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The Role of Vitamin K2 in Oral Health: A Narrative Review of Mechanisms and Clinical Applications.

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Abstract

Vitamin K2, in its menaquinone-4 (MK-4) and menaquinone-7 (MK-7) forms, has been identified as an essential cofactor in the activation of γ-carboxylated proteins (Gla proteins) involved in mineral homeostasis, bone regeneration, and inhibition of ectopic calcification. While extensively studied in cardiovascular and osteometabolic medicine, its impact on oral health has been less thoroughly explored.

The objective of this study is to review the current literature on the relationship between vitamin K2 and various aspects of oral health, including craniofacial development, periodontology, cariology, dentin physiology, and pulp regeneration.

Methods:
A narrative review was conducted based on literature indexed in PubMed, Scopus, and Google Scholar. Included sources comprised experimental studies, scientific reviews, observational research, and anthropological reports relevant to the systemic and oral roles of vitamin K2.

Results:
Vitamin K2 is involved in the activation of osteocalcin and Matrix Gla Protein, promoting dental remineralization, alveolar bone regulation, and inflammatory modulation in periodontal tissues. In vitro and animal studies support its beneficial effects on the pulp-dentin complex and osseointegration. Additionally, anthropological evidence suggests that ancestral populations with menaquinone-rich diets exhibited a lower prevalence of oral diseases.

Conclusions:
Vitamin K2 is a micronutrient with therapeutic potential in dentistry, particularly in the prevention of dental caries, periodontal therapy, interceptive orthodontics, and regenerative treatments. However, robust clinical evidence is required to validate its use as an adjunct in dental treatment protocols.

Keywords:

- Vitamin K2
- Oral health
- Dental caries
- Periodontal disease

Osteocalcin

Matrix Gla Protein

Dentin regeneration

Osseointegration

Ancestral diet

1. Introduction

In recent decades, there has been growing interest in the role of fat-soluble vitamins in both systemic and oral health, particularly those involved in bone metabolism and the modulation of inflammatory processes. Within this group, vitamin K2 (menaquinone) has emerged as a key micronutrient in biological functions that extend beyond its classical role in blood coagulation, most notably its involvement in the activation of regulatory proteins associated with bone mineralization and calcium homeostasis.

Unlike vitamin K1 (phylloquinone), whose primary function is to support hepatic synthesis of coagulation factors, vitamin K2 predominantly acts in extrahepatic tissues such as bone, vasculature, and potentially dental tissues. It modulates the activity of proteins such as osteocalcin and Matrix Gla Protein (MGP), both of which require γ-carboxylation to become functionally active. This functional distinction has prompted a growing body of research aimed at elucidating the impact of vitamin K2 on the craniofacial skeleton and oral health.

In the dental context, vitamin K2 has been associated with key physiological processes, including:

The development and growth of the maxillary bones

The formation and maintenance of alveolar bone

The structural integrity of enamel and dentin

The regulation of the periodontal inflammatory response

And the osseointegration of dental implants, via its influence on mineral metabolism and osteoblastic differentiation

Despite these potentially relevant associations, its integration into daily dental practice remains limited—largely due to insufficient dissemination of its specific mechanisms of action within dental tissues and the lack of robust clinical evidence. Nevertheless, preclinical and observational studies are beginning to establish a theoretical framework suggesting a significant impact of vitamin K2 on oral health, particularly when considered in synergy with vitamin D3 and calcium.

The aim of this narrative review is to critically and systematically analyze the existing literature on vitamin K2 in relation to oral health, highlighting its biological mechanisms, potential clinical applications, and emerging research areas within dentistry. In doing so, this work seeks to contribute to a more integrated understanding of the role of micronutrients in therapeutic and preventive dental care.

Review Methodology

A narrative review was conducted to explore the role of vitamin K2 in various aspects of oral health. Scientific articles indexed in the databases PubMed, Scopus, and Google Scholar published between 1980 and 2024 were reviewed. The selection included in vivo and in vitro experimental studies, systematic reviews, observational research, and relevant anthropological reports. Priority was given to publications in English and Spanish that addressed the relationship between vitamin K2 and processes such as bone mineralization, dentin physiology, dental caries, periodontal disease, maxillary development, and its clinical applications in dentistry.

Table 1 summarizes the studies included in this review:

Table 1. Bibliography on Vitamin K2 and Oral Health

Author and Year	Study Type	Subjects / Model	Key Findings
Shearer & Newman, 2008	Review	N/A	Metabolism and biological functions of vitamin K.
Walther et al., 2013	Review	N/A	Dietary sources of menaquinones (fermented foods, dairy).
Thijssen & Drittij-Reijnders, 1996	Experimental	Human tissues	Distribution of MK-4 in peripheral tissues.
Schurgers & Vermeer, 2002	Experimental	Humans (serum)	Lipoprotein transport of MK-7 vs. MK-4.
Sato et al., 2012	RCT	Healthy women	Higher bioavailability of MK-7.
Kamao et al., 2007	Observational	Humans (Japanese diet)	Vitamin K content in foods.
Booth, 2009	Review	N/A	Extra-coagulation functions of vitamin K.
Ferland, 1998	Review	N/A	Vitamin K-dependent proteins (Gla).
Cranenburg et al., 2007	Review	N/A	Vitamin K as a calcification modulator.
Price et al., 1986	Experimental	In vitro (osteocalcin)	Activation of osteocalcin by vitamin K.
Luo et al., 1997	Animal (knockout mice)	Mice	MGP prevents ectopic calcification.
Cockayne et al., 2006	Meta-analysis	Humans (fractures)	K2 supplementation reduces fracture risk.
Knapen et al., 2013	RCT	Postmenopausal women	MK-7 reduces bone loss.
Iwamoto et al., 2004	Review	N/A	Effects of K2 on osteoporosis.
Taira et al., 2012	Animal	Rats	MK-4 enhances mandibular bone regeneration.
Koshihara et al., 2003	In vitro	Bone marrow cells	K2 stimulates osteoblasts and inhibits osteoclasts.
Schurgers et al., 2007	Animal	Rats	K2 reverses warfarin-induced vascular calcification.
Kaneki et al., 2001	Observational	Humans (Japan)	Natto (MK-7) intake associated with lower fracture risk.
Iwamoto et al., 2000	Animal	Ovariectomized rats	K2 prevents post-ovariectomy bone loss.
Katsuyama et al., 2002	Animal	Rats	MK-4 reduces bone loss due to ovariectomy.
Schurgers & Vermeer, 2000	Review	N/A	MGP in bone mineralization.
Cui et al., 2023	Animal	Mice	MK-4 prevents medication-related osteonecrosis of the jaw via SIRT1 pathway.
Yamaguchi & Weitzmann, 2011	In vitro	Osteogenic cells	K2 activates BMP-2 and Runx2 for bone formation.
Price, 2008	Anthropological	Ancestral populations	K2-rich diets associated with better oral health.
Ma et al., 2022	Meta-analysis	Humans (postmenopausal osteoporosis)	Efficacy of K2 for osteoporosis.
Van Ballegooijen et al., 2017	Review	N/A	Synergy between vitamins D3 and K2.
Kambara & Yamaguchi, 2010	Animal	Rats	MK-7 reduces bone and tooth loss induced by LPS.
Price & Williamson, 1985	Experimental	Bovine	Structure of MGP.
Duerksen et al., 1983	Animal	Rats	K2 reduces incidence of dental caries.
Malin et al., 2024	Review	N/A	Role of diet in caries and hypothalamic-parotid axis.
Hara & Yamaguchi, 2009	In vitro	Osteoclasts	K2 inhibits bone resorption.
Bakhtiar et al., 2020	Review	N/A	Dental pulp stem cells and regeneration.
Olszewska-Czyz & Firkova, 2023	Case-control	Humans	Serum K2 levels correlate with periodontitis.
Iwasaki et al., 2009	Animal	Rats	K2 suppresses RANKL and osteoclastogenesis.
Cui et al., 2021	In vitro	Periodontal cells	MK-4 activates Wnt/β-catenin pathway for osteogenesis.
Schurgers et al., 2008	Review	N/A	MGP as a calcification inhibitor.
Ohsaki et al., 2006	Animal	Rats	K2 suppresses LPS-induced inflammation.
Kambara & Yamaguchi, 2010	Animal	Rats with periodontitis	MK-7 protects alveolar bone.
Vermeer et al., 2017	Review	N/A	Optimal doses of K2 for bone health.
Schurgers et al., 2007	Experimental	Humans	Comparison of K1 vs. MK-7 supplements.
Gast et al., 2009	Observational	Humans	High K2 intake reduces cardiovascular risk.
Larsen, 2015	Anthropological	Skeletal remains	Oral health in ancestral vs. modern populations.

f2. Metabolism and Biological Functions of Vitamin K2

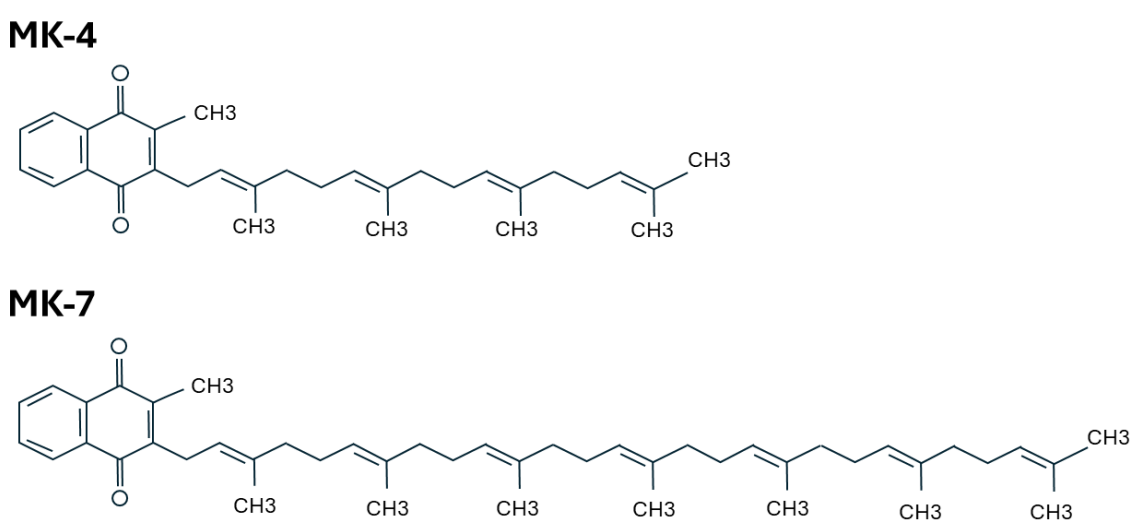
Vitamin K refers to a group of fat-soluble compounds divided into two major families: vitamin K1 (phylloquinone), which is predominant in green leafy vegetables, and vitamin K2 (menaquinones), primarily found in fermented products and produced by intestinal bacteria. The latter has been shown to possess distinct physiological functions of greater relevance in extrahepatic tissues, including bone, cartilage, blood vessels, and possibly dental structures【1,2】.

2.1. Vitamin K2 Isoforms: Menaquinones

Vitamin K2 comprises a range of isoforms known as menaquinones (MK-n), where "n" indicates the length of the isoprenoid side chain (Figure 1). The most relevant menaquinones for human health include:

- MK-4: Found in animal organs (e.g., liver, brain) and tissues such as the pancreas. It is synthesized via peripheral tissue conversion from K1【3】.
- MK-7: Derived from bacterial fermentation (e.g., natto). It exhibits a longer half-life and greater bioavailability than MK-4【4】.

Figure 1: Chemical structure of vitamin K2 (Menaquinones)



Both isoforms are capable of activating vitamin K–dependent proteins; however, MK-7 stands out for its superior efficacy in the sustained carboxylation of osteocalcin and Matrix Gla Protein (MGP)【5】.

2.2. Absorption, Transport, and Bioavailability

Vitamin K2, like all fat-soluble vitamins, requires the presence of dietary fats for intestinal absorption. Once absorbed, it is transported via chylomicrons through the lymphatic system and distributed to various tissues【6】. Unlike K1, which is preferentially taken up by the liver, K2 shows greater affinity for peripheral tissues, including bone and vascular walls, where it exerts longer-lasting effects【7】.

