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Theranostic Nanomaterials in Dentistry: Dual-Function Platforms for Diagnosis and Therapy

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ABSTRACT

Smart nanomaterials are redefining the future of dental science by offering dynamic, stimuli-responsive solutions that adapt to the oral microenvironment. Engineered to react to biochemical and physical triggers such as pH variations, bacterial metabolites, and enzymatic activity, these materials facilitate localized, on-demand therapeutic responses. Their versatility spans across preventive and therapeutic domains—ranging from anti-microbial implant coatings and biofilm-disrupting agents to bioactive remineralizers and site-specific drug delivery vehicles. Innovations such as nanostructured scaffolds for guided tissue regeneration, theranostic platforms for oral malignancies, and smart analgesic systems illustrate the expanding frontier of nanotechnology in dentistry. While challenges persist in terms of regulatory compliance, long-term safety, and commercial translation, smart nanomaterials stand at the forefront of personalized, minimally invasive, and multifunctional dental care.

Keywords: Dental nanotheranostics, Smart hydrogel systems, Oral microenvironment modulation, Nano-enabled caries prevention, Intelligent implant interfaces

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Introduction

Nanomaterials are materials with structural components smaller than 100 nanometers in at least one dimension (1-3). At this scale, materials often exhibit unique physical, chemical, and biological properties that differ significantly from their bulk counterparts (4, 5). These properties include increased strength, enhanced reactivity, and improved electrical or thermal conductivity, making nanomaterials highly valuable in various industries (6). Common types of nanomaterials include nanoparticles, nanotubes, nanowires, and quantum dots (7, 8), each with distinct applications in medicine (9, 10), dentistry (11, 12), electronics (13), energy storage (14), and environmental remediation (15). For example, silver nanoparticles are used for their antibacterial properties (16-18), while carbon nanotubes are prized for their exceptional strength and conductivity in advanced materials (19).

The development and use of nanomaterials also raise important considerations regarding safety and environmental impact. Due to their small size and high reactivity, nanoparticles can pose potential health risks if inhaled or absorbed, leading to ongoing research into their toxicological effects (20). Regulatory frameworks are still evolving to address the safe production, handling, and disposal of nanomaterials (21). Despite these challenges, the potential benefits of nanomaterials continue to drive innovation, with researchers exploring new ways to harness their properties for sustainable technologies (22, 23), targeted drug delivery (24), and next-generation electronics (25). As nanotechnology advances, it holds the promise of revolutionizing industries (26).

Smart nanomaterials

Smart nanomaterials are advanced materials engineered to respond dynamically to external stimuli such as temperature, light, pH, magnetic fields, or chemical signals, enabling precise control over their behavior (27, 28). These materials can adapt, self-repair, or release active agents on demand, making them ideal for applications like targeted drug delivery, responsive coatings, and adaptive sensors (29). For instance in case of oral health, smart nanomaterials respond to specific conditions in the mouth, such as pH changes or bacterial presence, to enhance treatment (30, 31). They can release antimicrobial agents (32), remineralize teeth (33) or detect early signs of decay, offering targeted and sustained therapy (34, 35)(Figure 1).

