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Nanoparticles in Endodontics

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Abstract: Nanotechnology has emerged as a transformative innovation in endodontics, significantly enhancing the effectiveness of root canal treatments and promoting tissue regeneration. The application of nanomaterials in endodontic procedures offers improved disinfection, enhanced mechanical properties of dental materials, and potential for regenerative healing. Due to their small size and large surface area, nanoparticles can deeply penetrate dentinal tubules, providing superior antimicrobial action and reducing the risk of reinfection compared to conventional methods. Nanomaterials also enhance the strength, fracture resistance, and adhesion of root canal sealers, thus increasing the durability of treatments. Moreover, nanotechnology shows promise in pulp tissue regeneration by facilitating targeted drug delivery and supporting stem cell differentiation. Despite these advancements, challenges regarding the safety, toxicity, and long-term biocompatibility of nanoparticles remain, necessitating ongoing research. This review explores the current applications and future potential of nanotechnology in endodontics, highlighting its transformative role in improving root canal therapy outcomes and advancing dental care.

***Keywords**: Nanoparticles , Nanotechnology ,Endodontics ,Regeneration , Durg Delivary*

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I. INTRODUCTION

Nanotechnology and the usage of materials at the nanoscale (1–100 nm), has emerged as a groundbreaking innovation in various scientific fields including dentistry. In particular, the application of nanotechnology in endodontics offers transformative potential, addressing many of the longstanding challenges in root canal therapy. Endodontics, which involves the treatment of the dental pulp and periapical tissues, requires effective disinfection, sealing of root canals, and potential tissue regeneration, all of which are critical to the success of the procedure. Traditional methods often fall short, especially given the complex and intricate nature of root canal anatomy, where reaching all infected areas can be difficult. (1)

Nanoparticles, such as silver, zinc oxide, and titanium dioxide, are being integrated into endodontic treatments due to their strong antimicrobial properties. These nanoparticles can penetrate deeply into dentinal tubules, areas that conventional irrigation and disinfection methods cannot adequately reach (1). Their small size and large surface area enable them to exert enhanced antibacterial effects against the broad spectrum of bacteria typically present in root canal infections. This improved disinfection capability significantly reduces the risk of reinfection, which prevents the endodontic treatment failure (2).

In addition to antimicrobial benefits, nanotechnology has shown promise in enhancing the mechanical properties of dental materials used in root canal procedures. For instance, the incorporation of silica nanoparticles into root canal sealers improves their strength, fracture resistance, and overall durability, providing more effective seals that prevent bacterial ingress (3). Moreover, nanoparticles can improve the adhesion of restorative materials to tooth structures, thereby increasing the longevity and success rate of endodontic treatments.

Nanotechnology also holds significant potential for tissue regeneration in endodontics. Nanoparticles can serve as carriers for bioactive molecules or growth factors, which could stimulate pulp tissue regeneration and facilitate the repair of periapical lesions .(4) This regenerative approach presents an alternative to tooth extraction, offering more sustainable solutions for preserving natural teeth. Furthermore, nanoparticles can be used in targeted drug delivery systems, ensuring precise and controlled release of antimicrobial agents, thus enhancing therapeutic efficacy while minimizing systemic side effects.(5)

However, the widespread clinical application of nanotechnology in endodontics is not without challenges. Issues related to the safety, toxicity, and long-term biocompatibility of nanoparticles need to be thoroughly

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addressed through rigorous testing .(6) Additionally, the complex anatomy of the root canal system and the presence of bacterial biofilms necessitate careful design and engineering of nanoparticles to ensure effective penetration and sustained release of therapeutic agents.

Nanotechnology presents a promising future for endodontics, offering more effective, precise and minimally invasive treatment options. As research progresses, nanomaterials are expected to play an increasingly significant role in revolutionizing root canal therapy and advancing dental care as a whole.

