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An antioxidant therapy - To maintain optimum health and wellbeing

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ABSTRACT

Antioxidants are our first line of defense against free radical damage, and are critical for maintaining optimum health and wellbeing. The need for antioxidants becomes even more critical with increased exposure to free radicals. Pollution, cigarette smoke, drugs, illness, stress, and even exercise can increase free radical exposure. Because so many factors can contribute to oxidative stress, individual assessment of susceptibility becomes important. Antioxidants terminate the chain reactions by removing free radical intermediates, and inhibit other oxidation reactions. They do this by being oxidized themselves, so antioxidants are often called as reducing agents such as thiols, ascorbic acid or polyphenols. Antioxidants are widely used as ingredients in dietary supplements and have been investigated for the prevention of diseases such as cancer, coronary heart disease and even altitude sickness. Many experts believe that the Recommended Dietary Allowance (RDA) for specific antioxidants may be inadequate and, in some instances, the need may be several times the RDA. As part of a healthy lifestyle and a well-balanced, wholesome diet, antioxidant supplementation is now being recognized as an important means of improving free radical protection. Damage to cells caused by free radicals is believed to play a central role in the aging process and in disease progression. The present paper Reviews the Role of Antioxidants in maintaining optimum health and wellbeing.

INTRODUCTION

OXIDATIVE STRESS

Oxidative Stress occurs in response to excessive levels of cytotoxic oxidants and free radicals in the environment. Antioxidant is a chemical compound or substance that inhibits oxidation, such as vitamin E, vitamin C, or beta-carotene, thought to protect body cells from the damaging effects of oxidation. The term “oxidative stress” has been coined to represent a shift towards the pro-oxidants in the pro-oxidant/antioxidant balance that can occur as a result of an increase in oxidative metabolism. Increased oxidative stress at the cellular level can come about as a consequence of many factors, including exposure to alcohol, medications, trauma, cold, infections, poor diet, toxins, radiation, or strenuous physical activity. Protection against all of these processes is dependent upon the adequacy of various antioxidant substances that are derived either directly or indirectly from the diet. Consequently, an inadequate intake of antioxidant nutrients may compromise antioxidant potential, thus compounding overall oxidative stress.

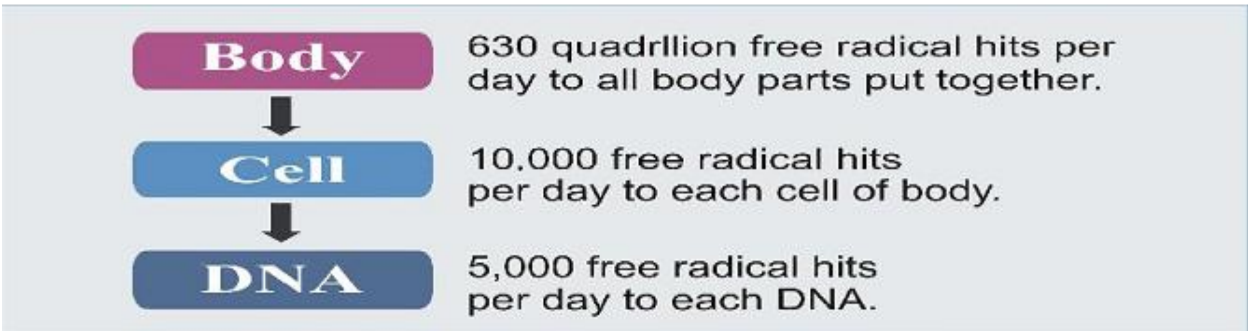


FIG.1: Oxidative stress to body, Cell & DNA

OXIDATIVE STRESS AND HUMAN DISEASE

Oxidative damage to DNA, proteins, and other macromolecules has been implicated in the pathogenesis of a wide variety of diseases, most notably heart disease and cancer. A growing body of animal and epidemiological studies as well as clinical intervention trials suggests that antioxidants may play a pivotal role in preventing or slowing the progression of wide variety of diseases, such as heart disease and some forms of cancer.

