



The Rise of Biomimetic Strategies and Materials in Restorative Dentistry and Endodontics - Review

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Abstract

The convergence of biology and materials science has catalyzed a transformative approach in dentistry—biomimetics—where restoration and regeneration are guided by the principles of natural tissue architecture and function. This review examines the progressive integration of biomimetic strategies in restorative and regenerative dentistry, emphasizing the role of bioactive materials such as calcium silicate-based cements, bioactive glass, and peptide-functionalized scaffolds. These innovations replicate the hierarchical structure of enamel and dentin while promoting remineralization, cellular differentiation, and tissue repair. Emerging

technologies in tissue engineering and nanomaterials have enabled the development of self-healing composites and smart adhesives that adapt to the oral microenvironment. By harmonizing synthetic interventions with biological models, biomimetic dentistry advances a minimally invasive, longevity-driven paradigm that enhances clinical outcomes. This synthesis highlights the translational potential of biomimetic materials in preserving pulp vitality, optimizing aesthetics, and restoring functional integrity.

Keywords: biomimetics, biomimetic protocols, biomimetic materials

Introduction

In an era where precision and preservation define modern dental practice, biomimetic dentistry emerges as a paradigm shift—drawing inspiration from nature's architecture to revolutionize restoration. This discipline transcends conventional treatment by embracing the principles of biological structure, mechanical integrity, and functional harmony, echoing the sophistication of natural dentition. Rather than merely repairing teeth, biomimetic strategies aim to recreate the innate form and resilience of enamel and dentin through advanced adhesive techniques, conservative preparation, and mineralizing protocols.

The term "biomimetic," first introduced in the 1950s by biophysicist and biomedical engineer Otto Schmitt, reflects a foundational shift in thinking—where engineering and design began to mirror biological systems to achieve functional harmony.¹⁻³ As the boundaries between material science, regenerative biology, and clinical application converge, biomimetic dentistry offers a framework that is not only minimally invasive but also biologically respectful. Modern dentistry emphasizes minimally invasive treatment strategies that utilize bioinspired materials to restore and remineralize defective or diseased dental tissues. The pivotal role of fluoride in reducing the incidence and preventing the progression of dental caries has been extensively documented in the literature for over 25 years.⁴⁻⁶ In recent years, diverse bioactive formulations—including micro- and nano-hydroxyapatite (HA), tricalcium phosphate, mineral trioxide aggregate, casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), and bioactive glasses—have gained attention for their superior biocompatibility,

biomimetic properties, bioactivity, and potential to promote dental remineralization.⁷⁻⁸

According to Vishal Mahajan et al, Unlike traditional restorative methods that often rely on mechanical retention and extensive tooth preparation, biomimetic dentistry prioritizes adhesive techniques, stress-reducing protocols, and bioactive materials that mimic the physical, optical, and physiological properties of enamel and dentin⁹. These innovations allow clinicians to restore teeth with minimal intervention, preserving pulp vitality and reducing the need for endodontic therapy or full-coverage crowns. The surge in biomimetic interest stems from synergistic advances across material science, tissue engineering, and adhesive dentistry—collectively driving innovations that foster durable restorations and elevate the standard of patient-centered care¹⁰. As dentistry continues to evolve toward minimally invasive and biologically harmonious practices, biomimetic dentistry stands at the forefront of this transformation. As advancements in interdisciplinary research accelerate, biomimetic dentistry emerges as a transformative approach—reshaping clinical protocols, minimizing retreatment rates, and significantly elevating patient-centered outcomes.

This article is designed to review about various advancements in protocols and materials used in biomimetic approach in restorative dentistry and endodontics.

Biomimetics in Restorations

At the macrostructural level, the biomechanical performance, structural resilience, and aesthetic harmony of teeth can be restored using a range of biomimetic materials.¹¹ During the restoration of damaged tooth structures, careful consideration of factors such as hue, shade, intra-coronal anatomy, mechanical function, and

the tooth's position within the arch is essential to uphold biomimetic principles. Magne et al 2022 stated that the Adhesive techniques constitute the cornerstone of BRD(Biomimetic restorative dentistry), and novel restorative designs are striking elements of this nascent approach to tooth restoration¹²

Biomimetic Protocols in Restoration

Biomimetic restorative dentistry employs stress-reducing protocols and bond-maximizing protocols to mitigate polymerization shrinkage and preserve structural integrity. These include using indirect or semi-direct restorations for enamel replacement, layering composite in <2 mm increments, integrating reinforcing fibers, and applying slow-start polymerization techniques. Clinicians also select dentin-replacing composites with low shrinkage and biomechanically compatible modulus, dual-cure materials for non-vital teeth, and limit cusp thickness to reduce flexural stress. Occlusal force verticalization is achieved through strategic composite placement. To optimize bonding, protocols emphasize a caries-free peripheral seal, enamel beveling, MMP deactivation, high-performance adhesives, immediate dentin sealing with resin coating, and margin elevation to supra-gingival levels—collectively enhancing bond strength and restoration longevity.