II. CLASSIFICATION

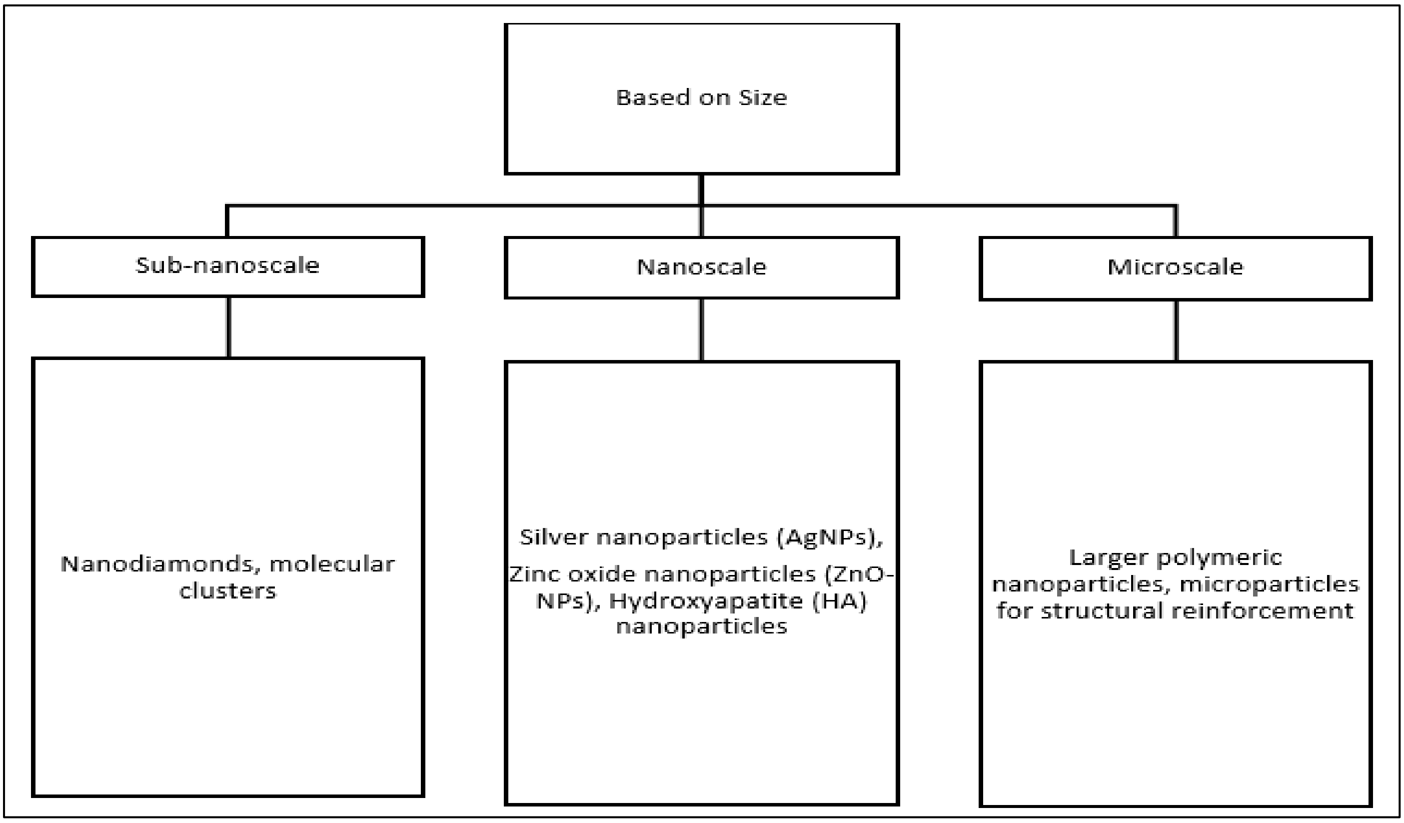

Fig 1 Based on Size

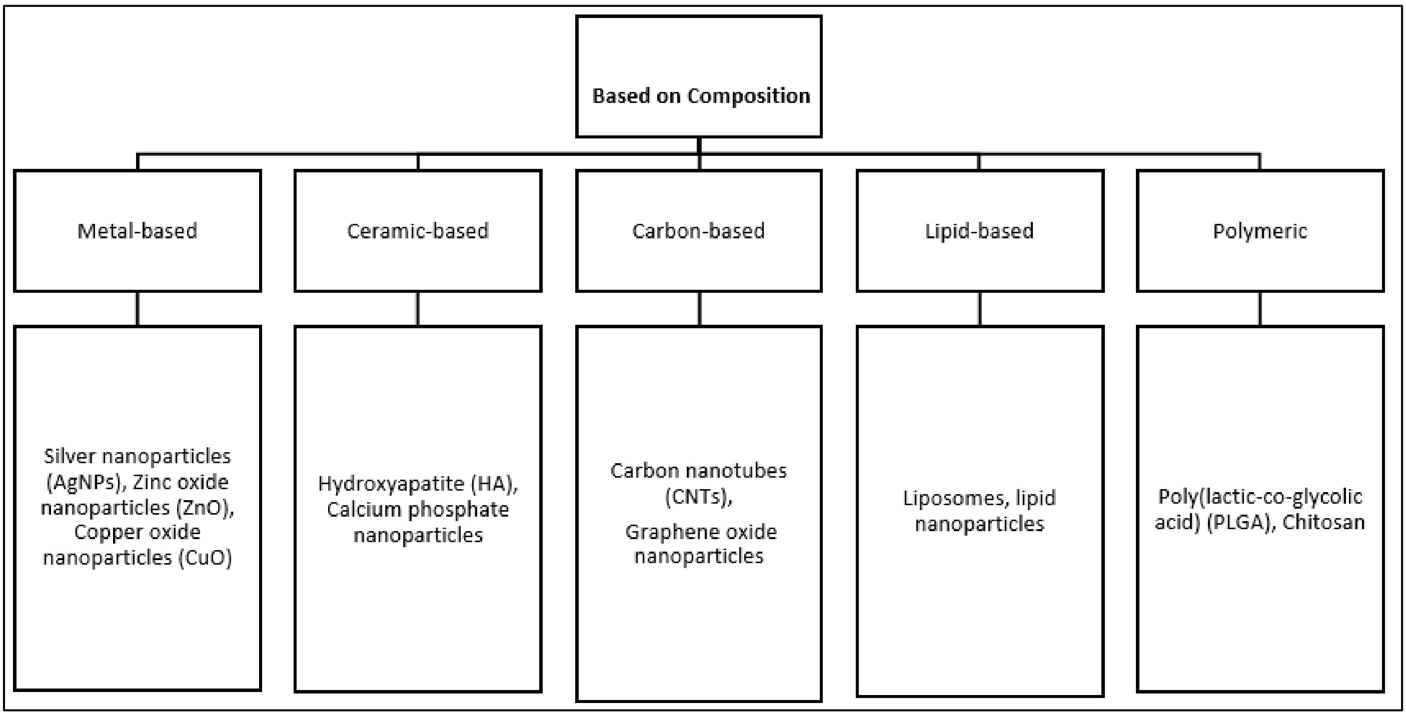

