Small Wonders In Dentistry: Nanoparticles In Endodontics – A Literature Review

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Abstract: Nanotechnology has greatly impacted dentistry, particularly endodontics, by addressing the challenge of fully eliminating microbial biofilms from root canals. Conventional materials often fall short in achieving complete disinfection, leading to the exploration of nanoparticles for their high reactivity, antimicrobial activity, and strong surface properties. Nanoparticles such as silver, graphene, chitosan, hydroxyapatite, titanium dioxide, zirconia, and bioactive glass have been incorporated into sealers, irrigants, obturating materials, and medicaments. These additions enhance antibacterial effects, smear layer removal, and bonding with dentin, offering notable improvements over traditional methods. The integration of nanoparticles marks a shift toward more effective, biocompatible treatments. Ongoing research continues to advance their role, aiming to improve outcomes and long-term success in root canal therapy.

Index Terms: Nanoparticles, Endodontics, Nanotechnology, Dentistry, Reactive Oxygen Species.

1. Introduction

Nanomaterial denotes a natural, incidental, or manufactured material containing particles in an unbound state or as an aggregate or agglomerate in which 50% or more of the organic and inorganic particles are present in different number, size, distribution, or one or more external dimensions [1]. The increased surface to volume ratio and increased number of atoms that are present near the surface compared with micro-/macrostructures contribute to the distinctly different properties of nanomaterials [2]. These advantages can be leveraged to build highly specialised materials and devices that interact at the subcellular and molecular level of the human body for maximum therapeutic efficacy with minimal adverse effects [3].

In order to improve overall oral health, the term "nanodentistry" refers to the use of dental nanorobots and nanomaterials for diagnosis and therapy. These tactics cover a wide range of oral health-related topics, including bone replacement materials, diagnosing and treating oral malignancies, treating dentin hypersensitivity, and removing biofilms. The development of nanomaterials in the field of endodontics is concentrated on actions that would enhance tissue regeneration, mechanical integrity of the previously damaged dentin matrix, and antibacterial activity [4]. Antimicrobial nanoparticles have been developed to address the shortcomings of traditional antibacterial agents and produce encouraging endodontic outcomes [5].

2. History

Dr. Richard Feynman introduced the concept of nanotechnology in 1959 after which Dr. Sumio Iijima proposed the idea of nanotubes in 1991. Later in 2000, Dr. Freitas Jr. coined the term "nano-dentistry," introducing innovations such as dentifrobots which are tiny robots designed for dental applications as well as nanomaterials and nanorobots which were intended to support dentition regeneration. Although initially dismissed as mere "science fiction" and deemed impractical, these groundbreaking ideas are now increasingly recognized and adopted by the medical and dental communities. [6].

3. Mechanism of action

Various mechanisms have been proposed to explain how nanoparticles exhibit their effects:

- Electrostatic interaction leading to cell membrane disruption

Positively charged nanoparticles react with the negatively charged surface of microorganisms, causing NPs to accumulate on the bacterial cell surface because negative and positive charges are attracted to one another. Effective bonding between these positively charged NPs and the cell membrane causes the cell wall framework to be upset, increasing the cell's permeability and allowing an increasing number of NPs to enter the bacteria and cause cellular content leakage. By attaching to mesosomes, these NPs impact DNA replication, respiration, and division [7].

- Metal ion homeostasis

The bacteria's capacity to hemostasize metal ions is crucial for metabolic functions. This essential function is disrupted by excess metal nanoparticles, which results in permanent harm that either stops the microorganism's growth or kills it [8].

- Production of Reactive Oxygen Species

When nanoparticles penetrate a microorganism's cell membrane, they generate Reactive Oxygen Species (ROS), causing oxidative stress within the cell that starts an attack on the bacterium. This attack results in reduced respiration and ATP synthesis, which damages the cell membrane. Active redox cycling and the pro-oxidant functional group on the metal oxide-nanoparticle interface are the two ways that a metal oxide produces ROS [9].

- Protein and enzyme dysfunction

By catalysing the oxidative process of the amino acid chain, nanoparticles produce carbonyls, which are naturally protein bound and induce protein breakdown, the inactivation of several enzymes, and disruption of catalytic activity [10].

