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Recent advancements in multifunctional nanomaterials for dental applications

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This review explores the transformative impact of smart nanomaterials on modern dentistry, a field where precision at the molecular level is unlocking innovative solutions. Nanodentistry leverages the unique properties of nanomaterials, such as their enhanced mechanical, optical, and chemical characteristics, to significantly improve oral healthcare. We delve into recent advancements in restorative dentistry, where novel nanocomposites are offering superior strength, wear resistance, and polish retention, while also minimizing polymerization shrinkage. In orthodontics, we highlight the use of nanomaterials with shape memory and antibacterial properties, which not only accelerate tooth movement but also actively reduce plaque formation and related complications. The article also examines the development of multifunctional nanomaterials for diagnostic and therapeutic applications, including highly effective antimicrobial agents designed to target and eliminate resilient biofilms. The use of nanoencapsulation is discussed for its ability to improve the efficacy, biocompatibility, and durability of dental treatments. Finally, we address the critical need for comprehensive biocompatibility assessments to ensure patient safety, emphasizing the development of materials that closely mimic natural tooth structure, such as hydroxyapatite-based enamel. Ultimately, this review emphasizes how these smart nanomaterials are not merely improving existing dental practices but are paving the way for a revolutionary approach to oral health diagnosis, treatment, and preventive care.

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1. Introduction

Nano dentistry is a developing field that utilizes nanotechnology and nanoparticles to enhance oral health and dental care.[1] This encompasses localized anesthetic, restoration of natural dentition, definitive treatment of hypersensitivity, accurate tooth realignment, enamel bonding with covalently bonded diamondized coatings, and oral hygiene management.[1,2] Nanotechnology applications in dentistry encompass nanocomposites, nano solutions, impression materials, and nanoencapsulation systems. For example, Nanoproducts Corporation has effectively manufactured stable, non-agglomerated nanoparticles, whereas the Southwest Research Institute has created tailored delivery systems for vaccinations, antibiotics, and pharmaceuticals that reduce adverse effects.[2,3]

Dental hypersensitivity, a prevalent clinical disease, arises when natural teeth display an increased density and diameter of dentinal tubules relative to non-sensitive teeth. Reconstructive nanoparticles can selectively and accurately occlude these tubules within minutes, providing a swift and enduring cure. The existence of natural cells in teeth further substantiates the viability of employing nanoparticles with cell-sized mobility for these exact functions. Improving the durability and appearance of teeth can be accomplished by substituting the outer enamel layer with covalently linked synthetic substances like sapphire or diamond.[2] Also, traditional dental imprint methods exhibit numerous constraints, notably patients' discomfort regarding the material's texture, flavor, and scent. Research indicates that conventional impressions may be uncomfortable during the production of fixed, detachable, and implant-supported prostheses.[4,5]Furthermore, the physical characteristics of these materials may hinder therapeutic procedures. Impression-taking frequently leads to the collection of material around the patient's lips, between teeth, or within the oral cavity.[5,6] Debris may also disperse onto the clinician's gloves, tools, and operatory surfaces. Certain patients may experience nausea or a gag response when impression materials are introduced into the oral cavity. Final cast inaccuracies may arise from air bubbles or debris in the

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impression material, with the extent of mistake influenced by the hydrophilicity of the materials employed.[6]

Progress in healthcare biotechnology consistently enhances diagnostic and therapeutic methodologies, with nanotechnology serving a pivotal function in this advancement. Nano dentistry, a specific sector of this discipline, utilizes nanomaterials, nanorobots, and nanoscale engineering for the detection, prevention, and treatment of oral illnesses.[7] The focus is on the accurate and specific administration of medicinal and diagnostic substances. Nanotechnology has enhanced dental materials, equipment, and therapies, rendering them stronger, more efficient, visually superior, and more biocompatible. Applications of nano dentistry encompass cavity replacement, teeth whitening, and orthodontic treatments, while simultaneously enhancing restorative lifetime and enabling the creation of new materials with superior durability and biocompatibility.[8] Nanomaterials, particularly nanoparticles (NPs), have been thoroughly examined as prospective therapeutic carriers in biomedical domains. In contrast to conventional techniques, nanoparticles provide enhanced regulation of biofilms by targeted distribution, increased antibacterial efficacy, and less toxicity. Their diminutive size facilitates infiltration into intricate biofilm architectures, rendering them optimal vehicles for antibacterial drugs. Moreover, nanoparticles can concurrently deliver many payloads, including pharmaceuticals and imaging agents, facilitating the integrated diagnosis and treatment of oral biofilms.[9,10]

Preserving oral health is crucial for overall well-being, as teeth are integral to nutrition and communication. Designing biocompatible nanoproducts necessitates a comprehensive understanding of the structure and function of the targeted tissues, including teeth and the oral cavity.[11] The behavior and destiny of nanomaterials in the body are contingent upon their proximity to biological nanoparticles and tissue interfaces. The human tooth consists of several tissues, and comprehending the composition and relative prevalence of each component offers critical insights for the development of effective dental nanomaterials. Tooth enamel, the most mineralized tissue in the human body, comprises 96% inorganic material (predominantly hydroxyapatite) and 4% organic matter and water. Hyaluronic acid is extensively utilized in dental materials, particularly in nanoscale formulations, owing to its bioactive and moisturizing characteristics.[1] This review highlights comprehensive insights of smart, multifunctional, and stimuli-responsive nanomaterials across restorative dentistry, endodontics, periodontology, and maxillofacial surgery, demonstrated how their mechanistic interactions with dental tissues drive clinically significant innovations.

2. Smart nanomaterials: tailored solutions for dental needs

2.1 Toxicity of nanomaterials

Nanotechnology has emerged as an innovative impact in dentistry, providing advanced materials for diagnosis, prevention, and therapy.[1] The toxicity of nanomaterials such as sliver, zinc oxide, and carbons nanoparticles in dentistry is an increasing concern due to their extensive application in restorative materials and procedures. Also, the toxicity of nanomaterials represents a major problem that requires attention to ensure patient safety and the effectiveness of dental treatments.[12] Other studies demonstrate that nanoparticles can induce cell death throughout different cell lines. Silver nanoparticles (AgNPs) demonstrate cytotoxic effects that are dependent on dose.[13] AgNPs are frequently used in dental materials and products due to their potent antibacterial activity towards oral pathogens such as *Enterococcus faecalis, Candida albicans*, *Porphyromonas gingivalis*, and *Streptococcus mutans*.[14] At low concentrations AgNPs demonstrate excellent biocompatibility, maintaining over 90% cell viability across 24–72 hours.[14] In recent studies, green synthesized AgNPs show high biocompatibility at concentrations up to 120 $\mu g\ mL^{-1}$, maintaining over 90% cell viability in human osteoblast-like cells, with minimal toxic effects in brine shrimp and zebrafish models.[15] Furthermore, zinc oxide nanoparticles (ZnO) exhibit cytotoxic effects on bacterial cells, enhancing their bactericidal efficacy, although are typically demonstrated to possess low toxicity towards human cells at concentrations effective against biofilms and oral infections.[16,17] Studies indicate that ZnO nanoparticles are nontoxic to human cells at lower concentrations (up to 20 $mg\ L^{-1}$ for HeLa cells and 120 μM in other lines), maintaining high viability. However, cytotoxicity increases at higher doses (around 240 μM), leading to reduced cell survival.[18,19] Also, many nanoparticles may penetrate the bloodstream *via* oral mucosa or ingestion, impacting organs such as the lungs, liver, and brain. This systemic exposure presents risks of neurotoxicity and other undesirable health outcomes.[20] In dental application such as polishing or shaping composites, inhalation of aerosolized particles may occur, resulting in respiratory difficulties along with potential systemic effects.[21,22] Furthermore, dental materials function directly in the oral cavity, facilitating absorption *via* mucosal membranes. Carbon nanotubes (CNTs) and graphene are commonly used nanomaterials in dental applications.[12] CNTs are unique *via* their high surface area and capability for active drug delivery, although they may provoke inflammatory and fibrotic responses.[12] There is a lack of comprehensive studies, especially evaluating the toxicity of dental nanomaterials, underlining the need for more study for determining safety profiles.[23] Although the potential adverse effects are associated with nanomaterials, their unique features remain in promoting advancements in dental therapies. Ongoing research is crucial for combining the advantages of nanotechnology with the significant of patient safety.

2.2 Nanoparticles for regeneration

Nanoparticles have revolutionized dental regeneration by providing novel approaches for addressing diverse dental problems, such as bone abnormalities, periodontal diseases, and improving tissue regeneration.[24,25] Nanoparticles enhance the regeneration of dental tissues by stimulating cellular proliferation and differentiation. A wide variety of nanoparticles, such as chitosan, gold nanoparticles, titanium oxide,

HA, and graphene oxide, have been employed to enhance osseointegration and enhance implant surface adhesion.[26] Bioactive glass nanoparticles have been demonstrated to improve dentine remineralization and promote odontoblast development from dental pulp stem cells (DPSCs).[26] Chitosan nanoparticles (CS-NPs) are observed for their osteoconductivity and capacity to promote osteoblast proliferation, rendering them beneficial for bone regeneration.[27,28]

Moreover, CS-NPs have found use in periodontal applications because of their biocompatibility and antibacterial characteristics, which promote periodontal tissue healing.[28,29] Also, multiple nanoparticles, such as HA and gold nanoparticles, have shown efficacy in combating periodontal diseases. Gold nanoparticles demonstrate antimicrobial characteristics and facilitate the remineralization process.[27]

Overall, the integration of nanoparticles in dentistry represents a notable progression in regenerative medicine. As shown in Fig. 1, nanoparticles demonstrate significant impact on implant surface enhancement, improvement of dental material characteristics, and play a vital role in bone regeneration, highlighting their essential role in modern dental therapies.

