International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Nanoparticles in Periodontics

Dr. Achsa Annie Kurian[1], Dr. Radhika B[2], Dr. Parikshith H M[3], Dr. Apoorva Gupta[4]

[1,4]2nd Year Postgraduate Student, Department Of Periodontics And Implantology, Coorg Institute Of Dental Sciences
[2]Professor, Department Of Periodontics And Implantology, Coorg Institute Of Dental Sciences
[3]Senior Lecturer, Department Of Periodontics And Implantology, Coorg Institute Of Dental Sciences

ABSTRACT

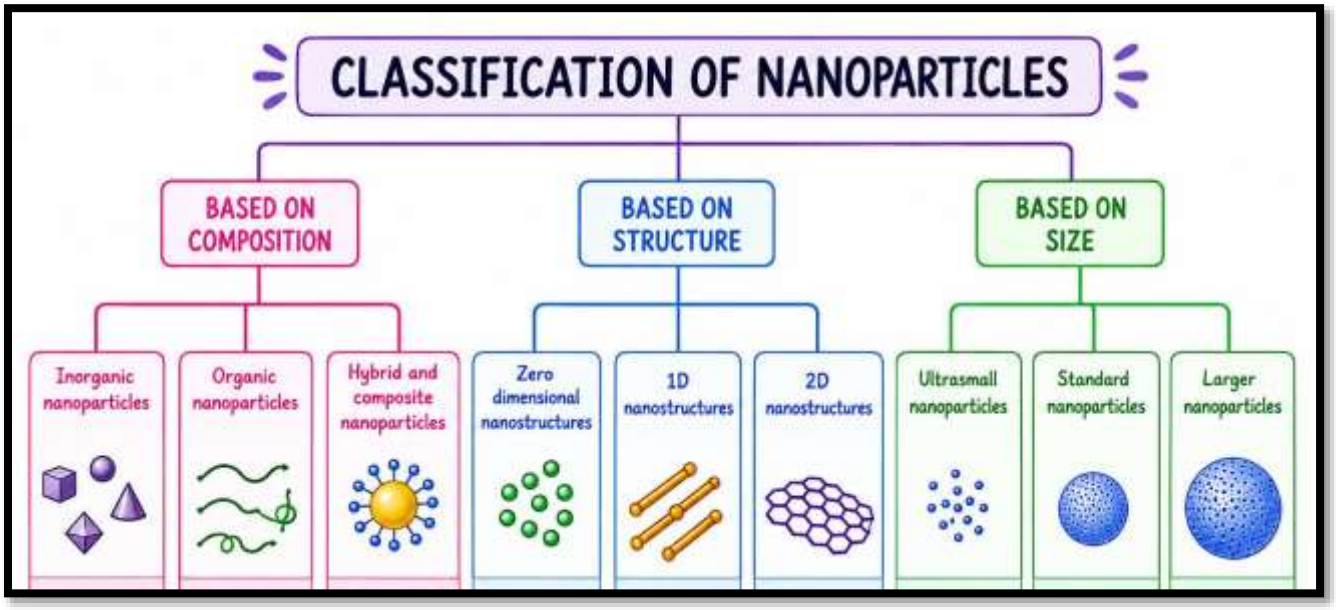
Numerous medical specialties have been transformed by nanotechnology, and its use in dentistry, especially periodontics, shows great potential for both diagnostic and therapeutic applications. Nanoparticles offer superior drug delivery systems, antibacterial properties, and regenerative capacities due to their unique physicochemical characteristics, including a high surface area-to-volume ratio and enhanced reactivity. They enable precise administration of antimicrobial medicines into periodontal pockets, resulting in prolonged release, improved treatment efficiency, and fewer systemic side effects.Strong antibacterial efficacy against periodontal infections is demonstrated by chitosan, zinc oxide, and silver nanoparticles. In order to promote healing and osseointegration, nanocomposites and nanofibers are being investigated for bone grafts and directed tissue regeneration. Early infection and inflammation detection is facilitated by diagnostic instruments such as nano sensors. To enhance results, periodontal therapy is increasingly incorporating drug delivery methods based on nanoparticles. Concerns about biocompatibility, toxicity, and long-term safety are still significant study topics despite these encouraging advantages. However, nanoparticles have the potential to revolutionise traditional periodontal treatment into a more accurate, efficient, and patient-friendly method with continued advancements and clinical testing. This review focuses on their recent developments, therapeutic uses, and potential future developments in periodontics.

