

Biomimetic Materials in Minimally Invasive Dentistry: Advances, Clinical Applications and Future Directions: A Narrative Review

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Abstract

Biomimetic dentistry represents a shift toward minimally invasive, biologically driven restorative care. Dental caries remains highly prevalent and are often treated with invasive techniques that compromise healthy tooth structure. This review highlights biomimetic materials such as glass ionomer cements, nano-hydroxyapatite, bioactive glass and calcium phosphate systems which promote a remineralization and a new era in the way clinicians practice dentistry. The reviewed studies showed the application in minimally invasive dentistry, especially in atraumatic restorative treatment. These Biomimetic Materials continue to show tissue preservation and promote restoration longevity. Although the findings are promising, more clinical studies are still needed.

Keywords: Biomimetic; Restorative; Remineralization; Demineralization; Glass Ionomer; Minimally Invasive; Composite; Fluoride; Bioactive

Biomimetic Dentistry

Dental caries has become the most prevalent disease worldwide, substantially affecting the most disadvantaged and underdeveloped regions, especially school-age children [1,2]. Traditional restorative techniques, such as invasive drilling and amalgam fillings, tend to increase dental anxiety. In addition, they involve the unnecessary removal of healthy tooth structure and cannot be performed in poor- resource settings. Patients may experience distress when faced with these traditional methods of caries restoration [1]. The principles of Minimally Invasive Dentistry (MID) can be applied to decrease dental anxiety and reduce patient stress levels [2].

This patient-centered philosophy, which prioritizes prevention, early caries detection and tooth preservation, has been driven by these challenges. MID proposes methods that are more friendly to the biological environment [3]. Unlike traditional restorative approaches that focus on the complete removal of decayed tissue, Minimal Intervention Dentistry (MID) has emerged as a preventive and conservative model [3]. This approach is based on a deeper understanding of the biology of dental caries. The philosophy of MID seeks to minimize operative trauma. To this end, it emphasizes early detection of caries, enamel remineralization and selective repair of affected tissues [4]. Instead of opting for extensive restorations, MID prioritizes chemical disinfection and control of dental biofilm. In this way, MID is emerging as a more conservative alternative that preserves healthy tooth structure, which is essential for maintaining long-term oral health [4,5].

Minimally invasive dentistry is based in three essential principles: early detection, prevention and intervention or treatment [5]. Early detection consists in using advanced diagnostic tools such as digital X-rays, laser fluorescence and transillumination, to detect cavities and other dental problems in their early stages [6]. Prevention focuses on patient education and to adopt good dental hygiene habits and solidify preventive measures, like, fluoride treatments and sealants. Finally, Intervention focuses on therapeutic methods that aim to preserve as much healthy tooth structure as possible [6].

The purpose is to study and replicate biological patterns to create solutions that the organism recognizes as its own, thus improving biocompatibility [5]. Among the materials that mimic enamel a hard, highly mineralized and wear-resistant tissue we have biomimetic hydroxyapatite and self-assembling peptides [7]. Materials that mimic dentin, which acts as the mechanical and biochemical support for enamel, have a more complex structure due to their high organic content. These include biomimetic composites and adhesives, collagen remineralization and bilayer systems such as bi-layered. All these results in multiple clinical benefits, such as improved adhesion, longevity and tissue regeneration [7].

Materials and Biomimetic Methods in Dentistry

The Biomimetic goal is to develop restorative materials that can restore the biomechanics of the natural tooth structure.

a. Glass Ionomer

It is considered as biomimetic materials because they have adhesiveness to tooth structure the same coefficient of thermal expansion as that of tooth structure, bond adhesively to enamel and dentin, have ability to release ions is responsible for the development of long-term durable bonds at the tooth versus restoration interface, its tensile strength is poor and is not advocated in areas of high occlusal stress and force concentration [12]. It releases fluoride over a prolonged period. The use of bioactive composites in restorative dentistry has changed from inert restorative materials to ones that actively promote tissue regeneration and reduce secondary caries [8]. Motivating the remineralization of dematerialized tooth structures and triggering the formation of hydroxyapatite, these composites are designed to release therapeutic ions like calcium, phosphate and fluoride, improving the marginal seal integrity and strengthening the tooth restoration interface [14].