Fig 2 Based on Composition

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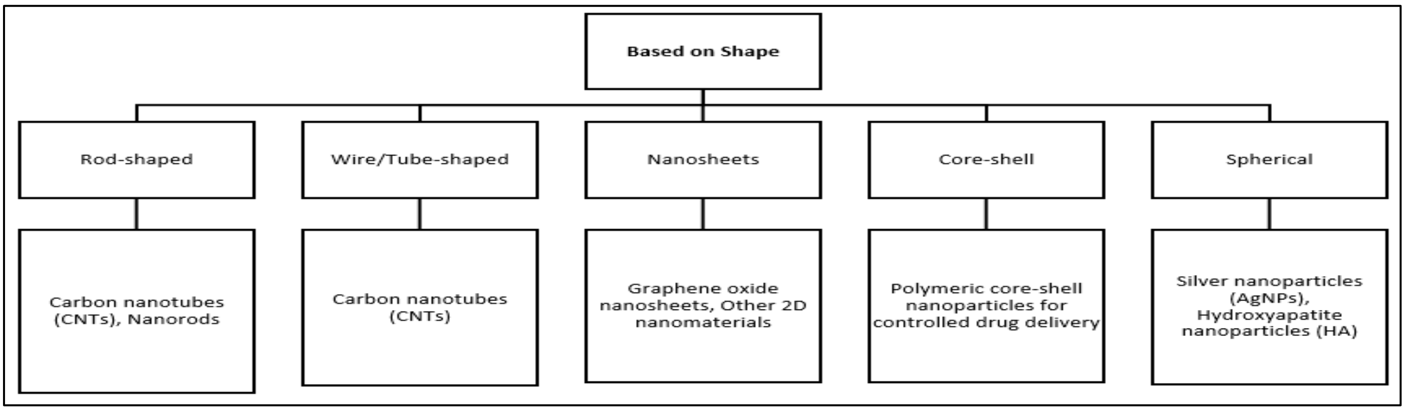