KEYWORDS: Nanoparticle, local drug delivery, silver nanoparticle, gold nanoparticle, periodontal regeneration

INTRODUCTION

Periodontal diseases are complex inflammatory disorders that begin with microbial biofilms and are further influenced by the body's immune response, ultimately resulting in the gradual breakdown of the tissues supporting the teeth[1].While traditional periodontal treatments like scaling, root planing, and surgery can effectively slow disease progression, they frequently do not fully eliminate periodontal pathogens or reliably restore lost tissues[2].Through nanoparticle-based systems, nanotechnology provides novel approaches that can improve bioavailability, sustain therapeutic release directly into periodontal pockets, and improve local drug delivery[3]. Because of their nanoscale size and adjustable surface characteristics, nanoparticles are more effective than traditional treatments at breaking up biofilms, facilitating targeted antibacterial actions, and regulating local inflammatory responses. In vitro and preclinical research has shown that a variety of nanoparticle classes, including as metallic (such as silver, gold), polymeric(such as poly lactic co-glycolic acid(PLGA), chitosan), lipid-based, and ceramic

carriers, offer promise for antibacterial and therapeutic potential against periodontal pathogens[4]. Although there is still little clinical evidence, silver nanoparticles (AgNPs) in particular have demonstrated robust antibacterial qualities and the ability to promote periodontal and peri-implant wound healing[5]. Optimising nanoparticle design, guaranteeing biocompatibility, and confirming long-term safety and performance in human subjects continue to be difficult tasks despite promising preclinical results. Research is still being done to improve the formulationsof nanoparticles and investigate how they might be combined with regenerative periodontal treatments[6].Classification of nanoparticles is given below based on their composition, structure and size Figure (1).



Figure(1)- Classification of Nanoparticles

Based on Composition

1. INORGANIC PARTICLES

Inorganic nanoparticles are nanosized particles composed mainly of metals, metal oxides, ceramics, or silica-based materials rather than carbon-based polymers. Common examples include silver (Ag), zinc oxide (ZnO), titanium dioxide (TiO_2), silica nanoparticles, hydroxyapatite, and bioactive glass nanoparticles. Due to their unique physicochemical properties, such as high surface area, enhanced reactivity, and nanoscale size, they are extensively investigated in periodontics for antimicrobial action, biofilm disruption, drug delivery, and periodontal regeneration[7].

Nanoparticles of metal

These elemental metal NPs have strong antibacterial properties.

- Broad-spectrum antibacterial drugs called silver nanoparticles (AgNPs) are utilised to combat periodontal infections.
- Gold nanoparticles (AuNPs) have photothermal and antibacterial uses.
- Copper nanoparticles: they have antibacterial properties against both positive and Gram-negative bacteria[7].

Nanoparticles of metal oxide

These include oxides that have antibacterial qualities and occasionally the ability to regenerate.

- Zinc oxide (ZnO) nanoparticles, have bactericidal properties against periodontal bacteria.
- Titanium dioxide (TiO_2) nanoparticles have antimicrobial properties and may activate salivary enzymes[8].
- The antibacterial and host-modulating properties of iron, magnesium, and cerium oxides have been investigated[7].

Nanoparticles built on silicon

Mesoporous silica nanoparticles (MSNs) have adaptable pore shapes for improved osteogenesis, antibacterial activity, and drug loading[7].

2. ORGANIC NANOPARTICLES

Biodegradable polymers or carbon-based materials make up the majority of organic nanoparticles (NPs), which are frequently used as medication or host-modulation agent carriers.

- **Polylactic-co-glycolic acid (PLGA)**is a biodegradable carrier with controlled release.
- **Chitosan nanoparticles** are a naturally occurring polymer with mucoadhesive and antimicrobial qualities.
- Highly branched polymers for targeted delivery are called dendrimers[9].

Lipid-based Nanoparticles: Liposomes and solid lipid nanoparticles are lipid bilayer systems used to encapsulate hydrophilic and lipophilic medications.

Organic Nanoparticles Based on Carbon

Graphene derivatives, such as carbon dots, have antibacterial properties and are employed in diagnostic applications[10].

3. HYBRID & COMPOSITE NANOPARTICLES

These are made up of two or more parts, frequently mixing organic and inorganic phases to serve several purposes (drug delivery, regenerative, and antimicrobial)[6].

Metal-doped Silica Nanoparticles: These are silica frameworks that have been infused with metal ions (such as Ag or Zn) to provide both structural and antibacterial characteristics[11].

Functional Hybrid Systems

- Metal-organic frameworks that carry ions and antibacterial medications, such as ZIF-8, a zinc-based metal-organic framework with organic ligand scaffolding.
- Composite carriers for tissue regeneration and controlled release (polymer + inorganic NP)[6].

Based on structure

Nanoparticles (NPs) and nanomaterials are typically classified by how many dimensions fall within the nanoscale (≤100 nm). This structural classification helps describe their geometry and possible interactions with biological systems.

Zero-Dimensional (0D) Nanostructures

Definition: The nanoscale (<100 nm) encompasses all three spatial dimensions. Examples include fullerenes, quantum dots, and spherical nanoparticles (Figure 2)

- Properties: Highest surface-to-volume ratio and can exhibit quantum confinement effects, impacting optical and chemical behaviour.
- Biomedical Relevance: Often utilised for medication delivery and antibacterial activities due to strong reactivity and cellular absorption.

One-Dimensional (1D) Nanostructures

Definition: The other two dimensions fall inside the nanoscale, with only one beyond it. Examples include nanorods, nanowires, and nanotubes (such as carbon nanotubes).