Biomimetics in Regenerative Endodontics

Regenerative endodontics aim to restore the biological function of the pulp–dentin complex rather than merely replacing lost tissue. Central to this philosophy is biomimetics.¹³

The foundation of regenerative endodontics lies in the triad of stem cells, scaffolds, and signaling molecules. Stem cells sourced from dental pulp or apical papilla possess the capacity to differentiate into odontoblast-like cells when exposed to appropriate biochemical cues¹⁴.

Scaffolds, whether natural (e.g., collagen) or synthetic (e.g., calcium silicate cements), provide a structural framework for cell attachment and tissue ingrowth. Signaling molecules such as bone morphogenetic proteins (BMPs), vascular endothelial growth factor (VEGF), and transforming growth factor-beta (TGF-β) orchestrate cellular behavior, promoting angiogenesis, neurogenesis, and mineralization.¹⁵

Biomimetic materials play a pivotal role in regenerative and restorative protocols. Calcium silicate-based cements like MTA, Biodentine, and CEM cement release bioactive ions that stimulate hard tissue formation and exhibit antimicrobial properties.¹⁶ Bioactive glass and hydroxyapatite-based materials mimic the mineral phase of dentin, supporting cellular adhesion and enhancing biological integration.¹⁷ These materials not only provide a seal but actively participate in the regenerative process.

Clinical techniques such as pulp revascularization and cell-homing leverage biomimetic principles. In revascularization, a blood clot formed within the canal acts as a natural scaffold, recruiting endogenous stem cells and initiating tissue repair¹⁸ Cell-homing strategies involve the delivery of chemotactic agents to attract stem cells to the site of injury, facilitating regeneration without exogenous cell transplantation¹⁹ Emerging technologies such as gene therapy and nanomaterials further enhance biomimetic outcomes. Campodoni E et al. described that Gene delivery systems aim to upregulate mineralizing genes within pulp tissues, while nanostructured scaffolds improve surface reactivity and enable controlled release of bioactive molecules.²⁰ These innovations are expanding the scope of regenerative endodontics toward more predictable and biologically integrated therapies.

Clinical evidence supports the efficacy of biomimetic regenerative procedures in restoring vitality, promoting root development, and improving structural integrity—especially in immature teeth.²¹ These outcomes align with the goals of minimally invasive dentistry and long-term preservation of tooth function.

The selection of an appropriate biomimetic scaffold for pulp-dentin regeneration aims to establish a microenvironment that closely mimics native tissue interactions—specifically, cell–cell, cell–ECM, and cell–soluble factor dynamics. An ideal scaffold should facilitate the proliferation, migration, and three-dimensional organization of stem cells, while promoting their differentiation into odontogenic, neurogenic, and vasculogenic lineages. Equally important is the scaffold's biocompatibility, ensuring harmonious integration with host tissues and minimizing adverse immune responses.

Scaffold design for pulp-dentin regeneration may incorporate hydrogels, porous three-dimensional (3D) structures, or a hybrid of both. Hydrogels, in particular, offer practical advantages—they can be easily delivered into root canal systems via syringe, enabling minimally invasive application. Evidence suggests that hydrogels support pulp regeneration by providing a conducive surface for cellular adhesion, proliferation, and differentiation into organized tissue architecture.

