Journal of Steroid Biochemistry and Molecular Biology 200 (2020) 105636

Contents lists available at ScienceDirect

Journal of Steroid Biochemistry and Molecular Biology

journal homepage: www.elsevier.com/locate/jsbmb

Review

Oral manifestations of magnesium and vitamin D inadequacy

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ARTICLE INFO

Keywords:
Vitamin D
Sunlight
Magnesium
Phosphorus
Calcium
Oral diseases

ABSTRACT

Adequate nutrition is essential for maintaining good oral health. Minerals such as magnesium, calcium, and phosphorus found in the diet constitute the main structural components of the tooth. Their inadequacy leads to absorption impairment, increased bleeding tendency, bone resorption, looseness, and premature tooth loss. Inadequacy of those essential minerals is associated with delayed tooth eruption and with enamel or dentin hypoplasia. Taking calcium without magnesium results in soft dental enamel, which cannot resist the acids causing tooth decay. In addition to magnesium, calcium, and phosphorus, adequate vitamin D is needed to maintain optimal oral health. Vitamin D exerts anti-inflammatory effects and helps in calcium absorption and bone remodeling. Moreover, adequate vitamin D status could reduce formation of dental caries by delaying its onset and progression. Here we summarize the oral manifestations of vitamin D and magnesium inadequacy.

1. Introduction

The prevalence of dental caries and periodontal diseases is high in humans and is the leading cause of tooth loss. It is the second-highest-occurring disease throughout the world according to the 2016 Global Burden of Disease study [1]. Many studies have established the connection between diet and dental caries [2–4]. The lack of calcium and vitamins D, A, B, and C leads to hypomineralization, delayed eruption of the tooth, bleeding gums, disturbed alveolar bone patterns, angular cheilitis, and periodontal diseases [5]. Adequate nutrition is paramount for good dental health because food contains minerals that constitute the main structure of a tooth. Those minerals interact with vitamins in their role of strengthening the teeth. Calcium, magnesium, zinc, and vitamin D are interrelated. Apart from bone strengthening, those nutritional agents actively maintain good oral health by reducing enamel loss and decay and by promoting stronger jawbone [6]. The lack of enough magnesium, calcium, and phosphorus in the diet is usually associated with loose teeth and premature tooth loss. In magnesium deficiency, the alveolar bone is fragile, and the gum becomes hypertrophic [7]; when such deficiency occurs during tooth formation, dental eruption would be delayed, and enamel or dentin hypoplasia can occur [8,9].

2. Ratio of calcium to magnesium in relation to dental health

For optimal health benefits, the typical advice has been to maintain a dietary calcium-to-magnesium ratio of around 2.0 in humans [10,11]; however, there is a paucity of scientific data to substantiate that assertion. Findings from a case–control study on colorectal cancer indicated an optimal dietary calcium-to-magnesium ratio of < 2.78 to reduce the risk of developing colorectal adenoma, and the risk was reduced also by increasing the magnesium concentration [12]. A follow-up clinical study reported that long-term treatment with 1200 mg/d of calcium lowered the risk of colorectal adenoma recurrence significantly, but only when the baseline calcium-to-magnesium ratio was < 2.626 [13]. Intake of additional calcium did not affect patients when the ratio was > 2.626 [13]. Findings from those studies, therefore, suggest that a ratio > 2.6–2.8 can have a negative effect on disease outcomes. Conversely, studies have also shown that ratios < 1.7 may also have negative effects and were associated with an increased

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https://doi.org/10.1016/j.jsbmb.2020.105636
Received 4 April 2019; Received in revised form 4 December 2019; Accepted 17 February 2020
Available online 18 February 2020
0960-0760/

risk of total mortality in both women and men [14]. Therefore, calcium-to-magnesium ratios < 1.7 and > 2.8 have been suggested to be detrimental, and optimal ratios may be around 2.0 [11]. One study determined the mineral content (calcium, magnesium, zinc, and phosphorus) from coronal dentin samples collected from premolar teeth removed for periodontal or prosthetic indications. A statistically significantly higher content of magnesium and a lower calcium-to-magnesium ratio were found in worn teeth, whereas the concentrations of the other minerals analysed were not significantly different between worn and intact teeth ($p < .05$ for all) [15]. Taken together, those studies indicate that an optimal calcium-to-magnesium ratio may exist. However, the exact ratio is unknown because of the paucity of studies that have investigated that relationship and the complex but interdependent relationship that exists between calcium and magnesium with regard to human tooth health. Hence, further studies are required to elucidate and clarify optimal calcium-to-magnesium ratios for good tooth health.