The plasma half-life of MK-7 is significantly longer (up to 72 hours), allowing stable serum levels with lower doses, in contrast to MK-4, which is eliminated more rapidly from the body【4】.

2.3. Activation of Gla Proteins: Osteocalcin and MGP

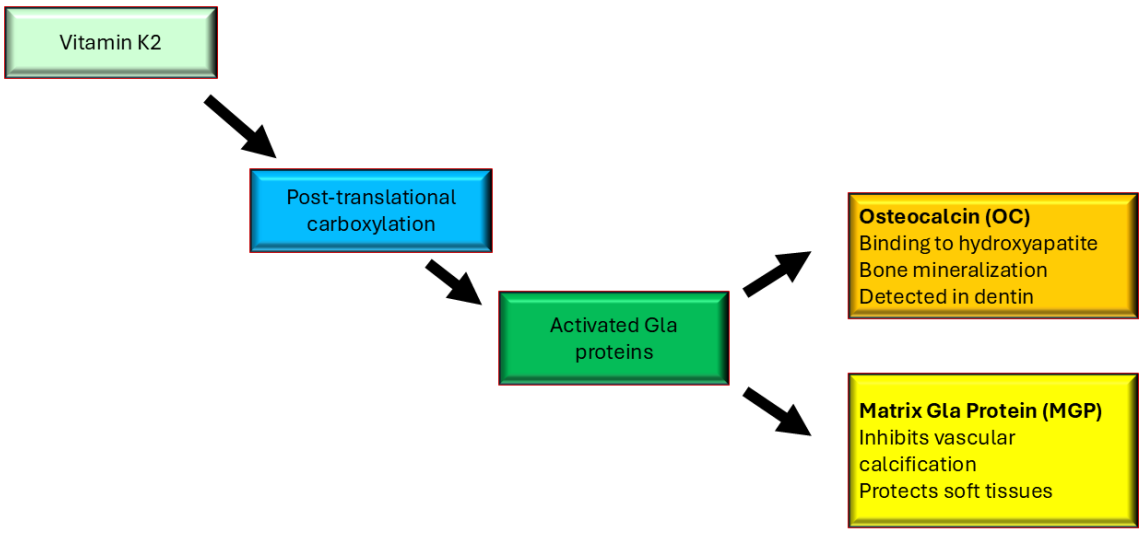
The central role of vitamin K2 in bone and dentoalveolar physiology lies in its ability to activate Gla (γ-carboxyglutamic acid-

containing) proteins through a post-translational carboxylation process【8】. This mechanism converts glutamic acid residues into γ-carboxyglutamic acid, allowing these proteins to bind calcium ions and direct them to specific tissues, thereby preventing ectopic deposition【9】 (Figure 2).

The two main proteins activated by K2 are:

- **Osteocalcin (OC):** Produced by osteoblasts. It must be carboxylated to bind hydroxyapatite and regulate bone mineralization. Osteocalcin has also been detected in dentin【10】.
- **Matrix Gla Protein (MGP):** Present in cartilage and blood vessels, it prevents pathological calcification of soft tissues【11】.

Figure 2: Activation of Gla proteins by vitamin K2



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2.4. Implications for Bone and Oral Health

Subclinical deficiency of vitamin K2 results in reduced carboxylation of these proteins, which may lead to bone fragility, alveolar bone demineralization, and inappropriate calcification of soft tissues—affecting both systemic and oral health【12,13】.

Adequate intake of vitamin K2 has been proposed to:

- Improve bone density in the maxillary and mandibular regions【14】.
- Support the osseointegration of dental implants【15】.
- Contribute to enamel and dentin integrity via its action on the extracellular matrix【10】.

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3. Role of Vitamin K2 in Bone and Maxillofacial Metabolism

Bone metabolism is fundamental to oral health, as much of the structure supporting the dentition—including the alveolar bone, maxilla, and mandible—undergoes continuous remodeling. In this context, vitamin K2 has demonstrated a crucial role in regulating bone mineralization and calcium homeostasis, particularly through the activation of Gla proteins such as osteocalcin and Matrix Gla Protein【16,17】.

3.1. Osteocalcin: Bridge Between Bone Metabolism and Dentistry

Osteocalcin, synthesized by osteoblasts, requires carboxylation to effectively bind to the hydroxyapatite in the bone matrix. In the presence of vitamin K2, the protein becomes active and promotes optimal bone mineralization. Elevated levels of uncarboxylated osteocalcin have been associated with decreased bone mineral density, which has clinical implications for periodontal stability and implant osseointegration【18】.

Experimental studies in K2-deficient rats have shown decreased trabecular bone volume in the mandible and alterations in alveolar bone architecture【19】. Administration of MK-4 in these models significantly improved bone quality, suggesting a direct impact on maxillofacial skeletal homeostasis.

3.2. Matrix Gla Protein (MGP) and the Prevention of Ectopic Calcification

MGP is another key protein modulated by vitamin K2, acting as a physiological inhibitor of calcification in soft tissues such as blood vessels and gingiva. Its K2-dependent activation prevents pathological mineralization of connective tissues—a phenomenon observed in advanced periodontal disease and cases of severe bone loss【11】.

The combined activity of osteocalcin and MGP under sufficient K2 availability suggests that this vitamin not only enhances bone formation at targeted sites but also protects against aberrant calcification, thereby improving the alveolar bone microenvironment.