Fig 3 Based on Shape

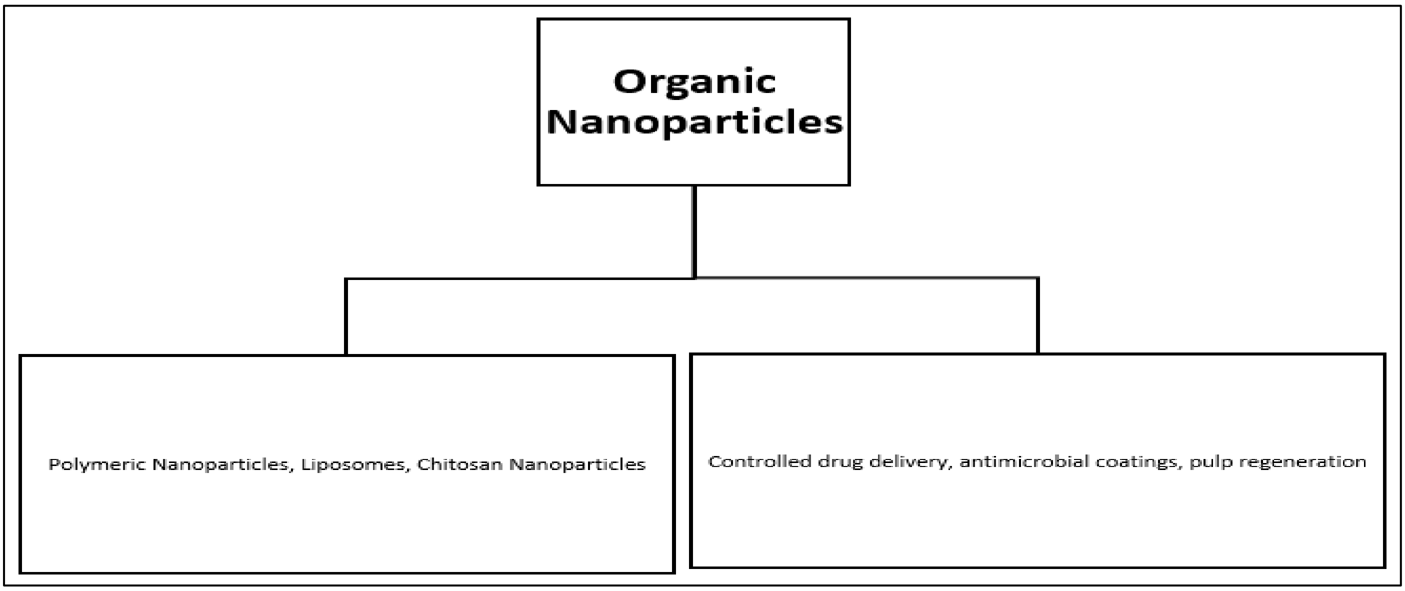

Fig 4 Organic Nanoparticles

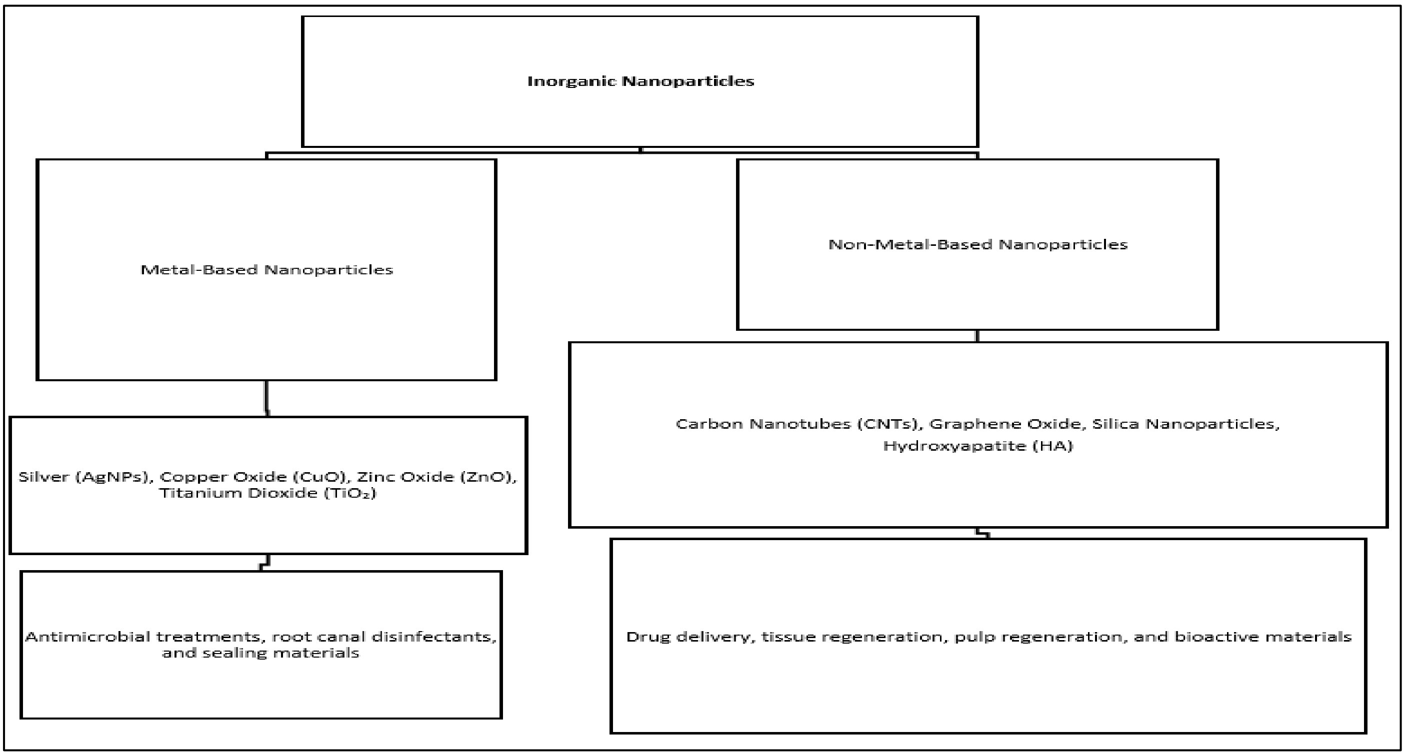

Fig 5 Inorganic Nanoparticles

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III. MECHANISIM OF ACTION OF NANOPARTICLES

- *Electrostatic Interactions and Disruption of the Cell Membrane:*

Positively charged NPs interact with the negatively charged bacterial cell membranes via electrostatic forces, causing their accumulation on the bacterial surface. This disrupts the cell wall framework and increases membrane permeability, allowing more NPs to enter the cell and causing leakage of cellular contents. Additionally, NPs can bind to mesosomes, disrupting bacterial respiration, division, and DNA replication, ultimately leading to bacterial death.(7)

- *Perturbations in Metal Ion Homeostasis:*

Microbial metabolic functions depend on the regulation of metal ions. Excessive metal NPs disrupt this balance, leading to irreversible damage, growth retardation, or microbial death by interfering with essential metabolic processes, particularly those involving metal ion regulation.(8)

- *Generation of Reactive Oxygen Species (ROS):*

NPs penetrate the bacterial cell membrane and trigger the release of ROS, inducing oxidative stress. This oxidative stress diminishes ATP production and disrupts cellular respiration, causing further damage to the cell membrane. ROS formation is amplified through redox cycling and pro-oxidant functional groups at the metal oxide-NP interface, intensifying the antimicrobial effect. (9) (10) (11)

- *Dysfunction of Proteins and Enzymes:*

NPs catalyze the formation of carbonyl groups by oxidizing amino acid chains in proteins. This leads to protein degradation, inactivation of enzymes, and disruption of enzymatic activity, impairing essential cellular functions and contributing to microbial death.(12) (13)

- *Genotoxicity and Inhibition of Signal Transduction:*

Due to their electrical properties, NPs interact with nucleic acids, negatively affecting the replication of chromosomal and plasmid DNA. This interaction inhibits signal transduction pathways, disrupting essential cellular processes and contributing to the death of the microorganism.(14) (15)

