10.5005/jp-journals-10011-1167
REVIEW ARTICLE

A Review of Antioxidants

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ABSTRACT

Antioxidants play the essential role in reducing the free radicals. Free radicals can cause various changes in human body from DNA mutation to cell death. Free radical formation form the biological basis of several medical problems including cancer. The antioxidants are useful in preventing the transfer of premalignant lesion to malignancy. Hence are usually prescribed in oral premalignant lesions like leukoplakia, lichen planus, oral submucous fibrosis. Antioxidants include beta carotene, carotenoid, vitamin C, vitamin E, trace elements like zinc and selenium. Functions of these antioxidants are discussed here.

Keywords: Oral cancer, Malignancy, Vitamin, Free radicals.

INTRODUCTION

Cancer is a dreaded disease with millions of new cases worldwide. The overall incidence rate of cancer is increasing by 2% per year and cancer ranks second only to coronary heart disease as the leading cause of death. Majority of human cancers is induced by environmental factors including lifestyle practices and specific occupation. It, thus, bears and preventive potential if the exogenous cause can be identified and eliminated. Oral cancer is a major form of cancer worldwide and is one of the most common malignancy in India accounting for 30 to 40% of all cancers.[1] Squamous cell carcinoma of the oral cavity is responsible for considerable morbidity and mortality in India where 60,000 new cases of oral cancer are reported to occur every year. Further, the combined effect of alcohol and tobacco is multiplicative with the risk of developing head and neck squamous cell carcinoma. Cigarette smoking and drinking alcohol cause significant oxidant stress, which increases DNA damage and, consequently, the malignant transformation of normal cells.[2] An antioxidant has been defined as 'any substance that when present at low concentrations compared to those of an oxidizable substrate (e.g. proteins, lipids, carbohydrates and nucleic acids), significantly delays or prevents oxidation of that substrate'.[3]

In 1981, Peto and his associates elaborate on the lower serum levels of beta cartone (BC) and cancer.[4] BC is an antioxidant. Retinol, retinoid, and tocopherol (vitamin E) are the other examples of antioxidants. Studies have shown the inverse relationship between the low dietary and serum levels of antioxidants and probability of development of cancer at various sites, including the head and neck. High consumption of antioxidants was associated with a decreased risk of head and neck squamous cell carcinoma among smokers, drinkers and those with both smoking and drinking habits. These findings suggest that dietary antioxidant intake prevents HNSCC in smokers and drinkers.[2]

Antioxidants are essential in reducing free radical reactions. Free radicals are chemical entities with one or more unpaired electrons. The free radicals can cause DNA mutations, change in enzymatic activity, lipid peroxidation of cellular membrane and may also cause death, unpaired anions of oxygen, hydroperoxides and superoxide are the most harmful free radicals. The free radicals are produced during normal cell metabolism. Under normal circumstances these free radicals, produced through biological processes and in response to exogenous stimuli are controlled by various eyzymes and antioxidants in the body, e.g. superoxide dismutase glutathione peroxidase. Metal binding proteins, e.g. ferritin and ceruloplasmin limit the availability to Fe necessary for formation of hydroxide radicals antioxidant system (Table 1).

Laboratory evidence suggests that oxidative stress which occurs when free radicals formation exceeds the ability to protect against them may form the biological basis of several medical problems, such as tissues injury after trauma and chronic contition, such as atherosclerosis and cancer.

The various antioxidants used are as follows:

1. *Beta carotene*: BC is a carotenoid that is mainly found in dark green, orange fruits or vegetables, such as spinach, carrots, sweet potatoes and in fruits like apricot, papaya, vegetable. In general the deeper the color of the vegetable or fruit the greater carotene content. Approximately 16% of ingested BC is transformed into retinol within the intestinal mucosa. The efficiency of BC absorption in the intestine dramatically decreases as the intake of BC increases. Serum BC levels reflect recent dietary intake.

Table 1: Antioxidant systems

	Primary	*Secondary*	*Tertiary*
Mode of action	This group prevents the formation of new radical species, i.e. either by converting existing free radicals into harmless molecules before they are able to react, or by preventing formation of free radicals from other molecules.	Trap free radicals, preventing chain reactions	Repair biomolecules damaged by free radicals
Example	*Superoxide dismutase (SOD) converts O_2 to H_2O_2 *Glutathione peroxidase (GPX). Converts H_2O_2 to less harmful molecules. *Metal binding proteins, e.g. ferritin and ceruloplasmin, limit the availability Fe necessary for formatin of OH radical	*Vitamin E *Vitamin C *B-carotene *Uric and *Albumin	*DNA repair enzyme *Methionine sulfoxide reductase

Lower than the normal are noted in cigarette smokers, alcoholics.