Vitamin D is a hormone necessary for the intestinal absorption of calcium, magnesium, and phosphorus, which are essential for proper mineralization of the bones and the teeth [16]. The osseointegration of dental implants with alveolar bone is enhanced when implants are coated with vitamin D [17]. Furthermore, injecting vitamin D_3 intraperitoneally accelerates orthodontic tooth movement, and with vitamin D, even patients undergoing bisphosphonate therapy can receive orthodontic treatment [18,19]. Magnesium influences dental and oral health, partly by enhancing the antimicrobial microenvironment, reducing oral inflammation, enhancing calcium absorption into the teeth, and enhancing tooth enamel pliability. Some clinical scientists believe that magnesium is more important than calcium in maintaining oral and dental health. Without adequate magnesium balance:

1 The salivary glands cannot remove excess food debris and provide a more basic environment to mitigate the effects of bacterial acid production.
2 The immune system cannot activate vitamin D, one of its primary forces.
3 The body cannot adequately make glutathione, an important anti-inflammatory agent that combats inflammation of teeth and gums.
4 The teeth can no longer absorb calcium, which instead enters the gums, where it calcifies and causes inflammation.
5 The tooth enamel lacks a primary constituent of its amorphous binding solution, the magnesium ion.

Magnesium deficiency, therefore, is apparently vital to protecting teeth and keeping them healthy [7,20,21].

3. Role of magnesium in vitamin D activation and function

Vitamin D and magnesium are some of the most studied nutrients in medicine because deficiency of either nutrient has enormous implications on public health [22]. Magnesium and vitamin D are two essential nutrients, and an adequate balance is essential for maintaining the physiologic functions of various organs [23–26]. Vitamin D helps regulate calcium and phosphate balance to maintain healthy bone function. Magnesium helps activate vitamin D, which helps regulate calcium and phosphate homeostasis to influence bone growth and maintenance. Magnesium is essential for the stability of cell function, RNA and DNA synthesis, and cell repair, as well as maintaining the cell's antioxidant status. Magnesium also is an important cofactor necessary for activating a variety of transporters and enzymes [27]. All the enzymes that metabolize vitamin D seem to require magnesium, which acts as a cofactor in the enzymatic reactions in the liver and kidneys (Fig. 1). Deficiency in either nutrient is associated with skeletal deformities, cardiovascular diseases, and metabolic syndrome [22,28–30].

Vitamin D deficiency is a common medical condition worldwide. Vitamin D supplementation increased because of the recent increase in global awareness, but magnesium deficiency remains less discussed [22]. More attention should be paid to possible consequences of insufficient or deficient magnesium supply in the general population [31]. Magnesium is the second-most-abundant intracellular cation, which plays a crucial role in the synthesis and metabolism of parathyroid hormone (PTH) and vitamin D [22,32,33]. Previous studies showed that several steps in vitamin D metabolism are magnesium-dependent, such as vitamin D binding to vitamin D binding protein, 25(OH)D synthesis, $1,25(OH)_2D$ synthesis, 25-hydroxylase synthesis, and vitamin D receptor expression for cellular effects [22,32,34]. Magnesium deficiency leads to impaired PTH secretion and response and can reduce the number of available vitamin D receptors in target cells [33,35–37]. Magnesium deficiency also reduces 1,25- dihydroxyvitamin D [$1,25(OH)_2D$] in vitamin D–resistant rickets [33], which can be corrected only after proper replacement of magnesium [22]. Studies showed that magnesium supplementation substantially reversed resistance to vitamin D in rickets in comparison with high intramuscular infusion of vitamin D alone [33]. Other studies reported that magnesium infusion plus oral vitamin D as 25(OH)D substantially increased both serum 25(OH)D and $1,25(OH)_2D$ in comparison with magnesium infusion alone, which led to a nonsignificant increase in both parameters [22,38]. Thus, a possible interaction exists between magnesium and vitamin D, which influences vitamin D status [39]. However, those findings need to be validated with large and multicenter clinical trials.

4. Magnesium deficiency and periodontal health and diseases

Periodontitis, multifactorial inflammatory disease of the supporting tissues of the teeth, is caused by specific microorganisms. *Streptococcus mutans*, *Lactobacillus*, and members of the genera *Bifidobacterium*, *Actinomyces*, *Propionibacterium*, and *Veillonella* are associated with dental caries in children and adults [40–42]. Among the factors associated with periodontitis are oral hygiene behavior, genetics, systemic health, and nutrition. The disease is characterized by the formation of pockets, which increase in depth progressively, and destruction of the alveolar bone and the periodontal ligament, with gingival recession. The World Health Organization has included the disease in priority prevention programs because it is a worldwide health problem leading to edentulism (toothlessness) in the adult population [43–45]. Periodontitis is the most prevalent bone disease in humans, affecting 40 %–90 % of the global population, and if untreated is severe enough to lead to tooth loss in 10 %–15 % of adults [46–48].