- *Improved Penetration:*

Nanoparticles enhance the penetration of irrigants into dentinal tubules and complex root canal anatomy, facilitating deeper disinfection, especially in the apical region. Their small size improves fluid dynamics, aiding in more thorough cleaning and debridement. (16)

- *Antibiofilm Activity:*

Nanoparticles, like silver and titanium dioxide, can penetrate and disrupt biofilm matrices, enhancing the efficacy of traditional disinfectants. This synergistic effect helps break down biofilms and improves their eradication.(17)

- *Controlled Release of Medicaments:*

Nanocarriers (liposomes, micelles, nanocapsules) provide controlled, sustained release of therapeutic agents such as antibiotics or growth factors, ensuring prolonged action at the target site while minimizing systemic side effects.(18)

- *Sealing and Bonding Enhancement:*

Incorporating nanoparticles like nano-hydroxyapatite (n-HAp) into root canal sealers enhances bonding, remineralizes dentin, and prevents bacterial infiltration. Nanocomposite materials improve the sealing ability and flowability of root canal fillings, ensuring better treatment outcomes.(19)

- *Remineralization of Dentin:*

Nano-hydroxyapatite (n-HAp) nanoparticles fill microscopic cracks and fissures in dentin, restoring its mineral content and enhancing structural integrity, thus reducing susceptibility to further demineralization and fractures.(19)

- *Regenerative Endodontics:*

Nanomaterials such as nanoscaffolds, bioactive nanoparticles, and nanogels promote pulp tissue regeneration by supporting stem cell differentiation into odontoblast-like cells. This encourages the formation of new dentin and pulp tissue, aiding in tissue healing and regeneration.(19)

- *Photocatalytic Action:*

Titanium dioxide (TiO_2) nanoparticles, when activated by UV light, generate ROS that degrade organic compounds and biofilms. This photocatalytic action aids in disinfection during root canal treatments and contributes to tooth whitening.

IV. APPLICATIONS OF NANOPARTICLES IN ENDODONTICS

- *Nanomaterials as Endodontic Irrigants*

Endodontic irrigation plays a critical role in disinfecting the root canal by removing bacteria, necrotic tissues, and dentine debris. Common irrigants like sodium hypochlorite (NaOCl) and chlorhexidine (CHX) are often used, but they have limitations, such as the inability of CHX to dissolve organic matter and potential toxicity. Nanoparticles (NPs), particularly silver nanoparticles (Ag NPs), have emerged as promising alternatives due to their high surface area and antimicrobial properties .(20,21)Silver nanoparticles have been shown to penetrate the smear layer and form a barrier that reduces bacterial invasion, all while maintaining dentine integrity.(22,23) Furthermore, silver nanoparticles can reach the apical third of the root canal and exhibit bactericidal effects against *E. faecalis*.(24) The use of low-level electric fields and magnetic fields can further enhance the penetration of nanoparticles into complex root canal systems .(25,26)

Recent innovations include combining nanoparticles with activation methods such as passive ultrasonic irrigation (PUI) and laser-assisted activation to enhance antibacterial efficacy. Studies have demonstrated that silver nanoparticles

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with laser activation or ultrasonic irrigation provide superior bacterial reduction compared to traditional methods .(27)Additionally, chitosan nanoparticles are gaining attention for their ability to remove the smear layer and enhance sealer penetration without compromising dentine's structural integrity. (28)These findings highlight the significant potential of nanoparticles to improve both the antimicrobial activity and mechanical properties of root canal irrigants.

➤ *Nanomaterials as Obturating Materials*

Gutta-percha remains the most widely used obturating material in endodontics, however, its lack of antibacterial properties limits its effectiveness. Incorporating nanomaterials such as silver nanoparticles and nanodiamonds into gutta-percha is an emerging strategy to enhance its antibacterial properties and improve clinical outcomes. Silver nanoparticles provide sustained release of silver ions, which exhibit antimicrobial effects against pathogens like *E. faecalis* and *C. albicans* .(29) Nanodiamonds, combined with amoxicillin, also show promise by enhancing antibacterial activity and improving the mechanical properties of gutta-percha .(30)

Further innovations include bioceramic calcium silicate nanoparticles, which can be coated onto or incorporated into gutta-percha points. These modifications increase fracture resistance and enhance obturation quality by improving sealer penetration and push-out bond strength .(31) These advancements in nanomaterial-based obturation materials highlight their potential to reduce the risk of reinfection and enhance the longevity and effectiveness of root canal treatments.