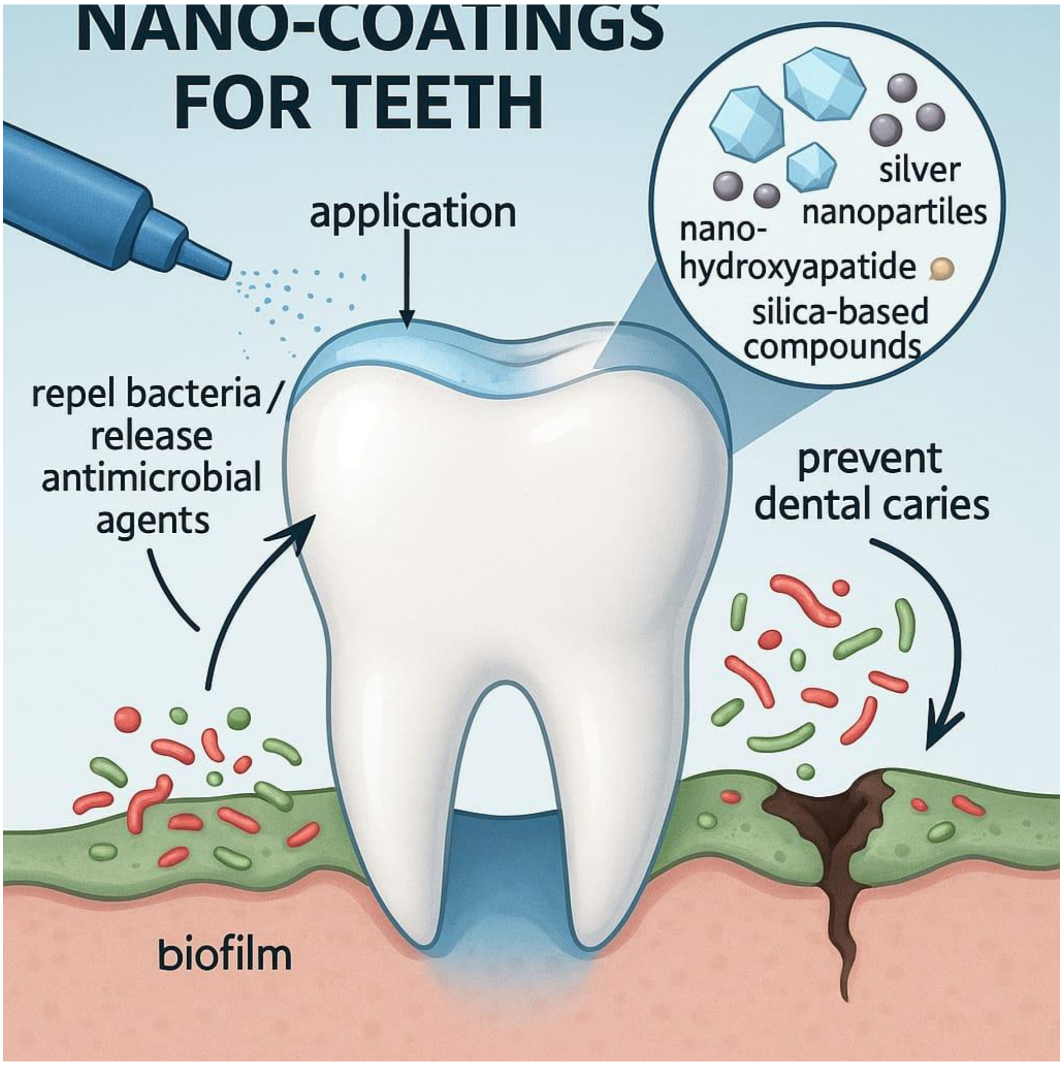

Figure.1: Smart nanomaterials are redefining the future of dental science by offering dynamic, stimuli-responsive solutions that adapt to the oral microenvironment.

Polymeric nanoparticles, such as chitosan (36) and PLGA (37), are designed for controlled drug release, allowing for sustained therapeutic effects with minimal dosing frequency especially useful in local delivery of antimicrobials or anti-inflammatory agents (38, 39). Metallic nanoparticles like silver, gold, and zinc oxide are prized for their potent antimicrobial properties, disrupting bacterial membranes and biofilms commonly found in dental infections (40, 41). Lipid-based nanoparticles further enhance drug bioavailability by facilitating penetration through the oral mucosa, making them valuable for systemic or local delivery in mucosal tissues (42).

In the diagnostic and regenerative realm, quantum dots (43) and carbon-based nanomaterials (like graphene and carbon nanotubes) (44) enable high-resolution bioimaging and biosensing, useful for early detection of oral pathologies and real-time monitoring of therapeutic delivery (45). Hydrogels and nanofibrous scaffolds, often combined with bioactive agents or growth factors, support tissue regeneration in periodontics by mimicking the extracellular matrix and guiding cell proliferation (46, 47). Meanwhile, stimuli-responsive nanomaterials add a layer of intelligence releasing their payload only in response to specific triggers such as acidic pH or enzymatic activity found in inflamed or infected tissues. This precision minimizes side effects and maximizes therapeutic efficacy, positioning smart nanomaterials as a cornerstone of next-generation oral treatments (48).

Applications (prevention)

Smart nano-based toothpaste and mouthwash:

Smart nano-based toothpaste and mouthwash utilize advanced nanomaterials to enhance fluoride delivery and improve antibacterial action for superior oral health. These formulations contain nanoparticles, such as hydroxyapatite or calcium phosphate, which bind more effectively to tooth enamel, promoting targeted remineralization and reducing cavities (49, 50). Additionally, nano-encapsulated fluoride ensures controlled release, maintaining optimal fluoride levels in the mouth for longer periods compared to traditional products (51, 52). Some smart systems even respond to acidic pH (indicating bacterial activity or plaque buildup), releasing antibacterial agents like silver or zinc oxide nanoparticles to combat harmful microbes while preserving beneficial oral flora (53-55).

