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Antibacterial functionalization of dental biomaterials: Mechanisms, materials, and emerging trends

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ABSTRACT

Dental caries, caused by dental plaque and microbial biofilms, is a prevalent disease that poses challenges to the success of prostheses and implants in dentistry. Both inorganic nanomaterials and organic polymeric biomaterials are employed for their antibacterial effects. Nanomaterials, with their high surface-to-volume ratio and diverse shapes, play a crucial role in preventing biofilm formation. Metal nanoparticles such as titanium, silver, copper, and zinc oxide, combined with advanced surface modifications like plasma therapy and coatings, effectively reduce bacterial adhesion and peri-implant inflammation. This review highlights the role of biological and antibacterial materials in managing dental infections and promoting oral health.

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1. Introduction

Dental caries is a common disease that can occur throughout life and is among the major health problems worldwide [1]. Although it has received less attention than some other diseases, it affects most adults and more than 60% of children in industrialized countries. In developed countries, the prevalence of dental caries has mainly been controlled through improved dental care and public health measures, such as the effective use of fluoride [2]. However, the incidence of dental caries is increasing in middle-income countries. The cost of traditional dental treatments imposes a heavy financial burden on these countries. Additionally, dental caries reduces individuals' quality of life by causing pain, nutritional problems, and social discomfort [3]. To better understand and prevent this disease, it is necessary to investigate the multiple factors that contribute to its development thoroughly.

Dental caries originates from dental plaque and is considered a multifactorial disease [4]. These microbes form complex communities, typically as thin layers called biofilms, on oral surfaces such as dental plaque [5]. Microbial biofilms also pose a significant challenge in dentistry, as they contribute to prosthetic failure and reduce the effectiveness of long-term treatments [6]. These biofilms serve as reservoirs for chronic infections and can evade both conventional antimicrobial therapies and the host immune system by forming protective extracellular matrices and employing innate resistance mechanisms [7]. Given these significant challenges, developing new strategies to combat biofilm-related complications in dentistry is essential.

Metal nanoparticles, such as silver, gold, and titanium, exhibit unique chemical, mechanical, physical, and optical properties that make them useful as carriers for the treatment of dental disorders and other diseases. In addition, their morphological features (e.g., spherical or rod-like structures) and high surface-to-volume ratios have enabled their widespread application in medical science, particularly in dentistry and dental surgery. Nanoparticles can also be classified into three categories: synthetic polymers, natural polymers, and alloys [8-11]. Leveraging these advanced materials, current research is particularly focused on enhancing the antimicrobial properties of dental implants.

Nevertheless, while such nanomaterials demonstrate strong antimicrobial potential, commercially pure titanium — the gold standard for dental implants — lacks this critical property and thus requires surface modifications. The most effective strategy to prevent biofilm formation on implant surfaces is to reinforce the peri-implant barrier. Antimicrobial materials incorporated into dental implants may exhibit either bactericidal or anti-adhesive properties, leading to direct cellular damage in adherent bacteria or preventing bacterial attachment to the implant surface. Most dental implants are fabricated from commercially pure titanium and its alloys, which are considered the gold standard. Although titanium fulfills the essential requirements of a successful implant biomaterial, it lacks inherent antimicrobial activity. Consequently, the development of modified titanium surfaces with enhanced antimicrobial potential has become a critical focus [12]. This challenge provides a foundation for exploring innovative materials and surface modifications to optimize dental implants and improve clinical outcomes.

This review highlights the pressing need for innovative antibacterial strategies to enhance the clinical performance of dental implants. In this context, the present study provides a comprehensive review of the mechanisms, materials, and novel approaches for the antibacterial functionalization of dental biomaterials. By elucidating the efficacy and limitations of emerging technologies, we aim to inform the development of next-generation implant surfaces with improved infection resistance and enhanced long-term clinical outcomes.

