

Antioxidants and cancer prevention - A review

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ABSTRACT

Antioxidant therapy and free radicals have attracted in a lot of consideration in recent years. Antioxidants are compounds that destroy the free radicals in the body, thereby preventing harmful oxidation-reduction reactions. Antioxidants are important for maintaining good health. The best sources of antioxidants are fruits and vegetables, which provide a variety of antioxidants such as Vitamins A, C, E, and carotenoids. Data that are presently available are compatible with the notion that these vitamins act as chemopreventives against some important cancers such as carotenoids for lung cancer, ascorbic acid for salivary gland cancer, and tocopherols for head-and-neck cancers. Hence, a greater consumption of fruits and vegetables should be encouraged as they are the natural sources of these chemopreventive antioxidants along with other protective factors packaged by nature.

KEY WORDS: Antioxidants, Cancer prevention, Cancer, Chemopreventive, Free radicals

INTRODUCTION

Antioxidants are substances which help and protect the cells from the harm caused by unstable atoms known as free radicals. Damage caused to these free radicals may lead to the development of cancer. Antioxidants are chemicals that interact with and neutralize free radicals, thus preventing them from causing damage. The part of dietary factors in balancing tumor keeps on being vigorously examined. Specifically, there has been expanded enthusiasm for different potential anticancer specialists, including natural cancer prevention agents which are known as biological antioxidants, for example, carotenoids, retinoids, ascorbic corrosive, and α -tocopherol. Extensive research center confirmation from chemical, cell culture, and animal studies shows that antioxidants may moderate or potentially prevent the improvement of cancer development. Be that as it may, data from late clinical trials are less certain. Finally, expansive scale, randomized clinical trials achieved conflicting conclusions.

ANTIOXIDANT AND CANCER PREVENTION IN 1997

A considerable wealth of information about the nutritional factors that affect cancer risk is available in the literature. This information has served as the basis for international dietary recommendations intended to reduce cancer risk^[1] and has moved into experimental trials designed to test the effects of single nutrients taken as supplements. Antioxidant nutrients, including beta-carotene and Vitamin C, have been a major focus of these studies, which to date have revealed either minimal effects^[2-5] or harm.^[6,7]

MECHANISM OF ACTION OF ANTIOXIDANT

Antioxidants neutralize free radicals by giving one of their electrons, which closes the electron taking response. The antioxidant supplement, be that as it may, does not turn into a free radical by giving an electron since they are steady in either shape.

Vital antioxidant incorporates the following:

1. Chain breaking or searching ones, for example, Vitamin E (alpha-tocopherol), Vitamin C (ascorbic corrosive), or Vitamin A (beta-carotene).

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- Preventative antioxidant which has the capacity to a great extent by sequestering change metal ions and preventing Fenton responses is along with these to a great extent proteins by nature (e.g., albumin, exchanging, or lactoferrin)^[8]

NATURAL ANTIOXIDANTS AND THEIR ROLE IN CANCER PREVENTION

Antioxidants are being credited for their ability to protect cells from the oxidative/electrophilic damage that makes them turn into cancerous agents. A number of antioxidants have shown to inhibit the induction of cancer by a wide variety of chemical carcinogens and/or radiation at many target sites in mice, rats, and hamsters. Epidemiological studies suggest that a diet rich in plant products containing natural antioxidants may be a deterrent to carcinogenicity. Many antioxidants were tested to determine if they would inhibit tumor initiation, promotion, and/or progression. Important antioxidants can be useful in the treatment of cancer, either as sole agents or as adjuncts to standard radiation and chemotherapy protocols. The knowledge of antioxidants in a cancer-curing or preventing methods is still in early stages. The relationship between antioxidant and cancer prevention cannot be depicted only on the basis of the presumed mechanism of action when used. Numerous natural antioxidants appear to have beneficial health effects. There is sufficient evidence to recommend consuming food sources rich in antioxidants. This chapter summarizes the current knowledge on the occurrence, types, and antioxidative properties of natural antioxidants, underlying the necessity of further research.^[9-12]