Dose: There is no recommended daily allowance specifically for BC. However, because BC is a vitamin A precursor, it can fulfill the nutritional requirement for vitamin A. The possible protective benefits of BC against cancer are probable related to its role and an antioxidant in decreasing free radical damage and its ability to quench singlet oxygen.[5] Carotenoids act as antioxidants and nuclear transcription factors, and reduce tumor formation via insulin-like growth factor (IGF)-receptor inhibition.[6]

2. BC also has immunoregulating properties that might retard the development of cancer cells.
   i. BC increases the no. of circulating lymphocytes
   ii. Enhances the proliferation and induction of cytotoxic T cells
   iii. Increases the number of helper T cells
   iv. Increases tumor necrosis factor and enables natural killer cells to be more effective.
3. Beta carotene might reduce the risk of cancer through a mechanism that does not involve its antioxidant property. The proposed novel mechanism of action of BC in cancer prevention relates to cell to cell communication. In the experimental study, it has shown that BC acts by arresting the progression of cancer—initiated cells into the transformed malignant state. BC increases the communication between the cells in a dose-dependent manner and proportionately reduces the ability of carcinogen-treated cells to undergo transformation to malignant cells.[7]
4. Around 16% beta carotene converted into vitamin A after ingestion which would allow an effect on cellular differentiation and cellular proliferation which becomes important during cancer promotion.[8,9]

Retinol: Also known as vitamin A, is an alcohol that can be converted into an aldehyde (retinol) or retinoic acid. As the intake of retinol increases the percentage of absorption remains the same. Vitamin A is found in dairy products, fish, egg and meat.

Hypervitaminosis occurs when the retinol intake exceeds the liver capacity to store it.

Vegetable which are rich source of carotene, e.g. carrot, spinach, green leaves, yellow fruits, such as mangoes, tomatoes, are also green source of vitamin A. One of the functions of vitamin A is to maintain the integrity and activity of the epithelial tissues and glands. It is concerned primarily with process of differentiation of epithelial cells. A low vitamin A intake has been linked with and increased risk for developing cancer of lung, colon, pharynx and breast.

Action: The possible protective roles of vitamin A include:

1. Vitamin A disturbs normal epithetical growth.
2. Tumor surveillance is dependent on adequate levels of vitamin A.
3. Vitamin A direct influences gene expression.

Vitamin C: Also known as ascorbic acid, is mainly found in citrus fruits, strawberry, honey dew, papaya and mangoes.

RDA: A total of 60 mg/per day, for smokers it increases up to 100 mg per day or more because there is decrease concentration of vitamin C in their serum and leukocytes.

Action: Hydroxylation reactions have the most common nutritional role for vitamin C. It is also essential in the synthesis of nor—epinephrine, serotonin carnitine. Besides the action as an antioxidant, it also acts as chemopreventive agent by decreasing nitrosation and also affect the action microphages and leukocytes.

Vitamin C readily scavenges reactive oxygen and nitrogen species, such as superoxide and hydroperoxyl radicals, aqueous peroxyl radicals, singlet oxygen, ozone, peroxynitrate, nitrogen dioxide, nitroxide radicals, and hypochlorous acid, thereby effectively protecting other substrates from oxidative damage.

Vitamin C can also act as a coantioxidant by regenerating α-tocopherol from the α-tocopheroxyl radical, produced via scavenging of lipid-soluble radicals.

Vitamin E: Alpha-tocopherol is the most active and common form of vitamin E is found in plant oils, wheat and green leafy vegetables.

RDA: 8 to 10 mg/day.

Absorption decrease as dose increase. After a small dose of 10 mg, vitamin E absorption is 50%.

While a large dose of 100 mg per day, absorption is 10%. According to one study excess intake of vitamin E may cause side effect mainly hemorrhagic strokes. Here, it is prudent to avoid large daily dose of vitamin E in patients taking anticoagulants drugs.

Action: Vitamin E is effective antioxidant mainly in hydroperoxide.

1. It protects cellular membrane from lipid peroxidation.
2. Patients immunoresponse can be increased as it enhances the mitogenic response, inhibit certain prostoglandins and improves T cell mediated response.

Vitamin E decreases the incidence of symptomatic oral radio-induced mucositis in patients with cancer of the oropharynx and oral cavity.

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