TABLE III: CONDITIONS ASSOCIATED WITH OXIDATIVE DAMAGE

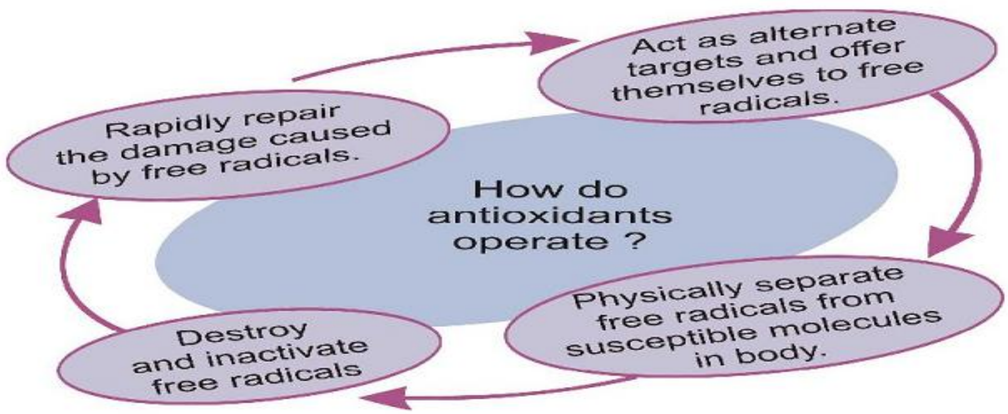
- Atherosclerosis
- Cancer
- Pulmonary dysfunction
- Cataracts
- Arthritis and inflammatory diseases
- Diabetes
- Shock, trauma, and ischemia
- Renal disease and hemodialysis
- Multiple sclerosis
- Pancreatitis
- Inflammatory bowel disease and colitis
- Parkinson’s disease
- Neonatal lipoprotein oxidation
- Drug reactions
- Skin lesion & Aging

WHAT ARE ANTIOXIDANTS?

Antioxidants are found in many foods. They work to keep our cells healthy by protecting them from damage by free radicals (molecules responsible for aging, tissue damage, and some disease). Free radicals damage cells in a process called oxidation. Oxidation results from everyday body functions such as breathing or walking, but certain processed and fatty foods, toxic substances, and sunlight can increase its effects. Antioxidants help repair damaged cells, which can prevent diseases, including cancer. A diet rich in a variety of plant-based foods provides all of the antioxidants the body needs. Research shows that vitamins, minerals, and phytochemicals from whole foods interact to boost their disease-fighting effects. These nutrients benefit both healthy people and those fighting disease. This is why it is important to focus on eating nutrient-rich foods rather than focusing on a single nutrient in supplement form. Here are some nutrients with antioxidant roles:

- Vitamins: A, C, and E
- Minerals: Zinc, copper, iron, manganese, and selenium
- Phytochemicals: Beta-carotene, lycopene, resveratrol, limonone, quercetin etc.

HOW DO ANTIOXIDANTS OPERATE?



NATURAL ANTIOXIDANTS TO NEUTRALIZE FREE RADICALS

To protect the cells and organ systems of the body against reactive oxygen species, humans have evolved a highly sophisticated and complex antioxidant protection system. It involves a variety of components, both endogenous and exogenous in origin, that function interactively and synergistically to neutralize free radicals. These components include:

- Nutrient-derived antioxidants like ascorbic acid (vitamin C), tocopherols and tocotrienols (vitamin E), carotenoids, and other low molecular weight compounds such as glutathione and lipoic acid.
- Antioxidant enzymes, e.g., superoxide dismutase, glutathione peroxidase, and glutathione reductase, which catalyze free radical quenching reactions.
- Metal binding proteins, such as ferritin, lactoferrin, albumin, and ceruloplasmin that sequester free iron and copper ions that are capable of catalyzing oxidative reactions.
- Numerous other antioxidant phytonutrients present in a wide variety of plant foods.

FIG.2: NATURAL ANTIOXIDANTS IN BODY

TABLE I: VARIOUS ROS AND CORRESPONDING NEUTRALIZING ANTIOXIDANTS

ROS	NEUTRALIZING ANTIOXIDANTS
Hydroxyl radical	Vitamin C, glutathione, flavonoids, lipoic acid
Superoxide radical	Vitamin C, glutathione, flavonoids, SOD
Hydrogen peroxide	Vitamin C, glutathione, betacarotene, vitamin E, CoQ10, flavonoids, lipoic acid
Lipid peroxides	Beta carotene, vitamin E, ubiquinone, flavonoids, glutathione peroxidase