- Genotoxicity and inhibition of signal transduction

The electrical characteristics of nanoparticles cause them to interact with nucleic acid molecules, which hinders signal transmission and negatively impacts chromosomal and plasmid DNA replication [11].

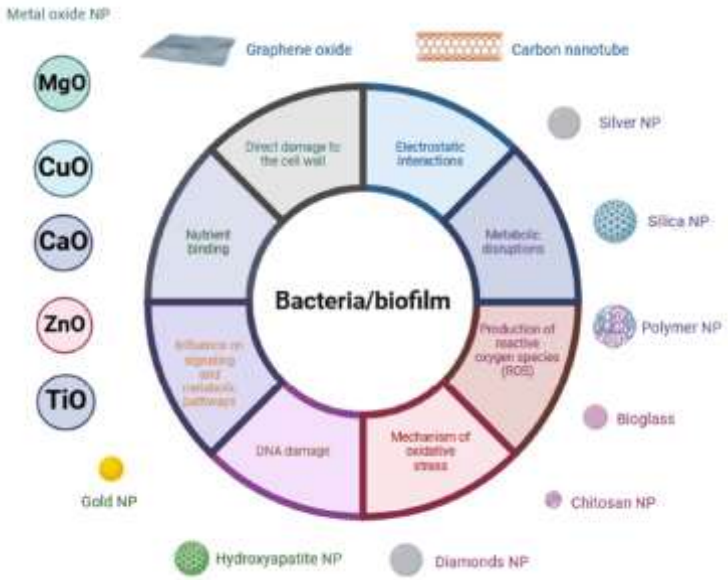

Figure 1. The effect of nanoparticles on the impairment of biofilm-forming bacteria

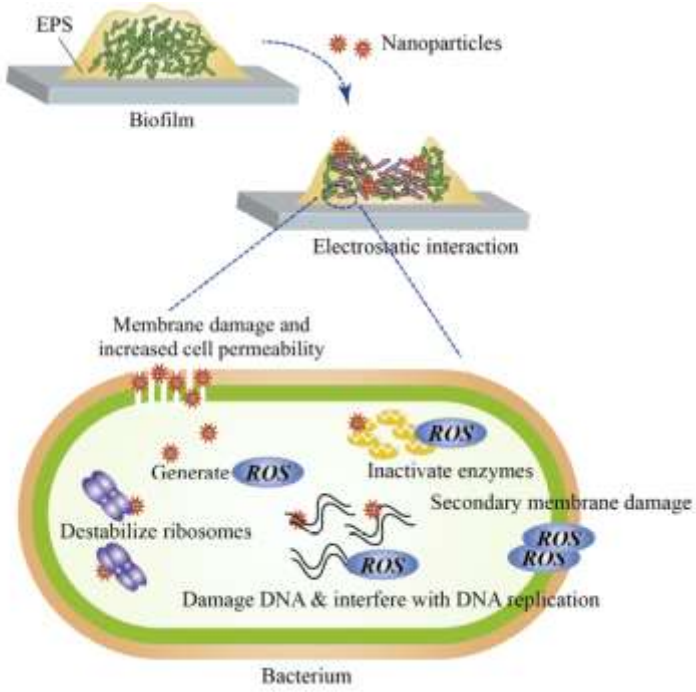

Figure 2: Antibacterial nanoparticles suggested modes of action: Nanoparticles interact electrostatically with bacterial cell walls after penetrating the biofilm. Increased cell permeability and the leakage of cellular components are the results of the ensuing breakdown of the cell wall and membrane. Additionally, nanoparticles can denature proteins, disrupt ribosome stability, and disrupt cellular processes. The interactions between membranes and nanoparticles result in the production of reactive oxygen species (ROS). ROS have the potential to disrupt DNA replication, destroy DNA, deactivate enzymes, and harm secondary membranes

4. Properties of nanoparticles

Its physicochemical characteristics, biocidal qualities, and potentially satisfying distribution capability allow for the introduction of nanoparticles against antimicrobial activity in the treatment of oral cavity infections.