3.3. Implications for Implant Osseointegration

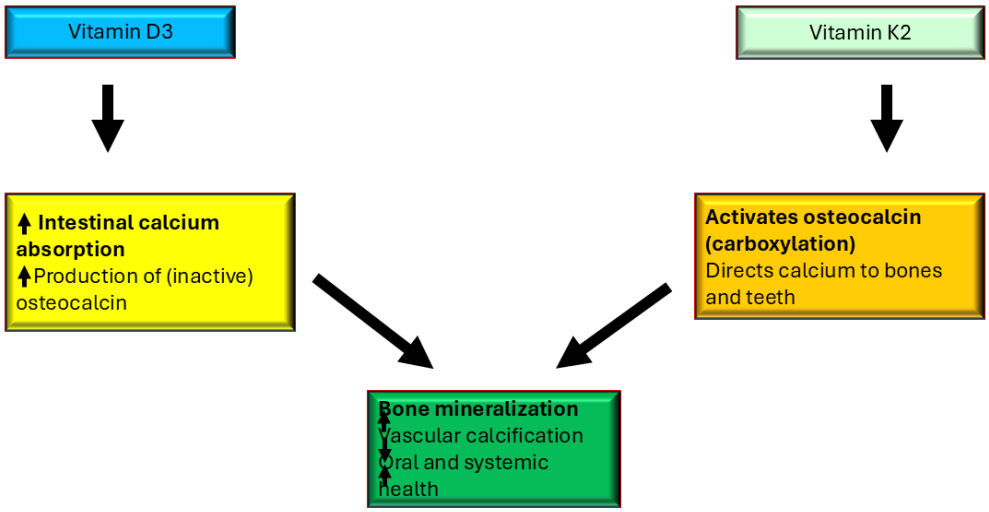
Osseointegration—defined as the direct structural connection between living bone and the surface of a dental implant—requires balanced osteoblastic activity and effective bone mineralization around the implant. Several preclinical studies have evaluated the effects of vitamin K2 supplementation on bone regeneration after implant placement, demonstrating increased peri-implant bone density, improved trabecular organization, and greater volume of newly formed bone【15,20】.

In an experimental rat model, oral administration of MK-4 significantly enhanced bone regeneration in mandibular defects treated with grafts, compared to unsupplemented controls【15】. These findings suggest a therapeutic potential for K2 as an adjunct in implantology and regenerative procedures.

3.4. Synergistic Interactions with Vitamin D3

Multiple studies have emphasized the synergistic interaction between vitamin D3 and K2 in regulating calcium metabolism. While vitamin D enhances intestinal calcium absorption and stimulates osteocalcin synthesis, vitamin K2 is essential to activate osteocalcin and direct calcium into the bone【21】. This synergy is particularly relevant in dentistry, where the efficiency of bone metabolism may determine the success of treatments such as bone grafts, orthodontics, and implant rehabilitation (Figure 3).

Figure 3: Synergy between Vitamins K2 and D3.



3.5. Prevention of Medication-Related Osteonecrosis of the Jaw (MRONJ)

Studies in murine models suggest that vitamin K2, particularly in its MK-4 form, may prevent medication-related osteonecrosis of the jaw (MRONJ) induced by zoledronic acid. This effect appears to be mediated by the inhibition of osteoblast apoptosis and the promotion of bone regeneration【22】.

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4. Role in Craniofacial Development and Maxillary Growth

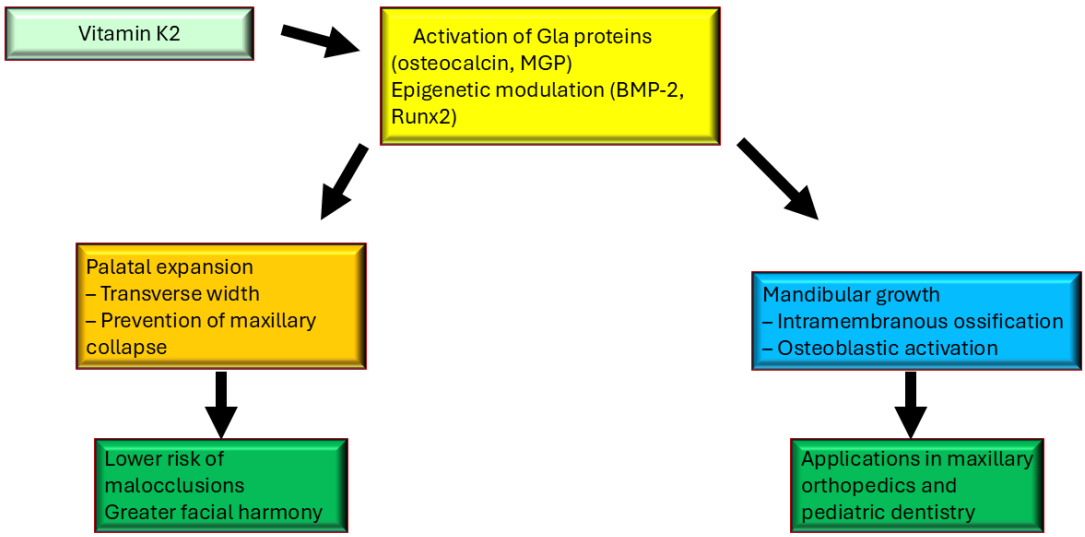
The harmonious development of the craniofacial complex depends on genetic, environmental, and nutritional factors. Vitamin K2, especially in its menaquinone-7 (MK-7) form, has been recognized as an essential cofactor for the activation of proteins involved in bone mineralization and maturation during growth. Its specific role in the formation and expansion of the maxillary bones has recently gained attention in emerging research.

4.1. Influence on Ossification and Bone Growth

During embryonic and postnatal development, the maxillary bones are formed through intramembranous ossification—a process highly dependent on osteoblastic activity. Vitamin K2 supports this activity by activating osteocalcin and other Gla proteins involved in calcium binding and mineralization regulation【16】.

Animal studies have associated vitamin K2 deficiency with delayed mandibular growth, palatal malformations, and reduced maxillary bone volume【19】. This evidence suggests that adequate levels of K2 are crucial for the proper three-dimensional development of the maxillofacial complex (Figure 4).

Figure number 4: Influence of vitamin K2 on craniofacial development:



4.2. Interaction with Epigenetic and Nutritional Factors

In addition to its direct action on mineralization, vitamin K2 may exert epigenetic effects by modulating the expression of osteogenic and remodeling-related genes. This hypothesis has been explored in studies showing that the carboxylation of osteocalcin by vitamin K2 can influence the signaling of growth factors such as BMP-2 and Runx2, both of which are critical for mandibular and palatal development【23】.

Furthermore, it has been proposed that chronic K2 deficiency—combined with other deficiencies such as vitamins D3 and A—may lead to phenotypic expression of hypoplastic maxillae and dental malocclusions, associated with mouth breathing patterns and transverse palatal collapse【24】.

