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The role of magnesium in the prevention and treatment of dental caries — the latest research

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Abstract: Magnesium is one of the bioelements necessary for proper human functioning. It is classified as a macronutrient. Together with calcium and phosphorus, it is the main building component of teeth. It has antibacterial properties, as consequence of which it can impede the formation of biofilm and thus reduce inflammation caused by bacterial toxins. Along with calcium, phosphorus and vitamins, magnesium helps maintain the health of the human body.

The scientific literature contains an increasing number of studies describing new methods for preventing caries resulting from interference with the oral microbiome. Modification of the microbiome and the use of prebiotics may prove to be groundbreaking. Magnesium may have the potential to function as a prebiotic because it promotes the colonization of commensal streptococci in the oral cavity. By changing the oral microbiome, it could play an important role in dental caries prevention.

Nanotechnology is a new concept of material production that has emerged both in dentistry and other fields. In view of the resistance of certain bacteria to antibiotics and other bactericidal agents, alternative dental materials with increased antibacterial properties are being sought by adding antibacterial nanoparticles (NPs) to their composition. One of the most commonly used metal oxides is magnesium oxide. Its antibacterial action involves disrupting the bacterial cell membrane. It seems that nanoparticles may be promising fillers for dental composites. However, due to the limited character of the clinical trials to date, there is a need for further experiments.

Keywords: magnesium, *Streptococcus mutans*, nanoparticles, microbiome, Mg-rich diet.

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Etiology of caries

According to FDI (World Dental Federation), dental caries is one of the most widespread diseases in the world today [1]. This infectious condition leads to the dissolution and demineralization of tooth structure [2]. The condition arises when there is a disturbance in the homeostasis of the oral microflora, which in turn results in a predominance of acid-forming bacteria in the microbiome [3], including *Streptococcus mutans, Streptococcus sobrinus* [4] and *Actinomyces viscosus* [5]. At the same time, people with oral caries and periodontal diseases have lower levels of commensal bacteria, such as *Streptococcus sanguinis* or *Streptococcus gordoni* [6]. Such a change in the balance in the oral cavity not only has local effects, but may also impact the general health of the patient [7]. Socio-economic, genetic and environmental factors such as pH, buffer capacity, saliva composition and an individual's diet also contribute to dental caries. A shift in the balance in a person's biofilm in favour of acidogenic bacteria causes demineralization of the tooth tissue. Therefore, caries prevention requires inhibiting the growth of biofilm [2].

Magnesium is a necessary bioelement for ensuring the proper functioning of the body [8]. It is classified as a macroelement that is essential for human life through its participation in biological processes, such as enzymatic catalysis or hormone production [9]. Together with calcium, this element helps maintain the proper density of bones and teeth [10]. Approximately half of all magnesium in the human body is located in the bones, and slightly less in the muscles [8]. Thanks to its antibacterial activity, magnesium can impair the formation of biofilm and thus reduce inflammation caused by bacterial toxins [11]. Together with calcium and phosphorus, it is the main building component of teeth. An insufficient quantity of these elements may, in extreme cases, even result in tooth loss [12]. Magnesium deficiency, which occurs during tooth formation, may delay tooth eruption as well as lead to hypoplasia of enamel and dentin [12].

Therapeutic/preventive methods using Mg^{2+} ions

One emerging trend in the literature has been the search for new methods of preventing dental caries caused by interference in the oral microbiome involving modification of the latter and the use of prebiotics [6]. Experimental research by Cheng *et al.* from 2020 confirmed that one potential prebiotic is Mg^{2+}. This is because it promotes the colonization of commensal streptococci in the oral cavity, which are capable of producing hydrogen peroxide with the participation of pyruvate oxidase. This compound inhibits growth of *Streptococcus mutans*, a pathogen closely associated with the development of dental caries [6]. In this way, magnesium could positively alter the ecology of the oral microbiome, thereby contributing to the prevention of dental caries. The authors of the publication also refer to previous studies showing that rinsing the mouth with a mouthwash containing a magnesium content similar to the one used in their research reduced the formation of dental plaque [6].