- Features include increased mechanical strength and transport along one axis and anisotropic (direction-dependent) behaviour.
- Biomedical Relevance: Frequently investigated for directed regeneration or scaffold reinforcement, particularly in tissue engineering templates.

Two-Dimensional (2D) Nanostructures

Definition: Thickness is still nanoscale, but two spatial dimensions are larger than the nano range. Examples include graphene/graphene oxide layers, nanosheets, and nanofilms.

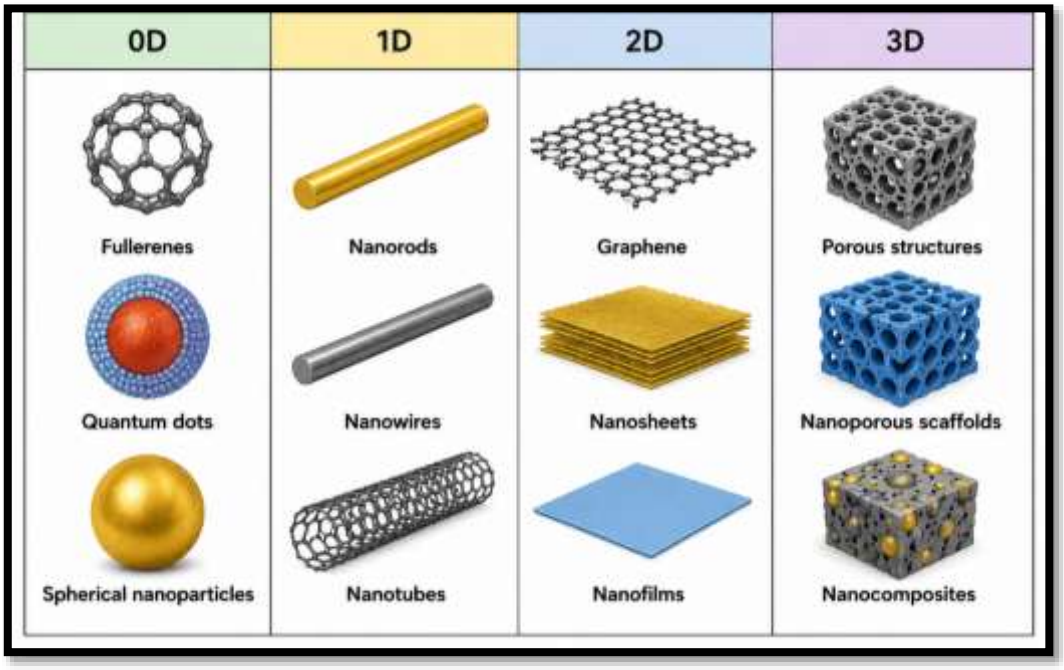
- Features: Suitable for coatings and surface functionalisation; large surface area with thin thickness.
- Biomedical Relevance: They can be used as controlled release platforms or implant surface modifications.

Three-Dimensional (3D) Nanostructures

Definition: Larger three-dimensional structures made of nanostructured materials.

Examples include porous structures, nanoporous scaffolds, and nanocomposites.

- Properties: Integration of nanoscale characteristics into macroscale structures.
- Biomedical Relevance: Because of the integrated macro- and nano-features, it is widely employed in GTR membrane scaffolds for tissue regeneration[12].Figure (2)



Figure(2) – Examples of nanoparticles based on structure.

Based on size

The numerical range of nanoparticles, which has a significant impact on biological behaviour, biodistribution, and cellular uptake, is the subject of size classification. The majority of created NPs fall between 1 to 100 nm, according to guidelines from nanotechnology literature, while functional differences can be made.

Ultra-Small Nanoparticles (<10 nm)

- Properties: High surface energy; frequently exhibits quantum size effects.
- Consequences: Quick cellular internalisation, however, reactivity may increase the danger of toxicity.
- Examples include ultrasmall metallic nanoparticles and quantum dots.
- Use: Targeted antibacterials, diagnostics, and precision imaging.
- **Standard Nanoparticles (10–50 nm)**
- Features: Excellent stability and surface area balance; frequently perfect for drug delivery vectors.
- Consequences: Reduced aggregation and excellent cellular absorption.
- Examples include metal and polymeric nanoparticles for controlled release .
- Use: Drug administration locally in periodontal pockets.
- **Larger Nanoparticles (50–100 nm)**
- Characteristics: Possibly delayed tissue clearance; good colloidal stability.
- Consequences: Lower systemic exposure and sustained delivery.
- Examples include polymeric carriers and lipid nanoparticles. \
- Use: Long-acting medications for persistent periodontitis[12].

- **MECHANISM OF ACTION**
- **Direct Antimicrobial Actions**

Nanoparticles exert direct antimicrobial activity against periodontal pathogens through multiple interconnected mechanisms that target bacterial structure, metabolism, and biofilm formation[13].