2. Antibacterial agents

Organic and polymeric biomaterials, along with inorganic nanomaterials, are increasingly used as antimicrobial strategies in dentistry. Excess carbohydrate consumption lowers oral pH, fostering acid-tolerant cariogenic bacteria that dominate plaque microflora, form biofilms, and eventually cause tooth decay. Root canal infections may also arise from trauma, caries, or pulp removal [13]. Antibacterial polymers have been engineered using various organic and inorganic compounds to enhance their antibacterial efficacy and durability. These agents include cationic polymers, metallic nanoparticles (e.g., silver and zinc), and natural compounds such as fatty acids and essential oils, which provide long-lasting, targeted antibacterial activity through molecular binding within the polymer matrix. These functionalization strategies help reduce toxicity and environmental impact while offering effective protection in dental restorations and implants [14]. For example, the antimicrobial activity of glass ionomer and zinc oxide cements has been enhanced by incorporating metal nanoparticles, quaternary ammonium compounds (QACs), chlorhexidine, and propolis [15].

Conventional antibiotic or biocide coatings are limited by the development of bacterial resistance and the depletion of active agents, driving interest in alternative approaches such as AMPs, nanostructured surface topographies, and polymer-modified coatings. For example, Tantalum-based bioactive coatings integrate passive bacteria-resistant surfaces with active bactericidal mechanisms to promote both osteointegration and antimicrobial efficacy [16].

Another approach to combating microbial resistance is to modify the structure of ionic liquids (ILs) using novel anions and cations. Combining ILs with active drugs can enhance antibacterial efficacy and drug delivery; however, the potential toxicity of some ILs requires further investigation through both in vitro and in vivo studies. In dentistry, bacterial resistance to drugs, such as penicillin, has also been observed in endodontic infections. As a result, the development of AMP, anti-adhesive polymers, surface modifications, and stimuli-responsive antimicrobial therapies is being explored as a preventive strategy [17].

Examples include zinc oxide (ZnO)-coated gutta-percha, which effectively inhibits *biofilm formation by Enterococcus faecalis and Staphylococcus aureus*, and nanoporous surfaces that reduce fungal adhesion. More advanced systems employ polymer layers or titanium nanotubes (TNTs), enabling pH-responsive, sustained release of antimicrobial agents. For instance, silver nanoparticles or AMP grafted onto TNTs enhance antibacterial activity in acidic environments while simultaneously supporting tissue integration [18].

Additionally, the creation of microstructural patterns such as laser-induced periodic surface structures (LIPSS) on titanium alloy surfaces using picosecond lasers has been shown to reduce bacterial adhesion and biofilm formation. Research indicates that laser microtexturing with various surface patterns increases surface roughness, energy, and wettability, while inhibiting microbial colonization. Furthermore, surface modification of titanium using a CO_2laser under active nitride conditions alters its microstructure and significantly reduces the biofilm-forming capacity of *Candida albicans* [19].

Moreover, microscopic features of the implant surface, such as bone-implant contact, surface roughness, and the host tissue's cellular response, enhance osseointegration and long-term implant

stability. Common methods of implant surface modification include sandblasting with abrasive particles, large-grit blasting, and acid-etching (SLA). Materials such as Al_2O_3 or TiO_2 are also used to create microscopic surface structures that promote faster healing and better integration with the bone [20].

2.1. Metallic nanoparticles

Nanoparticles with tunable physicochemical properties, high binding capacity, and enhanced antibacterial and biological performance are superior to bulk materials for dental applications. Among nanoparticles, copper nanoparticles (CuNPs) exhibit strong antibacterial activity, support disease control, and enable controlled release of therapeutic agents, thereby reducing toxicity [21, 22]. Silver nanoparticles (AgNPs) also exhibit antimicrobial, anti-inflammatory, and even anticancer properties. Their ability to target multidrug-resistant pathogens makes them important tools in biomedical applications [23]. Furthermore, in dentistry, silver–mercury amalgams have long been favored for cavity fillings due to their intrinsic antibacterial properties, low cost, and durability, whereas conventional resin composites lack such activity. However, degradation by-products of resin composites may promote bacterial growth. Emerging antibacterial biomaterials aim to address this limitation [24]. Moreover, zinc oxide nanoparticles (ZnONPs) exhibit antibacterial activity through mechanisms not yet fully elucidated, but thought to involve cellular uptake due to their small size and surface reactivity, followed by the generation of reactive oxygen species (ROS) within cells [25-27]. In titanium or hydroxyapatite coatings, elements such as zinc (Zn), copper (Cu), fluorine (F), selenium (Se), chlorine (Cl), iodine (I), calcium (Ca), or cerium (Ce) are incorporated by anodic oxidation, producing bactericidal effects through gradual ion release. Their antimicrobial mechanism primarily involves the generation of ROS, such as hydrogen peroxide (H_2O_2) and the superoxide anion (O_2^-), which damage bacterial membranes and lead to cell death. Similarly, ion-implanted surfaces exert antibacterial activity by disrupting bacterial metabolism [28-31].

