

Antioxidants in Periodontics - An Overview

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doi: 10.51505/ijmshr.2025.9401

URL: <http://dx.doi.org/10.51505/ijmshr.2025.9401>

Received: Jun 10, 2025

Accepted: Jun 23, 2025

Online Published: July 02, 2025

Abstract

Periodontitis is an inflammatory disease of supporting tissues of tooth caused by specific microorganisms. Bacterial endotoxins involved in the etiopathogenesis of periodontitis stimulate the polymorph nuclear neutrophils that releases free radicals as a part of host defense. The periodontal tissues are damaged due to increased release of free radicals. Damage mediated by free radicals can be mitigated by antioxidant defense system. Clinician must introduce adjunctive nutritional therapy to maintain optimal conditions and improve oral health. Dietary antioxidants offer remarkable benefits and valuable properties essential for periodontal health maintenance. Hence the present review focuses on antioxidants, its sources and mechanism by which they help in maintaining periodontal health.

Keywords- Periodontitis, Free radicals, Antioxidants

Introduction

Periodontal pathogens, host factors, and environmental factors all contribute to the development and progression of periodontal diseases. The immune response to periodontal disease leads to excessive inflammation, characterised by the release of proteolytic enzymes and reactive oxygen species. Researchers have increasingly implicated oxidative stress in the pathobiology of various human diseases, including periodontal disease, and are actively investigating its role (Sari A, Davutoglu V 2022). Periodontal diseases, including gingivitis and periodontitis, are widespread chronic conditions that affect populations worldwide.

Free Radicals

Free radicals are atomic or molecular species that exist independently with one or more unpaired electrons in their structures. Researchers have adopted the term "reactive oxygen species" (ROS) to describe molecules such as hydrogen peroxide (H₂O₂), hypochlorous acid (HOCL), and singlet oxygen (O₂), which, although not radicals themselves, can transform into radicals in both extracellular and intracellular environments.

Formation of free radicals: (Fig 1)

Cells convert most of the oxygen they take in into water through enzymatic action. However, some enzymes leak electrons onto oxygen molecules, generating free radicals. Free radicals form during normal biochemical reactions involving oxygen, from two key sources:

1. Internal factors: Cellular metabolisms, such as:
 - Mitochondrial electron transport chain activity
 - Endoplasmic reticulum oxidation
 - Various enzymatic activities
2. External factors: Environmental exposures, including:
 - Radiation
 - Engine exhaust oxidation
 - Carbon tetrachloride
 - Cigarette smoke (Kaur G, Kathariya R 2016)