Beyond fluoride delivery, nano-based oral care products leverage nanomaterials like chitosan nanoparticles or quantum dots for enhanced antibacterial and anti-inflammatory effects (56). These materials can penetrate biofilms more efficiently, disrupting plaque formation and preventing gum disease (57, 58). Some advanced mouthwashes incorporate nanosensors that detect early signs of decay or infection, providing real-time feedback for preventive care (59, 60). By combining sustained antimicrobial action with smart triggered responses, these innovations offer a more effective and personalized approach to maintaining oral hygiene compared to conventional toothpaste and mouthwash (61).

Smart dental implants

Smart nanotechnology dental implants with infection-resistant coatings represent a major advancement in dental care, particularly for patients requiring implants. These coatings are made from nanomaterials like silver nanoparticles (62), titanium dioxide (63), or bioactive polymers that actively prevent bacterial adhesion and biofilm formation (64, 65). Unlike traditional implants, which can become sites for infections like peri-implantitis, these smart coatings release antimicrobial agents in response to bacterial presence or changes in pH. Some coatings even have self-healing properties, repairing minor scratches that could otherwise harbor bacteria. This technology not only improves implant longevity but also reduces the need for antibiotics, lowering the risk of antimicrobial resistance (66, 67).

The development of these coatings involves advanced techniques such as layer-by-layer assembly or electrochemical deposition to ensure precise control over drug release (68, 69). Researchers are also exploring stimuli-responsive nanomaterials that activate only when an infection is detected, minimizing unnecessary chemical exposure. Clinical studies suggest that such implants significantly reduce post-surgical infections, improving patient outcomes (70). However, challenges remain, including long-term biocompatibility testing and large-scale manufacturing. If successfully optimized, smart nano-coated dental implants could become the standard in implantology, offering safer and more durable solutions for tooth replacement (71).

Nano-coatings for teeth

Nano-coatings for teeth are an innovative approach to preventing biofilm formation and protecting against dental caries. These ultra-thin coatings, often made from nanomaterials like nano-hydroxyapatite, silver nanoparticles, or silica-based compounds, create a protective barrier on the tooth surface (72). They work by either repelling bacteria or releasing antimicrobial agents that disrupt biofilm formation—the primary cause of plaque and cavities. Some coatings are also designed to slowly release fluoride or calcium phosphate, promoting enamel remineralization and strengthening teeth against acid erosion. Unlike traditional dental sealants, these nano-coatings are more durable and can be engineered to respond to changes in the oral environment, such as pH fluctuations caused by bacterial activity. This makes them highly effective in preventing early-stage tooth decay while maintaining a natural tooth appearance (73-75).

The application of nano-coatings involves techniques like spray deposition (76) or electrochemical bonding (77, 78), ensuring even coverage without altering tooth function or aesthetics. Recent advancements include smart coatings that activate only when harmful bacteria are present, reducing unnecessary chemical exposure. Studies show that these coatings significantly decrease the risk of cavities, particularly in high-risk patients, such as those with dry mouth or orthodontic appliances. Nano-coatings could revolutionize preventive dentistry, offering a long-lasting, non-invasive solution to maintain oral health and reduce the need for restorative treatments (79, 80)(Figure 2).

