Frontiers in Bioscience Elite

Front. Biosci. (Elite Ed) **2026**; 18(3): 41678
https://doi.org/10.31083/FBE41678

Review

Use of Nanotechnology in the Treatment of Periodontitis and Peri-Implantitis: A Narrative Review

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Academic Editor: Gaetano Isola
Submitted: 19 May 2025 Revised: 2 August 2025 Accepted: 19 August 2025 Published: 15 September 2026

Abstract

Nanotechnology has gained increasing attention as a promising approach for the management of periodontitis and peri-implantitis, providing innovative strategies for targeted drug delivery, antimicrobial action, and tissue regeneration. Nanostructured materials and nanocomposites have been developed to transport therapeutic agents directly to diseased sites, improving local therapeutic efficacy while minimizing systemic side effects. Additionally, certain nanoparticles, such as silver, chitosan-, and titanium-based nanomaterials, exhibit potent antimicrobial and anti-inflammatory properties, thereby helping to control microbial colonization, disrupt biofilm development, and modulate host responses. Nanotechnology also enables the functionalization of dental and implant surfaces to prevent bacterial adhesion and biofilm formation, two of the main factors associated with the onset and progression of these infections. Another important application is photodynamic therapy, in which nanoparticle-based delivery systems enhance the stability and targeted release of photosensitizers, allowing the selective destruction of pathogenic bacteria while causing minimal damage to surrounding tissues. Beyond its antimicrobial potential, nanotechnology has also demonstrated considerable promise in promoting periodontal tissue regeneration and improving implant surface bioactivity, highlighting its multifunctional role in contemporary periodontal therapy. Despite these promising advancements, several challenges remain. These include concerns regarding long-term safety, cytotoxicity, biocompatibility, and clinical translation, highlighting the need for well-designed clinical studies and extended follow-up before widespread implementation.

Keywords: nanotechnology; periodontitis; peri-implantitis; drug delivery systems; oral health

1. Introduction

Nanotechnology represents a field of science and technology dedicated to the study, design, production, and application of materials and devices at the nanometer scale, typically ranging from 1 to 100 nm [1]. The concept was first introduced in 1959 by Richard Feynman, who envisioned nanomachines or nanorobots capable of operating with high precision at the microscopic level, assembling structures atom by atom [2]. This vision laid the groundwork for the development of a wide range of microscopic instruments, marking a significant milestone in the history of modern science [3]. Seminal publications published outside this time window were retained when considered necessary to provide historical or conceptual context for manipulating materials at the atomic and molecular levels, enabling the creation of substances with unique and enhanced properties at the nanoscale [4]. These include improvements in physicochemical characteristics, magnetic behavior, light reflectivity, electrical and thermal conductivity, and increased sensitivity to specific stimuli, among others [5].

In recent years, nanotechnology has attracted considerable attention across biomedical fields, particularly in dentistry, for its capacity to improve the development of materials and systems with enhanced antimicrobial, regenerative, and drug-delivery properties [5,6]. Examples of the applications involving nanotechnology include the production of stronger and lighter materials, the fabrication of smaller and more efficient electronic devices, and the development of highly targeted therapeutic strategies [7,8]. Advances in regenerative nanotechnology and tissue engineering have enabled the creation of biological substitutes through innovations in cell transplantation, materials science, and bioengineering, thereby facilitating the restoration and maintenance of damaged or diseased tissues [8]. Targeted drug delivery systems have been refined to administer therapeutic agents directly to specific sites, thereby enhancing treatment efficacy while minimizing adverse systemic effects [9]. Together, these developments have expanded the therapeutic possibilities available in both medicine and dentistry [9,10].

In dentistry, nanotechnology has transformed the field by facilitating the development of more durable and robust materials while enabling increasingly precise diagnostic and therapeutic approaches, including tissue engineering and dental nanorobotics [5,11]. This has led to a wide

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range of new applications, such as innovative diagnostic strategies and enhanced disease prevention using functionalized nanoparticles [9]. Additionally, the integration of nanoscale devices with genetic engineering and biotechnology has paved the way for novel approaches to pain relief and the treatment of traumatic injuries [10]. Applications have also been proposed in areas such as diagnostic imaging, local anesthetics, restorative dentistry, and orthodontics [10,12].

Periodontitis and peri-implantitis represent important challenges in oral health. These chronic inflammatory diseases are initiated by dysbiotic bacterial biofilms and are characterized by the progressive destruction of the periodontal and peri-implant supporting tissues, ultimately compromising tooth and implant stability. Conventional treatments often fail to completely eliminate mature biofilms or achieve predictable regeneration of damaged tissues, underscoring the urgent need for more effective therapeutic strategies. In this context, nanotechnology has emerged as a promising alternative by enabling the development of targeted drug delivery systems, bioactive implant coatings, antimicrobial nanomaterials, and regenerative scaffolds designed to overcome many of the limitations associated with conventional therapies [7].

Nanomaterial production technologies are generally classified into two approaches: bottom-up and top-down [13]. The top-down method involves reducing bulk materials to submicron-sized particles by applying mechanical energy. Techniques such as high-pressure homogenization, microfluidization, and liquid-phase nanomilling are commonly employed to produce nanoscale structures from larger materials. Conversely, the bottom-up approach assembles structures through atom-by-atom or molecule-by-molecule processes [14,15]. Meanwhile, widely used materials include nanocrystals (e.g., potassium nitrate, calcium salts, calcium fluoride, and carbonate hydroxyapatite), as well as nanoparticles and metallic nanoparticles derived from pure metals such as gold, platinum, silver, titanium, zinc, iron, cerium, and thallium [15,16].

Recently, nanotechnology has been applied to treat periodontitis and peri-implantitis, with particular emphasis on targeting pathogenic biofilms while promoting tissue regeneration [6,17]. These diseases affect the tissues surrounding teeth and implants and are caused by bacterial accumulation that forms persistent biofilms adhering to dental surfaces [18,19]. One promising strategy involves silver nanoparticles (AgNPs), which can be applied to teeth or implants to eradicate pathogenic bacteria [17]. Similarly, chitosan-based nanofibrous membranes have been investigated as biomaterial scaffolds for guided bone regeneration, highlighting their potential applications in periodontal and regenerative therapies [20]. These nanoparticles not only exhibit antimicrobial properties but also possess anti-inflammatory capabilities, making them promising multifunctional candidates for managing periodontal and peri-implant diseases through the simultaneous control of microbial burden and host inflammatory responses.

Another significant approach involves drug-loaded nanoparticles designed to provide localized and sustained therapeutic delivery, thereby improving bioavailability and potentially reducing systemic exposure [21,22,23]. Silver, chitosan, gold, zinc oxide, and titanium dioxide nanoparticles have all been explored for their ability to inhibit bacterial growth and support tissue regeneration through complementary antimicrobial and bioactive mechanisms [24]. Additionally, nanostructured scaffolds and delivery systems have been designed to release antibiotics, anti-inflammatory agents, or antioxidants directly into periodontal pockets, providing sustained local drug release, improving bioavailability, and reducing the need for repeated systemic administration [15].

Photodynamic therapy (PDT) is another relevant application of nanotechnology that uses photosensitizers delivered via nanoparticles. Upon activation by specific wavelengths of light, these compounds produce reactive oxygen species (ROS) that selectively destroy bacteria within biofilms. Thus, PDT offers an effective means of reducing microbial load without relying on systemic antibiotics, thus lowering the risk of antibiotic resistance. Beyond antimicrobial activity, nanoparticle-assisted PDT has also shown potential to improve treatment selectivity and enhance photosensitizer stability, making it an increasingly attractive adjunctive therapy in periodontal care. Taken together, these findings support the potential role of nanotechnology in the prevention and treatment of periodontitis and peri-implantitis. This review examines the most recent and relevant applications of nanomaterials in the diagnosis, treatment, and regeneration of tissues affected by these diseases, while critically discussing their mechanisms of action, therapeutic advantages, current limitations, and future prospects for clinical translation.

2. Materials and Methods

A structured narrative review was conducted using PubMed® and ScienceDirect® as the primary literature databases, while Mendeley® was used as an additional tool for reference management and identification of relevant publications. The literature search was performed in English using the keywords “nanotechnology”, “periodontitis”, and “peri-implantitis”, combined primarily with the Boolean operator “AND” to identify studies addressing the intersection of these topics (Table 1).

The search strategy incorporated the following inclusion criteria: (i) articles published during the 15 years preceding the literature search; (ii) availability of full-text publications; and (iii) studies providing quantitative or clinically relevant data, including randomized clinical trials (RCTs), multicenter studies, systematic reviews, retrospective clinical studies, and well-designed preclinical investigations when relevant to the topic. Exclusion criteria

Table 1. Documents retrieved from the literature search conducted across the selected databases.

Search strategy	Database	Records retrieved	Duplicates removed	Records retained after title/abstract screening	Final articles included
	PubMed®	236	26	68	34
"*Nanotechnology*" AND "*Periodontitis*"	ScienceDirect®	619	21	83	42
	Mendeley®	65	9	15	12
	PubMed®	24	3	13	6
"*Nanotechnology*" AND "*Peri-implantitis*"	ScienceDirect®	30	3	26	9
	Mendeley®	3	1	1	1
Total		977	63	206	104

Note. The total number of final articles included (n = 104) corresponds to the sum of the studies retained from each database following the screening and eligibility assessment. Duplicate records identified across databases were removed prior to study selection.

included intervention proposals, case reports, and studies that, despite meeting the inclusion criteria, provided insufficient methodological detail, lacked reproducibility, or did not present robust or conclusive findings. Seminal publications published outside this time window were retained when considered necessary to provide historical or conceptual context.

Titles and abstracts were initially screened according to the predefined eligibility criteria. Whenever the information provided in the title or abstract was insufficient to determine eligibility, the full text was retrieved and evaluated to ensure that potentially relevant studies were not inadvertently excluded. The overall literature selection process is summarized in Fig. 1.

As this work was designed as a structured narrative review rather than a systematic review, no formal PRISMA protocol or standardized risk-of-bias assessment tool was applied. Instead, the included literature was critically evaluated based on its methodological quality, scientific relevance, study design, and contribution to the understanding of nanotechnology applications in periodontitis and peri-implantitis. Particular emphasis was placed on evidence derived from clinical studies, systematic reviews, and well-conducted experimental investigations to provide a balanced and up-to-date overview of the field.

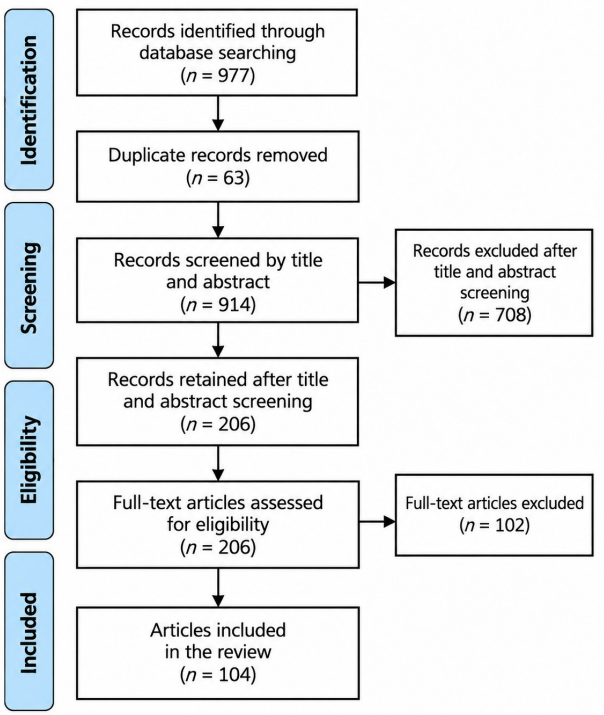

Fig. 1. Flowchart of the literature search and study selection process. Source: Authors' own elaboration. Figures were created using Microsoft PowerPoint 365 (Microsoft Corporation, Redmond, WA, USA) and exported as high-resolution images.

3. Discussion

The discussion is organized into thematic sections to provide a critical and integrated perspective on the current applications of nanotechnology in periodontal and peri-implant therapy. This literature review examines the growing role of nanotechnology in the management of oral diseases, with particular emphasis on periodontal and peri-implant diseases, while also considering advances that may be applicable to other areas of dentistry. Based on the available evidence, nanotechnology has evolved from an emerging concept to a multidisciplinary platform capable of addressing several of the biological and clinical challenges associated with conventional periodontal therapies. However, despite the encouraging experimental and early clinical findings, the level of evidence remains heterogeneous, highlighting the need for further well-designed clinical studies to confirm the long-term efficacy and safety of many nanotechnology-based approaches.

