

Free Radicals and Anti-oxidants in Health and Disease

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ABSTRACT

These days free radicals and free radical induced damage is becoming a topic of concern because of its serious consequences. Free radicals can result in various degenerative diseases like rheumatoid arthritis, aging and cancer. Mainly two types of free radicals are produced in the body which are responsible for the damage i.e. ROS (reactive oxygen species) and RNS (reactive nitrogen species). These are formed in our body during various physiological and pathological processes. Normally these are neutralized by the antioxidants but sometimes this neutralization is not complete leading to a phenomenon called oxidative stress which is responsible for the damage. Free radicals affect the proteins, lipids and DNA. Along with endogenous antioxidants, dietary components are a good source of natural antioxidants. Various fruits and vegetables are rich sources of antioxidants. Currently, many studies and research work is focusing in this direction so as to create new products or other sources which can act as antioxidants.

KEYWORDS: Antioxidants, Degenerative Diseases, Free Radicals, Oxidative Stress

INTRODUCTION

An antioxidant can be defined as: "any substance which is when present in low concentrations compared to that of an oxidisable substrate, significantly delays or inhibits the oxidation of that substrate".^{1,2} In our body various metabolic processes takes place like breakdown of fats and other food stuffs to release energy. Most of these metabolic processes utilize oxygen as a fuel and generates free radicals as by-products. These free radicals can be both useful and harmful to the body. They can destroy the various normal cells of our body by a phenomenon known as oxidation. The anti-oxidants function as reducing agents and are thus helpful in preventing this damage.³

ROLE OF ANTI-OXIDANTS

Anti-oxidants usually function in various ways: both endogenous and exogenous anti-oxidants prevent the damage to cells by the free radicals; protect from cancer and heart diseases; protect from exercise induced damage and helps in the recovery process; various neurological diseases like Alzheimer's disease, Parkinson's disease etc. can be prevented; and prevent various other oxidative stress induced diseases like Rheumatoid arthritis, Nephropathy and Pulmonary diseases.^{4,5}

CLASSIFICATION OF ANTIOXIDANTS

Depending upon its nature, antioxidants can be classified as: (i) Enzymatic: It includes superoxide dismutase, glutathione reductase, glutathione peroxidase, glucose 6-phosphate dehydrogenase and catalase; (ii) Non-

enzymatic: These are further divided into: (a) Metabolic antioxidants: These antioxidants can be produced within the body and includes L-arginine, melatonin, uric acid, lipid acid, bilirubin, coenzyme Q10, metal-chelating proteins, transferrin, glutathione etc.; and (b) Nutrient antioxidants: These cannot be produced within the body and have to take through exogenous sources like dietary components. It includes vitamin E, carotenoids, vitamin C, flavonoids, omega-3 and omega-6 fatty acids, metals (selenium, manganese, zinc) etc.^{6,7}

FORMATION OF FREE RADICALS

Free radicals are formed in the body by various mechanisms which may be endogenous or environmental. These can further be divided into enzymatic and non-enzymatic. Enzymatic reactions which generate free radicals are respiratory chain reaction, the cytochrome P450 system and the prostaglandin synthesis. For example, the superoxide anion radical (O_2^-) is formed via various cellular oxidase systems such as xanthine oxidase, peroxidases, NADPH oxidase etc. Non enzymatic reactions which lead to the formation of free radicals include reactions of oxygen with organic compounds and the reactions triggered via ionizing radiations. Oxidative phosphorylation in mitochondria also shows non-enzymatic reaction.^{8,9,10} Various electromagnetic radiations can also generate free radicals. For example gamma rays can split water in the body to generate hydroxyl radical i.e. OH^+ .⁶

OXIDATIVE STRESS

Mainly two types of free radicals are generated in the body which has very deleterious effects. These are ROS

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(reactive oxygen species) and RNS (reactive nitrogen species). Normally these free radicals are neutralized by various endogenous and exogenous anti-oxidants. However, when free radicals are produced in excess quantity, these are not completely neutralized and produce a condition known as oxidative stress. This condition has various degenerative effects on the cell membranes, Proteins, DNA etc. Damage to proteins can affect the enzymatic activity. This oxidative stress can also lead to various degenerative diseases like certain cancers, cardiovascular disease, neurodegenerative disorders, diabetes, aging, atherosclerosis, inflammatory conditions, eye disorders and fetal complications.^{6,11,12,13}

ANTIOXIDANT MECHANISM OF ACTION

Though there are various ways by which antioxidants can exert their action. But two mechanism of action are very important. First is the chain- breaking mechanism, in which the primary antioxidant donates an electron to the free radical and neutralizes it. In the second mechanism there is removal of ROS/reactive nitrogen species initiators by quenching chain-initiating catalyst. In both these mechanisms antioxidants neutralizes the free radicals and themselves become oxidized.^{14,15}