Biomineralization is a dynamic process, whereby living organisms can control the precipitation of inorganic nanocrystals in organic matrices to produce specific hybrid biological tissues such as bones, enamel, dentine, and cementum. Therefore, bones, and especially teeth, are continuously at risk of demineralization throughout life because of their location and arrangement in the mouth [20]. The oral environment can become acidic as a result of the types of consumed foods, especially sugary foods. Sugary foods are fermented by *S. mutans*, and the presence of bacteria increases the amount of acids on the surface of uncleaned teeth, which can erode enamel and demineralize other hard dental tissue. The way in which enamel can resist demineralizing acids will depend on how much mineral contents are found in its structure. Thus, it is important to determine the composition of saliva to determine that it favors mineralization or demineralization [49]. Previously it was believed that calcium promoted good mineralization, but more recent studies have established that magnesium instead helped resist decay because the mean concentration of magnesium was statistically significantly higher in healthy enamel than in mesiodens enamel [50]. Consuming calcium without magnesium will result in soft enamel, which cannot resist the acids causing the decay [51]. The role of magnesium in teeth remineralization process is crucial; it participates in the formation and growth of hydroxyapatite crystals [20]. When guinea pigs are fed with a magnesium-deficient diet, teeth fail to calcify

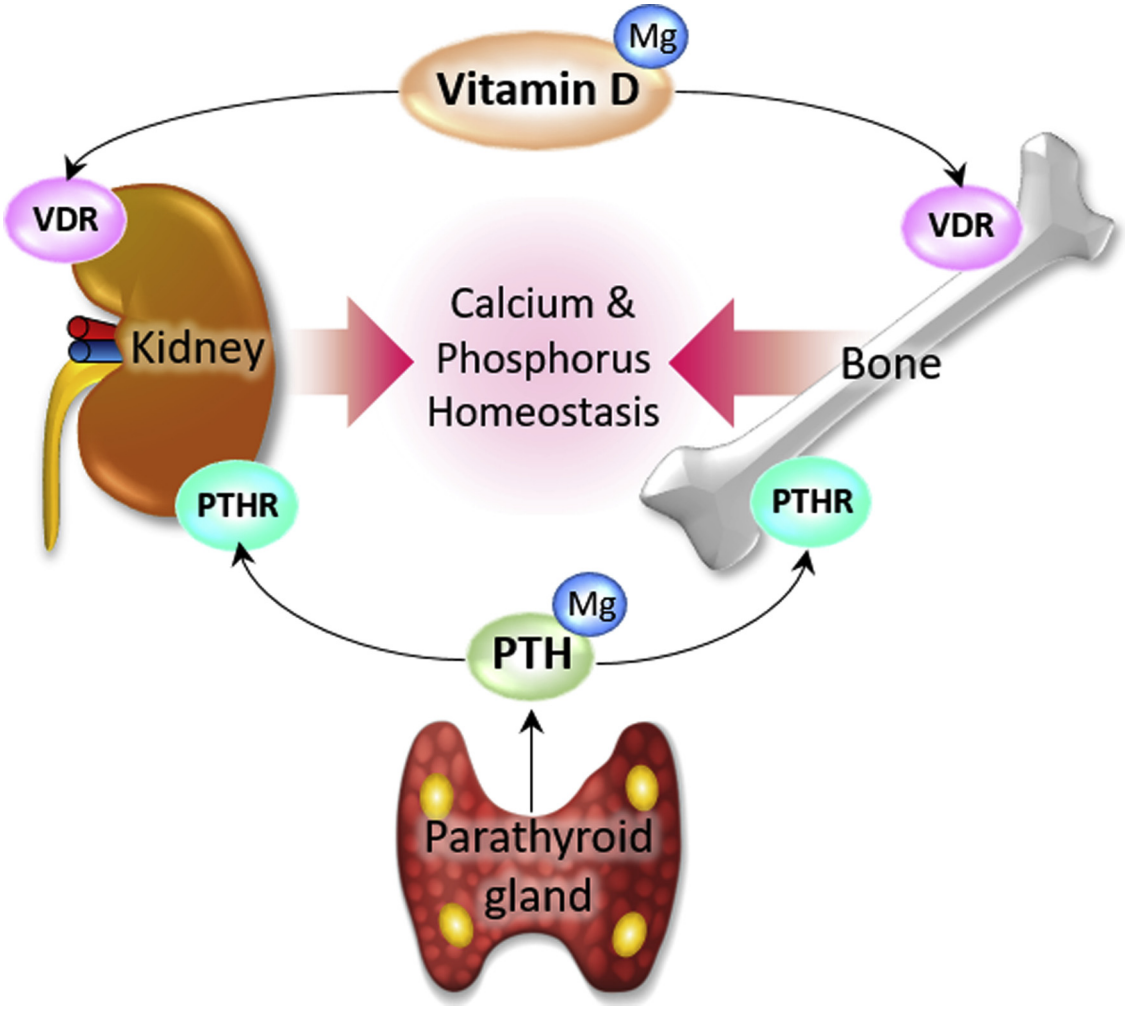

Fig. 1. Possible role of magnesium in vitamin D and PTH activation and function [28–30]. Both vitamin D and PTH exert important biological effects on tooth development and maintenance, including enhancing tooth movement to stabilize tooth position [94,130–132].
Abbreviations: Mg, magnesium; VDR, vitamin D receptor; PTH, parathyroid hormone; PTHR, parathyroid hormone receptor.

normally, leading to discoloration, erosion, and breaking of incisors at the gum line [51]. Danuta and colleagues determined the relationship between the content of magnesium and fluoride in superficial enamel and the depth of etching by perchloric acids. Their findings emphasized that the depth of etching and magnesium are interrelated, showing that magnesium enhances enamel resistance to erosion [52].