The evidence can be considered across four main therapeutic areas: antimicrobial strategies, tissue regeneration, immune modulation, and targeted drug delivery. This approach allows the evidence to be interpreted within a clinically meaningful framework, emphasizing not only the therapeutic potential of individual nanomaterials but also

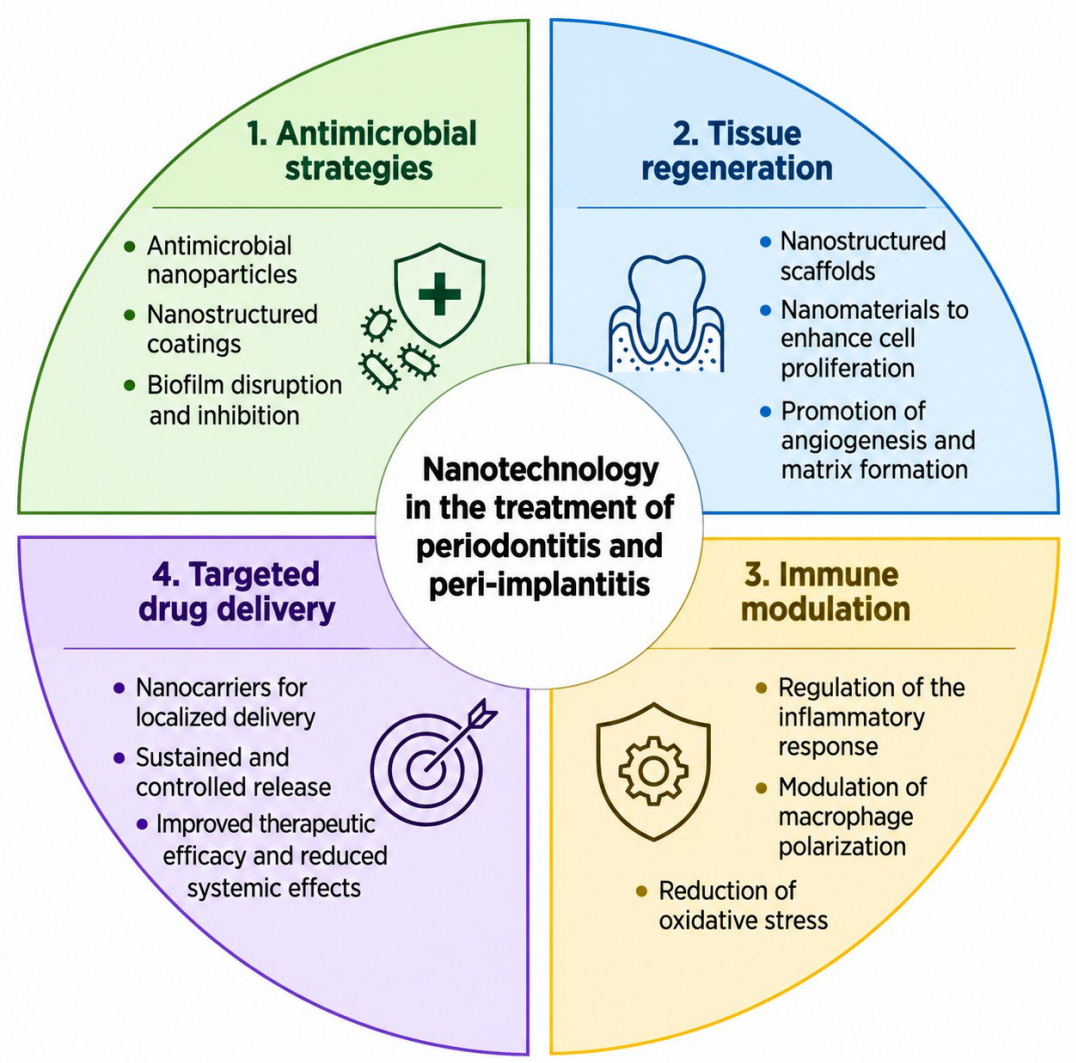

Fig. 2. Main therapeutic applications of nanotechnology in the management of periodontitis and peri-implantitis. Nanotechnology-based strategies are categorized according to four principal therapeutic objectives: antimicrobial strategies, tissue regeneration, immune modulation, and targeted drug delivery. Source: Authors' own elaboration. Figures were created using Microsoft PowerPoint 365 and exported as high-resolution images.

the biological mechanisms through which they may improve periodontal and peri-implant treatment outcomes. Rather than providing a purely descriptive summary, this review critically compares different nanomaterials according to their mechanisms of action, antimicrobial and regenerative performance, biocompatibility, translational potential, and current limitations. Special attention is also given to the challenges that continue to hinder clinical implementation, including potential cytotoxicity, variability in nanomaterial synthesis, regulatory considerations, and the limited availability of long-term human studies. The various applications of nanotechnology are categorized into distinct therapeutic uses (Fig. 2), providing an overview of the principal areas in which nanotechnology is currently contributing to the prevention, diagnosis, and treatment of periodontal and peri-implant diseases, while identifying the most promising directions for future clinical translation.

3.1 Antimicrobial Nanostrategies and Biofilm Control

The most extensively investigated application of nanotechnology in dentistry is its antimicrobial potential. Dental biofilms, particularly those formed in periodontal pockets and peri-implant sulci, are highly organized microbial communities that exhibit remarkable resistance to systemic antibiotics and conventional mechanical debridement due to their complex three-dimensional architecture, protective extracellular matrix, and altered metabolic activity. These characteristics allow pathogenic microorganisms to persist within the oral environment, contributing to chronic inflammation and disease progression. Nanoparticles offer a promising strategy to overcome these limitations by enhancing local drug concentration, facilitating penetration into biofilm layers, and exerting bactericidal effects through multiple complementary mechanisms.

Beyond their direct antimicrobial activity, several nanomaterials have demonstrated the ability to regulate oxidative stress, a key contributor to periodontal tissue destruction. Excessive production of reactive oxygen species (ROS) amplifies the inflammatory response and promotes extracellular matrix degradation, making oxidative stress an attractive therapeutic target. Sui et al. [24] demonstrated that nanotechnology-based antioxidant systems effectively reduced ROS levels while attenuating periodontal inflammation, suggesting their potential as adjunctive therapies for periodontitis. Nevertheless, the biological effects of nanomaterials are strongly influenced by their physicochemical properties, composition, and concentration. In this regard, Bressan et al. [25] reported that titanium nanoparticles may also stimulate ROS production, leading to neutrophil activation and increased matrix metalloproteinase expression. These apparently contrasting findings illustrate that the biological behavior of nanoparticles is highly context-dependent and emphasize the importance of carefully optimizing their composition and dosage to maximize therapeutic benefits while minimizing undesirable effects. Additional antioxidant approaches have also shown encouraging results. Swarnakar et al. [26] developed coenzyme Q10-loaded polymeric nanoparticles and reported enhanced ROS-scavenging activity compared with free coenzyme Q10, whereas Alvarez et al. [27] incorporated *Larrea divaricata* extracts into biodegradable nanocomposites, demonstrating that natural antioxidant compounds can be successfully integrated into nanodelivery systems. Likewise, Saita et al. [28] and Bao et al. [29] designed injectable and biodegradable nanoplatforms capable of scavenging ROS while simultaneously preserving alveolar bone integrity. Together, these findings suggest that nanotechnology may have applications beyond direct microbial control, including modulation of the host response.

Silver nanoparticles (AgNPs) remain one of the most extensively studied nanomaterials for periodontal and peri-implant applications because of their broad-spectrum antimicrobial activity and their ability to target microorganisms through multiple complementary mechanisms, thereby reducing the likelihood of resistance development compared with conventional antibiotics. These particles disrupt microbial membrane integrity, release Ag^{+} ions that interfere with DNA replication and essential enzymatic processes, and induce intracellular ROS generation, ultimately leading to bacterial cell death [30] (Fig. 3). The combination of these mechanisms may contribute to the antimicrobial activity of AgNPs against mature oral biofilms, which are generally less susceptible to traditional antimicrobial therapies.

They have been integrated into various clinical materials, including acrylic resins for prostheses [30,31], composite resins and porcelains used in restorative dentistry [32,33,34,35], and as components of root canal irrigants or gutta-percha in endodontic treatments [36,37,38,39,40]. Importantly, the available evidence suggests that incorporating AgNPs into these materials does not compromise their biological safety while providing additional antimicrobial benefits. For example, Suzuki et al. [37] demonstrated that AgNP-containing endodontic materials exhibited enhanced antimicrobial activity without increasing cytotoxicity compared with conventional formulations. Likewise, Mozayeni et al. [39] reported similar findings, indicating that AgNP formulations maintained acceptable biocompatibility while improving microbial eradication.

In orthodontics, AgNP coatings on brackets and wires have demonstrated antimicrobial activity without adversely affecting shear bond strength or enamel integrity [41,42,43,44]. This sustained antimicrobial effect is particularly relevant for orthodontic patients, in whom prolonged appliance wear favors plaque accumulation and increases the risk of enamel demineralization and gingival inflammation.

In periodontitis and peri-implantitis, AgNPs have been investigated both as stand-alone antimicrobial agents and in combination with conventional antibiotics. Their ability to disrupt mature subgingival biofilms through multiple mechanisms while exhibiting a low propensity for inducing bacterial resistance makes them particularly attractive for periodontal applications. Furthermore, when incorporated into implant surface modifications, AgNPs have been associated with reduced bacterial adhesion, lower biofilm formation, and improved osseointegration [45,46,47,48,49,50,51].

Lampé et al. [52] demonstrated that AgNP-coated titanium implants significantly reduced colonization by *Staphylococcus aureus* and *Pseudomonas aeruginosa* while simultaneously promoting osteoblastic proliferation and mineralization. Similarly, Pérez-Tanoira et al. [53] evaluated titanium surfaces functionalized with silver nanoparticles produced by laser ablation and demonstrated significant antimicrobial activity against clinically relevant peri-implant pathogens, including *Staphylococcus aureus, Streptococcus oralis, Actinomyces naeslundii, Porphyromonas gingivalis*, and *Veillonella dispar*. Moreover, repeated laser irradiation during nanoparticle production enhanced their antimicrobial performance, suggesting that laser-ablated AgNP coatings may represent a promising preventive strategy for reducing peri-implant biofilm formation. Comparable findings were reported by Drago et al. [54], who observed significantly lower biofilm formation on modified titanium implant surfaces than on untreated surfaces [55,56].

Beyond silver nanoparticles, photoresponsive nanomaterials such as fullerenes, graphene derivatives, and carbon nanotubes have further expanded antimicrobial strategies by combining photoactivation with targeted therapeutic delivery [57,58]. Upon light irradiation, these materials generate reactive oxygen species capable of selectively damaging bacterial membranes, proteins, and nucleic

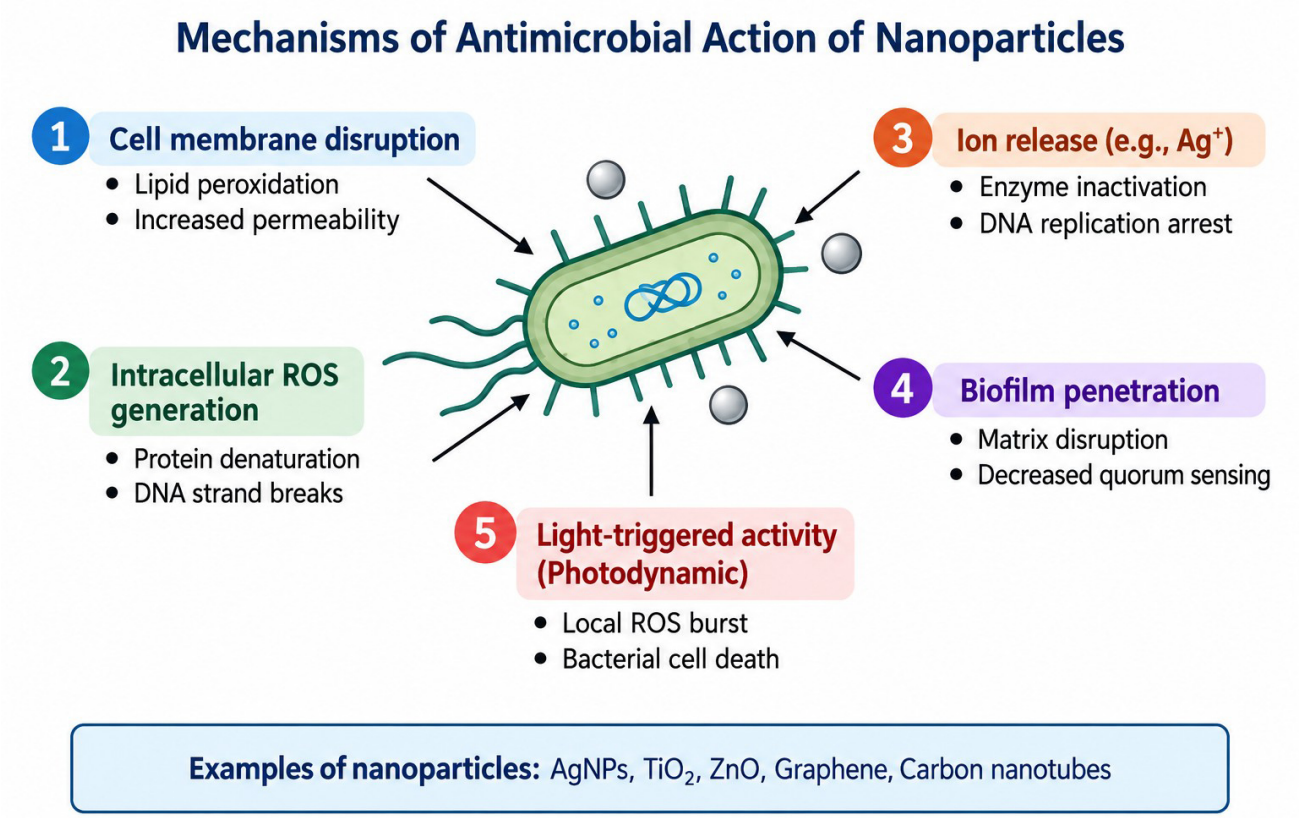

Fig. 3. Principal mechanisms by which nanoparticles exert antimicrobial activity against periodontal and peri-implant pathogens. These mechanisms include disruption of the bacterial cell membrane, intracellular reactive oxygen species (ROS) generation, release of antimicrobial metal ions (e.g., Ag^{+}), biofilm penetration and disruption, and light-triggered photodynamic activity. Collectively, these complementary mechanisms enhance bacterial eradication while potentially reducing the likelihood of antimicrobial resistance. Source: Authors' own elaboration. Figures were created using Microsoft PowerPoint 365 and exported as high-resolution images. AgNPs, silver nanoparticles; TiO_2, titanium dioxide; ZnO, zinc oxide.