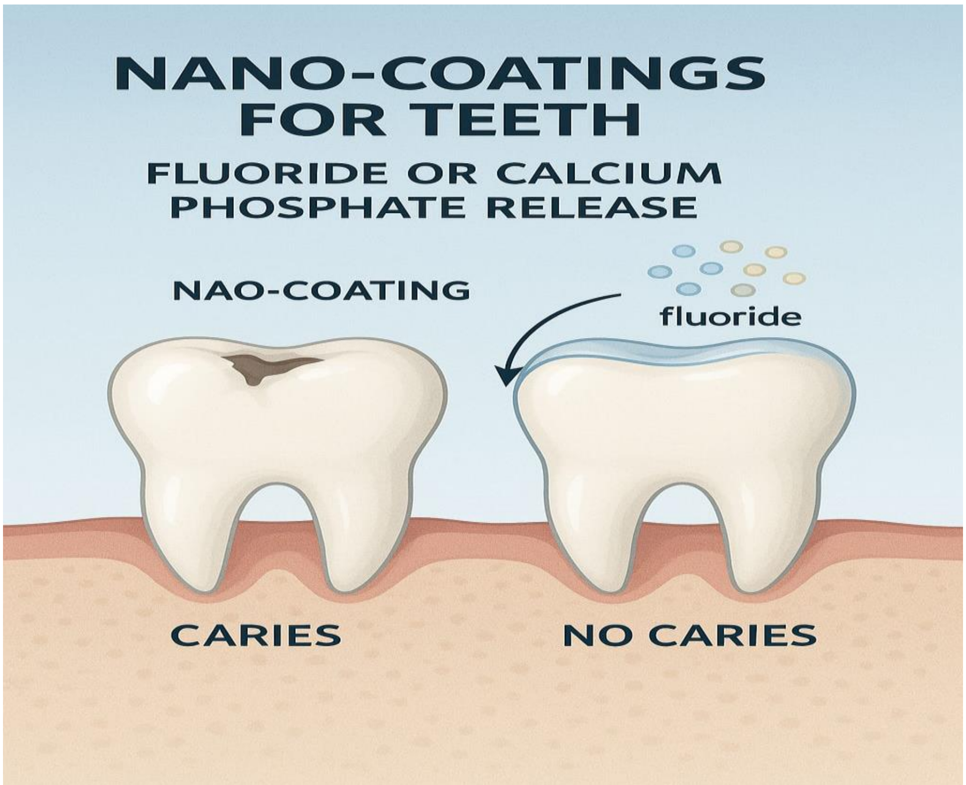

Figure.2: nano coatings significantly decrease the risk of cavities, particularly in high-risk patients.

Remineralization of enamel:

Smart remineralization of enamel using nano-hydroxyapatite represents a groundbreaking approach in preventive dentistry, offering a biomimetic solution for tooth repair (81). Hydroxyapatite is the natural mineral component of tooth enamel (82), and its nano-sized form has unique properties that enhance its effectiveness (83). Unlike traditional fluoride treatments, which only promote surface remineralization (84), nano-hydroxyapatite particles are small enough to penetrate microscopic enamel defects and rebuild the tooth structure from within. These nanoparticles can bind tightly to demineralized areas, filling in micro-cracks and early cavities while restoring the tooth's original strength and smoothness (85). Additionally, some advanced formulations include bioactive molecules that guide the crystalline growth of hydroxyapatite, mimicking the natural mineralization process. This makes nano-hydroxyapatite particularly effective for treating early-stage decay and reducing tooth sensitivity caused by enamel erosion (83, 86).

One of the key advantages of nano-hydroxyapatite is its biocompatibility, as it is chemically identical to the mineral found in natural teeth (87). This eliminates concerns about toxicity, making it suitable for long-term use in toothpaste, mouthwashes, and professional dental treatments (88, 89). Recent studies have shown that nano-hydroxyapatite forms a protective layer that resists acid attacks from bacteria and acidic foods. Some smart formulations are even designed to release minerals in response to pH changes, ensuring targeted remineralization when the oral environment becomes acidic (30, 83). Compared to fluoride, which primarily works by forming a more acid-resistant fluorapatite layer (90), nano-hydroxyapatite provides a more holistic repair mechanism by restoring the tooth's original mineral content. This makes it an attractive alternative for patients who prefer fluoride-free oral care products or are at high risk of cavities (85, 91).

Despite its promise, the widespread adoption of nano-hydroxyapatite in clinical dentistry faces some challenges. The long-term durability of remineralized enamel and the optimal concentration of nanoparticles for maximum efficacy still require further research. Additionally, manufacturing high-purity nano-hydroxyapatite at a cost-effective scale remains a hurdle for commercialization. However, ongoing advancements in nanotechnology and biomaterials are rapidly addressing these limitations. Future developments may include hybrid systems combining nano-hydroxyapatite with antimicrobial agents or bioactive peptides to enhance both repair and protection (92). As evidence of its effectiveness grows, nano-hydroxyapatite is poised to become a cornerstone of minimally invasive dentistry, offering a safe, natural, and highly effective way to preserve and restore enamel without the need for invasive procedures (93-95)(Figure 3).

