Review Article

PROSPECTS FOR THE USE OF SELENIUM-CONTAINING DRUGS IN DENTISTRY

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ABSTRACT

Periodontal diseases became widespread in the XX—XXI centuries. Almost 95% of the world's population is over 35 years old and 80% of children suffer from periodontal diseases of varying severity, while inflammatory periodontal diseases occur in 90-95% of cases. Periodontitis is a disease that causes damage to periodontal tissues, including gums, cement, and alveolar bone. This can be caused by various factors, including a violation of oral hygiene, smoking, genetic factors, and other causes. To date, scientists are trying to develop new methods and tools to effectively combat periodontitis. One of the innovative directions that make it possible to create an effective drug is the inclusion of selenium in the composition of drugs. Selenium is one of the trace elements necessary for the normal functioning of the human body. In recent years, it has been discovered that selenium plays an important role in dentistry: it is antioxidant properties, antimicrobial and anti-inflammatory properties open up new possibilities for use in dental practice. Nevertheless, both excess and lack of selenium can be extremely dangerous for the human body. This review article discusses the prospects for the use of selenium in dentistry, in particular in the treatment of periodontitis. In addition, the consequences of incorrect selenium dosages for the human body are described in detail.

Key words: Dentistry, Periodontitis, Selenium, Caries.

Introduction

Selenium is a trace element that was first described in 1817 by the Swedish chemist John Berzelius. In 1957, it was found that the addition of selenium to food prevented the development of muscular dystrophy and liver cirrhosis in rats [1]. In subsequent years, it was revealed that selenium is an important element of the enzyme glutathione peroxidase [2], after which the study of the effect of selenium deficiency on human health and the possibility of its use in medical practice began. Its role in the work of the immune, endocrine and reproductive systems, metabolism, cellular homeostasis, and carcinogenesis was revealed [3].

The main source of selenium for humans is food, therefore, the selenium content in the body is determined by a person's dietary preferences. The selenium content in plants varies significantly. It depends not only on the place of growth but also on the ability of plants to capture selenium from the soil and accumulate it. In general, the selenium content is higher in vegetables compared to fruits [4]. According to various studies, the main source of selenium for humans is meat products, fish, bread, and cereals [5, 6].

In nature, selenium exists in the form of organic (selenomethionine and selenocysteine) and inorganic compounds (selenite and selenate). Considering that organic forms are better absorbed in the gastrointestinal tract, some experts consider them the main ones for the prevention and treatment of diseases caused by selenium deficiency [7]. Selenomethionine is found in plants, mainly in cereals, and selenocysteine is mainly found in animal products.

For unknown reasons, the selenium content is lower in smokers and decreases with age. In addition, the selenium content is lower in people who consume a large amount of coffee and alcohol. Eating large amounts of rice and eggs is also associated with a reduced concentration of selenium in the body [8]. WHO recommends consuming 50-55 micrograms of selenium per day [9].

Both the lack of selenium and its excess are dangerous for humans. Manifestations of deficiency appear when using selenium less than 40 mcg/day, and excess – when using more than 400 µg / day [10]. Severe selenium deficiency leads to the development of Keshan's disease, manifested by heart failure due to cardiomyopathy, atrophy, degeneration, necrosis of articular cartilage, and fever [11]. In some studies, selenium deficiency was associated with an increased risk of cardiovascular disease, which decreased when the deficiency was replenished. Selenium has an anticarcinogenic effect on the prostate, liver, pancreas, and colon [12].

Some studies have shown that there is a U-shaped relationship between the concentration of selenium in the blood and the overall morbidity, i.e. the incidence is affected by both a lack and an excess of selenium [13]. Mortality from all causes also increases with a deficiency or excess of selenium.

General directions of selenium application in dentistry

Selenium is one of the trace elements necessary for the normal functioning of the human body. In recent years, it has been discovered that selenium is important in dentistry: its antioxidant properties, antimicrobial and anti-inflammatory properties open up new possibilities for use in dental practice.

Selenium is a key component of glutathione peroxidase, an enzyme that plays an important role in protecting organs from oxidative stress [14]. In dentistry, selenium can help prevent damage to the tissues of the oral cavity and teeth.