acids while minimizing injury to surrounding host tissues [59,60,61,62,63,64,65]. This approach is particularly attractive because it combines localized antimicrobial activity with a reduced dependence on systemic antibiotics. Likewise, photocatalytic nanomaterials such as TiO_2, ZnO, and Fe_3O_4 exhibit potent antimicrobial properties, particularly when used as implant surface coatings. Experimental studies have shown that these nanomaterials effectively reduce bacterial adhesion and biofilm maturation while maintaining favorable biocompatibility, with demonstrated activity against pathogens such as *Aggregatibacter actinomycetemcomitans* and *Fusobacterium nucleatum* in both *in vitro* and animal models [66,67,68,69,70].

Another area of investigation is the development of pathogen-targeted nanoplatforms capable of reaching deep periodontal pockets and disrupting mature biofilms, where conventional antimicrobial therapies often show limited efficacy. $NaYF_4$ and Fe_3O_4 nanoparticles, for example, have been incorporated into photodynamic therapy systems designed to enhance antimicrobial activity against periodontitis-related pathogens and biofilms [71,72,73].

Similarly, implant surfaces functionalized with ZnCuO or peptide-based nanocoatings have demonstrated substantial reductions in early bacterial adhesion, biofilm formation, and peri-implant inflammation, highlighting their potential as preventive strategies against peri-implant infections [74,75]. Dabbah et al. [74] reported that dental implants coated with ZnCuO nanoparticles exhibited significantly lower bacterial activity after 14 days compared with conventional titanium-coated implants. These findings suggest that ZnCuO nanocoatings may represent a promising surface modification to reduce early microbial colonization and improve peri-implant health. Besinis et al. [76] reported that titanium alloy implants modified with silver, titanium dioxide, and hydroxyapatite nanocoatings showed markedly reduced bacterial growth and biofilm formation compared with unmodified surfaces.

Fang et al. [75] evaluated peptide-functionalized implant coatings and demonstrated that their ability to inhibit the adhesion of *Porphyromonas gingivalis* significantly reduced early biofilm formation on implant surfaces. Chen et al. [77] investigated GL13K peptide coatings on titanium surfaces and found that the coatings reduced bacterial via-

Table 2. Representative nanoparticles used as drug delivery systems in periodontal therapy and their reported therapeutic applications.

Nanoparticle type	Carrier/Encapsulated agent	Target pathogen or condition	Key therapeutic benefits
Liposomes	Chlorin e6 (Ce6) and cetyltrimethylammonium bromide (CTAB)	*Candida albicans* biofilms	Enhanced photodynamic antimicrobial activity and membrane disruption
Gold nanoparticles	None (intrinsic surface activity)	*Staphylococcus aureus*	Sustained antimicrobial activity and inhibition of biofilm formation
Chitosan-based nanoparticles	Methylene blue	Mixed periodontal biofilms	Improved photodynamic antimicrobial efficacy and biodegradable drug delivery
Silk fibroin nanoparticles	Resveratrol	Periodontitis	Controlled drug release with anti-inflammatory and regenerative effects
Plant-derived exosome-like nanoparticles (ginger, coconut)	Plant-derived bioactive compounds	Periodontitis	Natural nanocarriers with immunomodulatory, anti-inflammatory, and regenerative properties

Note. Abbreviations: Ce6, chlorin e6; CTAB, cetyltrimethylammonium bromide.

bility and inhibited the formation and growth of biofilms. These findings support the use of peptide-functionalized titanium surfaces as a potential strategy for limiting bacterial colonization and biofilm formation around dental implants. Likewise, Rodríguez-Hernández et al. [78] investigated the antimicrobial properties of MgO nanoparticles and demonstrated activity against a broad spectrum of oral microorganisms, including *Capnocytophaga gingivalis, Eikenella corrodens, Streptococcus sanguinis, Actinomyces israelii, Fusobacterium nucleatum subsp. nucleatum, Porphyromonas gingivalis, Prevotella spp., Staphylococcus aureus, Streptococcus mutans,* and *Streptococcus sobrinus*. Many of these microorganisms are recognized as important contributors to periodontal biofilm formation and disease progression, supporting the potential use of MgO nanoparticles as broad-spectrum antimicrobial agents in periodontal therapy.

Taken together, the available evidence indicates that nanostructured implant coatings not only provide direct antimicrobial activity but also create surface environments that are less favorable for bacterial adhesion while maintaining compatibility with host tissues. Although most evidence currently derives from experimental and preclinical investigations, these approaches represent promising alternatives or adjuncts to conventional antimicrobial therapies and may eventually reduce the need for prolonged systemic antibiotic administration in the management of refractory periodontitis and peri-implantitis.

3.2 Targeted Drug Delivery and Controlled Therapeutics

Conventional pharmacological approaches may be limited by restricted drug penetration into periodontal tissues, rapid clearance from the periodontal pocket, and systemic exposure, all of which may compromise therapeutic outcomes. Nanotechnology addresses these limitations by enabling the development of engineered drug delivery systems capable of providing localized, sustained, and controlled release of therapeutic agents directly at the site of infection. This targeted approach not only increases local drug bioavailability but also reduces off-target exposure, thereby improving therapeutic efficacy while minimizing systemic toxicity, particularly in anatomically complex environments such as periodontal pockets and peri-implant crevices.

Nanocarriers, including liposomes, polymeric nanospheres, micelles, and dendrimers, can accommodate a broad range of therapeutic compounds, including antibiotics, anti-inflammatory drugs, photosensitizers, and bioactive plant-derived molecules [79,80,81,82,83]. Their nanoscale dimensions and tunable physicochemical properties allow these systems to improve drug stability, protect labile compounds from premature degradation, and achieve controlled release profiles that prolong therapeutic activity within periodontal tissues.

Gold nanoparticles have also been investigated for their antimicrobial activity against biofilm-forming microorganisms such as *Staphylococcus aureus*. Available evidence suggests sustained antimicrobial effects together with favorable biocompatibility, although the duration and clinical relevance of these effects require further investigation [84]. Similarly, silica nanoparticles and cationic liposomes have been shown to enhance cellular uptake, facilitate intracellular drug delivery, and prolong antimicrobial activity [85,86].

Guo et al. [79] reviewed the use of liposomal and other nanoarchitectured systems for oral drug delivery, achiev-

ing effective inhibition of *Candida biofilms* in experimental models through enhanced photodynamic activity. Polymeric nanocarriers have proven particularly valuable in antimicrobial photodynamic therapy because they improve photosensitizer stability, increase local retention, and enhance bacterial uptake. Studies employing methylene blue-loaded nanoparticles have demonstrated substantial antimicrobial effects [82], whereas chitosan-based nanocarriers have also shown significant antibacterial activity against periodontal pathogens [81,83]. These findings suggest that nanocarrier-based delivery systems may improve some aspects of nonsurgical periodontal therapy by increasing local drug concentrations while potentially reducing the need for repeated administration or prolonged systemic antibiotic use.

Collectively, the available evidence indicates that targeted nanodelivery systems represent one of the most promising applications of nanotechnology in periodontology (Table 2). Their ability to combine sustained drug release, selective tissue targeting, and multifunctional therapeutic effects may help overcome several of the limitations associated with conventional pharmacological approaches. Nevertheless, additional clinical studies are still required to determine the optimal formulations, long-term safety, and cost-effectiveness of these delivery platforms before their routine implementation in clinical practice.

Additionally, nanocarrier systems incorporating natural bioactive compounds have attracted increasing attention because they combine the intrinsic therapeutic properties of phytochemicals with the pharmacokinetic advantages provided by nanotechnology. Compounds such as resveratrol, melatonin, coenzyme Q10, and curcumin, whose clinical application has traditionally been limited by poor aqueous solubility, low stability, and restricted tissue penetration, can now be delivered directly to periodontal tissues through stable nanoformulations [87,88,89,90]. These delivery systems improve local drug retention, enhance bioavailability, and reduce systemic exposure.

Silver nanoparticle-based formulations have also demonstrated activity against multidrug-resistant oral pathogens. El-Telbany and El-Sharaki [91] investigated the antimicrobial activity of AgNPs against *Pseudomonas aeruginosa*, a microorganism frequently associated with biofilm-associated infections and recognized for its intrinsic resistance to multiple antimicrobial agents. Their results demonstrated that AgNPs effectively inhibited bacterial growth and biofilm development, supporting their potential use as antimicrobial coatings or adjunctive agents for preventing peri-implant infections. Similarly, Ansari et al. [92] developed gum arabic-coated silver nanoparticles, demonstrating enhanced antimicrobial activity against *P. aeruginosa*. The biopolymer coating improved nanoparticle stability while preserving their antibacterial efficacy, highlighting the potential of surface-functionalized nanomaterials for combating antibiotic-resistant microorganisms. Along the same line, Ali et al. [93] combined AgNPs with *Crataeva nurvala* extract, a medicinal plant known for its antioxidant, anti-inflammatory, and antimicrobial properties.

Plant-derived extracellular nanovesicles, often described as plant exosome-like nanoparticles, have been investigated as potential delivery and therapeutic platforms in periodontal research. Their reported biological effects include modulation of inflammatory responses and promotion of tissue repair [94,95,96,97,98,99,100].

Sundaram et al. [101] reported that plant-derived exosomal nanoparticles can inhibit the pathogenicity of *Porphyromonas gingivalis*, highlighting their potential as multifunctional platforms for periodontal therapy [101]. Numerous plant-derived extracts have also demonstrated biological activities relevant to periodontal therapy. Extracts from grapefruit, ginger, cabbage, carrot, blueberry, strawberry, ginseng, garlic, orange, and lemon exhibit anti-inflammatory and immunoregulatory effects that may contribute to the control of periodontal inflammation [100,102,103,104,105,106,107]. For example, plant-derived exosomal nanoparticles have been shown to inhibit *Porphyromonas gingivalis* [101], whereas lemon-derived nanoparticles have demonstrated the ability to induce tRNA degradation in *Clostridioides difficile*, thereby improving probiotic survival, and tea-derived catechins have been reported to inhibit the growth and virulence of oral pathogenic bacteria [108]. Furthermore, *Morinda officinalis*-derived extracellular vesicle-like particles have been shown to promote endothelial cell proliferation, migration, and tube formation, while enhancing angiogenesis and wound healing *in vivo* [109].

Arundina et al. [110] investigated nanoparticles derived from rice husk liquid smoke and demonstrated their capacity to stimulate osteoblast activity, suggesting a potential role in promoting alveolar bone regeneration during periodontal repair. Finally, Zhang et al. [111] developed microneedle patches capable of delivering tetracycline together with heparin-coated mesoporous silica microparticles directly into periodontal tissues. This approach combined local drug delivery with antibacterial activity and enhanced tissue regeneration, illustrating how next-generation nanodelivery systems may combine controlled drug release with regenerative therapies in a minimally invasive and patient-friendly approach.

3.3 Tissue Regeneration and Bone Remodeling

A central challenge in the treatment of periodontitis and peri-implantitis is the restoration of lost alveolar bone and periodontal attachment. Although conventional regenerative procedures have improved clinical outcomes, complete and predictable regeneration remains difficult to achieve, particularly in advanced defects where the inflammatory microenvironment compromises tissue healing. In this context, nanomaterials have provided additional ap-

Table 3. Bone regenerative nanomaterials and their reported applications and outcomes in periodontal and peri-implant tissue regeneration.

