

Cutting-Edge Biomaterials in Dentistry: A Biotechnological Perspective

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Abstract

Biotechnology has significantly advanced the field of dentistry, offering innovative biomaterials that enhance dental treatments and improve patient outcomes. One notable advancement is the use of hydroxyapatite and bioactive glass, which mimic the natural mineral components of teeth and bones, promoting better integration with the body's tissues. These materials are commonly used in bone grafts, dental implants, and coatings for implants, providing a foundation for successful dental restorations. Tissue engineering has also made significant strides with the development of collagen-based and polycaprolactone (PCL) scaffolds. These scaffolds support the growth and regeneration of dental tissues, facilitating the repair of periodontal structures and aiding in dental pulp regeneration. Stem cell therapy, leveraging dental pulp stem cells (DPSCs) and periodontal ligament stem cells (PDLSCs), further enhances regenerative dentistry by enabling the growth of new dental tissues, potentially leading to whole-tooth regeneration in the future. Biotechnologically derived growth factors and biologics, such as platelet-rich plasma (PRP), platelet-rich fibrin (PRF), and bone morphogenetic proteins (BMPs), are being incorporated into dental treatments to accelerate healing and promote bone growth. Additionally, antimicrobial peptides and proteins, like lysozyme and lactoferrin, are integrated into dental materials to reduce infection risks and improve the longevity of dental restorations. Furthermore, biodegradable and smart materials, including chitosan and responsive polymers, are being developed for controlled drug delivery and enhanced wound healing in dental applications. Genetically engineered proteins, such as recombinant human collagen and amelogenin, also make headway in tissue regeneration and enamel repair. Overall, biotechnology is revolutionizing dentistry, providing more effective, biocompatible, and patient-specific treatment options that significantly enhance the quality of dental care.

Keywords: biomaterials, biotechnology, dentistry.

1. Introduction

The convergence of biotechnology and dental materials science has significantly advanced dental treatment modalities. Traditional materials such as amalgam and inert composites, though effective, lack regenerative and biological activity. Biotechnologically enhanced materials have changed this paradigm by promoting active interactions with host tissues. These biomaterials – engineered using principles of tissue engineering, molecular biology, and nanotechnology – enable

tissue regeneration, enhance osseointegration, and mitigate infections through bioactivity. The field now includes bioactive ceramics like hydroxyapatite (HA), glass-based systems, polymeric scaffolds, and bioengineered proteins, but there are much more biomaterials used in dentistry (figure 1) [1].

In clinical dentistry, biotechnology facilitates development of regenerative therapies, including dental pulp and periodontal regeneration, alveolar ridge augmentation, and full-tooth tissue engineering. Stem cell technology and bioactive molecules like PRF and BMPs have particularly influenced regenerative outcomes. Furthermore, the introduction of smart materials responsive to

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stimuli such as pH or temperature has expanded capabilities in targeted drug delivery and wound healing. This review provides a comprehensive analysis of these biomaterials, focusing on their translational applications in clinical dentistry.

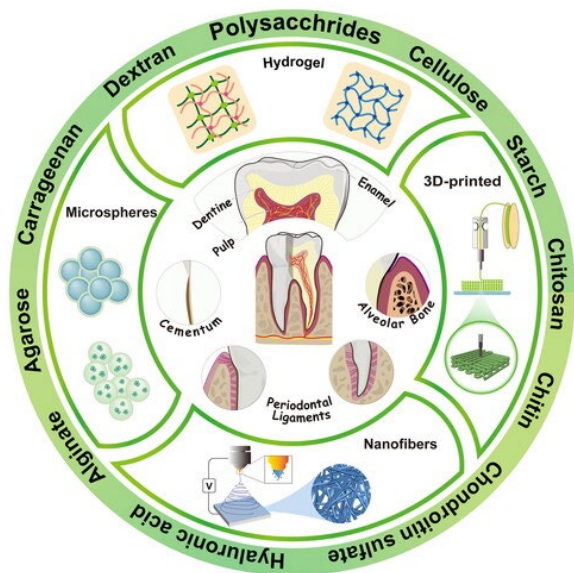


Figure 1. Polysaccharide-derived biomaterials and their dental applications in regeneration and repair

Polysaccharide-based biomaterials such as chitosan, alginate, cellulose, and hyaluronic acid play a crucial role in dentistry by forming hydrogels, nanofibers, and microspheres that support tissue regeneration, drug delivery, and periodontal healing [1-4].

