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Gold Nanoparticles in Dentistry- Where Cutting Edge Nanotechnology Meets Dazzling Dental Care

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ABSTRACT:

Gold nanoparticles (AuNPs) have emerged as a promising nanomaterial in modern dentistry due to their unique physicochemical properties, including high surface area-to-volume ratio, ease of functionalization, excellent biocompatibility, and intrinsic antimicrobial activity. This review highlights recent advances in the application of AuNPs across various dental domains, including periodontics, endodontics, prosthodontics, implantology, and oral cancer diagnostics. AuNPs have shown potential in enhancing the mechanical and biological performance of dental biomaterials, promoting osseointegration in implants, and serving as drug delivery vehicles for site-specific therapies.

Their ability to disrupt bacterial biofilms and fungal colonies further supports their role in combating oral infections and improving oral hygiene. Moreover, AuNPs can be utilized in biosensing platforms and imaging modalities, offering precise diagnostic capabilities. Despite these advantages, challenges such as cytotoxicity at higher concentrations, long-term stability, and regulatory concerns remain to be addressed. This review aims to provide a comprehensive overview of the synthesis, functionalization, and applications of AuNPs in dentistry, along with a discussion on current limitations and future prospects in clinical translation.

INTRODUCTION:

GOLD NANOPARTICLES (GNPS): ANCIENT ART AND MODERN TECHNOLOGY:

Gold nanoparticles have been used for centuries by artists, valued for the vibrant colours they produce through interactions with visible light. These striking hues arise from a phenomenon known as *surface plasmon resonance*, where conduction electrons on the gold surface oscillate in response to light, giving rise to vivid colours that vary with particle size and arrangement. In recent years, the unique optoelectronic properties of GNPs have found groundbreaking applications in high-tech fields such as organic photovoltaics, sensory probes, therapeutic agents, targeted drug delivery, electronic conductors, and catalysis. Nano gold can appear red, orange, or even blue depending on the size, shape, and spatial arrangement of the particles. For example, red-coloured gold nanoparticles are typically around 20 nanometres in diameter, whereas orange ones are closer to 80 nanometres. As these particles change in size or group together, their interaction with light shifts, resulting in dramatic colour changes[1-6].

GOLD NANOPARTICLES IN CALCIUM PHOSPHATE CEMENT:

The incorporation of gold nanoparticles (GNPs) significantly improved the behaviour of human dental pulp stem cells (hDPSCs) on calcium phosphate cement (CPC). This enhancement included a notable increase in cell adhesion—approximately a twofold rise in cell spreading—as well as improved cell proliferation and osteogenic differentiation, with a 2–3-fold increase observed at 14 days.

GNPs impart a micro-nano-scale structure to the CPC surface, thereby enhancing surface properties that promote cell adhesion and subsequent cellular behaviours. Furthermore, GNPs released from the GNP-

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CPC composite were internalized by hDPSCs, as confirmed by transmission electron microscopy (TEM), leading to enhanced cellular functions[6-8].

In addition, culture media supplemented with GNPs independently promoted hDPSC activity, further supporting the observed osteogenic induction effects of the GNP-CPC system. These findings collectively demonstrate that GNP-CPC significantly boosts the osteogenic functionality of hDPSCs. In conclusion, GNPs offer a promising approach to modifying CPC with nanoscale topography and serve as bioactive additives to enhance bone regeneration.

GOLD NANOPARTICLES IN IMPLANTS:

GOLD NANOPARTICLE-BASED BIOACTIVE COATING FOR ENHANCED PEEK IMPLANT PERFORMANCE:

Gold nanoparticles (AuNPs), a type of inorganic nanoparticle, have emerged as one of the most promising nanomaterials due to their unique optical, electronic, sensing, and biochemical properties. Polyetheretherketone (PEEK) is increasingly considered a promising material for dental implants, owing to its excellent physicochemical and mechanical characteristics. However, its widespread application is hindered by its biologically inert nature.