2.2. Organic antimicrobials

Plaque prevention strategies include pre-treatment with disinfectants (such as chlorhexidine (CHX), glutaraldehyde, or benzalkonium chloride), incorporation of leachable antibacterial agents, and embedding QACs or antimicrobial fillers into bonding agents. QACs disrupt bacterial membranes but raise concerns about cytotoxicity, limiting their clinical application. Additionally, antimicrobial coatings for orthopedic and dental applications often involve QACs, antimicrobial polymers (e.g., chitosan, ε-poly-L-lysine), AMP, antibiotics, or metal ions such as Ag and Zn [32]. Among disinfectants, chlorhexidine is widely used to control plaque and gingivitis. It acts by disrupting microbial membranes and inhibiting matrix metalloproteinase (MMP) activity, thereby helping protect the resin–dentin interface from enzymatic degradation. CHX has also been incorporated into titanium surfaces to reduce bacterial colonization, including *Streptococci* and *Staphylococcus aureus* [33].

2.3. Natural compounds

A nanocoating composed of natural and synthetic polymers, including chitosan and hyaluronic acid, was applied to dental implants as polyelectrolyte multilayers (PEMs). This coating enhances the titanium implant surface by improving its mechanical properties, topography, and biocompatibility. It exhibits strong antibacterial activity, particularly against *Staphylococcus aureus*, and offers significant advantages over conventional coatings by maintaining moisture, accelerating tissue repair, and reducing the risk of infection—ultimately promoting faster healing and improved osseointegration [34, 35]. Chitosan is a promising material for dental applications due to its bioactivity, antimicrobial properties, biocompatibility, and compatibility with other materials. It is used in the manufacture of mucosal adhesive patches for the prevention of caries, nanoparticles, and absorbable films for the local delivery of antibiotics such as metronidazole, chlorhexidine, and nystatin for the treatment of gingival, fungal, and mucositis infections (Fig. 1) [36, 37]. Also, the addition of natural essential oils such as clove oil [38, 39], eugenol [40, 41], trachyspermum copticum [42], mentha pulegium, satureja hortensis [43], geraniol [44], cuminum cyminum [45], ziziphora clinopodioides [46], and tarragon [47] Nanemulsions exhibit antibiofilm activity against microorganisms and are used in food, medicine, and various industries due to their antioxidant, antibacterial, and anti-inflammatory properties [48].

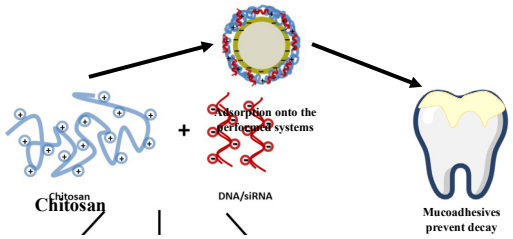

Fig. 1. Chitosan in the manufacture of mucoadhesives to prevent tooth decay by topically delivering various antibiotics.

3. Mechanisms of antibacterial action

The bactericidal effects of antimicrobial dental materials are generally attributed to physical damage to bacterial membranes, though exact mechanisms remain unclear [49]. Two main strategies exist: contact-killing materials and those that release antimicrobial agents. Contact-killing materials tend to offer longer-lasting effects, as ion release can decrease both stability and antibacterial efficacy [50].