Nanomaterial type	Scaffold/Coating use	Model/Context	Regenerative outcome
Alginate nanoparticles	Injectable guided tissue regeneration (GTR) matrix	General bone loss	Promoted mineralization and induced calcification
Graphene oxide + PDA + HAp	Diabetic bone scaffold	Diabetic rat periodontitis model	Reduced inflammation and enhanced bone regeneration
Silk fibroin nanoparticles	Implant surface coating	Dogs and human clinical studies	Antibacterial activity and improved osseointegration
Cerium oxide–gelatin nanoparticles	Resveratrol delivery carrier	Diabetic rat model	Reduced pro-inflammatory cytokine expression and improved tissue repair
Hydroxyapatite nanoparticles	Bone regenerative scaffold	*In vitro* and rat bone defect models	Promoted osteoblast proliferation, differentiation, and bone formation

Note. Abbreviations: GTR, guided tissue regeneration; PDA, polydopamine; HAp, hydroxyapatite.

proaches for guided tissue regeneration (GTR) and bone tissue engineering by modulating osteogenic, angiogenic, and immunological pathways. Their small size and high surface-area-to-volume ratio favor cell adhesion and signaling, enhance the delivery of bioactive molecules, and facilitate the integration of scaffolds with host tissues.

Alginate nanoparticles, given their generally favorable biocompatibility and ability to support mineralization without the need for additional chemical inducers, have been investigated as injectable and moldable matrices for GTR procedures [112]. Their physicochemical characteristics also allow them to adapt to irregular periodontal defects while serving as temporary extracellular matrices that support early tissue organization. Similarly, nanoparticles based on silk fibroin, titanium, and collagen have demonstrated promising results in enhancing osteoblast adhesion, proliferation, and extracellular matrix deposition [113,114,115,116,117]. Besides providing mechanical support, these biomaterials function as carriers for osteoinductive molecules and growth factors, allowing a more sustained and localized release during the different stages of tissue repair.

Preclinical studies and a limited number of early clinical investigations suggest that implant coatings incorporating silver, silica, and soda-lime glass nanoparticles not only reduce peri-implant bacterial colonization but also improve bone healing around implants, as reflected by increases in bone-to-implant contact and peri-implant bone density [118,119,120]. Pranno et al. [121], in an *in vitro* pilot study, reported that titanium surfaces coated with graphene nanoplatelets exhibited significant antibacterial activity, particularly against *Staphylococcus aureus*, without compromising osteoblast viability or the osteogenic properties of the implant surface. This combination of antimicrobial performance and preservation of the biological response is particularly relevant for implant dentistry, where successful osseointegration depends on maintaining a delicate balance between infection control and bone regeneration. Table 3 summarizes the principal nanomaterials investigated for bone regeneration, together with their scaffold applications, experimental models, and regenerative outcomes.

In a related approach, Maleki et al. [122] investigated the antibacterial potential of curcumin nanocrystals against *Porphyromonas gingivalis* in patients with peri-implantitis despite adequate oral hygiene. Their study was based on the observation that peri-implant disease may develop even in patients with satisfactory plaque control, largely due to persistent bacterial colonization and progressive peri-implant bone loss. The incorporation of curcumin into nanocrystalline formulations enhanced its local antimicrobial activity and contributed to reducing bacterial infection around dental implants. In a subsequent study, Maleki et al. [123] combined curcumin nanoparticles with gelatin-based nanocomposites to improve peri-implant healing and reduce the risk of postoperative infection. Although the results suggested biological compatibility and some regenerative potential, the therapeutic benefits were less pronounced than anticipated, leading the authors to recommend further experimental and clinical investigations before routine clinical application.

An area of particular interest is the use of nanotechnology in periodontal therapy for patients with diabetes, who frequently exhibit delayed wound healing, impaired bone regeneration, persistent oxidative stress, and a prolonged inflammatory response. These systemic alterations make periodontal and peri-implant regeneration especially challenging, encouraging the development of multifunctional biomaterials capable of addressing several biological pathways simultaneously. Li et al. [124] developed a conductive nanoscaffold composed of graphene oxide, polydopamine, and hydroxyapatite that promoted bone regeneration while simultaneously regulating the inflammatory microenvironment through macrophage polarization and mod-

ulation of cellular glycolysis. Rather than acting solely as a structural scaffold, this nanocomposite actively influenced the biological environment in which tissue regeneration occurred. Similarly, Giménez-Siurana et al. [125] demonstrated that resveratrol-loaded silk fibroin nanoparticles reduced inflammatory markers and improved periodontal healing in diabetic rats, whereas Ren et al. [126] reported that cerium oxide nanoparticles enhanced mesenchymal stem cell function while promoting angiogenesis and bone regeneration through their antioxidant activity.

The successful clinical translation of regenerative nanomaterials also depends on careful material design. Besides promoting tissue regeneration, nanomaterials must exhibit predictable degradation profiles, adequate biocompatibility, and controlled biological activity to avoid undesirable long-term effects. Vannozzi et al. [127] emphasized that regenerative nanoparticles should ideally be bioresorbable, thereby eliminating the need for surgical removal and reducing the risk of chronic foreign-body reactions. Likewise, Uskoković [128] argued that the osteogenic potential of nanomaterials should be precisely regulated rather than simply maximized, as excessive or uncontrolled mineralization may result in hypermineralization or ectopic bone formation. This consideration is particularly relevant in periodontal regeneration, where newly formed mineralized tissue must be spatially coordinated with the regeneration of periodontal ligament and surrounding soft tissues to restore the physiological architecture of the periodontium [129].

3.4 Immunomodulation and Microenvironmental Reprogramming

Nanomaterials may also influence the host immune response, which plays a pivotal role in determining whether periodontal and peri-implant tissues undergo destruction or successful repair. The progression of both diseases is driven not only by bacterial biofilms but also by a persistent and dysregulated inflammatory response characterized by excessive cytokine production, oxidative stress, and sustained activation of immune cells. For this reason, current therapeutic strategies increasingly aim to regulate the host response alongside controlling microbial infection. Nanotechnology offers new opportunities to modify the local inflammatory microenvironment, promoting conditions that favor tissue healing rather than chronic destruction.

Gold nanoparticles have demonstrated anti-inflammatory properties by modulating the secretion of cytokines such as IL-10 and TGF-β while promoting macrophage polarization toward the M2 phenotype, which is associated with inflammation resolution and tissue repair [130]. Similarly, nanoparticles loaded with indocyanine green and combined with polycationic polymers have shown dual antimicrobial and immunomodulatory activity, simultaneously suppressing bacterial growth while regulating local immune responses [131]. These findings illustrate the possibility of combining antimicrobial and immunomodulatory functions within a single nanoplatform. Cellulose nanofiber systems loaded with surfactin and κ-carrageenan oligosaccharides have also demonstrated the ability to reduce oxidative stress by suppressing reactive oxygen species production and decreasing the release of pro-inflammatory cytokines. Johnson et al. [132] reported that these nanomaterials effectively inhibited *Fusobacterium nucleatum* and *Pseudomonas aeruginosa*, two microorganisms frequently associated with periodontal dysbiosis and persistent biofilm formation, while contributing to a more balanced interaction between the biofilm and the host tissues.

Another approach involves the removal of extracellular DNA (eDNA), a structural component of the biofilm matrix that also acts as a danger-associated molecular pattern capable of amplifying the inflammatory response. Huang et al. [133] developed selenium-doped hydroxyapatite nanoparticles functionalized with polyamidoamine dendrimers that selectively captured and neutralized eDNA, thereby reducing inflammatory cell infiltration and limiting periodontal tissue damage in experimental models. Rather than acting exclusively through direct antimicrobial mechanisms, these nanoparticles interfere with one of the molecular signals responsible for maintaining chronic inflammation. Li et al. [134] further expanded this concept by developing bacteria-based systems capable of delivering therapeutic agents, allowing controlled modulation of the host immune response. These approaches reflect a shift in the role of nanotechnology, from serving solely as a drug delivery platform to actively participating in the regulation of the periodontal immune microenvironment through precisely targeted biological interactions.

3.5 Limitations, Safety Considerations, and Translational Challenges

Despite the considerable advances achieved in recent years, the incorporation of nanotechnology into routine periodontal and peri-implant therapy continues to face important scientific, clinical, and regulatory challenges. Although numerous experimental and preclinical studies have demonstrated encouraging results, the heterogeneity of nanomaterial formulations, study designs, and outcome measures makes it difficult to establish direct comparisons or define standardized therapeutic protocols. As a result, the translation of many nanotechnology-based approaches from laboratory research to everyday clinical practice remains limited.

Biocompatibility and cytotoxicity are among the main issues to be addressed. While many investigations report favorable safety profiles when nanomaterials are used at appropriate concentrations, their biological behavior is highly dependent on characteristics such as particle size, morphology, surface chemistry, concentration, and exposure time. This variability partly explains the apparently contradic-

Table 4. Functional classification of nanotechnology-based strategies for the management of periodontal and peri-implant diseases.

Therapeutic category	Representative nanomaterials/agents	Main applications	Principal therapeutic benefits
Antioxidant nanotherapies	Coenzyme Q10 (CoQ10), *Larrea divaricata* nanocomposites, injectable antioxidant nanoplatforms	Periodontitis, oxidative stress control	ROS scavenging, reduced inflammation, preservation of alveolar bone
Antimicrobial nanomaterials	Silver nanoparticles (AgNPs)	Prosthetic materials, restorative dentistry, endodontics, periodontitis, peri-implantitis	Broad-spectrum antimicrobial activity, inhibition of biofilm formation, reduced bacterial colonization
Photodynamic nanomaterials	Graphene derivatives, fullerenes, TiO_2, ZnO	Biofilm disruption, implant surface decontamination	Light-activated ROS generation and targeted bacterial killing
Targeted drug delivery systems	Liposomes, gold nanoparticles, polymeric nanocarriers	Local drug delivery, antimicrobial photodynamic therapy	Controlled drug release, enhanced bioavailability, improved therapeutic efficacy, reduced systemic toxicity
Bone regenerative nanomaterials	Collagen-, silica-, graphene-, and curcumin-based nanomaterials	Guided tissue regeneration, implant osseointegration	Enhanced osteogenesis, improved bone healing, simultaneous infection control
Biofilm-targeted nanostrategies	$NaYF_4$, Fe_3O_4, ZnCuO nanoparticles, antimicrobial peptides	Deep periodontal pockets, peri-implant biofilms	Improved penetration into mature biofilms and selective targeting of periodontal pathogens
Laser-generated nanoparticles	Laser-ablated AgNPs	Implant surface functionalization and biofilm prevention	Enhanced antimicrobial activity without chemical synthesis and reduced implant-associated biofilm formation
Plant-derived nanotherapeutics	Plant-derived exosome-like nanoparticles (ginger, coconut, blueberry), resveratrol, melatonin	Immunomodulation, anti-inflammatory therapy, periodontal regeneration	High biocompatibility, immunomodulatory activity, improved tissue repair, natural therapeutic delivery

Note. Abbreviations: AgNPs, silver nanoparticles; ROS, reactive oxygen species; TiO_2, titanium dioxide; ZnO, zinc oxide; $NaYF_4$, sodium yttrium fluoride; Fe_3O_4, magnetite nanoparticles.

tory findings reported for metal-based nanoparticles, particularly AgNPs and TiO_2. For example, although AgNPs consistently exhibit potent antimicrobial activity, high concentrations have also been associated with increased oxidative stress, fibroblast toxicity, and undesirable cellular responses [29,30]. These observations illustrate the complexity of designing nanoparticles capable of maintaining antimicrobial efficacy without disrupting the physiological balance required for periodontal tissue repair. A similar consideration applies to reactive oxygen species (ROS), whose antimicrobial properties are therapeutically advantageous but, when produced excessively, may contribute to oxidative damage and delayed healing.

Another important limitation concerns the scarcity of long-term clinical evidence. Most available studies evaluate short-term biological or microbiological outcomes, whereas information regarding long-term biodistribution, metabolic clearance, biodegradation, and possible tissue accumulation of nanoparticles remains limited [120]. Questions also remain regarding their potential interactions with distant organs and the consequences of repeated or prolonged exposure, particularly for non-biodegradable nanomaterials. This has increased interest in biodegradable and metabolically compatible nanomaterials that can exert their therapeutic effects without persisting indefinitely within the body.

