

REVIEW ARTICLE

Antioxidants In Oral Health

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ABSTRACT

Oral cavity is the mirror to general health as it is interconnected with other systems of the body. The human body has inbuilt defence mechanism against various disease causing agents. A free radical is one of the reactive oxygen species which causes oxidative stress and further lead to cell damage and progression to other severe diseases. Antioxidants are the first line of defence against these free radicals. Antioxidants like beta-carotene, lycopene, selenium are believed to have a preventive role against various oral diseases. This article overviews the different antioxidants available and their influence in the oral cavity.

Keywords: Antioxidants, Free Radical, Reactive Oxidative stress, Oxygen Species, Oral cavity

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INTRODUCTION

Oxygen is paramount for the existence of the living organisms, as it is required in many metabolic reactions of the body, particularly for the releasing of the energy. However, as per the saying “excess of everything is bad”, similar is the case with oxygen.¹ If the oxygen is present in

excess, it can lead to the production of some harmful or toxic reactions by producing free radicals. When there are too many free radical molecules, or “oxidants,” in the body, the imbalance is called “oxidative stress”.²

Free radicals are extremely reactive chemical species, with a very short half-life and are composed of a single atom or a group of atoms that form a molecule with a free electron.³ This high reactivity is due to free electron, which can bind other free radicals, or subtract an electron from the surrounding molecules. They are not always harmful, as they also serve useful purposes in the human body. For example, they play a role in the destruction of disease-causing microbes by specialized blood cells called phagocytes.^{4,5}

To simplify, the above described terms, antioxidants inhibit the “rusting” of cells in our body. Just as metals rust due to exposure to oxygen, cells in the body also become damaged by exposure to certain “Reactive Oxygen Species” (ROS). These damaging agents are caused by toxins present in the environment, smoking, bad eating habits, poor metabolism, lack of exercise and other factors. When uncontrolled, these ROS leads to degenerative diseases like diabetes, arthritis, cancer, brain disorders, and numerous aspects of aging. DNA damage is considered to be one of the most important contributors to cancer. Much of this damage is oxidative in nature.^{4,6} In the oral cavity, cells are uniquely susceptible to free radical damage as the mucus membranes rapidly imbibe the substances across their surfaces. The increase in free radicals from oxidative stress contributes to further breakdown of cell walls and oral tissue. In the oral cavity, oxidative stress is associated with gingivitis and other periodontitis.⁶ Nevertheless, factors including alcohol consumption, exposure to nicotine, dental procedures, bleaching agents, dental cements, composite fillings and metals used in dentistry also leads to oxidative stress.²

TYPES OF ANTIOXIDANTS⁴

There are various kinds of antioxidants, which are present in the food and as well as in the human body. Some foods that contain antioxidants are:

PRODUCT	ANTIOXIDANTS
Soya beans	Isoflavones, Phenolic Acids
Green tea, black tea	Polyphenols, Catechins
Coffee	Phenolic Esters
Red wine	Phenolic Acid
Rosemary, Sage	Carnosic Acid, Rosmaric Acid
Citrus and other fruits	Bioflavonoids, Chalcones
Onions	Quercetin, Kaempferol
Olives	Polyphenols

Saliva

In the oral cavity, saliva has various defence mechanisms such as enzymatic and immunological defence mechanism against bacteria, viruses, fungi, etc.⁷ Being a gateway for nutrients, xenobiotics and colonizing microorganisms, normal saliva is always exposed to a different variety of oxidants which may change the redox status and the integrity of oral structures.⁸ The salivary antioxidant system is made of various enzymes (peroxidase, catalase, super oxide dismutase, glutathione peroxidase) and small molecules (uric acid, vitamin E, C).⁹⁻¹⁰ Salivary albumin acts as antioxidant by non-specific binding of transition metals involved in ROS generation and by oxidation of albumin sulfhydryl groups. Hence, the salivary antioxidant system is considered to be very important in oral health.¹¹

Melatonin

Melatonin (MT) is a neuro- endocrine hormone produced mainly by the pineal gland.¹² The most important function of MT is being a potent antioxidant, immune-modulatory, protective and anti-neoplastic properties. It triggers the stimulation of type I collagen fibers and bone

formation. Therefore, MT might be used locally and therapeutically in the oral cavity damage as in case of post-surgical wounds caused by tooth extractions and other oral surgeries and helps in bone formation in various auto-immunological disorders such as Sjögren's syndrome and periodontal diseases.¹³ Subsequent studies proved that melatonin directly neutralizes a variety of ROS, including $\cdot\text{OH}$, the lipid peroxy radical ($\text{ROO}\cdot$), H_2O_2 , and singlet oxygen (O_2).^{14,15}

Lycopene

It has been hypothesized that lycopene prevents carcinogenesis by preserving critical cellular biomolecules, including lipids, proteins, lipoproteins and DNA. Several studies have shown that when lycopene is given orally in the dosage of 4.8 mg/day 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 increment in the mouth opening in oral sub-mucous fibrosis. On an average, the daily allowable intake of lycopene is estimated to be 3.7 mg.^{16,17} In vitro¹⁶ studies have shown lycopene to be twice as potent as β -carotene and ten times that of α -tocopherol in terms of its singlet oxygen quenching ability. Some other good sources of lycopene except tomatoes are papaya, guava, carrots, mango and grapes.