3.1. Contact-killing vs. release-based systems

Several approaches have been investigated to reduce biofilm formation at the tooth-restorative interface and on polymeric restorative materials. Among these, contact-killing compounds have shown promise in controlling dental biofilms [51]. These compounds can be immobilized within the polymer structure, providing long-term antibacterial effects without release or leakage, an advantage over release-based materials. Release-based approaches suffer from drawbacks such as sudden, uncontrolled antimicrobial release and a lack of long-term stability. In contrast, contact-based strategies address this limitation by forming covalent bonds that directly attach antibacterial molecules to the polymer backbone [52].

To minimize side effects, contact-killing antibacterial agents have been proposed. These agents are covalently incorporated into dental monomer formulations and exert their effects directly, without being released. This approach offers sustained antibacterial activity. Furthermore, their durability and mechanical properties are preserved even after water exposure, with minimal impact on the curing behavior [53].

For example, antimicrobial peptides (AMPs) have been reported to be immobilized on the surfaces of medical devices to confer contact-killing properties. Fig. 2 illustrates various

strategies developed to enhance the antibacterial properties of materials used in medical devices. AMP coatings on polyurethane catheters and titanium implants have been shown to inhibit the adhesion of various microbial species [54]. Titanium is widely used in dentistry; however, it lacks sufficient bioactivity for optimal integration with bone in orthopedic and dental implants. In tissue engineering, titanium dioxide (TiO_2) is employed to stimulate cell adhesion and migration, enhance wound healing, and promote osseointegration. Titanium implants, known for their high stability and favorable biocompatibility, play a significant role in modern dental applications. However, aesthetic concerns due to their metallic color, as well as the potential for corrosion and hypersensitivity, can be addressed by replacing titanium with ceramics such as zirconia, which offer superior mechanical strength, aesthetics, and biocompatibility [55].

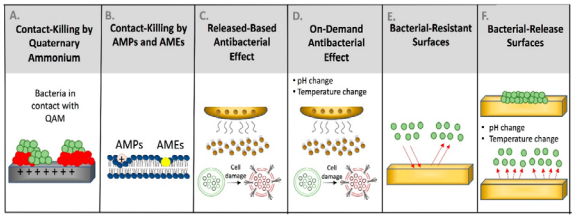

Fig. 2. Illustrates different antibacterial strategies: (A, B) contact killing through positive surface charge and membrane penetration by quaternary ammonium compounds or AMP; (C, D) continuous or intermittent release of antibacterial ions; and (E, F) resistant or bacteria-repellent surfaces that inhibit bacterial adhesion [54].

3.2. Disruption of bacterial membranes

In orthopedic applications, active antibacterial coatings incorporate various compounds, including antibacterial peptides, metal ions (such as zinc, copper, and silver), antibacterial polymers (such as ε-poly-L-lysine and chitosan), antibiotics, and quaternary ammonium compounds. For example, the primary antibacterial mechanism of quaternary ammonium compounds involves the disruption of bacterial cell membranes through their long cationic chains [32]. Moreover, due to its polycationic nature, chitosan interacts with the negatively charged bacterial membrane, disrupting its permeability and destabilizing its structure. This process ultimately leads to leakage of cellular contents and bacterial cell death [36]. On the other hand, metal nanoparticles disrupt the bacterial membrane, produce ROS, release metal ions, and damage vital cellular components, leading to leakage of cellular contents, inhibition of metabolic pathways, and bacterial death. These mechanisms have broad efficacy in combating drug-resistant bacteria [56].

3.3. Inhibition of biofilm formation

Dental plaque can contain more than 10^{11} microorganisms per milligram. The ability of biomaterials to prevent biofilm formation is considered a crucial factor for clinical success [57]. Consequently, considerable global attention has focused on reducing biofilm formation on biomaterials, as biofilm-related infections on medical devices cause serious complications in various parts of the body [58].