2. Inorganic biomaterials

2.1. Hydroxyapatite (HA)

Hydroxyapatite: $(\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2)$ represents the archetype of biomimetic inorganic biomaterials due to its close chemical similarity to the mineral phase of human bone and teeth. Its biocompatibility, osteoconductivity, and bioactivity make it a cornerstone in bone grafting and implant coatings [5,6]. In dentistry, HA is used for alveolar bone repair, ridge preservation, periodontal regeneration, and as a coating material for titanium implants. It facilitates rapid osseointegration by forming a direct chemical bond with surrounding bone tissue [6,7].

Biotechnological advancements have refined HA through doping with therapeutic ions (e.g., Zn^{2+} , Mg^{2+} , Sr^{2+}) and nanostructuring to improve resorption rates and antimicrobial properties.

Clinical studies show that nano-hydroxyapatite toothpastes promote enamel remineralization and hypersensitivity reduction. Moreover, combining HA with collagen or polymers such as polycaprolactone enhances mechanical strength and biological integration.

Bioactive Glass: Bioactive glass, first introduced by Larry Hench in 1969, represents a cornerstone in regenerative biomaterials due to its unique ability to bond chemically with both bone and soft tissues. Its classical formulation, Bioglass® 45S5, contains silicon dioxide (SiO_2), sodium oxide (Na_2O), calcium oxide (CaO), and phosphorus pentoxide (P_2O_5). When immersed in body fluids, it releases soluble silica, calcium, and phosphate ions that form a hydroxycarbonate apatite (HCA) layer on the surface, similar to the mineral phase of natural bone and dentin. This mechanism underpins its osteoconductive and osteoinductive capabilities, making it invaluable in clinical dentistry [2,3].

In recent years, the advent of ion-doped bioactive glasses has extended their biological functionality. Zinc (Zn^{2+}), strontium (Sr^{2+}), and silver (Ag^+) doping confer antibacterial, angiogenic, and osteogenic effects. Sharifianjazi et al. (2024) reported that Zn-doped glass promotes osteoblast proliferation while simultaneously inhibiting bacterial growth, reducing peri-implant infections [4]. Furthermore, the nanoscale engineering of bioactive glass has drastically improved its surface reactivity and integration with collagen or polymer matrices [5].

Clinically, bioactive glass is used in alveolar ridge preservation, sinus lift procedures, and periodontal regeneration. Commercially available formulations like PerioGlas, NovaBone, and BioGran demonstrate favorable outcomes in maintaining alveolar bone height after extractions. Injectable bioactive glass pastes now allow minimally invasive placement, and hybrid composites combining bioactive glass with hydrogels are being explored for pulpal regeneration.

The mechanistic interaction between bioactive glass and cells involves the upregulation of genes associated with bone morphogenesis (e.g., BMP-2, ALP, and COL1A1). The ionic dissolution products stimulate osteoprogenitor cell differentiation, providing a natural signal environment that bridges synthetic and biological domains. Future research is moving toward mesoporous bioactive glasses (MBGs) with high

surface area for growth factor delivery, and 3D-printed scaffolds that replicate alveolar bone microarchitecture.

3. Organic and hybrid biomaterials

Organic biomaterials represent a major evolution from purely inorganic constructs. These materials – often composed of collagen, elastin, fibrin, and synthetic polymers – are highly biocompatible and can mimic extracellular matrix (ECM) properties. The focus in modern dentistry is to combine their natural cell-friendly characteristics with the mechanical reinforcement of inorganic phases – such as calcium phosphate, creating hybrid scaffolds that promote predictable tissue regeneration [6].

3.1. Collagen-based scaffolds

Collagen, the most abundant ECM protein, is pivotal in tissue regeneration because of its ability to mediate cell adhesion and regulate signaling cascades. Type I collagen in particular provides tensile strength and supports fibroblast, osteoblast, and stem cell attachment. It is widely used in guided tissue regeneration (GTR) and guided bone regeneration (GBR) membranes, periodontal grafts, and pulp-capping materials [7, 9].

Biotechnological modification of collagen aims to improve its structural stability and biological performance. Cross-linking methods – such as enzymatic (using transglutaminase) or chemical (using carbodiimide) – extend collagen's degradation time without compromising its bioactivity. Recombinant human collagen (rhCollagen) offers a major advancement, eliminating zoonotic risks and variability seen in bovine or porcine-derived collagen [7].

