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MECHANISM OF DENTAL ENAMEL DEMINERALIZATION: THE ROLE OF ORGANIC ACIDS, PH, AND HYDROXYAPATITE DISSOLUTION

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ABSTRACT
Dental enamel demineralization is the initiating physicochemical event in the development of a carious lesion. This structured narrative review synthesizes evidence on the sequence linking carbohydrate metabolism in dental biofilm, organic-acid production, local pH decline, loss of mineral saturation, and dissolution of enamel apatite. Human enamel is a highly mineralized, carbonated apatite tissue that remains in dynamic equilibrium with calcium and phosphate in saliva and plaque fluid. Acidogenic and aciduric members of the dental biofilm convert fermentable carbohydrates to organic acids, creating repeated periods of undersaturation at the tooth surface. Although an enamel critical pH near 5.5 is commonly cited, the threshold is not a universal constant because it depends on calcium, phosphate, fluoride, and mineral composition. Experimental evidence further indicates that dissolution kinetics depend not only on pH but also on solution saturation, acid activity, acid identity, exposure time, and enamel architecture. At matched saturation and acid activity, lactic acid can produce faster enamel mineral loss than acetic or propionic acid, while time-lapse imaging demonstrates anisotropic lesion progression governed by enamel microstructure. Early mineral loss can be reversed when the environment becomes supersaturated again. Saliva contributes buffering, clearance, and mineral ions; fluoride primarily inhibits demineralization and accelerates remineralization at apatite surfaces, whereas calcium-phosphate systems provide additional mineral precursors. The evidence supports prevention strategies that reduce the frequency of acid challenges and maintain favorable oral-fluid chemistry rather than treating pH 5.5 or any single bacterial species as an absolute determinant of caries.

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Introduction

Dental caries is a biofilm-mediated, diet-modulated, dynamic disease in which repeated episodes of mineral loss and mineral gain occur at the tooth surface. Its earliest hard-tissue change is not an abrupt destruction of enamel but a shift in the chemical equilibrium between enamel mineral and the surrounding oral fluids. Enamel is approximately 96% mineral by weight and consists predominantly of substituted, carbonated apatite rather than perfectly stoichiometric hydroxyapatite. This distinction is important because substitutions within biological apatite influence crystal solubility and make enamel dissolution

more chemically complex than the dissolution of an ideal laboratory crystal (Abou Neel et al., 2016; Robinson et al., 2000).

The modern ecological view of caries also requires caution against assigning the disease to a single microorganism. Dental biofilm contains a diverse community whose composition and metabolic activity change in response to environmental conditions. Frequent exposure to fermentable carbohydrate favors organisms and metabolic pathways that are both acidogenic and aciduric, thereby increasing the duration and intensity of low-pH conditions. Streptococcus mutans can contribute to this ecology, but it is one member of a broader dysbiotic community rather than a sufficient cause by itself (Takahashi & Nyvad, 2011).

The mechanistic sequence that links this ecological shift to enamel mineral loss can be organized into three interdependent stages: production and transport of organic acids, reduction of plaque-fluid and tooth-surface pH with loss of mineral saturation, and dissolution of apatite crystallites. These stages are influenced by salivary flow and buffering, calcium and phosphate concentrations, fluoride availability, lesion diffusion pathways, enamel structure, and the frequency and duration of dietary challenges. The purpose of this review is to explain that sequence at a physicochemical level, critically compare the evidence that supports it, and identify implications for prevention and remineralization.

Methods

A structured narrative literature review was used because the objective was mechanistic synthesis rather than estimation of a pooled treatment effect. Relevant literature was identified through targeted searches of PubMed/MEDLINE and publisher databases, supplemented by backward citation searching from key papers. Search concepts included combinations of “enamel demineralization,” “hydroxyapatite dissolution,” “critical pH,” “dental biofilm pH,” “organic acid enamel,” “lactic acid enamel,” “saliva remineralization,” “fluoride mechanism caries,” and “amorphous calcium phosphate enamel.” The literature set was updated through August 2026.