Research has demonstrated that combining antimicrobial enzymes (AMEs) with AMPs produces a more pronounced inhibitory effect on biofilms [54]. For example, biofilm formation can be prevented by using enzymes such as Dispersin B, which degrades the biofilm polysaccharide matrix, often in combination with antibacterial peptides [59]. AMEs offer advantages, including bactericidal activity combined with targeted plaque degradation and disruption. Additionally, several types of hydrolytic enzymes, such as proteases, amylases, and lipases, each with distinct specificities, have been approved for use in food and oral care products [60]. Additionally, nanoparticles and plant compounds, including barberry root and bark extracts, help inhibit bacterial adhesion and accumulation, thereby preventing biofilm formation. Therefore, combining enzymatic, pharmaceutical, and antibacterial biomaterials is an effective strategy to prevent the formation and spread of biofilms both in the oral cavity and on medical surfaces [59].

3.4. Ion release and pH modulation

One novel antibacterial mechanism involves the use of pH-responsive, environmentally responsive nanocarriers. These smart nanocarriers are sensitive to pH changes in infectious environments. pH-sensitive chemical groups (such as amines or acid-labile bonds) undergo degradation or protonation upon entering acidic environments, such as those found in dental caries or bacterial biofilms. As a result, antibacterial drugs or metal ions are released in a controlled manner, specifically under these infectious, acidic conditions. This targeted release leads to biofilm destruction, promotes the growth of healthy microbiota, and reduces the growth of acidogenic bacteria [61].

Smart materials respond to changes in environmental pH to release drugs in a controlled, targeted manner under disease conditions, which is useful for treating dental caries. These materials contribute to a healthy microbial balance by reducing acidophilic bacteria. pH-sensitive drug carriers are usually made with specific chemical groups to release the drug when the pH changes. Studies on S. mutans biofilms showed that Ag-MSNs@CHX nanoparticles exhibit a significant antibacterial effect by releasing chlorhexidine and silver ions under low pH conditions and in the presence of GSH [3].

3.5. Photothermal and photodynamic mechanisms

Various stimulation methods are employed, including photothermal, magnetic, thermal, and mechanical approaches [62]. Among those, the photothermal mechanism, by applying heat to a system containing temperature-sensitive nanoparticles (e.g., thermally conductive polymers), induces the controlled release of antibacterial agents, such as silver ions, and reduces the bacterial load. In contrast, photodynamic therapy, by combining a photosensitizer, light at a specific wavelength, and molecular oxygen, produces ROS that lead to the destruction of bacterial cells and biofilms [63]. In one study, silver nitrate was encapsulated in thermoresponsive polymer nanogels that released the compound at 37 °C, thereby reducing bacterial growth. In clinical dentistry, antimicrobial photodynamic therapy (aPDT) is gaining interest for the disinfection of periodontal spaces and implants due to its antibacterial and antifungal properties [64]. aPDT is considered simpler and safer than traditional agents such as antibiotics and sodium hypochlorite. It involves three components: a non-toxic photosensitizer, visible light of an appropriate wavelength, and molecular oxygen, which together generate reactive oxygen species [13].

4. Dental biomaterials and their functionalization

Dental drug delivery materials encompass a range of polymeric carriers, including implant scaffolds, nanoparticles, nanofibers, films, and gels, designed to release therapeutic agents such as anti-inflammatory drugs and antibiotics in a controlled manner. These materials are primarily used to treat infections and repair

periodontal tissues and are also used in composite coatings, antibacterial formulations, adhesives, and sealants [65-70]. Kida et al. [71] examined the role of polymers in oral drug delivery systems, highlighting the use of carriers such as nanoparticles and hydrogels for the controlled release of anti-inflammatory drugs and antibiotics in the treatment of periodontal diseases. For dental applications, polymeric excipients represent a broad and diverse category. These include synthetic polymers such as acrylic acid polymers, polyethylene glycols, polylactides, poloxamers, and polyamides; semi-synthetic polymers such as cellulose derivatives; and natural macromolecular compounds such as hyaluronic acid, gelatin, xanthan gum, chitosan, sodium alginate, and fermentation-derived products. These polymers offer significant advantages by maintaining the drug at the target site and minimizing systemic side effects. Similarly, Zięba et al. [72] investigated polymer-based drug delivery systems, including hydrogels and nanoparticles, for the management of chronic periodontal diseases. These carriers increased local drug concentration at the infection site while reducing systemic adverse effects.