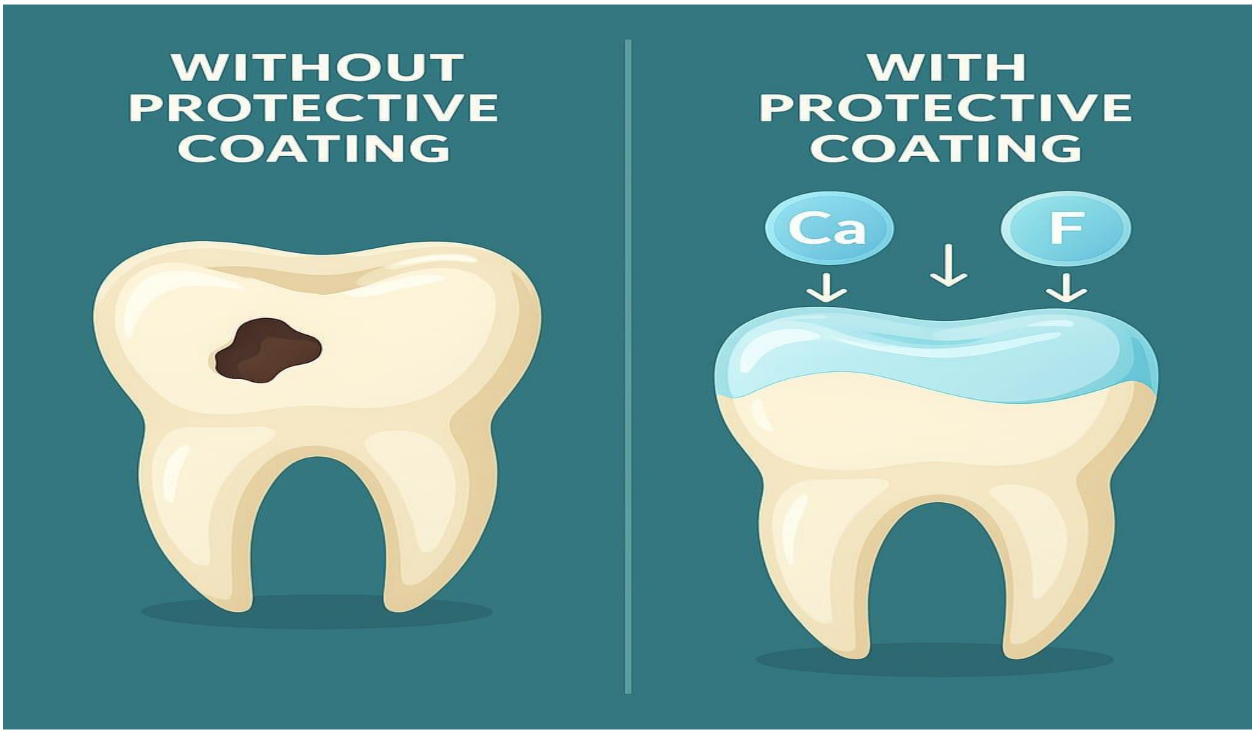

Figure.3: Smart remineralization of enamel using nano-calcium hydroxyapatite represents a groundbreaking approach in preventive dentistry.

Applications (treatment)

Targeted drug delivery for infections:

Targeted drug delivery using smart nanomaterials represents a transformative approach to treating oral infections, particularly in periodontal pockets where conventional treatments often fall short (96, 97). These advanced systems utilize nanoparticles engineered to release antibiotics directly at the infection site, responding to specific triggers like bacterial enzymes or acidic pH levels found in inflamed periodontal tissues (98). For instance, polymeric nanoparticles or liposomes can be loaded with antimicrobial agents such as doxycycline or metronidazole, then functionalized with targeting ligands that bind to bacterial biofilms (99, 100). This precision medicine approach ensures high drug concentrations exactly where needed while minimizing systemic exposure, reducing side effects and the risk of antibiotic resistance (101). Unlike traditional mouth rinses or oral antibiotics that disperse unevenly, smart nanocarriers penetrate deep into periodontal pockets, maintaining therapeutic drug levels for extended periods through controlled release mechanisms (102).

The design of these smart delivery systems incorporates several innovative features to enhance treatment efficacy. Some nanoparticles use pH-responsive polymers that swell and release their payload only in the acidic environment of infected pockets (103, 104), while others degrade in response to bacterial enzymes like matrix metalloproteinases (MMPs) (103). Additionally, researchers are developing multi-functional nanoparticles that combine antibacterial drugs with anti-inflammatory agents (e.g., curcumin or resolvins) (105) to simultaneously combat infection and modulate the host immune response (106, 107). Recent studies demonstrate that such systems can reduce periodontal pathogens like Porphyromonas gingivalis more effectively than conventional therapies, with animal models showing significant improvements in attachment loss and bone regeneration (108). Clinical trials are now exploring their use in adjunctive periodontal therapy, with some formulations designed for direct injection into pockets or as part of sustained-release gels applied during scaling and root planing procedures (109, 110).

Despite their potential, challenges remain in translating these laboratory successes into routine clinical practice. The long-term stability of nanoparticle formulations, precise control over drug release kinetics, and scalability of manufacturing processes require further optimization (111). Regulatory hurdles also exist, as the safety profiles of novel nanomaterials must be thoroughly evaluated, particularly regarding their potential accumulation in tissues or unintended immune responses. However, the field is advancing rapidly, with next-generation systems incorporating real-time monitoring capabilities using embedded nanosensors that could adjust drug release based on changing infection markers. As these technologies mature, smart nanomaterial-based drug delivery could redefine periodontal therapy, offering personalized, minimally invasive solutions that improve patient compliance and outcomes while addressing the global challenge of antimicrobial resistance in dentistry (112, 113).