➤ *Nanomaterials in Endodontic Sealers*

Root canal sealers play a crucial role in the obturation process, filling the space between bulk fillers (such as gutta-percha) and dentinal walls, and ensuring a three-dimensional seal that occludes lateral and accessory canals. To ensure long-term treatment success, endodontic sealers should provide a hermetic seal, remain stable over time, and exhibit bacteriostatic or bactericidal properties while being biocompatible with periapical tissues. Additionally, they must be insoluble in tissue fluids after setting but removable when necessary, in accordance with ISO 6876 and ANSI/ADA 57 standards.(32)

Various types of sealers have been developed, including zinc oxide-eugenol, calcium hydroxide ($Ca(OH)_2$), calcium phosphate, glass ionomer, calcium silicate, salicylate, methacrylate resin, silicone, and epoxy resin-based sealers. However, none meet all the ideal criteria.(33) Consequently, nanomaterials have gained attention for their potential to enhance sealer performance. Nanoparticles offer several benefits, such as sustained antimicrobial effects, which can improve the bactericidal properties of sealers. NPs can also serve as carriers for therapeutic agents, providing localized drug delivery, or act as surface modifiers, enhancing micromechanical adhesion to dentine. Furthermore, nanomaterials can improve bioactivity by promoting mineralization, contributing to better integration with the dentinal walls.(33)

Thus, the incorporation of nanomaterials into endodontic sealers offers significant potential for overcoming current limitations and improving the effectiveness of root canal obturation.

- *Metal and Metal Oxide Nanoparticles in Endodontic Sealers*

The incorporation of metal and metal oxide nanoparticles (NPs) into endodontic sealers enhances their antimicrobial properties and overall performance. Silver nanoparticles (Ag NPs) are particularly effective against a broad spectrum of pathogens, including *Candida albicans* and *Enterococcus faecalis*, and have been added to various sealers such as AH Plus, EndoSequence, MTA Fillapex, Sealapex, and TubliSeal .(34) Silver nanoparticles (20-54.2 nm) improve antibacterial efficacy, especially against *E. faecalis*. However, despite these benefits, silver-based sealers are not immune to bacterial leakage over time. Furthermore, concerns regarding cytotoxicity exist, as silver nanoparticles can generate reactive oxygen species (ROS), leading to oxidative damage and potential adverse effects on osteoblasts and fibroblasts.(35)

Zinc oxide nanoparticles (ZnO NPs), with superior bactericidal effects compared to other metal oxides (e.g., MgO, TiO_2), inhibit the growth of *E. faecalis* without compromising the physical properties of methacrylate resin-based sealers.(36) Zinc oxide nanoparticles (~40 nm) are less cytotoxic to fibroblasts compared to silver nanoparticles, supporting cell proliferation. Combining silver and Zinc oxide nanoparticles may offer an optimal balance between antimicrobial activity and cytocompatibility, although Zinc oxide nanoparticles (<50 nm) may pose toxicity risks to osteoblasts, highlighting the importance of nanoparticle size and shape in determining cytotoxicity .(31) Additionally, the inclusion of Zinc oxide nanoparticles has been shown to enhance the physical properties of sealers, such as flow and penetration into dentinal tubules.(37)

Other metal oxide nanoparticles, such as ferrimagnetic magnetite (Fe_3O_4) NPs (50-100 nm), have been explored for their potential to improve dentinal tubule penetration when applied under an external magnetic field.(38) These findings suggest that metal and metal oxide nanoparticles can improve the antimicrobial efficacy and physical properties of endodontic sealers, though careful consideration of their cytotoxicity and long-term performance is necessary.