DIETARY ANTIOXIDANTS

Vitamin C, vitamin E, and beta carotene are among the most widely studied dietary antioxidants. Vitamin C is considered the most important water-soluble antioxidant in extracellular fluids. It is capable of neutralizing ROS in the aqueous phase before lipid peroxidation is initiated. Vitamin E, a major lipid-soluble antioxidant, is the most effective chain-breaking antioxidant within the cell membrane where it protects membrane fatty acids from lipid peroxidation. Vitamin C has been cited as being capable of regenerating vitamin E. Beta carotene and other carotenoids are also believed to provide antioxidant protection to lipid-rich tissues. Research suggests beta carotene may work synergistically with vitamin E. A diet that is excessively low in fat may negatively affect beta carotene and vitamin E absorption, as well as other fat-soluble nutrients. Fruits and vegetables are major sources of vitamin C and carotenoids, while whole grains and high quality, properly extracted and protected vegetable oils are major sources of vitamin E.

PHYTONUTRIENTS

Many plant-derived substances, collectively termed “phytonutrients,” or “phytochemicals,” are becoming increasingly known for their antioxidant activity. Phenolic compounds such as flavonoids are ubiquitous within the plant kingdom. Flavonoids serve as protectors against a wide variety of environmental stresses while, in humans, flavonoids appear to function as “biological response modifiers”. Flavonoids have been demonstrated to have anti-inflammatory, antiallergenic, anti-viral, anti-aging, and anti-carcinogenic activity. The broad therapeutic effects of flavonoids can be largely attributed to their antioxidant properties. In addition to an antioxidant effect, flavonoid compounds may exert protection against heart disease through the inhibition of cyclooxygenase and lipoxygenase activities in platelets and macrophages.

ENDOGENOUS ANTIOXIDANTS

In addition to dietary antioxidants, the body relies on several endogenous defense mechanisms to help protect against free radical-induced cell damage. The antioxidant enzymes – glutathione peroxidase, catalase, and superoxide dismutase (SOD) – metabolize oxidative toxic intermediates and require micronutrient cofactors such as selenium, iron, copper, zinc, and manganese for optimum catalytic activity. It has been suggested that an inadequate dietary intake of these trace minerals may compromise the effectiveness of these antioxidant defense mechanisms. Research indicates that consumption and absorption of these important trace minerals may decrease with aging .Intensive agricultural methods have also resulted in significant depletion of these valuable trace minerals in our soils and the foods grown in them. Glutathione, an important water-soluble antioxidant, is synthesized from the amino acids glycine, glutamate, and cysteine. Glutathione directly quenches ROS such as lipid peroxides, and also plays a major role in xenobiotic metabolism. Exposure of the liver to xenobiotic substances induces oxidative reactions through the upregulation of detoxification enzymes, i.e., cytochrome P-450 mixed-function oxidase. When an individual is exposed to high levels of xenobiotics, more glutathione is utilized for conjugation (a key step in the body’s detoxification process) making it less available to serve as an antioxidant. Research suggests that glutathione and vitamin C work interactively to quench free radicals and that they have a sparing effect upon each other. Lipoic acid, yet another important endogenous antioxidant, categorized as a “thiol” or “biothiol,” is a sulfur-containing molecule that is known for its involvement in the reaction that catalyzes the oxidative decarboxylation of alpha-keto acids, such as pyruvate and alphaketoglutarate,in the Krebs cycle. Lipoic acid and its reduced form, dihydrolipoic acid (DHLA), are capable of quenching free radicals in both lipid and aqueous domains and as such has been called a "universal antioxidant." Lipoic acid may also exert its antioxidant effect by chelating with pro-oxidant metals. Research further suggests that lipoic acid has a sparing effect on other antioxidants. Animal studies have demonstrated supplemental lipoic acid to protect against the symptoms of vitamin E or vitamin C deficiency. Additional physiological antioxidants are listed in Table II.

TABLE II: ANTIOXIDANT PROTECTION SYSTEM

ENDOGENOUS ANTIOXIDANTS

- Bilirubin
- Thiols, e.g., glutathione, lipoic acid, N-acetyl cysteine
- NADPH and NADH
- Ubiquinone (coenzyme Q10)
- Uric acid
- Enzymes:

– Copper/Zinc and manganese - dependent superoxide dismutase (SOD)
– Iron - dependent catalase
– Selenium - dependent glutathione peroxidase

DIETARY ANTIOXIDANTS

- Vitamin C
- Vitamin E
- Beta carotene and other carotenoids and oxycarotenoids, e.g., lycopene and lutein
- Polyphenols, e.g., flavonoids, flavones, flavonols, and proanthocyanidins

