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Review Article

ANTIOXIDANTS IN PERIODONTAL DISEASES

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ABSTRACT

Periodontal disease is a chronic adult condition. Bacteria implicated in the etiology of this disease causes destruction of connective tissue and bone. As a result of stimulation by bacterial antigen polymorphic neutrophils (PMN) produces free radicals via respiratory burst as a part of host response to infection. The gingival tissue and periodontal ligament damaged due to increased release of free radicals. Damage mediated by free radicals can be mitigated by antioxidant defense system.

KEY WORDS: Reactive Oxygen Species/ Free radicals, Antioxidants, Periodontal disease.

INTRODUCTION

Periodontal diseases (gingivitis and periodontitis) are among the most widespread chronic conditions affecting populations worldwide. The incidence and progression of periodontal disease is related casually to periodontal pathogens as well as to various host and environmental factors. The aberrant response is characterized by exaggerated inflammation involving the release of excess of proteolytic enzymes and reactive oxygen species. A growing body of evidence implicates oxidative stress in pathobiology of many human diseases and recently in periodontitis.[1]

FREE RADICALS: DEFINITION

A free radical may be defined as an atomic or molecular species capable of independent existence with one or more unpaired electrons in its structures. In recent years the term "reactive oxygen species" (ROS) has been adopted to include molecule such as hydrogen peroxide (H_2O_2)

Hypochlorous acid (HOCL) and singlet oxygen (O_2), which though not radical in nature, are capable of radical transformation in the extra and intracellular environments.[2]

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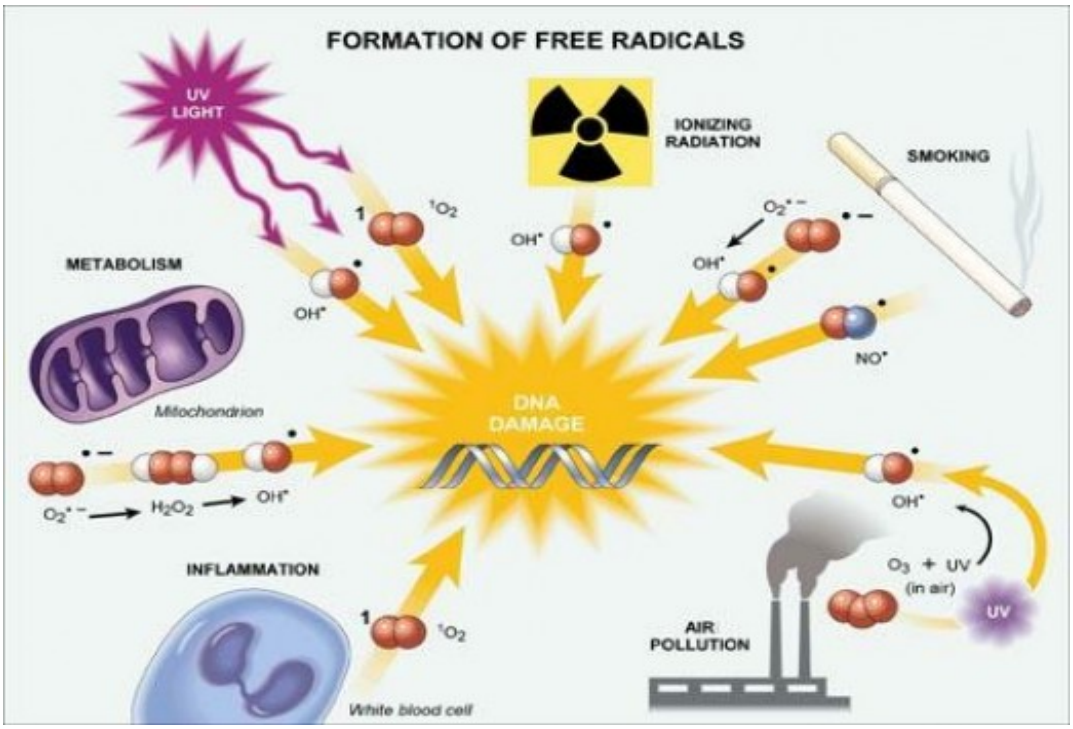