A. Size:

Nanoparticle size is a significant factor. The size falls between 10 and 100 nm. There is no therapeutic benefit at sizes smaller than 10 nm or larger than 100 nm. Large molecules are occupied by the reticuloendothelial system for disposal, while extremely minute particles are eliminated by the kidneys [12].

B. Surface Charge:

Nanoparticles are easily attached to the oppositely charged cell walls of the bacteria which improves the bactericidal potency. Stronger charges are more effective, but they also weaken the nanoparticles because of electric repelling forces between them. Therefore, nanoparticles should be loaded appropriately in relation to the amount of negative or positive charge [9].

C. Surface Configuration:

The surface of nanoparticles has a hydrophilic coating. The surface area to volume ratio of these particles is large. These characteristics are what give it its bioapplications since they boost its contact with cellular receptors by binding ligands on the outside of nanoparticles. Superparamagnetic iron oxide nanoparticles have been developed to use this surface composition [10].

D. Protein Adsorption:

Because of their electrical characteristics, polymers such as polyethylene glycol coated with nanoparticles interact with nucleic acid molecules, preventing signal transduction and negatively impacting chromosomal and plasmid DNA replication.

5. Classification of nanoparticles

5.1. On the basis of origin [13]

a. Natural

b. Artificial

5.2. On the basis of dimension

a. Zero dimension - nano structures or nanoparticles

b. One dimension - nano rods

c. Two dimensional - thin films

d. Three dimensional - nano cones

5.3. On the basis of structural configuration [13]

a. Carbon based nanoparticles

b. Metal nanoparticles

c. Dendrimers

d. Composites

5.4. On the basis of composition [14]

a. Inorganic - Zinc oxide, iron oxide, titanium dioxide, cerium oxide, aluminum oxide, bioactive glass.

b. Metallic - Gold, silver, iron, copper, magnesium

6. Nanomaterials in dentistry

In order to get excellent results in current endodontic therapy, it is crucial to fight bacterial infection. The traditional dental fillers and antibacterial medicines may not be sufficiently efficient against a variety of bacteria and frequently fail to reach all oral infection sites, which can result in illness recurrence [15].

Contrarily, nanoparticles can greatly enhance the effectiveness of antibacterial agents and fillers in dentistry, removing many of the aforementioned drawbacks. They can also deeply penetrate bacterial biofilm and tissues, delivering medications straight to the illness site [16]. A variety of bacteria, including resistant forms, can be defeated by some nanoparticles due to their potent antibacterial qualities. Additionally, nanoparticles can be engineered to regulate the slow release of active ingredients, guaranteeing persistent antibacterial activity [17].

Application	Nanoparticles	Features/Properties
sealing agents	silver nanoparticles (AgNPs)	provide long-lasting antibacterial protection, reducing the risk of root canal reinfection
	zinc oxide nanoparticles (ZnO-NPs)	exhibit antimicrobial properties, improve the mechanical and adhesive properties of sealants
filling materials	nanohydroxyapatite (nHAp)	added to filling materials improves their mechanical and biological properties and supports the regeneration of tooth hard tissues
	nanodiamonds	increase the mechanical strength of filling materials and improve their adhesive properties
intrathecal drugs	carbon nanoparticles (e.g., fullerenes, carbon nanotubes)	used as drug carriers, enabling precise delivery of active substances to infection sites.
	gold nanoparticles (AuNPs)	used for imaging, diagnostic and therapeutic purposes because of their optical and plasmonic properties, improving the effectiveness of intrathecal medications
irrigation solutions	titanium oxide nanoparticles (TiO_2-NPs)	in combination with UV radiation, TiO_2-NPs generate reactive oxygen species that effectively disinfect root canals
	silver nanoparticles (AgNPs)	adding to irrigation solutions increases their antimicrobial effectiveness, penetrate bacterial biofilm, used to disinfect root canals, effectively remove different strains of bacteria, including difficult-to-fight Gram-negative bacteria

Table 1. Characteristics of selected nanoparticles used in endodontic treatment [16]

7. Various nanoparticles used in endodontics

7.1. Organic Nanoparticles

- Graphene

Graphene forms antibacterial surfaces and is utilised for illness diagnosis and detection. In a study, He et al. examined the antibacterial activity of graphene oxide nanoparticles (NPs) against common infections such as S. mutans and found that these nanoparticles were very successful at stopping S. mutans growth [18].