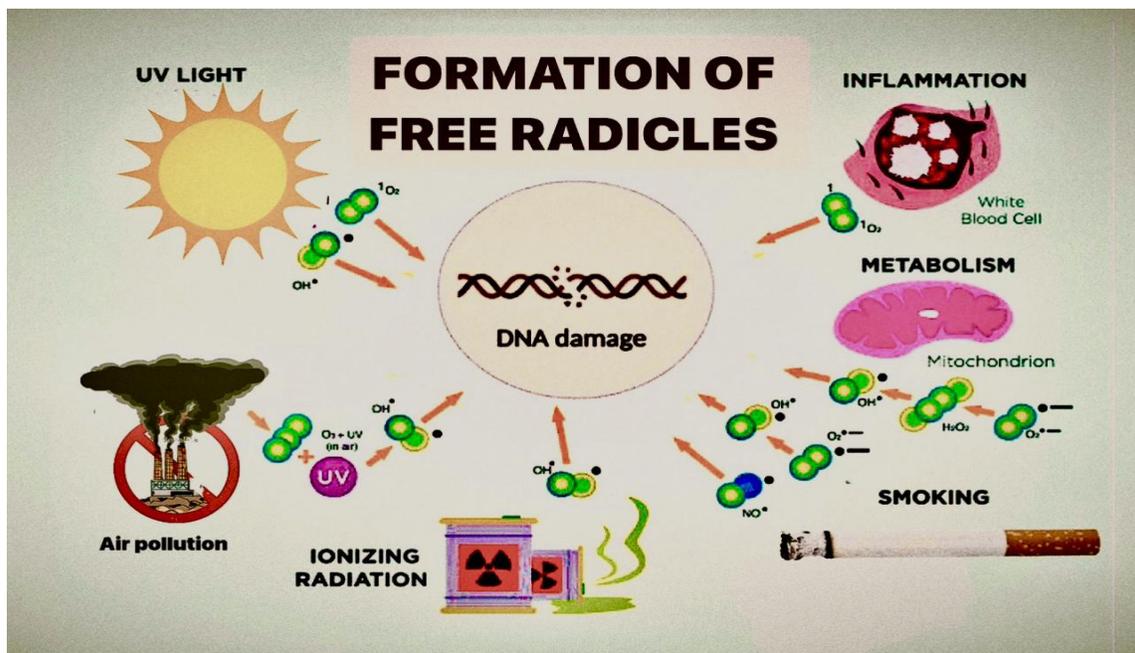


FIG 1: FORMATION OF FREE RADICALS

Antioxidants

Antioxidants are potent substances that effectively delay or prevent oxidation of susceptible substrates, even at low concentrations (Guo Q, Li F, Duan Y 2020). A diverse range of biologically significant compounds have been identified as antioxidants, including:

- Vitamins: C (ascorbic acid), E (α -tocopherol), and A
- Carotenoids: β -carotene
- Proteins: metallothionein, glutathione peroxidase, superoxide dismutase, catalase, nitric oxide synthase, heme oxygenase-1, and eosinophil peroxidase.
- Amino acids: cysteine, homocysteine, taurine, methionine, and S-adenosyl-l-methionine
- Polyphenolic compounds: polyphenols, flavonoids, phytoestrogens, and resveratrol
- Other antioxidants: melatonin, nicotinamide adenine dinucleotide phosphate, adenosine, co-enzyme Q-10, urate, ubiquinol, nitroxides, and reduced glutathione (GSH)

These antioxidants play a crucial role in protecting cells from oxidative damage, promoting overall health and well-being (Kaur G, Kathariya R 2016).

