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THE IMPACT OF ANTIOXIDANTS ON OXIDATIVE STRESS AND ORAL LESIONS: A REVIEW

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Abstract

Oral cancer is the deadliest of diseases all over the world. It can be treated primarily by surgery with or without adjuvant radiotherapy and or chemotherapy. Antioxidants are intimately involved in preventing cell damage or death of the cells. Whether antioxidants can protect the human population from diseases like leukoplakia, lichen planus, carcinoma in situ or oral cancer and also from cancers of the upper aero digestive tract i.e. larynx, pharynx and esophagus and increase the life expectancy is still a debate. Recently, there is an upsurge in prevention of diseases induced by free radicals. This review elicits the impact of antioxidants on oral lesions.

Introduction

Merriam-Webster defined Antioxidant as "a substance that inhibits oxidation, especially one used to counteract the deterioration of stored food products". Antioxidants are substances which slow down the rate at which something decays because of oxidization[1]. The process of oxidation is a natural phenomenon of energy generation system and it's by- product called "Free Radicals" can damage healthy cells of the body[2]. In a normal cell there is a balance between formation and removal of free radicals. When there is imbalance, there is more formation of free radicals or levels of antioxidants are diminished. This state is called "Oxidative Stress" and can result in serious cell damage if the stress is massive and prolonged. Majority of the diseases / disorders are mainly linked to oxidative stress due to free radicals. Antioxidants are capable of stabilizing or deactivating free radicals by donating their electrons before they attack cells[3]. This review discusses the antioxidants and its role in oral diseases.

Sources of Free Radicals

Free radicals can be formed from both endogenous and exogenous substances[4].

Exogenous sources include electromagnetic radiation, cosmic radiation, UV-light, Ozone, X-rays, gamma rays, cigarette smoke and microwave radiation.

Endogenous sources are mitochondrial electron transport chain, β-oxidation of fat. Neutrophils stimulated by exposure to microbes, metabolism of arachidonic acid and platelets. Industrial effluents, excess chemicals, alcoholic intake, certain drugs, asbestos, certain pesticides and herbicides, some metal ions, fungal toxins and xenobiotics.

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The antioxidants can be categorized as enzymatic and non-enzymatic type (fig.1)

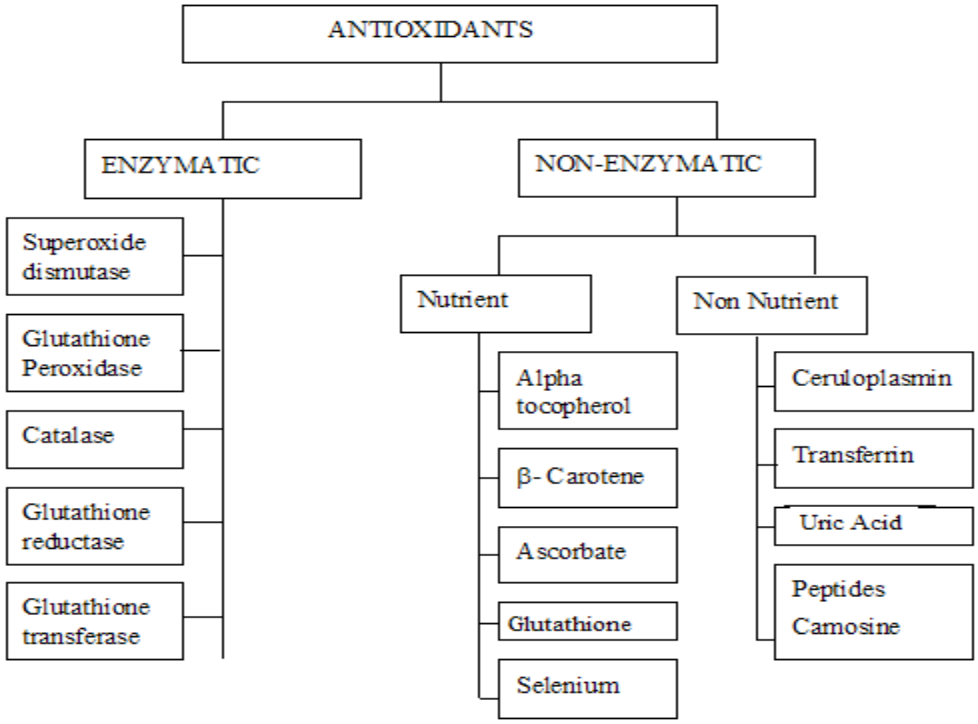

Fig 1. Classification of free radicals

Mechanism of Action

A free radical is defined as any species that contains one or more unpaired electron occupying an atomic or molecular orbital by itself (Fig 2). Antioxidants neutralize free radicals by donating one of their electrons[5]. Free radicals cause tissue damage by Lipid peroxidation, protein damage, DNA damage, enzyme oxidation and stimulation of pro-inflammatory cytokines release[6].

