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DENTAL SCIENCE
Review Article

Antioxidants in Dentistry: A Review

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Abstract

Free radicals play an important role in aging process and disease progression by damage to the cells. They have been implicated in the pathogenesis of various chronic and degenerative conditions including cancer, arthritis, aging, autoimmune disorders, cardiovascular and neurodegenerative diseases. Antioxidants are capable of deactivating free radicals before they attack human cells. In humans, highly complex antioxidant systems (enzymatic and non enzymatic) are generated, which work synergistically and in combination with each other to prevent cells or organs against free radicals. This review discusses the role of antioxidants and their applications in various fields of dentistry.

Keywords: *Antioxidants; Reactive oxygen species; Dental caries; Periodontal tissue damage; Gingivitis; Oxidative stress*

Introduction

Oxygen is an element which is indispensable for life and it plays an important role in promoting and deteriorating human health. Gershman's free radical theory of oxygen toxicity in 1954 threw light on the toxicity of oxygen due to its partially reduced form [1]. When cells use oxygen to generate energy in the form of ATP in the mitochondria, free radicals are created [2,3]. A free radical is defined as "any species capable of independent existence that contains one or more unpaired electrons [2]. They are a family of highly reactive and diverse species, capable of extracting electrons and thereby oxidizing a variety of bio molecules vital to cell and tissue function, which not only includes oxygen free radicals, but also nitrogen and chlorine species [4].

In recent years, the term "reactive oxygen species" (ROS) has been adopted to include molecules such as hydrogen peroxide (H_2O_2), hypochlorous acid (HOCl) and singlet oxygen ($^1O_2$), which though, not radical in nature, are capable of radical transformation in the extra- and intracellular environments [5].

Whilst most ROS have extremely short half lives, they can cause substantial tissue damage by initiating free radical chain reactions. Therefore the human body contains a number of protective Anti Oxidant (AO) mechanisms, whose specific role is to remove harmful oxidants (ROS), as soon as they form and repair the damage caused by ROS *in vivo* [5].

Antioxidants are defined as "those substances which when present at low concentrations, compared to those of an, oxidizable substrate, will significantly delay or inhibit oxidation of that substrate [6].

In normal physiology, there is a dynamic equilibrium between ROS activity and antioxidant defence capacity and when that equilibrium shifts in favour of ROS, either by reduction in anti oxidant defence or an increase in ROS production or activity, oxidative stress results [5].

Oxidative stress is defined as "disturbance in the pro oxidant - anti oxidant balance in favour of former, leading to potential damage" (Sies 1991) []. It has been implicated in the pathogenesis of various chronic and degenerative conditions including cancer, arthritis, aging, autoimmune disorders, cardiovascular and neurodegenerative diseases [7].

Antioxidants are capable of deactivating free radicals before they attack human cells. Humans do generate highly complex antioxidant systems (enzymatic and non enzymatic), which work synergistically and in combination with each other to prevent cells or organs against free radicals [8].

Antioxidants are produced from several sources including minerals, vitamins, food and herbs. They can also be acquired in capsule, liquid or tablet form. In dentistry they are incorporated in the form of toothpastes, sprays, mouth rinses or as supplements [9,10]. Antioxidants can be categorised by several methods: [11]

According to their mode of action:-

Preventative	Enzymes- superoxide dismutase, catalase, glutathione peroxidase, DNA repair enzymes.
	Metal ion sequestrators- albumin, lactoferrin, transferrin, Ceruloplasmin, uric acid, polyphenolic flavonoids
Scavenging	Ascorbate, carotenoids, uric acid, vitamin E, bilirubin, reduced glutathione & other thiols

II. According to their location:-

Intracellular	Superoxide dismutase enzymes-1 & 2, catalase, glutathione peroxidase, DNA repair enzymes and reduced glutathione.
Extracellular	Superoxide dismutase enzyme-3, selenium glutathione peroxidase, reduced glutathuione,
Membrane associated	α-tocopherol

III. According to their solubility:-

Water soluble	Haptoglobin, Ceruloplasmin, albumin, Ascorbate, uric acid, polyphenolic flavonoids, reduced glutathione and other thiols, cysteine and transferring
Lipid soluble	α-tocopherol, carotenoids, bilirubin, quinones

IV. According to structures they protect:-

DNA protective antioxidants	Superoxide dismutase enzymes 1 and 2, glutathione peroxidase, DNA repair enzymes, reduced glutathione, cysteine
Protein protective antioxidants	Sequestration of transition metals by preventative antioxidants Scavenging by competing substances Antioxidant enzymes
Lipid protective antioxidants	α-tocopherol, Ascorbate, carotenoids, reduced ubiquinone, reduced glutathione, glutathione peroxidase, bilirubin

The commonly used antioxidants are discussed below.