Priority was given to peer-reviewed primary experimental studies that directly measured mineral loss, lesion depth, microhardness, or dissolution kinetics, together with authoritative mechanistic and clinical reviews. Seminal studies published before 2000 were retained when they provided foundational kinetic or chemical evidence that remained directly relevant. Educational webpages and duplicate or substantially overlapping secondary publications were not used as independent evidence. Because the search was iterative and designed for a narrative review, no PRISMA flow diagram, pooled effect estimate, or formal risk-of-bias score was generated. Accordingly, conclusions are framed as a mechanistic synthesis of the included literature rather than as a systematic estimate of the entire evidence base.

Mechanistic Basis of Enamel Demineralization

Enamel Mineral and the Mineral-Solution Equilibrium

The conventional formula $Ca_{10}(PO_4)_6(OH)_2$ is useful for representing ideal hydroxyapatite, but human enamel is a substituted biological apatite containing carbonate and other ions. Its crystallites are organized within enamel rods and interrod enamel, with water-filled microscopic pathways between crystallites. These pathways allow diffusion of acids and dissolved ions even though mature enamel is acellular and highly mineralized (Abou Neel et al., 2016; Robinson et al., 2000).

At the tooth surface, the direction of mineral exchange depends on the degree of saturation of plaque fluid or saliva with respect to enamel mineral. When the surrounding fluid is saturated or supersaturated, net dissolution is not thermodynamically favored and mineral may precipitate onto residual crystal surfaces. When acid production lowers phosphate activity and the solution becomes undersaturated, the chemical driving force reverses and apatite dissolves. Thus, pH is important because it changes the distribution of phosphate species and the saturation state; pH does not act as an isolated variable independent of calcium, phosphate, fluoride, and mineral composition (Dawes, 2003; Margolis et al., 1999).

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Organic-Acid Production in Dental Biofilm

Fermentable carbohydrates entering dental biofilm are metabolized through microbial glycolytic and related pathways. The acids generated during this metabolism reduce extracellular pH and create selective pressure favoring acid-tolerant organisms. The resulting ecological feedback can increase both the capacity of the biofilm to generate acid and its ability to remain metabolically active under acidic conditions (Takahashi & Nyvad, 2011). Frequent carbohydrate intake is therefore mechanistically important because it increases the number of acidification episodes and reduces the interval available for salivary neutralization and mineral recovery.

Lactic acid is commonly prominent during rapid carbohydrate fermentation, but plaque contains multiple organic acids, including acetic and propionic acids. Weak acids can exist in both dissociated and undissociated forms, and their behavior within plaque and porous enamel is not determined by bulk pH alone. Margolis et al. (1999) demonstrated this point experimentally. Human enamel sections were exposed to partially saturated acid solutions while pH, degree of saturation, and acid activity were controlled. In the direct acid comparison performed at pH 4.3, demineralization rates were similar in acetic and propionic acid solutions but were higher in lactic acid at the same enamel saturation and acid activity. The result does not establish that lactic acid is universally "more cariogenic" in vivo; rather, it shows that acid-specific interactions can modify dissolution kinetics after major thermodynamic variables are controlled.

pH Decline and the Critical-pH Concept

After a carbohydrate challenge, plaque pH typically falls rapidly as acids accumulate and then recovers more gradually as substrates are cleared and acids are buffered or metabolized. Repeated excursions into an undersaturated state constitute the chemical episodes during which net enamel mineral loss can occur. This dynamic pattern is more informative than a single resting-pH measurement because caries reflects the cumulative balance of multiple demineralization and remineralization periods (Featherstone, 2004; Takahashi & Nyvad, 2011).