2.3 Antibacterial nanofillers and coatings

Periodontal disease results in tooth loss and health complications, as regular brushing is inadequate for eliminating bacterial biofilms. Antibiotics have limited efficacy in treating infections that have biofilms adhered to the surface of the tooth.[30,31] There is a need for a new approach to fighting microbes, and researchers have conducted experiments to examine the effectiveness of antibacterial nanoparticles as a method of delivering drugs directly to the affected area.[32] Oral bacterial cells were significantly affected by metallic nanoparticles, demonstrating strong antibacterial properties. However, additional investigation is required to confirm the durability, long-term efficacy, and safety of these nanoparticles.[32] Nanofillers such as Ag, platinum, Zn/zinc oxide (ZnO), Ti/titanium dioxide (TiO_2), and zirconia (ZrO_2) have been utilized in biomaterials to augment antibacterial efficacy, with TiO_2 nanoparticles demonstrating extensive antibacterial properties. Nanotechnology has facilitated the creation of two approaches to combat dental caries: the integration of inorganic antibacterial nanoparticles into resin composites, and the use of chemicals that directly diminish microbial biofilm upon contact.[33]

In recent years, nanoparticles and smart materials have garnered heightened interest in dental applications. While the two phrases are occasionally employed synonymously, they denote separate things. Nanomaterials has nanoscale dimensions (1–100 nm), endowing them with distinctive physical and chemical properties, including increased strength, surface area, and bioactivity.[16] Conversely, smart materials are engineered to react to environmental stimuli-such as variations in pH, temperature, or mechanical stress-by modifying their behavior or function in a predictable and advantageous manner.[2,34]

In contrast, Composite resins containing 1% AgNPs or ZnO NPs have demonstrated enhanced antibacterial properties, with ZnO NPs effectively suppressing the activity of *Streptococcus mutans*. Nevertheless, certain studies indicate the absence of any antibacterial impact on *S. mutans*.[35,36] Colloid metal oxide nanoparticles exhibit exceptional antibacterial efficacy.[35,36] Also, glass ionomer cements (GICs) that release fluoride ions have been used to reduce the occurrence of secondary caries.[35,37] Furthermore, the use of TiO_2 NPs has greatly enhanced both the mechanical strength and antibacterial properties.[38] Also, hexametaphosphate nanoparticles in GICs results in better antibacterial capabilities and increased release of fluoride ions.[38] The addition of ZnO nanoparticles to GICs did not enhance the antibacterial efficacy against S.[38]

Additionally, nanofibers are utilized as carriers with high-loading capacity because of their expansive contact surface area, whilst micelles are favored for their ease of manipulation

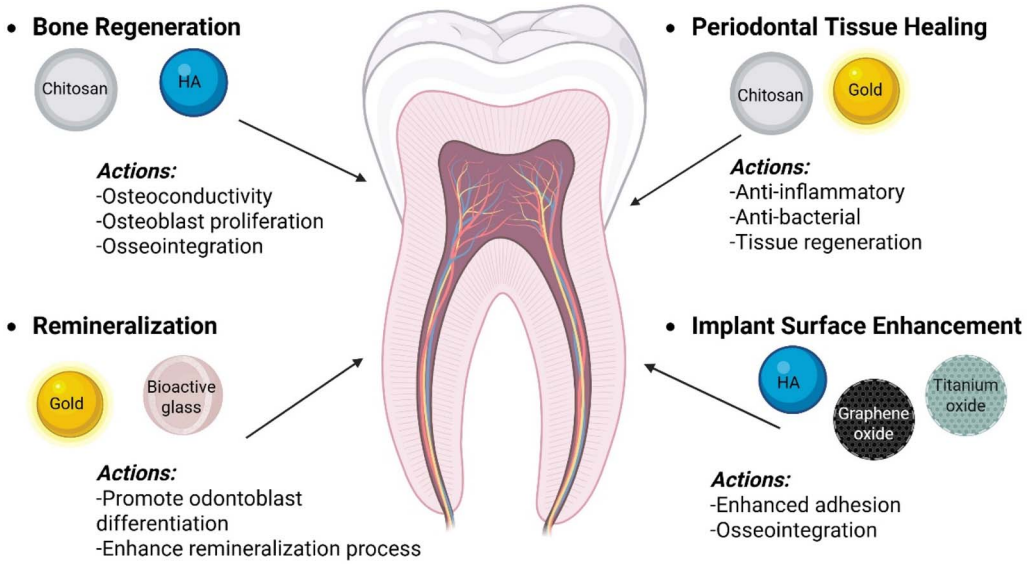

Fig. 1 Roles of various nanoparticles in dental regeneration.

and encapsulation.[39,40] Applying bioactive fillers is a viable approach to address the issue of antibiotic resistance.[41] They introduce additives into the microenvironment to discourage the growth of infections. The customization options encompass altering the size of the filler, the ratio of surface area to mass, the morphologies of the particles, the surface charge, the dosage, and the coatings of the nanoparticles. Fillers can be altered to specifically target infections, resulting in reduced side effects. The effectiveness of dental composites is influenced by the quantity of filler present, which can reduce biofilms by up to 7.5% when ZnO NPs are used.[42]

2.4 Biosensing nanomaterials for diagnostics

Biosensing nanomaterials have completely altered diagnostics by increasing sensitivity, specificity, and the capacity to do high-density analyses.[43] Nanoparticle-based detection techniques use plasmonic and fluorescent nanoparticles for identifying biomarkers related with periodontitis, allowing for prompt intervention.[44] Furthermore, nanomaterials, including quantum dots and CNTs, are used for molecular imaging and the detection of premalignant lesions, hence enhancing early diagnosis.[45] Also, advancements in digital radiography *via* nanophosphor scintillators lower radiation exposure while retaining image quality.[46] By applying X-ray imaging, nanoparticles such as hafnium oxide can be tailored to specifically target oral pathogens, therefore enabling exact localization of bacterial infections.[47,48] Another approach based on biosensing is based on incorporating nanomaterials such as gold–silver nanorods (Au@Ag NRs) attached to polydimethylsiloxane (PDMS) for detecting volatile organic compounds generated by bacterial decay at lesion locations, therefore offering direct visualization of dental lesions.[49–51] As a result, nanotechnology improves the resolution and accuracy of dental imaging *via* unique characteristics including large surface area and conductivity.[3] Overall, future studies need to focus on creating more bio-compatible nanomaterials with improved assembly approaches to improve treatment efficacy and diagnosis accuracy.

3. Applications of smart nanomaterials in dentistry

The integration of nanotechnology has been instrumental in the development of biocompatible and safe dental restorative materials like glass ionomer cement, dental composites, dental implants, and endodontic materials. Significant progress has been witnessed in resin-based dental restorative materials in recent years. Incorporating nanoparticles into the dental composite resin matrix can notably improve its mechanical properties, minimize polymerization shrinkage, while enhancing abrasion resistance and surface hardness.[7] Smart materials are those having the ability to express an alteration in their characteristics in regulated behavior when they are exposed to specific external stimuli. Temperature, pH or moisture fluctuations, mechanical stress, and electric or magnetic fields are examples of such stimuli. In dental composites, this function was utilized to react against the following sections different types of smart fillers well be discussed according to their responses, such as self-healing and antibacterial activity.[52] These advancements in smart materials hold promise for innovative applications in dentistry and other fields, offering the potential for tailored responses to environmental changes in a reliable and reversible manner.

3.1 Restorative dentistry

Restorative dentistry uses advanced methods to repair and replace damaged tooth structures, restore functionality, and improve aesthetics.[53] The use of dental fillers is among the most common dental materials utilized in restorative procedures performed on humans.[54] Nanotechnology has found applications across various domains of dentistry, including restorative dentistry, offering substantial potential for enhancing the clinical performance of restorative materials like composite resins, dental adhesives, and glass ionomer materials. The primary aim is to augment their strength, aesthetics, and therapeutic attributes, such as bioactivity and antibacterial effects, to effectively manage and reduce bacterial biofilm formation on tooth surfaces or at the tooth–restoration interface. In today's dental market, nanocomposites, nano-filled adhesives, nano-ionomers, and even nano-amalgam restorative materials have been introduced.[55]

3.1.1 Smart fillings and adhesives with self-healing properties. Researchers have developed self-healing materials inspired by nature. Certain natural materials, like bones, function as self-healing composite materials. Due to physical, chemical, and biological stresses, most materials degrade over time. The material eventually fails due to this degradation. Self-repairing composites formulated on microcapsules may be more effective than macroscopic repair techniques, which have been found to not produce sufficient mechanical properties with an appealing outcome. A self-healing composite contains silica nanoparticle-encapsulated healing powder and liquid. This liquid contains water and polyacrylic acid. Silica particles strengthen resin bonds and reduce fracture. If the self-healing composite cracks, silica particles enter and release liquid, which reacts with powder to form GIC and heals the crack. As GIC forms, it forms an ionic bond with the composite and stops cracking immediately.[56] Self-healing polymer nanocomposites benefit from the addition of fillers like clay, cellulose, metals, and carbon materials, which enhance properties such as toughness, strength, and Young's modulus. The healing ability of these composites can be activated through methods like the Joules effect, where electrical current triggers thermal healing in the nanostructured network. Self-healing materials have intrinsic properties (*e.g.*, block copolymers with reactive groups that respond to external stimuli) and extrinsic properties (which provide limited healing capacity once a threshold is surpassed). The self-healing process in polymers is influenced by factors such as chemical interaction,[57] physical association, cross-linking, chain movement, and polymerization. Nanostructures improve polymer properties, but achieving uniform dispersion of nanomaterials is crucial for high-performance self-healing

composites. Factors like morphology, nanoparticle content, and microphase separation further enhance healing capabilities.[58] There are many studies that incorporate nanomaterials in self-healing systems, as demonstrated in Table 1.

3.1.2 Antibacterial fillings for combating cavity recurrence. Traditional dental composites have primarily focused on improving mechanical and physical properties, but they lack bioactive functions to prevent secondary cavities. These cavities occur at the interface between the tooth and filling due to bacterial activity, particularly from *S. mutans*, which produce acids that degrade the tooth structure. Biofilm formation on dental composites is a major concern, as composites tend to accumulate thicker biofilms compared to materials like glass ionomers and amalgams, which release caries-inhibiting ions. This increased biofilm can elevate the risk of cavities, highlighting the need for antibacterial and demineralizing composites. To address this issue, researchers have developed anti-cavity composites by incorporating antibacterial particles such as bioactive glass, metal/metal oxides, and polymer nanoparticles, which help manage biofilm formation and reduce the risk of recurrent decay.[69]

3.1.2.1 Silver nanoparticles. In dentistry, silver nanoparticles have been extensively studied for antimicrobial properties in dental restorative nanocomposites, prostheses, and implants, demonstrating their versatility and efficacy. The potent antibacterial, antifungal, and antiviral properties of Ag