Ascorbic acid [12]

It is the only endogenous antioxidant in plasma that can completely protect against peroxidative damage induced by the oxidants released from activated neutrophils. The protection is provided by scavenging superoxide and peroxyl radicals and decrease the pro-inflammatory gene expression via effects on nuclear factor κβ transcription factor.

α tocopherol (Vitamin E) [11,13]

It is generally regarded as the most important and effective lipid soluble antioxidant *in vivo*. The antioxidant activity can be attributed to the single phenolic OH group, which when oxidised gives rise to vitamin E radical. Vitamin E helps in scavenging of free radicals, maintenance of membrane integrity and inhibition of cancer cell growth or differentiation by inhibition of DNA & RNA and protein synthesis in cancer cells.

Carotenoids [11]

The only source of carotenoids is from diet which includes green vegetables, tomatoes, red grapefruits and water melon.

Polyphenols [14]

They exert their antioxidant effect by their direct antioxidant properties (Eg by sparing vitamin E or by regenerating vitamin C) or to their inhibitory effect towards lipoxygenase.

Coenzyme Q10 [15]

It exists in an oxidised form (ubiquinone or CoQ) and a reduced form (ubiquinol or CoQH2) and both of them possess antioxidant activity. CoQ10 is also regarded as a pro-oxidant molecule in response to various pathophysiological events.

Lazaroids [11]

They are 21-aminosteroids. They are a newly identified family of compounds which are derived from glucocorticoids but lack activity of both glucocorticoids and mineralocorticoids. These compounds scavenge lipid peroxyl radicals and inhibit iron dependent lipid peroxidation by a mechanism similar to that of vitamin E.

Applications in various fields of dentistry

Periodontology

The reactive oxygen species cause periodontal tissue damage by [11]

1. Ground substance degradation
2. Collagenolysis either directly or indirectly or as a result of oxidation of proteases.
3. Stimulation of excessive pro-inflammatory cytokine release through NF-κβ activation.
4. PG-E2 production via lipid peroxidation and superoxide release, both of them have been linked to bone resorption.
5. The additive effects of endotoxin mediated cytokine production and that arising from respiratory burst of PMNLs in response to the same organisms lead to periodontal inflammation and subsequent attachment loss.

Evidence [16,17] suggests that scaling stimulates the increase in superoxide dismutase (SOD) levels, various other antioxidants and total antioxidant capacity (TAOC) of saliva and thus can be considered as prognostic bio markers of periodontal treatment.

It has also been shown that antioxidant therapy can be used as an adjunct to the non surgical periodontal therapy [18].

Restorative dentistry

Higher levels of salivary Vitamin E and C levels have been seen in overweight and obese subjects respectively. The elevated antioxidant levels might provide protection against dental caries activity [19]. The oxidative carbohydrate metabolism within the dental plaque might be adversely affected by these antioxidants and thus reducing bacterial activity and growth and consequently dental caries activity [20].

Manimaran., *et al*. [21] studied the application of proanthocyanidin agent (PA) that improves the bond strength of root dentin treated with sodium hypochlorite (NaOCl).

Orthodontics

Application of a topical antioxidant-essential oil gel has been shown to be an effective means of reducing inflammation in orthodontic patients with gingivitis [22]. Bond strength of brackets bonded to bleached human tooth enamel can be increased by pine bark extract [23]. Statistically significant results have been obtained with respect to bone formation when vitamin C and resveratrol were used in the expanded pre maxillary suture [24,25].

Oral medicine

Oxidative damage plays a key role in the pathogenesis of cancer by causing DNA damage. Antioxidant nutrients act to inhibit the development of cancer cells and destroy them through apoptosis, by stimulation of cytotoxic cytokines, by their action on gene expression, by preventing the development of tumour's necessary blood supply or by cellular differentiation [26].

Intervention trials on betel, quid tobacco chewers show that the administration of Vitamin A causes complete remission of leukoplakia [27]. However synthetic retinol 13 cis retinoic acid is toxic even when given at very low dose. Therefore increased emphasis has been placed on the use of relatively nontoxic antioxidants such as beta carotene and vitamin E [28,29].

Dental Implantology [30]

Antioxidant supplementation with grape seed extract has shown to have a positive effect on treating periimplantitis.

Conclusion

The antioxidant micronutrients are important not only for limiting oxidative and tissue damage but also in preventing increased cytokine production, which is a result 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. Thus, it is important to have an adequate antioxidant intake from both diet and supplements and therefore can be a valuable adjunct in the treatment of chronic dental inflammatory disorders.

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