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Review Article

Current Perspectives on Gold Nanoparticles in Endodontic Tissue Engineering

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ABSTRACT

Gold nanoparticles (AuNps) have emerged as promising agents in endodontic tissue engineering, offering a range of properties and functionalities that can revolutionize dental treatments. From their unique antimicrobial activity to their ability to enhance mechanical properties and facilitate targeted drug delivery, AuNps hold great potential for improving the efficacy and outcomes of endodontic procedures. This review article highlights the properties and characteristics of AuNps and their interaction as well as regenerative impact on pulp, dentin and periapical bone.

Keywords: Gold nanoparticles, Endodontic tissue engineering, Dental pulp regeneration, Dentin formation, Periapical bone regeneration

INTRODUCTION

In recent years, nanotechnology has emerged as a promising field in various branches of science and medicine, including dentistry. The application of nanotechnology in dentistry has shown great potential for improving the efficacy and outcomes of dental procedures. One such area of research is the use of metallic nanoparticles, particularly gold nanoparticles, in endodontic regeneration.[1] Nanotechnology involves the manipulation and control of matter at the nanoscale level, which is approximately 1 to 100 nm. At this scale, materials exhibit unique physical, chemical, and biological properties that differ from their bulk counterparts. These properties make nanoparticles ideal for various biomedical applications, including tissue regeneration.[2]

Endodontic regeneration, specifically pulp regeneration, is a significant focus of research in the field of dentistry. The traditional approach to endodontic treatment involves removing infected dental pulp and filling the root canal with inert materials. However, this approach fails to restore the full functionality and vitality of the tooth. [1,2]

Gold nanoparticles (AuNps) hold immense potential in endodontic regeneration as they can influence cellular behaviour, promote tissue growth, and modulate the immune response. They can be incorporated into scaffolds, medicaments, or injectable formulations to enhance the regenerative capacity of dental pulp stem cells, promote dentin formation, and combat bacterial infections commonly associated with endodontic procedures. [3]

METHODS

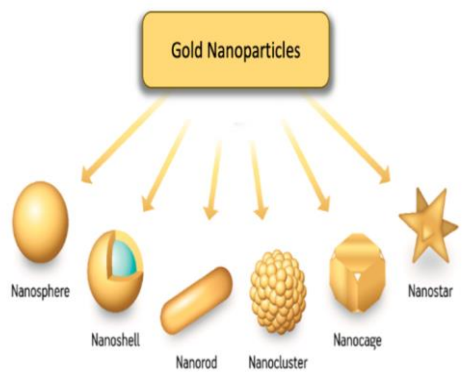
A search was done in PubMed and Google scholar by using the following keywords: gold nanoparticles, metallic nanoparticles, regenerative endodontics, tissue engineering, dentin regeneration, pulp regeneration, stem cells, nanotechnology, drug delivery, scaffolds.

The search was restricted to in-vitro studies. In addition hand search of most relevant scientific journals in endodontics and Conservative dentistry such as Journal of endodontics, International endodontic journal, Journal of Conservative dentistry, Operative dentistry and Journal of Restorative dentistry was also done. Researches with relevant information and published in English language were considered for inclusion in the literature review.

Based on the inclusion and exclusion criteria defined, titles isolated from the electronic databases were analysed. The abstracts of selected titles were screened by one reviewer. The full texts of 20 publications selected by the reviewer were further studied, which led to the exclusion of 3 articles. Finally, 17 publications were included for this literature review.

PROPERTIES AND CHARACTERISTICS OF GOLD NANOPARTICLES

Size and Shape Control: Gold nanoparticles can be synthesized with precise control over their size and shape. They can range from a few nanometres to several hundred nanometres in diameter. The shape of gold nanoparticles can vary from spheres to rods, triangles, cubes, and other complex geometries [4].



Optical Properties: Gold nanoparticles exhibit unique optical properties due to their size and shape-dependent localized surface plasmon resonance (LSPR). LSPR results in the absorption and scattering of light at specific wavelengths, giving rise to intense colours, such as red or purple. This optical property is exploited in various applications, including biosensing, imaging, and photothermal therapy [5].

Surface Chemistry and Functionalization:
The surface of gold nanoparticles can be readily functionalized with different molecules, ligands, or biomolecules. This surface chemistry allows for specific targeting, enhanced stability, and controlled interactions with other molecules or systems [4].