Figure 1: Formation of free radicals

FORMATION:

Most of the oxygen taken up by the cells is converted to water by the action of cell enzymes. However some of these enzymes leak electrons into the oxygen molecule and lead to the formation of free radicals. They are formed during normal biochemical reaction involving oxygen. There are two important sources of free radical formation. One of the internal factors i.e. normal cellular metabolisms like mitochondrial ETC, endoplasmic reticulum oxidation and many enzymatic activities[3, 4]. Other external factors like radiation, oxidation of engine exhaust, carbon tetrachloride, cigarette smoke and oxygen itself.[5]

MECHANISM OF TISSUE DAMAGE:

The reactive oxygen species may cause damage to various cellular and extracellular tissues by targeting the following substances.

1. **Protein damage:** It results in fragmentation and polymerization reactions of various Protein molecules leading to the formation of protein radicals and protein-bound ROS.[6]
2. **Lipid peroxidation:** It is the one of the most important reactions of free radical species. Hydroxyl and

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peroxynitrate anions are most effective in activating this process.[7]

3. DNA damage: The mechanism of damage by peroxynitrate and hydroxyl radical include strand breaks, base pair mutation, deletion, insertions, nicking and sequence amplifications.[8]

EFFECT OF ROS ON PERIODONTAL TISSUES AND COMPONENTS:

The reactive oxygen species cause periodontal tissue damage by

- ❖ Ground substance degradation.
- ❖ Collagenolysis either directly or indirectly or as a result of oxidation of proteases.
- ❖ Stimulation of excessive pro-inflammatory cytokine release through NK-kB activation.[9]
- ❖ PG - E_2 production via lipid peroxidation and superoxide release, both of which have been linked with bone resorption.
- ❖ Since 1L-1 &TNF- α positively regulate their own production, the additive effects of endotoxin mediated cytokine production and that arising from respiratory burst of PMNLs in response to the same organism, lead to periodontal inflammation and subsequent attachment loss.[10]
- ❖ In a normal cell there is balance between formation and removal of free radicals. However this balance can be shifted towards more formation of free radicals or when levels of antioxidants are diminished. This state is called oxidative stress and can result is serious cell damage if the stress is massive and prolonged. Oxidative stress plays a major role in the development of chronic and degenerative diseases such as cancer, arthritis, aging, auto immune disorders, cardiovascular and neurodegenerative diseases[11].

ANTIOXIDANTS:

Antioxidants may be defined as substances which present at low concentrations, compared to an oxidisable substrate, will significantly delay or inhibit oxidation of substrate[12].The antioxidants may be exogenous or endogenous in nature. The endogenous antioxidants can be classified as enzymatic and non enzymatic. The antioxidant enzymes include glutathione peroxidase (GP_X), glutathione reductase (GR_X), superoxide dismutase (SOD), catalase (CAT).[13]

The non-enzymatic antioxidants are also divided into metabolic antioxidants and nutrient antioxidants. Metabolic includes lipoic acid, glutathione, L-arginine, uric acid, bilirubin etc[14].

While nutrient antioxidant belonging to exogenous antioxidants are compounds which not cannot produced in the body and must be provided through foods such as vitamin E, vitamin C, carotenoids, trace elements(Se, Cu, Zn,Mn).[15]

ANTIOXIDANTS IN PERIODONTAL DISEASE:

- ❖ Periodontal disease has now been linked to oral cancer, heart disease, stroke, lung infections, pre-term and low birth weight babies, osteoporosis, and other chronic diseases.
- ❖ Patients with periodontitis tend to have lower antioxidant capacity – both locally and systemically.
- ❖ Oral biologist from university at buffalo's school of dental medicine have shown for the first time that a diet low in antioxidant vitamins can increase the risk of developing gum disease.
- ❖ The research was conducted in the university of buffalo's periodontal disease research center .They evaluated the examined serum levels of antioxidant nutrients and their relationship to periodontal disease. Results showed that selenium has the strongest association with gum diseases, with low levels increasing the risk by 13 fold. Low levels of vitamin

