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THE ROLE OF SALIVARY ANTIOXIDANTS IN THE PROTECTION OF ORAL TISSUES

УЛОГАТА НА САЛИВАРНИТЕ АНТИОКСИДАНСИ ВО ЗАШТИТАТА НА ОРАЛНИТЕ ТКИВА

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Abstract

As a secrete, saliva comes into direct contact with all oral structures in the oral cavity. Antioxidants are essential for the protection of oral tissues. Antioxidants play an important role in the pathogenesis of inflammatory processes such as periodontal disease. Saliva contains enzymatic antioxidants such as glutathione peroxidase (GPx), superoxide dismutase (SOD), etc., as well as non-enzymatic antioxidants such as uric acid, albumin, etc. According to the findings of the literature and some of our studies, a lower concentration of antioxidants in saliva has been found in patients with chronic periodontitis. Following the causal treatment, a correlation was established between the clinical parameters for the condition of the periodontium and the level of antioxidants in saliva. The importance of these studies is that they demonstrate the possibility of using saliva as a valid diagnostic tool in the monitoring of periodontitis and other inflammatory diseases. The non-invasive determination of antioxidants in saliva allows for analysis of the results and the generation of useful recommendations for the development and monitoring of new treatment strategies, as well as the prevention of many pathological conditions and the prevention of inflammatory diseases in the oral cavity. **Key words:** saliva, antioxidants, periodontitis.

Апстракт

Плунката како секрет е во непосреден контакт со сите орални структури во усната празнина. Во заштита на оралните ткива значајна улога имаат антиоксидантите. Антиоксидантите играат важна улога во патогенезата на воспалителните процеси, вклучувајќи ја и пародонталната болест. Плунката содржи ензимски антиоксиданси, какошто се глутатион пероксидаза (GPx), супероксид дисмутаза (SOD) итн., неензимски антиоксиданси и тоа мочна киселина, албумини и др. Според наодите од литературата и од некои наши истражувања утврдена е намалена концентрација на антиоксидантите во плунка кај пациенти со хронична пародонтопатија. По спроведениот каузален третман воспоставена е корелација помеѓу клиничките параметри за состојбата на пародонциумот и нивото на антиоксиданси во плунка. Важноста на овие студии е да се прикаже можноста за употреба на плунката како валиден дијагностички медиум во следењето на пародонтопатијата и другите инфламаторни заболувања. Со неинвазивното определување на антиоксидантите во плунка се овозможува анализа на постигнатите резултати и се добиваат корисни препораки за развој и следење на нови стратегии за третман и можност да се спречат многу патолошки состојби и да се овозможи превентивно делување на инфламаторните заболувања во усната празнина. **Клучни зборови:** плунка, антиоксиданси, пародонтопатија.

Introduction

Saliva as an oral cavity secrete, is produced by the large and small mucous glands and comes into direct contact with all oral structures[1]. It is made up of 99% water, and the rest is made up of organic and inorganic substances. The biochemical composition of saliva enables numerous functions in the oral environment[2]. Saliva plays the most important role in maintaining oral homeostasis, self-cleansing of the mouth from leftover food particles, maintaining physiological pH values, maintaining the integrity of hard and soft tissues, and providing specific and non-specific antimicrobial and antioxidant protection. Saliva, with its multifunctional role in the oral cavity, is an important component of oral health maintenance[3].

Antioxidants play an important role in protecting oral tissues from the harmful effects of free radicals[4].

The history of free radicals began when McCordKelle and Fridovich discovered the enzyme superoxide dismutase, which catalyzes the decomposition of the superoxide anion created by the uniform reduction of oxygen[5].

Free radicals are highly reactive transient chemicals (atoms, ions, or molecules) with one or more electrons in their structure[6]. Once created, a free radical can cause a series of chain reactions and then react with less reactive molecules. This chain reaction is interrupted by the action of non-enzymatic antioxidants and enzyme mechanisms[7].

The most well-known are the free radicals of the oxygen-superoxide anion O^2; perhydroxy anion - HOO; hydrogen peroxide - H_2O_2; hydroxyl radical – OH, and so on.

Increased production of these radicals may be associated with increased activity of inflammatory cells and polymorphonuclear leukocytes present in the gingival epithelium in aggressive and chronic forms of periodontitis[8].

In recent years, in the pathogenesis of many inflammatory diseases, including chronic periodontitis, free radicals and antioxidants have received special attention. Numerous studies have been conducted to examine free radicals and antioxidants in serum and gingival tissue. In the examination of our material, an increase in the value of free radicals in serum and gingival tissue was observed with the progression of the clinical stage of periodontitis in non-smokers. In the second and third clinical stages of chronic periodontitis, patients with antioxidant stress have lower antioxidant levels[9].