Due to their nanoscale size and high surface-area-to-volume ratio, nanoparticles interact with bacterial cell walls and cytoplasmic membranes, causing membrane depolarization, increased permeability, leakage of intracellular contents, and eventual bacterial cell death[14].Positively charged nanoparticles can bind electrostatically to negatively charged bacterial membranes, resulting in membrane destabilization, structural disruption, and impairment of essential cellular functions[15].Many metal and metal oxide nanoparticles, particularly silver nanoparticles (AgNPs), zinc oxide nanoparticles (ZnO NPs), and titanium dioxide nanoparticles (TiO_2 NPs), generate reactive oxygen species (ROS) such as hydroxyl radicals and superoxide ions that induce oxidative stress and damage bacterial DNA, proteins, lipids, and membranes.The excessive accumulation of ROS overwhelms bacterial antioxidant defence systems, ultimately leading to microbial destruction and inhibition of bacterial growth[14].Certain nanoparticles also release antimicrobial metal ions such as Ag^+ and Zn^{2+}, which interact with thiol groups of enzymes and proteins, disrupt metabolic pathways, interfere with ATP production, alter membrane permeability, and inhibit bacterial replication.Silver ions released from AgNPs can denature ribosomes, inhibit protein synthesis, disrupt respiratory enzymes, and interfere with DNA replication, thereby enhancing antibacterial efficacy. Nanoparticles can penetrate bacterial biofilms and inhibit biofilm formation by reducing bacterial adhesion, disrupting the extracellular polymeric matrix, interfering with quorum-sensing pathways, and preventing biofilm maturation within periodontal pockets.Since periodontal biofilms protect microorganisms from antibiotics and host immune responses, nanoparticle-mediated biofilm disruption significantly improves bacterial susceptibility and enhances periodontal treatment outcomes[13].Figure (3)

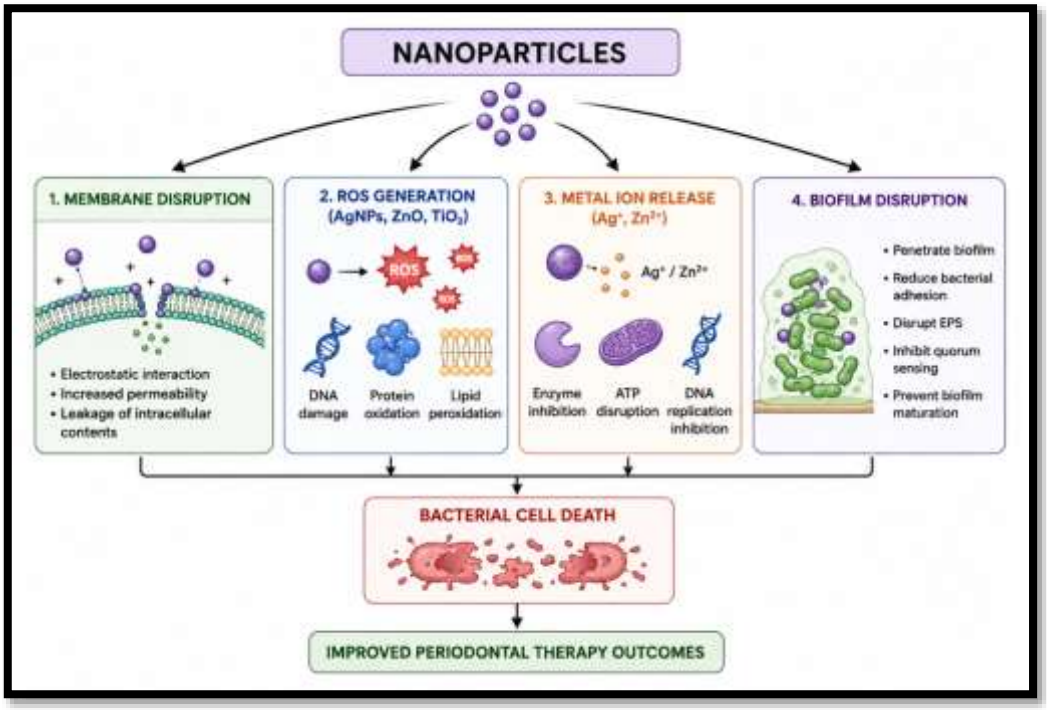


Figure (3) – Antimicrobial action of nanoparticles

1. Drug Delivery and Penetration Mechanisms

Nanoparticles are highly effective drug delivery systems in periodontics because they enable targeted localisation, enhanced tissue penetration, and controlled release of therapeutic agents. Polymeric nanoparticles (e.g., PLGA), liposomes, and mesoporous silica nanoparticles can deliver antimicrobial, anti-inflammatory, and regenerative molecules directly into periodontal pockets, resulting in higher local drug concentrations and reduced systemic adverse effects.Their nanoscale dimensions facilitate penetration into periodontal tissues and biofilms, improving the efficacy of locally delivered drugs .Furthermore, nanoparticle-based carriers provide sustained and controlled drug release, maintaining therapeutic concentrations for prolonged periods, reducing dosing frequency, and minimising burst release of antibiotics such as minocycline and doxycycline[3].Encapsulation within nanoparticles also protects bioactive molecules from enzymatic degradation and premature inactivation, thereby enhancing their stability and bioavailability in the periodontal environment[16].In addition, mesoporous silica nanoparticles possess high drug-loading capacity and stimuli-responsive release properties, making them promising carriers for targeted and controlled periodontal drug delivery [17].