Regulatory considerations also represent a substantial barrier to clinical implementation. Despite the growing number of experimental nanoplatforms described in the literature, relatively few nanotechnology-based approaches have progressed from experimental research to established clinical applications in dentistry. In addition to demonstrating efficacy, future nanomaterials will need to satisfy increasingly stringent requirements related to manufacturing consistency, quality control, long-term safety, and regulatory compliance before widespread clinical adoption becomes feasible. This limited transition from experimental research to clinical application also reflects the need for fur-

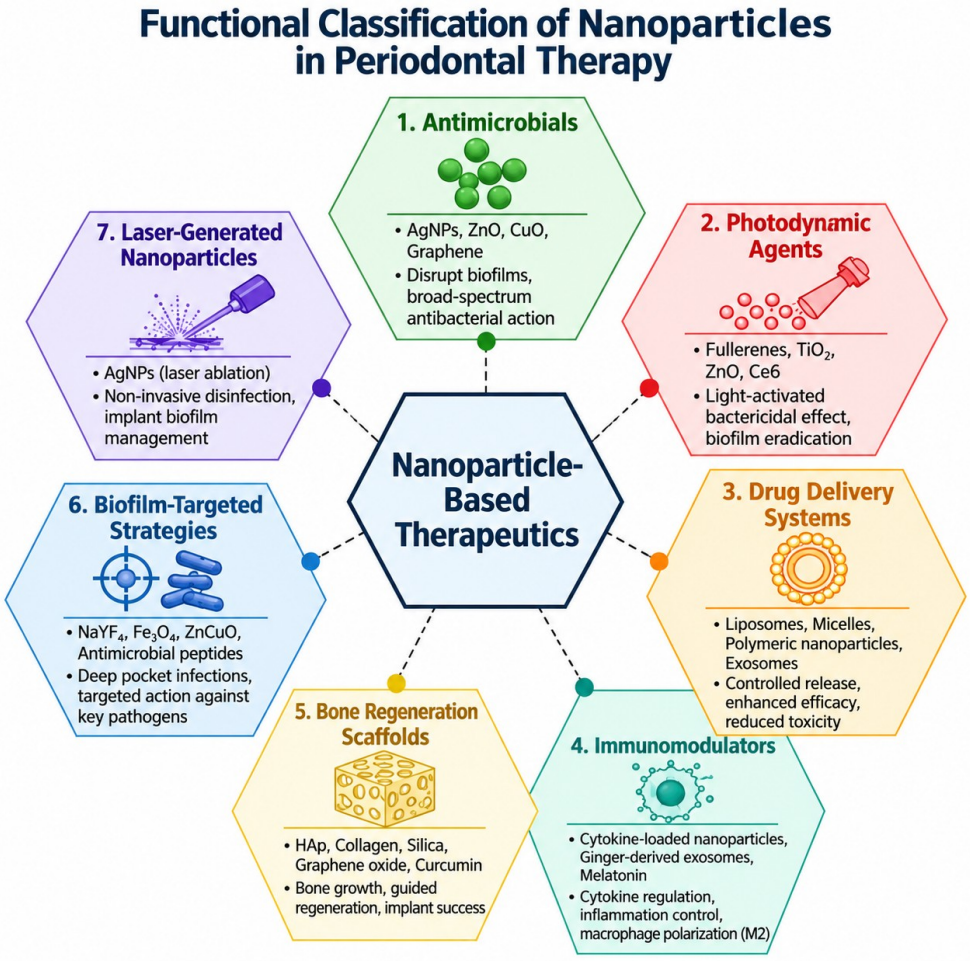

Fig. 4. Functional classification of nanoparticle-based therapeutic strategies in the management of periodontitis and peri-implantitis. Source: Authors' own elaboration. Figures were created using Microsoft PowerPoint 365 and exported as high-resolution images.

ther evidence regarding the long-term safety, reproducibility, and clinical effectiveness of these materials. This review also has methodological limitations. It was designed as a structured narrative review rather than a systematic review; therefore, no formal risk-of-bias assessment was performed. As a structured narrative rather than a systematic review, no formal risk-of-bias assessment was performed. Although a rigorous literature search and critical appraisal of the available evidence were conducted, these methodological limitations may affect the reproducibility of the literature selection and should be considered when interpreting the findings.

Economic and environmental aspects are likewise becoming increasingly relevant. The synthesis of advanced nanomaterials frequently requires specialized equipment, sophisticated manufacturing processes, and high-purity raw materials, all of which may increase production costs and limit large-scale implementation. These factors may pose additional challenges for healthcare systems with limited resources, where cost-effectiveness remains an essential component of therapeutic decision-making. At the same time, relatively little attention has been devoted to the environmental impact associated with the production, clinical use, and disposal of nanomaterials. Metal-based nanoparticles, in particular, may enter aquatic ecosystems after disposal, interact with environmental microorganisms, and potentially accumulate within food webs if appropriate waste management strategies are not implemented. Addressing these issues will require interdisciplinary collaboration between materials scientists, clinicians, toxicologists, environmental researchers, and regulatory authorities to ensure that future nanotechnology-based therapies are not only effective but also safe, accessible, and environmentally sustainable.

3.6 Functional Criteria and Key Properties of Nanomaterials for Periodontal Therapy

The therapeutic success of nanotechnology in periodontics depends not only on the intrinsic biological activity of nanomaterials but also on their ability to meet a series of functional and physicochemical requirements that allow

them to perform effectively within the complex periodontal microenvironment. Compared with conventional biomaterials, the nanoscale dimensions and high surface-area-to-volume ratio of nanoparticles can facilitate deeper penetration into periodontal tissues, enhance interactions with cellular and extracellular components, and improve the localized delivery of therapeutic agents. These properties enable nanomaterials to reach anatomical sites that are often inaccessible to conventional treatments while maintaining high biological activity using relatively low concentrations.

An ideal nanoparticle intended for the treatment of periodontitis and peri-implantitis should exhibit adequate mucoadhesion to ensure prolonged retention within periodontal pockets and peri-implant sulci, allowing sustained therapeutic activity despite the continuous flow of gingival crevicular fluid. At the same time, it should combine antimicrobial activity with regenerative capacity, eliminating pathogenic microorganisms while creating a biological environment that favors new bone formation and periodontal attachment. Rather than functioning through a single mechanism, next-generation nanomaterials are increasingly being designed as multifunctional platforms capable of simultaneously controlling infection, modulating inflammation, and promoting tissue regeneration.

Besides these biological functions, the physicochemical characteristics of nanomaterials play a decisive role in determining their clinical performance. Controlled biodegradability, high biocompatibility, structural stability, selective molecular interactions, and efficient uptake by target cells all contribute to therapeutic precision while minimizing undesirable effects on surrounding tissues. The balance between persistence and degradation is particularly important, as nanoparticles should remain active long enough to exert their therapeutic function without accumulating within tissues or eliciting chronic foreign-body responses.

The diversity of these functional characteristics is summarized in Table 4, which classifies the principal nanotechnology-based approaches according to their therapeutic role, including antimicrobial agents, photodynamic therapies, targeted drug delivery systems, regenerative scaffolds, immunomodulatory nanomaterials, and plant-derived formulations. Rather than representing isolated therapeutic strategies, these categories frequently overlap, reflecting the multifunctional nature of many contemporary nanoplatforms. For example, a single nanomaterial may simultaneously provide antimicrobial activity, regulate the inflammatory response, and serve as a controlled drug delivery vehicle. Fig. 4 complements this overview by illustrating the main classes of nanoparticle-based therapeutics, their mechanisms of action, and their principal biological targets within periodontal and peri-implant tissues, illustrating how current nanotechnology approaches increasingly combine several therapeutic functions within the same platform.

4. Conclusions

Nanotechnology is emerging as an increasingly investigated strategy for improving the prevention and treatment of periodontitis and peri-implantitis, offering therapeutic approaches that extend beyond the capabilities of conventional periodontal therapies. The evidence reviewed in this study shows that nanomaterials can perform multiple complementary functions, including targeted drug delivery, antimicrobial activity, modulation of the host inflammatory response, and promotion of periodontal and peri-implant tissue regeneration. Rather than acting through a single mechanism, many of the currently investigated nanoplatforms combine several biological activities within the same system, making them of particular interest for the management of these multifactorial diseases.

The literature also demonstrates that nanotechnology has enabled the development of implant surface coatings, injectable biomaterials, regenerative scaffolds, photodynamic systems, and multifunctional nanoparticles capable of reducing bacterial colonization while simultaneously enhancing bone healing and tissue repair. These approaches may be particularly relevant in clinical situations where conventional therapies have limitations, such as deep periodontal pockets, mature biofilms, peri-implant infections, or patients with systemic conditions that compromise healing.

Despite these encouraging developments, most available evidence still originates from experimental models or early-stage clinical studies, and important challenges remain before these technologies can be routinely incorporated into clinical practice. Long-term safety, standardized manufacturing protocols, regulatory approval, cost-effectiveness, and environmental sustainability remain important areas for future research to ensure that future nanotechnology-based therapies are not only effective but also safe and accessible.

Overall, the current evidence suggests that nanotechnology should be viewed not as a replacement for conventional periodontal therapy, but as a complementary platform capable of enhancing existing therapeutic approaches. Further collaboration among clinicians, biomaterials scientists, microbiologists, and biomedical engineers will be important for translating these approaches into predictable, evidence-based treatments.

Author Contributions

Conceptualization, VN and DS; methodology, DS; validation, KCS; literature search and study selection, VN and DS; writing—original draft preparation, VN and DS; writing—review and editing, KCS; visualization, KCS; supervision, DS. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

The authors would like to express their sincere gratitude to everyone who contributed to the development and preparation of this manuscript.

Funding

This research received no external funding.

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] Bao G, Mitragotri S, Tong S. Multifunctional nanoparticles for drug delivery and molecular imaging. Annual Review of Biomedical Engineering. 2013; 15: 253–282. https://doi.org/10.1146/annurev-bioeng-071812-152409

[2] Feynman RP. There's plenty of room at the bottom. Journal of Microelectromechanical Systems. 1992; 1: 60–66. https://doi.org/10.1109/84.128057

[3] Drexler KE. Engines of Creation: The Coming Era of Nanotechnology (pp. 99–129). Anchor Press: New York. 1986.

[4] Hosseini Hooshiar M, Mozaffari A, Hamed Ahmed M, Abdul Kareem R, Jaber Zrzo A, Salah Mansoor A, et al. Potential role of metal nanoparticles in treatment of peri-implant mucositis and peri-implantitis. Biomedical Engineering Online. 2024; 23: 101. https://doi.org/10.1186/s12938-024-01294-0

[5] Jhaveri HM, Balaji PR. Nanotechnology: The future of dentistry. The Journal of Indian Prosthodontic Society. 2005; 5: 15–17. https://doi.org/10.4103/0972-4052.16335

[6] Saravana KR, Vijayalakshmi R. Nanotechnology in dentistry. Indian Journal of Dental Research : Official Publication of Indian Society for Dental Research. 2006; 17: 62–65. https://doi.org/10.4103/0970-9290.29890

[7] Yih TC, Moudgil VK. Nanotechnology comes of age to trigger the third industrial revolution. Nanomedicine : Nanotechnology, Biology, and Medicine. 2007; 3: 245. https://doi.org/10.1016/j.nano.2007.10.083

[8] Patil M, Mehta DS, Guvva S. Future impact of nanotechnology on medicine and dentistry. Journal of Indian Society of Periodontology. 2008; 12: 34–40. https://doi.org/10.4103/0972-124X.44088

[9] Saleh MHA, Roh A, Martin K, Mianecki M, Tariq Sheikh A, Singh P, et al. Cargo-less Nanoparticles Prevent Bone Loss in Periodontitis and Peri-implantitis. Journal of Dental Research. 2025; 104: 862–869. https://doi.org/10.1177/00220345251319256

[10] Freitas RA, Jr. Nanotechnology, nanomedicine and nanosurgery. International Journal of Surgery (London, England). 2005; 3: 243–246. https://doi.org/10.1016/j.ijsu.2005.10.007

[11] Freitas RA, Jr. Nanodentistry. Journal of the American Dental Association (1939). 2000; 131: 1559–1565. https://doi.org/10.14219/jada.archive.2000.0084

[12] Freitas RA, Jr. Welcome to the future of medicine. Studies in Health Technology and Informatics. 2009; 149: 251–256.

[13] Joudeh N, Linke D. Nanoparticle classification, physicochemical properties, characterization, and applications: a comprehensive review for biologists. Journal of Nanobiotechnology. 2022; 20: 262. https://doi.org/10.1186/s12951-022-01477-8

[14] Abid N, Khan AM, Shujait S, Chaudhary K, Ikram M, Imran M, et al. Synthesis of nanomaterials using various top-down and bottom-up approaches, influencing factors, advantages, and disadvantages: A review. Advances in Colloid and Interface Science. 2022; 300: 102597. https://doi.org/10.1016/j.cis.2021.102597

[15] Gleiter H. Nanostructured materials: basic concepts and microstructure. Acta Materialia. 2000; 48: 1–29. https://doi.org/10.1016/S1359-6454(99)00285-2

[16] Nano A. The A to Z of nanotechnology and nanomaterials. The Institute of Nanotechnology, Azom Co., Ltd.: London. 2003.