A value near pH 5.5 is often used as a practical approximation for the "critical pH" of enamel. However, the term should not be interpreted as a fixed biological constant. Dawes (2003) emphasized that the pH at which oral fluid becomes unsaturated with respect to enamel varies inversely with the calcium and phosphate concentrations of that fluid. Fluoride and the variable composition of biological apatite can shift the equilibrium further. Therefore, one plaque sample may remain mineral-saturated at a pH at which another sample is already undersaturated. The clinically relevant question is not simply whether pH crossed 5.5, but how far the fluid moved from saturation, for how long, and how frequently the challenge was repeated.

Hydroxyapatite Dissolution at the Crystal Surface

Acidification promotes protonation of phosphate and hydroxyl groups associated with apatite. As phosphate species shift toward HPO_4^{2-} and $H_2PO_4^-$, the activity of PO_4^{3-} falls and the surrounding solution becomes less saturated with respect to enamel mineral. The equilibrium then shifts toward dissolution, releasing calcium and phosphate species from the crystal surface. A simplified reaction for ideal hydroxyapatite can be represented as $Ca_{10}(PO_4)_6(OH)_2 + 8H^+ \rightarrow 10Ca^{2+} + 6HPO_4^{2-} + 2H_2O$, although real enamel dissolution involves substituted apatite, multiple aqueous calcium-phosphate species, diffusion, and possible reprecipitation (Robinson et al., 2000).

This chemistry corrects a common oversimplification: hydrogen ions do not merely "push calcium out" of the lattice by direct one-for-one displacement. Protonation changes the solution chemistry and mineral saturation, and mineral ions are subsequently released as the system approaches a new equilibrium. Margolis et al. (1999) showed that enamel mineral loss increased as pH decreased and as the degree of saturation decreased, demonstrating that the magnitude of undersaturation is a major kinetic determinant.

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Enamel Structure, Lesion Pattern, and Duration of Acid Exposure

Enamel does not dissolve uniformly. Its crystallites are organized into rods, interrod regions, and larger decussating structures such as Hunter-Schreger bands. Using time-lapse microradiography and polarized-light imaging, Harper et al. (2021) demonstrated that mineral loss progressed anisotropically and was influenced by intrinsic enamel architecture. In their acid model, progression from the surface toward dentin was faster than lateral progression, and demineralization preferentially followed Hunter-Schreger bands once the lesion front reached them. These findings support a diffusion-reaction model in which local structure modifies the route and rate of mineral loss.

A relatively intact surface layer can coexist with substantial subsurface mineral loss. Margolis et al. (1999) observed well-defined surface layers in lesions produced at pH 4.3 and 5.0, whereas lesions formed at pH 6.0 lacked an apparent surface layer under their experimental conditions. Such observations show that early caries is not equivalent to uniform surface etching. Selective dissolution, diffusion gradients, and reprecipitation can preserve the outer surface while mineral is lost beneath it (Robinson et al., 2000).

Exposure time is also important. Ersen et al. (2025) reported, in an in vitro human-enamel model, that longer demineralization periods were associated with increasing lesion depth and decreasing surface microhardness. Their design does not reproduce the fluctuating chemistry of the oral cavity, but it reinforces the general principle that duration of an acid challenge changes the magnitude of tissue damage. In vivo, this duration is strongly influenced by salivary clearance and buffering.

Remineralization and Protective Oral-Fluid Factors

Saliva

Saliva is central to the reversal of early mineral loss. Its protective functions include dilution and clearance of fermentable substrates and acids, bicarbonate-dependent buffering, contribution to the acquired pellicle, and maintenance of calcium and phosphate in solution. When acid production declines and pH recovers, these ions can support supersaturation and redeposition onto partially dissolved crystals (Dawes et al., 2015). This is why salivary dysfunction increases caries susceptibility even when enamel composition is unchanged.

The demineralization-remineralization balance is therefore temporal. A brief episode of undersaturation does not inevitably produce a permanent lesion if sufficient recovery follows. Repeated or prolonged acid challenges, especially when salivary flow is low, can shift the cumulative balance toward mineral loss. Conversely, preserving or stimulating salivary flow supports both chemical neutralization and mineral availability (Featherstone, 2004).

