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RESEARCH ARTICLE

BIOACTIVE MATERIALS IN DENTISTRY – A NARRATIVE REVIEW OF THE LITERATURE

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ABSTRACT

Bioactive dental materials are increasingly utilized in restorative dentistry because they interact beneficially with biological tissues. These materials, including bioceramics, calcium phosphates, and bioactive glasses, exhibit biocompatibility, bioactivity, and the ability to promote tissue regeneration. The FDI Policy Statement emphasizes that bioactive materials should have local, intended, and non-toxic effects without compromising their primary function of dental tissue replacement. Recent systematic reviews and studies have explored the bioactivity of various restorative materials, including resin composites and resin cements, which often incorporate additives like bioactive glass and hydroxyapatite. These materials can induce hydroxyapatite formation, release therapeutic ions, and promote remineralization at the dentin-material interface. Calcium silicate-based materials, such as mineral trioxide aggregate and Biodentine, are particularly noted for their use in endodontics and pulp therapy due to their excellent biocompatibility and bioactivity. These materials can set in moist environments and promote dentin bridge formation, making them suitable for vital pulp therapy and root-end fillings. Despite their advantages, the mechanical properties of bioactive materials can be a concern, and their clinical benefits are still being evaluated, particularly for resin-based composites. Ongoing research aims to optimize these materials' physical and mechanical properties to enhance their clinical performance and longevity. Bioactive dental materials significantly advance restorative dentistry, offering potential benefits in tissue regeneration and caries prevention. However, further clinical studies are needed to establish their long-term effectiveness and fully establish guidelines for their use.

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INTRODUCTION

Bioactive materials in dentistry are a class of biomaterials designed to interact positively with living tissues, promoting beneficial biological responses such as remineralization, tissue regeneration, or antibacterial effects (1). Unlike traditional inert materials (e.g., amalgam, resin composites), bioactive materials actively engage with the oral environment to enhance healing, repair, or prevent further damage (2). These materials are increasingly used in restorative dentistry, endodontics, implantology, periodontology, and caries management to enhance the longevity and effectiveness of dental treatments (3).

Definition of Bioactive Materials in Dentistry: Bioactivity in dentistry refers to a material's ability to elicit a specific, beneficial biological response when in contact with living tissues or cells (4). Many bioactive materials induce the precipitation of hydroxyapatite crystals on their surface, mimicking the mineral component of teeth and bone, which enhances bonding to dental tissues (5). Materials that stimulate repair, regeneration, or remineralization of dental tissues (e.g., dentin, enamel, pulp, or bone) can also be bioactive (6). Some bioactive materials release ions or molecules to inhibit bacterial growth or biofilm formation, reducing the risk of secondary caries or infections (7). However, the term "bioactive" is debated due to its broad and sometimes vague use in marketing (8). Some experts argue that "biointeractive" may be more accurate for materials that exchange ions without direct cellular stimulation, reserving "bioactive" for materials that provoke a positive cellular response (9). This distinction highlights the need for precise terminology and scientific validation. Bioactive materials are categorized by composition, application, or mechanism (10-16). The main types are described in table 1. In addition to the materials listed in the table, there are also other substances that qualify as bioactive. These include Giomers, peptide-based materials, graphene-based materials, and plant-derived biomaterials (17-21). Giomers are hybrids of glass ionomer cements and composites, such as Beautifil Flow Plus (21). They combine the benefits of fluoride release with the aesthetic qualities of composites. Peptide-based materials promote dentin regeneration through growth factors, with Emdogain being one example used for periodontal regeneration (18). Graphene-based materials have gained attention for their antibacterial and remineralizing properties, particularly in caries management (17). Lastly, plant-derived biomaterials, which consist of polysaccharides or extracts (like Cissusquadrangularis combined with hydroxyapatite), are utilized for periodontal regeneration and as coatings for implants (20, 21).