The Bioactive Components (BAGs) and Amorphous Calcium Phosphate (ACP) facilitate this biomineralization, while the incorporation of antimicrobial agents like quaternary ammonium methacrylate and silver nanoparticles provide intrinsic bacterial inhibition. Nano-Hydroxyapatite (HA) particles have been added to GIC to produce GIC-HA hybrids, which showed improved release of fluoride ions and improved mechanical and antibacterial properties This complex bioactivity prolonging their lifespan by lowering microleakage and secondary decay but also promotes pulp vitality and general oral health [11].

b. Nano-Hydroxyapatite

This releases fluoride ions and increases the antibacterial properties, reducing the risk of secondary caries, ultimately contributing to the longevity and clinical success of the restoration. The nano-hydroxyapatite and calcium phosphate into composites resins enhances mechanical properties and reduces polymerization shrinkage [13]. Nanotechnology transforms biomimetic restorative dentistry by enabling the precise manipulation of materials at the nanoscale to simulate the natural tooth's involute structure and function. This nanostructured approach allows for superior aesthetics in translucency and light copying the properties of the enamel and its distribution can be optimized to mimic the natural restoration. However, the Polyvinyl Phosphonic Acid (PVPA) is one of the polyelectrolytes that are used [11]. Its biomimetic property is related to its ability to form nanocrystals that stimulate intrafibrillar and interfibrillar remineralization at the resin-dentin interface, to promote the remineralization of demineralized dentin, preventing secondary caries. Nanoparticles actively release calcium and phosphate ions, additionally, the integration of antimicrobial nanoparticles impregnated in these materials inhibits biofilm formation [8].

c. Bioactive Glass (BAG)

BAG has showed an important regenerative capacity for repairing hard tissues due to the ability to release ions for apatite crystals formation that mimics the natural apatite found in bone and dental hard tissues when BAG contacts water or saliva, it releases calcium, sodium and phosphorous ions, which promotes remineralization at surfaces of dental tissues [12]. Moreover, the calcium phosphate precipitates occlude the dentinal tubules and prevent movement of dentinal fluids. BAG can also be used in pulp capping procedures since they are non-cytotoxic and were reported to promote the formation of reparative dentin [9,10].

d. Casein Phosphopeptide–Amorphous Calcium Phosphate (CPP-ACP)

Precursor in the biological formation of hydroxyapatite. CPP-ACP has substantial potential to prevent enamel demineralization and enhance enamel and dentine remineralization [9,10].

e. Calcium Hydroxide (CaOH₂)

Are responsible for its antibacterial properties due to the alkaline pH and hard tissue regeneration effects. and it may aid in dissolving necrotic tissue remnants, bacteria. It also could induce tertiary dentin formation [13].

f. CaPO₄

Biocompatible as a material for bone replacement is its chemical resemblance to the mineral elements of mammalian teeth and bones and non-toxic and exhibits bioactive behavior while assimilating into biological tissue via the same processes present in healthy bone remodeling [14].

Clinical Applications and Advantages in Restorative Dentistry

Restorative dentistry aims to preserve healthy tooth structure while providing durable and esthetic restorations. One important advancement in this area is the use of magnification devices. According to Bud, et al., Dental Operating Microscopes (DOM) significantly improve precision and visualization compared to loupes [15].

While loupes are more commonly used due to affordability and ease of use, they have limitations such as disturbances caused by small head movements and the need to adjust magnification. In contrast, DOM allows minimal adjustment, reduces postural deviations and facilitates better evaluation of restorations. The use of DOM supports minimally invasive dentistry principles, encouraging conservative handling of dental tissues, enhancing treatment quality and improving patient outcomes [16].

Another example of a minimally invasive approach is the digitally guided direct composite injection technique, described by Araujo, et al. This technique uses a bi-layer clear mini-index for the management of extensive occlusal caries in a pediatric patient [17]. The digital guidance allows precise placement of composite resin, reproducing accurate occlusal anatomy while preserving healthy tooth structure. This case demonstrates the integration of digital tools in pediatric restorative procedures, improving precision, predictability and overall quality of Class I restorations [16].

Together, these advancements illustrate how clinical applications combining magnification and digital guidance can enhance restorative dentistry by improving precision, preserving dental tissues and supporting minimally invasive approaches [15].