Key challenges associated with these systems include ensuring long-term stability, maintaining sustained antimicrobial activity, and preventing systemic drug absorption. Drug depletion may compromise mechanical strength and result in the formation of porous structures. As a result, surface coatings are often preferred, as they preserve mechanical integrity and can be reapplied to various surfaces, including tooth enamel and dental implants, when necessary [69].

4.1. Resin-based composites

The incorporation of mineral fillers into resin-based dental composites generally increases mechanical properties, such as stiffness, hardness, compressive strength, and flexural strength, though it may decrease flexural modulus. To improve the adhesion between the resin matrix and the fillers, a silane coupling agent such as 3-methylacryloxypropyl-trimethoxy-silane (MPTS) is commonly used. Studies have shown that silanes improve mechanical properties and particle adhesion to the epoxy resin [73].

In terms of sealer materials, epoxy resin-based sealers such as AH Plus may have antibacterial properties due to the release of formaldehyde during curing. Methacrylate-based sealers also exhibit antibacterial properties due to the low pH and the release of unreacted monomers. Silicate-based sealers exhibit antibacterial properties by forming a calcium silicate hydrogel and calcium hydroxide via a hydration reaction [74-76]. Liang et al. [77] synthesized two tertiary amine-based monomers, DMAEM and HMAEM, and incorporated them into adhesive resins. In acidic environments, these monomers are protonated at the amine nitrogen, forming quaternary ammonium compounds with antibacterial properties. The modified resins exhibit antibacterial activity selectively under acidic conditions.

4.2. Dental adhesives and sealants

Dental resin composites are more susceptible to secondary caries due to biofilm accumulation and accelerated degradation caused by direct contact with the oral mucosa and salivary proteins. Dental luting cements securely bond indirect restorations by filling gaps to prevent dislodgement, while composite resins are widely used for direct tooth restoration. In Fig. 3, dental implants replace missing teeth, endodontic treatments eliminate root canal infections, and regenerative materials promote new bone and tissue growth in cases of periodontitis. Shrinkage during light polymerization can create marginal gaps, facilitating bacterial infiltration. Recurrent decay is the most common reason for restoration replacement, which may compromise the remaining tooth structure and ultimately lead to tooth loss [15].

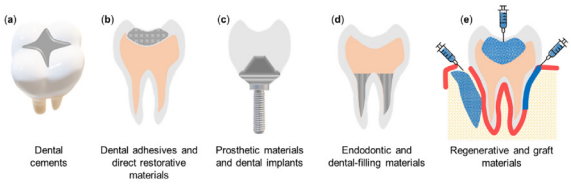

Fig. 3. Images of applications of dental materials requiring antimicrobial and anti-adhesive properties: (a) dental cements; (b) adhesives and direct restorative materials; (c) dental implants and prosthetic materials; (d) restorative materials and endodontic; (e) grafting materials and reconstructive [15].

4.3. Ceramics and glass ionomers

Glass-ionomer cements (GICs) are versatile materials in clinical dentistry, commonly used for restorations, liners, bases, luting agents, fissure sealants, and orthodontic adhesives. Their advantages include biocompatibility with tooth tissue, fluoride release, strong adhesion, and a thermal expansion coefficient similar to that of natural teeth. Resin-modified GICs set through a combination of acid–base neutralization and polymerization, forming a hybrid structure composed of polymers and polysalts [78].

Zhu et al. [79] The growth of bacteria such as S. aureus and P. aeruginosa is inhibited by metal ions such as zinc and silver when coated on metal and ceramic implants, leading to a reduced inflammatory response. This application of ceramics is of great interest in dentistry due to their high biocompatibility and effective antibacterial properties.

While titanium and its alloys have long dominated as dental implant materials due to their strength and biocompatibility, ceramics are increasingly recognized as viable alternatives [80].