Many studies have established the connection between diet and dental caries [53]. Good nutrition is essential for fighting bacteria, maintaining tissue integrity, and repairing injured tissues [54]. People have been informed that eating sugary foods and not brushing teeth contribute to forming dental caries by fermentation, leading to pH below 7 [55]. However, many people are not aware that ultraviolet-B irradiance and vitamin D supplementation will produce more vitamin D, which also reduces dental caries [56]. Vitamin D supplementation can prevent caries onset and progression. That is why recommending vitamin D supplementation for children at risk of dental caries may decrease the overall prevalence of severe early-childhood caries [57,58]. Magnesium has proven essential for the activity of calcium and phosphorus in inhibiting caries. Consuming calcium and phosphorus without taking magnesium at the same time, instead of strengthening teeth, might have the opposite effect, causing structures beneath the surface to dissolve [51]. Researchers from Otago University in New Zealand have shown that magnesium, not calcium, contributes to reducing enamel caries. Those authors studied 200 patients aged 5–56 years, giving them an alkaline phosphate and then monitoring them for 3 years. At the end of that period, all participants showed reduced incidence of caries. The extracted teeth of the case group had twice the amount of magnesium of the teeth of the control group, who did not receive magnesium. The investigators concluded that consumed magnesium contributed to reduced cavities in the case group. The susceptibility of tooth enamel to caries development is proportional to its amount of magnesium content [51].

Because the foods we consume can affect dental health, we should eat magnesium-rich foods to prevent dental caries. However, instead of eating magnesium-rich leafy vegetables, people tend to consume phosphorus-rich foods [59]. A study assessed calcium, magnesium, and fluoride in bottled and natural drinking water in Saudi Arabia. The authors recommended that, as part of the preventive measures against dental caries, manufacturers consider bottling waters with optimum mineral compositions that are beneficial for both the systemic and dental health of the public [60]. Emphasis should be put on improving the magnesium consumption in the population to fight its deficiency instead of thinking that increased consumption of calcium will prevent dental caries. Because milk is rich in calcium and phosphorus but poor in magnesium, it may interfere with magnesium metabolism and antagonize magnesium action, thus compromising caries prevention [51,61]. Magnesium is statistically significantly higher than sodium and phosphorus in healthy and mesiodens enamel, which indicates magnesium's role in preventing dental caries [50].

Low dietary intake of magnesium can lead to deficiency and has

been associated with many pathologies, such as periodontitis and diabetes mellitus [62]. A single-blinded, randomized study evaluated serum magnesium levels in patients with type 2 diabetes mellitus and chronic periodontitis. Researchers evaluated how serum magnesium levels affected periodontal health before and 21 days after scaling and root planing. In comparison with healthy control patients (nondiabetic, with no periodontitis), serum magnesium levels were significantly decreased in patients with chronic periodontitis and diabetic patients. However, the levels increased significantly in all groups after scaling. The authors inferred that the increase in serum magnesium level might be attributed to reduced inflammation after the scaling procedure [63]. A longitudinal study in an elderly Japanese population evaluated the association between calcium/magnesium ratio and serum calcium levels and periodontitis progression in smokers versus nonsmokers. The authors reported a link with low serum calcium/magnesium ratio and periodontal disease progression in smokers who also had lower serum calcium levels than nonsmokers. The researchers suggested that the calcium/magnesium ratio was more important than calcium concentration in disease progression [64].

Oral bone mass increases from infancy to early adulthood, up to a genetically determined peak mass [7]. Generally, a balanced diet helps in maintaining healthy bone growth and periodontal health, especially when it is rich in magnesium [50]. Early experimental and clinical studies have shown that when the calcium-to-magnesium ratio is low, as with magnesium supplementation, periodontitis can be prevented or slowed [65,66]. That result was evidenced by a study done by Meisel and colleagues (2005) on an adult population aged 40 or more years. Serum magnesium levels were significantly associated with reduced probing depth, less attachment loss, and more remaining teeth [67]. Those results indicated that nutritional magnesium supplementation may improve periodontal health. The median number of remaining teeth was 17 in the case group (Mg users) and 14 in the control group (no Mg drugs) [67]. Eleven years later, those researchers conducted another study and arrived at similar results: that an adequate magnesium supply may be important in preventing periodontal diseases and future tooth loss [68]. They found again that a magnesium-rich diet could improve periodontal health and that low bone mass characterized in the oral cavity by the loss of alveolar crestal bone height and tooth loss may result from magnesium deficiency accompanied by the stimulation of proinflammatory cytokines [42]. The authors concluded that “taking magnesium supplements could prevent tooth loss in the middle-aged and delay tooth loss in the elderly, improving the well-being of the individual and reducing costs for prosthodontic treatment” [67,68].