In this study, a near-infrared (NIR) light-responsive bioactive coating incorporating AuNPs and metronidazole was applied to the PEEK surface via dopamine-assisted polymerization. Compared to untreated PEEK, the modified surface demonstrated significantly enhanced hydrophilicity, promoting better biological interaction. Moreover, under NIR irradiation, the coating exhibited a notable photothermal conversion effect, enabling controlled release of both the gold nanoparticles and the antibiotic from the surface. This multifunctional system offers an innovative strategy for improving the bioactivity and therapeutic performance of PEEK-based implants[9-11].

ENHANCED OSSEOINTEGRATION OF TITANIUM IMPLANTS VIA DOUBLE LAYERS OF GOLD NANOPARTICLES IN OSTEOPOROTIC CONDITIONS:

Osseointegration is a critical factor in the success of implants, particularly in patients with osteopenia or osteoporosis, where low bone density compromises bone healing and integration. Gold nanoparticles (GNPs) have demonstrated significant potential as osteogenic agents due to their bioactive properties.

This study aimed to investigate the osseointegration performance of titanium (Ti) implants coated with double layers of GNPs (referred to as GNP2). The physicochemical characteristics of the modified Ti surfaces were evaluated using scanning electron microscopy (SEM), atomic force microscopy (AFM), water contact angle measurements, and x-ray photoelectron spectroscopy (XPS). These analyses confirmed successful surface modification and enhanced surface properties conducive to cellular interaction.

In vitro assays demonstrated that human bone-marrow-derived mesenchymal stem cells exhibited enhanced osteogenic differentiation on GNP2 surfaces compared to controls. Furthermore, an in vivo study was conducted using hydroxyapatite (HA)-coated and GNP2-coated spinal pedicle screws implanted in ovariectomized (OVX) and SHAM rabbit models. Osseointegration parameters—including bone-to-implant contact and bone volume—were significantly higher in the GNP2 group compared to the HA group, particularly in osteoporotic (OVX) conditions.

These results suggest that titanium implants modified with double layers of gold nanoparticles may serve as an effective alternative to conventional materials for improving osseointegration, especially in patients with compromised bone quality[12-18].

THE MODIFICATION METHODS OF AUNPS TO IMPLANT MATERIALS:

The integration of gold nanoparticles (AuNPs) into implant materials can be achieved through several modification strategies, including **immersion**, **sputtering**, **self-assembly**, and **mixing** techniques. Following modification, AuNPs may be present either on the surface or embedded within the implant material matrix. AuNPs or gold nanorods (AuNRs) can be directly coated onto substrates such as titanium dioxide (TiO_2) nanotubes, pure titanium, hydroxyapatite (HA) particles, or polymers using simple immersion, sputtering, or self-assembly methods. For example, TiO_2 nanotubes and polydimethylsiloxane (PDMS) can be immersed in a chloroauric acid solution, where the AuNPs are generated via in situ reduction and

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deposited onto the material surface under ultraviolet (UV) light exposure.

In addition to surface coating methods, AuNPs can also be incorporated into implant materials by mixing. Different concentrations of AuNPs can be directly blended with polymer matrices to create composite materials. Moreover, chloroauric acid solutions can be reduced in situ by biocompatible agents such as chitosan to form AuNPs, which are then embedded within hydrogel composites.

It is important to note that during the coating preparation process, both the AuNPs and the substrate materials may require **chemical pretreatment** to enhance binding affinity and therapeutic functionality. One commonly employed method is **polyethylene glycolation (PEGylation)**, which improves biocompatibility, stability, and surface interaction. These versatile modification approaches enable the tailored design of nanocomposite implants with enhanced biological activity, particularly for applications in bone regeneration, antibacterial coatings, and osteointegration in compromised bone environments[19- 25].

ANTIBACTERIAL PROPERTIES:

THE ANTIBACTERIAL MECHANISM OF GOLD NANOPARTICLES:

Implant materials modified with gold nanoparticles (AuNPs) demonstrate excellent antimicrobial properties, largely attributed to the unique biological activity of the AuNPs themselves. Gold nanoparticles electrostatically adsorb onto bacterial membranes, particularly interacting with lysine residues found on the surface of Gram-positive bacteria. This interaction disrupts membrane integrity, leading to the formation of irreversible pores and ultimately causing bacterial cell death.

Upon internalization into bacterial cells, AuNPs further contribute to antimicrobial action by reducing intracellular adenosine triphosphate (ATP) levels, thereby impairing cellular metabolism and energy production.