In 2020, Steiger *et al.* studied the ability of divalent cations (magnesium, zinc, calcium) to modify the *Streptococcus mutans* biofilm on tooth surfaces. The researchers were also interested in the possibility of combining the tested cations with cariogenic exopolysaccharides (EPS). It should be emphasized that the majority of the plaque biofilm is made up of a matrix with extracellular polysaccharides (EPS). The researchers concluded that zinc inhibited bacterial adhesion and had an antibacterial effect. However, in an environment saturated with magnesium, the bacteria were able to dissolve far more Ca^{2+} cations, which resulted in the binding of calcium in the plaque. Due to

the deficiency of the calcium levels necessary for remineralization, the disease progressed. Hence, in a magnesium-saturated environment, an effect different from the one desired was achieved [2].

Due to the observed tendency of magnesium levels to decline in teeth as patients age, this element is used as an ingredient in teeth cleansing agents, with the aim of protecting teeth against external acids and providing additional strengthening [2].

In order to prevent white spot lesions (WSL), Lale *et al.* (2020) used a gel with medical minerals in their in vitro studies which, in addition to bioavailable calcium and phosphates, included magnesium. The research results were promising because the compounds contained in the gel had a longer demineralization inhibitory effect compared to fluoride varnish [13].

However, in 2022 Yilmaz *et al.* from conducted a study on children with WSL. They were offered a number of toothpastes intended to promote remineralization, including one toothpaste containing calcium glycerophosphate (CaGP), magnesium chloride ($MgCl_2$) and 12% xylitol (45 mg tube of children's toothpaste R.O.C.S., DRC Group, Moscow, Russia). The paste turned out to have the remineralizing properties needed for treating WSL [14].

Research by Degli Esposti, Ionescu *et al.* from 2020 confirmed the possibility of using magnesium as an ingredient in toothpastes with a remineralizing effect. The paste used in this experiment contained biomimetic hydroxyapatite HA doped with CO_3^{2-}, F^-, Mg^{2+} and Sr^{2+} ions [15].

The possible use of magnesium for remineralization purposes was also tested by Yavuz and Kargul in 2021 based on samples of human enamel featuring artificially created carious defects. The remineralizing substances used by the researchers also included one containing calcium glycerophosphate, magnesium chloride and xylitol. Greater remineralization was observed in the study sample in which this element was used compared to the control group. Unfortunately, despite this observation, the differences in the results were not statistically significant [16].

Application of nanotechnology methods

Nanotechnology is a new approach to material production that has been developed in, among other fields, medicine, including dentistry, as well as in agriculture [11]. Due to the resistance of certain strains of bacteria to antibiotics and other bactericidal agents, alternative bactericidal dental materials are being sought [4]. In the case of dentistry, nanotechnology is being applied in the production of dental materials with enhanced antibacterial properties achieved thanks to the addition of antibacterial nanoparticles to their composition. The main applications are inorganic, nanocrystalline metal oxides, such as zinc oxide, to which magnesium oxide is added to improve its antibacterial properties [11]. The antibacterial effect of magnesium oxide is based on the release of trace amounts of metal ions and, as a consequence, on the disruption of the bacterial cell membrane [17]. Magnesium oxide nanoparticles have also been used for bone regeneration and tumor inhibition. They appear to be promising fillers for dental composites. However due to limited clinical research, further research in this direction is needed [17] (Table 1). Moreover, in 2024 Khursheed *et al.* demonstrated the effectiveness of reducing microleakage by means of nanoparticles modified with ZnO and MgO [18].

In an experiment conducted in 2023 Tanveer *et al.* used composites with ZnO doped with Mg^{2+} ions on models of secondary caries in rats. Compared with composites without magnesium these materials were characterized by higher levels of antibacterial activity against such strains of bacteria as *Streptococcus mutans, Enterococcus faecalis* and the diabetic saliva microbiome, which contained a greater number of acid-forming bacteria, including streptococci and lactic acid bacilli.