4.3. Human Studies and Clinical Perspectives

Although most of the evidence comes from animal models or cell cultures, there are indirect clinical observations linking the consumption of vitamin K2-rich foods (such as Japanese natto) with a lower prevalence of craniofacial deformities and greater mandibular development【18】. These associations still require validation through longitudinal human studies.

In pediatric dentistry and maxillary orthopedics, vitamin K2 may be considered a therapeutic adjunct during growth phases, especially in interceptive orthodontics or in patients at risk of skeletal malformations. However, further research is needed to determine optimal dosages, intervention windows, and follow-up biomarkers.

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5. Vitamin K2 and Dental Caries

Dental caries is a multifactorial disease influenced by the interaction of acidogenic microorganisms, diet, saliva composition, and the structural resistance of enamel and dentin. While classical etiology focused on bacteriology and fermentable sugars, recent approaches also consider mineral metabolism and local immune responses. In this context, vitamin K2 emerges as a potentially relevant cofactor in the prevention and management of dental caries.

5.1. Regulation of Calcium and Phosphorus Metabolism

By activating proteins such as osteocalcin and Matrix Gla Protein, vitamin K2 contributes to calcium and phosphorus regulation in hard tissues. These minerals are essential to maintain enamel integrity and dentin resilience against acid attacks from cariogenic bacteria such as Streptococcus mutans【25】.

An adequate nutritional status in vitamin K2 may enhance mineral incorporation into the dental matrix, both during formation and in saliva-induced remineralization processes.

5.2. Interaction with Vitamin D3 and Remineralization Synergy

The synergy between vitamin D3 and K2 is well documented in bone metabolism and extends to the oral environment. Vitamin D stimulates osteocalcin production and enhances intestinal calcium absorption, while K2 activates osteocalcin to direct calcium toward mineralized tissues, including teeth【26】.

Experimental studies have shown that combined administration of D3 and K2 enhances enamel remineralization in animal models, particularly under acid and oral biofilm exposure conditions【27】.

5.3. Dentin Density and Structure

As a vital tissue, dentin can benefit from proper systemic nutrition. Osteocalcin has been detected in the dentin matrix, and its K2-mediated activation may influence the organization of dentinal tubules and the response to early carious lesions【28】.

It has also been suggested that K2 could play an indirect role in activating cells of the pulp-dentin complex, potentially enhancing the defensive response to carious progression toward the pulp.

5.4. Preclinical and Observational Evidence

Although direct clinical evidence is limited, animal studies have reported a lower incidence of caries in rats fed vitamin K2-supplemented diets【29】. Additionally, epidemiological observations by Weston A. Price noted a lower prevalence of caries in populations consuming diets rich in fat-soluble nutrients, including vitamin K2, although lacking the analytical precision of modern studies【24】.

5.5. Role in the Endocrine System

Evidence suggests that the hypothalamus, under nutritional regulation, controls dentinal fluid flow via the hypothalamic-parotid axis, essential for tooth nutrition and defense. A sugar-rich diet induces oxidative stress in the brain, disrupting this fluid flow and facilitating bacterial adhesion and enamel demineralization. It also triggers inflammatory responses that degrade dentin via matrix metalloproteinases. Therefore, vitamin K2—with its antioxidant properties in the central nervous system—may help preserve this defensive mechanism【30】.

6. Influence on Dentin and Dental Pulp Physiology

Dentin and pulp form a functional biological complex that responds coordinately to external stimuli, injury, and reparative processes. Dentin, although mineralized, is vital and contains a matrix rich in specific proteins, while the pulp hosts mesenchymal stem cells capable of differentiating into odontoblasts and participating in tissue regeneration. In this context, vitamin K2 may play a significant physiological role, especially through Gla protein activation and regulation of cell differentiation processes.

6.1. Presence and Function of Gla Proteins in Dentin

Osteocalcin, a vitamin K2-dependent protein, has been detected in dentin matrix and is believed to regulate mineralization in this tissue. Its post-translational activation by carboxylation is essential for its function, enabling proper calcium binding and incorporation into dentin hydroxyapatite【10】.

Moreover, other Gla proteins such as Matrix Gla Protein (MGP) may help regulate mineral deposition and prevent inappropriate calcification within the pulp【20】.

6.2. Differentiation of Pulp-Dentin Complex Cells

Vitamin K2 has demonstrated direct effects on mesenchymal stem cells, promoting their osteogenic and potentially odontoblastic differentiation via activation of signaling pathways such as Runx2 and BMP-2—essential for dentin formation【23】. This property is particularly relevant to the regenerative response to carious lesions or thermal stimuli.

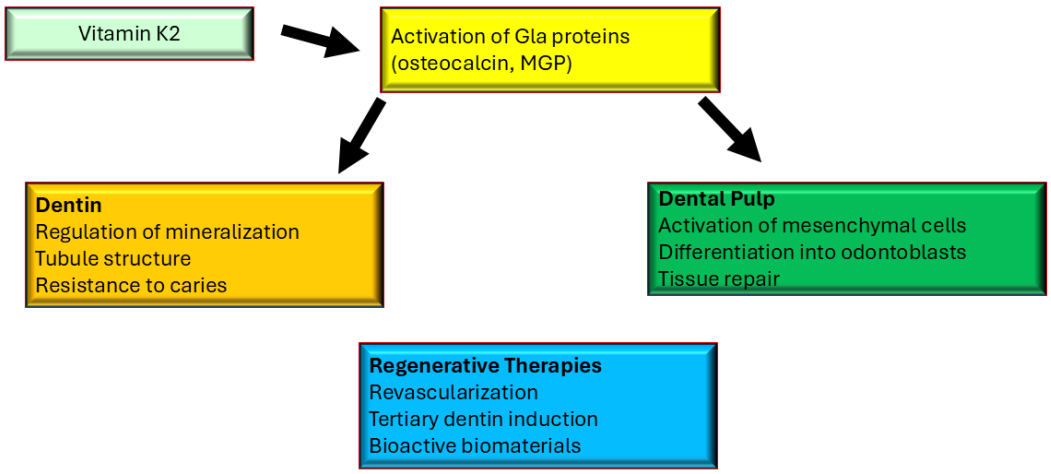
In vitro studies have shown that vitamin K2 stimulates the expression of differentiation markers such as alkaline phosphatase and osteocalcin in dental pulp-derived cell cultures【31】.