In addition, gold nanoparticles enhance the photocatalytic activity of semiconductor oxides such as titanium dioxide (TiO_2) and zinc oxide (ZnO). This leads to the generation of reactive oxygen species (ROS), including peroxides, hydroxyl radicals, and elevated levels of singlet oxygen, which collectively damage cellular components and induce bacterial lysis.

Furthermore, under near-infrared (NIR) light irradiation, AuNPs exhibit strong photothermal effects. When local temperatures exceed 50 °C, bacterial proteins undergo denaturation, resulting in effective thermal ablation of pathogens.

These multifaceted antimicrobial mechanisms make AuNP-modified implants a promising strategy for preventing post-implantation infections and enhancing the long-term success of biomedical implants[26- 32].

ADVANTAGES OF AUNPS AS ANTIBACTERIAL AGENTS

1. High Biosafety: Gold is chemically inert, and the absorption/metabolism of gold nanomaterials can be regulated through design, providing high biosafety.
2. Chemical Manipulability: The antibacterial effects of AuNPs can be enhanced by controlling their size, shape, and surface chemistry. Surface modifications with various molecules allow tuning of their properties.
3. Low Resistance Induction: AuNPs are less likely to induce bacterial resistance compared to standard antibiotics.
4. Functionalization Potential: AuNPs can be functionalized using antioxidants, biological ligands, organic molecules, or dendrimers. These functionalized nanomaterials show enhanced bacterial targeting, biocompatibility, and cellular uptake.[33-35]

In this systematic review, we summarize the antibacterial effects of AuNP-modified medical implants, current modification methods, types of

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implant materials used, microbial effects, and technological limitations.

TITANIUM-BASED IMPLANTS AND TIO_2 NANOTUBES

Titanium and its alloys are commonly used in orthopaedic implants. Titanium dioxide nanotubes (TNTs), formed via anodization, mimic natural bone matrix due to their nanoscale structure .

However, pristine TiO_2 lacks antibacterial properties unless activated by ultraviolet (UV) light, which cannot penetrate tissues effectively. Near-infrared (NIR) light (650–900 nm), with better tissue penetration and less damage, activates AuNP-decorated TiO_2 nanotubes for enhanced photocatalysis and antibacterial effects[36,37].

Even without NIR excitation, AuNP-modified TNTs have shown antibacterial activity against *Streptococcus gordonii*, *Porphyromonas gingivalis*, and *Fusobacterium nucleatum*, along with reduced inflammatory responses in vivo.

PHOTOTHERMAL AND OPTICAL PROPERTIES OF AUNPS

AuNPs—especially nanorods and nanoshells—absorb NIR light and convert it into heat via the surface plasmon resonance (SPR) effect. This photothermal property enables localized heating and bacterial cell destruction. The optical behavior of AuNPs is affected by size, shape, and surrounding dielectric environment: Smaller particles (~30 nm) show stronger field enhancement than larger ones (~60 nm).Oblate-shaped particles exhibit a red-shift in resonance[38].

ANTIBACTERIAL EFFICIENCY AND DESIGN VARIABLES

AuNPs appear in various shapes (spheres, rods, stars, flowers), and nanostars show the strongest antibacterial effects [10]. However, in implant applications, shape alone was not a dominant factor; particle quantity and distribution were more significant .

FUNCTIONALIZATION AND SYNERGISTIC EFFECTS

Functionalized AuNPs exhibit superior antibacterial activity due to: Enhanced receptor targeting, Better uptake and aggregation control and Tuned optical and catalytic properties

CHALLENGES OF ANTIBIOTIC RESISTANCE

Antibiotic therapy remains the standard for treating post-surgical infections. However, the rise of antibiotic resistance makes treatment more difficult and expensive. In some cases, device removal is necessary, with one study reporting a five-fold increase in mortality after revision surgery due to infection, compared to aseptic failure .

Emerging Antibacterial Alternatives for Implants-Alternative strategies include:

Antimicrobial Peptides (AMPs): While effective against resistant bacteria, AMPs suffer from poor biodistribution, toxicity, and degradation.

Quaternary Ammonium Compounds: Broad-spectrum activity but pose toxicity and resistance challenges.