- Chitosan

Chitosan (poly[1,4-b-D-glucopyranosamine]), a deacetylated derivative of chitin, is the second most abundant natural biopolymer. Nanoparticles of chitosan have been developed mainly for antibacterial and drug/gene delivery applications. The mechanism of action of Chitosan nanoparticles is based on the principle of electrostatic interaction leading to cell membrane disruption. This results in increased permeability of cell wall, eventually causing cell death and microleakage of its intracellular components [19].

7.2 Non-Organic Nanoparticles

- Bioactive glass

The primary constituents of bioactive glass-based NPs are SiO_2, Na_2O, and P_2O_5 at varying quantities. They are between 20 and 60 nm in size. Bioactive glass is beneficial as the osmotic effects due to ion release in an aqueous environment cause alkaline pH; high osmotic pressure above 1% leads to disruption of microorganisms and precipitation of calcium phosphate causes remineralization of surface enamel [20].

- Mesoporous calcium silicate

These are NPs with a high specific surface area and pore volume ratio that range in size from 80 to 100 nm. Because of their extremely viscous nature, these NPs are used to fill the apical third of root canals [21].

- Tetracycline loaded Calcium Deficient Hydroxyapatite

Tetracycline-loaded Calcium Deficient Hydroxyapatite (TC-CDHA) nanocarriers showed antibacterial efficacy against E. coli and S. aureus bacteria. Interestingly, human periodontal ligament fibroblast cells proliferated more when drug-loaded CDHA was absorbed by their cells. Therefore, it can be said that CDHA nanocarriers are excellent drug delivery vehicles with the ability to regenerate bone for local periodontal applications [22].

7.3 Metallic Nanoparticles

- Gold

Gold nanoparticles when attach to the membrane, alters the membrane potential and lowers the ATP level. Additionally, it prevents transfer ribonucleic acid (tRNA) from attaching itself to the ribosome. Non-toxicity, functionalization, multifunctional effects, ease of detection, and photothermal activity are a few benefits [16].

- Silver

Silver compounds have antimicrobial properties, especially in nanoparticle form. Silver has antibacterial properties and acts on a variety of targets. The particles change hydrogen bonds, cause DNA to unwind, and ultimately disrupt cell-wall formation by successively interacting with the sulfhydryl groups of proteins and DNA. Ag-NPs, or silver nanoparticles, boost penetrability by disrupting the microbial cell sheet. Cell contents are released as a result [19].

7.4 Metal Oxides Nanoparticles

- Zinc oxide

Nanoparticles of zinc oxide are very powerful against microorganisms. Microbial cells are destroyed by its high pH environment. Zinc oxide nanoparticles promote cell death, increase cell wall permeability, and leak out cytoplasmic material. The size of the particles has a direct impact on the bactericidal effect. The antibacterial action increases with size. Zinc oxide NP causes additional harm by dissociating zinc ions within the microbial cell and interfering with its adjuvant function. Its concentration determines how effective it is against bacteria. The antibacterial action is greatest at higher doses [23].

- Titanium dioxide

As an antibacterial agent, titanium dioxide nanoparticles (TNPs) have also been applied in dentistry. TNPs are aesthetically attractive, highly biocompatible, and have stronger antibacterial qualities than chlorhexidine. Through the production of ROS and lipid peroxidation, it induces oxidative stress, which impairs cell integrity and increases membrane permeability. It is an efficient antifungal for fluconazole-resistant microbial strains and possesses good stability and appropriate photocatalytic qualities [24].

- Zirconia

Zirconia (ZrO_2) is commonly used in dentistry because to its tooth-like optical and metallic properties. It is a high-performance ceramic with superior toughness, strength, chemical stability, and corrosion resistance. Its water insolubility contributes to it's ability to resist bacterial colonisation while being low in cytotoxicity, making it a biocompatible and beneficial material in dental applications [25,26].

