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# **Review Article**

# Salivary antioxidants and dental problems - A review literature

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#### ABSTRACT

Antioxidants deficiency is indirectly related with a group of diseases worldwide. Dental studies related with free radicals and their toxic effects in dentistry have been focused recently. Major inflammation in periodontics and gingivitis is treated with antioxidants by its free radical scavenging activity. Recent studies with oral cancer incidence and its adjuvant treatment with antioxidants sustain the preventive effect of various antioxidants. Reactive oxygen species and other hydroxyl radicals tend to degrade the oral maxillary and induce carcinoma in a step-wise manner which ultimately leads to death. Data correlating the anticarcinogenic properties of antioxidants provide major insight in the mechanism of action.

Keywords: Antioxidants, oral cancer, salivary antioxidants

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#### **INTRODUCTION**

#### Antioxidants are substances that inhibit oxidation in the cellular environment and maintain homeostasis.<sup>[1]</sup> They are natural or man-made substances that can neutralize free radicals and eliminate them. Free radicals are chemical species having a single unpaired electron in its outer orbit, which create an imbalance in the microenvironment of the cells and reconstitute a pathological effect.<sup>[2]</sup> Free radicals such as reactive oxygen species (ROS) are formed within the mitochondrial inner membrane and induce lesions in the nucleoproteins which serve as a binding protein during carcinogenic process.<sup>[3]</sup> DNA damage can result in dysfunction, mutation, or oxidation of protein. Antioxidants can be enzymatic or non-enzymatic which donate an electron to the free radical and make them stable.<sup>[4]</sup> Polyphenol antioxidant is a type of antioxidant derived from fruits and vegetables and is considered as a major therapeutic drug in treating dental pathologies.<sup>[5]</sup> It contains a polyphenolic substructure with the presence of catechol group in the polyphenol which acts as an electron acceptor.<sup>[6]</sup> Polyphenol antioxidants are mainly obtained from diet rich in honey, legumes, apple, blackberry, blueberry, grapes, cherries, pomegranate, strawberry, and vegetables such as broccoli, cabbage, onion, and parsley.<sup>[7]</sup>

#### SALIVARY ANTIOXIDANTS

Saliva is rich in antioxidants and acts a first-level defense along with immune response during oral inflammation.<sup>[8]</sup> Dental studies reveal that primary inflammation in the mouth cavity if left untreated with adequate consumption of dietary antioxidant might lead to chronic conditions.<sup>[9]</sup> Thus, salivary antioxidants such as uric acid, albumin, ascorbic acid, and glutathione act as a medium of natural defense in maintaining oral health and can be measured by total antioxidant capacity (TAC).<sup>[10]</sup> It has been reported that periodontal diseases are high in patients with significant decrease in salivary antioxidants. In periodontal diseases such as gingivitis, there is an increased amount of free radicals released due to inflammation.<sup>[11]</sup> Bacteria such as *Porphyromonas gingivalis* and Entamoeba gingivalis are causative agents of Gingivalis, and hence, enhanced salivary antioxidants are known to reduce inflammation by quenching the free radicals produced by pathogens.<sup>[12]</sup> In response to the bacteria which acts as a pathogen, our body produces a number of inflammatory mediators such as cytokines, prostaglandins, and certain enzymes. Neutrophils appear due to the inflammatory responses which phagocytose the bacteria.<sup>[13]</sup> This process results in the formation of large quantities of ROS.

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## **DENTAL CARIES**

It is a common oral disease which is caused by the interaction of bacteria and dietary carbohydrates, leading to the destruction of tooth structure.<sup>[14]</sup> It is an infectious transmissible disease having a multifactorial etiology which depends on the interaction of three main group factors that must exist simultaneously for sufficient time including host, microbial, and substrate factors.<sup>[15]</sup> Saliva plays an important role in caries prevention. Saliva has an antibacterial action due to its complex structure of organic and inorganic molecules, such as electrolytes, mucins, antiseptic substances, immunoglobulin, proteins, and various enzymes.<sup>[16]</sup> Saliva peroxidase controls oral bacteria which lead to dental caries and periodontal diseases. Statistical comparisons have correlated the levels of TAC in saliva where significantly increased in caries patient in comparison to non-caries subjects.<sup>[17]</sup>