In regenerative endodontics, scaffolds play a crucial role in supporting tissue healing and regeneration. Natural scaffolds such as collagen, chitosan, silk, fibrin, and blood-derived matrices like blood clot, platelet-rich plasma (PRP), and platelet-rich fibrin (PRF) have shown promising results. PRP, a first-generation autologous platelet concentrate, is rich in growth factors including PDGF, TGF- β , IGF, VEGF, EGF, and epithelial cell

growth factor, which are released via α -granule degranulation to stimulate bone and soft tissue repair. PRF, known as Choukroun's PRF, is a second-generation concentrate prepared by centrifuging blood without anticoagulants, forming a fibrin matrix that gradually releases bioactive molecules. Synthetic scaffolds like polyglycolide and polyglycerol sebacate also offer structural support but lack the intrinsic bioactivity of platelet-derived matrices. Natural scaffolds such as collagen and chitosan are widely employed in tissue engineering due to their inherent biocompatibility and enzymatic degradability. Increasingly, biomimetic scaffolds derived from natural materials are favored over synthetic polymers, which often lack the mechanical integrity and biological responsiveness of their natural counterparts. Recent advancements in scaffold fabrication techniques—such as electrospinning, freeze-drying, and 3D printing—have enabled the creation of porous, biocompatible structures tailored for bone tissue engineering.²²⁻²⁸

Biomimetic Materials in Dentistry

Biomimetic materials in dentistry can be categorized based on their interaction with biological tissues. Bioinert materials, such as titanium alloys, serve primarily structural roles and exhibit minimal interaction with surrounding tissues. In contrast, bioactive materials like bioactive glass engage dynamically with the oral environment, promoting physiological processes such as remineralization and tissue regeneration. More advanced are bioresponsive materials, which demonstrate adaptive behavior by responding to external stimuli—such as changes in pH, temperature, or moisture—to facilitate repair and healing. This classification aids clinicians and researchers in selecting appropriate materials tailored to specific therapeutic needs and biological contexts⁹

Mineral Trioxide Aggregate (MTA), derived from purified Portland cement, comprises tricalcium silicate, dicalcium silicate, tricalcium aluminate, tetracalcium aluminoferrite, bismuth oxide for radiopacity, and gypsum. It is available in gray and white formulations, with the latter lacking iron compounds to reduce discoloration. MTA exhibits favorable physical and chemical properties, including hydrophilicity, an alkaline pH (~12.5), high biocompatibility, excellent sealing capability, and radiopacity. These characteristics make it an ideal material for a range of clinical applications such as pulp capping, pulpotomy, apexification, apexogenesis, root-end filling, perforation repair, regenerative endodontics, internal resorption management, and vital pulp therapy. The advantages of MTA include superior biocompatibility compared to calcium hydroxide, promotion of cementogenesis and osteogenesis, effectiveness in moist environments, and consistent long-term clinical success. However, it is limited by its long setting time (approximately 2.5–3 hours), handling difficulties due to its sandy consistency, potential for discoloration—particularly in the gray variant—and relatively high cost with limited shelf life. To address these drawbacks, research has focused on modified formulations such as fast-setting MTA with additives like calcium chloride, resin-modified variants, and nanoparticle-infused alternatives, as well as the integration of antimicrobial and smart biomaterial technologies to enhance performance and clinical versatility.²⁹⁻³³

Biodentine is a bioactive dentin substitute composed of tricalcium silicate as its main reactive component, along with dicalcium silicate, calcium carbonate, zirconium oxide for radiopacity, and iron oxide for coloration.³⁴ Its liquid phase contains calcium chloride to accelerate

setting and a hydrosoluble polymer to reduce water content.³⁵ It sets within 9–12 minutes and achieves a compressive strength of ~220 MPa in 24 hours, closely resembling natural dentin³⁵. Biodentine shares a similar elastic modulus with dentin, ensuring effective stress distribution²¹. Zirconium oxide enhances radiographic visibility.³⁶ while its low porosity minimizes microleakage and bacterial ingress.³⁷ Biologically, it promotes hydroxyapatite formation and releases calcium ions that stimulate pulp cell differentiation into odontoblast-like cells.³⁸⁻³⁹ Its alkaline pH imparts antibacterial properties and supports pulpal healing without triggering inflammation²⁵, making it highly biocompatible. Clinically, Biodentine is suitable for both crown and root procedures—including pulp capping, pulpotomy, apexification, and root-end fillings—and is effective in both primary and permanent teeth. Compared to MTA, it offers faster setting, improved handling, no risk of tooth discoloration, and comparable or superior sealing ability. However, its higher cost, suboptimal radiopacity in some studies, and requirement for mechanical mixing are noted limitations.⁴⁰⁻⁴²