Fluoride: Fluoride is a well-known bioactive material that aids in the remineralization of enamel and dentin and inhibits bacterial activity, although its concentration must be carefully controlled to avoid toxicity (10). The American Academy of Pediatrics recommends fluoride varnish application as a standard of care in pediatric primary care settings to maximize caries prevention (11). Fluoride is a well-established bioactive material in dentistry, primarily recognized for its role in preventing dental caries. The cariostatic effect of fluoride is mainly topical, enhancing the deposition of calcium phosphates during remineralization of enamel and dentin, and reducing the dissolution of calcified tissues even at low concentrations (<1 mg/L) (22). Fluoride's mechanism of action includes inhibiting acid formation by bacteria, reducing extracellular polysaccharide production, and enhancing remineralization (23). Fluoride-releasing dental materials, such as glass ionomers and resin composites, have shown promise in slowing down caries progression adjacent to restorations, although their efficacy in clinical trials remains less clear (24). Additionally, fluoride exposure can shift the composition and activity of oral biofilms, reducing the prevalence of saccharolytic organisms and inhibiting sugar fermentation pathways, which contributes to its anti-caries effect (25). Fluoride-doped amorphous calcium phosphate nanoparticles have also demonstrated potential in promoting enamel remineralization and occluding dentinal tubules (26). In general, fluoride is a critical bioactive material in dentistry due to its ability to enhance remineralization, inhibit demineralization, and modulate oral biofilm activity, thereby preventing dental caries.

Amorphous calcium phosphate: Amorphous calcium phosphate (ACP) is a bioactive material commonly used in dentistry due to its potential benefits in enamel remineralization and dentinal tubule occlusion. ACP provides essential calcium and phosphate ions, which are necessary for the remineralization process. However, it does not possess the mechanical strength required for chewing (12). When ACP releases calcium and phosphate ions, these ions precipitate to form hydroxyapatite, the main mineral component of tooth enamel (26, 27). This process helps restore the mineral content and structural integrity of the teeth. Fluoride-doped ACP can further enhance this process by accelerating the transformation to crystalline apatite, which improves remineralization and offers additional anti-caries benefits (27). ACP can effectively induce the formation of enamel-like hydroxyapatite, thus remineralizing demineralized enamel and dentin (26, 28). Additionally, ACP formulations can occlude dentinal tubules, helping to reduce sensitivity in dentin (26). ACP is biocompatible and can be used in various dental applications without causing adverse effects (29). Stabilizers such as casein phosphopeptides (CPP) can help maintain ACP in its amorphous state, which enhances its remineralization potential (28). ACP is incorporated into toothpaste and topical mousse formulations to provide daily remineralization and protection against caries (27). There are also ACP-based composites designed to release calcium and phosphate ions in a controlled manner, promoting remineralization around dental restorations (30). ACP agents are utilized in preventive dentistry to inhibit demineralization and support the natural repair of tooth structures (28).

Bioactive glass: Bioactive glass is another material that releases calcium, phosphate, and fluoride ions, promoting remineralization and exhibiting antimicrobial properties (13). Bioactive glass (BAG) is a versatile biomaterial used in dentistry due to its ability to bond with hard tissues and promote regeneration. BAG primarily comprises silicate-based systems, which release therapeutic ions such as calcium, phosphate, and fluoride upon immersion in physiological solutions. This ion release leads to the formation of an "apatite-like" phase, enhancing remineralization and filling marginal gaps in dental restorations (31). In dentistry, BAG is utilized in various applications, including dental restorative materials, pulp capping, root canal treatments, and coatings for dental implants. It is also employed in air-abrasion techniques and as a mineralizing agent (13). BAG's biocompatibility and antibacterial properties make it suitable for treating dentin hypersensitivity and pulp-dentine tissue engineering (32). The sol-gel synthesis method of BAG offers improved biological properties, although it presents challenges in terms of cost-effectiveness and fluoride incorporation (31, 32). Despite these challenges, BAG's ability to form a hydroxyapatite layer upon contact with biological fluids is a key feature that facilitates bonding to bone and soft tissues, making it a valuable material in both dental and orthopedic applications (33).

Pediatric patients with high caries risk are common user groups for bioactive glass in dentistry due to its remineralization and antimicrobial properties. This is particularly beneficial for children who may have difficulty maintaining optimal oral hygiene, as bioactive glass can help prevent and arrest dental caries by inhibiting cariogenic bacteria like Streptococcus mutans (34, 35). Orthodontic patients are another group that benefits from bioactive glass, especially in the form of enhanced bonding resins. These resins help prevent demineralization around brackets, a common issue during orthodontic treatment. Bioactive glass's ability to neutralize acids and release remineralizing ions makes it effective in maintaining enamel integrity in these patients (13, 36). Additionally, children with enamel hypoplasia or developmental defectsmay benefit from bioactive glass applications. Its ability to form a mineralized layer on enamel surfaces can help restore the structural integrity of compromised teeth (36, 37).