5. Vitamin D inadequacy and periodontal health

Vitamin D influences the status of periodontal health and disease [69–75]. Vitamin D affects the pathogenesis of periodontal diseases through its anti-inflammatory and immune-modulatory activities. Vitamin D increases bone mineral density, reduces bone resorption, and can suppress inflammatory processes associated with periodontal disease [76]. Significant associations exist between periodontal pathology, increased bone mineral density in the mandible, and reduced alveolar bone resorption and intake of vitamin D and calcium [77–79]. Long-term vitamin D supplementation (daily for 3 years) reduced risk of tooth loss by 60 % in one study [80]. Another study recorded significant improvement in both alveolar bone mass and alveolar crest height in periodontally healthy postmenopausal women who received daily calcium and vitamin D supplementation and were evaluated for 3 years [81]. Dietrich and colleagues analysed the Third National Health and Nutrition Examination Survey (NHANES III) data and found an inverse relationship between serum vitamin D levels and attachment loss in participants with lower levels of vitamin D [71]. In a randomized controlled trial on postmenopausal women who received 400 IU/day of vitamin D and increased calcium intake to 1000 mg/day for 2 years, more than 80 % of participants either maintained or gained mandibular bone mass [82]. In a case-control study, patients on vitamin and calcium supplements had shallower probing depths, fewer bleeding sites, lower gingival index values, fewer furcation involvements, less attachment loss, and less alveolar crest height loss [83].

Another study using the NHANES III data showed that vitamin D reduced risk of gingival inflammation in patients with the highest 25(OH)D levels—they experienced 20 % less bleeding on probing than patients with the lowest levels [84]. A case-control study associated vitamin D deficiency with periodontal disease among pregnant women [70]. Vitamin D deficiency also negatively affects treatment outcomes by delaying postsurgical healing [85]. Vitamin D levels play an important role in bone homeostasis, especially on attachment, bone growth, and tooth formation. Therefore, vitamin D dysregulation is linked to periodontal diseases. Depleted bone can rebuild with vitamin D supplementation [86,87]. In addition to the direct effects on bone metabolism, the direct antibiotic effect of vitamin D on periodontal pathogens may contribute to healing from periodontitis. Vitamin D inhibits inflammatory mediators that cause periodontal destruction [69]. Because the dietary content of vitamin D will affect healing after periodontal surgery [7,88], deficiency will negatively affect the healing of periodontal tissues [85,89,90]. Animal clinical studies have shown that vitamin D_3 supplementation is positively correlated with dental implant osseointegration [45,91]. Because vitamin D directly affects bone metabolism and has anti-inflammatory properties, more research on the vitamin will potentially contribute to a better understanding of periodontal disease [16,69].

The quality of host immune response correlates highly with nutritional status. Vitamin D is important not only for periodontal disease prevention but also for the reversal effect when gingivitis and periodontitis have already caused tissue damage, to convert diseased tissue into healthy tissue by eating healthy food. Good nutrition is needed for sustaining healthy tissues, maintaining the immune system, and protecting against periodontal disease. When a patient is malnourished, immunity will be compromised, increasing the risk and extent of oral infection. Malnutrition will delay the repair process in the gingival sulcus and can increase epithelial attachment permeability, making it easier for bacteria to enter [7].

An important way that vitamin D affects the immune system is by inducing human cathelicidin, LL-37 [92] (Fig. 2). LL-37 has both antimicrobial and antiendotoxin activities [93]. Vitamin D induces cathelicidin in oral epithelial cells [94], and children with high dental caries activity have low concentrations of LL-37 [95]. Several epithelial antimicrobial peptides, including LL-37, have been called the “guardian of the oral cavity” [96] and have been found to play important roles in oral health [97]. LL-37 also has important benefits in reducing risk of gingivitis [98]. Maternal vitamin D deficiency also increases the DMFT (decayed, missing, filled, primary teeth) score for children aged 12–35 months [99]. Therefore, vitamin D may be of benefit in treating periodontitis because of its direct effects on bone metabolism as well as its possible anti-inflammatory effects on periodontopathogens.

6. Contribution of phosphorus and calcium in oral health and diseases

The role of essential minerals in metabolism, general physiology, and tooth health has been well studied; however, studies on their possible interactions are lacking. Magnesium is required for the synthesis and metabolism of vitamin D, the latter of which is important in regulating calcium and phosphorus. Deng and colleagues (2013) investigated the interaction between magnesium and vitamin D in the general population. They found that magnesium intake may contribute to vitamin D status and modify any links between serum vitamin D level and mortality risk [39]. Taking vitamin D supplements enhanced magnesium and calcium absorption, increased excretion of magnesium and decreased magnesium retention in animals [100], and reduced