Nano-antibiotics against resistant bacteria:

Smart nanomaterials have emerged as powerful weapons against antibiotic-resistant bacteria in oral infections, particularly against formidable pathogens like methicillin-resistant Staphylococcus aureus (MRSA) (114). Silver nanoparticles (AgNPs) are among the most promising nano-antibiotics, offering a multi-pronged attack on resistant bacteria. These tiny particles, typically ranging from 1-100 nm, exert antimicrobial effects through multiple mechanisms: they disrupt bacterial cell membranes, generate reactive oxygen species, and interfere with DNA replication and enzyme functions (115). Unlike conventional antibiotics that target specific bacterial pathways (which microbes can evolve to resist) (116), silver nanoparticles attack several cellular processes simultaneously, making it extremely difficult for bacteria to develop resistance. In oral health applications, AgNPs have been incorporated into dental adhesives, implant coatings, and even antimicrobial gels, effectively combating MRSA and other resistant strains in periodontal pockets, peri-implantitis, and oral mucosal infections (117-119).

The versatility of nano-antibiotics allows for innovative delivery methods that enhance their therapeutic potential. Silver nanoparticles can be combined with other nanomaterials, such as chitosan or graphene oxide, to create synergistic antimicrobial effects while improving biocompatibility (120, 121). Some advanced formulations use "smart" triggers, where the antibacterial activity of AgNPs is amplified in response to specific conditions like acidic pH or bacterial enzymes present in infected oral cavities (53, 122). Researchers are also developing hybrid systems where silver nanoparticles are loaded into hydrogel scaffolds or electrospun nanofibers, enabling controlled release directly at infection sites over extended periods (123, 124). These approaches are particularly valuable for treating deep periodontal infections or infected root canals, where traditional antibiotics often fail to penetrate effectively (125, 126). Studies demonstrate that nano-silver formulations can reduce MRSA biofilm formation by over 90%, while also preventing the colonization of other problematic oral pathogens like Pseudomonas aeruginosa and Enterococcus faecalis (62, 127).

Looking ahead, nano-antibiotics like silver nanoparticles represent a paradigm shift in managing resistant oral infections. Their broad-spectrum activity extends beyond bacteria to combat fungi and viruses, making them useful for treating opportunistic infections in immunocompromised patients (128, 129). New generations of "intelligent" nano-antibiotics are being engineered with surface modifications that enhance targeting specificity to infected tissues while sparing beneficial oral microbiota. Some experimental systems even combine AgNPs with photothermal therapy, where near-infrared light activation boosts their antibacterial potency. As dental research continues to refine these nanomaterials, they are poised to become indispensable tools in combating the growing crisis of antimicrobial resistance, offering more effective and durable solutions for maintaining oral health in an era of diminishing antibiotic efficacy (130-134).

Nano-enabled photodynamic therapy:

Nano-enabled photodynamic therapy (NE-PDT) represents a significant advancement in the targeted treatment of oral cancers and premalignant lesions. This approach utilizes light-activated smart nanoparticles that selectively destroy malignant cells while minimizing damage to surrounding healthy tissue. The therapeutic mechanism involves photosensitizing nanoparticles, typically composed of porphyrin derivatives, chlorophyll, or novel metal-organic frameworks, which generate cytotoxic reactive oxygen species (ROS) upon exposure to specific light wavelengths (135, 136). Compared to conventional PDT, nano-formulations offer enhanced tumor targeting through both passive accumulation (via the enhanced permeability and retention effect) and active targeting using surface-conjugated ligands that bind to overexpressed cancer biomarkers. This dual targeting capability significantly improves treatment precision while reducing common side effects associated with systemic photosensitizers, such as prolonged photosensitivity (137). Recent studies demonstrate that NE-PDT can achieve up to 90% cancer cell apoptosis in oral squamous cell carcinoma models, with particular efficacy against therapy-resistant tumor stem cells (138).

The design of these smart nanosystems incorporates several innovative features to optimize therapeutic outcomes. Some advanced platforms employ stimuli-responsive release mechanisms, where the photosensitizer remains inactive until encountering the tumor microenvironment's characteristic acidic pH or specific enzymes (139). Other systems combine PDT functionality with imaging capabilities, allowing real-time monitoring of treatment efficacy through fluorescence or photoacoustic imaging (140, 141). Particularly promising are transition metal-doped nanoparticles that enhance ROS generation through plasmonic effects, as well as upconversion nanoparticles that convert near-infrared light to visible wavelengths, enabling deeper tissue penetration for treating subepithelial lesions. These technological refinements address traditional PDT limitations related to poor light penetration in oral tissues and hypoxia-induced treatment resistance (142). Clinical trials investigating NE-PDT for oral leukoplakia have shown complete lesion resolution in some cases, with significantly reduced recurrence rates compared to surgical excision (143).