Studies show that selenium can reduce the level of free radicals in the tissues of the oral cavity, which can lead to a decrease in inflammatory processes and increase wound healing [15].

Selenium has antimicrobial properties, which makes it useful in the fight against oral infections [16]. It can help in the fight against bacteria, viruses, and fungi that cause various dental problems, such as caries, periodontitis, and stomatitis.

Selenium is also able to enhance the effect of antibiotics, which can be useful in the treatment of oral infections.

Inflammation is a common problem in dentistry, and selenium can help reduce inflammation in the oral cavity. It can reduce swelling and pain associated with gum disease and other inflammatory conditions.

Periodontitis as a serious problem in modern dentistry

Periodontitis is a disease that leads to damage to periodontal tissues, including gums, cement, and alveolar bone [17]. This type of disease is one of the most common dental diseases.

Periodontitis begins with gum disease, which becomes inflamed and red. This can lead to pockets between the gum and the tooth that allow bacteria to penetrate deeper and attack additional periodontal tissues **(Figure 1)**. As a result, the destruction of cement and alveolar bone may occur, which can lead to tooth loss [18]. The main characteristics of this disease are presented in **Table 1**.

Periodontitis develops when bacteria form plaque on the teeth and in the area around them. Plaque contains microbes that can cause inflammation in the gums and bones supporting the teeth.

Table 1. General characteristics of periodontitis

Causes and risk areas of the disease	Symptoms and signs of the disease
Smoking and tobacco use;	Bleeding gums during brushing or chewing;
Stress and fatigue;	Detachment of the gums from the teeth;
Genetic predisposition to gum disease;	An increase in the notches on the surface of the teeth when the gum moves away from them;
Poor nutrition and lack of vitamins;	Calcareous deposits on teeth;
Other diseases such as diabetes, cardiovascular diseases, and diseases of the immune system.	Periodic pain in the teeth and gums.

Periodontal diseases became widespread in the XX—XXI centuries. Almost 95% of the world's population is over 35 years old and 80% of children have periodontal diseases of varying severity, while inflammatory periodontal diseases occur in 90-95% of cases [19].

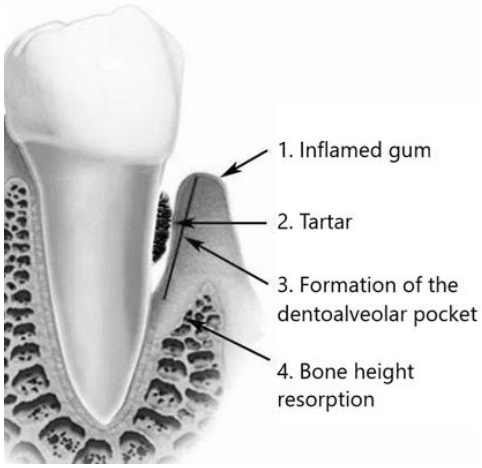

Figure 1. The principle of the occurrence of periodontitis

The pathogenesis of periodontitis is a research area of interest for many authors. Some authors assign an important role in the formation of periodontal diseases to the microbiological factor. The entire XX century was devoted to the study of the influence of microorganisms on the progression of periodontal diseases [20]. At the same time, inflammatory mediators, such as, for example, prostaglandins and interleukins, and together with their enzymes, metalloproteinase matrix, were identified and recognized as important participants in the destruction of periodontal tissues [21]. The discovery of antibiotics made it

possible to control periodontal diseases by affecting the inflammatory process.

This concept was questioned already in 1982, when researchers, based on the results of their work, stated that a severe form of periodontitis was detected only in 8% of 600 patients in the age range from 40 to 70 years [22]. This discovery led to a new era of understanding the epidemiology of periodontal diseases. In 1983, several other scientific papers were carried out, which confirmed the fact that periodontal diseases do not necessarily proceed at a constant rate if left without therapeutic correction, which contradicts the concept of their bacterial nature.

Scientific knowledge of modern dentistry pays more and more attention to the peroxide oxidation of lipids in the oral cavity. Damage to cellular and subcellular membranes in chronic periodontitis is becoming an increasingly urgent problem in modern dentistry.