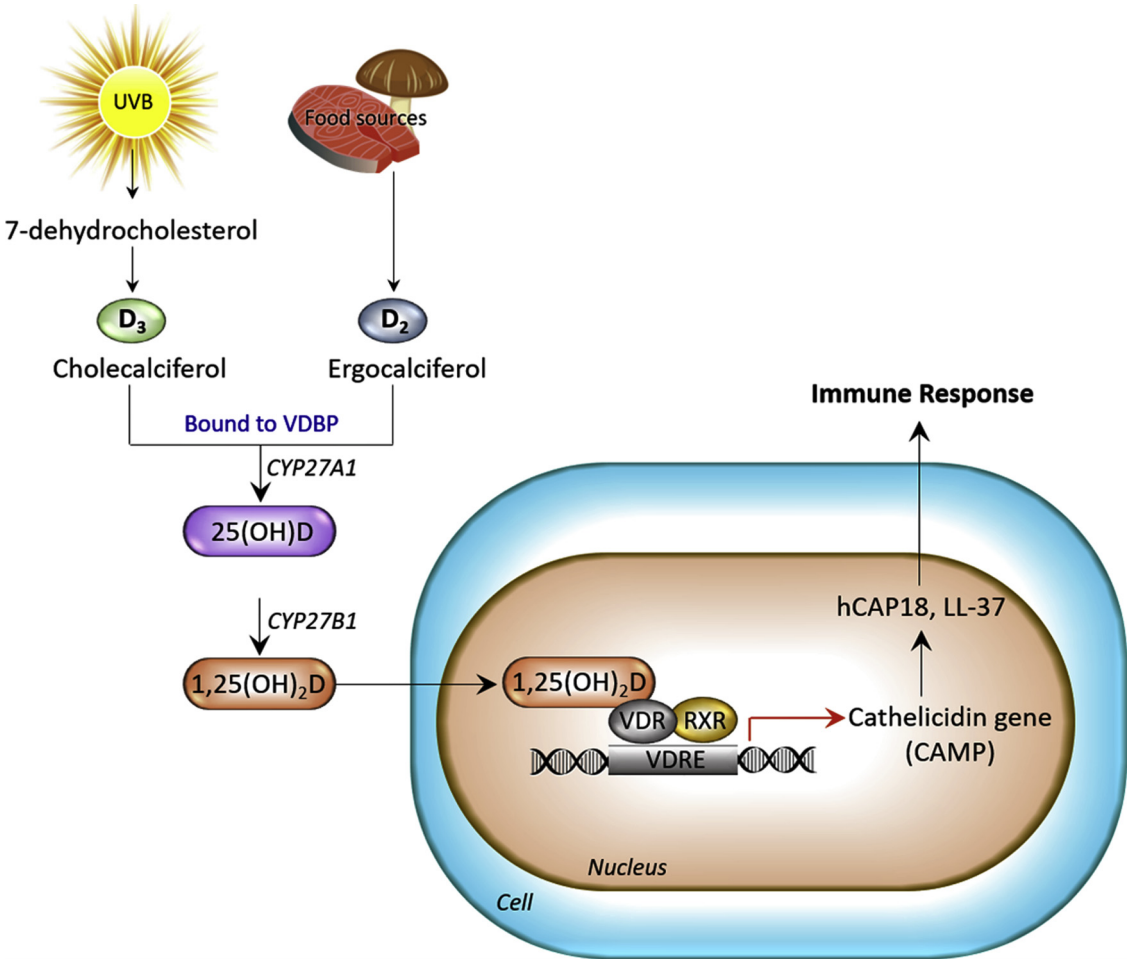

Fig. 2. Cathelicidin LL-37–induced gene expression by vitamin D. Vitamin D—synthesized in the skin (cholecalciferol) or by plants (ergocalciferol) after exposure to UVB radiation—binds to vitamin D binding protein (VDBP). Vitamin D is converted to 25-hydroxyvitamin D [25(OH)D] and then activated to 1,25-dihydroxyvitamin D [1,25$(OH)_2$D]. Activated 1,25$(OH)_2$D regulates expression of hCAP18 (proprotein) and LL-37 (protein), which is important for immune response, by interacting with the vitamin D receptor (VDR), which dimerizes with the retinoid X receptor (RXR) and binds to the vitamin D response element (VDRE) site on the cathelicidin (*CAMP*) gene promoter.

magnesium retention in humans [101].

Magnesium is a direct antagonist of intracellular calcium [102], whose intestinal absorption is primarily under the control of 1,25$(OH)_2$D. PTH, whose synthesis and metabolism is magnesium-dependent, regulates calcium secretion in the kidney tubules and increases the conversion of 25(OH)D to 1,25$(OH)_2$D in the kidney, thereby increasing gastrointestinal calcium absorption [103]. The association between magnesium and calcium has been widely investigated [104–106]. Excessive calcium affects magnesium absorption, whereas slight reduction in magnesium causes increased calcium retention [11]. One study reported that when serum magnesium was low and serum calcium and phosphorus were higher, the risk of heart failure increased in a large population of whites and African Americans [104]. Song and colleagues showed that when serum calcium levels were lower than the mean values of 9.3 ± 0.5 mg/dl, serum magnesium levels affected bone mineral density more than serum calcium levels [106]. In a rodent model that determined the effects of a moderate dietary magnesium restriction (10 % of nutrient requirement) on bone and mineral metabolism assessed over 6 months, the resulting bone loss was linked with decrease in serum magnesium levels and increased serum calcium levels [105]. In addition, consuming calcium and phosphorus without adequate intake of magnesium can lead to soft enamel and dental caries [51]. Collectively, those studies offer evidence to support an interplay between magnesium and calcium. Hence, balancing those two minerals in the correct ratios is vital for maintaining optimal bone density and teeth health.