[17] Kong LX, Peng Z, Li SD, Bartold PM. Nanotechnology and its role in the management of periodontal diseases. Periodontology 2000. 2006; 40: 184–196. https://doi.org/10.1111/j.1600-0757.2005.00143.x

[18] Serrano-Granger J, Herrera D. La placa dental como biofilm: ¿cómo eliminarla? RCOE. 2005; 10: 431–439. (In Spanish)

[19] Mlachkova A, Dosseva-Panova V, Maynalovska H, Pashova-Tasseva Z. Nanoparticles as Strategies for Modulating the Host's Response in Periodontitis Treatment. Nanomaterials (Basel, Switzerland). 2025; 15: 476. https://doi.org/10.3390/nano15070476

[20] Shin SY, Park HN, Kim KH, Lee MH, Choi YS, Park YJ, et al. Biological evaluation of chitosan nanofiber membrane for guided bone regeneration. Journal of Periodontology. 2005; 76: 1778–1784. https://doi.org/10.1902/jop.2005.76.10.1778

[21] Shaheen MA, Elmeadawy SH, Bazeed FB, Anees MM, Saleh NM. Innovative coenzyme Q_{10}-loaded nanoformulation as an adjunct approach for the management of moderate periodontitis: preparation, evaluation, and clinical study. Drug Delivery and Translational Research. 2020; 10: 548–564. https://doi.org/10.1007/s13346-019-00698-z

[22] Rizvi SAA, Saleh AM. Applications of nanoparticle systems in drug delivery technology. Saudi Pharmaceutical Journal : SPJ : the Official Publication of the Saudi Pharmaceutical Society. 2018; 26: 64–70. https://doi.org/10.1016/j.jsps.2017.10.012

[23] Horie RT, Sakamoto T, Nakagawa T, Tabata Y, Okamura N, Tomiyama N, et al. Sustained delivery of lidocaine into the cochlea using poly lactic/glycolic acid microparticles. The Laryngoscope. 2010; 120: 377–383. https://doi.org/10.1002/lary.20713

[24] Sui L, Wang J, Xiao Z, Yang Y, Yang Z, Ai K. ROS-Scavenging Nanomaterials to Treat Periodontitis. Frontiers in Chemistry. 2020; 8: 595530. https://doi.org/10.3389/fchem.2020.595530

[25] Bressan E, Ferroni L, Gardin C, Bellin G, Sbricoli L, Sivolella S, et al. Metal Nanoparticles Released from Dental Implant Surfaces: Potential Contribution to Chronic Inflammation and Peri-Implant Bone Loss. Materials (Basel, Switzerland). 2019; 12: 2036. https://doi.org/10.3390/ma12122036

[26] Swarnakar NK, Jain AK, Singh RP, Godugu C, Das M, Jain S. Oral bioavailability, therapeutic efficacy and reactive oxygen species scavenging properties of coenzyme Q10-loaded polymeric nanoparticles. Biomaterials. 2011; 32: 6860–6874. https://doi.org/10.1016/j.biomaterials.2011.05.079

[27] Alvarez Echazú MI, Olivetti CE, Peralta I, Alonso MR, Anesini C, Perez CJ, et al. Development of pH-responsive biopolymer-silica composites loaded with Larrea divaricata Cav. extract with antioxidant activity. Colloids and Surfaces. B, Biointerfaces. 2018; 169: 82–91. https://doi.org/10.1016/j.colsurfb.2018.05.015

[28] Saita M, Kaneko J, Sato T, Takahashi SS, Wada-Takahashi S, Kawamata R, et al. Novel antioxidative nanotherapeutics in a rat periodontitis model: Reactive oxygen species scavenging by redox injectable gel suppresses alveolar bone resorption. Biomaterials. 2016; 76: 292–301. https://doi.org/10.1016/j.biomaterials.2015.10.077

[29] Bao X, Zhao J, Sun J, Hu M, Yang X. Polydopamine Nanopar-

ticles as Efficient Scavengers for Reactive Oxygen Species in Periodontal Disease. ACS Nano. 2018; 12: 8882–8892. https://doi.org/10.1021/acsnano.8b04022

[30] Yin IX, Zhang J, Zhao IS, Mei ML, Li Q, Chu CH. The Antibacterial Mechanism of Silver Nanoparticles and Its Application in Dentistry. International Journal of Nanomedicine. 2020; 15: 2555–2562. https://doi.org/10.2147/IJN.S246764

[31] de Castro DT, do Nascimento C, Alves OL, de Souza Santos E, Agnelli JAM, Dos Reis AC. Analysis of the oral microbiome on the surface of modified dental polymers. Archives of Oral Biology. 2018; 93: 107–114. https://doi.org/10.1016/j.archoralbio.2018.06.005

[32] Li Z, Sun J, Lan J, Qi Q. Effect of a denture base acrylic resin containing silver nanoparticles on Candida albicans adhesion and biofilm formation. Gerodontology. 2016; 33: 209–216. https://doi.org/10.1111/ger.12142

[33] Dias HB, Bernardi MIB, Marangoni VS, de Abreu Bernardi AC, de Souza Rastelli AN, Hernandes AC. Synthesis, characterization and application of Ag doped ZnO nanoparticles in a composite resin. Materials Science & Engineering. C, Materials for Biological Applications. 2019; 96: 391–401. https://doi.org/10.1016/j.msec.2018.10.063

[34] Ai M, Du Z, Zhu S, Geng H, Zhang X, Cai Q, et al. Composite resin reinforced with silver nanoparticles-laden hydroxyapatite nanowires for dental application. Dental Materials : Official Publication of the Academy of Dental Materials. 2017; 33: 12–22. https://doi.org/10.1016/j.dental.2016.09.038

[35] Cheng L, Weir MD, Xu HHK, Antonucci JM, Kraigsley AM, Lin NJ, et al. Antibacterial amorphous calcium phosphate nanocomposites with a quaternary ammonium dimethacrylate and silver nanoparticles. Dental Materials : Official Publication of the Academy of Dental Materials. 2012; 28: 561–572. https://doi.org/10.1016/j.dental.2012.01.005

[36] Ioannidis K, Niazi S, Mylonas P, Mannocci F, Deb S. The synthesis of nano silver-graphene oxide system and its efficacy against endodontic biofilms using a novel tooth model. Dental Materials : Official Publication of the Academy of Dental Materials. 2019; 35: 1614–1629. https://doi.org/10.1016/j.dental.2019.08.105

[37] Suzuki TYU, Gallego J, Assunção WG, Briso ALF, Dos Santos PH. Influence of silver nanoparticle solution on the mechanical properties of resin cements and intrarradicular dentin. PloS One. 2019; 14: e0217750. https://doi.org/10.1371/journal.pone.0217750

[38] Mishra P, Tyagi S. Surface analysis of gutta percha after disinfecting with sodium hypochlorite and silver nanoparticles by atomic force microscopy: An *in vitro* study. Dental Research Journal. 2018; 15: 242–247.

[39] Mozayeni MA, Dianat O, Tahvildari S, Mozayani M, Paymanpour P. Subcutaneous Reaction of Rat Tissues to Nanosilver Coated Gutta-Percha. Iranian Endodontic Journal. 2017; 12: 157–161. https://doi.org/10.22037/iej.2017.31

[40] Vazquez-Garcia F, Tanomaru-Filho M, Chávez-Andrade GM, Bosso-Martelo R, Basso-Bernardi MI, Guerreiro-Tanomaru JM. Effect of Silver Nanoparticles on Physicochemical and Antibacterial Properties of Calcium Silicate Cements. Brazilian Dental Journal. 2016; 27: 508–514. https://doi.org/10.1590/0103-6440201600689

[41] Al-Thomali Y. Shear bond strength of orthodontic brackets after adding silver nanoparticles to a nano-bond adhesive at different thermal cycles and cyclic loading—An in vitro study. Journal of Orthodontic Science. 2022; 11: 28. https://doi.org/10.4103/jos.jos_183_21

[42] Hernández-Gómora AE, Lara-Carrillo E, Robles-Navarro JB, Scougall-Vilchis RJ, Hernández-López S, Medina-Solís CE, et al. Biosynthesis of Silver Nanoparticles on Orthodontic Elastomeric Modules: Evaluation of Mechanical and Antibacterial Properties. Molecules (Basel, Switzerland). 2017; 22: 1407. https://doi.org/10.3390/molecules22091407

[43] Takallu S, Mirzaei E, Zakeri Bazmandeh A, Ghaderi Jafarbeigloo HR, Khorshidi H. Addressing Antimicrobial Properties in Guided Tissue/Bone Regeneration Membrane: Enhancing Effectiveness in Periodontitis Treatment. ACS Infectious Diseases. 2024; 10: 779–807. https://doi.org/10.1021/acsinfecdis.3c00568

[44] Metin-Gürsoy G, Taner L, Akca G. Nanosilver coated orthodontic brackets: in vivo antibacterial properties and ion release. European Journal of Orthodontics. 2017; 39: 9–16. https://doi.org/10.1093/ejo/cjv097

[45] Panáček A, Smékalová M, Večeřová R, Bogdanová K, Röderová M, Kolář M, et al. Silver nanoparticles strongly enhance and restore bactericidal activity of inactive antibiotics against multiresistant Enterobacteriaceae. Colloids and Surfaces. B, Biointerfaces. 2016; 142: 392–399. https://doi.org/10.1016/j.colsurfb.2016.03.007

[46] Halkai KR, Mudda JA, Shivanna V, Rathod V, Halkai RS. Biosynthesis, Characterization and Antibacterial Efficacy of Silver Nanoparticles Derived from Endophytic Fungi against *P. gingivalis*. Journal of Clinical and Diagnostic Research : JCDR. 2017; 11: ZC92–ZC96. https://doi.org/10.7860/JCDR/2017/29434.10681

[47] Chi M, Qi M, A L, Wang P, Weir MD, Melo MA, et al. Novel Bioactive and Therapeutic Dental Polymeric Materials to Inhibit Periodontal Pathogens and Biofilms. International Journal of Molecular Sciences. 2019; 20: 278. https://doi.org/10.3390/ijms20020278

[48] Singh P, Ahn S, Kang JP, Veronika S, Huo Y, Singh H, et al. In vitro anti-inflammatory activity of spherical silver nanoparticles and monodisperse hexagonal gold nanoparticles by fruit extract of Prunus serrulata: a green synthetic approach. Artificial Cells, Nanomedicine, and Biotechnology. 2018; 46: 2022–2032. https://doi.org/10.1080/21691401.2017.1408117

[49] Gunputh UF, Le H, Lawton K, Besinis A, Tredwin C, Handy RD. Antibacterial properties of silver nanoparticles grown *in situ* and anchored to titanium dioxide nanotubes on titanium implant against *Staphylococcus aureus*. Nanotoxicology. 2020; 14: 97–110. https://doi.org/10.1080/17435390.2019.1665727

[50] Pokrowiecki R, Zaręba T, Szaraniec B, Pałka K, Mielczarek A, Menaszek E, et al. In vitro studies of nanosilver-doped titanium implants for oral and maxillofacial surgery. International Journal of Nanomedicine. 2017; 12: 4285–4297. https://doi.org/10.2147/IJN.S131163

[51] Massa MA, Covarrubias C, Bittner M, Fuentevilla IA, Capetillo P, Von Marttens A, et al. Synthesis of new antibacterial composite coating for titanium based on highly ordered nanoporous silica and silver nanoparticles. Materials Science & Engineering. C, Materials for Biological Applications. 2014; 45: 146–153. https://doi.org/10.1016/j.msec.2014.08.057

[52] Lampé I, Beke D, Biri S, Csarnovics I, Csik A, Dombrádi Z, et al. Investigation of silver nanoparticles on titanium surface created by ion implantation technology. International Journal of Nanomedicine. 2019; 14: 4709–4721. https://doi.org/10.2147/IJN.S197782

[53] Pérez-Tanoira R, Fernández-Arias M, Potel C, Carballo-Fernández R, Pérez-Castro S, Boutinguiza M, et al. Silver Nanoparticles Produced by Laser Ablation and Re-Irradiation Are Effective Preventing Peri-Implantitis Multispecies Biofilm Formation. International Journal of Molecular Sciences. 2022; 23: 12027. https://doi.org/10.3390/ijms231912027

[54] Drago L, Bortolin M, De Vecchi E, Agrappi S, Weinstein RL, Mattina R, et al. Antibiofilm activity of sandblasted and laser-modified titanium against microorganisms isolated from peri-

implantitis lesions. Journal of Chemotherapy (Florence, Italy). 2016; 28: 383–389. https://doi.org/10.1080/1120009X.2016.1158489

[55] Salaie RN, Besinis A, Le H, Tredwin C, Handy RD. The biocompatibility of silver and nanohydroxyapatite coatings on titanium dental implants with human primary osteoblast cells. Materials Science & Engineering. C, Materials for Biological Applications. 2020; 107: 110210. https://doi.org/10.1016/j.msec.2019.110210