Beyond standalone applications, NE-PDT is being integrated into multimodal treatment regimens to combat advanced oral malignancies (144). Researchers are developing combinatorial platforms that couple photosensitizing nanoparticles with chemotherapeutic agents or immune checkpoint inhibitors, creating synergistic antitumor effects (145, 146). For instance, light-activated nanoparticles carrying both a photosensitizer and cisplatin demonstrate enhanced DNA damage in cancer cells while simultaneously overcoming chemoresistance mechanisms (147, 148). Another emerging approach involves photodynamic immunotherapy, where nanoparticle-generated ROS not only directly kill tumor cells but also stimulate potent antitumor immune responses through immunogenic cell death. These developments are particularly relevant for treating HPV-positive oropharyngeal cancers, where the immune-modulating effects of NE-PDT could potentially clear both primary tumors and metastatic foci (149-152).

The continued evolution of NE-PDT is being facilitated by advancements in material science and optical technologies. Next-generation systems now incorporate machine learning algorithms to optimize light dosimetry and nanoparticle distribution patterns, enabling personalized treatment protocols. With ongoing improvements in biocompatibility, manufacturing scalability, and regulatory approval pathways, NE-PDT is transitioning from experimental research to clinical reality. Its minimally invasive nature, precision targeting, and compatibility with other treatment modalities position this technology as a transformative approach in oral oncology, offering improved outcomes for patients with malignancies that are challenging to treat using conventional modalities (153, 154).

Future directions include the development of implantable light-emitting devices for repeated PDT sessions and the engineering of microbial-derived photosensitizers for targeted ablation of tumor-associated microbiota (155-157).

Smart Nano-scaffolds for Bone Regeneration and Periodontal Repair:

Periodontal disease and bone defects resulting from trauma or pathology present significant challenges in dental rehabilitation, necessitating innovative approaches for tissue regeneration (158). Smart nano-scaffolds have emerged as a promising solution, offering three-dimensional structures that mimic the extracellular matrix to guide cell proliferation and differentiation (159, 160). These scaffolds are engineered from biocompatible nanomaterials such as nano-hydroxyapatite, graphene oxide, or electrospun polymeric fibers, which provide both mechanical support and bioactive cues for tissue regeneration (161). Unlike traditional grafts, smart scaffolds can be functionalized with growth factors (e.g., BMP-2, PDGF) or gene therapies that are released in response to local microenvironmental cues, such as pH or enzymatic activity. This dynamic interaction enhances osteogenesis and periodontal ligament regeneration while minimizing off-target effects (162-164). Preclinical studies demonstrate that such nano-scaffolds can accelerate alveolar bone healing better compared to conventional materials, with simultaneous promotion of cementum and soft tissue attachment (165).

The regenerative capacity of these scaffolds is further augmented by their ability to recruit endogenous stem cells and modulate immune responses. Advanced designs incorporate mesenchymal stem cell (MSC)-specific binding peptides or chemotactic signals that direct host cells to the defect site, bypassing the need for exogenous cell transplantation (166). Some scaffolds are combined with conductive nanomaterials (e.g., carbon nanotubes) to deliver electrical stimuli that enhance osteogenic differentiation, particularly in large mandibular defects (167, 168). Additionally, 4D-printed smart scaffolds with shape-memory properties can adapt to complex anatomical contours upon implantation, improving surgical handling and tissue integration (169, 170). Research highlights their efficacy in treating intrabony periodontal defects, where hybrid nano-scaffolds loaded with amelogenin peptides have shown simultaneous regeneration of bone, periodontal ligament, and cementum—a critical triad for functional tooth support (171).

A key innovation in this field is the development of immunomodulatory nano-scaffolds that actively steer the healing process toward regeneration rather than fibrosis. By incorporating anti-inflammatory cytokines (e.g., IL-4, IL-10) (172, 173) or macrophage-polarizing nanoparticles, these scaffolds can resolve chronic inflammation associated with periodontitis and create a pro-regenerative microenvironment (174). For example, scaffolds releasing resolvin D1 from biodegradable nanoparticles have demonstrated significant reductions in periodontal inflammation coupled with enhanced bone formation in animal models (175, 176). Other systems leverage CRISPR-Cas9-loaded nanoparticles within scaffolds to locally edit genes involved in bone metabolism, offering potential for correcting genetic disorders affecting oral tissues. Such multifunctional platforms are being tested for complex reconstructions, including maxillofacial defects and peri-implant bone loss, where they outperform static biomaterials by dynamically interacting with the host tissue (177-179).