In the United States, dietary intake of phosphorus in adults have increased and is above the recommended daily allowance of 700 mg/d [103,107]. Phosphorus interacts with calcium, magnesium, and vitamin D. Calcium and phosphorus concentrations in dental plaque and the calcium/phosphorus ion levels in saliva can affect the balance between demineralization and remineralization of enamel [108]. Lin and colleagues investigated the link between caries experienced and daily intake of calcium, phosphorus, magnesium, and calcium/phosphorus ratio in children by dental examination, questionnaire interviews about 24 -h dietary recalls, and food frequency. The daily intakes of calcium, phosphorus, magnesium, and calcium/phosphorus ratio were inversely related to primary caries index; however, only the calcium/phosphorus ratio remained significant after adjustment for potential confounders. On the basis of the Taiwanese dietary reference intakes, the calcium/phosphorus ratio was linked to caries in both primary and permanent teeth. The authors concluded that daily intake of calcium/phosphorus ratio was an important factor for caries after considering potential confounding factors [109]. Conversely, there is a paucity of scientific data regarding the interaction of phosphorus and magnesium; however, because phosphorus is associated with calcium, a phosphorus-rich diet may affect persons who consume a low-magnesium diet. In support of that assertion, a study linked lower serum magnesium and higher concentrations of phosphorus and calcium with a greater risk factor for heart failure [104].

Table 1
Effect of vitamin D, calcium, and magnesium on oral health.

No.	Author	Country; Year	Type of study	Methodology	Key findings
1.	Schroth et al. [58]	Canada; 2013	Case–control	n = 266; preschool children; 144 with severe early-childhood caries and 122 caries-free	Children with severe early-childhood caries have low vitamin D and calcium levels
2.	Shetty et al. [63]	India; 2016	Single-blinded, randomized study	n = 120; periodontitis and type 2 diabetes mellitus	Imbalance of serum magnesium level in patients with chronic periodontitis and type 2 diabetes mellitus
3.	Meisel et al. [67]	Germany; 2005	Cross-sectional	n = 4290; aged 20–80 yrs	Nutritional magnesium supplementation may improve periodontal health
4.	Meisel et al. [68]	Germany; 2016	Cross-sectional	n = 3300	Adequate magnesium serum level and Mg/Ca balance may prevent progression of attachment level and tooth loss, especially in inflammatory states
5.	Boggess et al. [70]	USA; 2011	Case–control	n = 246; 123 cases, 123 controls; pregnant women	Vitamin D insufficiency [serum 25(OH)D $<$ 75 nmol/l] associated with maternal periodontal disease during pregnancy
6.	Dietrich et al. [71]	USA; 2004	Cross-sectional	n = 11,202; aged $\geq$20 y	Low serum 25(OH)D_3 concentrations may be associated with periodontal disease independently of bone mineral density
7.	Joseph et al. [75]	India; 2015	Cross-sectional	n = 141, including 48 controls; chronic periodontitis patients with and without type 2 diabetes mellitus	Low levels of serum vitamin D in chronic periodontitis patients with type 2 diabetes mellitus
8.	Krall et al. [80]	USA; 2001	Randomized controlled trial	n = 145; healthy subjects aged $\geq$65 years; 82 patients took vitamin D and calcium supplementation, and 63 took placebo	Calcium and vitamin D supplements reduce tooth loss in the elderly
9.	Miley et al. [83]	USA; 2009	Cross-sectional	n = 51; periodontal maintenance therapy; 23 took vitamin D ($\geq$400 IU/day) and calcium ($\geq$1000 mg/day) supplementation, and 28 took no supplementation	Periodontal maintenance therapy group showed a trend for better periodontal health with vitamin D and calcium supplementation
10.	Bashutski et al. [85]	USA; 2011	Randomized controlled trial	n = 40; severe chronic periodontitis; periodontal surgery and teriparatide administration in vitamin D–sufficient and –insufficient individuals	Vitamin D deficiency at the time of periodontal surgery negatively affects treatment outcomes
11.	Garcia et al. [88]	USA; 2011	Observational clinical trial	n = 51; 23 patients took vitamin D ($\geq$400 IU/day) and calcium ($\geq$1000 mg/day) supplementation, and 28 took no supplementation	Calcium and vitamin D supplementation has a modest positive effect on periodontal health
12.	Zhou et al. [126]	China; 2012	Case–control	193 cases, 181 controls	Decreased serum 25(OH)D concentrations were significantly associated with poor periodontal health
13.	Chhonkar et al. [127]	India; 2018	Case–control	n = 60; 3 and 6 years; 30 children with caries and 30 without caries	Vitamin D deficiency is risk factor both for incidence of dental caries and for its severity in children
14.	Adegboye et al. [128]	Denmark; 2012	Cross-sectional	n = 135; adults	Dairy calcium, particularly from milk and fermented products, may protect against periodontitis
15.	Staudte et al. [129]	Germany; 2012	Case–control	n = 80; 42 chronic periodontitis and 38 healthy subjects	Patients with periodontitis have less intake of magnesium than healthy subjects

Taken together, the aforementioned studies indicate that potential interactions may exist between magnesium, vitamin D, calcium, and phosphorus. However, to the best of our knowledge, no single study has investigated the collective interactions of those minerals regarding tooth health. Many unanswered questions remain, such as:

- whether one, a combination, or all of those minerals work independently or in synergy to activate and/or inhibit each other and hence affect their functions;
- how deficiency in one or more of those minerals affects bone and tooth health and/or gives rise to disease development; and
- what their optimal ratios are in terms of the optimal tooth health.