[56] Zhou W, Jia Z, Xiong P, Yan J, Li Y, Li M, et al. Bioinspired and Biomimetic AgNPs/Gentamicin-Embedded Silk Fibroin Coatings for Robust Antibacterial and Osteogenetic Applications. ACS Applied Materials & Interfaces. 2017; 9: 25830–25846. https://doi.org/10.1021/acsami.7b06757

[57] Aoshima H, Kokubo K, Shirakawa S, Ito M, Yamana S, Oshima T. Antimicrobial activity of fullerenes and their hydroxylated derivatives. Biocontrol Science. 2009; 14: 69–72. https://doi.org/10.4265/bio.14.69

[58] Yin R, Wang M, Huang YY, Landi G, Vecchio D, Chiang LY, et al. Antimicrobial photodynamic inactivation with decacationic functionalized fullerenes: oxygen-independent photokilling in presence of azide and new mechanistic insights. Free Radical Biology & Medicine. 2015; 79: 14–27. https://doi.org/10.1016/j.freeradbiomed.2014.10.514

[59] Huang L, Bhayana B, Xuan W, Sanchez RP, McCulloch BJ, Lalwani S, et al. Comparison of two functionalized fullerenes for antimicrobial photodynamic inactivation: Potentiation by potassium iodide and photochemical mechanisms. Journal of Photochemistry and Photobiology. B, Biology. 2018; 186: 197–206. https://doi.org/10.1016/j.jphotobiol.2018.07.027

[60] Ouyang K, Dai K, Chen H, Huang Q, Gao C, Cai P. Metal-free inactivation of E. coli O157:H7 by fullerene/C_3N_4 hybrid under visible light irradiation. Ecotoxicology and Environmental Safety. 2017; 136: 40–45. https://doi.org/10.1016/j.ecoenv.2016.10.030

[61] Wang Y, Jin Y, Chen W, Wang J, Chen H, Sun L, et al. Construction of nanomaterials with targeting phototherapy properties to inhibit resistant bacteria and biofilm infections. Chemical Engineering Journal. 2019; 358: 74–90. https://doi.org/10.1016/j.cej.2018.10.002

[62] Ristic BZ, Milenkovic MM, Dakic IR, Todorovic-Markovic BM, Milosavljevic MS, Budimir MD, et al. Photodynamic antibacterial effect of graphene quantum dots. Biomaterials. 2014; 35: 4428–4435. https://doi.org/10.1016/j.biomaterials.2014.02.014

[63] Sah U, Sharma K, Chaudhri N, Sankar M, Gopinath P. Antimicrobial photodynamic therapy: Single-walled carbon nanotube (SWCNT)-Porphyrin conjugate for visible light mediated inactivation of Staphylococcus aureus. Colloids and Surfaces. B, Biointerfaces. 2018; 162: 108–117. https://doi.org/10.1016/j.colsurfb.2017.11.046

[64] Xiao H, Zhu B, Wang D, Pang Y, He L, Ma X, et al. Photodynamic effects of chlorin e6 attached to single wall carbon nanotubes through noncovalent interactions. Carbon. 2012; 50: 1681–1689. https://doi.org/10.1016/j.carbon.2011.12.013

[65] Banerjee I, Mondal D, Martin J, Kane RS. Photoactivated antimicrobial activity of carbon nanotube-porphyrin conjugates. Langmuir : the ACS Journal of Surfaces and Colloids. 2010; 26: 17369–17374. https://doi.org/10.1021/la103298e

[66] Tsai YH, Milbrandt NB, Prado RC, Ponce NB, Alam MM, Qiu SR, et al. Effect of Nitrogen Doping on the Photocatalytic Properties and Antibiofilm Efficacy of Reduced TiO_2 Nanoparticles. ACS Applied Bio Materials. 2024; 7: 4580–4592. https://doi.org/10.1021/acsabm.4c00459

[67] Podporska-Carroll J, Myles A, Quilty B, McCormack DE, Fagan R, Hinder SJ, et al. Antibacterial properties of F-doped ZnO visible light photocatalyst. Journal of Hazardous Materials. 2017; 324: 39–47. https://doi.org/10.1016/j.jhazmat.2015.12.038

[68] Sethi D, Sakthivel R. ZnO/TiO_2 composites for photocatalytic inactivation of Escherichia coli. Journal of Photochemistry and Photobiology. B, Biology. 2017; 168: 117–123. https://doi.org/10.1016/j.jphotobiol.2017.02.005

[69] Gao L, Giglio KM, Nelson JL, Sondermann H, Travis AJ. Ferromagnetic nanoparticles with peroxidase-like activity enhance the cleavage of biological macromolecules for biofilm elimination. Nanoscale. 2014; 6: 2588–2593. https://doi.org/10.1039/c3nr05422e

[70] Suketa N, Sawase T, Kitaura H, Naito M, Baba K, Nakayama K, et al. An antibacterial surface on dental implants, based on the photocatalytic bactericidal effect. Clinical Implant Dentistry and Related Research. 2005; 7: 105–111. https://doi.org/10.1111/j.1708-8208.2005.tb00053.x

[71] Qi M, Li X, Sun X, Li C, Tay FR, Weir MD, et al. Novel nanotechnology and near-infrared photodynamic therapy to kill periodontitis-related biofilm pathogens and protect the periodontium. Dental Materials : Official Publication of the Academy of Dental Materials. 2019; 35: 1665–1681. https://doi.org/10.1016/j.dental.2019.08.115

[72] Sun X, Wang L, Lynch CD, Sun X, Li X, Qi M, et al. Nanoparticles having amphiphilic silane containing Chlorin e6 with strong anti-biofilm activity against periodontitis-related pathogens. Journal of Dentistry. 2019; 81: 70–84. https://doi.org/10.1016/j.jdent.2018.12.011

[73] Sun X, Sun J, Sun Y, Li C, Fang J, Zhang T, et al. Oxygen self-sufficient nanoplatform for enhanced and selective antibacterial photodynamic therapy against anaerobe-induced periodontal disease. Advanced Functional Materials. 2021; 31: 2101040. https://doi.org/10.1002/adfm.202101040

[74] Dabbah K, Perelshtein I, Gedanken A, Houri-Haddad Y, Feuerstein O. Effects of a ZnCuO-Nanocoated Ti-6Al-4V Surface on Bacterial and Host Cells. Materials (Basel, Switzerland). 2022; 15: 2514. https://doi.org/10.3390/ma15072514

[75] Fang D, Yuran S, Reches M, Catunda R, Levin L, Febbraio M. A peptide coating preventing the attachment of Porphyromonas gingivalis on the surfaces of dental implants. Journal of Periodontal Research. 2020; 55: 503–510. https://doi.org/10.1111/jre.12737

[76] Besinis A, Hadi SD, Le HR, Tredwin C, Handy RD. Antibacterial activity and biofilm inhibition by surface modified titanium alloy medical implants following application of silver, titanium dioxide and hydroxyapatite nanocoatings. Nanotoxicology. 2017; 11: 327–338. https://doi.org/10.1080/17435390.2017.1299890

[77] Chen X, Hirt H, Li Y, Gorr SU, Aparicio C. Antimicrobial GL13K peptide coatings killed and ruptured the wall of Streptococcus gordonii and prevented formation and growth of biofilms. PloS One. 2014; 9: e111579. https://doi.org/10.1371/journal.pone.0111579

[78] Rodríguez-Hernández AP, Vega-Jiménez AL, Vázquez-Olmos AR, Ortega-Maldonado M, Ximenez-Fyvie LA. Antibacterial Properties In Vitro of Magnesium Oxide Nanoparticles for Dental Applications. Nanomaterials (Basel, Switzerland). 2023; 13: 502. https://doi.org/10.3390/nano13030502

[79] Guo J, Wang P, Li Y, Liu Y, Ye Y, Chen Y, et al. Advances in hybridized nanoarchitectures for improved oro-dental health. Journal of Nanobiotechnology. 2024; 22: 469. https://doi.org/10.1186/s12951-024-02680-5

[80] Deng X, Liang Y, Peng X, Su T, Luo S, Cao J, et al. A facile strategy to generate polymeric nanoparticles for synergistic chemo-photodynamic therapy. Chemical Communications (Cambridge, England). 2015; 51: 4271–4274. https://doi.org/10.1039/c4cc10226f

[81] Mukherjee M, De S. Inactivation of Pseudomonas aeruginosa by Chitosan Coated Iron Oxide Nanoparticles. Recent Patents on Biotechnology. 2016; 10: 133–139. https://doi.org/10.2174/1872208310666160805113554

[82] Klepac-Ceraj V, Patel N, Song X, Holewa C, Patel C, Kent R, et al. Photodynamic effects of methylene blue-loaded polymeric nanoparticles on dental plaque bacteria. Lasers in Surgery and Medicine. 2011; 43: 600–606. https://doi.org/10.1002/lsm.21069

[83] Ono K, Hayashi JI, Suzuki Y, Yamashita M, Nishikawa K, Higuchi N, et al. Photodynamic disruption of a polymicrobial biofilm of two periodontal species using indocyanine green-loaded nanospheres. Photodiagnosis and Photodynamic Therapy. 2024; 50: 104421. https://doi.org/10.1016/j.pdpdt.2024.104421

[84] Qi M, Chi M, Sun X, Xie X, Weir MD, Oates TW, et al. Novel nanomaterial-based antibacterial photodynamic therapies to combat oral bacterial biofilms and infectious diseases. International Journal of Nanomedicine. 2019; 14: 6937–6956. https://doi.org/10.2147/IJN.S212807

[85] Wysocka-Król K, Olsztyńska-Janus S, Plesch G, Plecenik A, Podbielska H, Bauer J. Nano-silver modified silica particles in antibacterial photodynamic therapy. Applied Surface Science. 2018; 461: 260–268. https://doi.org/10.1016/j.apsusc.2018.05.014

[86] Jin CS, Zheng G. Liposomal nanostructures for photosensitizer delivery. Lasers in Surgery and Medicine. 2011; 43: 734–748. https://doi.org/10.1002/lsm.21101

[87] Kara A, Akman S, Ozkanlar S, Tozoglu U, Kalkan Y, Canakci CF, et al. Immune modulatory and antioxidant effects of melatonin in experimental periodontitis in rats. Free Radical Biology & Medicine. 2013; 55: 21–26. https://doi.org/10.1016/j.freeradbiomed.2012.11.002

[88] Murgia D, Angellotti G, D'Agostino F, De Caro V. Bioadhesive Matrix Tablets Loaded with Lipophilic Nanoparticles as Vehicles for Drugs for Periodontitis Treatment: Development and Characterization. Polymers. 2019; 11: 1801. https://doi.org/10.3390/polym11111801

[89] Menon VP, Sudheer AR. Antioxidant and anti-inflammatory properties of curcumin. Advances in Experimental Medicine and Biology. 2007; 595: 105–125. https://doi.org/10.1007/978-0-387-46401-5_3

[90] Goyal G, Garg T, Rath G, Goyal AK. Current nanotechnological strategies for an effective delivery of drugs in treatment of periodontal disease. Critical Reviews in Therapeutic Drug Carrier Systems. 2014; 31: 89–119. https://doi.org/10.1615/critrevtherdrugcarriersyst.2014008117

[91] El-Telbany M, El-Sharaki A. Antibacterial and anti-biofilm activity of silver nanoparticles on multi-drug resistance *pseudomonas aeruginosa* isolated from dental-implant. Journal of Oral Biology and Craniofacial Research. 2022; 12: 199–203. https://doi.org/10.1016/j.jobcr.2021.12.002

[92] Ansari MA, Khan HM, Khan AA, Cameotra SS, Saquib Q, Musarrat J. Gum arabic capped-silver nanoparticles inhibit biofilm formation by multi-drug resistant strains of Pseudomonas aeruginosa. Journal of Basic Microbiology. 2014; 54: 688–699. https://doi.org/10.1002/jobm.201300748

[93] Ali SG, Ansari MA, Khan HM, Jalal M, Mahdi AA, Cameotra SS. Crataeva nurvala nanoparticles inhibit virulence factors and biofilm formation in clinical isolates of Pseudomonas aeruginosa. Journal of Basic Microbiology. 2017; 57: 193–203. https://doi.org/10.1002/jobm.201600175

[94] Zhang Z, Yu Y, Zhu G, Zeng L, Xu S, Cheng H, et al. The Emerging Role of Plant-Derived Exosomes-Like Nanoparticles in Immune Regulation and Periodontitis Treatment. Frontiers in Immunology. 2022; 13: 896745. https://doi.org/10.3389/fimmu.2022.896745

[95] Mu J, Zhuang X, Wang Q, Jiang H, Deng ZB, Wang B, et al. Interspecies communication between plant and mouse gut host cells through edible plant derived exosome-like nanoparticles. Molecular Nutrition & Food Research. 2014; 58: 1561–1573. https://doi.org/10.1002/mnfr.201300729