The processes of lipid peroxidation are accelerated in inflammatory diseases, immunological damage to cell membranes, exposure to various stress factors, carcinogenesis, lack of vitamins and some trace elements, radiation sickness, and aging [23]. It is known that protein synthesis is disrupted by the products of free radical processes, respectively, protein synthesis of the alveolar bone is disrupted. According to several authors, the importance of free radicals synthesized during the vital activity of macrophages is especially great at the early stages of periodontal tissue damage [24]. In other studies, it was shown that under the influence of emotional and painful stress in the soft tissues of the periodontal period in rats, activation of lipid peroxidation was noted at the very beginning of the process [25]. In tissue sections, loosening of the epithelium, edema, expansion of the gum base, and resorption of the alveolar process were observed.

The intensity of free radical processes is regulated by the action of antioxidants, which allows the use of various antioxidants for the treatment of chronic periodontitis in patients [26].

It is known that to neutralize the development of destructive effects of reactive oxygen species in a living organism, there is a special antioxidant defense, the key component of which is selenium-dependent glutathione peroxidase, a homotetrameric selenoprotein, which is the first barrier to cell protection and the formation of which requires selenium [27]. Modern scientists have derived a whole group of plasma glutathione peroxidases, for which a detailed characteristic has been created [28]. In the physiology of oxidant stress, nitrite hydroperoxide, released during the activity of endothelial cells, macrophages, and neutrophils, is of great importance [29]. The powerful oxidizing abilities of this ion determine its leading place in the formation of inflammatory processes as an inducer of toxicity, while protection from the action of this compound is formed due to the activity of selenium-dependent glutathione peroxidase, which reduces peroxide to a nitrite ion [30]. In addition, antioxidant protection, in addition to an important link in the process of neutralizing free radicals, is directly involved in the formation of various metabolic processes.

Prospects for the use of selenium in the treatment of periodontitis

In modern sources of literature, more and more attention is paid to compounds with antioxidant properties, an important place among which is selenium, as an integral part of selenium-dependent glutathione peroxidases and thioredoxin reductases. In 2005, the therapeutic dental toothpaste "Anthoxide" was developed and patented in Russia, which is a gel toothpaste containing zinc chloride, cobalt nitrate, copper sulfate, and selenium sulfate, i.e. the paste contains the main structural trace elements of enzyme antioxidants.

Of particular interest is selenium as an element of the synthesis of glutathione peroxidase. Additional administration of selenium may be recommended to optimize the tissue activity of glutathione peroxidase in the thyroid gland, to prevent the possible development of oxidative stress [31].

There is a population deficit of many trace elements and vitamins in a significant territory of Russia [32]. A deficiency of iodine, selenium, and cobalt compounds during pregnancy is a trigger factor that provokes the birth of a small child. The combined deficiency of iodine and selenium was established during the physiological course of pregnancy in a larger number of mothers [33]. Thus, many studies confirm that selenium deficiency poses a threat not only to the development of periodontal diseases but also to the formation of various somatic pathologies [34], which makes it relevant to further study the effects of selenium deficiency on the human body.

In the Russian Federation, in the treatment of inflammatory diseases of periodontal tissues, inorganic selenium-containing drugs are used in large quantities as part of multivitamins, as well as in the form of biologically active additives.

Studies have proven that selenium normalizes the balance of antioxidant protection and promotes recovery in the pathological focus [35]. It has been established that reparative processes in the bone tissue of the mandible occur against the background of microcirculation disorders, tissue hypoxia phenomena, as well as activation of oxidative stress occurring in an infected bone wound against the background of a pronounced deficit of bone tissue restoration [36]. Against the background of selenium deficiency in patients with mandibular fractures, inhibition of antiradical protection and accumulation of lipid peroxidation products were noted, thereby slowing down the recovery process in the fracture zone [37]. The results obtained during the study

confirm the presence of an imbalance in the "lipid peroxidation — antioxidant protection" system in patients with mandibular fractures [38]. When examining the blood, they revealed selenium deficiency against the background of its increased excretion in urine and saliva. Under the action of routine methods of therapy, blood parameters do not have dynamics to full normalization [39]. The introduction of a medicinal selenium-containing drug into complex therapy contributed to the normalization of selenium levels, as well as to the elimination of an imbalance in the parameters of the antioxidant system in biological fluids, which also significantly affected the positive prognosis in treatment.

