antioxidants in cardiovascular health and disease. Internet J Med Update; 1:1-17.
3. Beatty S, Koh HH, Phil M, Henson D, Boulton M. (2000) The Role of oxidative stress in the pathogenesis of age-related macular degeneration. Survophthalmol; 45: 115-34.
4. Benabadji, S.H., Wen, R., Zheng, J.B., Dong, X.C. and Yuan, S.G. (2004). Anticarcinogenic and antioxidant activity of diindolylmethane derivatives. 25, 666-671.
5. D. V. Ratnam, D. D. Ankola, V. Bhardwaj, D. K. Sahana and M. N. V. R. Kumar, (2006) "Role of Antioxidants in Prophylaxis and Therapy: A Pharmaceutical Perspective," Journal of Controlled Release, Vol. 113, No. 3, pp. 189-207.

ISBN 978-93-5457-774-1

6. Deepa, G., Ayesha, S., Nishtha, K. and Thankamani, M., (2013) Comparative evaluation of various total antioxidant capacity assays applied to phytochemical compounds of Indian culinary spices, International Food Research Journal 20(4): 1711-1716.
7. Dhanasekaran M, Ran J, (2005), the emerging role of coenzyme Q-10 in aging, neurodegeneration, cardiovascular disease, cancer and diabetes mellitus. CurrNeurovasc Res; 2: 447-59.
8. Donaldson MS. (2004) Nutrition and cancer: A review of the evidence for an anti-cancer diet. Nutr J; 3:19-25.
9. Genestra M. (2010) Oxylradicals, redox sensitive signaling cascades and antioxidants. Review. Cell Signal; 19:1807-19.
10. Gulcin I, Alici HA, Cesur M (2005) Determination of in- vitro antioxidant and radical scavenging activities of propofol. Pharmacology Bulletin 2005; 53:281-285.
11. Hracsko Z, Orvos H, Novak Z, Pal A, Varga IS. (2008) Evaluation of oxidative stress markers in neonates with intra-uterine growth retardation. Redox Rep; 13:11-6.
12. Huang DH, Chen C, Lin C, Lin Y, (2005) Antioxidant and ant proliferative activities of water spinach (Ipomoea aquatic Forks.) constituents. Botanical Bulletin of Academic Science; 46:99-106.
13. K. Rahman, (2007) "Studies on Free Radicals, Antioxidants, and Co-Factors," Clinical Interventions in Aging, Vol. 2, No. 2, , pp. 219-236.
14. Khilfi S, Hachimi E, Khalil A, Es-Safi A, Belahyam A, Tellal A, El Abbouyi A. (2006) In-vitro antioxidant properties of Salvia verbenaca. L. hydromethanolic extract. Indian Journal of Pharmacology; 38:276-280.
15. M. Carocho and I. C. F. R. Ferreira, (2013) "A Review on Anti- oxidants, Prooxidants and Related Controversy: Natural and synthetic compounds. Screening and Analysis Methodologies and Future Perspectives," Food and Chemical Toxicology, Vol. 51, pp. 15-25. doi:10.1016/j.fct.2012.09.021
16. Mahajan A, Tandon VR. (2004). Antioxidants and rheumatoid arthritis. J Indian Rheumatol Ass.12:139-42.
17. Mark L Wahlqvist, (2013) Antioxidant relevance to human health, Asia Pac J Clin Nutr;22 (2):171-176.
18. Meyer CH, Sekundo W. (2005). Nutritional supplementation to prevent cataract formation. Devophthalmol; 38:103-19.
19. MacNee W. (2001) Oxidative stress and lung inflammation in airways disease. Eur J Pharmacol; 429:195-207.
20. Nantz MP, Rowe CA, Nieves C Jr, Percival SS. (2006). Immunity and antioxidant capacity in humans is enhanced by consumption of a dried, encapsulated fruit and vegetable juice concentrate. J Nutr 136(10):2606-10.
21. Saima Hamid, AdilaSahar, Farnaz Malik, ShahzadHussain, Rashid Mahmood, Kazi Muhammad Ashfaq, Tanveer Akhtar Malik, Abbas Hassan and Asif Hanif Chaudhry, (2014) Physico- chemical investigation and antioxidant activity studies on extracts of Eruca sativa seed, International Journal of Pharmaceutical Chemistry, ISSN: 2249-734X (Online), 160-164.

ISBN 978-93-5457-774-1