4.4. Hydrogels and scaffolds

Bi-network hydrogels, such as those made from chitosan and polyacrylamide, exhibit very high antibacterial activity while providing good mechanical strength, making them ideal for soft tissue repair and drug delivery. These dressings also prevent bacterial growth by retaining moisture and creating a protective environment, which helps wounds heal more quickly [81].

The design of biofunctional scaffolds is crucial for tissue regeneration, and hydrogels (HGs) are emerging as leading candidates due to their resemblance to the natural extracellular matrix (ECM), which supports cell adhesion, proliferation, and vascularization. Collagen-based HGs mimic cell–ECM interactions and allow for biofunctionalization, while hyaluronic acid-based HGs can be engineered with DNA, polymers, or matrix metalloproteinase (MMP)-sensitive peptides to modulate particle delivery. Gelatin HGs are biocompatible, low-immunogenic, and biodegradable, making them versatile for biomedical applications such as tissue matrices, drug delivery systems, and contact lenses. Chitosan-based HG composites with silica nanoparticles have also been developed as pH-responsive scaffolds that promote fibroblast proliferation and bone remineralization [82].

Integrating AMPs into HG scaffolds holds promise for tissue engineering but poses challenges due to HGs' low mechanical strength, particularly in load-bearing applications such as dentistry. Scaffold biomaterials more broadly include polymers, ceramics, and composites, with polymers favored for their tunable

physicochemical properties [83]. Dental tissue engineering imposes unique requirements, aiming to regenerate enamel, dentin, and pulp. Critical scaffold features include interconnected porosity to support the transport of oxygen, nutrients, and waste. Recent studies report that HG scaffolds derived from decellularized bone ECM enhance the odontogenic differentiation of dental pulp stem cells (DPSCs), increasing the expression of markers such as DSPP, DMP-1, and MEPE, and promoting greater mineral deposition compared to collagen-only scaffolds [84].

5. Evaluation of antibacterial performance

To ensure clinical durability, long-term evaluation of dental materials is essential, including investigations of their antibacterial and mechanical properties. The potential for bacterial resistance to these materials should also be assessed [85].

In vitro testing methods, such as zone of inhibition and colony-forming unit (CFU) counting, are commonly employed to evaluate antibacterial performance. For example, in a study, composites containing AgNPs resulted in bidirectional reductions in microbial CFU, with the greatest reduction observed for S. sanguis biofilms, and only at the highest nanoparticle dose (5 wt%) did the growth inhibition zone develop. Addition of 0.5–1.5% diamond nanoparticles (NDs) to acrylic resin reduced C. albicans adhesion and CFU to approximately 290 per microliter, while improving surface roughness and mechanical properties, thereby reducing microbial adhesion and increasing denture comfort. Addition of 1% AgNPs to orthodontic retainer composites also reduced biofilm growth and T. denticola CFU from $3\times10^{\wedge6}$ μL^{-1} to $6\times10^{\wedge4}$ μL^{-1} [86].

Most studies on dental materials containing nanoparticles have been conducted in vitro, whereas in vivo investigations involving complex biofilms are of greater clinical relevance [86]. Evidence suggests that Chlorhexidine can alter the oral microbiome and pH [61]; however, further animal and clinical studies are needed to fully understand these effects and to evaluate the short- and long-term consequences of nanoengineered surfaces [87-89].

Omadacycline, the first oral and injectable 9-aminomethylcycline antibiotic of the tetracycline family, has strong activity against a wide range of anaerobic, gram-positive, and some gram-negative bacteria, including resistant strains and microorganisms that form biofilms in the oral cavity. *In vitro* and *in vivo* studies have shown that this drug is effective not only in inhibiting biofilm-forming bacteria in the oral cavity but also in treating clinical infections such as ABSSSI, CABP, and UTI. It has potential for clinical use in the treatment of oral and gingival infections. However, similar to other tetracyclines, it may cause tooth discoloration and inhibit bone growth [90].