Table 1 Summarize different studies on self-healing nanocomposite fillers

Aim	Self-healing system	Key findings	Self-healing efficiency (%)	Additional properties	Ref.
Investigate the effect of triethylene glycol dimethacrylate (TEGDMA) microcapsules on dental composites	TEGDMA self-healing microcapsules (0–10 wt%), 20 wt% silica nanoparticles	No significant changes in transmittance, conversion degree, hardness, or elastic modulus; bending strength decreased	Not reported	Potential for mechanical performance optimization	59
Develop self-healing dental composites (SHDC) with antibacterial and remineralization functions	Dimethylaminohexadecyl methacrylate (DMAHDM), calcium phosphate (CP) nanoparticles, poly(urea-formaldehyde) (PUF) microcapsules (7.5 wt%)	Maintained mechanical strength; achieved antibacterial, remineralization, and self-healing properties	65–81%	Antibacterial, remineralization	60
Enhance healing ability of acrylic resin with PMMA microcapsules	poly(methyl methacrylate) (PMMA) shell microcapsules with TEGDMA healing agent, nano-silicon dioxide (SiO_2) modified with 3-methacryloxypropyltrimethoxysilane (MPS)	No significant mechanical property loss or cytotoxicity	78–121%	Biocompatibility confirmed	61
Optimize mechanical properties of self-healing nanocomposites	Nanoclay, PUF nanocapsules (7.5 wt%), different stirring rates	Optimal mechanical properties at 1300 rpm; stable self-healing performance over 90 days	54–58%	High durability in water aging	62
Improve thermoplastic polyurethanes (TPU) self-healing using NIR activation	Polypyrrole (PPy) nanoparticles, TPU	Increased thermal stability and hydrogen bonding with ester/urethane bonds	~100%	NIR-heated healing activation	63
Develop humidity-activated self-healing nanocomposites	Carbon nanotube (CNT)-based carboxyl methyl cellulose (CMC) with murexide salt	Healing at ambient temperature & 80% humidity; Young's modulus increased with CNT content	70% (20–30 °C), 50% reduction at 60–100 °C	Thermal stability (400–580 °C)	64
Improve anti-corrosion and self-healing in epoxy coatings	Titania nanotubes, epoxy monomer (EM), dodecylamine (DDA)	Accelerated healing *via* nanotube EM release; improved anti-corrosion properties	63%	Mechanical reinforcement, corrosion resistance	65
Enhance mechanical and self-healing properties of epoxy	β-Cyclodextrin/graphene (CD-G) epoxy nanocomposite	Enhanced mechanical properties, defect repair, and corrosion resistance	Not reported	Anti-penetration properties	66
Develop self-healing polyurethane nanocomposites with graphene oxide	Polyurethane graphene oxide nanocomposites	Stress–strain analysis showed healing in 48 h	70%	Anti-corrosion properties	67
Improve self-healing and anti-corrosion in epoxy coatings	Epoxy coatings with mesoporous silica (MSP) and polyethyleneimine (PEI)	Inhibitor effect blocked coating defects, improving corrosion resistance	Not reported	Anti-corrosion ability	68

nanoparticles make them popular nanofillers. The release of Ag^+ ions makes silver nanoparticles antibacterial. Ag^+ ions may kill bacteria by damaging cell walls, inhibiting DNA replication, and denaturing cytoplasmic enzymes. Smaller silver nanoparticles with higher specific surface areas have effective antibacterial properties even at low concentrations. Ag nanoparticles in the 1–100 nm range have been shown to kill Gram-negative and Gram-positive bacteria.[70,71]

Cheng *et al.* developed silver nanoparticles with a diameter of approximately 3 nm using an *in situ* method. By dissolving silver 2-ethylhexanoate in 2-(*tert*-butyl) amino ethyl methacrylate (TBAEMA) and mixing it with dental monomers like bis-phenol-A-dimethacrylate (BisGMA) and TEGDMA, they successfully reduced Ag^+ to Ag during photopolymerization. This *in situ* synthesis method prevented nanoparticle agglomeration without significantly altering the material's flexural strength and silver nanoparticle composites reduced bacterial colonization with as low as 0.03% (by mass) silver salt, but more did not.[72] In another study, Durner *et al.* explored the impact of silver nanoparticles on the leaching of substances from dental resin composites (DRCs). They observed increased release of organic small molecules from the samples containing silver nanoparticles, suggesting a potential influence on polymerization.[73]

Recent studies have demonstrated the effectiveness of silver nanoparticles in reducing lactic acid formation, inhibiting biofilm growth, and preventing secondary caries in dental materials.[74] Incorporating silver nanoparticles in dental composites has been shown to enhance both strength and antibacterial activity without compromising aesthetic or mechanical properties.[75] Combining silver nanoparticles with other bioactive agents has been explored to achieve dual-action properties such as remineralization alongside antibacterial effects, highlighting their potential in improving dental materials.[76]

Ai *et al.* synthesized HA nanowires coated with polydopamine (PDA) and loaded with AgNPs to create HA-PDA–Ag nanowires for integration into resin composites, demonstrating prolonged antibacterial efficacy without cytotoxic effects as the Bis-GMA/TEGDMA composites with ≥8% HA-PDA–Ag-1.0 exhibit nearly total bacterial death rate and silver ion release <0.05 ppm per day under AO/EB staining.[77] Barot *et al.* used halloysite nanotubes (HNT) to encapsulate AgNPs, improving antibacterial activity and mechanical properties in dental resin composites. The 5 wt% HNT/Ag composite that increased flexural strength by 54% (133.4 MPa *vs.* 86.5 MPa in control) and had good antibacterial activity against *S. mutans* would support these assertions. Another study involved mixing silver sulfadiazine with glass powders to create antibacterial materials for dental resins, showing potent antimicrobial effects over eight weeks.[78]

3.1.2.2 Zinc oxide nanoparticles. ZnO is a white inorganic compound insoluble in water with a ZnO formula. In dentistry, ZnO macro and micro-sized particles have been examined as an inorganic filler in restorative materials. Composites, adhesive resins, sealers, and cement are among the materials studied by ZnO. Smaller particles of ZnO nanoparticles demonstrated a superior antimicrobial activity than larger particles against both Gram-negative and Gram-positive bacteria. ZnO nanoparticles at the nanoscale exhibit potent antibacterial activity by interacting with bacterial cell membranes, disrupting membrane integrity, and inducing cell death. In addition, nano-sized particles have a high surface area to volume ratio; therefore, they have a higher percentage of atoms on the material's surface, leading to an increased surface reactivity. Nano-sized ZnO particles through bioactivity can enable mineral growth and negatively affect bacteria growth. Consequently, their biological properties could be mainly related to their higher reactivity and low dimensionality.[79]

The antibacterial mechanism of ZnO, known as photocatalytic sterilization, involves the generation of reactive oxygen species (ROS) through light-induced electron transfer processes. Even in dark conditions, ZnO crystals' surface defects contribute to ROS production. Additionally, the release of Zn^{2+} ions and interactions with bacteria also play crucial roles in ZnO nanoparticles' antibacterial effects.[70]

Studies show that incorporating ZnO nanoparticles into matrices can effectively inhibit bacterial growth and enhance compressive strength, with the addition of 1% ZnO nanoparticles significantly boosting mechanical properties. However, increasing ZnO nanoparticle content can reduce curing depth and weaken flexural and compressive strength due to opacity issues.[80]

Unlike silver, ZnO nanoparticles have a color like natural teeth, making them more aesthetically suitable for DRCs. Wang *et al.* developed strategies such as creating cellulose nanocrystals (CNC)/ZnO nanohybrids and coating ZnO particles with mesoporous SiO_2 to enhance the mechanical properties of DRCs. These approaches combine the reinforcement effects of CNC with the antibacterial properties of ZnO nanoparticles. The addition of 2 wt% CNC/ZnO nanohybrids reduced bacterial numbers by 78%, while incorporating 7 wt% ZnO@m-SiO_2 nanoparticles significantly increased flexural strength, flexural modulus, and compressive strength of DRCs without compromising other properties like degree of conversion and depth of cure.[81] Chen developed ZnO@m-SiO_2 nanoparticles by coating ZnO particles with mesoporous SiO_2, leading to improved bonding between fillers and matrices in dental resin composites. This enhancement resulted in increased compressive strength (32.5%), flexural strength (121.2%), and modulus (67.1%) in composites containing 7 wt% ZnO@m-SiO_2 compared to control fillers with SiO_2. The antibacterial efficacy of these composites surpassed 99.9% without significant alterations to other properties.[82]

3.1.2.3 Titanium dioxide nanoparticles. Nanostructured titanium dioxide materials are widely utilized in various medical and nonmedical fields due to their abundance. TiO_2, a white material with low solubility, finds applications in medical, pharmaceutical, and cosmetic industries. These nanostructures are cost-effective, non-toxic, and have diverse potential applications, being approved by the Food and Drug Administration (FDA) for use in food and drug-related products.[79] In the dental field, TiO_2 nanoparticles have been integrated into dental resin to combat caries, a prevalent chronic disease with significant health and economic implications. Incorporating TiO_2 into resin matrices has demonstrated

potent antibacterial effects in various dental applications such as composites, sealants, bases, liners, adhesives, and cements.[79]

The antibacterial mechanism of TiO_2 nanoparticles involves photocatalysis when exposed to UV radiation, generating ROS that disrupt bacterial osmotic balance and interfere with cellular processes, leading to oxidative cell death. Notably, TiO_2 nanoparticles may exhibit antibacterial properties even without UV irradiation, although the exact mechanism remains unclear.[83]

In dentistry, studies have highlighted the antimicrobial properties of TiO_2 nanostructures against various bacteria and fungi. Welch *et al.* incorporated TiO_2 NPs into dental adhesives to achieve bioactivity and bactericidal effects, positively impacting tooth remineralization by interfering with bacterial acidity.[84] Sun *et al.* integrated acid-modified TiO_2 nanoparticles into dental adhesives at a mixture of BisGMA and TEGDMA, resulting in improved resin mixtures when used in small amount of acid-modified TiO_2 nanoparticles.[85] In another study, Neel *et al.* examined the addition of TiO_2 NPs to Transbond XT, an orthodontic composite paste, to use as nanofillers, resulting in enhanced antibacterial effects and reduced enamel demineralization without affecting bond strength compared to conventional composites.[86]

Due to the challenges of dispersing TiO_2 nanoparticles, Xia *et al.* modified them with organosilane allyltriethoxysilane (ATES) to improve dispersion within resin-based composites, enhancing microhardness and flexural strength. Composites with 1.0 wt% modified nano-TiO_2 exhibited significantly better mechanical properties ($P < 0.05$) than controls.[87]

3.1.2.4 Copper nanoparticles. Copper nanoparticles (CuNPs) are recognized for their antimicrobial properties and potential applications in dentistry. They attach to microbial surfaces, disrupting cell membranes and causing cell death by generating free radicals that affect DNA replication and protein synthesis. Incorporating CuNPs into dental adhesives has shown effective antimicrobial activity against *S. mutans* without compromising mechanical properties, suggesting a promising avenue for combatting dental diseases.[88]