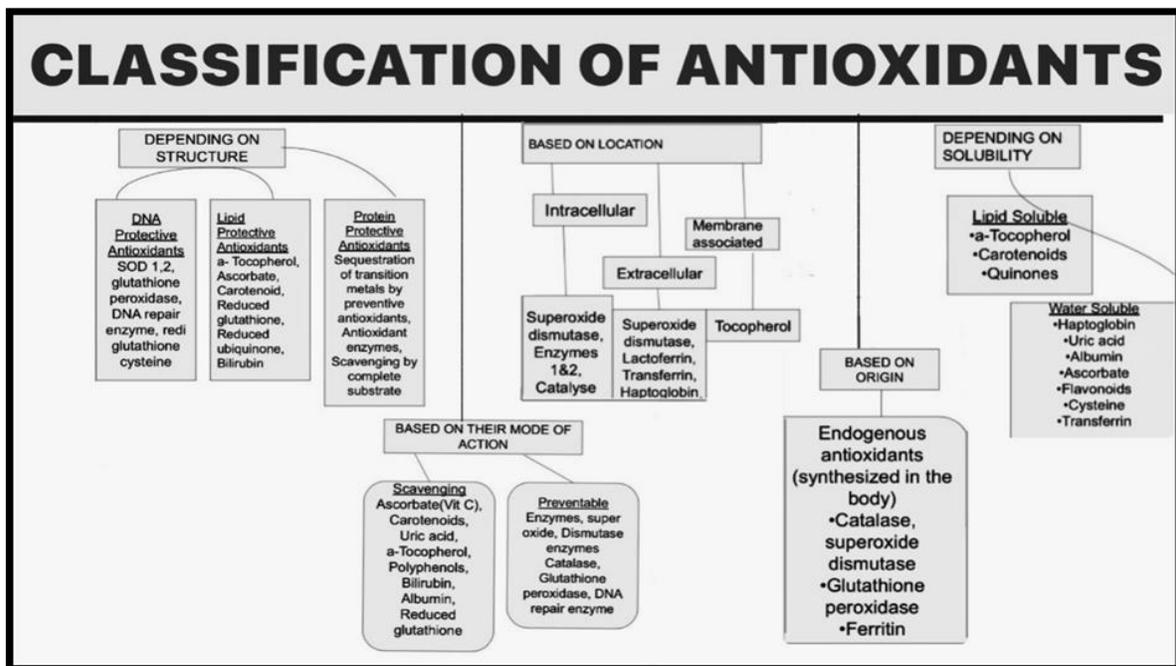


FIG 2: CLASSIFICATION OF ANTIOXIDANTS

Endogenous Antioxidants: The Body's Natural Defence

The body has a robust antioxidant system, comprising enzymatic and non-enzymatic antioxidants, to counteract oxidative stress and protect against cell damage.

Enzymatic Antioxidants

- Glutathione peroxidase (GSH-Px) reduces hydro peroxides and hydrogen peroxide, preventing lipid per-oxidation and cell damage.
- Glutathione reductase (GSH-Red) maintains glutathione in its reduced state, crucial for antioxidant enzyme activity.
- Glutathione transferase (GSH-Tr) detoxifies lipid hydro peroxides, supporting antioxidant defence.
- Catalase converts hydrogen peroxide to water and oxygen, protecting against hyper-lipid per-oxidation.
- Superoxide dismutase (SOD) eliminates superoxide radicals, safeguarding cells against oxidative damage.
- Mitochondrial cytochrome oxidase detoxifies superoxide, playing a critical role in the respiratory chain.

Non enzymatic Antioxidants

- Melatonin quenches hydroxyl and superoxide radicals, exhibiting strong antioxidant properties.
- Ceruloplasmin prevents the Fenton reaction, reducing hydroxyl radical formation.
- Transferrin binds free iron ions, inhibiting the Fenton reaction.
- Lactoferrin binds iron ions, protecting against oxidative stress.
- Glutathione (GSH and GSSG) eliminates harmful compounds, regulating antioxidant enzymes.
- Cysteine scavenges superoxide and hydroxyl radicals.
- Uric acid functions as an endogenous free radical scavenger and antioxidant.
- Glucose scavenges hydroxyl radicals.
- Albumin defends against free radicals, contributing to the extracellular antioxidant defence system.
- Bilirubin scavenges peroxy radicals, protecting against oxidative damage.

Exogenous Antioxidants: Dietary Supplements

Vitamin C (ascorbic acid)

Strengthens the immune system, supports collagen synthesis, Vitamin C, or ascorbic acid, plays a vital role in maintaining periodontal health. Its significance extends beyond being a potent

antioxidant radical scavenger, as it is essential for collagen synthesis, iron-dependent oxidation prevention, and tyrosine metabolism (Kaur G, Kathariya R 2016).

Deficiency and Depletion

Severe vitamin C deficiency leads to scorbutic gingivitis or scurvy, characterised by ulcerative gingivitis, rapid periodontal pocket formation, and attachment loss. Inadequate consumption of fruits and vegetables, key sources of vitamin C, can lead to depletion. Ascorbic acid is rapidly depleted and oxidised during oxidative stress, but adequate glutathione levels prevent this oxidation (Kaur G, Kathariya R 2016).

Role in Periodontal health (Kaur G, Kathariya R 2016)

- Supports collagen synthesis and hydroxylation
- Maintains high matrix turnover in periodontal ligament (PDL) cells
- Accumulates in high concentrations in PMNLs, mononuclear cells, platelets, and endothelial cells
- Enhances phagocytic ability of neutrophils
- Shows an inverse relationship with periodontal disease

Sources and Recommended Dietary Allowance- Rich sources: natural fruits and vegetables like gooseberry, broccoli, kiwi fruit, paprika, and citrus fruits

- **Recommended daily intake:** 90 mg for men and 75 mg for women (Food and Nutrition Board, 2000)

- **Optimal intake:** 200 mg daily from a range of fresh fruits and vegetables (Levine et al) (Kaur G, Kathariya R 2016)

regenerates vitamin E.- Vitamin E (tocopherol) inhibits lipid peroxidation, protecting cell membranes (Guo Q, Li F, Duan Y 2020)