Hydroxyapatite and tri-calcium phosphate: Hydroxyapatite (HA) and tri-calcium phosphate (TCP) are bioceramics that mimic the mineral composition of natural tooth structures, enhancing biocompatibility and promoting tissue regeneration (12). Hydroxyapatite and tricalcium phosphate are prominent bioactive materials used in dentistry due to their biocompatibility and similarity to the mineral components of human hard tissues. HA is a stable and biocompatible calcium phosphate with low solubility, making it suitable for various dental applications. It is used for tooth remineralization, reduction of tooth sensitivity, oral biofilm control, and tooth whitening. HA's chemical similarity to the inorganic fraction of bone and teeth allows it to integrate well with natural tissues, promoting osteoconductivity and osseointegration (12, 37).In conservative dentistry and oral implantology, HA is employed as a coating for dental implants, in cements, and as a bone substitute material (37). However, clinical data on HA's effectiveness compared to fluoride in oral care products is

Table 1. Bioactive materials in dentistry

Material	Example	Composition	Mechanism	Applications	Advantages	Limitations
Calcium Silicate-Based Materials	Mineral Trioxide Aggregate (MTA), Biodentine	Derived from Portland cement, often mixed with bismuth oxide (MTA) or other additives	Release calcium and hydroxide ions, creating a high pH environment (~12.5) that promotes hydroxyapatite formation. Stimulate dentin bridge formation in pulp capping by inducing odontoblast activity.	Endodontics: Vital pulp capping, apexification, apexogenesis, root canal sealing, perforation repair, retrograde filling. Restorative Dentistry: Biodentine serves as a dentin substitute, temporary restorative material, or base/liner.	Excellent biocompatibility and sealing ability. Hydraulic nature allows setting in moist environments Promotes tissue regeneration and remineralization	MTA has long setting times, poor handling, and potential discoloration. Biodentine improves handling but may have lower mechanical strength than composites.
Calcium Phosphate-Based Materials	Hydroxyapatite (HA), Tricalcium Phosphate (TCP), Amorphous Calcium Phosphate (ACP)	Calcium and phosphate compounds with varying Ca/P ratios, influencing resorption rates.	Mimic the mineral phase of teeth and bone, promoting apatite formation. Release calcium and phosphate ions to support remineralization.	Implantology: Coatings on titanium implants to enhance osseointegration Restorative Dentistry: Additives in toothpastes or restorative materials (e.g., casein phosphopeptide-ACP in chewing gums) for caries prevention. Periodontology: Bone grafting for alveolar ridge preservation post-extraction.	High bioactivity and osteoconductivity. Natural compatibility with dental and bone tissues.	Variable resorption rates depending on Ca/P ratio. Limited mechanical strength for load-bearing restorations.
Bioactive Glass (BAG)	45S5 Bioglass, S53P4, QMAT3	Silica-based glasses with calcium, phosphate, and sometimes additives (e.g., silver, zinc, fluoride).	Dissolve in aqueous environments, releasing ions (Ca^{2+}, PO_4^{3-}, Si^{4+}) that form hydroxyapatite. Exhibit antimicrobial properties due to high pH and ion release.	Restorative Dentistry: Additives in dental adhesives, composites, or toothpastes for remineralization and desensitization. Endodontics: Root canal sealers; Implantology: Coatings to improve osseointegration. Periodontology: Bone regeneration and periodontal defect repair. Orthodontics: Air abrasion for adhesive removal with minimal enamel damage.	Versatile applications across dentistry. Antibacterial and remineralizing properties. FDA-approved formulations	Lower mechanical strength than traditional composites Bioactivity depends on glass composition and dissolution rate.
Glass Ionomer Cements (GICs) and Resin-Modified GICs (RMGICs)	ActivaBioACTIVE Restorative, Beautifil II, Fuji IX	Fluoroaluminosilicate glass with polyacrylic acid (GICs) or resin components (RMGICs).	Release fluoride ions, which convert hydrox apatite to fluorapatite, enhancing enamel resistance to acid. Bond chemically to dentin and enamel, reducing microleckage. Some RMGICs incorporate calcium phosphate fillers for enhanced bioactivity.	Restorative Dentistry: Fillings, liners, bases, and pediatric restorations. Prosthodontics: Luting cements for crowns and bridges. Preventive Dentistry: Sealants and caries prevention in high-risk patients.	Fluoride release and recharge capability. Aesthetic properties similar to composites. Good adhesion to tooth structure.	Lower flexural strength and wear resistance than composites. ActivaBioACTIVE has high water sorption, reducing hardness over time.
Fluoride-Based Materials	Silver Diamine Fluoride (SDF), Sodium Fluoride, Nano-Hydroxyapatite (nHA)	Fluoride compounds, sometimes combined with silver (SDF) or hydroxyapatite nanoparticles.	Fluoride promotes remineralization by forming fluorapatite. SDF combines fluoride's remineralizing effect with silver's antibacterial properties. nHA fills microdefects in enamel, mimicking natural hydroxyapatite.	Caries Management: SDF for arresting caries in children and high-risk patients. Preventive Dentistry: nHA in toothpastes for remineralization and desensitization.Restorative Dentistry: Additives in composites or sealants.	Non-invasive caries control. nHA is a natural alternative to fluoride, avoiding potential risks.	SDF causes black staining. nHA's long-term efficacy requires further clinical studies.