2. Modulation of Host Immune Response

Nanoparticles can modulate the host immune response by regulating inflammatory pathways involved in periodontal disease progression. Gold nanoparticles have been shown to suppress the production of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6 through inhibition of NF-κB signalling, thereby reducing tissue inflammation[18].Certain nanoparticles promote macrophage polarization from the pro-inflammatory M1 phenotype toward the anti-inflammatory M2 phenotype, enhancing tissue repair and resolution of inflammation[19]. Cerium oxide nanoparticles possess potent antioxidant and immunomodulatory properties that reduce oxidative stress and inflammatory cytokine production while protecting surrounding tissues from inflammatory damage [20].Chitosan nanoparticles have demonstrated the ability to downregulate inflammatory mediators and reduce activation of NF-κB and MAPK

signaling pathways, thereby limiting periodontal tissue destruction[21].Nanoparticles can also regulate T-cell responses and cytokine balance, promoting immune homeostasis and improving the regenerative potential of periodontal tissues [18].

3. Support of Tissue Regeneration

Nanoparticles contribute to periodontal tissue regeneration by providing bioactive surfaces that enhance cell adhesion, proliferation, and differentiation, thereby creating a favourable microenvironment for the regeneration of periodontal ligament, cementum, and alveolar bone [22].When incorporated into scaffolds, hydrogels, and guided tissue regeneration membranes, nanoparticles improve mechanical properties and enable the localized delivery of growth factors and bioactive molecules that support tissue repair[23].Furthermore, bioactive nanoparticles such as nano-hydroxyapatite and bioactive glass nanoparticles stimulate osteogenic signaling pathways by upregulating bone-related markers including BMP-2, Runx2, osteocalcin, and alkaline phosphatase, thereby promoting osteoblast differentiation, mineralization, and alveolar bone formation.These regenerative effects make nanoparticles promising tools for enhancing periodontal wound healing and tissue regeneration [24].

4. Photothermal and Photodynamic Effects

Nanoparticles can enhance periodontal therapy through light-activated mechanisms. In photothermal therapy (PTT), nanoparticles such as gold nanoparticles absorb near-infrared light and convert it into heat, resulting in localized bacterial destruction and biofilm disruption[25].In photodynamic therapy (PDT), photosensitizer-loaded nanoparticles generate reactive oxygen species (ROS) upon light activation, leading to targeted microbial killing and enhanced healing [26].

APPLICATIONS OF NANOPARTICLES IN PERIODONTICS

1. Antimicrobial Therapy against Periodontal Pathogens

Controlling subgingival biofilms and pathogenic microorganisms that cause periodontitis is one of the main uses of nanoparticles in periodontics. Because of their large surface area and capacity to interfere with bacterial cell membranes and biofilm development, nanoparticles like metal (such as AgNPs and AuNPs) and metal oxide NPs exhibit strong antibacterial effects. In addition to conventional mechanical therapy (scaling and root planing), these NPs are being researched[8].

- Silver nanoparticles (AgNPs): They can improve the results of traditional periodontal treatments and have shown potent antibacterial action against periodontal infections[28].
- Gold nanoparticles and other metal nanoparticles: These have been demonstrated to have broad-spectrum antibacterial effects and are used to prevent the growth of multiple strains of bacteria[8].

2. Local Drug Delivery Systems

Antibiotics, anti-inflammatory drugs, and host-modulating substances can be specifically delivered into periodontal pockets using nanoparticles. This reduces systemic negative effects while increasing medication concentration at the illness location.

- Polymeric NPs, such as PLGA, are used to administer antimicrobials and anti-inflammatory medications in a sustained and controlled manner.
- Nanocarriers: Nanocarriers enhance drug absorption by diseased periodontal tissues and improve drug retention within periodontal pockets, thereby increasing the efficacy of local drug delivery [3].

3. Anti-Inflammatory and Host-Modulating Applications

One of the main clinical characteristics of periodontitis is chronic inflammation, which can be resolved by using nanoparticles to modify host immune responses. Some NPs improve healing by reducing pro-

inflammatory cytokines and shifting macrophage polarisation towards anti-inflammatory phenotypes.
Nanoparticles containing anti-inflammatory agents: Nanoparticles loaded with anti-inflammatory agents have demonstrated enhanced resolution of inflammation and reduced periodontal tissue destruction in experimental studies [10].

4. Regenerative and Tissue-Engineering Applications

In order to encourage the regeneration of periodontal tissues (alveolar bone, periodontal ligament, and cementum) lost as a result of disease, nanotechnology is being thoroughly investigated.