Collagen scaffolds also serve as delivery systems for biologics such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), or bone morphogenetic proteins (BMPs). These bioactive composites provide spatiotemporal control of tissue regeneration. Recent developments include collagen-nanohydroxyapatite composites, which improve osteoconduction and stiffness. Clinical evidence suggests that collagen matrices enhance soft tissue thickness around dental implants and support long-term esthetic outcomes [1,7].

3.2. Polycaprolactone (PCL) Scaffolds

Polycaprolactone (PCL) is a synthetic aliphatic polyester prized for its slow biodegradation, excellent mechanical properties, and high processability. It is particularly suited to long-term regenerative applications such as alveolar bone augmentation and pulp–dentin complex reconstruction.

PCL scaffolds fabricated via electrospinning or 3D printing provide interconnected pores that facilitate cell migration and vascularization. Their hydrophobicity can be modulated through surface plasma treatment or blending with hydrophilic polymers like gelatin or collagen [8]. When combined with nanohydroxyapatite or bioactive glass, PCL scaffolds exhibit enhanced compressive strength and osteogenic potential.

In regenerative endodontics, PCL scaffolds seeded with dental pulp stem cells (DPSCs) have shown capacity to regenerate pulp-like tissue with vascular networks. In alveolar defects, PCL-based membranes have demonstrated comparable outcomes to collagen-based GTR systems. The future trajectory of PCL biomaterials lies in growth factor incorporation—for instance, embedding BMP-2 or VEGF for controlled release—to achieve multi-phase tissue regeneration.

4. Cellular biotechnology in regenerative dentistry

Cell-based therapies are at the heart of biotechnological innovation in regenerative dentistry. Stem cells, when combined with bioactive scaffolds and signaling molecules, can restore complex structures like the dentin–pulp complex, periodontal ligament, and alveolar bone. Two key stem cell types dominate dental biotechnology: Dental Pulp Stem Cells (DPSCs) and Periodontal Ligament Stem Cells (PDLSCs).

4.1. Dental pulp stem cells (DPSCs)

Discovered by Gronthos et al. (2000), DPSCs are mesenchymal-like stem cells derived from the dental pulp of permanent or deciduous teeth [9]. They possess multilineage potential, capable of differentiating into odontoblasts, chondrocytes, adipocytes, and osteoblasts. Their accessibility

and ethical acceptability make them ideal for regenerative therapies.

Cell homing-based regenerative endodontic therapy represents an innovative approach in pulp–dentin complex regeneration. Rather than relying on transplanted cells, it leverages chemotactic cues and biomaterial scaffolds to recruit the body’s own progenitor cells from periapical tissues toward the site of injury [9]. These scaffolds, enriched with growth factors, provide both mechanical support and biochemical signaling necessary for tissue repair and vascularization (figure 2).

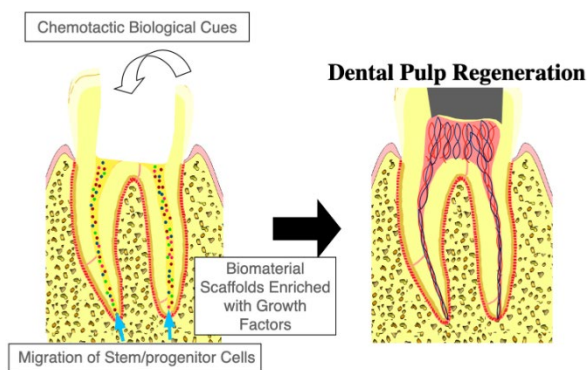


Figure 2. Schematic overview of cell homing-based regenerative endodontic therapy in dental pulp regeneration [10]

In regenerative endodontics, DPSCs are employed to restore the vitality of necrotic teeth by regenerating pulp-like tissues and dentin. They are cultured within biodegradable scaffolds (e.g., collagen or PCL) and stimulated by growth factors like TGF- β or BMP-2 to induce odontogenic differentiation. Preclinical models have shown the regeneration of pulp tissue with neovascularization and innervation, marking a major shift from conventional root canal therapy to biologically driven regeneration [11].

Furthermore, gene modification of DPSCs – for example, overexpressing VEGF or Runx2 – enhances angiogenic and osteogenic potential. Cryopreservation protocols now allow the creation of “tooth banks” for autologous DPSC storage, making clinical translation increasingly feasible.