In recent decades, analysis of the biochemical composition of saliva has been used as an additional diagnostic test. Numerous biochemical parameters of pathological processes in the oral cavity can be determined in the saliva.

Aim of the study

The aim of this study is to highlight the role of antioxidants in saliva in the protection of oral tissues.

Material and methods

Data from published scientific and scientific-professional journals and books were used to achieve the aim of this study, Electronic journal data from the ISSN database was also used. This paper examines foreign and domestic journals and books from 1992 to 2021.

All data is displayed according to the set goal.

We explained the obtained data for using the analysis of the biochemical composition of saliva as an additional diagnostic test that can demonstrate a number of biochemical parameters of pathological processes in the oral cavity. The topic of research in a number of studies is the analysis of the total antioxidant capacity in saliva and its significance for the occurrence of oral diseases. Studies have highlighted the link between salivary antioxidants and chronic periodontal disease.

Results and discussion

Antioxidants and saliva (Biochemical properties of antioxidants in saliva)

During the course of growth and development of the human body, a specific defense system, namely an antioxidant system, is established to protect the body from the harmful effects of free radicals. There is a balance between ROC (reactive oxygen compounds) and antioxidants in physiological states. Oxidative stress occurs only when the antioxidant defense system cannot neutralize the increased ROC production. According to the mode of action, antioxidants are divided into two groups: enzymatic and non-enzymatic antioxidants.

Superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), oral peroxidase (OP) are among the first group od enzyme antioxidants. Non-enzymatic antioxidants in the second group include ascorbic acid (Vitamin C), retinol (Vitamin A), alpha-tocopherol (Vitamin E), uric acid, glutathione reductase, polyphenols and albumin.

Superoxide dismutase (SOD) is an enzyme that catalyzes the dismutation of the superoxide anion into hydrogen peroxide and oxygen.

There are more isoform forms of superoxide dismutase in humans. Copper, zinc and manganese-dependent extra cellular superoxide dismutase are the three forms.

Studies have shown increased SOD activity in saliva in patients with recurrent aphthous stomatitis relative to the control group. The authors believe that the increased activity of this antioxidant enzyme is a host adaptation mechanism as a result of the increased production of free radicals by the defense cells[10,11].

Oral peroxidase (OP) is a salivary enzyme that contains two peroxidase enzymes, salivary peroxidase (80%) and myeloperoxidase (20%).

Salivary peroxidase (SP) is mostly secreted by the parotid salivary glands. This enzyme contains selenium in its composition. The most important function of salivary peroxidase is to reduce hydrogen peroxide in the presence of thiocyanate ions. These ions are produced by tobacco smoke during liver detoxification, and are then transported through the blood to the salivary glands and reach the saliva by ultrafiltration. SP catalyzes the reaction of hydrogen peroxide and thiocyanate ions. Hypothiocyanate acid and hypothiocyanate ions are obtained as a result of this reaction,. Thus, this enzyme participates in the non-specific antibacterial protection and in the efficient removal of hydrogen peroxide from the oral environment[12].

In some studies, the activity of SP in cigarette smokers has been studied in terms of the occurrence of oral cancer. Cigarette smoking is one of the risk factors for developing this malignant disease. In smokers, SP activity is significantly reduced. Incomplete elimination of hydrogen peroxide occurs, and in reaction with other free radicals, more reactive radicals are formed, causing oxidative damage to biomolecules and this leads to malignant transformation and the appearance of oral cancer[13].

Myeloperoxidase (MPO) is a HEM-dependent enzyme found in neutrophil leukocytes and monocytes. In the presence of hydrogen peroxide, a complex is formed that has the ability to oxidize iodides and chlorides, creating toxic products. The chlorine ion is distributed in biological systems and its oxidation produces hypochlorous acid. This acid has oxidative properties, resulting in active forms of oxygen that participate in the breakdown of toxins, inflammatory regulators and other compounds[11].

In some studies, some authors have noted increased MPO activity in saliva during inflammatory processes in the oral cavity[11].

Among the enzymatic antioxidants found in saliva is catalase, which is a tetramer in structure and contains HEM in each subunit. This enzyme inhibits the formation of more hydrogen peroxide and catalyzes its breakdown into water and molecular oxygen[14].

Uric acid (acidum uricum) is the most important non-enzymatic antioxidant followed by albumin, and other non-enzymatic antioxidants that are found in small concentrations in saliva.

Uric acid is the end product of purine nucleotide metabolism. It is found in higher concentrations in the blood plasma, because it is not degraded due to a lack of the enzyme uricase. It is present in saliva in lower concentrations as uric acid salts (urates) and enters[4] through passive diffusion from the circulation. In patients with oral cancer who smoke, a reduced concentration of uric acid is observed compared to the control group, as a result of its consumption, because it participates in the neutralization of the increased concentration of free radicals[15].