Table 1. Examples of possible applications of nanotechnology in dentistry described in publications.

	Dental nanomaterial	Publication
1	glass ionomer cement with the addition of magnesium oxide nanoparticles	Noori *et al.* (2019) [4]
2	composite material based on resins enriched with magnesium oxide nanoparticles MgONPs	Wang *et al.* (2023) [19]
3	composite material with ZnO and magnesium ions	Tanveer *et al.* (2023) [11]
4	resin composite with nanoparticles of magnesium oxide (nMgO) and bioactive glass (BAG)	Tian *et al.* (2023) [20]
5	orthodontic composite with an admixture of hydroxyapatite, iron and magnesium nanoparticles (FeMgHAPn)	Nagesh *et al.* (2024) [21]
6	self-adhesive resin-based cement with the addition of zein-coated magnesium oxide nanoparticles (zMgO NPs)	Naguib *et al.* (2024) [22]
7	ZnO and MgO modified nanoparticles	Khursheed *et al.* (2024) [18]

These composites were safe with low magnesium concentrations, i.e. 1% and 2.5%. However, concentrations of 5% and higher turned out to be harmful to human cells. The materials used by the researchers also proved to be effective in preventing secondary caries in a rodent model in which diabetes was present. Zinc and magnesium cations released into the environment interact with the negatively charged bacterial cell membranes, thereby increasing their permeability. They then negatively affect the respiratory chain and cell division, which ultimately results in the death of the bacteria [11]. The results of the study appear so promising that this direction of research should be continued.

Another study with similarly interesting findings, was conducted Wang *et al.* in 2023, and involved observing the antibacterial properties of a composite material based on resins, and enriched with the addition of fillers, and antibacterial magnesium oxide nanoparticles (MgONPs). The researchers noted an improvement in the anti-biofilm properties of this material, but without any deterioration in its mechanical, physicochemical and biocompatibility properties. It should be pointed out, however, that this is still an experimental model and thus may require many more studies before its clinical application [19]. Nanomaterials could play an important role in the prevention and treatment of dental caries [4].

An *in vitro* study conducted by Noori *et al.* in 2019 looked at the possible application of a material formed by adding MgO nanoparticles to glass ionomer cement. The researchers pointed out the beneficial properties of this chemically synthesized magnesium oxide, including its antibacterial and antibiofilm effects [4]. MgO nanoparticles also have the ability to inhibit bacterial enzymes, and additionally increase their antibacterial effectiveness thanks to the alkaline pH [4].

The literature includes more and more studies claiming that fluoride therapy is not an entirely effective treatment WSL. As a consequence, researchers are looking for new materials with both antibacterial and antibiofilm properties as well as a remineralizing capability. For example, in 2024, Nagesh *et al.* reported an experiment aimed at assessing the properties of an orthodontic composite with admixtures of hydroxyapatite, Fe and Mg (FeMgHAPn) nanoparticles. The authors of the study also assessed whether this material had antibacterial properties in relation to such bacteria as *Streptococcus mutans*, *Streptococcus aureus* and *Escherichia coli*. They made use of the agar-well diffusion method. These tests confirmed the antibacterial properties of the

composite when applied against *Streptococcus mutans*, provided that the minimum concentration of MgNps is 1%. They concluded that the antibacterial properties of such material increase when there is an accompanying increase in the concentration of iron and magnesium ion nanoparticles [21]. The experiment is one example of an analysis of the possible application of dental materials featuring an admixture of FeMgHAPn nanoparticles in the prevention of dental caries [21].

However, we should also not overlook the concerns raised by some researchers regarding the use of nanoparticles, in particular the possible cell damage caused by the small size of such particles, as well as the risk of changes occurring in the mechanical properties of the composite resin. Therefore, not only are their biological safety and antibacterial activity important for the future use of nanoparticles, but so too are the mechanical properties of the material [5].