- Hydrogels and nanocomposite scaffolds: Nanoparticle-incorporated hydrogels and nanocomposite scaffolds promote angiogenesis and osteogenesis within periodontal defects, thereby enhancing bone regeneration and supporting periodontal tissue repair.
- Nanostructured membranes: Used to enhance cell adhesion and regulate the release of growth-promoting substances during guided tissue regeneration[6].

5. Biofilm Disruption and Prevention

Nanoparticles can stop biofilm formation and slow the maturation of bacterial communities in periodontal pockets when added to different formulations (such as gels, coatings, and local delivery systems). Nanoparticles aid in breaking up preexisting biofilms and preventing new bacteria from adhering to tooth surfaces[8].

6. Photothermal and Photodynamic Adjuncts

Certain nanoparticles are employed in light-activated periodontal disease treatments:
Photothermal therapy (PTT): When activated by near-infrared (NIR) light, nanoparticles such as gold-based hybrid systems convert light into heat, effectively destroying bacteria within periodontal biofilms. This approach provides targeted antibacterial activity with minimal damage to the surrounding healthy tissues[29].

7. Antioxidant and Host-Protective Applications

Some nanoparticles have antioxidant properties that lessen oxidative stress, which is a major factor in the deterioration of periodontal tissue. Preclinical models have demonstrated the antibacterial and antioxidant properties of environmentally friendly synthesised AgNPs against inflammation and periodontal infections[30].

8. Enhanced Osseointegration and Bone Regeneration

Nanoparticle-Coated Implant Surfaces

By enhancing surface characteristics that promote bone cell adhesion and proliferation, implant surface modification with nanoparticles greatly improves osseointegration, the direct structural and functional connection between bone and implant. Nanocoatings promote early implant stability, vascularisation, and bone remodelling, which may result in a quicker and more robust integration of the implant with the jawbone[31].

9. Diagnostic applications

- Gold and silver nanoparticle-based biosensors detect periodontal inflammatory biomarkers like MMP-8, IL-1β, and TNF-α in saliva and gingival crevicular fluid, enabling early and non-invasive diagnosis of periodontitis [32]. Nanoparticles are used in periodontal diagnostics because their high surface area and distinct physicochemical properties significantly enhance the sensitivity and accuracy of disease detection.
- Plasmonic nanoparticles enhance colorimetric and optical biosensing systems, enabling quick and highly specific chairside identification of periodontal disease activity[10].

10. Potential Diagnostic Aids

Nanoparticles have been suggested for highly sensitive detection of periodontal pathogens and biomarkers utilising nanodiagnostic platforms (e.g., quantum dots, nanosensors), opening the door to early disease identification, albeit this is still primarily in the research stages[10].

ADVANTAGES OF NANOPARTICLES IN PERIODONTICS

- **Strong antimicrobial and antibiofilm properties:** When compared to traditional methods, nanoparticles' unique antibacterial, anti-inflammatory, and antioxidant qualities help prevent periodontal infections and biofilm formation[6].
- **Enhanced targeted drug delivery:** Targeted and sustained local delivery of antibacterial and anti-inflammatory drugs to periodontal pockets is made possible by nanoparticle-based systems, which increase therapeutic efficacy while lowering systemic side effects[3].
- **Modulation of host inflammatory responses:** In order to help resolve periodontal inflammation and promote tissue repair, nanotechnology makes it possible to implement techniques that modify host immune responses, such as lowering pro-inflammatory cytokines[10].
- **Potential for enhanced regeneration:** By establishing microenvironments that promote cell attachment and differentiation, nanoparticles integrated into scaffolds, hydrogels, or delivery systems enhance alveolar bone regeneration and periodontal tissue healing[6].
- **Improved tissue penetration:** Because of their nanoscale size, nanoparticles can reach infection and inflammatory sites more easily by penetrating deeper into periodontal tissues and biofilms[33].

LIMITATIONS OF NANOPARTICLES IN PERIODONTICS

Toxicity and biocompatibility concerns: One significant drawback is the possibility of harmful nanoparticle buildup in cells and tissues, which could have negative consequences and obstruct clinical translation. Long-term toxicity profiles are not yet fully understood[6].

Poor in vitro–in vivo correlation: It is challenging to forecast clinical efficacy since results from laboratory (in vitro) research frequently do not translate to animal models or human clinical outcomes[6].

Limited clinical evidence: There are few reliable human clinical trials to confirm safety and efficacy, and the majority of research on nanoparticles in periodontal therapy is still preclinical (animal or laboratory studies)[9].

I**mmune system interactions:** Because nanoparticles can be recognised by the immune system, their safe use may be complicated by the possibility of inflammation, immunological activation, or allergic reactions[9].

FUTURE PERSPECTIVES

Smart nanomaterials and responsive systems: In order to improve controlled and on-demand therapy, future nanoparticles may be designed as "smart" nanosystems that release therapeutic chemicals in reaction to particular triggers, such as pH shifts or bacterial enzymes in periodontal pockets[10].