#### **ORAL CANCER**

Oral cancer is a class of disease characterized by uncontrolled cell growth to form masses of tissue called tumors. Tumor development might occur due to imbalanced cell proliferation and cell death which can further progress into cancer.<sup>[18]</sup> In addition, genetic and epigenetic alterations drive cellular transformation with multiple signals delivered within the tumor microenvironment by modifier genes<sup>[19]</sup> with an accumulation of mutations in oncogenes, tumor suppressor genes, and genes that maintain the genomic integrity of the cell.<sup>[20]</sup> Cancer development is characterized by cumulative action of multiple events occurring in single cell and can be described by three stages: Initiation, promotion, and progression.<sup>[21]</sup> ROS is involved in all these stages. The effect of oxidative stress at a certain stage of carcinogenesis is directly proportionate to the type and the reactivity of radicals involved.<sup>[22]</sup> During tumor development, tumor cells release nucleic acids into the blood circulation, and this process occurs by apoptotic and necrotic cell deaths along with active cell secretion. Increased ROS levels report the imbalance between the generation and elimination, leading to oxidative stress-related malignancy characterized by functional decline of the cellular antioxidants during the primary defense.<sup>[23]</sup> Antioxidants act as reducing agents to get oxidized and prevent excess free radical production, but under malignant condition, the levels of antioxidants provided are insufficient to overplay the emerging free radicals all over. Hence, treatment with antioxidants in the initial stages might reduce the effect of cancer metastasis.[24]

## **MECHANISM OF ACTION**

Enzymic and non-enzymic antioxidants deliver a wide variety of action against dental and other disease conditions. Hence, a detailed mechanism of action is studied and followed with yet future research. Superoxide dismutase, catalase, glutathione peroxidase, and glutathione reductase are considered as the primary antioxidant enzymes since they are involved in the direct elimination of ROS.<sup>[25]</sup> They catalyze the dismutation of the superoxide ( $O_2^-$ ) radical into either ordinary molecular oxygen ( $O_2$ ) or hydrogen peroxide ( $H_2O_2$ ), and the regulation of hydrogen peroxide provides a key in the downregulation of cellular damage. Salivary antioxidants enhance a wide variety of action as the majority of saliva is watery, and hence, function in the transport and lubrication in the body.<sup>[26]</sup>

#### **CONCLUSION**

Antioxidant review helps us to understand the potent activity in scavenging the free radicals and maintaining homeostasis. Salivary antioxidant present naturally may be enriched with proper hygiene and a dietary habit as per dental research explains. Various researches on natural products reveal the antioxidant and anticarcinogenic effects which emphasize the intake of natural food. Recent research has focused mainly in antioxidant study and its action mechanism for various diseases. Hence, in the future, antioxidant-based artificial drugs will be prescribed and followed in curing ailments for the betterment of humanity.

#### REFERENCES

- 1. Dröge W. Free radicals in the physiological control of cell function. Physiol Rev 2002;82:47-95.
- Reşat A, Özyürek M, Güçlü K, Çapanoğlu E. Antioxidant activity/ capacity measurement. 1. Classification, physicochemical principles, mechanisms, and electron transfer (ET)-based assays. J Agric Food Chem 2016;64:997-1027.
- O'Brien TJ, Ceryak S, Patierno SR. Complexities of chromium carcinogenesis: Role of cellular response, repair and recovery mechanisms. Mutat Res 2003;533:3-36.
- 4. Michael TL, Beal MF. Mitochondrial dysfunction and oxidative stress in neurodegenerative diseases. Nature 2006;443:787-95.
- Hamid AA, Aiyelaagbe OO, Usman LA, Ameen OM, Lawal A. Antioxidants: Its medicinal and pharmacological applications. Afr J Pure Appl Chem 2010;4:142-51.
- Carreras A1, Mateos-Martín ML, Velázquez-Palenzuela A, Brillas E, Sánchez-Tena S, Cascante M, *et al.* Punicalagin and catechins contain polyphenolic substructures that influence cell viability and can be monitored by radical chemosensors sensitive to electron transfer. J Agric Food Chem 2012;60:1659-65.
- Amarowicz R1, Carle R, Dongowski G, Durazzo A, Galensa R, Kammerer D, *et al.* Influence of postharvest processing and storage on the content of phenolic acids and flavonoids in foods. Mol Nutr Food Res 2009;53 Suppl 2:S151-83.
- 8. Fisinin VI, Surai P. Gut immunity in birds: Facts and reflections. Agric Biol 2013;4:3-25.
- 9. Logan EI. Dietary influences on periodontal health in dogs and cats. Vet Clin North Am Small Anim Pract 2006;36:1385-401.
- 10. Vincent SD. Inter-Individual Variation in Saliva Antioxidant Status in Relation to Periodontal Disease, Dissertation University