Tian *et al.* from 2023 demonstrated the effective antibacterial action of a resin composite with an admixture featuring a nanoparticle of magnesium oxide (nMgO), responsible for the antibacterial effect, and bioactive glass (BAG), acting as a remineralizing agent, when compared to a resin composite containing only one of these compounds, nMgO or BAG [20].

The bacteriostatic effect against *Streptococcus mutans* of experimentally created resin cement with the addition of magnesium oxide nanoparticles (MgONPs) has been confirmed by Wang *et al.* from 2023, but the need to conduct further research on this issue is emphasized [23].

In 2024, Naguib *et al.* conducted a study on self-adhesive resin cement with the addition of zein-coated magnesium oxide nanoparticles (zMgO NPs), which could potentially improve the adaptation of the cement. A material constructed in this way could help reduce both marginal leakage and the risk of secondary caries. The study analyzed resin posts cemented in extracted human teeth [22].

A diet rich in magnesium

To maintain good health, not only is the absorption of bioelements vitally important but so too is a properly composed diet, containing appropriate amounts of bioelements such as magnesium, which when combined with calcium, phosphorus and vitamins helps maintain the health of the human body [12]. Magnesium affects not only the metabolism and synthesis of parathyroid hormone (PTH), but also the metabolism of vitamin D. This is necessary, among other things, for the synthesis of 25 (OH)D and 1,25 $(OH)_2D$ [12]. The relationship between magnesium intake and vitamin D levels has been described by Deng *et al.* in 2013 [24].

The normal level of this bioelement in blood serum ranges from 0.8 to 1 mmol/L. However, the daily requirement depends on the patient's age. In the case of children it is between 30 and 240 mg, for women it is 310–360 mg, and for men 400–420 mg (Table 2). Some general diseases and factors, such as a poor diet with increased amounts of sugar and highly processed food, increase the body's demand for this bioelement [8].

Table 2. Daily magnesium requirement.

	Individual group	Range [mg]
1	Children	30–240 mg
2	Females	310–360 mg
3	Men	400–420 mg

Another factor that plays an important role in a human's diet is the composition of drinking water. If it contains calcium, magnesium and fluorine, it may have a remineralizing effect on dental tissue. A deficiency in bioelements in water may occur when reverse osmosis (RO) water purification systems are used. These feature special filters capable of removing 92–99% of all beneficial minerals, including magnesium [10]. In 2020, Almejrad *et al.* conducted a study analyzing the composition of 92 different bottled waters and concluded that most of those tested did not provide the necessary daily dose of minerals, including magnesium [25]. As a consequence, in order to prevent caries, the elemental composition of water consumed by humans needs to be controlled.

Despite a lack of clinical evidence, the literature recommends maintaining an appropriate ratio of calcium to magnesium in the diet, namely at the level of 2: 0 [12]. Thus, Ma *et al.* conducted a study in which children with early childhood caries (ECC) had higher dietary magnesium intake than healthy children [26]. The higher intake of magnesium might have disturbed the ionic balance of calcium and magnesium, and as a consequence resulted in the dissolution of hydroxyapatite and the release of calcium ions [26]. In turn, Madali *et al.* (2023) observed a relationship between magnesium deficiency and high values of the following indicators: DMFT (decayed, missing, and filled teeth) and the DMFS surfaces index (surfaces with caries, removed and filled surfaces) [27].

In 2020, Klitynska *et al.* conducted research on the content of macro- and microelements in hair, saliva, serum, as well as on the relationship between incidence of dental caries in children and their anxiety levels. In one of the studied groups, reduced levels of magnesium in the body correlated not only with high levels of anxiety, but also with a high incidence of dental caries [28].

Conclusions

Magnesium is the one of the bioelements, which together with calcium and phosphorus is the main building component of teeth. Thanks to its antibacterial properties it can affect the formation of biofilm. It can play an important role in the prevention and perhaps treatment of dental caries.

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