Non-Carious Cervical Lesions

Non-Carious Cervical Lesions (NCCLs) are defects at the cervical region of teeth not caused by caries. They are frequently associated with abrasion, erosion, abfraction and attrition and may occur alongside gingival recession, forming complex combined defects. NCCLs present a clinical challenge due to their multifactorial etiology and the need for conservative, minimally invasive treatment [17]. Recent evidence supports several restorative and clinical strategies

Material Selection

Systematic reviews and clinical trials show that both Glass Ionomer Cement (GIC) and Composite Resin (CR) provide satisfactory restoration of NCCLs, with no significant differences in clinical performance, retention or longevity [18]. Resin-Modified Glass Ionomer Cements (RMGIC) enriched with bioactive fillers also offer remineralization potential and may enhance the preservation of affected dentin, supporting minimally invasive restorative approaches.

Combined Lesions Management

In cases where NCCLs coexist with gingival recession, treatment decisions must consider both soft tissue and tooth structure. Mild lesions can be managed with standard root coverage procedures alone, while more advanced lesions may require combined restorative and surgical approaches, including composite restorations and soft tissue grafts [19].

Management of Deep Caries: Stepwise Excavation Technique

A conservative approach for treating deep carious lesions that avoids pulp exposure and preserves tooth structure [19]. The procedure involves two or more stages:

1. Initial Partial Caries Removal:

Soft, infected dentin is removed, leaving affected dentin near the pulp to prevent exposure [22]. Temporary restoration: A biocompatible material (e.g., calcium hydroxide or glass ionomer) is placed to promote dentin remineralization and allow pulp healing [20].

2. Second Excavation (after several months):

Residual caries is removed and a permanent restoration is placed [22].

Bioactive Sealants

E-Sealant, a novel autologous fibrin sealant derived from Plasma Rich in Growth Factors (PRGF), demonstrates excellent biological and adhesive properties. *In-vitro*, it promotes cell adhesion, proliferation and migration, outperforming commercial fibrin sealants [21]. *In-vivo*, it ensures strong graft adhesion, tissue integration, minimal inflammation and reduced fibrosis, supporting regenerative healing. These characteristics make E-Sealant a promising bioactive sealant for applications requiring tissue preservation and regeneration [21].

Process of Demineralization and Remineralization with Biomimetic Materials

The process of dental demineralization and remineralization is like a cycle that varies constantly according to the metabolism of carbohydrates in bacterial plaque. This process begins when sugars decompose, generating acids that reduce the plaque pH below the critical level of 5.5, dissolving the enamel apatite crystals. Although fluoride has been a standard tool to promote remineralization and create fluorapatite (a mineral more resistant to acids), its effectiveness decreases in advanced lesions or with dental caries [22]. For this reason, the use of biomimetic materials, such as hydroxyapatite nanoparticles, is presented as an alternative to simulate the natural structure of the tooth and with this favor a better mineral recovery [23].

a. Mechanism of Action and Comparative

It is known that fluoride improves the speed with which calcium and phosphate are deposited, so that in this way a strong protective layer of fluorapatite is produced. The biomimetic options try to copy the original architecture of the dental tissue; in this way a more integral and profound repair would be promoted [23].

b. In-vitro vs. Clinical Evidence

When evaluating all these treatments, it is necessary to know between the results obtained in the laboratory (*in-vitro*) and those observed in patients. The *in-vitro* analyses allow measuring in a controlled way how effectively these materials penetrate and what capacity they must organize the crystals [28]. In contrast, clinical evidence is more complex, since factors such as saliva, plaque and diet affect the repair process. Although biomimetic materials show great potential in controlled experiments, much more validation is required in the physiological environment to confirm their use as a standard treatment [24].

c. Penetration Depth and Crystal Formation

An important factor is how much these materials manage to deepen within the enamel lesions. Unlike traditional methods, these systems support the creation of organized crystals that join with precision in the affected structure. The success will depend on the capacity of the material to permeate the surface and deposit minerals that reconstruct the structure beyond working on the surface layer. This does not mean that this new tissue guarantees an exact copy of the original structure of the tooth [24].

d. Limitations in Advanced Lesions

It is notable to note that the benefits of remineralization are shown in these initial states, such as white spots. When the loss of minerals reaches a cavity, the enamel presents technical obstacles that neither conventional nor biomimetic materials have been able to resolve in their totality [22]. In more advanced cases, the formation of new tissues does not manage to restore the anatomy of the tooth, which leads to resorting to restorative treatments to ensure functional integrity [26].