6.3. Potential in Regenerative Therapies

Due to its ability to activate structural proteins, modulate inflammation, and promote controlled mineralization, vitamin K2 has been proposed as an adjunct in regenerative therapies such as pulp revascularization, tertiary dentin induction, and enhancement of bioactive dental materials.

While these applications remain experimental, they represent a promising avenue of research in biological and regenerative dentistry—aligned with minimally invasive, conservative clinical approaches【32】 (Figure 5).

Figure number 5: Influence of vitamin K2 on dentin and dental pulp:



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7. Periodontal Disease and Vitamin K2

Periodontal disease is a chronic inflammatory condition that affects the supporting tissues of the tooth, including the gingiva, periodontal ligament, and alveolar bone. It is mediated by an immune-inflammatory response to dysbiosis in the subgingival biofilm, leading to progressive destruction of connective tissue and bone. Various studies have indicated that mineral homeostasis, inflammation control, and bone remodeling are key processes in periodontal progression—and within this context, vitamin K2 may play a significant protective role.

A human study found that serum levels of vitamin K2 correlated with the presence and severity of periodontitis, including its complexity, extent, and stage. K2 levels progressively decreased as all clinical parameters of periodontitis worsened【33】.

7.1. Regulation of Alveolar Bone Resorption

Alveolar bone is particularly sensitive to imbalances between osteoclastogenesis and bone formation. Vitamin K2, through osteocalcin activation and inhibition of osteoclastogenesis, has been shown to reduce bone loss induced by inflammatory processes in animal models【16】. Specifically, menaquinone-7 supplementation has been reported to downregulate RANKL expression and upregulate OPG (osteoprotegerin), thereby modulating local bone balance【34】. Another in vitro study showed that MK-4 promotes the osteogenic differentiation of periodontal ligament stem cells, likely via activation of the Wnt/β-catenin signaling pathway【35】.

7.2. Activation of Matrix Gla Protein and Prevention of Pathological Calcification

Matrix Gla Protein (MGP), which requires vitamin K2 for its activation, acts as an inhibitor of vascular and soft tissue calcification. Insufficient vitamin K2 levels have been associated with increased calcification in inflamed periodontal tissues, potentially impairing periodontal ligament regeneration and the functionality of root cementum【36】.

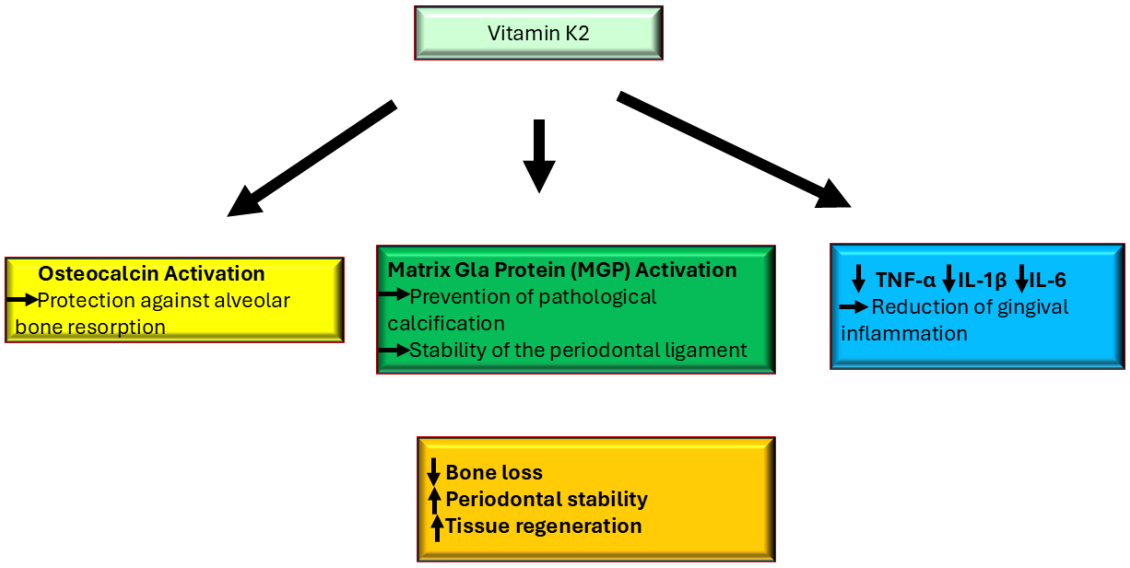
7.3. Immunomodulatory and Anti-Inflammatory Effects

Vitamin K2 has demonstrated anti-inflammatory properties in various cellular models, inhibiting the expression of cytokines such as TNF-α, IL-1β, and IL-6【37】. These cytokines are strongly implicated in the destruction of periodontal tissues, and their modulation represents a promising strategy to slow periodontitis progression.

7.4. Preclinical Evidence and Clinical Perspectives

In experimental rat models of periodontitis, oral administration of K2 significantly reduced interdental bone loss and the number of osteoclasts in molar furcations【38】. Although clinical trials in humans directly evaluating the effect of K2 in periodontal treatment are still lacking, its properties position it as a potential adjunct in supportive therapies—especially in patients at risk of osteoporosis or with deficiencies in fat-soluble nutrients (Figure 6).

Figure 6: Vitamin K2 and periodontal disease:



8. Clinical and Therapeutic Considerations

The growing body of evidence regarding the systemic and oral benefits of vitamin K2—particularly in its menaquinone-7 (MK-7) form—has sparked interest in its integration as a therapeutic adjunct in dentistry. However, for its safe and effective clinical implementation, factors such as bioavailability, recommended dosages, potential interactions, and at-risk populations must be considered.

8.1. Recommended Dosages and Safety

Although there is no specific Recommended Daily Intake (RDI) for vitamin K2 distinct from K1, an effective dose for bone and cardiovascular functions is estimated to range between 90 and 180 µg/day of MK-7【39】. This form has a long half-life and high bioavailability, allowing for once-daily dosing.