Cationic Polymers: Show strong bactericidal activity but are hindered by non-degradability and toxicity.

Inorganic Nanoparticles: Offer photocatalytic and photothermal effects with low resistance induction.

ANTIBACTERIAL PROPERTIES OF FUNCTIONALIZED GOLD NANOPARTICLES AND THEIR APPLICATION IN ORAL BIOLOGY

As bacterial resistance is becoming increasingly serious, the development of antibacterial nanomaterials is an effective method of solving this problem. Gold nanoparticles have good stability and excellent biocompatibility and are easily modified, and their antibacterial properties can be enhanced by changing their structure and size or adding ingredients. Gold nanoparticles are also excellent drug carriers that can improve the antibacterial effects of loaded antibacterial drugs. After being modified and combined with other antibacterial drugs, gold nanoparticles can also play a better antibacterial role for effective antibacterial strategies against some resistant bacteria. Gold

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nanoparticles have photothermal effects, and modified gold nanoparticles can be a good medium for photothermal treatments to kill bacteria. By adding functionally modified gold nanoparticles, many materials can obtain much needed antibacterial properties. Gold nanoparticles can also be combined with cations, low-temperature plasma, various surface ligands, and other potential antibacterial agents. In short, the antibacterial characteristics of functionalized gold nanoparticles demonstrate that they have considerable practical application value and provide more ideas to solve antibacterial problems. At the same time, the application of gold nanoparticles in oral biology is also increasing[39-42].

JOINT ANTIBACTERIALS

Titanium and its alloys are widely used in orthopedic implants due to their excellent mechanical strength, corrosion resistance, and biocompatibility. However, they are vulnerable to bacterial colonization and biofilm formation, which can lead to implant-associated infections.

A common strategy to enhance the antibacterial properties of titanium is the formation of titanium dioxide nanotubes (TNTs) on its surface through anodization. These nanotubes provide a nanoscale topography similar to bone matrices and can act as carriers for antibacterial agents. However, pristine TiO_2 has minimal intrinsic antibacterial activity unless activated by ultraviolet (UV) light, which cannot penetrate deeply into tissue. In contrast, near-infrared (NIR) light (650–900 nm) offers deeper tissue penetration due to lower absorption by water and biological components, making it suitable for in vivo activation.

When TNTs are decorated with gold nanoparticles (AuNPs), the resulting nanocomposite exhibits enhanced antibacterial effects. AuNPs can induce a photothermal effect under NIR light through surface plasmon resonance (SPR), converting light into heat that can kill bacteria. This photothermal enhancement improves the photocatalytic antibacterial activity of TiO_2 even under mild irradiation.

Importantly, studies have shown that AuNP-modified TNTs can exhibit significant antibacterial properties even without external light activation. These modified surfaces have demonstrated strong inhibitory effects against common implant-related pathogens such as *Streptococcus gordonii*, *Porphyromonas gingivalis*, *Fusobacterium nucleatum*, and *Escherichia coli*. In vivo, these surfaces reduce inflammatory responses, suggesting their potential for clinical applications.

The effectiveness of these AuNP-TiO_2 systems is influenced by several factors, including nanoparticle size, distribution, and concentration. Uniform dispersion of AuNPs is typically achieved with concentrations below 10 wt%, while higher concentrations may lead to aggregation and reduced efficacy[43-52].

BIOCOMPATIBILITY OF IMPLANT MATERIALS MODIFIED BY AUNPS

Biomaterials come into contact with cell surfaces, tissues, organs, and blood components. The toxicity assessment of implant materials is a principal issue for potential medical applications. Gold nanoparticles have good biocompatibility at the appropriate concentration and size, and excessive concentrations will cause toxicity. Some literature illustrated that gold nanoparticles with reasonable size and concentration have good cytocompatibility. The results of cytocompatibility studies showed that AuNPs (of approximately 20 nm) did not cause HDF-f cell death at a maximum concentration of 300 μM . The 20 nm AuNPs exhibited the lowest uptake by reticuloendothelial cells and the slowest clearance from the body. As the size of the AuNPs increased, the permeability and diffusion coefficients decreased .The results of an in vivo experiment showed that AuNPs of 3, 5, 50, and 100 nm did not show harmful effects, whereas AuNPs ranging from 8 to 37 nm induced severe sickness in mice at a dose of 8 mg/kg per week. Other studies showed that 10 nm nanoparticles and 15 nm nanoparticles both showed the most widespread organ distribution.