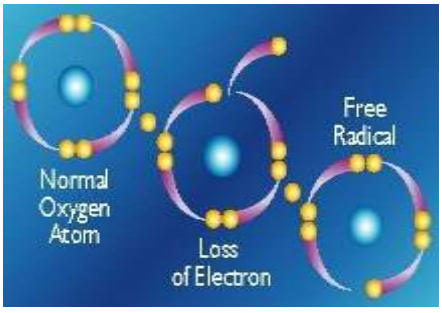

Fig.2 Formation of free radical.

Assay Methods for Antioxidants

For purpose of assessing antioxidant capacity (AOC) in foods, botanicals, nutraceuticals, and other dietary supplements dealing with analytical issues, the First International Congress on Antioxidant Methods was convened in Orlando, FL, in June 2004 [7]. These assay methods are popular due to their ease, speed and sensitivity. The presence

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of antioxidants leads to the disappearance of these radical chromogens, the most widely used are total radical-trapping antioxidant parameter (TRAP) and Oxygen radical absorbance capacity (ORAC) assay. Some other commonly used assays are Trolox equivalent antioxidant capacity (TEAC), FRAP, ABTS and DPPH methods.

Antioxidant Role in Oral Lesions

Antioxidant therapy for leukoplakia

Proliferative verrucous leukoplakia has a high rate of malignant transformation (70.3%) to verrucous carcinoma or squamous cell carcinoma[8]. Silverman SJR, Kaugars GE in their study used 13cRA (13-Cis Retinoic acid) in the range of 0.5 to 1 mg/kg/d as a starting dose for the treatment of premalignant oral lesions. For patients presented with an extensive premalignant oral lesion, it was advisable to begin with 50 mg of 13-cRA/d. The maximum duration of continuous 13-cRA is 3 months. They also found more than a 50% reduction in the clinical size of the lesion with 13-Cra[9]. Shah et al., treated 16 patients with oral leukoplakia with topical doses of 13-cRA, which ranged from 3 to 10 mg/day for 6 months delivered by lozenges. Five (31.2%) of the patients dropped out because of the side-effects, and 2 of the 3 patients who showed complete clinical resolution had recurrences within 5 weeks of discontinuing the medication[10].

Antioxidant Therapy in Oral Lichen Planus

It has been found ROS (Reactive oxygen species) produced by keratinocytes, fibroblasts and pro-inflammatory cells results in disequilibrium of pro-oxidants and antioxidants[11]. Petruzzi M *et al*., used tazarotene for the treatment of lichen planus. Tazarotene has an effect on the growth and differentiation of keratinocytes[12]. A total of 37 biopsy-proven symptomatic OLP patients were selected for this randomized double-blind placebo-controlled trial. Purslane (n = 20) and placebo (n = 17) were advised for lichen planus cases for 3 months. Assessments were made at baseline, after 2 weeks and each month for 6 months, based on the visual analog scale (VAS) and clinical improvement including lesion type and size. Approximately 83% of the purslane patients showed partial to complete clinical improvement but 17% had no response[13].

Antioxidant Therapy in Oral Sub Mucous Fibrosis

Malondialdehyde is a biomarker of oxidative stress and it is an end product of LPO. There is alteration in biological parameters leading to depletion of antioxidants. The supplementation of antioxidants may prevent oxidative damage in betel nut and tobacco users[14]. Borle *et al*., reported that vitamin A, 50,000 IU chewable tablets, if given once daily could cause symptomatic improvement. Soma gupta *et al*., assessed the non-enzymatic antioxidant defense status of the body in a study by plasma β-carotene and vitamin E level, β-carotene level was decreased in all grades of OSMF cases[15]. Maher *et al*., evaluated the role of multiple micronutrients consisting of retinol, vitamin E, vitamin D, vitamin B complex and some minerals in the management of oral sub mucous fibrosis (OSMF) and reported clinical improvement[16].

Role of Antioxidants in Immune-Mediated Systemic Diseases

An association between lipid peroxidation and impaired glucose level have been stated in diabetics mellitus. In diabetic patients, elevated levels of pro-oxidants protein such as ferritin found in homocysteine and intestine are the probable sources of oxidative stress. By the peroxidation of arachidonic acid the prostaglandin like compounds F-2 isoprostanes are formed mediated by free radicals[17]. Glutathione levels showed elevation with an increase in periodontal probing depth in both type 1 and 2 diabetes samples. Glutathione levels have been found to influence signal transduction and gene expression events in T-lymphocytes. HIV-infected patients show have increased serum cytokine level leading to oxidative stress, thus altering glutathione levels. Glutathione supplements was found to increase the survival rate in patients with low CD4 T-cell counts. Depletion of liver glutathione levels below a certain threshold value in HIV patients is a hallmark in the transformation of HIV-infected to full-blown AIDS patient. Hence, glutathione is essential to for the balance between the T-helper cell 1 and T-helper-2 type cells[18].

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Role of Antioxidants in Oral Cancer

Ames, suggested that antioxidants produce cancer regression, prevention of carcinogenesis and prevention of carcinogenesis[19]. Hristozov *et al*., found signifiantly higher levels of lipid peroxidation products (malonaldehyde) in early and advanced cancers in comparison to controls[20]. Das suggested that tumor cells have relatively low amounts of SOD, which quenches superoxide anion and as a result of a higher level of aerobic metabolism, higher concentration of hydroxyl ion compared with normal cells. He also suggested that ionizing ration radiation and chemotherapeutic agents like anthracyclines and bleomycin exert their anticancer effect by producing free radicals[21].