EndoSequence BC Sealer and Root Repair Material (RRM), developed by Brasseler USA, are calcium silicate-based bioceramics designed to mimic the biological and mechanical properties of dentin. Composed of tricalcium silicate, calcium phosphate, zirconium oxide, and tantalum oxide, they release calcium and hydroxyl ions upon contact with moisture, initiating a mineralization process that resembles natural hard tissue formation.⁴³ These materials, including iRoot SP and iRoot BP, are phosphate-containing and aluminum-free, offering excellent sealing ability and biocompatibility. Ponnada N et al stated that Endosequence and RRM promote dentin

remineralization and hydroxyapatite-like formation at the dentin–material interface, supporting clinical success in apexification and regenerative procedures.⁴⁴ Mechanically, EndoSequence matches dentin in modulus of elasticity and compressive strength, encouraging odontoblast-like cell activity and secondary dentin formation. It adheres well to dentin, remains dimensionally stable, and performs reliably in moist environments.⁴⁵ Biologically, EndoSequence exhibits strong antibacterial properties and high biocompatibility, aiding periapical tissue regeneration and reducing complications. Its superior sealing prevents microleakage, offering better longevity and tissue response than traditional sealers.⁴⁶⁻⁴⁷

Bio Aggregate (BA), marketed as Diaroot by Innovative Bioceramics, is a nanoparticulate calcium silicate-based bioceramic developed as a biomimetic alternative to MTA. It contains calcium silicate, calcium phosphate, silicon dioxide, and tantalum oxide, while excluding aluminum and bismuth. Its nanoparticle formulation enhances sealing and tubule penetration, and it forms hydroxyapatite during setting, enabling chemical bonding with dentin.⁴⁸ BA releases calcium and hydroxyl ions, contributing to its antibacterial properties and promoting osteoblastic differentiation. This ion exchange supports dentin bridge formation and regeneration of pulp and periapical tissues. Its high pH boosts antimicrobial efficacy, and the material maintains excellent dimensional stability and sealing ability.⁴⁹ Functionally, BA has a modulus of elasticity similar to dentin, allowing it to behave like natural tooth structure. It is chemically stable, non-toxic, and biocompatible, making it suitable for direct contact with vital tissues and effective in regenerative applications. Designed with biomimetic principles, BA encourages remineralization

and tissue healing through ion exchange and hydroxyapatite formation. Its bioinductive nature promotes favorable cellular responses, making it ideal for minimally invasive restorative techniques.⁵⁰ Clinically, BA is used in apexification, root-end fillings, perforation repairs, and pulp capping. Compared to MTA, it offers better handling, reduced discoloration, and improved aesthetics. Its mechanical and biological properties closely resemble dentin, reinforcing its role in regenerative dentistry.⁵¹

Calcium-Enriched Mixture (CEM) cement is a bioactive calcium silicate-based material designed as a biomimetic alternative to MTA. Its composition includes multiple calcium compounds that support its biological compatibility and functional mimicry.⁵² CEM releases calcium and phosphate ions, promoting hydroxyapatite formation and sealing at the tissue interface. It sets in moist conditions and maintains an alkaline pH, enhancing antibacterial activity and healing.⁵³ Campodoni E described that it induces dentinogenesis and cementogenesis by stimulating stem cell differentiation, making it suitable for pulp therapy, apexification, perforation repair, and root-end fillings. CEM offers good handling, color stability, and sealing ability comparable to MTA, improving its clinical performance.⁵⁴ Biocompatible and bioactive, CEM supports cellular attachment and resists bacterial infiltration, aligning with biomimetic principles for long-term success.⁵⁵

Glass Ionomer Cement (GIC), introduced by Wilson and Kent in 1972, is a widely recognized biomimetic material in restorative dentistry due to its chemical bonding to tooth structure, fluoride release, and resemblance to dentin and enamel properties.⁵⁶ Composed of fluoroaluminosilicate glass and

polyalkenoic acid, GIC sets via an acid-base reaction that releases calcium, phosphate, and fluoride ions, promoting remineralization and antibacterial effects.⁵⁷ Its coefficient of thermal expansion closely matches natural tooth structure, reducing marginal stress, while its chemical adhesion to moist enamel and dentin preserves healthy tissue. GIC's fluoride recharge and high pH environment support caries prevention and tissue healing.⁵⁸ Modified variants, including resin-modified and nano-bioceramic GICs, offer enhanced mechanical properties for high-stress and pediatric applications.⁵⁹ Bioactive glass-modified GICs further stimulate hydroxyapatite formation, improving integration and regeneration.⁶⁰ Clinically, GICs serve as liners, bases, sealants, and restorations, especially in Class V lesions, due to their biocompatibility and low cytotoxicity.⁶¹ Their ion exchange capabilities also make them promising as bone cements.⁶² Recent studies highlight GIC's role in biomimetic dentistry by replicating natural biomechanics and aesthetics.