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TABLE 1

Antioxidants in Oral Healthcare

Antioxidant	Source	Mechanism	Clinical Significance
Beta carotene	Dark green, orange or yellow vegetables and fruits	Scavenging effect (traps peroxyl free radicals in tissue at low partial pressure of oxygen	Deficiency can lead to periodontal destruction (plasma)
Alpha tocopherol	Plant oil, margarine, wheat germ and green and leafy vegetables	Scavenging effect (breaks free radical chain reaction)	Prostaglandin inhibitory effect can contribute in reducing periodontal inflammation. Plasma, saliva, GCF, synovial fluid
Ascorbic acid	Citrus fruits, cruciferous vegetables	Scavenging and preventive (binds metal ion) effect. Acts by decreasing nitrosation and also affects the activity of leucocytes and macrophages	Gingival bleeding is a common result of ascorbate depletion. Plasma, saliva, GCF, synovial fluid
Minerals (zinc, copper, manganese, selenium)	Legumes, nuts, whole grains, green vegetables	Enzyme activators and subunits of antioxidant defense mechanism	Cytotoxic in reaction
Curcuminoids	Turmeric	Inhibits the generation of potent free radicals like superoxide and hydroxyl radical	Antibacterial, fungicidal, wound healing, cytotoxic
Epigallocatechin-3-gallate	Green tea	Scavenging effect	Reduce the risk of dental caries and plaque formation. Effective in oral leukoplakia
Spirulina fusiforms	Blue green microalgae	Potent quencher of highly reactive singlet oxygen	Effective in buccal squamous cell carcinoma
Eugenol	Clove	Scavenging and preventive effect. Enzyme activator for antioxidant action	Effective in toothache

Adapted from Cabrera C, Artacho R, Gimenez R. Beneficial effects of green tea—a review. *J Am Coll Nutr.* 2006;25(2):79-99.
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❖ A and C, a-carotene, and b-crytoxanthin also increased the risk of gum disease significantly.[16]

❖ Krol's study of total antioxidant status in peripheral and gingival serum correlated with periodontal clinical status showing significantly lower total antioxidant status in venous blood serum in each subgroup as compared with controls. He concludes that oxidative stress in periodontitis expressed by elevated concentration of ROS and accompanied by suppressed antioxidant activity in gingival blood may accelerate lesion formation in periodontal tissues.[17]

❖ Panjamurthy et al observed lower plasma vitamin C, vitamin E and reduced GHS in periodontitis subjects. Total antioxidant capacity (TAOC) concentration was found to be reduced in serum and plasma of periodontitis patients.[18]

❖ Chapple et al found lower total antioxient concentration in the saliva of periodontitis patients when compared to periodontally healthy control[19]

❖ Similar results were observd in a larger cohort study and in small case control studies (Diab ladki et al and Brock et al[20]). Lower TAOC was reported in women than men. A higher level of protin carbonyls (oxidative stress) was found in periodontitis patients than in controls.[21]

❖ Salivary antioxidant levels (SOD, GPX, reduced GHS, Ascorbic acid, α-

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tocopherol) were observed to be lower in periodontitis patients[22,23] as well as in patients under antiepileptic therapy with gingival hyperplasia[24].

- ❖ Marker of oxidative damage such as malondialdehyde[25], 8-hydroxy-deoxy-gunosine [26]were found to be higher in saliva of patients with periodontitis.
- ❖ Periodontal dieases are associated with an imbalance between oxidants and antioxidants in favour of the former due to an increase in free radical production and a defect in antioxidant level.[27, 28.]

CONCLUSION

Oxidative stress lies at the heart of periodontal tissue damage that result from host microbial interaction. While a myriad of possible mechanism leading to the destruction of periodontal tissue exist, ROS would appear to play a significant role in the pathology of periodontal disease. Antioxidants remove these harmful oxidants (reactive oxygen species) as soon as they form or repair the damage caused by ROS in vivo. Novel adjunctive antioxidant and anti-inflammatory strategies to the traditional periodontal therapy can help us in achieving good clinical results.

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