4.2. Periodontal ligament stem cells (PDLSCs)

PDLSCs, isolated from periodontal ligament tissue, exhibit strong regenerative potential for the periodontium, including cementum, alveolar bone,

and connective fibers [12]. When seeded on scaffolds such as collagen-hydroxyapatite composites, PDLSCs regenerate oriented fiber bundles and cementum-like structures.

Recent *in vivo* studies have demonstrated that PDLSCs combined with PRF or BMP-2 significantly improve periodontal attachment and reduce pocket depth in chronic periodontitis models. These results illustrate the synergy between stem cells and biologics in functional tissue restoration.

Emerging technologies like 3D bioprinting now allow precise spatial deposition of PDLSCs and biomaterials to mimic natural tissue architecture. Additionally, the use of exosomes derived from PDLSCs—which carry bioactive RNAs and proteins—has been proposed as a cell-free alternative for promoting regeneration and immune modulation [13]

5. Growth factors and biologics

Growth factors and biologics are essential in accelerating and regulating tissue regeneration in dentistry. They function by stimulating cellular migration, proliferation, differentiation, and matrix formation. In regenerative dentistry, these biologics are commonly used in conjunction with scaffolds or autologous blood derivatives to enhance healing and osseointegration,

5.1. Platelet-Rich Plasma (PRP) and Platelet-Rich Fibrin (PRF)

Platelet concentrates such as PRP and PRF are autologous biologics obtained from patient blood, enriched with growth factors like platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and transforming growth factor-beta (TGF- β) (figure 3). These molecules play crucial roles in angiogenesis, osteogenesis, and soft-tissue regeneration [14].

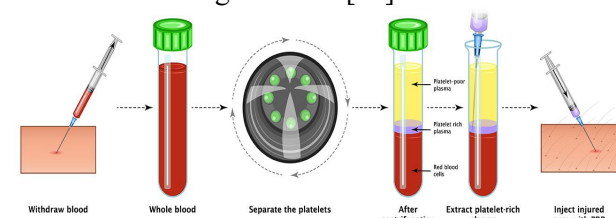


Figure 3. Platelet-Rich Plasma (PRP) preparation

PRP was the first-generation concentrate and involves centrifugation followed by activation with thrombin or calcium chloride. Although effective, PRP's liquid nature and use of anticoagulants can limit its matrix-forming potential. PRF, developed later, overcame these limitations by forming a natural fibrin network without external additives.

PRF's fibrin matrix acts as a reservoir for gradual release of cytokines and growth factors, sustaining cellular activity and tissue repair for longer durations. Clinical trials demonstrate its success in enhancing bone density around dental implants, reducing alveolar ridge resorption post-extraction, and accelerating healing in periodontal defects.

Liu et al. (2023) [15] observed that combining PRF with autogenous bone grafts significantly improved alveolar ridge regeneration and reduced healing time (figure 4). The use of injectable PRF (i-PRF) has further simplified clinical application, allowing minimally invasive delivery to soft and hard tissues [16].

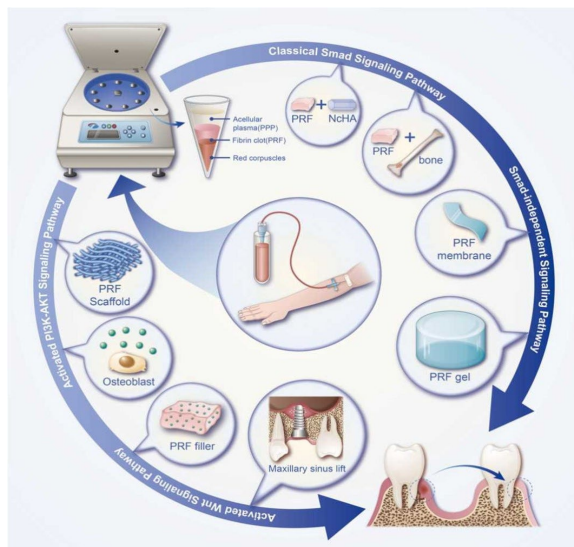


Figure 4. PRF, obtained by blood centrifugation, enhances alveolar bone regeneration alone or with grafts

In the context of regenerative endodontics, PRF provides a matrix for revascularization of necrotic immature teeth, guiding stem cells from the apical papilla (SCAPs) to regenerate pulp-like tissue. Overall, PRP and PRF exemplify the integration of biotechnology and clinical dentistry, offering autologous, cost-effective, and biocompatible regenerative tools

5.2. Bone morphogenetic proteins (BMPs)

BMPs, members of the transforming growth factor-beta (TGF- β) superfamily, are pivotal in skeletal development and bone regeneration. BMP-2 and BMP-7 are particularly significant in dentistry for promoting osteoblastic differentiation and matrix mineralization.