Stability and Biocompatibility: Gold nanoparticles are generally stable and resistant to oxidation. They exhibit excellent biocompatibility and low toxicity, making them suitable for various biomedical applications. However, it is important to consider the surface functionalization and concentration of nanoparticles to ensure their biocompatibility [6].

Catalytic Activity: Gold nanoparticles exhibit catalytic activity due to their unique surface properties. They can act as efficient catalysts in various chemical reactions, including oxidation, hydrogenation, and carbon-carbon bond formation. Their catalytic activity can be further enhanced by modifying their size, shape, and surface chemistry [7].

Colloidal Stability: Gold nanoparticles can form stable colloidal suspensions in various solvents. Their colloidal stability is attributed to the electrostatic repulsion or steric hindrance provided by surface functionalization or capping agents [6].

INCORPORATION STRATEGIES OF GOLD NANOPARTICLES

Specific strategies for incorporating gold nanoparticles may vary depending on the intended application and the desired properties or functionalities required. Common incorporation strategies for gold nanoparticles are listed in Figure 1.

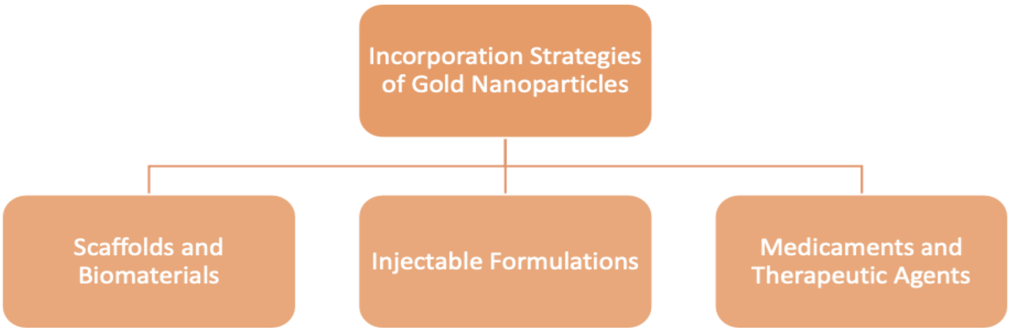


Figure 1: Incorporation Strategies of Gold Nanoparticles Original work of the authors

Scaffolds and Biomaterials: Incorporated into scaffolds and biomaterials to enhance their mechanical, electrical, and biological properties. By incorporating gold nanoparticles into the matrix of a scaffold or biomaterial, researchers can take advantage of the unique properties of gold nanoparticles, such as their high surface area-to-volume ratio, biocompatibility, and plasmonic properties. These properties can be utilized for various purposes, such as improving the mechanical strength of the scaffold, enabling targeted drug delivery, or enhancing tissue regeneration.

Injectable Formulations: Formulated into injectable systems, such as hydrogels or nanocomposites, for targeted drug delivery or therapeutic applications. By incorporating gold nanoparticles into these formulations, they can be transported to specific sites within the body, enabling localized drug delivery or imaging. The surface of the gold nanoparticles can also be functionalised with specific ligands or molecules to target specific cells or tissues, increasing the efficacy and specificity of the therapeutic treatment.

Medicaments and Therapeutic Agents: Utilized as carriers or delivery systems for various medicaments and therapeutic agents, such as drugs, genes, or proteins. The surface of gold nanoparticles can be modified with specific molecules or functional groups to enable the attachment or encapsulation of therapeutic agents. This allows for controlled release, increased stability, and improved bioavailability of the loaded agents. Additionally, the unique plasmonic properties of gold nanoparticles can be exploited for various therapeutic applications, including photothermal therapy, photodynamic therapy, or imaging-guided therapy [8].

ANTIBACTERIAL EFFECTS OF GOLD NANOPARTICLES

Gold nanoparticles have demonstrated significant antibacterial properties, making them a promising candidate for various antibacterial applications.

Broad-Spectrum Activity:
Gold nanoparticles exhibit antibacterial activity against a wide range of bacteria, including both Gram-positive and Gram-negative strains. This includes common pathogenic bacteria such as Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, and Streptococcus species. Figure 2 represents bacteria susceptible to the antimicrobial action of AuNps.