Moreover, biofilm models play a central role in endodontic research, as they simulate the real conditions of root canal infections. Single-species biofilm models are valuable for their high reproducibility, simplicity, and experimental controllability; however, they do not accurately reflect the complexity of clinical infections, which typically involve multispecies communities. Compared to single-species biofilms, multispecies biofilms generate more biomass, have higher virulence, and demonstrate increased resistance to the host immune response. These interspecies interactions and the dynamic infection environment underscore the importance of using multispecies models to more accurately replicate clinical conditions [91].

The flow cell system is one of the most effective methods for modeling biofilm formation, as it enables live, non-destructive observation using confocal laser scanning microscopy (CLSM). In this method, bacteria are cultured in a continuous flow of medium delivered via a silicone tube and attach to non-fluorescent, transparent surfaces such as microscope slides to allow direct observation of biofilm growth. Additionally, laminar flow provides stable, uniform conditions for biofilm development [92].

6. Emerging trends and future directions

In dentistry, biopolymers such as collagen, hyaluronic acid, chitosan, and gelatin are widely explored for their ability to mimic natural tissues, while advances in nano- and microcomposites have significantly improved the performance of dental materials. Beyond their structural roles, these systems serve as smart drug-delivery carriers, enabling targeted therapeutic applications [93-97]. Smart materials that reversibly respond to external stimuli such as pH and temperature have further enabled the development of antibacterial surfaces capable of releasing agents at infection sites [98].

Recent strategies focus on anti-adhesive and antimicrobial approaches, employing nanoparticles, covalent surface modifications (such as QPEI or QAP), and silver-incorporated resins that maintain mechanical strength while suppressing biofilm growth. Multifunctional systems integrating chitosan, quaternary ammonium compounds, and bioactive glass exemplify synergistic effects, although careful control of ion release and nanoparticle stability remains vital. Emerging materials such as QAMs and graphene oxide highlight future directions, where multi-stimulus responses to pH, enzymes, and redox signals could enable more precise, durable, and tissue-integrated dental treatments [99-101].

7. Regulatory and translational challenges

The complexity of periodontal ligament function and its integration with cementum and alveolar bone pose a significant challenge for tissue engineering, necessitating the development of multiphase, multilayer scaffolds. While bioactive materials such as bioactive glasses (BGCs) show promise by releasing therapeutic ions (e.g., Ca^{2+}, PO_4^{3-}, Zn^{2+}, Sr^{2+}), concerns remain regarding the toxicity of certain metal ions (e.g., Ag^{+}, Cu^{2+}) and the potential for excessive local pH shifts, which raise safety and biocompatibility issues [102-104].

The clinical translation of nanomaterials and engineered surfaces is further complicated by the diversity of nanostructures, compound variability, and emerging mechanisms like immunomodulation and photodynamic therapy, all of which challenge existing regulatory frameworks. Moreover, antimicrobial resistance, driven by bacterial strategies such as outer membrane remodeling, biofilm formation, enzymatic inactivation, and target modification, complicates the design and approval of antibacterial surfaces. To overcome these hurdles, especially for release-based systems, surface designs must not only address microbial defense mechanisms but also meet stringent safety and efficacy standards to enable successful clinical adoption [105].

8. Conclusion

The antibacterial performance of dental biomaterials has effectively addressed the challenge of biofilm-associated infections in oral healthcare. By integrating multiple mechanisms, including ion release, biofilm inhibition, and contact killing, and employing innovative agents such as natural compounds, metal nanoparticles, and organic molecules, microbial colonization prevention has advanced significantly. Improvements in surface modification techniques, smart materials, and pH-sensitive nanocarriers have enhanced the control of drug release and the biocompatibility of dental implants. However, engineering and

regulatory obstacles continue to slow the translation of these technologies from laboratory research to clinical use. Future studies should prioritize optimizing multifunctional systems, standardizing assessment protocols, and increasing long-term stability and compatibility. Ultimately, ongoing innovation in materials science and practical implementation will lead to a new generation of antibacterial biomaterials that are more robust, safer, and longer-lasting, thereby improving patient quality of life.

Author contributions

Mohammad Hassan Shahavi: Conceptualization, Writing – original draft, Writing – review & editing, Supervision; **Nazanin Jafari:** Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare no conflict of interest.

Data availability

No data is available.

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