Enzymatic antioxidants and its role in oral diseases

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ABSTRACT

Antioxidants are substances that when present at very low concentration inhibits the oxidation of a molecule. It has the capacity to nullify the ill effects of oxidation caused by free radicals in the living organisms. The unpaired electrons of these free radicals are highly reactive and neutralize the harmful reactions of human metabolism. Protection of the body against free radicals is provided by some enzymes which come under a distinctive group, concerned solely with the detoxification of these radicals. Superoxide dismutase (SOD), glutathione peroxidase (GPX) and catalase are the key enzymatic antioxidants of this defense system by which the free radicals that are produced during metabolic reactions are removed. This review highlights the mechanism of action of enzymatic antioxidants SOD, GPX and catalase and its role in oral disease.

KEY WORDS: Catalase, enzymatic antioxidant, glutathione peroxidase, oral disease, superoxide dismutase

A substance that is capable of neutralizing the harmful effects of free radicals in the human body is termed as an antioxidant. Antioxidants can be defined as a substance which when present at very low concentration inhibits the oxidation of any molecule.[1] The harmful effects of free radicals obtained as products of metabolism are inactivated by antioxidants.[2] Free radicals are molecules that are extremely reactive and either donate or extract electrons from neighboring molecules that it reacts with.[3] Aerobic organisms have an antioxidant defense system that neutralizes these free radicals. This system includes both enzymes and nonenzymatic antioxidants that play an important role in scavenging these free radicals. Antioxidants present in cells, function to prevent the damage done by oxidative stress.

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Discussion

The different type of antioxidants is glutathione, Vitamin A, Vitamin E, enzymes catalase, superoxide dismutase, (SOD) and various peroxidases. This review discusses the enzymatic antioxidants and its role in oral diseases. The prime antioxidant enzymes highlighted in the current review are SOD, glutathione peroxidase (GPX), catalase.

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Superoxide dismutase

Superoxide dismutase is an enzyme with a generalized presence in the body which catalyzes the dismutation of superoxide. As a by-product of this reaction hydrogen peroxide is produced which helps to conduit in transmission of the injury caused by free radicals. The human body produces an incredible number of reactive oxidants such as hydrogen peroxide, superoxide and hydroxyl radicals. The hydroxyl radical is the most catastrophic to the tissue causing destruction of the adjacent cells. The enzyme SOD has three variants. The predominant copper-zinc containing enzymes are found in the cytoplasm while manganese SOD is located in the mitochondria. A third type is present extracellularly.[2]

Glutathione

Glutathione peroxidase and glutathione reductase are enzymes that act as antioxidants. The reduced form of glutathione is defensive in nature. The oxidized form is not protective. Reduced glutathione helps to neutralize hydrogen peroxide produced inside the cell.[4] These enzymes are key players in preventing increased levels of oxidative stress.[5] This repeated oxidization and reduction of glutathione makes it a free radicals scavenger.[6]

Catalase

Catalase is an antioxidant enzyme that acts as a catalyst for the conversion of hydrogen peroxide to oxygen and water. It nullifies the effect of hydrogen peroxide that is present intracellularly. The precise amount of catalase present in the cytoplasm cannot be assessed because most of it is lost during tissue manipulation.[7] Oxidative stress is caused by an imbalance between the reactive oxygen species and antioxidant interaction. Oxidative stress is an etiologic and aggravating factor in a number of diseases.

Role of antioxidants in periodontal lesion

Oxidative stress has a significant role in the pathogenesis of periodontitis. SOD levels were found to be elevated in chronic periodontitis cases.[8] This enzyme present in periodontal ligament neutralizes the effect of reactive oxygen species. It is hypothesized that bacterial polysaccharides stimulate the release of superoxide which in turn leads to induction of the enzyme SOD. The amount of GPX has shown considerable variability in chronic periodontitis patients. Some studies have shown a decrease in the level of this enzyme in chronic periodontitis patients while other studies are contrary to the same.

Role of antioxidants in oral mucosal lesions

The role of this enzyme in cancer patients was studied, and it was observed that most tumor cells lacked superoxides of manganese.[9] Manganese SOD was found to be a tumor suppressor.[10] The expression of SOD can thus also be used as oxidative biomarker for cancer.[11] The alteration in glutathione levels in carcinogenesis of hamster buccal pouch induced was observed. Gamma-glutamyl transpeptidase is an enzyme that removes the toxic effect of carcinogens, and it catalyzes the breakdown of glutathione. There was a gradual elevation in the levels of glutathione which doubled in level in the test pouch compared to the control. The preneoplastic pouch epithelium was found to be resistant to the toxic effects of the carcinogen. This could be due to an increase in reduced glutathione and gamma-glutamyl transpeptidase.[12]

The erythrocyte catalase activity was decreased in oral cancer patients as compared to the patients with precancer. An increase in production of superoxide anion or a decrease in antioxidant scavenging activity of the enzyme could be responsible for this.[13]

The erythrocyte SOD activity of oral submucous fibrosis patients was compared to the stage of this disease. As there was no change in levels, it was not revelatory.[14] Literature in the past states that there is a gradual reduction in the SOD level which had a positive correlation with clinical grades of oral submucous fibrosis.[15] Mean hemolysate levels of both the antioxidant enzymes SOD and GPX were decreased in the patients of oral submucous fibrosis compared to control healthy volunteers.[16]

Antioxidants have a significant correlation in individuals with recurrent aphthous stomatitis with decreased erythrocyte SOD level. The other two enzymes GPX and catalase showed no significant difference compared to controls.[17]

Lichen planus is an autoimmune disease. The evaluation of oxidative stress in lichen planus on estimating the serum levels of SOD and catalase, showed an increase in the levels of SOD, with decreased catalase levels than controls. Catalase is the main enzyme in eliminating peroxides. A disturbance in the balance between the antioxidant and free radicals results in the accumulation of hydrogen peroxide, thus leading to the vacuolization of the basal cells seen in histopathological sections of lichen planus.[7]

Expression of antioxidants glutathione and SOD by oral mucosal fibroblasts in cell cultures in response to arecoline, the cytotoxic betel quid constituent was tested for their protective effects. Decreased glutathione prevents the arecoline cytotoxicity. While catalase and SOD have no role in preventing cytotoxicity.[18]

Role of antioxidants in immune-mediated systemic diseases

Diabetes (type 1 and type 2) induced inflammatory periodontal disease were evaluated for the levels of oxidized and reduced glutathione levels. The levels of glutathione in unstimulated saliva were significantly lower than control group diabetics. Glutathione levels showed elevation with an increase in probing depth in both type 1 and 2 diabetes samples. This substantiates the fact that generation of free radical is increased in chronic hyperglycemia leading to increased reduced glutathione.[19]

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.[20] 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.[21]

Summary

Oxidative stress that results in DNA damage is the root cause of physiologic and pathologic diseases aging, atherosclerosis and cancer. Hence, SOD and glutathione levels can be considered as indicators of oxidative stress. Hence, a diet with increased antioxidants from fruits and vegetables makes an individual less prone to oral diseases including periodontal, mucosal, immune-mediated, malignancies. Antioxidants also have a chemopreventive potential to reduce betel quid-associated premalignant and malignant lesions.[22]

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