limited and shows varied results (38). Tricalcium Phosphate exists in two polymorphs, α-TCP and β-TCP, both of which are used in dental applications. TCP is more soluble than HA, which makes it useful in situations where faster resorption is desired. It is often used in bone graft materials and as a component in biphasic calcium phosphate (BCP) formulations, which combine HA and TCP to balance stability and resorption rates (39, 40). TCP's bioresorbability allows it to be gradually replaced by natural bone, making it suitable for bone repair and regeneration (40). Combining HA and TCP with bioactive glasses can enhance the mechanical properties and biological response of these materials. This synergy allows for better control over the dissolution rates and improves the overall performance of the composite in dental applications (39). These composites are used in maxillofacial surgery, periodontal treatments, and as scaffolds for tissue engineering (39, 40). HA and TCP are integral to modern dental materials due to their biocompatibility, osteoconductivity, and ability to integrate with natural tissues. Their applications range from dental implants and bone grafts to oral care products, with ongoing research aimed at optimizing their properties and expanding their clinical use.

Calcium silicate-based materials: Calcium silicate-based materials, such as mineral trioxide aggregate (MTA) and Biodentine, are widely used in dentistry for their excellent sealing properties and ability to promote hard tissue formation(13, 14). This makes them particularly suitable for procedures like pulp capping and root repair. These materials are known for their outstanding biocompatibility, bioactivity, and capacity to encourage tissue regeneration (13, 14). Calcium silicate-based materials can stimulate cellular responses, such as osteoblast differentiation and proliferation (41, 42). Additionally, when in contact with biological fluids, they can induce the formation of hydroxyapatite on their surfaces, which aids in the remineralization of dentin and the regeneration of bone tissue (41, 42). One of the advantages of these materials is their ability to set in the presence of moisture, allowing their use in clinical environments where blood and saliva may be present (41). They typically possess adequate mechanical strength; however, some formulations may face challenges such as long setting times and handling difficulties (43). Calcium silicate-based materials are commonly employed in vital pulp therapy procedures, including both direct and indirect pulp capping, due to their effectiveness in promoting the formation of a dentin bridge (41).

Resin-based materials: Resin-based materials have been modified to include bioactive fillers, such as nano-sized amorphous calcium phosphate and quaternary ammonium compounds, to enhance their remineralizing and antibacterial properties. These materials are designed to prevent secondary caries by inhibiting bacterial biofilm formation and promoting mineral gain (16). Additionally, carboxymethyl chitosan lysozyme nanogels loaded with antibacterial drugs have shown significant inhibitory effects against Streptococcus mutans and good remineralization outcomes, making them promising for early enamel caries treatment in children (19). These bioactive materials are integral in pediatric dentistry for their dual functionality in promoting remineralization and providing antimicrobial effects, thereby enhancing the longevity and effectiveness of dental treatments in children. **Conclusion:** Bioactive materials in dentistry are designed to interact beneficially with biological tissues, promoting remineralization and exhibiting antimicrobial properties. These materials are increasingly used in dentistry to enhance the longevity and effectiveness of dental treatments. Overall, the integration of bioactive materials in dentistry aims to improve clinical outcomes by enhancing the biological response, promoting tissue regeneration, and preventing recurrent decay. Bioactive materials such as fluoride, amorphous calcium phosphate, bioactive glass, and resin-based materials with bioactive fillers significantly influence the long-term oral health of patients by promoting remineralization and providing antimicrobial effects.

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