Pathophysiology of Demineralization

Dental health depends on a dynamic balance between the enamel and the oral fluids; this is when the process of demineralization occurs:

1. *Mechanism:* It begins when the oral pH drops below 5.5 (the critical point). Hydrogen ions (H^+) react with the hydroxyapatite crystals of the enamel, dissolving them and releasing calcium and phosphate into the environment [25].
2. *Structural Effect:* This generates surface porosity. If this process is not suspended, the structural protein matrix collapses, which leads to the formation of advanced caries [26].

The Biomimetic Approach (Remineralization):

Conventional fluoride acts more on the surface, in contrast to the biomimetic approach, which seeks to simulate nature:

1. *Diffusion and Penetration:* It utilizes nanoparticles or calcium complexes which, due to their small size, achieve a superior depth of penetration, reaching the body of the lesion beneath the surface [27].
2. *Formation of Organized Crystals:* Biomimetic materials act as a scaffold. They do not merely deposit minerals at random; rather, they additionally promote epitaxial growth, ensuring that the new apatite crystals align with the original structure of the enamel prisms [28].
3. *Limitations:* This process is highly effective in white spots (incipient lesions). However, it is limited in processes where the caries is advanced, where there is no longer an organic base structure to guide the formation of new crystals [27].

Analysis of Antimicrobial Strategies in Composite Resins

The persistent challenge of secondary caries at the margins of dental restorations has pushed material science toward "active" chemistry. Rather than simply filling a cavity, modern resins aim to create a hostile environment for the bacteria that cause decay [29]. Recent literature identifies three major players in the quest for "bioactive" composites:

Quaternary Ammonium Compounds (QAMs): These are integrated into the resin's molecular backbone. Because they are chemically bonded, they don't wash away, providing a permanent "electric shield" on the restoration surface [30].

Silver Nanoparticles (AgNPs): Silver is prized for its high potency. In nanoparticle form, it offers a massive surface area that can disrupt bacterial functions even at very low concentrations [31].

Zinc Oxide Nanoparticles (ZnO): Beyond killing germs, these particles are studied for their "biomimetic" qualities, helping to protect the tooth structure and potentially assisting in the repair of the dentin-resin interface [32].

a. How They Work: Contact Killing vs. Ion Release: The way these materials fight bacteria generally falls into two categories: The release and the contact model.

1. The "Release" Model: Materials containing silver or zinc often work by slowly leaking ions into the surrounding saliva. This creates a "cloud" of protection that kills bacteria even if they aren't touching the tooth [29]. However, this can leave tiny holes in the resin over time, potentially weakening the filling [32].
2. The "Contact" Model: This is the specialty of QAMs. These molecules act like microscopic "needles" that pop the membranes of bacteria on contact. Since the molecules are anchored to the resin, the effect doesn't "run out," and the physical density of the filling stays intact [33].
3. Fighting *Streptococcus mutans*: The primary target of these technologies is *S. mutans*, the main culprit behind plaque and acid production. Research shows that both nanosilver and QAM-loaded resins drastically lower the ability of these bacteria to stick to the restoration [31]. By stopping the "first responders" of plaque from colonizing the surface, the material prevents the formation of the thick biofilms that eventually lead to cavities [30].

b. Balancing Strength and Longevity: Adding these "germ-fighters" to resin is a delicate balancing act.

1. Longevity: While QAMs provide a permanent defense, their surface can eventually get coated in a layer of saliva proteins, which acts like a "shield" for the bacteria, hiding the active killing sites [34].
2. Mechanical Integrity: If you add too many nanoparticles, the resin might not harden correctly under the curing light. This can lead to a "soft" filling that wears down too fast or becomes rough. However, when used in the right amounts, these nanoparticles can make the resin tougher and more resistant to the pressures of chewing [34]. The most recent research (2024) suggests that the future lies in "smart" resins that combine these antibacterial effects with the ability to "self-heal" micro-cracks before they turn

into major failures [33].