Vitamin E: A Powerful Antioxidant with Immune-Boosting Properties

Vitamin E is a collective term for eight natural compounds, including tocopherols and tocotrienols, with α -tocopherol being the most biologically active form. As the most potent oil-soluble antioxidant in nature, vitamin E plays a crucial role in:

- Protecting cell membranes from lipid per-oxidation
- Inhibiting per-oxidation of membrane phospholipids
- Preventing damage to cell membranes
- Supporting immune system functions

- Acting as a prostaglandin inhibitor to reduce inflammation

Comprising alpha, beta, gamma, and delta tocopherols, vitamin E is stored in the liver and found in cell membranes and lipoproteins. Its antioxidant properties make it the first line of defence against free radical attacks, safeguarding polyunsaturated fatty acids in membranes, erythrocytes, lipoproteins, brain, and other tissues.

Research has also demonstrated vitamin E's significance in preventing alveolar bone destruction and reducing periodontal inflammation, solidifying its importance in maintaining overall health (Kaur G, Kathariya R 2016).

Vitamin D and Calcium: Essential Nutrients for Periodontal Health(Kaur G, Kathariya R 2016)

Vitamin D and calcium play a crucial role in maintaining periodontal health, with limited evidence suggesting a link between their deficiency and periodontal disease.

Role of Vitamin D and Calcium

Vitamin D:

- Regulates bone and calcium homeostasis
- Acts as an anti-inflammatory agent
- Inhibits immune cell cytokine expression
- Has antibiotic effects on periodontal pathogens
- Inhibits inflammatory mediators contributing to periodontal destruction

- Calcium:

- Essential for bone health
- Low daily consumption linked to more severe periodontal disease (Kaur G, Kathariya R 2016)

Sources and Recommended Dietary Allowance(Kaur G, Kathariya R2016)

- Vitamin D:

- 95% synthesised in skin upon sun exposure
- Dietary sources: oily fish, fortified milk, and orange juice
- Recommended daily intake: 400-1000 IU

- Calcium:

- Recommended daily intake: 1000-1200 mg
- National Osteoporosis Foundation recommendations vary by age
- Polyphenols exhibit anti-inflammatory, antiallergic, antiviral, anti-aging, anti-carcinogenic, and antioxidant properties.

- Flavonoids (Sczepanik FSC, Grossi ML2020)

Scavenge free radicals, protecting against oxidative stress and inflammation.

Flavonoids: Powerful Compounds for Periodontal Health

Flavonoids, polyphonic compounds, exhibit antioxidant, anti-inflammatory, and anti-allergic properties, making them beneficial for periodontal health. They inhibit bacterial collagenous, show a synergistic relationship with vitamin C, and protect against oxygen damage and excessive inflammation.

Role in Periodontal health

- Inhibit periodontal pathogens and prevent tissue destruction
- Reduce gingival bleeding index
- Inversely related to mean pocket depth, bleeding on probing, and clinical attachment level
- Inhibit collagenase activity in aggressive periodontitis patients
- May restore alveolar bone by inhibiting lipopolysaccharides

Sources of Flavonoids

- Parsley, onions, blueberries, black tea, green tea, oolong tea, bananas, citrus fruits, Ginkgo biloba, red wine, sea buckthorns, and dark chocolates ($\geq 70\%$ cocoa)

Recommended Dietary Allowance

- Tea is the primary source, contributing 157 mg of flavonoid daily
- Supplement doses range from 30 mg to 2000 mg daily
- Therapeutic range: 50 mg to 500 mg daily

Carotenoids: Antioxidant Powerhouses for Periodontal Health

Carotenoids, a group of naturally coloured pigments, play a crucial role in periodontal health due to their antioxidant properties. They protect vitamins C and E, scavenge reactive nitrogen species, and influence other antioxidants.