The mechanism of Cu nanocompounds involves aggregating bacterial cell surfaces, disrupting membrane integrity, and penetrating cells to induce leakage of intracellular components. Cu nanoparticles can release ions that disrupt ROS balance, leading to cell damage. These nanoparticles interact with sulfhydryl groups, inhibiting essential enzymes and proteins, further contributing to their antibacterial activity against various microorganisms, including oral pathogens like *S. aureus*, *E. coli*, and *S. mutans*.[71]

Copper oxide nanoparticles (CuO) exhibit semiconductor properties and antimicrobial effects by generating reactive hydroxyl radicals. Studies have demonstrated the efficacy of copper and copper alloys in killing bacteria, yeasts, and viruses through direct contact.[79] Copper-catalyzed azide–alkyne cycloaddition (CuAAC)-based resin have shown promise in reducing biofilm formation as it exhibited at least a fourfold reduction in *S. mutans* metabolic activity and biofilm viability and enhancing mechanical properties compared to conventional BisGMA-based polymers, offering enhanced strength and reduced shrinkage stress.[89] Additionally, CuAAC resin-based composites with microfillers enhanced mechanical performance, including over twofold lower shrinkage stress (0.43 ± 0.01 MPa), equivalent flexural modulus (6.1 ± 0.7 GPa) and strength (107 ± 9 MPa), and more than tenfold higher energy absorption (10 ± 1 MJ m^{-3}), as well as a $\sim$20 °C reduction in reaction heat at 60 wt% filler loading compared to BisGMA-based composites, highlighting their potential in dental applications.[90]

3.1.2.5 Gold nanoparticles. Gold has captivated researchers for its biocompatible behavior and antibacterial properties over the years. Utilizing gold nanoparticle-based materials in dental restorations offers numerous advantages. These materials effectively protect against microbial growth, particularly in dental caries prevention, and maintain long-term defense against caries. Notably, they exhibit chemical inertness, ensuring compatibility with dental materials and remaining active during restoration light curing. This characteristic preserves restoration color integrity and promotes superior composite bonding to tooth tissues, ultimately extending the lifespan of dental restorations.[91]

Dadkan *et al.* demonstrated that incorporating gold nanoparticles into dental adhesives enhances antibacterial properties. Incorporating colloidal gold nanoparticles (<20 nm) into dentin adhesives improved performance, including 75% increase in flexural strength, 60% improvement in micro-shear bond strength, and 65% increase in tensile strength at 5× NP concentration. Additionally, the adhesive showed antibacterial activity through a 2 mm inhibition zone, reduced bacterial growth in pour plate assays, and improved cell viability. Furthermore, the pure gold nanoparticles showed no harmful effects on cells and actually increased cell viability in the adhesive formulation.[92]

3.1.2.6 Iron oxide nanoparticles. Iron oxide (Fe_2O_3) has shown promise in various fields including tissue engineering, cancer therapy, imaging, and restorative dentistry. In dentistry, Fe_2O_3 nanoparticles have been studied for their ability to enhance bonding strength in dental adhesives.[79] Research has demonstrated that incorporating Fe_2O_3 nanoparticles in specific concentrations can significantly improve bond strength, even under conditions like exposure to a magnetic field and simulated pulpal pressure. The longer and denser resin tags observed in Fe_2O_3 adhesive suggest potential for improved bonding durability.[93] Additionally, combining magnetic nanoparticles such as Fe_2O_3 nanoparticles in the adhesive with a magnetic field enhanced resin penetration into dentin and dentin bond strength by 59%, while the incorporation of antibacterial agents and remineralization fillers further improved the adhesive's properties.[94] These findings highlight the potential of using multiple agents to enhance the characteristics of dental restorative materials. Future studies may investigate the durability of magnetic nanoparticles in dental adhesives under various stress conditions like thermocycling and water aging.

3.1.2.7 Fluoride nanoparticles. Fluoride nanoparticles have shown promise in dental restorative materials by promoting remineralization, inhibiting microbial activity, and combating recurrent caries. Their large surface area allows for high fluoride release rates with minimal filler usage.[95] Mitwalli *et al.*

developed a dental nanocomposite, nanoparticles of calcium fluoride ($nCaF_2$) +DMAHDM, incorporating calcium fluoride nanoparticles, demonstrating effective ion release and strong antibacterial properties by lowering biofilm CFU by 4 logs and reducing metabolic activity and lactic acid production in comparison to the control ($p < 0.05$). This composite has the potential to reduce biofilm acid production, prevent recurrent caries, and improve the durability of dental restorations.[96]

3.1.2.8 Polymeric nanoparticles. Polymerisable antibacterial monomer particles in dental composites prevent porosity and poor mechanical characteristics by adding unleachable antimicrobial age. Copolymerizing resin with antibacterial monomer prevents composite surface bacterial development during contact. MDPB, the most studied antibacterial quaternary ammonium (QA) chemical, is employed for repairs where appearance is not important due to its color instability. Ionic dimethacrylates (IDMAs) were approved for dentistry in 2012. IDMA, like MDPB, was bactericidal in Bis-GMA/TEGDMA matrices. Unfortunately, polymerisable agents only work when bacteria touch them.[97]

Antibacterial quaternary ammonium methacrylate nanoparticles (QAM) can be utilized as dental fillings as their antibacterial properties induce cytoplasmic leakage in microbial cell walls, leading to cell death. QAM resins and bacterial cell walls have positively and negatively charged surfaces, respectively, which favors ionic attachment and produces an electric imbalance in the cell membrane, raising osmotic pressure and cell death. Li demonstrated that increasing DMAHDM content in resin-based bonding agents improved antibacterial performance, reducing early bacterial attachment and biofilm CFU by nearly 5 logs at 10% DMAHDM. All groups maintained similar microtensile bond strengths (~60 MPa, $p > 0.1$), indicating that higher quaternary amine charge density inhibits biofilm formation without compromising adhesion.[98] A unique attribute of QAM resins is their ability to suppress 3D biofilms.[99] QAM enhances bacterial stress and death due to its antibacterial effects. QAM resins link well with restorative dental adhesive materials and are antimicrobial, which may help build better adhesives.[100]

Antibacterial nanomaterials in dentistry go beyond inorganic nanocompounds. Functional fillers include quaternary ammonium polyethylenimine (QAPEI). The resin composite was tested for *S. mutans* and *Actinomyces viscosus* antibacterial activity by direct contact and agar diffusion. After polishing the foundation material, nanoparticle-containing specimens reduced the two bacteria by 6 orders of magnitude. Nanoparticle-free QAPEI did not suppress bacteria, but optimized QPEI produced with regulated $NaHCO_3$ neutralization and *N*-lauroylsarcosine surface treatment showed considerable antibacterial activity at 0.5% wt/wt in acrylate and epoxy resin dental materials.[101] $NaHCO_3$ neutralizes acid during manufacture, improving QAPEI nanoparticles' *E. faecalis* antibacterial action. Antibacterial activity in acrylate and epoxy resin dental materials is increased by *N*-lauroylsarcosine surface treatment.[71]

3.2 Endodontics: revolutionizing root canal treatments

Endodontics is the branch of dentistry that studies the biology of normal dental pulp and treats pulp diseases and periradicular conditions. Dental caries can be caused by oral microorganisms, requiring root canal treatment. Nanotechnology can help develop advanced endodontic materials. Endodontic treatments require dental amalgam, GIC, composite, gutta-percha, root canal disinfectant, and sealers. Nanotechnology can improve endodontic materials by adding anti-bacterial nanoparticles to prevent root canal infection and failure. The studies have shown that biopolymeric nanoparticles in root canal disinfectants significantly enhance antibacterial activity, while QAPEI nanoparticles improve the antibacterial properties of root canal sealers against *Enterococcus faecalis* biofilms, a common cause of root canal treatment failure.[102]

3.2.1 Nanoparticle-based antiseptics for effective disinfection. Nanotechnology has emerged as a promising approach for improving root canal disinfection, as demonstrated in recent studies[103] Alfirdous *et al.* explored the use of nanostructure-based antimicrobial photodynamic therapy, utilizing polymeric nanoparticles and nanoemulsions to enhance penetration and light propagation within dentinal tubules.[103] These advancements address the limitations of conventional endodontic disinfection by providing deeper bacterial eradication and more effective canal sealing also, CuONPs play a significant role in endodontic disinfection due to their strong antibacterial properties. Despite being non-biodegradable, CuONPs have emerged as a promising alternative for controlling biofilm formation in the oral cavity. Their disinfection mechanism involves restricting bacterial growth by disrupting cell membrane permeability, thereby preventing essential nutrient uptake and leading to bacterial inhibition. This makes CuONPs highly effective in endodontic treatments, offering a potent strategy for biofilm control and infection prevention within the root canal system.[104]

The disinfection role of amorphous iron nanoparticles (AIronNPs) highlighted by Gao *et al.* (2020) in antimicrobial therapy, particularly when combined with an alternating magnetic field (AMF).[105] AIronNPs exhibited potent antibacterial effects by generating ROS through Fenton chemistry, effectively decomposing hydrogen peroxide into hydroxyl radicals for enhanced microbial eradication. The study demonstrated that AMF significantly boosted the catalytic activity and antibacterial efficiency of AIronNPs, leading to broad-spectrum disinfection. Additionally, this approach accelerated wound healing by promoting granulation tissue formation in an infected model. The synergistic use of AIronNPs and AMF presents a novel strategy for precise and controlled antibacterial activity, paving the way for advanced magnetic nanoantibiotics in disinfection and tissue healing applications.[105]

CS-NPs have demonstrated strong antimicrobial, antifungal, and antiviral properties, making them highly effective in root canal disinfection. Their antibacterial mechanism relies on electrostatic interactions that disrupt bacterial cell membranes, increasing permeability and ultimately causing cell death through leakage of intracellular components.[106] Kishen *et al.* were the first to explore the use of CS-NPs in endodontic disinfection, highlighting their ability to penetrate the complex anatomy of the root canal and dentinal tubules, ensuring long-term antimicrobial effects even after three months.[107] These

findings confirm that CS-NPs hold great potential for enhancing root canal disinfection and improving treatment outcomes.