In addition, in antimicrobial strategies for bone defect restoration and dental implants, AuNPs exhibit good biological activity, such as in the promotion of fibroblast adhesion, proliferation, and migration .

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Moreover, AuNPs can stimulate osteogenic differentiation of bone marrow mesenchymal stem cells (BMSCs) and promote the bone-forming effect of implant materials. Osteogenesis is significantly promoted when combined with bioactive materials. Furthermore, gold nanoparticles exhibit anti-inflammatory effects. In wound-dressing antibacterial applications, AuNPs exhibit good collagen fiber regeneration to promote wound healing.

Of the included articles, most also investigated the biocompatibility of modified implant materials. Cytotoxic and inflammatory responses have been previously described; however, none of the modified surfaces exhibited significant cytotoxicity in vitro. Most AuNPs were approximately 20 nm in size. The addition of 5% gold content to the surface of TNT showed the best anti-inflammatory effect , promoted initial adhesion, and enhanced the spreading and proliferation of rat bone marrow mesenchymal stem cells (rBMSCs) , evenly stimulating the ALP activity of rBMSCs . However, one study showed that chitosan hydrogels with AuNPs led to a higher thickness of the fibrous tissue capsule

BIOSYNTHESIS OF GOLD NANOPARTICLES BY VASCULAR CELLS

Biosynthesis of gold nanoparticles (AuNPs) for antimicrobial and chemotherapeutic applications is a well-established process in microbial hosts such as bacterial, fungi, and plants. However, reports on AuNPs biosynthesis in mammalian cells are scarce. In this study, bovine aortic endothelial cells (BAECs) and bovine aortic smooth muscle cells (BASMCs) were examined for their ability to synthesize AuNPs *in vitro*. Cell culture conditions such as buffer selection, serum concentration, and $HAuCl_4$ concentration were optimized before the biosynthesized AuNPs were characterized through visible spectrometry, transmission electron microscopy, X-ray diffraction, and Fourier transform infrared (FTIR) spectroscopy. BAECs and BASMC produced small, spherical AuNPs that are semi-crystalline with a similar diameter (23 ± 2 nm and 23 ± 4 nm). Hydrogen peroxide pretreatment increased AuNPs synthesis, suggesting that antioxidant enzymes may reduce Au^{3+} ions as seen in microbial cells. However, buthionine sulfoximine inhibition of glutathione synthesis, a key regulator of oxidative stress, failed to affect AuNPs generation. Taken together, these results show that under the right synthesis conditions, non-tumor cell lines can produce detectable concentrations of AuNPs *in vitro*.

GOLD NANOPARTICLES IN ORAL CANCER BEYOND DRUG DELIVERY

Gold nanoparticles (AuNPs) have been widely employed as carriers for drug delivery and small-molecule therapeutics targeting cancer cells. Studies have demonstrated that AuNPs functionalized with nuclear localization sequences (NLS) can traverse the nuclear membrane and trigger cellular apoptosis. To evaluate their therapeutic potential, two types of AuNP–doxorubicin (DOX) conjugates were compared: one linked via a pH-sensitive bond and the other through a pH-resistant linker.

CONCLUSION:

The primary objective of dental treatment is to eliminate existing oral diseases and implement preventive strategies to control their progression. Various therapeutic interventions have been developed to address these conditions. Due to their nanostructure, high surface area-to-volume ratio, and excellent biocompatibility, gold nanoparticles (GNPs) have been explored in the management of periodontal diseases, dental caries, tissue engineering, dental implantology, and cancer diagnostics. GNPs exhibit significant antifungal and antibacterial properties, making them valuable additives in biomaterials to enhance antimicrobial efficacy. Furthermore, their incorporation improves the mechanical properties of these materials, contributing to better clinical outcomes. GNPs are available in a range of sizes and concentrations, allowing for tailored applications. These attributes make GNPs ideal candidates as fillers in various dental and medical biomaterials. This review aims to examine the impact of GNP incorporation on the performance of biomaterials used in dental and biomedical fields.

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