METAL BINDING PROTEINS

- Albumin (copper)
- Ceruloplasmin (copper)
- Metallothionein (copper)
- Ferritin (iron)
- Myoglobin (iron)
- Transferrin (iron)

SUMMARY

Antioxidants are an inhibitor of the process of oxidation, even at relatively small concentration and thus have diverse physiological role in the body. Antioxidant constituents of the plant material act as radical scavengers and helps in converting the radicals to less reactive species. A variety of free radical scavenging antioxidants is found in dietary sources like fruits, vegetables and tea, etc. Oxygen is absolutely essential for the life of aerobic organism but it may become toxic if supplied at higher concentrations. Dioxygen in its ground state is relatively unreactive; its partial reduction gives rise to active oxygen species (AOS) such as singlet oxygen, super oxide radical anion, hydrogen peroxide etc. This is partly due to the oxidative stress that is basically the adverse effect of oxidant on physiological function. Free oxygen radicals plays cardinal role in the etiology of several diseases like arthritis, cancer, atherosclerosis etc. The oxidative damage to DNA may play vital role in aging and the presence of intracellular oxygen also can be responsible to initiate a chain of inadvertent reaction at the cellular level and these reaction cause damage to critical cell biomolecules. These radicals are highly toxic and thus generate oxidative stress in plants. Plants and other organism have in built wide range of mechanism to combat with these Free

Radical problems. Free radicals are an atom or molecule that bears an unpaired electron and is extremely reactive, capable of engaging in rapid change reaction that destabilize other molecules and generate many more free radicals. In plants and animals these free radicals are deactivated by antioxidants. These antioxidants act as an inhibitor of the process of oxidation, even at relatively small concentration and thus have diverse physiological role in the body. Antioxidant constituents of plat materials act as radical scavengers, and convert the radicals to less reactive species. Plants have developed an array of defense strategies (antioxidant system) to cope up with oxidative stress. The antioxidative system includes both enzymatic and non-enzymatic systems. The non enzymatic system includes ascorbic acid (vitamin C); ά-tocopherol, cartenes etc. and enzymic system include superoxide dismutase (SOD), catalase (CAT), peroxidase (POX), ascorbate peroxidase (APX), glutathione reductase (GR) and polyphenol oxidase (PPO) etc. The function of this antioxidant system is to scavenge the toxic radicals produced during oxidative stress and thus help the plants to survive through such conditions. Spices and herbs in food as medicine is a current hot trend that is capturing everyone's imagination with images of a new magic bullet or fountain of youth. The intake of antioxidant compounds present in food is an important health-protecting factor. Natural antioxidants present in foods and other biological materials have attracted considerable interest because of their presumed safety and potential nutritional and therapeutic effects. Because extensive and expensive testing of food additives is required to meet safety standards, synthetic antioxidants have generally been eliminated from many food applications. The increasing interest in the search for natural replacements for synthetic antioxidants has led to the antioxidant evaluation of a number of plant sources. Antioxidants that have traditionally been used to inhibit oxidation in foods also quench dreaded free radicals and stop oxidation chains in-vivo, so they have become viewed by many as nature's answer to environmental and physiological stress, aging, atherosclerosis, and cancer. The nutraceutical trend towards doubling the impact of natural antioxidants that stabilize food and maximize health impact presents distinct challenges in evaluating antioxidant activity of purified individual compounds, mixed extracts, and endogenous food matrices and optimizing applications. It is well known that Mediterranean diet, which is rich in natural antioxidants, leads to a limited incidence of cardio- and cerebrovascular diseases. It is known that compounds belonging to several classes of phytochemical components such as phenols, flavonoids, and carotenoids are able to scavenge free radical such as $O2^{\cdot}$, $OH^{\cdot}$, or lipid peroxyl radical $LOO^{\cdot}$ in plasma. The effective intake of single food antioxidants and their fate in the human body have been defined only for a few compounds. It is reasonable that the higher the antioxidant content in foods is, the higher the intake by the human body will be. Natural antioxidants occur in all parts of plants. These antioxidants include carotenoids, vitamins, phenols, flavonoids, dietary glutathione, and endogenous metabolites. Plant-derived antioxidants have been shown to function as singlet and triplet oxygen quenchers, free radical scavengers, peroxide decomposers, enzyme inhibitors, and synergists. The most current research on antioxidant action focuses on phenolic compounds such as flavonoids. Fruits and vegetables contain different antioxidant compounds, such as vitamin C, vitamin E and carotenoids, whose activities have been established in recent years. Flavonoids, tannins and other phenolic constituents Present in food of plant origin are also potential antioxidants. These components include:

- Nutrient-derived antioxidants like ascorbic acid (vitamin C), tocopherol and tocotrienols (vitamin E), carotenoids, and other low molecular weight compounds such as glutathione and lipoic acid.
- Antioxidant enzymes, e.g., super oxide dismutase, glutathione peroxidase, and glutathione reductase, which catalyze free radical quenching reactions.
- Metal binding proteins, such as ferritin, lactoferrin, albumin and ceruloplasmin that sequester free iron and copper ions that are capable of catalyzing oxidative reactions.
- Numerous other antioxidant phytonutrients present in a wide variety of plant foods.

ANTIOXIDANTS AND AGE-RELATED MACULAR DEGENERATION (AMD)

Cataracts and age-related macular degeneration (AMD) are the leading causes of visual impairment and acquired blindness .Approximately 10 million people suffer from early signs of AMD and almost a half million people have significant visual loss from late-stage AMD. Cataract extractions are the most common surgical procedure performed accounting for more than 2 million procedures a year. It has been estimated that if the progression of cataracts could be delayed by 10 years, the number of cataract extraction surgeries per year would be reduced by 45 percent. Both the severity and irreversibility of cataracts and AMD have generated interest in ways to either prevent or delay their progression. Nutrition is one promising means of protecting the eyes from these diseases. The Age-Related Eye Disease Study from the National Eye Institute (NEI) is the first large clinical trial to test the effect of a high dose antioxidant vitamin combination plus zinc on preventing or delaying the progression of AMD and its associated vision loss. The antioxidant vitamins and zinc supplement reduced the risk of developing advanced AMD by about 25 percent in the study subjects who were at high risk for developing the advanced stage of this disease. In the same high-risk group, the supplements also reduced vision loss by 19 percent. The doses tested were: • 500 milligrams (mg) vitamin C • 400 IU vitamin E • 15 mg beta-carotene • 80 mg zinc • 2 mg copper (to prevent anemia from high dose zinc) According to researchers, this supplement combination is the first effective treatment to slow the progression of AMD. The NEI concluded that persons older than 55, with signs of intermediate to late vision loss due to AMD, should consider taking a supplement such as that used in this trial. Effective treatment can delay progression to advanced AMD in about 300,000 people who are at high risk.

ANTIOXIDANTS AND CATARACTS

Some recent studies compared dietary and supplemental intake of antioxidant vitamins with development of cataracts. Many of these studies have shown that antioxidant vitamins may decrease the development or progression of this disease. The Nutrition and Vision Project found that higher intakes of vitamin C led to a reduced risk for cortical and nuclear cataracts. Results also showed that people who used vitamin C and E supplements for more than ten years had decreased progression of nuclear cataracts. • A recent analysis of results from a national dietary study (National Health and Nutrition Examination Survey) found that higher levels of vitamin C in the diet were associated with lower risk of cataracts. • In the Nurses' Health Study, the need for cataract surgery was lower among women who used vitamin C supplements for ten years or longer. The Roche European American Cataract Trial found that an antioxidant supplement with vitamins C and E and beta-carotene lead to a small decrease in the progression of cataracts in less than 3 years. In the Longitudinal Study of Cataract, vitamin E supplement use for at least a year was associated with a reduced risk of nuclear cataracts becoming more severe. The five year follow-up to the Beaver Dam Eye Study showed a reduced risk for nuclear and cortical cataracts among people using multivitamins or any supplement containing vitamins C and E.

CONCLUSION

The most important free radical in biological systems is radical derivatives of oxygen with the increasing acceptance of free radical as common place and important biochemical intermediate. Antioxidants are believed to play a very important role in the body defense system against reactive oxygen species (ROS), which are the harmful byproducts generated during normal cell aerobic respiration. Increasing intake of dietary antioxidants may help to maintain an adequate antioxidant status and, therefore, the normal physiological function of a living system. To protect the cells and organ systems of the body against reactive oxygen species, humans have evolved a highly sophisticated and complex antioxidant protection system. It involves a variety of components, both endogenous and exogenous in origin, that function interactively and synergistically to neutralize free radicals.

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