3.2.2 Regenerative therapies for pulp tissue repair. The dental pulp is unmineralized soft tissue beneath a tooth. Pulp contains connective tissue, immune cells, odontoblasts, nerve fibers, and blood vessels. Due to its unique composition, the pulp produces and maintains dentin, provides immunity, nutrition, tooth vitality, and sensation. Worse, caries, trauma, and infections can cause pulpitis, painful and permanent pulp inflammation. Necrosis of the pulp kills teeth. Pulp tissue restoration after disease or damage is difficult. Revascularization of pulp tissue is difficult due to the tiny blood flow source at the tooth root apex. A lack of blood vessels reduces nutrient diffusion. To preserve the tooth's hard tissues, patients often need a root canal, weakening and killing the tooth.[108]

3.2.2.1 Materials for dental pulp regeneration. In tissue engineering and regenerative dentistry, biocompatibility, bioactivity, cell growth and differentiation make natural biomaterials essential. Studies like the AceCol scaffold showed superior biological properties for collagen, which is used for tissue regeneration.[109] Another promising material, chitosan, promotes odontogenic differentiation and antimicrobial effects in scaffolds. Ultrasmall superparamagnetic iron oxide (USPIO)-labeled HA and silk fibroin (SF) composites are low-cytotoxic and effective in dental pulp regeneration. Composite scaffolds that boost DPSC differentiation use gelatin and fibrin, which support cells well. Bioprinting with alginate supports pulp–dentin complex engineering.[110] Hyaluronic acid hydrogels promote vascularization and odontoblastic differentiation, demonstrating their regenerative potential. Platelet concentrates like platelet-rich-plasma (PRP), platelet-rich-fibrin (PRF), and concentrated growth factor (CGF) boost cell proliferation and differentiation, with PRF working best in inflammatory conditions.[111,112] Studies have shown that decellularized extracellular matrix (dECM) scaffolds can regenerate dental tissues and even teeth. Regenerative medicine is evolving with these natural biomaterials for dental pulp and dentin repair.[113]

Synthetic materials like poly(α-hydroxy ester)-based polymers, gelatin methacryloyl (GelMA), and self-assembling peptides demonstrate potential for pulp–dentin complex regeneration. Scaffolds can be made from polyglycolic acid (PGA), polylactic acid (PLA), poly lactic-*co*-glycolic acid (PLGA), and polycaprolactone (PCL), which have controlled biodegradability, mechanical strength, and bioactivity. Studies using bioactive molecules like PGA-melanocortin peptides (PGA-α-MSH) and PLGA/PEG hydrogels show improved cell adhesion, proliferation, and differentiation, promoting angiogenesis and osteogenesis. 3D bioprinting pulp regeneration scaffolds with GelMA, a modified gelatin derivative, is common. Self-assembling peptides mimic the extracellular matrix *via* nanoscale structures, providing DPSC proliferation and differentiation in 3D. Using bioactive composites and hybrid scaffolds to improve cell adhesion and tissue regeneration has advanced synthetic materials in regenerative pulp therapy.[114]

3.2.2.2 Pre-clinical trails. The table summarizes various studies that explore the use of nanoparticle-based biomaterials for dental pulp regeneration and endodontic therapies. These studies highlight the potential of bioactive nanoparticles and scaffolds to promote cell proliferation, differentiation, and tissue regeneration, with a focus on enhancing pulp healing, antibacterial properties, and angiogenesis. Key findings show that nanoparticles such as bioactive glass, curcumin, and clindamycin-loaded PLA significantly improve pulp healing, cell recruitment, and antibacterial efficacy. Additionally, hydrogels enriched with CNC and platelet lysate support growth factor release and enhance cell recruitment. Scaffolds loaded with fibronectin also boost cell migration and gene expression related to pulp regeneration. Despite promising results, challenges remain in clinical translation, including scaling production, ensuring long-term stability, and optimizing dosing for specific applications. Overall, these studies demonstrate the great potential of nanomaterials in advancing regenerative endodontics and improving pulp tissue regeneration outcomes as demonstrated in Table 2.

3.3 Periodontology: combating gum disease at the nanoscale

Gum inflammation and bone loss (alveolar bone loss) characterize periodontitis, the most common oral disease. The main reason is the accumulation of plaque on dental and gingival surfaces, which is influenced by elements related to unclean behavior, the oral cavity's internal environment, and the creation of plaque.[125] Periodontal disease, caused by opportunistic infections, is challenging to treat due to bacteria in biofilms that resist antimicrobials and the body's defenses. Periodontitis is characterized by inflammation of the gums, bleeding gums, and foul breath. When periodontal collagen deteriorates and alveolar bone resorbs, gingival epithelial tissue migrates, and teeth become less supported, pockets form. If left untreated, teeth can become loose and eventually fall out, and the best way to treat the issue depends on how far along it is in its evolution.[126]

Traditional treatment for periodontal issues typically includes scaling and root planing to reduce biofilm under gums, alongside antibacterial therapies such as probiotics, antiseptics, and antibiotics. Recent research indicates that metal and metal oxide nanoparticles exhibit antimicrobial properties effective against different Gram-positive and Gram-negative bacteria, including resistant strains.[127] As a result, nanotechnologies offer a promising alternative to conventional periodontitis treatment.

3.3.1 Targeted drug delivery for periodontal regeneration. Nanoparticles enhance the *in vivo* effectiveness of bioactive molecules, allowing for regulated distribution, improved drug release, and simple penetration, all of which contribute to the successful regeneration of periodontal tissue. Liposomes, inorganic nanoparticles, nanotubes, dendrimers, micelles, and polymeric nanoparticles are some of the nanoparticulate delivery strategies that have been studied for periodontal tissue regeneration.

3.3.1.1 Liposomes. Liposomes serve as versatile drug delivery systems owing to their bi-layered structure, biocompatibility, and biodegradability. They can encapsulate molecules of varying solubility while considering factors such as

Table 2 Pre-clinical (*in vitro* and *in vivo*) studies of nanoparticle-based biomaterials for dental pulp regeneration

Type	Nanoparticle type	Affected tissue/cells	Key findings & conclusion	Ref.
In vitro	Bioactive glass (BG) + tideglusib	Human dental pulp stem cells (hDPSCs)	BG + tideglusib promoted pulp healing and hDPSC proliferation, showing potential for pulp regeneration	115
In vitro	Phytosomal curcumin (PC)	DPSCs	Low doses enhanced DPSCs, while high doses were cytotoxic. PC-NPs are promising for regeneration at low doses	116
In vivo & *in vitro*	Polyvinyl alcohol (PVA)/ chitosan nanofibers + ciprofloxacin & IDR-1002	hDPSCs & dental pulp tissue	Nanofibers demonstrated antimicrobial, anti-inflammatory, and regenerative properties for pulp revascularization	117
In vitro	Polyamidoamine (PAMAM) dendrimers	DPSCs	PAMAM dendrimers facilitated differentiation, while DNCP outperformed in mineralization	118
In vitro	Dicalcium phosphate dihydrate (DCPD) & HA	DPSCs	NP-HA promoted early differentiation, while NP-DCPD supported osteoinduction	119
In vitro	PCL nanofiber scaffolds + fibronectin (FN)	Human apical papilla cells (hAPCs)	FN-loaded scaffolds promoted proliferation, migration, and pulp regeneration	120
In vitro	Clindamycin-PLA (CLIN-PLA) in fibrin hydrogel	Dental pulp mesenchymal stem cells (DP-MSCs)	CLIN-PLA-NPs had antibacterial properties and supported collagen synthesis without cytotoxicity	121
In vivo	USPIO-labeled HA/silk fibroin scaffold	DPSCs	Scaffold supported pulp regeneration and enabled MRI-based monitoring	122
In vitro	Hyaluronic acid, CNCs and platelet lysate (PL) hydrogel	Human dental pulp cells (hDPCs)	Hydrogels promoted cell recruitment and angiogenesis, supporting pulp revascularization	123
In vitro	Mesoporous calcium silicate (MesoCS)	DPSCs & bone cells	MesoCS supported mineralization and osteogenic differentiation	124

drug/lipid ratio, release kinetics, and stability. Ultrasound has shown effectiveness in delivering biomolecules for periodontal regeneration. Negatively charged liposomes are highlighted for their dual hydrophobic and hydrophilic traits, and modifications with viral fusion proteins enable the delivery of antigenic substances into cell cytosol.[128] A novel pH-activated nanoparticle, *N*,*N*,*N*-trimethyl chitosan, a liposome, and doxycycline (TMC-Lip-DOX NPs), inhibited free mixed bacteria and biofilm formation and showed excellent biocompatibility with human periodontal ligament stem cells (hPDLSCs) suggesting potential use for periodontal inflammation treatment.[129] Resveratrol-loaded liposomal system (Lipo-RSV), a nonflavonoid polyphenol, inhibited inflammatory progression and was biocompatible. However, liposomes face challenges such as limited stability, drug leakage, and augmenting output procedures[130] as demonstrated in Table 3.

3.3.1.2 Polymeric nanoparticles. Polymeric nanoparticles, with their non-immunogenicity and biological inactivity, are crucial in drug delivery systems, particularly in treating periodontal defects through various methods and carrier surfaces.[131] Superior bioactivity, biocompatibility, and osteoconductivity have been demonstrated by composite biomaterials composed of biodegradable polymers with bioactive glasses[131] as demonstrated in Table 3. By utilizing a porous composite of chitosan/collagen encapsulated with platelet-derived growth factor (PDGF), a 3D carrier for improved proliferation of periodontal ligament cells can be created. This carrier releases growth factors over the course of six weeks.[132]

The best guided tissue regeneration (GTR) membranes are chorionic membranes (CM) or amnion/chorion membranes (ACM), which have many desirable properties such as being biocompatible, having minimal immunogenicity, being

Table 3 The advantages and disadvantages of targeted NPs used in drug delivery for periodontal regeneration

Name of nano	Advantages	Disadvantages	Ref.
Liposomes	• Biodegradability, biocompatibility, and non-toxicity • Versatile in drug delivery systems; potential for modifying with viral fusion proteins and specific applications in periodontal inflammation treatment	• Stability issues • Drug leakage • Challenges in increasing output	129
Polymeric nanoparticles	• Biological inactivity and non-immunogenicity • Widely used for drug delivery in periodontal treatment • Specific properties with chitosan: antibacterial, biodegradable, biocompatible, non-toxic, tissue healing, and osteoinducting	• Need for further research to confirm effectiveness in bone ridge restoration and bone deformities fixing	142
Inorganic nanoparticles and nanocrystals	• Exhibit significant antimicrobial and regenerative capabilities • These materials have potential applications in bone reconstruction, particularly MgO, silver, and zinc nanoparticles • Bioactive glasses containing strontium and zinc promote osteogenesis	• Possible accumulation of heavy metals in the body from silver and zinc nanoparticles	138
Small filaments (nanofibers)	• Exhibit biomimetic characteristics that enhance cell adhesion, differentiation, and proliferation • Flexibility in application and processability • These nanofibers can improve the local environment for periodontal regeneration by incorporating biomolecules • Biodegradability and biocompatibility	• Requires precise structural mechanics and chemistry research for specific applications in GBR therapies	140

permeable, stable, and resorbable.[133] CM and ACM have shown potential in tissue regeneration treatment for various defects, but further studies are needed to demonstrate their role in repairing bone defects and preserving bone ridges.[133] Because of its biodegradability kinetics, tractability mechanical qualities, and biocompatibility, PLGA is a biodegradable polymer that is utilized for therapeutic drug delivery systems.[134]

Due to their unique features, nanogels nanosized cross-linked hydrophilic polymeric networks have been investigated for drug delivery. A novel asymmetric barrier membrane with antibacterial activity was developed by him and colleagues by combining nanoscale agarose hydrogel, hollow carbonated HA, and ε-poly-lysine. The membrane shows promise for periodontal tissue engineering due to its enhanced biocompatibility and mechanical qualities.[135]

3.3.1.3 Inorganic nanoparticles and nanocrystals. Periodontitis treatment options including inorganic nanoparticles have received a lot of attention. These include metallic nanoparticles with antibacterial and regenerative properties, as well as nanobiomaterials containing calcium for bone rebuilding.[131] Although nanoparticles derived from silver and zinc have important antibacterial and osteogenic effects, the buildup of heavy metals in the body could result from their breakdown,[136] magnesium oxide nanoparticles (MgO) have recently attracted a lot of interest in periodontal regeneration biomedical applications. Periodontal tissue regeneration could be facilitated by the fabrication of a membrane containing MgO nanoparticles which is composed of PCL and gelatin core–shell nanocellulose[137] as demonstrated in Table 3.