Several studies have confirmed that vitamin K2, even at high doses (up to 360 µg/day), does not present known toxicity in healthy individuals【40】. However, caution is advised in patients taking vitamin K antagonists such as warfarin, as K2 may interfere with their anticoagulant effects【41】.

8.2. Available Forms and Absorption

Vitamin K2 can be obtained from the diet (e.g., fermented cheeses, natto, egg yolk) or as a supplement in the form of MK-4 or MK-7. MK-7 is preferred for systemic use due to its greater stability and half-life.

It is recommended to consume vitamin K2 with dietary fat to optimize intestinal absorption, given its fat-soluble nature【6】.

8.3. Synergy with Vitamin D3 and Calcium

The combination of vitamin K2 with vitamin D3 has shown synergistic effects on bone and dental health. Vitamin D3 enhances calcium absorption and stimulates osteocalcin synthesis, while K2 activates osteocalcin through carboxylation, directing calcium to bones and teeth instead of soft tissues【26】.

Therefore, in patients receiving D3 and calcium supplementation, co-administration of vitamin K2 is advisable to prevent ectopic calcification and optimize dentoalveolar mineralization.

8.4. Clinical Applications in Dentistry

Potential clinical applications of vitamin K2 in dentistry include:

Support in patients with periodontal disease or alveolar bone loss.

Adjunctive therapy in dental implant osseointegration.

Complementary use in orthopedic and orthodontic therapies during growth.

Modulation of caries risk in patients with demineralizing diets or enamel hypoplasia.

Use in pulp or dentin regeneration protocols in conjunction with emerging biological therapies.

Although clinical trials in dentistry are still lacking, the physiological rationale, preclinical studies, and extrapolations from bone medicine support its evaluation in future dental research.

9. Discussion

The literature review suggests that vitamin K2 plays multiple relevant roles in oral physiology—from its involvement in bone mineralization and inflammatory modulation to its possible impact on dental tissue formation and repair. However, most available studies are preclinical, observational, or extrapolated from the fields of bone or cardiovascular medicine.

9.1. Need for Controlled Clinical Trials

Despite strong biological plausibility supported by well-described mechanisms—such as the activation of Gla proteins (osteocalcin, MGP) and synergy with vitamin D3—there remains a significant gap in direct clinical evidence within dentistry. Most beneficial effects have been reported in animal models or cell cultures.

It is therefore essential to develop controlled clinical trials and cohort studies, especially in the following contexts:

Chronic periodontitis, evaluating progression under K2 supplementation.

Osseointegration of dental implants, measuring quality and speed of peri-implant bone formation.

Orthodontics and pediatric dentistry, assessing K2's impact on maxillary development.

Incipient caries, analyzing its role in remineralization and pulpodentinal responses.

Validation of these effects through rigorous study designs and representative populations would allow for the potential clinical inclusion of vitamin K2 as part of preventive or therapeutic dental strategies.

9.2. Relationship with Ancestral Dietary Patterns

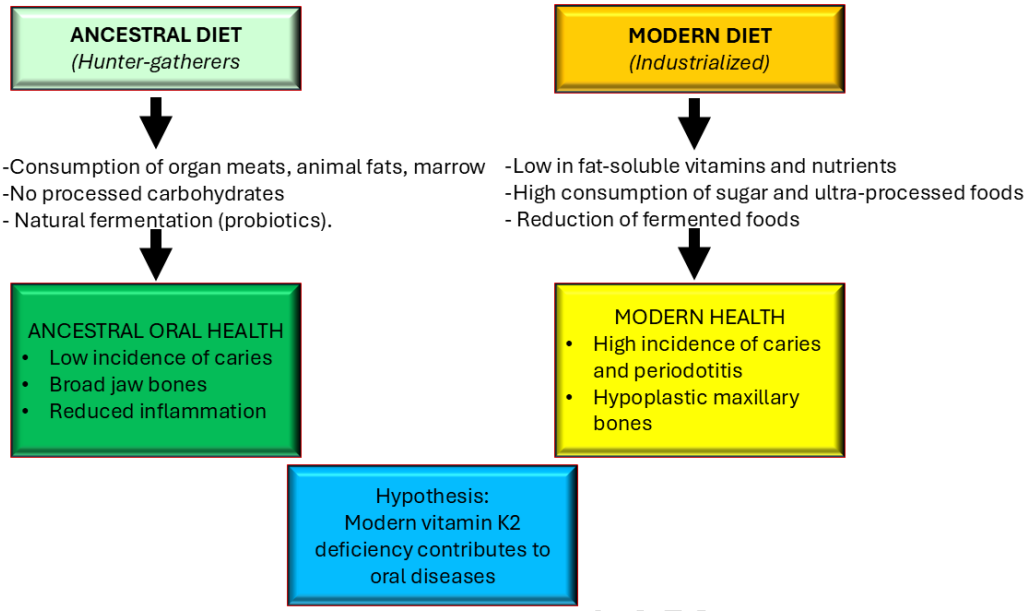
An important aspect to consider is the difference in oral health between modern populations and ancestral groups, particularly hunter-gatherers. Various anthropological and bioarchaeological studies have documented a low incidence of caries and periodontal disease in pre-agricultural populations, even in the absence of modern oral hygiene【42】.

One hypothesis, proposed by authors such as Weston A. Price, attributes this difference in part to the higher nutritional density of ancestral diets, which were rich in fat-soluble vitamins like A, D, and K2—found in organ meats, bone marrow, wild game, and animal fats【24】. These foods were abundant in menaquinones, especially MK-4, the active form of K2 present in animal tissues.

In contrast, modern diets—characterized by ultra-processed foods low in natural animal fats and fermented products—may contribute to subclinical vitamin K2 deficiencies, promoting demineralization, oral dysbiosis, and chronic inflammation.

This comparison underscores the need to revisit ancestral nutrition as a reference model for oral health and to systematically investigate how chronic K2 deficiency may contribute to modern oral pathologies. Figure 7 compares both types of nutrition..

Figure 7: Impact of ancestral and modern nutrition on oral health.