[96] Zhang M, Viennois E, Prasad M, Zhang Y, Wang L, Zhang Z, et al. Edible ginger-derived nanoparticles: A novel therapeutic approach for the prevention and treatment of inflammatory bowel disease and colitis-associated cancer. Biomaterials. 2016; 101: 321–340. https://doi.org/10.1016/j.biomaterials.2016.06.018

[97] Chen X, Zhou Y, Yu J. Exosome-like Nanoparticles from Ginger Rhizomes Inhibited NLRP3 Inflammasome Activation. Molecular Pharmaceutics. 2019; 16: 2690–2699. https://doi.org/10.1021/acs.molpharmaceut.9b00246

[98] You JY, Kang SJ, Rhee WJ. Isolation of cabbage exosome-like nanovesicles and investigation of their biological activities in human cells. Bioactive Materials. 2021; 6: 4321–4332. https://doi.org/10.1016/j.bioactmat.2021.04.023

[99] De Robertis M, Sarra A, D'Oria V, Mura F, Bordi F, Postorino P, et al. Blueberry-Derived Exosome-Like Nanoparticles Counter the Response to TNF-α-Induced Change on Gene Expression in EA.hy926 Cells. Biomolecules. 2020; 10: 742. https://doi.org/10.3390/biom10050742

[100] Zhao WJ, Bian YP, Wang QH, Yin F, Yin L, Zhang YL, et al. Blueberry-derived exosomes-like nanoparticles ameliorate nonalcoholic fatty liver disease by attenuating mitochondrial oxidative stress. Acta Pharmacologica Sinica. 2022; 43: 645–658. https://doi.org/10.1038/s41401-021-00681-w

[101] Sundaram K, Miller DP, Kumar A, Teng Y, Sayed M, Mu J, et al. Plant-Derived Exosomal Nanoparticles Inhibit Pathogenicity of Porphyromonas gingivalis. iscience. 2019; 21: 308–327. https://doi.org/10.1016/j.isci.2019.10.032

[102] Perut F, Roncuzzi L, Avnet S, Massa A, Zini N, Sabbadini S, et al. Strawberry-Derived Exosome-Like Nanoparticles Prevent Oxidative Stress in Human Mesenchymal Stromal Cells. Biomolecules. 2021; 11: 87. https://doi.org/10.3390/biom11010087

[103] Cao M, Yan H, Han X, Weng L, Wei Q, Sun X, et al. Ginseng-derived nanoparticles alter macrophage polarization to inhibit melanoma growth. Journal for Immunotherapy of Cancer. 2019; 7: 326. https://doi.org/10.1186/s40425-019-0817-4

[104] Liu B, Li X, Yu H, Shi X, Zhou Y, Alvarez S, et al. Therapeutic potential of garlic chive-derived vesicle-like nanoparticles in NLRP3 inflammasome-mediated inflammatory diseases. Theranostics. 2021; 11: 9311–9330. https://doi.org/10.7150/thno.60265

[105] Bruno SP, Paolini A, D'Oria V, Sarra A, Sennato S, Bordi F, et al. Extracellular Vesicles Derived From *Citrus sinensis* Modulate Inflammatory Genes and Tight Junctions in a Human Model of Intestinal Epithelium. Frontiers in Nutrition. 2021; 8: 778998. https://doi.org/10.3389/fnut.2021.778998

[106] Lei C, Teng Y, He L, Sayed M, Mu J, Xu F, et al. Lemon exosome-like nanoparticles enhance stress survival of gut bacteria by RNase P-mediated specific tRNA decay. iscience. 2021; 24: 102511. https://doi.org/10.1016/j.isci.2021.102511

[107] Şahin F, Koçak P, Güneş MY, Özkan İ, Yıldırım E, Kala EY. In Vitro Wound Healing Activity of Wheat-Derived Nanovesicles. Applied Biochemistry and Biotechnology. 2019; 188: 381–394. https://doi.org/10.1007/s12010-018-2913-1

[108] Xu X, Zhou XD, Wu CD. The tea catechin epigallocatechin gallate suppresses cariogenic virulence factors of Streptococcus mutans. Antimicrobial Agents and Chemotherapy. 2011; 55: 1229–1236. https://doi.org/10.1128/aac.01016-10

[109] Zhao Q, Hu QX, Li JP, Su HB, Li ZY, He J, et al. *Morinda Officinalis*-Derived Extracellular Vesicle-like Particles Promote

Wound Healing via Angiogenesis. ACS Applied Materials & Interfaces. 2025; 17: 30454–30464. https://doi.org/10.1021/acsami.5c01640

[110] Arundina I, Diyatri I, Juliastuti WS, Budhy TI, Surboyo MDC, Iskandar B, et al. Osteoblast Viability of Liquid Smoke Rice Hull and Nanoparticles Form as Periodontitis Treatment. European Journal of Dentistry. 2023; 17: 450–455. https://doi.org/10.1055/s-0042-1745772

[111] Zhang X, Hasani-Sadrabadi MM, Zarubova J, Dashtimighadam E, Haghniaz R, Khademhosseini A, et al. Immunomodulatory Microneedle Patch for Periodontal Tissue Regeneration. Matter. 2022; 5: 666–682. https://doi.org/10.1016/j.matt.2021.11.017

[112] Wang H, Leeuwenburgh SCG, Li Y, Jansen JA. The use of micro- and nanospheres as functional components for bone tissue regeneration. Tissue Engineering. Part B, Reviews. 2012; 18: 24–39. https://doi.org/10.1089/ten.TEB.2011.0184

[113] Rodríguez-Lozano FJ, García-Bernal D, Aznar-Cervantes S, Ros-Roca MA, Algueró MC, Atucha NM, et al. Effects of composite films of silk fibroin and graphene oxide on the proliferation, cell viability and mesenchymal phenotype of periodontal ligament stem cells. Journal of Materials Science. Materials in Medicine. 2014; 25: 2731–2741. https://doi.org/10.1007/s10856-014-5293-2

[114] Vera-Sánchez M, Aznar-Cervantes S, Jover E, García-Bernal D, Oñate-Sánchez RE, Hernández-Romero D, et al. Silk-Fibroin and Graphene Oxide Composites Promote Human Periodontal Ligament Stem Cell Spontaneous Differentiation into Osteo/Cementoblast-Like Cells. Stem Cells and Development. 2016; 25: 1742–1754. https://doi.org/10.1089/scd.2016.0028

[115] Ren N, Li J, Qiu J, Yan M, Liu H, Ji D, et al. Growth and accelerated differentiation of mesenchymal stem cells on graphene-oxide-coated titanate with dexamethasone on surface of titanium implants. Dental Materials : Official Publication of the Academy of Dental Materials. 2017; 33: 525–535. https://doi.org/10.1016/j.dental.2017.03.001

[116] De Marco P, Zara S, De Colli M, Radunovic M, Lazović V, Ettorre V, et al. Graphene oxide improves the biocompatibility of collagen membranes in an in vitro model of human primary gingival fibroblasts. Biomedical Materials (Bristol, England). 2017; 12: 055005. https://doi.org/10.1088/1748-605X/aa7907

[117] Radunovic M, De Colli M, De Marco P, Di Nisio C, Fontana A, Piattelli A, et al. Graphene oxide enrichment of collagen membranes improves DPSCs differentiation and controls inflammation occurrence. Journal of Biomedical Materials Research. Part a. 2017; 105: 2312–2320. https://doi.org/10.1002/jbm.a.36085

[118] Martinez A, Guitián F, López-Píriz R, Bartolomé JF, Cabal B, Esteban-Tejeda L, et al. Bone loss at implant with titanium abutments coated by soda lime glass containing silver nanoparticles: a histological study in the dog. PloS One. 2014; 9: e86926. https://doi.org/10.1371/journal.pone.0086926

[119] Godoy-Gallardo M, Manzanares-Céspedes MC, Sevilla P, Nart J, Manzanares N, Manero JM, et al. Evaluation of bone loss in antibacterial coated dental implants: An experimental study in dogs. Materials Science & Engineering. C, Materials for Biological Applications. 2016; 69: 538–545. https://doi.org/10.1016/j.msec.2016.07.020

[120] Nakajima M, Yanagawa M, Takikawa H, Thien TT, Zegarra-Caceres L, Yan C, et al. Advances in Local Drug Delivery for Periodontal Treatment: Present Strategies and Future Directions. Biomolecules. 2025; 15: 903. https://doi.org/10.3390/biom15060903

[121] Pranno N, La Monaca G, Polimeni A, Sarto MS, Uccelletti D, Bruni E, et al. Antibacterial Activity against *Staphylococcus Aureus* of Titanium Surfaces Coated with Graphene Nanoplatelets to Prevent Peri-Implant Diseases. An In-Vitro Pilot Study. International Journal of Environmental Research and Public Health. 2020; 17: 1568. https://doi.org/10.3390/ijerph17051568

[122] Maleki Dizaj S, Shokrgozar H, Yazdani J, Memar MY, Sharifi S, Ghavimi MA. Antibacterial Effects of Curcumin Nanocrystals against *Porphyromonas gingivalis* Isolated from Patients with Implant Failure. Clinics and Practice. 2022; 12: 809–817. https://doi.org/10.3390/clinpract12050085

[123] Maleki Dizaj S, Torab A, Kouhkani S, Sharifi S, Negahdari R, Bohlouli S, et al. Gelatin-Curcumin Nanocomposites as a Coating for Implant Healing Abutment: In Vitro Stability Investigation. Clinics and Practice. 2023; 13: 88–101. https://doi.org/10.3390/clinpract13010009

[124] Li Y, Yang L, Hou Y, Zhang Z, Chen M, Wang M, et al. Polydopamine-mediated graphene oxide and nanohydroxyapatite-incorporated conductive scaffold with an immunomodulatory ability accelerates periodontal bone regeneration in diabetes. Bioactive Materials. 2022; 18: 213–227. https://doi.org/10.1016/j.bioactmat.2022.03.021

[125] Giménez-Siurana A, Gómez García F, Pagan Bernabeu A, Lozano-Pérez AA, Aznar-Cervantes SD, Cenis JL, et al. Chemoprevention of Experimental Periodontitis in Diabetic Rats with Silk Fibroin Nanoparticles Loaded with Resveratrol. Antioxidants (Basel, Switzerland). 2020; 9: 85. https://doi.org/10.3390/antiox9010085

[126] Ren S, Zhou Y, Zheng K, Xu X, Yang J, Wang X, et al. Cerium oxide nanoparticles loaded nanofibrous membranes promote bone regeneration for periodontal tissue engineering. Bioactive Materials. 2021; 7: 242–253. https://doi.org/10.1016/j.bioactmat.2021.05.037

[127] Vannozzi L, Pucci C, Trucco D, Turini C, Sevim S, Pané S, et al. Biodegradable Piezoelectric Micro- and Nanomaterials for Regenerative Medicine, Targeted Therapy, and Microrobotics. Small Science. 2025; 5: 2400439. https://doi.org/10.1002/smsc.202400439

[128] Uskoković V. When 1+1>2: Nanostructured composites for hard tissue engineering applications. Materials Science & Engineering. C, Materials for Biological Applications. 2015; 57: 434–451. https://doi.org/10.1016/j.msec.2015.07.050

[129] Bose S, Roy M, Bandyopadhyay A. Recent advances in bone tissue engineering scaffolds. Trends in Biotechnology. 2012; 30: 546–554. https://doi.org/10.1016/j.tibtech.2012.07.005

[130] Ni C, Zhou J, Kong N, Bian T, Zhang Y, Huang X, et al. Gold nanoparticles modulate the crosstalk between macrophages and periodontal ligament cells for periodontitis treatment. Biomaterials. 2019; 206: 115–132. https://doi.org/10.1016/j.biomaterials.2019.03.039

[131] Shi E, Bai L, Mao L, Wang H, Yang X, Wang Y, et al. Self-assembled nanoparticles containing photosensitizer and polycationic brush for synergistic photothermal and photodynamic therapy against periodontitis. Journal of Nanobiotechnology. 2021; 19: 413. https://doi.org/10.1186/s12951-021-01114-w

[132] Johnson A, Kong F, Miao S, Thomas S, Ansar S, Kong ZL. In-Vitro Antibacterial and Anti-Inflammatory Effects of Surfactin-Loaded Nanoparticles for Periodontitis Treatment. Nanomaterials (Basel, Switzerland). 2021; 11: 356. https://doi.org/10.3390/nano11020356

[133] Huang H, Pan W, Wang Y, Kim HS, Shao D, Huang B, et al. Nanoparticulate cell-free DNA scavenger for treating inflammatory bone loss in periodontitis. Nature Communications. 2022; 13: 5925. https://doi.org/10.1038/s41467-022-33492-6

[134] [136] Li Z, Wang Y, Liu J, Rawding P, Bu J, Hong S, et al. Chemically and Biologically Engineered Bacteria-Based Delivery Systems for Emerging Diagnosis and Advanced Therapy. Advanced Materials. 2021; 33: 2102580. https://doi.org/10.1002/adma.202102580