Role in Periodontal health

- Predictors of overall antioxidant status
- Associated with reduced periodontitis prevalence
- Low serum levels linked to increased periodontitis risk

- β -Cryptoxanthin has anabolic effects on bone metabolism
- Lycopene, a potent antioxidant, reduces oxidative stress and inflammation

Sources of Carotenoids

- Lycopene: tomatoes, apricots, guavas, watermelons, papayas, and pink grapefruits
- Other carotenoids: alpha-carotene, beta-carotene, cryptoxanthin,
- **Coenzyme Q10: A Vital Energy-Boosting Antioxidant (ubiquinone)** supports energy production, strengthens the immune system, and protects against free radicals (Toczewska J, Zalewska A 2023)
- Selenium, a trace mineral, regulates thyroid function, supports the immune system, and acts as an antioxidant enzyme cofactor (Toczewska J, Zalewska A 2023)

Coenzyme Q10, also known as ubiquinone, is a naturally occurring substance found in all living cells, with high concentrations in veal, fish, and chicken. This essential nutrient plays a crucial role in:

- Energy production within the body
- Strengthening the immune system by increasing immune resistance
- Protecting against free radicals
- Supporting heart muscle function
- Maintaining circulatory system health

As a fat-soluble nutritional supplement, Coenzyme Q10 exhibits antioxidant properties similar to vitamin E. Notably, research has shown that individuals with periodontitis tend to have lower Coenzyme Q10 levels in their gingival tissues. Fortunately, local or systemic administration of Coenzyme Q10 during treatment can help reduce inflammation in periodontal tissues, highlighting its potential benefits for oral health(Kaur G, Kathariya R2016)

Selenium: A Trace Mineral with Mighty Antioxidant Powers

Selenium, a essential trace mineral, plays a vital role in the body's antioxidant defences and overall health. It is a key component of:

- Selenoproteins, which regulate thyroid function and support immune system function
- Glutathione peroxidase, a crucial antioxidant enzyme that protects cells from damage

Despite being a essential nutrient, the body only requires tiny amounts of selenium to function properly. It helps in maintaining overall health and well-being (Mohapatra A, Panda A2024)

Implications of Antioxidants in Periodontal Health (Fig3)

Antioxidants play a crucial role in maintaining periodontal health by regulating fibroblast migration and proliferation during gingival healing and periodontal repair. They contribute to bone remodeling processes by promoting bone formation, inhibiting resorption, and supporting periodontal tissue regeneration through extracellular matrix synthesis and cell proliferation (Pattnaik N, Satpathy A 2015). They exert their beneficial effects through three key mechanisms:

1. Modulating the immune response: Antioxidants reduce the production of pro-inflammatory cytokines, chemokine, and proteins by leukocytes, thereby preventing cellular destruction.
2. Neutralising oxidative stress: Antioxidants protect fibroblasts from toxic substances that generate ROS, reversing oxidative damage and promoting cellular health.
3. Enhancing wound healing: Antioxidants actively promote the wound healing process, facilitating tissue repair and regeneration (Kaur G, Kathariya R 2016)