However, it should be borne in mind that several studies indicate the toxicity of inorganic selenium preparations. Morphological examination of the bones of the lower jaws was carried out on laboratory white male rats under the condition of acute intoxication with sodium selenite. It has been proven that hypertrophic processes in bone tissue are activated during acute intoxication with sodium selenite [40].

It should be noted that inorganic selenium compounds have a low minimum threshold of toxicity due to the limited possibilities of neutralizing their leading toxic metabolite — hydrogen selenium.

The toxicity of organic selenium is significantly lower than that of inorganic selenium, which means there is less risk of possible overdose. In addition, the bioavailability of organic selenium in the body is usually much higher than that of inorganic selenium. That is why, as a result of research, it was proved that the organic form of selenium is preferable when supplying the body with a trace element for preventive purposes [5].

It is important to understand that in the natural environment, selenium enters the human and animal bodies primarily in the form of selenium-containing amino acids - selenomethionine (Se-Met) and selenocysteine (Se-Cys). The intake of selenium artificially with its alimentary deficiency into the body is carried out in the form of selenite or sodium selenate. At the same time, selenate and selenite anions that come from food can be rapidly restored under the action of the protein thioredoxin to hydrogen selenium, which is present at physiological pH values mainly in the form of hydroselenide anion. Only a certain amount of selenium, which is part of hydrogen selenium, is included in the highly specific process of synthesis of selenoproteins, including components of vital antioxidant systems. If an excessive amount of inorganic selenium enters the body, it can accumulate in tissues in the form of a free hydroselenide anion, which is extremely dangerous and toxic.

Conclusion

Selenium is one of the trace elements necessary for the normal functioning of the human body. In recent years, it has been discovered that selenium is important in dentistry. Studies show that selenium can reduce the level of free radicals in the tissues of the oral cavity, which can lead to a decrease in inflammatory processes and increase wound healing. Selenium is also able to enhance the effect of antibiotics, which can be useful in the treatment of oral infections. It can reduce swelling and pain associated with gum disease and other inflammatory conditions.

Thus, selenium is an important element in the structure of antioxidant protection in the body. In periodontal diseases, the use of selenium preparations reduces the effect of lipid peroxidation, which leads to accelerated recovery of periodontal tissues and improves the prognosis in patients.

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References

1. Hawkes WC, Wilhelmsen EC, Tappel AL. Abundance and tissue distribution of selenocysteine-containing proteins in the rat. J Inorg Biochem. 1985;23(2):77-92. doi:10.1016/0162-0134(85)83011-7
2. Nagdalian AA, Blinov AV, Siddiqui SA. Effect of selenium nanoparticles on biological and morphofunctional parameters of barley seeds (Hordéum vulgáre L.). Sci Rep. 2023;13(1):6453. doi:10.1038/s41598-023-33581-6
3. Minich WB. Selenium Metabolism and Biosynthesis of Selenoproteins in the Human Body. Biochemistry (Mosc). 2022;87(Suppl 1):S168-S02. doi:10.1134/S0006297922140139
4. Hu J, Wang Z, Zhang L, Peng J, Huang T, Yang X, et al. Seleno-Amino Acids in Vegetables: A Review of Their Forms and Metabolism. Front Plant Sci. 2022;13:804368. doi:10.3389/fpls.2022.804368
5. Xie M, Sun X, Li P, Shen X, Fang Y. Selenium in cereals: Insight into species of the element from total amount. Compr Rev Food Sci Food Saf. 2021;20(3):2914-40. doi:10.1111/1541-4337.12748
6. Kiani AK, Dhuli K, Donato K, Aquilanti B, Velluti V, Matera G, et al. Main nutritional deficiencies. J Prev Med Hyg. 2022;63(2 Suppl 3):E93-E101. doi:10.15167/2421-4248/jpmh2022.63.2S3.2752
7. Kieliszek M. Selenium–Fascinating Microelement, Properties and Sources in Food. Molecules. 2019;24(7):1298. doi:10.3390/molecules24071298
8. Blinov AV, Nagdalian AA, Siddiqui SA. Synthesis and characterization of selenium nanoparticles