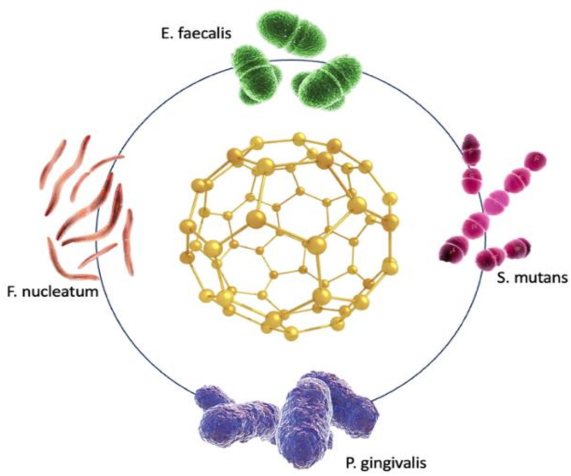


Figure 2: Bacteria susceptible to antimicrobial action of AuNps Original work of the authors

Size-Dependent Activity: The size of gold nanoparticles plays a crucial role in their antibacterial efficacy. Smaller nanoparticles tend to have greater antibacterial activity due to their higher surface area-to-volume ratio, allowing for increased interaction with bacterial cells.

Mechanisms of Action: The antibacterial mechanisms of gold nanoparticles are multifaceted and can vary depending on the nanoparticle size, shape, surface chemistry, and bacterial species. Gold nanoparticles can exhibit synergistic effects when combined with other antibacterial agents, such as antibiotics or photo-thermal agents. This combination approach enhances the antibacterial efficacy and helps overcome bacterial resistance.

Biofilm Inhibition: Gold nanoparticles have shown the ability to inhibit the formation and growth of bacterial biofilms, which are highly resistant to conventional antibacterial treatments. Disrupting biofilms is critical for effective bacterial eradication and prevention of recurrent infections.

Controlled Release Systems: Gold nanoparticles can be incorporated into controlled release systems, such as hydrogels or coatings, to provide sustained and localised antibacterial effects. This controlled release approach improves the long-term antibacterial activity and reduces the risk of bacterial resistance.

Biocompatibility and Safety: Gold nanoparticles have demonstrated excellent biocompatibility, low toxicity, and minimal impact on mammalian cells. This is crucial for their potential use in biomedical applications, such as wound dressings, implant coatings, and drug delivery systems [9].

PROMOTION OF PULP, DENTIN AND PERIAPICAL BONE REGENERATION

Influence of Gold Nanoparticles on Dental Pulp Stem Cells (DPSCs)

Specific effects of AuNps on DPSCs can vary depending on several factors, including the size, shape, concentration, and surface functionalization of the nanoparticles, as well as the experimental conditions and protocols used.

Biocompatibility: AuNps have been found to be biocompatible with DPSCs, they do not cause significant toxicity or adverse effects on cell viability. This is crucial for their potential use in dental applications, as it ensures the safety of DPSCs when in contact with AuNps [4]. DPSCs have the ability to internalize AuNps, either through passive diffusion or active cellular uptake mechanisms. Once internalized, these nanoparticles can interact with cellular components and influence various cellular processes [6].

Xia, et al., 2021, low concentrations of AuNps can promote the proliferation of DPSCs. This may be attributed to the activation of signalling pathways involved in cell growth and division. The presence of AuNps can stimulate the production of growth factors and cytokines that support cell proliferation [10]. AuNps have the potential to influence the differentiation of DPSCs into various cell lineages. For example, GNPs have been shown to enhance the osteogenic differentiation of DPSCs, promoting the formation of mineralized tissue. This property is valuable in tissue engineering and regenerative medicine applications, particularly in the context of dental and bone regeneration [7]. AuNps can modulate signalling pathways within DPSCs, influencing their behaviour and function. For instance, AuNps have been reported to activate the Akt signalling pathway, which is involved in cell survival and proliferation. By activating or inhibiting specific signalling pathways, AuNps can regulate various cellular processes in DPSCs [10].

Enhancement of Dentin Formation and Mineralization

Gold nanoparticles can promote the odontogenic differentiation of dental pulp stem cells (DPSCs), which are responsible for dentin formation. AuNps can induce the expression of odontogenic markers, such as dentin sialophosphoprotein (DSPP), alkaline phosphatase (ALP), and osteocalcin. This stimulation of odontogenic differentiation can lead to increased dentin matrix deposition and subsequent mineralization. DPSCs can be influenced by AuNps to produce an extracellular matrix rich in dentin-specific proteins and minerals. The presence of gold nanoparticles has been reported to upregulate the secretion of collagen, fibronectin, and other extracellular matrix components. This enhanced extracellular matrix production provides a favourable environment for dentin formation and mineralization [11].