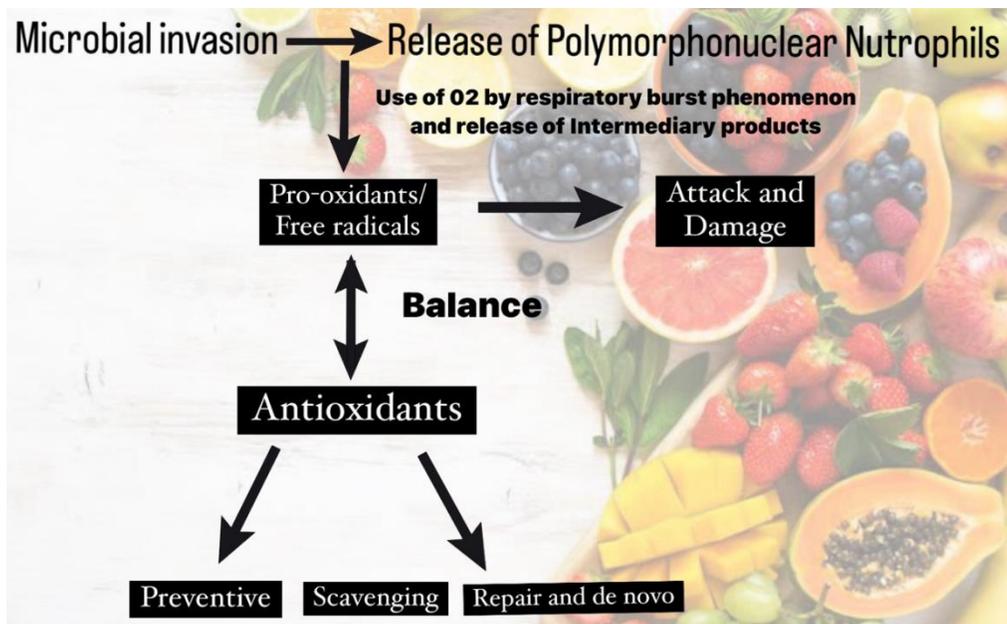


FIG 3: Interrelationship between free radicals and antioxidants antioxidants

Antioxidants Play a Crucial Role in Mitigating Oxidative Stress

To combat the harmful effects of excessive free radicals, our body has a robust antioxidant defence system. Antioxidants actively neutralise and reduce the damage caused by these destructive molecules, promoting overall health and well-being (Guo Q, Li F, Duan Y

2020). They also protect against oxidative damage by scavenging ROS and enhancing endogenous antioxidant enzyme activity (Chen M, Cai W 2019).

Found in a variety of sources, including nutrient-rich foods, tea, vitamins, minerals, and more, antioxidants offer a natural defence against oxidative stress. Furthermore, they are utilised in adjunctive treatments for conditions like cardiovascular diseases, pulmonary diseases, aging, and atherosclerosis, which share physiological connections with periodontal diseases. This suggests that antioxidants may also hold potential in supporting periodontal health and management (Guo Q, Li F, Duan Y 2020)

Total Antioxidant Capacity: A Key Indicator of Periodontal Health

The antioxidant system is complex, and measuring Total Antioxidant Capacity (TAOC) helps to assess its overall activity. Research has shown that periodontitis is linked to compromised local TAOC, with decrease in TAOC in periodontitis patients.

TAOC levels in plasma and saliva have been found to correlate with periodontal parameters, but there is conflicting evidence on whether periodontal treatment can improve compromised TAOC. A recent study found no relationship between TAOC and bacterial load in periodontitis, suggesting that changes in TAOC may be related to the host immune response rather than bacterial load.

Systemic conditions like gender, smoking, pregnancy, and systemic diseases can influence TAOC associated with periodontitis (Toczewska J, Zalewska A 2023)

Antioxidants in Periodontal Therapy

Preclinical studies have demonstrated the therapeutic potential of antioxidants in periodontal disease. Antioxidants like curcumin, resveratrol, and green tea polyphenols have shown anti-inflammatory effects, reducing inflammation and oxidative damage in periodontal tissues and immune cells. (Scannapieco FA, Gershovich E 2020)

Dietary Impact on Wound Healing in Periodontal Procedures

A well-balanced diet, rich in micronutrients and macronutrients, can significantly enhance wound healing after periodontal procedures.

- Vitamin D: Higher serum levels (>50 /L) before surgery lead to improved clinical attachment and reduced probing depths.
- Vitamin B complex: Supplements benefited patients after access flap surgery, promoting healing.
- Omega-3 fatty acids (DHA and EPA): Combination with acetylsalicylic acid reduced inflammation, improved clinical attachment, and decreased probing depths.

- Antioxidants: Topical application facilitates wound healing by promoting fibroblast migration and lowering inflammatory markers, particularly beneficial for smokers.

These studies emphasise the importance of dietary supplements in improving periodontal outcomes and wound healing after procedures. (Goldie MP2005)

Conclusion

Periodontitis, a chronic inflammatory disorder, occurs when the balance between antioxidant defenses and repair efforts is disrupted, leading to tissue damage. To prevent this, sufficient antioxidant levels must be present in oral fluids. As the body cannot produce many of these nutrients, a diet rich in antioxidants is essential. Dietary antioxidants play a crucial role in maintaining oral health and managing periodontal disease, positively impacting clinical outcomes. A strong link exists between periodontal health and antioxidants, with an inverse relationship. Therefore, consuming enough antioxidants through diet is vital to minimise the harmful effects of free radicals and promote healthier tissues, highlighting the essential role of dietary antioxidants in periodontal health.

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