Fluoride

Fluoride should not be described simply as converting bulk enamel into fluorapatite. Its principal anticaries effects are topical and occur at the mineral-fluid interface. During an acidic challenge, low concentrations of fluoride associated with apatite surfaces can reduce mineral dissolution. When pH rises again, fluoride increases the driving force for precipitation of less soluble fluoridated apatite and accelerates remineralization. Higher topical fluoride exposures can also create calcium-fluoride-like reservoirs that release fluoride during subsequent acidic challenges (Buzalaf et al., 2011).

This mechanism explains why regular exposure to topical fluoride is effective even though the fluoride concentration incorporated throughout the enamel crystal lattice is relatively small. The important clinical objective is to maintain biologically useful fluoride availability at the tooth-biofilm-fluid interface during repeated cycles of acidification and recovery.

Calcium-Phosphate Remineralizing Systems

Calcium-phosphate systems act through a different but complementary principle: they increase the availability of calcium and phosphate precursors that can participate in mineral reprecipitation. Amorphous calcium phosphate (ACP) is of interest because it can serve as a transient precursor to apatite, but its

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instability in aqueous environments requires stabilization or delivery strategies. Yan et al. (2022) reviewed approaches including casein phosphopeptides, amelogenin-related systems, polymers, and other stabilizers designed to maintain ACP in a reactive state.

These agents should not be presented as mechanistically interchangeable with fluoride or as established substitutes for fluoride-based prevention. A recent systematic review of randomized trials evaluating CPP-ACP and bioactive glass for early enamel lesions found remineralizing potential but substantial heterogeneity and generally low-to-moderate certainty, with evidence insufficient to replace fluoride as the standard preventive therapy (Mishra et al., 2026). Their most defensible role is therefore as adjunctive or context-specific strategies rather than universal alternatives.

Comparative Synthesis and Critical Appraisal

The strongest mechanistic evidence in the literature comes from controlled physicochemical and imaging studies in which pH, acid activity, degree of saturation, or exposure time can be manipulated independently. Margolis et al. (1999) demonstrated that enamel dissolution kinetics depend simultaneously on pH, mineral saturation, and acid species. Harper et al. (2021) extended the mechanistic picture by showing that enamel architecture introduces directional differences in lesion progression. These studies provide direct evidence for causal chemical and structural determinants, but they remain laboratory models.

Clinical translation is more complex because oral biofilm is spatially heterogeneous and saliva continuously changes the local concentrations of acids, buffers, calcium, phosphate, and fluoride. Consequently, it would be inappropriate to infer a patient's caries risk from acid identity or a single pH threshold alone. Likewise, the observation that lactic acid produced faster mineral loss than acetic or propionic acid under matched in vitro conditions should be interpreted as evidence of acid-specific kinetics, not as a basis for assigning dietary recommendations to a particular acid species without clinical validation.

The evidence also clarifies the relationship between remineralizing interventions. Fluoride, calcium-phosphate systems, salivary support, and dietary modification act at different points within the same chemical cycle. Fluoride modifies dissolution and reprecipitation at apatite surfaces; calcium-phosphate agents increase mineral-ion availability; saliva governs buffering, clearance, and supersaturation; and dietary behavior determines the frequency of substrate-driven acid challenges. A mechanism-based prevention strategy should therefore combine these approaches according to caries risk rather than treating them as interchangeable products.