Dental composites are among the most widely used biomimetic materials in restorative dentistry due to their ability to replicate the mechanical, optical, and adhesive properties of enamel and dentin. Their micromechanical bonding capabilities, facilitated by adhesive systems that form a hybrid layer resembling the dentinoenamel junction, help distribute stress and minimize marginal failure.⁶³ Nanohybrid and microfilled composites enhance enamel-like aesthetics through improved polishability, translucency, and strength. Innovations such as fiber-reinforced composites and self-healing resins mimic dentin's resilience, with polyethylene fibers reinforcing weakened cusps and reducing fracture risk.⁶⁴ while preserving tooth integrity during failure.⁶⁵ Bioactive fillers like nano-hydroxyapatite and calcium

phosphate promote remineralization and apatite formation at the restoration interface, supporting biological integration and regeneration of demineralized tissues.⁶⁶⁻⁶⁷ In pediatric and esthetic applications, composites offer conservative treatment options, compatibility with tooth structures, and long-term aesthetic success.⁶⁸⁻⁶⁹ Though challenges like polymerization shrinkage remain, advancements in low-shrinkage monomers and bulk-fill technologies have improved marginal integrity and reduced sensitivity.⁷⁰

Bioactive glass (BG), a silica-based biomimetic material pioneered by Hench, is renowned for its ability to bond chemically with bone and dental tissues through the formation of a hydroxyapatite-like layer that promotes regeneration and cellular activity.⁷¹⁻⁷⁴ Nanostructured BGs, including bioactive glass nanoparticles (BGNs), enhance surface reactivity and are used in bone grafts, pulp capping, and drug delivery due to their controlled porosity and ion release.⁷⁵ Composite systems combining BGs with polymers or ceramics improve mechanical properties and enable applications in tissue regeneration and wound healing.⁷⁶ In dentistry, BGs support enamel and dentin remineralization, antimicrobial protection, and acid resistance, particularly in fluorapatite-forming variants.⁷⁷ Their biocompatibility and alkaline pH make them suitable for pediatric therapies like pulp vitality preservation and apexification, while their angiogenic and immunomodulatory effects extend to soft tissue repair.⁷⁸ Advanced techniques like 3D printing allow for scaffold designs that mimic the extracellular matrix though challenges remain in optimizing mechanical strength and degradation rates, prompting research into ion doping and multifunctional composites.⁷⁹

Biomimetic Mineralization (BIMIN) for Enamel and Dentin Regeneration

Biological mineral synthesis offers a level of precision in controlling particle size, morphology, texture, composition, and structure that surpasses conventional mineral processing techniques.⁸⁰ Among emerging strategies, Biomimetic Mineralization (BIMIN) has gained attention for its ability to induce the formation of enamel-like fluorapatite layers on mineral substrates, presenting a viable approach for the remineralization of superficial enamel defects and exposed dentin.

The BIMIN technique involves the diffusion of calcium ions from an aqueous solution into a glycerine-enriched gelatin gel containing phosphate and fluoride ions. When this conditioned gel is applied directly to the tooth surface, it facilitates the nucleation and growth of a firmly adherent mineral layer within approximately eight hours.⁸¹ The resulting layer exhibits structural and compositional similarities to native enamel, supporting its potential application in minimally invasive restorative dentistry.

Conclusion

Biomimetic dentistry marks a transformative approach in restorative care, prioritizing the replication of natural dental tissue architecture, function, and regenerative capacity. The incorporation of bioactive materials—such as Biodentine, mineral trioxide aggregate (MTA), and bioactive glass—facilitates improved outcomes in pulp vitality preservation, dentin repair, and structural longevity. This synergy between advanced material science and regenerative techniques supports minimally invasive treatment protocols and aligns with the principles of biologically driven, patient-focused dentistry. Ongoing interdisciplinary research and rigorous clinical trials are vital to optimizing biomimetic

strategies, enhancing material efficacy, and broadening their clinical scope. As innovation progresses, biomimetic dentistry is poised to redefine restorative benchmarks and foster biologically harmonious dental interventions.

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