stabilized with Cocamidopropyl betaine. Sci Rep 2020;12:21975. doi:10.1038/s41598-022-25884-x
9. Khanam A, Platel K. Bioaccessibility of selenium, selenomethionine, and selenocysteine from foods and influence of heat processing on the same. Food Chem. 2016;194:1293-9. doi:10.1016/j.foodchem.2015.09.005
10. Takata N, Myburgh J, Botha A, Nomngongo PN. The importance and status of the micronutrient selenium in South Africa: a review. Environ Geochem Health. 2022;44(11):3703-23. doi:10.1007/s10653-021-01126-3
11. Bachinina KN, Povetkin SN, Simonov AN, Pushkin SV, Blinova AA, Sukhanova ED. Effects of Selenium Preparation on Morphological and Biochemical Parameters of Quail Meat. Int Trans J Eng Manag Appl Sci Technol. 2021;12(13):1-7. doi:10.14456/ITJEMAST.2021.263
12. Steinbrenner H, Duntas LH, Rayman MP. The role of selenium in type-2 diabetes mellitus and its metabolic comorbidities. Redox Biol. 2022;50:102236. doi:10.1016/j.redox.2022.102236
13. Qiu Z, Geng T, Wan Z, Lu Q, Guo J, Liu L, et al. Serum selenium concentrations and risk of all-cause and heart disease mortality among individuals with type 2 diabetes. Am J Clin Nutr. 2022;115(1):53-60. doi:10.1093/ajcn/nqab241
14. Kiełczykowska M, Kocot J, Paździor M, Musik I. Selenium - a fascinating antioxidant of protective properties. Adv Clin Exp Med. 2018;27(2):245-55. doi:10.17219/acem/67222
15. Cai Z, Zhang J, Li H. Selenium, aging and aging-related diseases. Aging Clin Exp Res. 2019;31(8):1035-47. doi:10.1007/s40520-018-1086-7
16. Hou J, Tamura Y, Lu HY, Takahashi Y, Kasugai S, Nakata H, et al. An In Vitro Evaluation of Selenium Nanoparticles on Osteoblastic Differentiation and Antimicrobial Properties against Porphyromonas gingivalis. Nanomaterials (Basel). 2022;12(11):1850. doi:10.3390/nano12111850
17. Tonetti MS, Greenwell H, Kornman KS. Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. J Periodontol. 2018;89 Suppl 1:S159-S72. doi:10.1002/JPER.18-0006
18. Kinane DF, Stathopoulou PG, Papapanou PN. Periodontal diseases. Nat Rev Dis Primers. 2017;3:17038. doi:10.1038/nrdp.2017.38
19. Darby I. Risk factors for periodontitis & peri-implantitis. Periodontol 2000. 2022;90(1):9-12. doi:10.1111/prd.12447
20. Shi B, Chang M, Martin J, Mitreva M, Lux R, Klokkevold P, et al. Dynamic changes in the subgingival microbiome and their potential for diagnosis and prognosis of periodontitis. mBio. 2015;6(1):e01926-14. doi:10.1128/mBio.01926-14
21. Gemmell E, Marshall RI, Seymour GJ. Cytokines and prostaglandins in immune homeostasis and tissue destruction in periodontal disease. Periodontol 2000. 1997;14:112-43. doi:10.1111/j.1600-0757.1997.tb00194.x
22. Williams RC. Understanding and managing periodontal diseases: a notable past, a promising future. J Periodontol. 2008;79(8 Suppl):1552-9. doi:10.1902/jop.2008.080182
23. Veljovic T, Djuric M, Mirnic J, Gusic I, Maletin A, Ramic B, et al. Lipid Peroxidation Levels in Saliva and Plasma of Patients Suffering from Periodontitis. J Clin Med. 2022;11(13):3617. doi:10.3390/jcm11133617
24. Battino M, Bullon P, Wilson M, Newman H. Oxidative injury and inflammatory periodontal diseases: the challenge of anti-oxidants to free radicals and reactive oxygen species. Crit Rev Oral Biol Med. 1999;10(4):458-76. doi:10.1177/10454411990100040301
25. Ma F, Luo S, Lu C, Jiang X, Chen K, Deng J, et al. The role of Nrf2 in periodontal disease by regulating lipid peroxidation, inflammation, and apoptosis. Front Endocrinol (Lausanne). 2022;13:963451. doi:10.3389/fendo.2022.963451
26. Sczepanik FSC, Grossi ML, Casati M, Goldberg M, Glogauer M, Fine N, et al. Periodontitis is an inflammatory disease of oxidative stress: We should treat it that way. Periodontol 2000. 2020;84(1):45-68. doi:10.1111/prd.12342
27. Bhagat S, Singh P, Parihar AS, Kaur G, Takkar H, Rela R. Assessment of Levels of Plasma Oxidative Stress in Patient Having Aggressive Periodontitis before and after Full Mouth Disinfection. J Pharm Bioallied Sci. 2021;13(Suppl 1):S432-S5. doi:10.4103/jpbs.JPBS_599_20
28. Patel SP, Rao NS, Pradeep AR. Effect of nonsurgical periodontal therapy on crevicular fluid and serum glutathione peroxidase levels. Dis Markers. 2012;32(1):1-7. doi:10.3233/DMA-2012-0855
29. Titov VY, Petrenko YM. Nitrite-catalase interaction as an important element of nitrite toxicity. Biochemistry (Mosc). 2003;68(6):627-33. doi:10.1023/a:1024609624652
30. Takahashi K, Cohen HJ. Selenium-dependent glutathione peroxidase protein and activity: immunological investigations on cellular and plasma enzymes. Blood. 1986;68(3):640-5.
31. Silvestrini A, Mordente A, Martino G, Bruno C, Vergani E, Meucci E, et al. The Role of Selenium in Oxidative Stress and in Nonthyroidal Illness Syndrome (NTIS): An Overview. Curr Med Chem. 2020;27(3):423-49. doi:10.2174/0929867325666180201111159
32. Kolmykova LI, Korobova EM, Baranchukov VS, Kurnosova IV, Silenok AV, Makarova EM. Chemical composition of groundwater used for drinking in conditions of natural deficiency of iodine and selenium and evaluation of its health effect: the case of Bryansk region (Russia). Environ Geochem Health.