BMPs signal through SMAD-dependent pathways, activating transcription of osteogenic genes such as Runx2 and Osterix. Their recombinant human forms (rhBMP-2, rhBMP-7) are biotechnologically produced and incorporated into scaffolds or collagen sponges to enhance bone repair.

In dental applications, BMPs are used for sinus floor elevation, alveolar ridge augmentation, and implant site preparation. Studies demonstrate that rhBMP-2-loaded collagen membranes can regenerate vertical bone defects with success rates comparable to autografts [17].

However, BMP use is not without limitations. Supra-physiological doses can trigger inflammatory responses or unwanted ectopic bone formation. Hence, recent biotechnology efforts focus on controlled-release systems, using biodegradable polymers (e.g., PCL, PLGA) to ensure sustained, localized delivery of BMPs.

Combination therapies using BMPs and stem cells (e.g., DPSCs or PDLSCs) represent the next frontier, as these synergize signaling cues with cell-based regeneration, resulting in superior osteogenesis and integration

6. Antimicrobial and smart materials

Post-surgical infection remains a major challenge in dental regenerative procedures. Antimicrobial and smart biomaterials address this by actively preventing bacterial colonization while supporting tissue regeneration (figure 5). Advances in biotechnology have led to materials capable of stimulus-responsive behavior, such as drug release in response to pH or temperature changes in infected tissue [18].

The emergence of antimicrobial smart dental materials marks a transformative shift in dentistry. These materials respond to environmental or physical stimuli – such as pH, light, magnetic and electric fields, or enzymatic activity – to deliver targeted antimicrobial effects, enhance healing,

and prevent biofilm formation, ensuring longer-lasting, adaptive dental restorations.

6.1. Antimicrobial Peptides and Proteins

Antimicrobial peptides (AMPs) such as lysozyme, lactoferrin, defensins, and histatins are naturally occurring molecules that form part of the body's innate defense mechanism. They act by disrupting bacterial membranes, neutralizing toxins, and modulating immune responses.

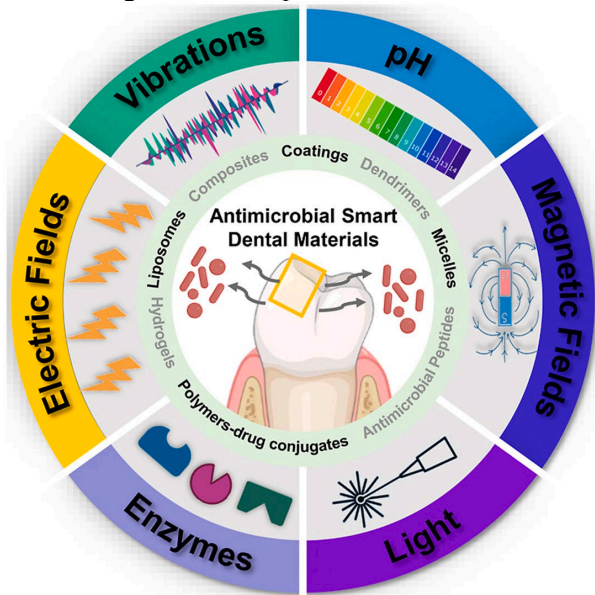


Figure 5. Stimuli-responsive antimicrobial smart materials for adaptive and self-regulating dental applications [17]

In dentistry, AMPs have been integrated into resin composites, dental sealants, and adhesive systems to reduce bacterial biofilm formation and secondary caries. For example, lactoferrin-enriched composites inhibit *Streptococcus mutans* colonization while maintaining material strength. Biotechnological approaches have allowed synthesis of engineered AMPs (eAMPs) with enhanced resistance to proteolytic degradation. These peptides can be covalently bonded to material surfaces for long-lasting antimicrobial functionality. Hybrid systems incorporating AMPs with nanoparticles (e.g., silver or zinc oxide) demonstrate synergistic antibacterial and regenerative potential.