Translational and clinical research expansion: Although the majority of the evidence is now preclinical, there is a noticeable push towards larger clinical trials and in vivo validation to verify the safety, effectiveness, and best dosing strategies for periodontal therapy based on nanoparticles[3].

Integration with new treatment modalities: Nanotechnology can be used in conjunction with photothermal therapy, immunomodulation, and sophisticated scaffolds to treat infection, inflammation,

and tissue regeneration all at once on a single therapeutic platform[29].

AI-integrated nano diagnostics: Combine artificial intelligence's capacity for pattern recognition with the great sensitivity and specificity of nanoparticle biosensing. In comparison to traditional clinical diagnostics alone, this synergy promises earlier, more precise, and more individualised identification of periodontal disease, indicating a future trend in precision periodontology[34].

CONCLUSION

Nanoparticles represent a promising advancement in periodontal therapy, offering therapeutic and diagnostic benefits beyond those of conventional treatment approaches. Their unique properties enable targeted antimicrobial activity against periodontal pathogens, modulation of host inflammatory responses, and promotion of periodontal tissue and alveolar bone regeneration. Through their antibacterial, anti-inflammatory, immunomodulatory, and regenerative effects, nanoparticles have demonstrated significant potential in improving the management of periodontitis. Although encouraging results have been reported in preclinical studies, concerns regarding biocompatibility, toxicity, long-term safety, and clinical effectiveness remain. Therefore, further well-designed in vivo studies and large-scale clinical trials are required to validate their safety and efficacy and to establish nanoparticle-based therapies as a routine component of periodontal treatment.

REFERENCES

1. Kinane DF, Stathopoulou PG, Papapanou PN. Periodontal diseases. Nature reviews Disease primers. 2017 Jun 22;3(1):1-4.
2. Lang NP, Lindhe J, editors. Clinical periodontology and implant dentistry, 2 Volume Set. John Wiley & Sons; 2015 Mar 25.
3. Basudan AM. Nanoparticle based periodontal drug delivery–a review on current trends and future perspectives. The Saudi dental journal. 2022 Dec 1;34(8):669-80.
4. Alavi SE, Ebrahimi Shahmabadi H, Sharma LA, Sharma A. Nanoparticle-based drug delivery systems for non-surgical periodontal therapy: innovations and clinical applications. 3 Biotech. 2025 Aug;15(8):269.
5. Siddiqi A, Zafar S. Scope of Silver Nanoparticles in Periodontal and Peri-Implant Wound Healing: A Systematic Review of Translation Research. Essentials of Dentistry. 2023 May 1;2(2):55-65.
6. Wang D, Li Q, Xiao C, Wang H, Dong S. Nanoparticles in periodontitis therapy: a review of the current situation. International Journal of Nanomedicine. 2024 Dec 31:6857-93.
7. Shi R, Zhu Y, Lu W, Zhai R, Zhou M, Shi S, Chen Y. Nanomaterials: innovative approaches for addressing key objectives in periodontitis treatment. RSC advances. 2024;14(38):27904-27.
8. Kiarashi M, Mahamed P, Ghotbi N, Tadayonfard A, Nasiri K, Kazemi P, Badkoobeh A, Yasamineh S, Joudaki A. Spotlight on therapeutic efficiency of green synthesis metals and their oxide nanoparticles in periodontitis. Journal of nanobiotechnology. 2024 Jan 5;22(1):21.
9. Mlachkova A, Dosseva-Panova V, Maynalovska H, Pashova-Tasseva Z. Nanoparticles as Strategies for Modulating the Host's Response in Periodontitis Treatment. Nanomaterials. 2025 Mar 21;15(7):476.
10. D'Amico E, Aceto GM, Petrini M, Cinquini C, D'Ercole S, Iezzi G, Pierfelice TV. How Will Nanomedicine Revolutionize Future Dentistry and Periodontal Therapy?. International Journal of Molecular Sciences. 2025 Jan 12;26(2):592.