New Generation of Glass Ionomers (GICs)

Glass ionomer cements (GICs) continue to be important materials in restorative dentistry because of their chemical adhesion to dental tissues, fluoride release and usefulness in minimally invasive procedures. However, conventional GICs also have limitations, mainly related to mechanical strength and clinical durability. For this reason, newer formulations have been introduced, such as High-Viscosity Glass Ionomer Cements (HVGICs), Resin-Modified Glass Ionomer Cements (RMGIs) and experimental bioactive glass-enhanced formulations [35, 41].

a. High-Viscosity Glass Ionomers

In the reviewed studies, HVGICs were the most frequently evaluated materials. Their clinical use was mostly reported in pediatric dentistry, especially in primary molars and Atraumatic Restorative Treatment (ART). Yunus, et al., conducted a randomized clinical trial comparing HVGIC restorations placed with conventional cavity preparation and with ART in children with dentinal caries in primary molars. After 36 months, no statistically significant difference in survival was found between the two approaches, supporting the use of HVGIC in minimally invasive restorative care [35].

Princy, et al., also compared HVGIC with alkasite in ART restorations in primary molars and found that both materials showed clinically acceptable short-term performance, although HVGIC showed numerically better anatomic form and marginal adaptation [36]. Mondal, et al., also reported a survival advantage for ART restorations using HVGIC over conventional composite restorations in primary molars during a 24-month follow-up [37]. However, when HVGIC was evaluated as a pit and fissure sealant, Ghosh, et al., found that resin-based sealants had better short-term retention, suggesting that the performance of HVGIC may vary depending on the indication [38].

b. Resin-Modified Glass Ionomers (RMGIs)

The evidence for RMGIs was more limited, but still relevant. Bågesund, et al., conducted a randomized controlled split-mouth clinical trial comparing resin-based sealing without caries removal and caries removal followed by RMGI restoration in cavitated dentine lesions in primary molars. After 3 years, the defect-free rate was higher in the RMGI group, although the difference was not statistically significant. These findings support the clinical acceptability of RMGIs in minimally invasive treatment of primary teeth [39]. Islam, et al., also reported that some resin-modified glass ionomer materials showed improved fluoride recharge capacity when compared with other restorative materials [40].

c. Bioactive Glass-Enhanced Formulations

Bioactive glass-enhanced formulations represent a more recent development in glass ionomer technology. Kim, et al., evaluated the incorporation of bioactive glass into glass ionomer cement and found that the modified material promoted mineral deposition on demineralized dentin, suggesting a favorable interaction at the dentin-restoration interface [41]. Likewise, Šošić, reported increased calcium and fluoride ion release together with preserved fluoride recharge capacity in glass ionomer materials modified with experimental bioactive glass [42].

d. Fluoride Release and Recharge Capacity

One of the main advantages of glass ionomer-based materials is their ability to release fluoride and, in some cases, recharge fluoride from external sources. Krajangta, et al., found that high-viscosity glass ionomer cements were able to release fluoride over time and showed fluoride recharge capacity, even when protective surface coatings were used [43]. Islam, et al., reported that conventional GICs showed higher initial fluoride release, while some resin-modified materials showed better fluoride recharge ability [40]. In addition, Šošić, demonstrated that bioactive glass-modified glass ionomer materials could enhance fluoride and calcium ion release while maintaining recharge capacity [42].

e. Mechanical Properties, Current Indications and Future Directions

Improving the mechanical limitations of conventional GICs has been one of the main reasons for developing newer formulations. Yu, et al., developed a novel glass ionomer cement and compared it with conventional GIC in an *in-vitro* study. Their results showed enhanced mechanical and chemical properties, together with increased release of fluoride and other ions, suggesting that modified formulations may help overcome some of the traditional weaknesses of conventional glass ionomers [44]. Overall,

the reviewed studies suggest that newer glass ionomer formulations do not completely replace conventional GICs, but they do expand their clinical possibilities. HVGICs showed acceptable survival and clinical usefulness in ART and pediatric restorative care, while RMGIs demonstrated favorable performance in minimally invasive treatment of primary molars [35-39].

Most of the clinical studies were carried out in minimally invasive dentistry, especially in children and primary molars. This makes these materials especially relevant in conservative restorative approaches and in high-caries-risk pediatric patients [43]. Although the reviewed evidence supports their use, the available literature is still limited. Stronger clinical evidence was found for HVGICs, while bioactive glass-enhanced formulations were supported mainly by *in-vitro* studies. More randomized clinical trials with longer follow-up periods are still needed and the possible integration of these materials with digital dentistry may represent a future area of development [44].

Conflict of Interest

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The project did not meet the definition of human subject research under the purview of the IRB according to federal regulations and therefore, was exempt.

Informed Consent Statement

Informed consent was taken for this study.

Authors' Contributions

All authors contributed equally to this paper.

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