2021;43(12):4987-5009. doi:10.1007/s10653-021-01022-w
33. Schomburg L. Selenium Deficiency Due to Diet, Pregnancy, Severe Illness, or COVID-19-A Preventable Trigger for Autoimmune Disease. Int J Mol Sci. 2021;22(16):8532. doi:10.3390/ijms22168532
34. Farias PM, Marcelino G, Santana LF, de Almeida EB, Guimarães RCA, Pott A, et al. Minerals in Pregnancy and Their Impact on Child Growth and Development. Molecules. 2020;25(23):5630. doi:10.3390/molecules25235630
35. Huang S, Jin M, Su N, Chen L. New insights on the reparative cells in bone regeneration and repair. Biol Rev Camb Philos Soc. 2021;96(2):357-75. doi:10.1111/brv.12659
36. Anthonymuthu TS, Kenny EM, Bayır H. Therapies targeting lipid peroxidation in traumatic brain injury. Brain Res. 2016;1640(Pt A):57-76. doi:10.1016/j.brainres.2016.02.006
37. Sadeghi M, Rahimi M, Poornoroz N, Jahromi FF. Patient satisfaction with hospital services after the implementation of the health system. Arch Pharm Pract. 2021;12(1):31-6.
38. Lampasona M, Pantaleo L. The role of pharmacies in immunization programs and health promotion. Arch Pharm Pract. 2022;13(2):62-5.
39. Florina MG, Mariana G, Csaba N, Gratiela VL. The Interdependence between diet, microbiome, and human body health-a systemic review. Pharmacophore. 2022;13(2):1-6.
40. Alzain HM, AlJabr IA, Al AK, Jaafari HA, AlSubaie AS, Hussein KM. The Impact Of Industrial And Community Noise Nuisance On Global Health And Economies. Pharmacophore. 2021;12(3):64-7.