Portland cement is a prime component of Mineral trioxide aggregate which is most widely used as root end filling material. Tanamaru et al. examined zirconia nanoparticles as potential radiopacifying agents in Portland cement. The results showed that adding zirconia did not reduce the material's biocompatibility. Both micro and nano-sized zirconia particles were evaluated, and both showed increased radiopacity levels that met the ISO/ADA minimum criterion of 3 mm aluminium equivalent [27].

By mixing ZrO_2 nanoparticles with Polymethyl Methacrylate (PMMA), Chęcińska et al. examined the use of zirconium oxide in dentistry. Zirconium oxide ceramics outperformed aluminum oxide ceramics in terms of strength and flexural resistance, based on quantitative testing. Souza et al. observed that incorporating ZrO_2 nanoparticles to glass ionomer cement enhanced compressive strength and resistance to cracking [28].

7.5 Approaches in Regenerative Dental Care

The objective of regenerative endodontic treatment (RET), an emerging discipline of dentistry, is to regenerate a tooth's healthy pulp tissue in order to ensure it continues to develop and function normally [29]. Regenerative endodontics activates the tooth's inherent healing mechanisms by using innovative materials and advanced biological procedures. Stem cells used in regenerative endodontic therapy (RET) can be derived from sources like dental pulp, alveolar bone, and peripheral blood, and possess the ability to differentiate into multiple cell types involved in dental pulp tissue formation [30,31].

Type of Stem Cells	Function in Regenerative Endodontics
Dental Pulp Stem Cells (DPSCs)	Have the ability to develop into various cell types, including odontoblasts that produce dentin.
Stem Cells from Human Exfoliated Deciduous Teeth (SHEDs)	Represent immature pulp stem cells that can transform into odontoblasts and other cells aiding pulp repair, as well as endothelial cells that help form blood vessels within the pulp.
Dental Follicle Stem Cells (DFSCs)	Can mature into cells that contribute to the regeneration of periodontal tissues.
Periodontal Ligament Stem Cells (PLSCs)	Possess the capacity to regenerate periodontal structures such as cementum, ligament, and alveolar bone.
Stem Cells from Apical Papilla (SCAPs)	Able to differentiate into odontoblasts, which form dentin, and pulp-like cells involved in vascular tissue regeneration.
Supernumerary Tooth Stem Cells (SNTSCs)	Their potential for regenerative applications is still being explored.

Table 2. Stem cells in regenerative endodontic treatment [32,33,34]

Nanoparticle-based carrier systems have been proposed as a method for the sustained release of bioactive molecules, which are a crucial component of regenerative endodontics as they modulate cellular activity, such as proliferation, migration and differentiation. [35] As nano particles possess enhanced solubility, high surface-area-to- volume ratio and minute dimensions, nanoparticle-based carrier systems may improve the dissolution and absorption of bioactive molecules and drugs. [36]

Bellamy et al. discovered that a scaffold consisting of carboxymethyl chitosan when used with transforming growth factor-β1-loaded chitosan nanoparticles significantly improved the viability, differentiation, and migration of stem cells from the apical papilla (SCAP). This was achieved by utilizing chitosan's adaptability, swelling ability to conform to different anatomical sites, and ease of molecular conjugation [37]. Nanoparticles have also been used in novel methods to assess regenerative outcomes. Biz et al. combined gold nanoparticles with L-lysine to create materials readily absorbed by stem cells. The increased radiopacity allowed microtomographic imaging to identify viable cells after treatment, without significant cytotoxicity [38].

8. Conclusion

Nanoparticles represent a significant advancement in endodontics, offering enhanced antimicrobial effects, improved drug delivery, and support for tissue regeneration. Their small size enables better penetration into the complex root canal system, effectively

targeting bacterial biofilms and aiding healing. Metal nanoparticles like silver and copper have strong antibacterial properties, while biodegradable options such as chitosan provide biocompatibility and lower toxicity. Nanoparticles in scaffolds and sealers promote regenerative treatments by supporting stem cell growth and differentiation.

However, concerns about cytotoxicity, environmental effects, and long-term safety remain. Future studies should focus on optimizing nanoparticle formulations, reducing adverse effects, and developing standardized clinical protocols. Overall, nanoparticles have the potential to improve endodontic success and shift dental care toward more biologically based approaches.

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Nil

10. Conflict of interest

There is no conflict of interest

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