In periodontal therapy, AMP-loaded membranes have been used to prevent infection and support soft tissue healing. Future developments aim to combine AMPs with growth factors or stem cells,

creating multifunctional scaffolds that promote regeneration while mitigating microbial invasion

6.2. Biodegradable and Smart Polymers

Smart materials represent an exciting frontier in regenerative dentistry. These are engineered to respond to physiological stimuli such as pH, temperature, or enzymatic activity. When incorporated into scaffolds or coatings, they can release therapeutic agents in a controlled, site-specific manner.

Chitosan, derived from chitin, is a key biodegradable polymer with intrinsic antimicrobial and hemostatic properties. It supports fibroblast adhesion and accelerates wound healing. Its cationic nature allows electrostatic binding to bacterial cell walls, disrupting their membranes [19].

In periodontal regeneration, chitosan-based dressings and hydrogels deliver antibiotics, growth factors, or stem cells directly to defect sites. Studies report enhanced bone and ligament regeneration with minimal inflammatory response. Beyond chitosan, other smart materials like poly(*N*-isopropylacrylamide) (PNIPAAm) and pH-responsive poly(acrylic acid) are being investigated for drug-releasing membranes. For instance, acidic conditions in infected root canals can trigger the release of antimicrobials from pH-sensitive scaffolds.

These smart polymers can be functionalized with nanocarriers, such as liposomes or dendrimers, to achieve controlled release of growth factors or antibiotics. Clinically, this minimizes systemic exposure and supports sustained local regeneration [20].

7. Genetically Engineered Proteins

Genetic engineering enables precise synthesis of biomolecules identical to natural human proteins, ensuring purity, safety, and predictable biological performance. In dentistry, recombinant proteins have gained traction as bioactive components for enamel, dentin, and soft tissue regeneration [17]. Recombinant human collagen (rhCollagen), produced using yeast or plant-based expression systems, eliminates zoonotic risks associated with animal-derived collagen. It serves as a matrix for cell adhesion, proliferation, and differentiation. rhCollagen membranes have demonstrated

superior tensile strength and integration in guided tissue regeneration (GTR) and implant therapy [21].

Another key protein is amelogenin, a crucial regulator of enamel matrix formation. Recombinant amelogenin has been utilized in products like Emdogain® for periodontal regeneration. It stimulates cementoblast differentiation and regeneration of acellular cementum, essential for periodontal attachment [22]. Research in recombinant amelogenin and tuftelin proteins explores enamel remineralization and caries prevention. These proteins can be incorporated into toothpaste formulations or resin infiltrants to promote biomimetic enamel repair [22].

Future directions include gene-activated scaffolds, which release plasmid DNA encoding therapeutic proteins such as BMPs or VEGF, turning the scaffold itself into a localized protein factory. This biotechnological integration could revolutionize regenerative dentistry, offering self-regulating healing systems,

8. Challenges and Future Perspectives

While progress in biotechnological biomaterials is impressive, translation to routine clinical dentistry faces multiple barriers. Biocompatibility testing, immune response control, and regulatory approval remain major challenges. Furthermore, reproducibility and scalability of cell-based therapies require strict quality control.

Ethical issues arise in stem cell sourcing, particularly for embryonic or allogeneic cells. To address this, autologous sources (DPSCs, PDLSCs) and induced pluripotent stem cells (iPSCs) are gaining favor [23].

The future lies in integrating 3D bioprinting, AI-guided design, and nanotechnology to develop personalized, smart, and adaptive biomaterials. Hybrid systems combining biosensing capabilities with regenerative potential could monitor healing and adjust release profiles in real time [24].

Conclusions

Biotechnology has redefined the future of restorative and regenerative dentistry. From hydroxyapatite and bioactive glass to collagen scaffolds, stem cells, and gene-activated materials, the field is shifting toward personalized, biologically integrated solutions. The emergence of

smart biomaterials, nanotechnology, and bioresponsive systems now allows for precise control of cellular behavior, drug delivery, and tissue regeneration. Continued interdisciplinary collaboration between materials scientists, biotechnologists, and clinicians will accelerate the translation of these innovations into clinical practice. In the near future, dentistry is expected to move beyond repair toward true biological restoration—enabling natural tissue regeneration, improved longevity of dental treatments, and enhanced patient outcomes through personalized, biotechnology-driven care.

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