11. Nawaz MZ, Alghamdi HA, Zahoor M, Rashid F, Alshahrani AA, Alghamdi NS, Pugazhendhi A, Zhu D. Synthesis of novel metal silica nanoparticles exhibiting antimicrobial potential and applications to combat periodontitis. Environmental Research. 2024 Jan 15;241:117415.
12. Joudeh N, Linke D. Nanoparticle classification, physicochemical properties, characterization, and applications: a comprehensive review for biologists. Journal of nanobiotechnology. 2022 Jun 7;20(1):262.
13. 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 Apr 17:2555-62.
14. Govindarajan DK, Mohanarangam M, Kadirvelu L, Sivaramalingam SS, Jothivel D, Ravichandran A, Periasamy S, Kandaswamy K. Biofilms and oral health: nanotechnology for biofilm control. Discover Nano. 2025 Jul 16;20(1):114.
15. Yang M, Sun M, Wang J, Cao Q, Xian CJ, Zhai Y. The Application of Metal Nanoparticles in Oral Inflammatory Diseases. International Dental Journal. 2025 Dec 1;75(6):103881.
16. Baeza A, Colilla M, Vallet-Regí M. Advances in mesoporous silica nanoparticles for targeted stimuli-responsive drug delivery. Expert opinion on drug delivery. 2015 Feb 1;12(2):319-37.
17. Song Y, Li Y, Xu Q, Liu Z. Mesoporous silica nanoparticles for stimuli-responsive controlled drug delivery: advances, challenges, and outlook. International journal of nanomedicine. 2017 Dec 20:87-110.
18. Dykman LA, Khlebtsov NG. Immunological properties of gold nanoparticles. Chemical science. 2017;8(3):1719-35.
19. Ding H, Zhang Y, Mao Y, Li Y, Shen Y, Sheng J, Gu N. Modulation of macrophage polarization by iron-based nanoparticles. Medical Review. 2023 Apr 25;3(2):105-22.
20. Heckert EG, Karakoti AS, Seal S, Self WT. The role of cerium redox state in the SOD mimetic activity of nanoceria. Biomaterials. 2008 Jun 1;29(18):2705-9.
21. Kean T, Thanou M. Biodegradation, biodistribution and toxicity of chitosan. Advanced drug delivery reviews. 2010 Jan 31;62(1):3-11.
22. Bottino MC, Thomas V, Schmidt G, Vohra YK, Chu TM, Kowolik MJ, Janowski GM. Recent advances in the development of GTR/GBR membranes for periodontal regeneration—A materials perspective. Dental materials. 2012 Jul 1;28(7):703-21.
23. Ivanovski S, Vaquette C, Gronthos S, Hutmacher DW, Bartold PM. Multiphasic scaffolds for periodontal tissue engineering. Journal of dental research. 2014 Dec;93(12):1212-21.
24. Mourino V, Cattalini JP, Boccaccini AR. Metallic ions as therapeutic agents in tissue engineering scaffolds: an overview of their biological applications and strategies for new developments. Journal of the Royal Society Interface. 2012 Mar 7;9(68):401-19.
25. Wang S, Chen KJ, Wu TH, Wang H, Lin WY, Ohash M, Chiou PY, Tseng HR. Photothermal effects of supramolecularly assembled gold nanoparticles for the targeted treatment of cancer cells. Angewandte Chemie (International ed. in English). 2010 May 17;49(22):3777.
26. Maisch T. Anti-microbial photodynamic therapy: useful in the future?. Lasers in medical science. 2007 Jun;22(2):83-91.
27. Hayat S, Ashraf A, Siddique MH, Aslam B, Shafaqat H, Javed S, Taj Z, Sarfraz MH, Rafiq H, Muzammil S. Nanoparticle-mediated approaches to combat antibiotic resistance: a comprehensive

review on current progress, mechanisms, and future perspectives. RSC advances. 2025;15(50):42460-78.

28. Liang Y, Wang B, Yu Q, Wang W, Ge S, Shao J. Ebselen optimized the therapeutic effects of silver nanoparticles for periodontal treatment. International Journal of Nanomedicine. 2023 Dec 31:8113-30.
29. Nasiri K, Masoumi SM, Amini S, Goudarzi M, Tafreshi SM, Bagheri A, Yasamineh S, Alwan M, Arellano MT, Gholizadeh O. Recent advances in metal nanoparticles to treat periodontitis. Journal of nanobiotechnology. 2023 Aug 21;21(1):283.
30. Barik B, Satapathy BS, Pattnaik G, Bhavrao DV, Shetty KP. Sustainable synthesis of silver nanoparticles from Azadirachta indica: antimicrobial, antioxidant and in silico analysis for periodontal treatment. Frontiers in Chemistry. 2024 Oct 15;12:1489253.
31. Soe ZC, Wahyudi R, Mattheos N, Lertpimonchai A, Everts V, Tompkins KA, Osathanon T, Limjeerajarus CN, Limjeerajarus N. Application of nanoparticles as surface modifiers of dental implants for revascularization/regeneration of bone. BMC Oral Health. 2024 Oct 4;24(1):1175.
32. Hooshiar MH, Moghaddam MA, Kiarashi M, Al-Hijazi AY, Hussein AF, A. Alrikabi H, Salari S, Esmaelian S, Mesgari H, Yasamineh S. Recent advances in nanomaterial-based biosensor for periodontitis detection. Journal of biological engineering. 2024 Apr 18;18(1):28.
33. Nakajima M, Yanagawa M, Takikawa H, Thien TT, Zegarra-Caceres L, Yan C, Tabeta K. Advances in Local Drug Delivery for Periodontal Treatment: Present Strategies and Future Directions. Biomolecules. 2025 Jun 19;15(6):903.
34. Jundaeng J, Chamchong R, Nithikathkul C. Artificial intelligence-powered innovations in periodontal diagnosis: a new era in dental healthcare. Frontiers in Medical Technology. 2025 Jan 10;6:1469852.