- Vitamin C** - Vitamin C, also known as ascorbic acid, is a water-soluble vitamin. It is essential for collagen, carnitine, and neurotransmitters biosynthesis. Health benefits of Vitamin C are antioxidant, anti-atherogenic, anticarcinogenic, and immunomodulator. Vitamin C works synergistically with Vitamin E to quench free radicals and also regenerates the reduced form of Vitamin E. Natural sources of Vitamin C are acid fruits, green vegetables, and tomatoes.^[8]
- Vitamin E** - Vitamin E is a fat-soluble vitamin with high antioxidant potency because it is fat-soluble, α -tocopherol safeguards cell membranes from damage by free radicals. Its antioxidant function mainly resides in the protection against lipid peroxidation. The dietary sources of Vitamin E are vegetable oils, wheat germ oil, whole grains, nuts, cereals, fruits, eggs, and poultry meat. Vitamin E has been proposed for the prevention against colon, prostate and breast cancers, some cardiovascular diseases, ischemia, cataract, arthritis, and certain neurological disorders.^[9]

- Beta-carotene** - Beta-carotene is a fat-soluble member of the carotenoids which are considered provitamins because they can be converted to active Vitamin A. Beta-carotene is converted to retinol, which is essential for vision. It is a strong antioxidant and is the best quencher of singlet oxygen. Beta-carotene is present in many fruits, grains, oil, and vegetables (carrots, green plants, squash, and spinach).^[9]
- Selenium** - Selenium is a trace element. It forms the active site of several antioxidant enzymes including glutathione peroxidase. Similar to selenium, the minerals manganese and zinc are trace elements that form an essential part of various antioxidant enzymes.^[8] Se is a trace mineral found in soil, water, vegetables (garlic, onion, grains, nuts, and soybean), seafood, meat, liver, and yeast. At a low dose, health benefits of Se are antioxidant, anticarcinogenic, and immunomodulators.
- Lycopene** - Lycopene is an antioxidant which has been hypothesized to prevent carcinogenesis and atherogenesis by protecting cellular biomolecules which includes lipids, lipoproteins, proteins, and DNA. Lycopene, when given in the dosage of 4.8 mg/day orally for 3 months, leads to the reversal of dysplastic changes in leukoplakia and when given in the dosage of 16 mg/day leads to substantial increase in the mouth opening in oral submucous fibrosis. The major dietary source of lycopene is tomatoes, with the lycopene in cooked tomatoes, tomato juice, and tomato sauce included, being more bioavailable than that in raw tomatoes.^[13]
- Omega-3 and omega-6 fatty acids** - They are essential long-chain polyunsaturated fatty acids. Dietary sources of omega-6 fatty acids (linoleic acid) include vegetable oils, nuts, cereals, eggs, and poultry. It is important to maintain an appropriate balance of omega-3s and omega-6s in the diet, as these two substances work together to promote health.^[13]

FREE RADICALS

It is frequently stated that 90% of the incidence of cancer in a population is due to environmental factors including food consumption and lifestyle.^[14,15] The definition “environmental” implies non-genetic factors though, clearly, genetic predisposition plays a role in determining the susceptibility of an individual to become a victim of the disease.^[16]

Free radical scavengers such as endogenous and exogenous antioxidants act by preventing and repairing damages which are caused by reactive oxygen species (ROS) and RNS and thereby help in enhancing the immune defense and lower the risk of cancer and degenerative diseases.

Mechanism of Free Radicals

Free radicals are chemically active atoms that have a charge due to an excess or deficient number of electrons. The most biologically important free radical is known as ROS which are the free radicals containing oxygen.^[8] In the recent years, the term “ROS” or “reactive oxygen intermediates” is a collective term which has been adopted to include molecules such as hydroxyl radical (OH), superoxide anion (O₂), hydrogen peroxide (H₂O₂), hypochlorous acid (HClO) While most reactive oxygen species have extremely short half-life, they can cause substantial tissue damage by initiating free radical chain reaction. Reactive oxygen species can cause tissue damage by a variety of different mechanism which includes DNA damage, lipid peroxidation through activation of cyclooxygenase and lipoxygenase pathway, protein damage including gingival hyaluronic acid and proteoglycans, oxidation of important enzymes, for example, antiprotease such as 1 antitrypsin, stimulation of pro-inflammatory cytokine release by monocytes, and macrophages by depleting intracellular thiol compounds and activating nuclear factor.^[13]

HOW MIGHT ANTIOXIDANTS PREVENT CANCER?