Albumins are plasma proteins that are synthesized in the liver. In addition to participating in antioxidant protection, they also play a role in regulating blood pH, transporting various substances and arriving in saliva from the blood by ultrafiltration[16].

Glutathione reductase is a tetrapeptide and consists of glutamic acid, cysteine and glycine. It facilitates the activity of the antioxidant enzyme - glutathione peroxidase[16.]

The effects of the antioxidant system depend on the intake of vitamins and micronutrients through diet, as well as the synthesis of antioxidant enzymes, which can be influenced by physical activity, nutrition, and genetic predisposition[17,18].

Antioxidants in saliva and periodontitis

A number of studies have been conducted to examine the total antioxidant capacity in saliva and its significance in the occurrence of oral diseases.

Studies have been performed with meta-analysis of antioxidants in saliva in patients with oral lichen planus (OLP), which is a type of premalignant disease. The authors noted a reduced antioxidant capacity compared to the control group[19].

Many studies have examined the association between antioxidants in saliva and periodontal disease.

Many authors compare antioxidant levels in saliva in patients with chronic periodontitis and individuals with clinically healthy periodontitis[20]. Other studies have determined the level of antioxidants in saliva in patients with chronic periodontitis before and after causal therapy[21].

Canacki et al.[22] in their study on 30 patients with chronic periodontitis and 30 individuals in the control group, obtained results indicating lower levels of superoxide dismutase (SOD) and glutathione peroxidase (GPx) in saliva. Other authors conducted studies with the same number of patients with chronic periodontitis and control group, and found lower activity of the enzyme antioxidants SOD, GPx and catalase (CAT) in saliva, which is negatively correlated with the clinical parameters of periodontitis[23]. Other studies have found a significant negative correlation between the antioxidant enzymes SOD, CAT and glutathione reductase activity and periodontal parameters in patients with periodontal disease[24]. A group of authors[25] found lower values of GPx and the non-enzymatic antioxidant uric acid in patients with chronic periodontitis,. Uric acid activity in saliva is reduced in patients with periodontitis and has a negative correlation with bone resorption biomarkers such as collagen C-terminal telopeptide type 1 and matrix metalloproteinases 8 (MMP-8)[26].

In contrast, some authors[27] studied saliva in 43 patients with chronic periodontal disease who had received periodontal treatment. They received higher values for SOD, GPx, as well as for the albumins. Other studies found the opposite results for SOD after periodontal treatment compared to the previous authors but increased values for GPx, albumin and uric acid[28]. Other authors show increased concentration of antioxidants in saliva (uric acid, total antioxidant status, SOD and GPx) after causal therapy, as well as a positive correlation with clinical parameters of the periodontal condition (gingival index, plaque index and gingival bleeding)[29].

A number of studies[30] have examined the correlation between GPx activity in gingival fluid and clinical signs of the periodontal tissue (gingival index, plaque index, bleeding index, periodontal pocket depth, and loss of epithelial attachment) in patients and individuals with a clinically healthy periodontium. A positive correlation was found between GPx and the noted clinical parameters, as well as higher GPx activity in the gingival fluid relative to saliva.

The SOD activity was reduced following periodontal treatment. Bacterial polysaccharides stimulate the release of oxygen from fibroblasts during inflammation. Increased oxygen release may lead to increased SOD activity in order to balance oxidative stress with antioxidant protection. Increased SOD activity allows for increased activity of GPx, which removes hydrogen peroxide. Following the analyses, a progressive reduction of the SOD activity was observed with the increase of the depth of the periodontal pockets.

The differences in the results obtained for the enzyme antioxidants in saliva presented in the studies are due to how the mixed unstimulated saliva is collected and stored.

The SOD and CAT activity has also been determined in gingival tissue in patients with periodontal disease, and their reduced activity has been observed with increasing depth of periodontal pockets[31].

A group of authors suggests that non-enzyme antioxidants in saliva such as vitamin C, vitamin E, and glutathione reductase have decreased activity in patients with periodontitis, whereas enzyme antioxidants such as SOD and GPx have increased activity[32].

The opposite results between periodontal status and antioxidant protection have been obtained from the conducted researches. Some studies performed with meta-analyzes have obtained results for SOD levels that indicate insignificant differences between patients with periodontitis and the control group[33]. Studies of non-enzymatic antioxidants in saliva have shown a greater association between clinical parameters of periodontitis and decreased activity of non-enzymatic antioxidants.

Conclusion

The significance of these studies is that they indicate that saliva can be used as a valid diagnostic medium. Saliva is in constant and direct contact with the tissues in the oral environment and thus can follow physiological conditions, pathological changes and changes at the cellular molecular level. Non-invasive determination of antioxidants in saliva allows for analysis of the achieved results and the generation of useful recommendations for development and monitoring of new treatment strategies, as well as the possibility of preventing many pathological conditions and preventing inflammatory diseases in the oral cavity.

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