9.3. Implications for Public Health and Education

If its benefits are confirmed, vitamin K2 could become part of integrated oral health strategies at both preventive and therapeutic levels. This would include:

• Nutritional education focused on natural sources of K2.
• Food fortification in at-risk populations.
• Targeted supplementation in specific clinical contexts (orthodontics, periodontics, implantology).

As with vitamin D3, the approach to this vitamin should evolve beyond its classical role in coagulation, toward a systemic and interdisciplinary perspective that incorporates its impact on bone, inflammation, microbiota, and mineral metabolism.

9.4 Study Limitations

This work constitutes a narrative review of the literature, which inherently carries certain limitations associated with this type of design. First, neither a systematic review nor a meta-analysis was conducted, meaning that the selection of articles may have been subject to search or interpretation bias. Although efforts were made to include the most relevant and up-to-date sources, it is possible that some pertinent studies were omitted—particularly those published in languages other than English or Spanish, or those indexed in databases not consulted.

Second, much of the available evidence on the role of vitamin K2 in dentistry originates from preclinical studies, including animal models and cell cultures. While these studies provide physiological foundations and plausible mechanisms, their direct clinical applicability in humans has yet to be sufficiently validated. Therefore, many of the associations described should be interpreted with caution until more robust evidence becomes available, ideally from randomized controlled trials and cohort studies.

Furthermore, extrapolations from research in bone or cardiovascular health to the dental field may not fully capture the specific characteristics of the oral environment, such as the microbiota, pulpal physiology, or masticatory forces. Likewise, the heterogeneity in the forms of vitamin K2 used in studies (MK-4 vs. MK-7), their dosages, routes of administration, and treatment durations limits the ability to establish clear and standardized clinical recommendations.

Lastly, economic, regulatory, and availability-related aspects of vitamin K2 supplementation were not addressed in detail, which may represent a barrier to its practical implementation in certain clinical or population-based contexts.

10. Conclusions

This narrative review concludes that vitamin K2, in its menaquinone-4 (MK-4) and menaquinone-7 (MK-7) forms, plays key roles in various aspects of oral health, beyond its well-known function in blood coagulation. Its central mechanism—activation of Gla proteins—links K2 to bone mineralization, inflammation modulation, and dentin formation, offering new perspectives in both clinical and preventive dentistry.

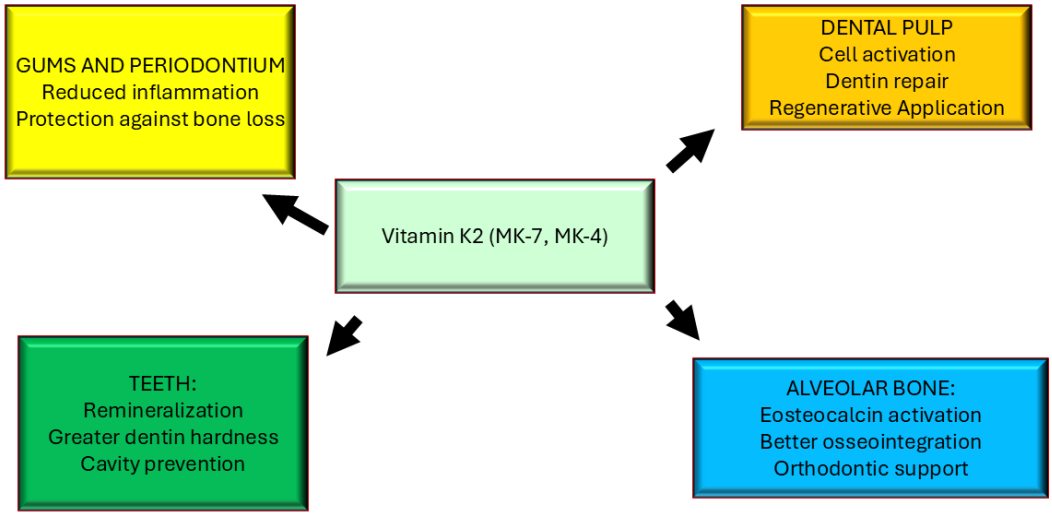
10.1. Main Findings

• Vitamin K2 activates proteins such as osteocalcin and

Matrix Gla Protein, regulating calcium incorporation into mineralized tissues and preventing its accumulation in soft tissues.
• It plays a significant role in the formation and remodeling of alveolar bone, positioning it as a potential adjunct in periodontics, implantology, and maxillary orthopedics.
• Its presence in dentin and influence on pulp cell differentiation suggest involvement in tissue repair and regeneration processes.
• In caries prevention, it may improve dentin structural quality and promote remineralization, especially in synergy with vitamin D3.
• Epidemiological and anthropological evidence suggests that ancestral diets rich in K2 may have contributed to better oral health compared to the modern industrialized diet.

Figure 8 summarizes the potential effects of vitamin K2 in dentistry.

Figure number 8: Summary of the effects of Vitamin K2 in Dentistry:



10.2. Clinical Implications

Although preclinical evidence is promising, there is an urgent need for controlled clinical trials to confirm the benefits of K2 supplementation in specific dental contexts. In the meantime, preventive strategies could benefit from promoting natural dietary sources of K2 (fermented foods, fatty animal products), especially in populations at risk of bone or dental demineralization.

10.3. Future Research Directions

Clinical trials in periodontitis, caries, implantology, and maxillary growth.

Cohort studies correlating serum K2 levels with oral health indicators.

Development of bioactive dental biomaterials incorporating vitamin K2 in their formulation.

Evaluation of the role of K2 in dental pulp homeostasis and its potential in regenerative therapies.

Statement of interest

The author declares that **there are no conflicts of interest** of a financial, personal, academic, or other nature that could have inappropriately influenced the conduct of this work, the interpretation of the data, or the preparation of the manuscript.

The author further states that **no financial, material, or institutional support** has been received from any public or private entity that could generate bias or affect the objectivity of the results and conclusions presented herein.

This declaration is made in accordance with international standards of transparency and ethical conduct in scientific publishing.

Disclaimer

This publication has not been subjected to peer review. It responds to the author's academic need to examine the current state of the art on this particular topic.

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