Antioxidants neutralize free radicals as the characteristic result of normal cell processes. Free radicals are particles with incomplete electron shells which make them more chemically responsive than those with complete electron shells. Introduction to different natural factors, including tobacco smoke and radiation, can likewise prompt free radical development. In humans, the most widely recognized type of free radicals is oxygen. At the point when an oxygen molecule (O₂) turns out to be electrically charged or “radicalized,” it tries to take electrons from different molecules, making harm to the DNA and different molecules. After some time, such harm may become plainly irreversible and prompt illness including cancer (malignancy). Antioxidants are regularly portrayed as “mopping up” free radicals, which means they neutralize the electrical charge and keep the free radical from taking electrons from different molecules.^[5,17-20]

RECENT ADVANCES IN ANTIOXIDANT

Many years of research have demonstrated that exact blends of the antioxidants phloretin, tetracurcuminoid, and ferulic acid, including formulations applied topically, can neutralize cell-damaging free radicals, especially those caused by UV beams, nicotine, alcohol, and hydrogen peroxide.^[21] Recent research

has additionally affirmed that specific antioxidants, including phloretin, silymarin, and hesperetin, essentially inhibit the inflammation response related with *Actinobacillus actinomycetemcomitans*, one of the pathogens that cause periodontal disease.^[22] Lutein, dark green vegetables, for example, kale, broccoli, kiwi, sprout, and spinach. Lignan; oat meal, barley, and rye. Herbs; turmeric (curcumin), grape seed, or pine bark extricates, they can likewise give intense antioxidant protection for the body^[13,23]

Protective Roles of Micronutrients in Carcinogenesis^[24]

1. Beta-carotene: Beta-carotene acts as a precursor of Vitamin A. It is an antioxidant and free radical scavenging. It has properties of immunomodulation, stimulation of increase in the numbers of T- helper and NK cells as well as cells with interleukin-2 receptors. It helps in inhibition of mutagenesis and cancer cell growth.
2. Vitamin A (retinoids): Vitamin A helps in inhibiting keratinization and terminal differentiation of epidermal cells. It also helps in enhancement of cellular immunity and reverses or arrests leukoplakia progression. It induces cytotoxic and cytostatic effects on cancer cells. Vitamin A plays a role in influencing DNA, RNA, and gene expression and interferes with carcinogenic stimulation and binding.
3. Vitamin E (A-tocopherol): Vitamin E is a free radical scavenging. It helps in maintenance of membrane integrity and immune function. It helps in inhibiting cancer cell growth/differentiation, mutagenicity, nitrosamine formation, DNA, RNA, and protein synthesis in cancer cells.
4. Vitamin C (ascorbic acid): Vitamin C is an antioxidant and helps in reducing Vitamin E degradation and oncogene expression. It enhances the process of chemotaxis, phagocytosis, collagen synthesis, and detoxification through cytochrome P450. It also inhibits nitrosamine formation and formation of fecal mutagens.

Controversial Areas in Antioxidants Therapy

Current literature reports that a half century of data demonstrates the lack of predictability of antioxidant therapy and it has not been validated by the scientific method. Widespread use of antioxidants has failed to quell the current pandemic of cancer, diabetes, and cardiovascular disease or to stop or reverse the aging process. Antioxidant treatment protocol in human reproductive medicine is still controversial. High doses of Vitamin A can cause embryotoxic and teratogenic effects seen.^[25] Large doses of ascorbic acid may be associated with the inhibition of ovarian steroidogenesis and increased probability of abortion.^[26]

CONCLUSION

The antioxidant micronutrients are essential not only for the limitation of oxidative property and tissue damage but also it is useful in preventing the increase in cytokine production which is an end product of prolonged activation of immune response. Dietary and other enzymatic antioxidants protect the lipids of lipoprotein and other biomembranes against oxidative damage by intercepting oxidants before they can attack the tissues. Antioxidants are used widely in daily clinical practice. They are used in the prevention of cellular damage, the most common pathway for cancer, aging, and a variety of disease. Dietary antioxidants such as Vitamin C, Vitamin E, and carotenoids may likewise be used in the prevention of degenerative disease and maintenance of good health. There is now convincing evidence that foods containing antioxidants may be of major importance in disease prevention.

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