Hence, future studies are needed to elucidate the correlation between those minerals with regard to tooth health. Such endeavors should use research studies to explore any underlying molecular and cellular mechanisms that may be involved as well as large multicenter clinical trials for validation.

7. Optimal diet and oral health

Dairy products such as milk, cheese, and yogurt can protect teeth against demineralization [110,111]. Daily consumption of milk products is related to a lower risk of caries [112,113] and reduces caries in the elderly [108]. Milk has properties akin to those of saliva and can reharden human enamel that has softened after exposure to acidic beverages [110]. Milk contains calcium, vitamin D, phosphorus, riboflavin, B-complex vitamins, and vitamin A [114]. Casein, a protein in milk, strengthens and repairs tooth enamel [115]. Therefore, consuming milk products is good for oral health. Conversely, because milk is poor in magnesium but rich in calcium and phosphorus, magnesium-rich foods such as green leafy vegetables and quinoa, or magnesium supplements, should be consumed at the same time to prevent caries and promote tooth mineralization. In support of that recommendation, one study showed that the number of periodontal disease events decreased significantly with greater intake of dark green and yellow vegetables [108].

Starch-rich staple foods have low cariogenic ability, and consuming a high-starch, low-sugar diet (compared with a low-starch, high-sugar diet) positively correlates to caries prevention [116,117]. By contrast, intake of cereals, nuts and seeds, sugar and sweeteners, and confectioneries positively correlated with periodontal disease events [108]. Furthermore, deficiencies of vitamins A, C, and E, related to the production of reactive oxygen species, have been linked to periodontal disease, as well as folic acid deficiency [118]. A positive correlation between low vitamin C intake and periodontal disease was demonstrated in a study using the NHANES III data [119]. Consuming foods rich in antioxidant nutrients such as vitamins A, C, and E is therefore important in maintaining periodontal health. Those antioxidants are found in many fruits, vegetables, and grains [120]. Omega-3 fatty acid–rich foods also reduce periodontitis [121,122]. Those foods, such as wild-caught salmon and sardines, are full of vitamin D, which helps the body absorb calcium and phosphorus and helps protect tooth enamel. In addition, foods such as celery, chewing gums, and lemons help stimulate salivary production and reduce cariogenicity [120].

Collectively, findings from some studies mentioned here indicate that the key to optimal dental health is to prevent caries and periodontal disease by lowering intake of phosphorus-rich foods; foods rich in phytic acid, which can interfere with vitamin D metabolism [123]; and foods that promote demineralization, while increasing intake of foods that promote tooth remineralization such as dark leafy greens and healthful fats. Consuming a diverse, balanced diet containing a variety of vital macronutrients including calcium, magnesium, vitamin D, and phosphorus at optimal ratios, along with other vitamins and oral probiotics [124], is therefore important in promoting tooth mineralization and good oral health. Those vitamins and minerals are best absorbed in the body when they are obtained through natural food sources; however, supplements can also be taken to augment their intake.

8. Conclusion

Several studies have reported the importance of micronutrients for maintaining good periodontal health and have provided some evidence to demonstrate a causal link with periodontal disease. However, further research is needed in this emerging field. Observational cross-sectional studies investigating associations between vitamin D and chronic periodontitis, for instance, yield only weak evidence [125]. Moreover, there is a paucity of general evidence to support any relationship between micronutrients in general and periodontal disease. Expanding on such studies and conducting well-designed, randomized clinical trials on vitamins such as vitamin D and minerals such as magnesium are needed. Doing so would lead to further insight and knowledge on causal associations or underlying mechanisms regarding periodontal health as well as their potential role in preventing and treating periodontal disease. Further studies on the interactions between magnesium supply and vitamin D status with a more detailed assessment of individual magnesium status need to be conducted [31] (Table 1).

Good oral health cannot be achieved and sustained without rectifying nutrient deficiencies. Because diet plays a predominant modifying role in the progression of periodontal disease, dentists should educate patients about how good nutrition affects the supportive structures of the teeth, such as the importance of consuming healthy food rich in magnesium and vitamin D in preventing dental caries. A sufficient amount of minerals such as magnesium and calcium is needed to keep teeth healthy. Knowing which nutrients maintain oral health or resolve unhealthy areas will help people select foods appropriately. Controlled studies should be conducted to establish the extent to which adequate intakes of magnesium and vitamin D can stabilize or improve periodontal health and maintain oral health in general.

Acknowledgments

Thanks to Dr. Nuraly Akimbekov of Al-Farabi Kazakh National University, Almaty (Kazakhstan) for help in drawing the illustrations. Dr. Razzaque is a Visiting Professor at the Harvard School of Dental Medicine, Boston (USA), and an Honorary Professor at the University of Rwanda College of Medicine & Health Sciences, Kigali (Rwanda).

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