- *Organic Nanoparticles in Endodontic Sealers*

Organic nanoparticles (NPs), such as chitosan and quaternary ammonium compounds (QACs), are increasingly utilized in endodontic sealers due to their biocompatibility and antimicrobial properties. Chitosan nanoparticles, incorporated into epoxy-based sealers, enhance antibacterial effects against *E. faecalis*, with prolonged efficacy observed even after one month.(39) Their synergy with chlorhexidine (CHX) further improves antimicrobial performance, although some studies suggest that increasing chitosan nanoparticle

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concentration does not always yield better results.(40,41) Additionally, chitosan nanoparticle protect collagen from enzymatic degradation, improving the sealer's durability.(39) Quaternary ammonium polyethyleniminenanoparticles, another type of quaternary ammonium compounds, provide long-lasting antimicrobial activity without compromising sealer properties. They disrupt *E. faecalis* biofilm and prevent collagen degradation by inhibiting matrix metalloproteinases (MMPs).(42,43)

➢ *Nanomaterials as Nanocarriers*

Nanomaterials like halloysite nanotubes (HNTs) and multi-walled carbon nanotubes (MWCNTs) serve as effective nanocarriers in endodontic sealers. Halloysite nanotubes, loaded with antimicrobial agents, significantly reduce *E. faecalis* growth compared to conventional sealers.(44) Multi-walled carbon nanotubes also enhance antimicrobial efficacy when used with agents like Chlorhexidine and silver nanoparticles (Ag NPs).(44) Mesoporous silica nanoparticles (MSNs) and mesoporous calcium-silicate nanoparticles (MCS NPs) exhibit excellent dentinal tubule infiltration and sustained antimicrobial agent release, offering enhanced antimicrobial and healing properties .(45,46) Additionally, Ppolylactic-co-glycolic acid nanoparticle, used to deliver propolis and other agents, provide prolonged release and robust antibacterial effects against *E. faecalis* and other pathogens.(47)

➢ *Nanomaterials in Retro-Filling and Root-Repair Materials*

Root-end fillings are critical in periapical surgery, with mineral trioxide aggregate (MTA) being the gold standard. However, MTA has limitations, such as handling difficulties, prolonged setting time, and poor antimicrobial properties. Nanoparticles (NPs) incorporated into MTA and other bioactive endodontic cements improve their properties. Silver nanoparticles (Ag NPs) enhance antimicrobial activity, biocompatibility, calcium ion release, and dimensional stability, while reducing setting time and improving radiopacity. (48,49)Other nanoparticles, like bismuth lipophilic NPs, TiO2 NPs, and ZnO NPs, further enhance properties like antimicrobial activity, strength, and radiopacity, although careful consideration is needed to avoid compromising compressive strength .(50,51) Hydroxyapatite nanopartricles improve radiopacity and antibiofilm activity, but negatively affect compressive strength and solubility.(52) Additionally, incorporating nanoparticles like titanium dioxide and silver nanoparticle can enhance bond strength in MTA, while silicon dioxide nanoparticles have negligible impact.(53)

➢ *Nanomaterials for Pulpal Repair and Regeneration*

Pulpal regeneration involves stem cells, scaffolds, and bioactive molecules to repair the pulp–dentin complex. Scaffolds must mimic the extracellular matrix (ECM), with nanofibrous scaffolds promoting positive cell interactions and differentiation by providing mechanical support and facilitating stem cell growth.(54,55) Nanofibers promote cell attachment, protein adsorption, and integrin expression, influencing stem cell differentiation and activation of signaling pathways.(56) Nanoparticle-based systems offer promising scaffold materials for pulpal repair. Magnetic nanoparticless, titanium dioxide (TiO2) nanoparticles, and hydroxyapatite nanoparticles support stem cell attachment, proliferation, and differentiation.(57) Mesoporous bioactive nanoparticles and zinc bioglass nanoparticles further enhance odontoblast differentiation and angiogenesis, demonstrating potential in regenerative dentistry.(58) Chitosan nanoparticles widely used in drug delivery, impact stem cell differentiation based on encapsulation techniques, while mesoporous bioglass nanospheres offer antimicrobial and regenerative benefits.(59)

V. CONCLUSION

In conclusion, nanoparticles hold significant promise in enhancing endodontic treatment outcomes. Their unique properties enable more effective root canal disinfection, targeted drug delivery, and improved tissue regeneration. Nanoparticle-based antimicrobial agents and root canal sealers show improved efficacy in combating biofilm and promoting better sealing and biocompatibility. Despite encouraging results, further research is needed to optimize formulations, ensure safety, and establish standardized clinical applications. Ultimately, nanoparticles have the potential to revolutionize endodontic treatments, improving success rates and patient outcomes.

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