AuNps can act as nucleation sites for the deposition of mineral crystals during dentin mineralization. Surface properties, such as their high surface area and ability to bind calcium ions, can promote the nucleation and growth of hydroxyapatite crystals, the primary mineral component of dentin. This interaction between AuNps and calcium ions facilitates the biomineralization process, leading to increased dentin mineralization. Expression of genes associated with dentinogenesis and mineralization can be modulated by AuNps, which is capable of upregulating the expression of key genes involved in dentin formation, including dentin matrix protein 1 (DMP1), bone sialoprotein (BSP), and osteopontin (OPN). These genes play essential roles in regulating dentin matrix deposition and mineralization [12].

AuNps can be functionalised or loaded with bioactive molecules, such as growth factors or signalling molecules, to enhance dentin formation and mineralization. This can facilitate the controlled release of these molecules, providing sustained and localized delivery to the site of dentin regeneration. This controlled release can promote the recruitment and differentiation of DPSCs, as well as enhance the mineralization process [13].

Periapical Bone Formation Influenced by Gold Nanoparticles

Periodontal ligament stem cells (PDLSCs) have the potential to contribute to periodontal tissue regeneration, including periodontal bone formation. Gold nanoparticles have been investigated for their potential role in enhancing the regenerative capabilities of PDLSCs in the context of periodontal tissue engineering.

AuNps have been shown to promote the osteogenic differentiation of PDLSCs. They can stimulate the expression of osteogenic markers, such as osteocalcin, alkaline phosphatase, and runt-related transcription factor 2 (RUNX2), which are essential for bone formation. GNPs can provide cues and signals that drive PDLSCs towards an osteogenic lineage, facilitating periodontal bone formation. Signalling pathways involved in PDLSC behaviour and differentiation can be modulated by AuNps, which can impact periodontal bone formation. AuNps have been reported to activate the Wnt/β-catenin signalling pathway, which plays a crucial role in osteogenesis and bone formation. Activation of this pathway by GNPs can enhance the osteogenic potential of PDLSCs, contributing to periodontal bone regeneration [14].

Adequate blood supply is crucial for successful periodontal tissue regeneration, including bone formation. AuNps have shown the potential to promote angiogenesis, the formation of new blood vessels, which supports the oxygen and nutrient supply to the regenerating tissue [15]. This enhanced angiogenic response facilitated by AuNps can positively influence the regenerative capacity of PDLSCs and contribute to periodontal bone formation [16]. AuNps can be functionalized to carry and release bioactive molecules, such as growth factors or osteogenic factors. By loading these molecules onto AuNps, controlled release can be achieved, allowing for sustained delivery to PDLSCs and the surrounding tissue. This controlled release of bioactive molecules can enhance the osteogenic differentiation of PDLSCs and promote periodontal bone formation [17].

CONCLUSION

The use of gold nanoparticles (AuNps) in endodontics holds great promise and has been the subject of extensive research. AuNps offer unique properties such as antimicrobial activity, drug delivery capabilities, and enhanced mechanical properties, making them attractive for various applications in endodontic treatments. Studies have demonstrated the antimicrobial efficacy of AuNps against endodontic pathogens and their ability to disrupt biofilms. Additionally, these nanoparticles have shown potential for targeted drug delivery within the root canal system, improving the effectiveness of treatment while minimizing side effects. Furthermore, their incorporation into dental materials and restorations has shown to enhance their mechanical properties, resulting in improved longevity and durability.

However, there are still important aspects that require further investigation. Biocompatibility, long-term safety, and the potential systemic effects of AuNps in the endodontic environment need to be thoroughly assessed. Optimizing the characteristics such as size, shape, surface charge, and coating, is crucial to maximize their efficacy and minimize any adverse effects. Mechanistic studies are needed to better understand the interactions between AuNps and microbial pathogens, as well as their modes of action.

Future research should include well-designed in vivo studies to validate the effectiveness and safety of GNP-based therapies in animal models that mimic human endodontic infections. Clinical trials with long-term follow-up are also necessary to evaluate the clinical outcomes, patient acceptance, and cost-effectiveness of gold nanoparticle-based treatments in endodontics.

Overall, with continued research and development, gold nanoparticles have the potential to revolutionize endodontic treatments by providing enhanced antimicrobial properties, targeted drug delivery, and improved restorative materials. However, it is essential to address the remaining research gaps, ensure safety, and establish robust clinical evidence before widespread implementation in routine endodontic practice.

Declaration by Authors

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