Table 1

Key Variables Governing Enamel Demineralization

Variable	Evidence-based interpretation	Representative source
Biofilm acid production	Fermentable carbohydrate drives acid production and selects for an acidogenic/aciduric ecology; no single species is sufficient to explain caries.	Takahashi & Nyvad (2011)
pH and saturation	A pH near 5.5 is only an approximation. The actual dissolution threshold depends on calcium, phosphate, fluoride, and mineral composition.	Dawes (2003)
Acid identity	At matched enamel saturation and acid activity at pH 4.3, lactic acid produced faster mineral loss than acetic or propionic acid; acetic and propionic rates were similar.	Margolis et al. (1999)
Enamel structure	Mineral loss is anisotropic; intrinsic rod architecture and Hunter-Schreger bands influence lesion progression.	Harper et al. (2021)
Exposure time	Longer sustained acid exposure increases lesion depth and reduces surface microhardness in vitro.	Ersen et al. (2025)

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Variable	Evidence-based interpretation	Representative source
Remineralization	Recovery requires a return toward supersaturation. Saliva supplies buffering and mineral ions; fluoride inhibits dissolution and accelerates reprecipitation.	Dawes et al. (2015); Buzalaf et al. (2011)

Note. The table summarizes mechanistic evidence and does not imply that any single variable independently determines clinical caries risk.

Clinical Implications

The mechanistic evidence supports prevention strategies aimed at reducing the cumulative time during which enamel is exposed to an undersaturated environment. Reducing the frequency of fermentable-carbohydrate intake can reduce repeated acidification episodes; maintaining normal salivary flow supports clearance, buffering, and mineral availability; and regular topical fluoride exposure increases resistance to demineralization while promoting remineralization. These measures address the chemistry of the disease rather than relying solely on removal of a named microorganism (Buzalaf et al., 2011; Dawes et al., 2015; Featherstone, 2004).

For early noncavitated lesions, preservation of the surface layer is clinically important because residual mineral provides a scaffold for remineralization. Once structural integrity is lost and cavitation develops, simple mineral replacement becomes less capable of restoring original anatomy. This distinction supports early detection and nonoperative management of lesions that remain cleansable and structurally intact.

Limitations of the Evidence

Several limitations constrain interpretation. First, many mechanistic studies use sectioned or polished enamel exposed to simplified acid solutions, which cannot reproduce the spatial heterogeneity, microbial metabolism, salivary flow, pellicle, and intermittent dietary challenges of the oral cavity. Second, the frequently cited critical pH is context dependent; reporting it as an absolute threshold can obscure clinically important variation in mineral saturation. Third, evidence on newer calcium-phosphate systems remains heterogeneous, and in vitro remineralization does not automatically predict superior clinical outcomes. Finally, this paper is a structured narrative review rather than a systematic review; its purpose is to integrate mechanisms, not to establish exhaustive effect estimates or formal certainty ratings for every intervention.

These limitations also define useful research directions. Experimental work should increasingly combine controlled mineral chemistry with realistic biofilm and salivary conditions, and clinical studies should connect measurable physicochemical variables—such as plaque-fluid saturation, acid-challenge duration, and fluoride availability—to lesion progression over time. Such designs would strengthen the bridge between dissolution kinetics and patient-level outcomes.

Conclusion

Dental enamel demineralization is best understood as a dynamic mineral-solution process produced by the interaction of biofilm metabolism, oral-fluid chemistry, and enamel structure. Fermentable carbohydrates support acid production within a dysbiotic biofilm; the resulting fall in pH reduces phosphate activity and can make plaque fluid undersaturated with respect to enamel; and this undersaturation drives dissolution of substituted apatite crystals. The rate of mineral loss is modified by the degree of saturation, acid activity and identity, exposure duration, diffusion pathways, and enamel architecture.

The same framework explains why early lesions can recover. When acid production decreases and pH rises, saliva restores buffering and provides calcium and phosphate, while fluoride inhibits further dissolution and favors precipitation of less soluble fluoridated mineral. Calcium-phosphate technologies may supplement, but not automatically replace, fluoride. Effective prevention therefore depends on shifting

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repeated demineralization-remineralization cycles toward net mineral gain through dietary control, salivary support, fluoride, and appropriate adjuncts.

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