Conclusion

The imbalance between reactive oxygen species and antioxidants defence systems increases oxidative burden and lead to damage of macromolecules such as DNA, proteins,carbohydrates. Antioxidants also have a role in the prevention of degenerative disease, premalignant and malignant lesions and maintenance of good health. So, some researchers have suggested using combined antioxidant supplements will provide higher protection against free radicals. So if the knowledge of free radicals and the impact of antioxidants in oral lesions is well accomplished, we can easily prove the proverb "PREVENTION IS BETTER THAN CURE" but at the same time we should remember, "ONE CARROT PER DAY KEEPS A DOCTOR AWAY". Future approach include gene therapy to produce more antioxidant in the body, genetically engineered plant products with higher level of antioxidant, synthetic antioxidant enzymes (SOD mimics), novel biomolecules and the use of functional foods enriched with antioxidant.

References

1. *Saikat Sen et al., Free Radicals, Antioxidants, Diseases and Phytomedicines: Current and Future prospect International Journal of Pharmaceutical Sciences Review and Research Volume 3, Issue 1, July – August 2010*
2. *Anil Kumar Nagarajappa et al., Role of Free Radicals and Common Antioxidants in Oral Health, an Update British Journal of Medicine & Medical Research BJMMR, 9(4): 1-12, 2015*
3. *Arvind Shetti et al., Antioxidants: Enhancing oral and general health Journal of Indian Academy of Oral Medicine and Radiology / Jan-Mar 2009 / Volume 21 / Issue*
4. *Shahin Sharif Ali et al.,Review Indian medicinal herbs as sources of antioxidants Food Research International 41 (2008) 1–15*
5. *Kumar S. Free radical in andioxidants: Human and food system. AASR 2011;129-35.*
6. *Harsh Mohan., Essential pathology 3rd edition*
7. *Ronald l. Prio et al., Standardized Methods for the Determination of Antioxidant Capacity and Phenolics in Foods and Dietary Supplements, J. Agric. Food Chem. 2005; 53, 4290-430*
8. *Hsue SS, Wang WC, Chen CH, Lin CC, Chen YK, Lin LM. Malignant transformation in 1458 patients with potentially malignant oral mucosal disorders: A follow-up study based in a Taiwanese hospital. J Oral Pathol Med 2007;36:25-9.*
9. *Kaugars GE, Silverman S Jr, Lovas JG, Brandt RB, Riley WT, Dao Q.A clinical trial of antioxidant supplements in the treatment of oral leukoplakia. Oral Surg Oral Med Oral Pathol 1994;78:462 8*
10. *Shah JP, Strong EW, DeCosse JJ, Itri L, Sellers P. Effcts of retinoids on oral leukoplakia. Am J Surg 1983;146:466 70.*
11. *Mishra SS, Maheshwari TN. Evaluation of oxidative stress in oral lichen planus using malonaldehyde: a Systematic review; Journal of dermatology and dermatology surgery; 2014.*
12. *Petruzzi M, De Beneditts M, Grassi R, Cassano N, Vena G, Serpico R. Oral lichen planus: A preliminary clinical study on treatment with tazarotene. Oral Dis 2002;8:291 5.*
13. *Agha Hosseini F, Borhan Mojabi K, Monsef Esfahani HR, Mirzaii Dizgah I, Etemad Moghadam S, Karagah A Efficacy of purslane in the treatment of oral lichen planus. Phytother Res 2010;24:240 4*
14. *P Rajakumar et al., Role of Antioxidants in Oral Submucous Fibrosis; Journal of International Oral Health 2016; 8(3):412-414*

15. *Gupta S, Reddy MV, Harinath BC. Role of oxidative stress and antioxidants in aetiopathogenesis and management of oral submucous fibrosis. Indian J Clin Biochem 2004;19:138 41*
16. *Maher R, Aga P, Johnson NW, Sankaranarayanan R, Warnakulasuriya S. Evaluation of multiple micronutrient supplementation in the management of oral submucous firosis in Karachi, Pakistan. Nutr Cancer 1997;27:41 7*
17. *Davies KJ. Protein damage and degradation by oxygen radicals: IV, Degradation of denatured protein, J BiolChem 1997; 262:9914-20*
18. *De la Fuente M. Effects of antioxidants on immune system ageing. Eur J Clin Nutr. 2002; 56: 5–8.*
19. *Ames BN, Shigenaga MK, Hagen TM. Oxidants, antioxidants, and the degenerative diseases of aging. Proc Natl Acad Sci USA 1993;90:7915-22.*
20. *Hristozov D, Gadjeva V, Vlaykova T, Dimitrov G. Evaluation of oxidative stress in patients with cancer. Arch Physiol Biochem 2001;109:331 6*
21. *Das U. A radical approach to cancer. Med Sci Monit 2002;8:RA79 92*

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