College Northampton; 2004.

- 11. Diab-Ladki R, Pellat B, Chahine R. Decrease in the total antioxidant activity of saliva in patients with periodontal diseases. Clin Oral Investig 2003;7:103-7.
- Moya IA, Su Z, Honek JF. Current and future perspectives on the chemotherapy of the parasitic protozoa *Trichomonas vaginalis* and *Entamoeba histolytica*. Future Med Chem 2009;1:619-43.
- Smith JA. Neutrophils, host defense, and inflammation: A doubleedged sword. J Leukoc Biol 1994;56:672-86.
- 14. Selwitz RH, Ismail AI, Pitts NB. Dental caries. Lancet 2007;369:51-9.
- 15. Baydaa AY. The relation of salivary antioxidants to dental caries among overweight and obese adult aged 30-40 year-old at textile factory in Mosul city. Children 2011;17:18.
- González S, Sung H, Sepúlveda D, González M, Molina C. Oral manifestations and their treatment in Sjögren's syndrome. Oral Dis 2014;20:153-61.
- 17. Preethi BP, Reshma D, Anand P. Evaluation of flow rate, pH, buffering capacity, calcium, total proteins and total antioxidant capacity levels of saliva in caries free and caries active children: An *in vivo* study. Indian J Clin Biochem 2010;25:425-8.
- Elise CK, Liotta LA. Molecular insights into cancer invasion: Strategies for prevention and intervention. Cancer Res 1995;55:1856-62.
- Prendergast GC, Jaffee EM. Cancer immunologists and cancer biologists: Why we didn't talk then but need to now. Cancer Res 2007;67:3500-4.

- 20. Forouzanfar MH, Alexander L, Anderson HR, Bachman VF, Biryukov S, Brauer M, *et al.* Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015;386:2287-323.
- 21. Kemp CJ, Donehower LA, Bradley A, Balmain A. Reduction of p53 gene dosage does not increase initiation or promotion but enhances malignant progression of chemically induced skin tumors. Cell 1993;74:813-22.
- 22. Valko M, Rhodes CJ, Moncol J, Izakovic M, Mazur M. Free radicals, metals and antioxidants in oxidative stress-induced cancer. Chem Biol Interact 2006;160:1-40.
- 23. Holdenrieder S, Stieber P. Clinical use of circulating nucleosomes. Crit Rev Clin Lab Sci 2009;46:1-24.
- Lokeshkumar B, Sathishkumar V, Nandakumar N, Rengarajan T, Madankumar A, Balasubramanian MP. Anti-oxidative effect of myrtenal in prevention and treatment of colon cancer induced by 1, 2-dimethyl hydrazine (dmh) in experimental animals. Biomol Ther (Seoul) 2015;23:471-8.
- 25. Rice-Evans CA, Diplock AT. Current status of antioxidant therapy. Free Radic Biol Med 1993;15:77-96.
- Ali AA, Alqurainy F. Activities of antioxidants in plants under environmental stress. The Lutein: Prevention and Treatment for Diseases 2006. Kerala: Transworld Research Network; 2006. p. 187-256.