Vitamin C (Ascorbic Acid)

It is an important free radical scavenger in plasma and helps to reinforce active Vitamin E in lipid membranes.¹⁸ As Vitamin C act as a powerful antioxidant, through its ability to scavenge free radicals, it also shows its protective effects on biopolymers such as DNA. Like Vitamin E, Vitamin C may be protective for both initiation and promotion of carcinogenesis.¹⁹ Sagan et al²⁰ suggested that dietary Vitamin C enters the mitochondria and protects against oxidative injury. Some foods that contain vitamin C are chilly pepper, bell peppers, kale, and broccoli.

Beta Carotene (βC)

Carotenoids are a widespread group of naturally occurring fat-soluble colorants. Of the more than

700 naturally occurring carotenoids identified thus far, approx fifty are present in the human diet and can be absorbed and metabolized by the human body.²¹ A precursor of vitamin A helps in immune modulation, promotes increase in the numbers of T-helper and NK cells as well as cells with IL-2 receptors and inhibits mutagenesis and cancer cell growth.¹

It has been assumed that beta carotene exhibits property of quenching single oxygen or scavenge free radical with a multiple higher efficiency, which is much higher than α tocopherol.²² Some other good sources of beta carotene are: sweet potato, carrot, spinach, apricots, broccoli, turnip green, butternut squash, prunes, peaches, tomatoes.

Green Tea/ Polyphenols

One of the most ancient and popular beverage consumed around the world is green tea, especially in India, China, Japan and Thailand, which is made from the leaves of the plant "Camellia sinensis".²³ The antioxidant activity of green tea is due to the polyphenols either directly by scavenging reactive oxygen and nitrogen species and chelation of redox-active transition of metal or indirectly by hindering pro oxidant enzymes, redox sensitive transcription factors and inducing antioxidant enzymes.²⁴

Selenium

This is a trace element and a critical co-factor for the major antioxidant enzyme glutathione-peroxidase, which catalyses the oxidation of hydroperoxide. Selenium is also implicated in cell signaling and immune reactions, which may furnish to its cancer chemo preventive potential. Both selenium and vitamin E mutually reimburse deficiency to each other and synergistically acts to slow down carcinogens. Some of the good sources of selenium are sea food, liver and meat.¹

ROLE OF ANTIOXIDANTS IN ORAL CAVITY

Dental Caries

Saliva exhibit several defence mechanisms in oral

health such as salivary flow rate, buffer capacity, pH, electrolytes, total protein, etc which inhibit caries formation.²⁵ These days, it has been assumed that the role of elevated antioxidant levels might provide protection against elevated dental caries activity.²⁶ Recently, it has been affirmed that the onset and development of dental caries is due to imbalances in levels of free radicals, reactive oxygen species, and antioxidants in saliva.²⁷ A study conducted by Amitha M²⁸ assessed the relation between that Total Antioxidant Capacity (TAC) of saliva and early childhood caries and rampant caries. The result revealed that TAC of saliva was increased in children with dental caries. Another study revealed that total protein and total antioxidant level of saliva were increased with caries activity.²⁶ However, till date there are very few studies that have discussed about the relationship between TAC of saliva and dental caries. Further studies should be carried out to know the beneficial role of antioxidants in preventing some major diseases should be recognized.

Periodontal Health

Periodontal pathogens can induce over production of ROS and leads to collagen and periodontal tissue breakdown. These antioxidants scavenge the ROS, which minimize the collagen breakdown.²⁹

Free radical bursts from the phagocytic cells, such as neutrophils and macrophages migrating to the inflammation site, damage the gingival tissue significantly.¹³ It has also compared the generation O₂ by the activated Polymorphonucleosides in the gingival crevicular fluid (GCF) of patients with acute periodontitis. Due to countless evidences that suggest a participation of the ROS in the pathogenesis of the periodontal disease, it has been raised that the factors that promote a rupture of the antioxidant physiological system, contribute to the development of oxidative mechanisms that initiate the periodontitis. Melatonin boosts the osteoblast differentiation and bone formation. Melatonin encourages the synthesis of type I collagen fibers in human osteoblasts at micromolar concentration.³⁰ Broke et al. in 2004 studied the total antioxidant capacity of serum in

periodontitis found higher serum total antioxidant capacity for healthy controls than periodontitis cases.³¹ Pavlica et al. in 2004 investigated the total antioxidant capacity of serum and concluded that the total antioxidant capacity in periodontitis was lower than in health and suggested a negative correlation between total antioxidant capacity and periodontal parameters.³²