For nano-DDSs to aid in periodontal regeneration, they need to promote osseointegration with host tissues while also limiting the activity of bacterial pathogens. The inclusion of strontium and zinc in bioactive glasses is a potential approach to promote osteogenesis in living things. A combination of polymers and ceramic nanoparticles would be used to create these glasses. Adding the BMP activator phenamil to Sr-doped mesoporous bioglass nanoparticles improved the osteo/odontogenesis of human mesenchymal stem cells, according to an additional investigation.[138]

Due to its dual biological activity of osteoanabolic and anti-resorptive actions, strontium ranelate has been acknowledged as a therapeutic medication for osteoporosis and bone repair.

Recent research has demonstrated that osteogenic-differentiating MSCs exhibit a marked upregulation of osteoblast and alkaline phosphatase (ALP) gene expression after treatment with strontium.[139]

3.3.1.4 Nanofibers. Nanofibers exhibit significant potential as a nanomedicine for periodontal tissue regeneration due to their biomimetic properties, which enhance cell adhesion, differentiation, and proliferation. Key attributes include optimal porosity, high surface-to-volume ratio, improved mechanical qualities, and adjustable flexibility, making them an excellent choice for electrospinning. This method allows for the creation of nanofiber membranes that provide an ideal environment for cell growth and can be tailored with biomolecules to further promote periodontal regeneration.[140] Because of its adaptable biodegradability, excellent biocompatibility, minimal bacterial adhesion, high structural integrity, fabricability of customizable sizes, desirable mechanical properties, and interactions with biomolecular components, SF is regarded as one of the most utilized natural biopolymers as nanofiber drug carriers.[141] For guided bone regeneration (GBR) treatments, a new bilayer membrane was created, which consists of nanocalcium-phosphate with a PCL membrane layer and an electrospun layer of silk fibroin-PCL-PEG-PCL. Potential uses for GBR treatments were foreseen by structural, chemical, and mechanical investigations.[140]

3.3.2 Nanobiosensors for early detection of periodontal disease. Nanoparticles (NPs), including metallic, fluorescent, and magnetic types, enhance point-of-care testing (POCT) for infectious diseases, especially in areas with limited healthcare resources. In periodontal disease, markers such as MMP-8, IL-1β, and TNF-α indicate tissue degradation. Detection typically relies on saliva or gingival crevicular fluid (GCF) samples, although GCF's limited volume affects specificity.[143] Biosensors are analytical tools that measure chemical concentrations by combining biologically active components with appropriate physical transducers to generate a quantifiable signal. These nanosensors make advantage of the enhanced sensitivity and accuracy offered by metal nanoparticles like magnetic nanoparticles, CNTs, and quantum dots, as illustrated in Fig. 2. The production of damaging proteases, gingipains, by *P. gingivalis* is the primary cause of gingival disease. To aid in early diagnosis and therapy, a nanoplasmonic biosensor based on nanoparticles can detect the activity of these proteases.[144,145] Research shows *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis* can easily cling to Ag-coated magnetic nanoparticles, allowing a microfluidic chip to separate tested bacteria from other sample components. The Raman signal is amplified by magnetically drawing the NPs towards the Si/Ag surface-enhanced Raman spectroscopy (SERS) platform, recording SERS spectra.[146] Metal nanoparticle platforms have been developed to accurately detect biomarkers linked to periodontal disorders. The platform uses Cu NPs@Cu-MOF and Ti carbide nanosheets to detect H_2O_2 levels in saliva and gingival crevicular fluid, distinguishing between healthy individuals and those with gingivitis or periodontitis.[147] Ag nanoplates show great selectivity and recovery for detecting ALP and IL-1β.[148] AuNPs can detect *P. gingivalis* with a limit of less than 0.1 μg mL^{-1}, and the detection limit for methyl mercaptan increases to 50 ppb when mixed with ZnO NPs and AuNPs.[144] Magnetic nanobeads can detect *P. gingivalis*-specific gingipains, and Fe_2O_3@AgNPs can reliably distinguish *A. actinomycetemcomitans* and *P. gingivalis*. Wearable fluorescent mouthguards made of ZnO–PDMS have excellent sensitivity and specificity for detecting volatile sulfur compounds.[143]

3.4 Oral and maxillofacial surgery: enhanced implants and tissue engineering

Tissue engineering offers a multidisciplinary solution for restoring normal shape, function, and appearance after tooth loss and supporting bone and tissue. Dentures or fixed prostheses are the standard of care, but they cannot always repair problems caused by trauma, tumors, or birth anomalies in the

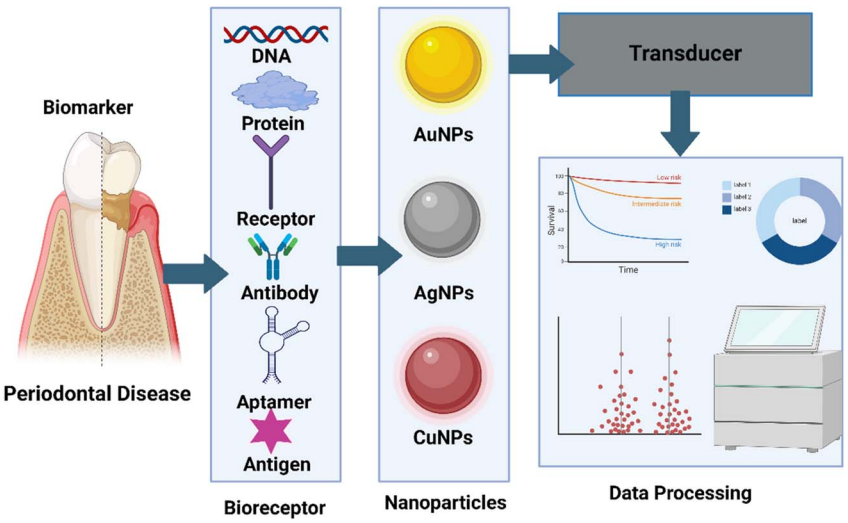

Fig. 2 A biosensor, consisting of bioreceptors, nanoparticles, transducers, signal processors, and display components, can detect biomarkers in circulation, such as periodontitis, by converting electrical signals to the correct format.

maxillofacial region.[149] Traditional therapies like autogenous grafts and osteo-cutaneous free flaps can be time-consuming and expensive. Recent biotechnology advancements allow for the growth of artificial versions of injured or missing components, replicating stem cells, cytokines, and growth factors, enabling tissue regeneration. Oral and maxillofacial features like tooth structures, periodontium, temporomandibular joint, condyle, and cranial sutures can be regenerated using mesenchymal stem cells, which can be produced from embryos or adults and develop into mesodermal lineages. Biobanking allows for the preservation and retrieval of dental stem cells.[149,150]

3.4.1 Biocompatible nanomaterials for implant-bone bonding. Problems with bacterial adhesion, low cell proliferation, and inadequate corrosion resistance are common with orthopedic implants, despite their critical role in bone formation and treatment. Exceptional tribological properties, great wear and tear resistance, osseointegration, tissue regeneration, and drug release maintenance are just a few of the ways nanotechnology could improve orthopedic research. To promote cell proliferation, decrease infection rates, and avoid biofilm formation, nanostructured materials imitate the characteristics of original bones. Nanostructured metals, ceramics, polymers, and carbon materials have opened up new avenues of inquiry in orthopaedics.[151]

3.4.1.1 Metallic and metallic oxide nanoparticles for implant-bone bonding. Magnesium is crucial for human health, as insufficient levels can lead to osteopenia and bone loss. Medical implants made of magnesium are biocompatible, biodegradable, and low toxicity, making them suitable for orthopedics. Nanoparticles of MgO have antibacterial, economical, and eco-friendly properties as demonstrated in Table 4, making them useful for dental and orthopedic implant preservation. Researchers have enhanced the mechanical strength and antibacterial activity of porous scaffolds, bioactive glass scaffolds, and prosthetic bandages using Mg nanoparticles. However, cell death, DNA damage, and intracellular ROS generation can occur, and the processes contributing to Mg poisoning require further investigation.[152]

Tantalum is a biometal ideal for orthopedic implants due to its anti-corrosion and high biocompatibility properties. It is used in hernia mesh, frontal sinus reconstruction tubes, and peripheral nerve repair foil as demonstrated in Table 4. Porous Ta mimics osseous tissue and provides superior fixing strength. Tantalum oxide (Ta_2O_5) nanoparticles are ideal for X-ray and Computed Tomography (CT) contrast agents. They improve Young's elasticity and compressive strength and have been used to fortify polyetheretherketone (PEEK) scaffolds. However, they are not suitable for load-bearing implants due to their density, high elastic modulus, and poor compatibility with bone.[153]

Titanium and TiO_2 nanoparticles are ideal materials for dental and orthopedic implants due to their biocompatibility, high specific strength, corrosion resistance, stiffness, and tensile strength as demonstrated in Table 4. They can enhance osteogenic differentiation and improve bone healing capabilities. However, they can disrupt bacterial cell membrane integrity and release harmful metal ions. Titania nanoparticles can also cause hypersensitivity reactions near implants, potentially entering the bloodstream or cells. To ensure the safety and long-term durability of orthopedic implants, effective ways to incorporate titanium nanoparticles and alloys are crucial.[154] Silver nanoparticles are favored in bone tissue engineering due to their antibacterial and proliferation-inhibiting properties as demonstrated in Table 4. They are biocompatible and can increase cell division rates. They stimulate the HIF-1 gene, promoting osteoblast development and differentiation. They also lower inflammation and improve osteogenesis. Further research is needed to understand their effect on MSCs.[155]