ROLE OF VARIOUS NUTRIENTS AS ANTIOXIDANTS

Various dietary components and nutrients act as natural antioxidants and are very useful to the body. They supplement the action of various endogenous antioxidants to combat the deleterious effects of free radicals. All the dietary nutrients are quite specific in its structure and function. Lack of these various antioxidants in the diet on long term basis can lead to various progressive and degenerative diseases in the body. It includes three components mainly i.e. vitamin C, vitamin E and carotenoids.^{6,16}

Vitamin C: It is a water soluble vitamin and is very potent anti-oxidant. It mainly acts as a scavenger for the free radicals. Its main site of action is extracellular fluid and water compartments. It plays protective role in various diseases like coronary artery disease, cancer, aging and arthritis.¹⁷

Vitamin E: It is a water soluble vitamin with high antioxidant potential. It is present in the cell membranes of the body and is usually stored in the form of adipose tissue. It consists of total of eight compounds, of which four are tocopherols and four tocotrienols. Among all these types, only α -tocopherol is the most bioactive form in humans. The main site of action of vitamin E is cell membranes, where it prevents the damage from free radicals by preventing the lipid peroxidation. Vitamin E has been thought to be effective against various types of cancers like prostate cancer, breast cancer and colon cancer. It also gives protection against various degenerative diseases like arthritis, cardiovascular

diseases and neurological disorders.¹⁸ A recent trial study has raised some questions regarding its dosage that should be given. According to this study, α -tocopherol doses of 400 IU or more are dangerous and can lead to death of the patient, but on the other hand dose of 200 IU per day or less is quite safe with no deleterious effects on the body.¹⁹ So it should be used with caution keeping the adverse effects in mind. Various sources of vitamin E include whole grains, eggs, poultry, meat, wheat germ oil, vegetable oils etc.⁶

Carotenoids: Various types of carotenoids are present in the dietary supplements. It includes β -carotene, α -carotene, lutein, β - cryptoxanthin, lycopene etc. Among all these carotenoids, β -carotene is the most effective and important antioxidant. It is fat soluble and is considered to be the precursor of Vitamin A. It protects against the free radical damage by quenching the singlet oxygen and protects the lipid-rich tissues. Lycopene is another potent antioxidant and is protective against the prostate cancer. These carotenoids are also effective against cardiovascular diseases and eye disorders.^{5,20} Few other dietary antioxidants are also of great significance in protection against free radicals. Various minerals like selenium play role against cancer. Long term dietary deficiency of selenium can lead to atherosclerosis and myocardial ischemia. Red wine is protective against the cardiac diseases due to its antioxidant properties. Most of these antioxidants like Vitamin E; Vitamin C etc cannot be produced in our body and hence should be taken in the diet. Fortunately most of these antioxidants are present in fruits and vegetables. So, fruits and vegetables should be taken daily on regular basis so that various chronic diseases can be prevented.²⁰

SOURCES OF ANTIOXIDANTS

Good sources of antioxidants include beverages such as tea; Indian medicinal plants like garlic; fruits like apples, grapes, blackberries, blueberries, citrus fruits, apricot; olive oil; vegetables like cabbage, onion, pepper, mushroom, beetroot, brinjal, sweetcorn, corn; chocolates; legumes like beans, horsegram, peas; red palm oil; amla; groundnut oil; cardamom; cloves; cinnamon; and red wine.

CURRENT APPROACHES TO PREVENT THE FREE RADICAL INDUCED DAMAGE

These days many approaches are being followed to prevent the free radical induced damage to the body. Few studies have found the relation between loss of memory and lack of antioxidants in the diet. So intake of good diet rich in various natural anti-oxidants is mandatory. Recently a new class of SOD mimetic drugs, like tempol, was also developed to alleviate acute and chronic pain. Genetically engineered plants are being generated so that the vegetables thus produced has ample amount of required antioxidants. Tomatoes has been developed which has three times lycopene amount.²¹ Many

antioxidant herbal formulations are available in the market like Geriforte, Reaktiv, Brahma rasayana, HD-3 and MAK- 4. Indian medicinal plants and spices has good antioxidant potential. Antioxidant supplements are also available which are either prepared artificially by a chemical process or are extracted from the plants or other natural food sources. But the usefulness versus adverse effects of these products is still controversial. These supplements if taken in excess amount can produce the oxidative stress.²²

CONCLUSION

Free radicals are responsible for large number of diseases in the body. These free radicals are formed both as a result of normal physiological processes and environmental interactions. They act at different biological molecules leading to various adverse effects. Antioxidants counteract their effect and neutralize the free radicals. These oxidants can be endogenous (produced within the body) or exogenous (taken from outside sources). Dietary components mainly the fruits and vegetables are the major and important source of exogenous antioxidants. Research involving the combined efforts of the biomedical scientists, nutritionists and physicians can help in controlling the adverse effects caused by these free radicals. The better and thorough understanding of the biochemical processes occurring at a cellular level is required so that the steps can be taken in right direction to prevent the oxidative damage. People should also be made aware about the damage caused by free radicals and importance of antioxidants in our routine life. Sources of oxidants like cigarette, alcohol and stress should be avoided. We can say that a healthy lifestyle can lead to a healthy life.^{4,6,22}

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