Oral Cancer

Oral cancers is one of the ten most persistent cancers in the world as to 25% of all malignancies are found in the oral cavity.³³ These oral cancers unluckily have a very poor survival rate of 50% or less. One of the major reasons for oral cancer is the use of tobacco, and the best treatment one could get for himself is prevention by stopping the habit of smoking or chewing tobacco. Other prevention modalities, such as nutritional agents, may similarly be beneficial for several chronic diseases.³⁴ As the process of carcinogenesis occurs by the generation of reactive oxygen species, administration of non-enzymatic antioxidants especially β -carotene, Vitamin E and Vitamin C can effectively prevent the process of carcinogenesis caused by these free radicals.³⁵ A study showing that lycopene effect on the oral cancer has provided that high doses of lycopene (8mg/day) are useful in improvement of oral health.¹⁹ Polyphenols present in green tea have shown the capability to inhibit tumor cell proliferation and induce apoptosis in laboratory and animal studies.²³

Leukoplakia

In the oral cavity, Leukoplakia is the most common pre-cancerous lesion. In 1957, Sugar and Banoczy, hinted the malignant potential of leukoplakia.³⁶ From the various studies undergone, there is no doubt that the association exists between tobacco chewing and smoking with oral leukoplakia.³⁷ Tobacco smoke contains NOO_ radicals, which are carcinogenic. Free radical scavengers should be the necessary part of the treatment regimen in tobacco chewers or smokers to prevent the formation, induce the remission or inhibit the progression of pre-cancerous lesions into malignancies. Lycopene, is

a very effective natural antioxidant and quencher of free radicals. A study conducted by Mohitpal singh et al.¹⁷ has shown that lycopene is very promising antioxidant in the treatment modality in oral leukoplakia.

Barth et al. observed increased reversion of oral mucosa in leukoplakia on treating them with vitamin C, E and β -carotenes, which indicates their strong positive role in decreasing oxidative stress like environment in disease.³⁸

Oral Sub-Mucous Fibrosis

In the oral cavity, various premalignant changes are seen, among them, the most important precancerous condition is Oral Sub mucous Fibrosis (OSMF) which illustrates an increase in the prevalence in different states of India.³⁹ OSMF has a similarity in behaviour and malignant changes to other premalignant lesions of the oral cavity. So, it has been felt that the disease process in OSMF also could be reversed and inhibited by the use of anti-oxidants, as is observed in other pre malignant lesion therapies of the oral cavity.⁴⁰ The benefits of antioxidants specially lycopene is being relatively non toxic and can be supplemented easily in the diet. Borle et al.⁴¹ reported that Vitamin A, 50,000 IU chewable tablets, if given once daily could cause symptomatic improvement. Trismus (Tonic spasm of masticatory muscles) did not improve with this treatment. Maher et al.⁴¹ evaluated the role of multiple micronutrients consisting of retinol, vitamin E, vitamin D, vitamin B complex and some minerals in the management of OSMF and reported clinical improvement.

LIMITATIONS OF ANTIOXIDANTS

Although there are various benefits of fruits and vegetables as they helps in reducing the free radical damage from environmental pollutants (including radiation) in observational studies, supplements of Vitamins C and E and beta-carotene generally do not reduce DNA damage from irradiation in many in vitro and animal studies. Reasonable data is available which suggests that Vitamin C has no effect on cancer.⁴² High doses of Vitamin A showed to have embryo toxic and teratogenic effects. Large doses of

Vitamin C may be associated with the inhibition of ovarian steroidogenesis and increased probability of abortion.³⁸

Some studies have shown that, people whose diets are rich in fruits and vegetables have a reduced chance of developing cancer and an increase in the concentration of beta-carotene in their blood. However, supplements of beta-carotene do not have an anticancer effect, and they actually increase cancer in smokers.⁴²

CONCLUSION

Antioxidants as studied in the above article are very important in health. However, data regarding the beneficial role of antioxidants in oral as well as general health is very scarce. Therefore, further studies should be conducted to know the beneficial role of anti oxidants in the oral cavity, as we know it can hugely change the scenario of treatments related to non-curable diseases of oral cavity like cancers and periodontium.

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