Zirconium and ZrO_2 nanoparticles offer improved mechanical properties, biocompatibility, and corrosion resistance in various bio-applications like dental procedures, orthopaedic devices, and biosensors as demonstrated in Table 4. However, their lack of activity may limit their usefulness. Metal nanocomposites have been integrated with bioactive substances to reduce toxicity and enhance antibacterial properties.[156] Copper and silver nanoparticles have been used to treat osteomyelitis, eradicating bacteria while maintaining antibacterial properties. Synergistic applications of nanocomposites are being explored for improved bioactivity, corrosion protection, and antibacterial function.[156]

3.4.1.2 Nonmetal nanoparticles for implant-bone bonding. Amorphous glasses, carbon composites, crystalline ceramics, and polymeric materials are ideal for structural implantation due to their unique properties as demonstrated in Table 4. However, their bio-incompatibility and poor mechanical qualities have limited their application. Nanophase components, such as composites, polymers, and ceramics, have improved osseo-integration and bone-formation capabilities, making them ideal for osteoblast function and ingrowth. Polymer-based materials are preferred for controlled drug delivery vehicles and porous tissue engineering scaffolds due to their superior osseointegration and bone regeneration properties. Bioglass, silicon oxide, HA, and calcium phosphates are non-metallic materials with desirable properties but high noncompliant elastic modulus, making them susceptible to acetabular socket loosening and fractures. More progress is needed to improve the ability to target and influence cell and tissue activities in anticipation of implantation at specific sites.[157,158]

3.4.1.3 Smart orthopedic implants for implant-bone bonding. Bone grafting is a promising method for addressing patients' reconstructive demands, with biomaterials and their three-dimensional structures being enhanced to create smart or intelligent implants. Stimuli, including physical, chemical, electrical, or magnetic, can promote tissue regeneration in the interior microenvironment.[158] Designing biomaterials with light and magnetic fields integrated into their structure allows for precise delivery of medications and growth factors. Magnetite nanoparticles have been used to stimulate and accelerate osteogenic processes, while a bioactive coating has been created for titanium substrates used in bone implants. Light-responsive biomaterials can control the position, wavelength, duration, and intensity of a harmless light source as demonstrated in Table 4, with some devices targeting biofilm-forming bacteria.[158,159] Sulfonated long carbon fiber reinforced

Table 4 The advantages and disadvantages of NPs for implant-bone bonding

Nanoparticles	Advantages	Disadvantages	Ref.
Magnesium and MgO	• Non-toxic and biodegradable • Antibacterial properties • Cost-effective • Environmentally friendly • Improve antimicrobial and mechanical properties	• Potential toxicity issues (cell death, DNA damage, ROS formation) • Requires further research to understand toxicity mechanisms	152 and 158
Tantalum and Ta_2O_5	• Excellent biocompatibility • Anti-corrosion • Significant fixing strength (mimics bone tissue) • Effective as X-ray and CT contrast agents	• High density and modulus of elasticity (unsuitable for load-bearing implants) • Lack of sufficient bone compatibility	153 and 158
Titanium and TiO_2	• Excellent biocompatibility • High strength, stiffness, and tensile strength • Corrosion resistance • Promote bone healing and osteogenic differentiation	• Potential to emit toxic metal ions • Risk of hypersensitivity reactions • Can damage bacterial cell membranes and enter bloodstream or cells	154 and 158
Silver	• Strong antibacterial and proliferation-inhibiting properties • Promote osteoblast growth and differentiation • Reduce inflammation • Accelerate cell division	• More research needed to understand the impact on MSCs	158
Zirconium and ZrO_2	• Enhanced mechanical properties – excellent biocompatibility • High corrosion resistance	• Limited utility due to inactivity • Requires enhancement for better antimicrobial properties	156 and 158
Copper	• Strong antibacterial and bactericidal properties • Potential to enhance bioactivity when used in nanocomposites • Useful in protecting against corrosion	• Potential toxicity • More studies needed to fully understand effects and optimize use	156 and 158
Polymeric materials, ceramics, glasses, carbon composites	• Excellent osseo-integration and bone-formation capabilities • Effective for controlled drug delivery and tissue engineering scaffolds • Superior bone regeneration capabilities	• Limited applicability due to bio-incompatibility • Generally, have subpar mechanical properties • Prone to socket loosening and fractures	157 and 158
Smart or intelligent implants	• Can promote tissue regeneration using stimuli (physical, chemical, electrical, magnetic) – accurate administration of growth factors and pharmaceuticals	• Requires further research to optimize stimuli and effects	158 and 159

polyetheretherketone (LCFRPEEK) implants have been treated with hydrogels made of multifunctional stimuli-responsive metal–organic frameworks (MOFs) by UV-grafting, which show superior *in vivo* immunomodulatory, angiogenesis, osteogenic differentiation, and osseointegration capabilities. Wang *et al.* reduced graphene oxide (GO) injected into a hydrogel film based on chitosan and teriparatide, allowing for angiogenesis and local bone regeneration in an osteoporotic bone defect. More research is needed to find the optimal pulsatile schedule, indicating that automation could be a part of the design plan to improve the regenerative effect.[158]

3.4.2 Nanoparticles for guided tissue regeneration. Periodontitis, a severe inflammation, can cause teeth to fall out. Two basic surgical techniques for periodontal tissue regeneration and repair are GTR and GBR. GTR uses an occlusive substance to prevent the growth of connective and epithelial tissues into defects, allowing periodontal tissues to regenerate. GBR is used for posterior implant implantation to correct defective alveolar areas. Membranes used in GTR and GBR must be biocompatible, have a degradation profile aligned with tissue regeneration, exhibit high tear and rupture resistance, be porous, osteoconductive, and antibacterial.[160]

A monolayer directed tissue regeneration membrane including drug-loaded CS-NPs was the goal of Ghaffar *et al.* (2024) study. The chitosan GTR membrane was treated with the nanoparticles that had been produced by the ionotropic gelation process and then applied by the freeze gelation method. Compared to the control membrane, the GTR membrane containing ciprofloxacin nanoparticles exhibited a markedly quicker rate of drug release. CS-NPs coated with antibiotics enhanced the membrane's drug release capability.[161]

In study by Abdelaziz *et al.* (2021) a new line of scaffolds containing nanofibers and nanoparticles has been designed for directed periodontal tissue and bone regeneration with increased antibacterial activity. These scaffolds were constructed using electrospinning with different concentrations of hydroxyapatite nanoparticles (HANPs) and AgNPs from PCL or PLA/cellulose acetate (CA) in a 7 : 3 ratio. The nanofibers improved cell survival by 50% and maintained antibacterial activity for 32 days, demonstrating their potential for GTR/GBR applications. The nanofibers also showed optimal mechanical properties, with a tensile modulus of 20 MPa for PCL-based nanofibers and 38 MPa for PLA/CA nanofibers. The scaffolds loaded with HANPs predicted improved *in vivo* bone production, facilitating the creation of apatite and mesenchymal stem cell proliferation.[160]

4. Challenges and future directions

The process of using smart nanomaterials in dentistry depends on the type of nanomaterial used. The practicality of nanotechnology in medicine is widely known and available. However, the main impact of its use *in vivo* or *in vitro* experimentation is the safety in the use of any type of nanomaterials. In dentistry, it is a priority to overlook the toxicity of the nanomaterial, overly due to the nanomaterial impacts directly towards living tissue. Even if the nanomaterial is highly regarded in its application in a dental disease or surgery, the risks of its use must be outweighed, especially to the patient's cells and homeostasis of their oral cavity.[162]

All nanomaterials used in any consumer and environmental field must prologue to their impact on human health and the environment. As such, the properties of the nanomaterials of its physical, mechanical, chemical, and biological properties must be tested and adhered to chemical & biological standards. Such standards help to specify the most appropriate material in dental work that is biocompatible and biodegradable without the cause of toxic agents causing any adverse effects.[163] Vasiliu *et al.* (2021) highlight that the biocompatibility of a dental material must depend on several factors of the chemical and physical characteristics of the nanoparticle. Further noting the concept of biocompatibility of a dental material is only said to be biocompatible under five objectives: (1) when harmless to soft tissues, (2) doesn't have the potential of being carcinogenic, (3) doesn't contain agents resulting in allergic reactions, and (4) doesn't negatively affect the blood–brain barrier, and (5) doesn't cause genotoxicity, cellular toxicity, immunotoxicity or dissolution of toxic ions into the bloodstream.[3,21,163,164] Moreover, "smart/intelligent" materials have been declared as "passive materials" and are ideal for dental applications. Mainly due to their focus on no interactions in the oral environment. The purpose of pursuing the use of smart nanomaterials in dental applications is due to their ability to modify their shape, color, and size under the external stimulus of temperature, light, pH, moisture, electric/magnetic fields, chemical compounds, or stress.[163]

Furthermore, to impact the quality of smart nanomaterials, nanomaterials result in the generation of ROS. To avoid the formation of ROS or even the induction of toxicity in the body through dissolution and binding. One may coat the nanoparticle in a polymeric coating or another coating of a neutral charge. The purpose of a neutral charge is due to the ionic behavior of the nanoparticle, which requires a coating to prevent the dissolution of the nanoparticle systemically or in the oral environment of the affected area. Polymeric coating aids as a barrier to prevent nanoparticle dissolution and the formation of free radicals. Moreover, another prospect one may use is to have the nanoparticle to be negatively charged instead of positively charged, to reduce nanotoxicity and bind to the cell's surface.[21]

Another option to help with safety considerations in dental applications is using materials in tissue engineering. Tissue engineering has been aimed at its futuristic use with the requirements of using biocompatible green materials with long-term stability. These factors help to avoid the adverse health effects nanoparticles or 3D scaffolds may induce. Instead of materials that contain cationic toxicity and diffusely long-term immunogenicity. Although 3D scaffolds may also seem to be another alternative to use, there are some complications in their use. Including immune rejection, low bioactivity, irreversible genotoxicity, and ethical considerations.[164] To combat and avoid the use of a nanomaterial deemed non-biocompatible/biodegradable, lab-on-a-chip technologies have advanced to enable rapid and sensitive detection of nanotoxicity of the material through biological fluid.[21] The use of this technology beforehand in any *in vitro* and *in vivo* short-term or long-term experimentation, can help to shorten the span of testing and assessing the issues and toxicity of the nanomaterial.

The main goal of commercializing dental nanoproducts is to ensure the product's safety beforehand and the understanding of implementing certain laws. Of which lays rest of high importance, due to the biodegradability, biocompatibility, physical, mechanical, biological, and chemical properties of the nanoparticles at the nanoscale, and their unknown side effects and biological interactions they propose.[165] After these ethical concerns of animal and human testing are then followed. Such ethical concerns must be applied to avoid future issues, these

include "patient approval, family consent, dosage consideration, prior animal testing and informed consent for human experimentation". Once such challenges can be perceived, aspects of private companies commercializing the product may follow. Such concerns may be difficult to overcome because many of the population may have social xenophobia towards the new and unknown technologies of nanotechnology.[3] Without the procedures of ethical regulations, the prospect of the nanoproduct being in the market would be deemed difficult.

Frameworks have been adopted in the US federal and state agencies to assess and evaluate any health concern. Such a framework is established on a four-stage framework: (I) identifying the problem, (II) assessment of the dose–response, (III) assessment of exposure and (IV) characterization of the risks.[166]

Ideally, frameworks such as the one above help to implement the correct laws, regulations, and policies for the market of dental nano products. However, the stages of the framework don't suit their own with the US federal and state agencies. They rely on the coherence of the government to sponsor and encourage private companies to perform post-marketing studies. These studies allow the proper investigation of the long-term effects and adverse side effects of the target nanoproduct. The studies then are directed to the legislative and regulatory bodies (*e.g.* FDA) to assess and examine the nanomaterial.[166]

However, one issue does affect the commercialization of any type of nanoproduct. Not just in the dental sciences. And that is society itself. The main prospect of the success of commercialization of any product is focused on the consumer, funding parties, and policy & decision makers. The success and failure of any nanoproduct rests on the public's attitude toward the concept of nanotechnology. The ethics, morals, and values of people today control mainly the concepts of acceptance of ideas of new technologies of the benefits outweighing the risks. And, in the case of fear, the concept of using nanotechnology is led into society. There is a call for immediate action on the collaboration of the public's concerns and spreading awareness of the various applications of nanotechnology currently enrolls in and in the future. Such an action can aid in the support of the public for the commercialization of nanoproducts.[166]

Furthermore, dental products to be left on the market must satisfy the regulatory standards of ISO 10993-series and ISO 7405 of evaluation and management of medical grade materials of biocompatibility, biodegradability, sustainability and *etc.*[167–169] With such standards already deeply entrenched in the dental market, many types of innovative products have begun to emerge. Such products have been mixed with biosensors, nanocomposite adhesives, and the involvement of AI into the vast field of dental science. JHCIB biosensors (Dentalis Bio Solutions) is an innovative biosensor made of micro disposable polymer kit sensor, which can allow the detection of charged and uncharged molecules.[169] Biosensor, when equipped with an AI integration system, like Overjet, can enhance the utility in the care of the patient. Allowing the point-of-care diagnostics to achieve significantly higher standards towards smart patient care in regards of cavity, disease, or pathogen formation and detection.[170] Even though this biosensor, has not yet been on the market officially, the outlook of reach & development in these sections have progressed with the ventures and use of various interdisciplinary fields: biomedical, material science, computational biology, AI, and bio nanotechnology, *etc.* that influence the progress and advancements of innovative and pioneering devices and products onto the market. Other implantations include the use of various types of material in the synthesis of nanocomposite formulations of cement, adhesives, and creams of metal/metal oxide nanoparticles, including zirconia,[171] calcium hydroxide,[172] silver nanoparticles,[173] titania,[174] zinc oxide, copper oxide,[175] and much more. These have all been either experimentally proven in various literature at a higher degree or had successful clinical trials in treatment and outcomes towards patient status and care. Especially with such nanoparticles on the market: Filtek™ Supreme XTE (3M), Composan Bio-esthetic Cream (Promedica), Composan Bio-esthetic Flow Nanocomposite (Promedica), Provilat (Promedica), Solobond M Dentine & Enamel Bond (VOCO), and Diafil Nanocomposite (DiaDent). Thus, the progress of the use of smart nanomaterials is still advancing, but to this point, the progress of associating nanotechnological material on the market has grown. And with the involvement of 3D and 4D printing and AI, the creation of such products may soon be accessible in dental science at a near stage. Hence, it can be summarized that the futuristic applications of smart nanomaterials rely on future studies and examination of the properties of smart nanomaterials. Including the prospect of determining new nanomaterials to be used in the applications of the "smart" properties. And, with the evolution of new smart nanomaterials being designed leads to further studies to be performed to understand the impact of these nanomaterials used in the dental field. Especially with the development and use of smart nanomaterials in tissue engineering & regeneration and dental implants. With complex structures being in use, it is a must for one to acknowledge the impact of smart nanomaterial in studies of long-term effects. To determine the validity of the future applications of smart nanomaterials in dental sciences.

5. Conclusion

Smart nanomaterials are a promising new tool for dentists to employ in their attempts of providing better, more personalized care to their patients. Stronger, more biocompatible, and more effective dental treatments can be made with the help of these nanoparticles, which have unique physicochemical features. Orthodontics, periodontology, implantology, and restorative dentistry all make use of them to effectively address persistent clinical issues such bacterial colonization, tissue regeneration, and material degradation. Nanoparticles have the potential to merge conventional dental materials with the intricate oral biome, according to new research. A well-rounded approach prioritizing long-term safety, regulatory approvals, and standardized methods to test biocompatibility and cytotoxicity is necessary for clinical applications to be successful. To improve material formulations and ensure they operate effectively *in vivo*, it will be crucial for materials

scientists, clinicians, and bioengineers from many sectors to continue collaborating. Finally, intelligent nanomaterials have the potential to revolutionize restorative, preventative, and regenerative dentistry by offering new tools for treatment. Research in the future should aim towards creating biocompatible materials with several functions that can simulate the structure of real teeth and lead to long-term improvements in oral health. Future dental nanotechnology research will center on developing controlled-release therapeutic nanostructured delivery systems, discovering environmentally friendly nanomaterials derived from bio-based sources, and conducting longitudinal studies to better understand the interplay between structure, property, and function. To enhance restorative and regenerative dental care, contemporary engineering is being combined with environmentally friendly materials. In the long run, this will lead to the development of multipurpose systems that restore long-term oral health by imitating the architecture of real teeth.

Abbreviations

TBAEMA	2-Ethylhexanoate in 2-(*tert*-butyl)amino ethyl methacrylate
MPS	3-Methacryloxypropyltrimethoxysilane
ALP	Alkaline phosphatase
AMF	Alternating magnetic field
ACM	Amnion/chorion membranes
AIronNPs	Amorphous iron nanoparticles
BG	Bioactive glass
BisGMA	Bis-phenol-A-dimethacrylate
CP	Calcium phosphate
CNTs	Carbon nanotubes
CMC	Carboxyl methyl cellulose
CA	Cellulose acetate
CNC	Cellulose nanocrystals
CS-NPs	Chitosan nanoparticles
CM	Chorionic membranes
CLIN-PLA	Clindamycin-PLA
CT	Computed tomography
CGF	Concentrated growth factor
CuNPs	Copper nanoparticles
CuAAC	Copper-catalyzed azide–alkyne cycloaddition
dECM	Decellularized extracellular matrix
DP-MSCs	Dental pulp mesenchymal stem cells
DPSCs	Dental pulp stem cells
DRCs	Dental resin composites
DMAHDM	Dimethylaminohexadecyl methacrylate
DDA	Dodecylamine
EM	Epoxy monomer
e-PTFE	Expanded polytetrafluoroethylene
FN	Fibronectin
FDA	Food and drug administration
GelMA	Gelatin methacryloyl
GICs	Glass ionomer cements
Au@Ag NRs	Gold–silver nanorods
GO	Graphene oxide
GBR	Guided bone regeneration
GTR	Guided tissue regeneration
HNT	Halloysite nanotubes
hAPCs	Human apical papilla cells
hDPCs	Human dental pulp cells
hDPSCs	Human dental pulp stem cells
hPDLSCs	Human periodontal ligament stem cells
HA	Hydroxyapatite
HANPs	Hydroxyapatite nanoparticles
IDMAs	Ionic dimethacrylates
Fe_2O_3	Iron oxide
LCFRPEEK	Long carbon fiber reinforced polyetheretherketone
MesoCS	Mesoporous calcium silicate
MSP	Mesoporous silica
MOFs	Metal–organic frameworks
MDPB	Methacryloyloxydodecylpyridinium bromide
TMC-Lip-DOX NPs	*N*,*N*,*N*-Trimethyl chitosan, a liposome, and doxycycline
NPs	Nanoparticles
ATEs	Organosilane allyltriethoxysilane
PGA-α-MSH	PGA-melanocortin peptides
DCPD	Phosphate dihydrate
PC	Phytosomal curcumin
PDGF	platelet-derived growth factor
PRF	Platelet-rich-fibrin
PRP	Platelet-rich-plasma
POCT	Point-of-care testing
PLGA	Poly lactic-*co*-glycolic acid
PLGA	Poly(lactic-*co*-glycolic acid)
PMMA	Poly(methyl methacrylate)
PUF	Poly(urea-formaldehyde)
PAMAM	Polyamidoamine
PCL	Polycaprolactone
PDMS	Polydimethylsiloxane
PDA	Polydopamine
PEEK	Polyetheretherketone
PEI	Polyethyleneimine
PGA	Polyglycolic acid
PLA	Polylactic acid
PPy	Polypyrrole
PTFE	Polytetrafluoroethylene
PVA	Polyvinyl alcohol
QA	Quaternary ammonium
QAMs	Quaternary ammonium methacrylates
QAPEI	Quaternary ammonium polyethylenimine
ROS	Reactive oxygen species
Lipo-RSV	Resveratrol-loaded liposomal system
GCF	Saliva or gingival crevicular fluid
SHDC	Self-healing dental composites
SiO_2	Silicon dioxide
SF	Silk fibroin
AgNPs	Silver nanoparticles
SERs	Surface-enhanced Raman spectroscopy
TPU	Thermoplastic polyurethanes
TEGDMA	Triethylene glycol dimethacrylate
USPIO	Ultrasmall superparamagnetic iron oxide
ZnO NPs	Zinc oxide nanoparticles
CD-G	β-Cyclodextrin/graphene

Conflicts of interest

There are no conflicts to declare.

Data availability

No primary research results, software or code are included, and no new data were generated or analyzed as part of this review.

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