Despite these advances, clinical translation requires optimization of scaffold degradation rates to match tissue formation kinetics and standardization of manufacturing protocols. Emerging trends include the use of AI to design patient-specific scaffold architectures based on CT/MRI data and the integration of biosensors for real-time monitoring of healing progress. With ongoing clinical trials demonstrating safety and efficacy, smart nano-scaffolds are poised to revolutionize periodontal and bone regenerative therapies. Future directions include leveraging microbiome-modulating nanoparticles to prevent microbial disruption of healing and developing scaffolds with built-in antimicrobial properties for use in infected defect sites (180, 181).

Pain management:

Smart nanomaterials are transforming the landscape of pain management in dentistry through the development of advanced nano-carrier systems engineered for sustained and targeted anesthetic delivery (182). Traditional local anesthetics like lidocaine and bupivacaine are often constrained by their short duration of action, necessitating repeated administration and contributing to patient discomfort (183). Nano-carriers such as liposomes, polymeric nanoparticles, and solid lipid nanoparticles offer a promising solution by encapsulating anesthetic agents and modulating their release kinetics. These systems enable the maintenance of therapeutic concentrations at nerve terminals for extended durations, potentially ranging from several hours to multiple days, depending on their structural and compositional characteristics (184, 185). Notably, thermoresponsive liposomes can release their cargo in response to localized temperature changes at inflamed sites, while pH-sensitive nanoparticles exploit the acidic microenvironment of infected tissues to achieve targeted delivery. By enhancing the retention of anesthetics at the site of action and limiting systemic diffusion, these strategies not only prolong analgesia but also reduce the risk of adverse effects (186, 187).

The multifunctionality of nano-carrier platforms further allows for integrated approaches to pain control that combine anesthetics with anti-inflammatory or antimicrobial agents (188). For instance, hybrid nanoparticles co-loaded with ropivacaine and dexamethasone have demonstrated synergistic efficacy in mitigating postoperative pain and inflammation (189, 190). Recent innovations include the development of nerve-specific nano-formulations functionalized with targeting ligands, such as peptide-modified tetrodotoxin analogs, which exhibit selective binding to sodium channels on peripheral nerves, thereby enhancing anesthetic efficiency (191). Clinical studies have reported that bupivacaine-loaded nanocarriers can extend analgesic effects up to 72 hours following procedures like third molar extractions, a significant improvement over the 4–8 hours observed with conventional formulations. Moreover, the integration of imaging agents, such as quantum dots, into these systems facilitates real-time visualization of drug distribution, offering precise delivery within the complex anatomy of the oral cavity (185, 192-194).

Ongoing research is increasingly focused on the development of personalized and minimally invasive delivery systems. Mucoadhesive nano-gels designed for topical application to the oral mucosa provide controlled release of anesthetics in response to salivary conditions, while injectable nano-hydrogels form in situ depots that respond to enzymatic activity at inflamed sites (195, 196). Despite challenges related to scalability, reproducibility, and biodegradation, early clinical data underscore the significant potential of these technologies to reshape dental pain management. As these smart nano-systems continue to evolve, they may ultimately reduce or eliminate the reliance on opioid analgesics, offering more effective, longer-lasting, and patient-specific alternatives across a broad spectrum of dental procedures (197).

Challenges

Despite their immense potential, the widespread adoption of smart nanomaterials in dentistry faces several significant challenges. One major hurdle is ensuring biocompatibility and long-term safety, as nanoparticles may accumulate in tissues or trigger unintended immune responses (198, 199). Rigorous toxicological studies are needed to evaluate potential risks, particularly for metallic nanoparticles like silver or zinc oxide, which could exhibit cytotoxicity at higher concentrations (200, 201). Another critical issue is the stability and controlled degradation of these materials. some nano-formulations may break down too quickly, reducing their therapeutic efficacy, while others might persist too long, raising concerns about chronic exposure (202, 203).

Manufacturing complexities also pose barriers, as scaling up production while maintaining consistency in nanoparticle size, shape, and functionality remains technically demanding and costly (202). Regulatory frameworks for nano-dental products are still evolving, creating uncertainties in approval pathways and delaying clinical implementation (198). Additionally, the reproducibility of stimuli-responsive behaviors in diverse oral environments (e.g., varying pH, saliva composition, and microbial activity) requires further optimization to ensure reliable performance across patient populations (204, 205).

Patient-specific variability, such as differences in oral microbiome or healing responses, further complicates personalized applications (206). Finally, cost-effectiveness and accessibility must be addressed to ensure these advanced therapies benefit broader populations (207- 209). Overcoming these challenges will require interdisciplinary collaboration among material scientists, clinicians, and regulatory bodies to translate laboratory innovations into safe, effective, and affordable dental solutions (210- 212).

Conclusion

The integration of smart nanomaterials into dentistry represents a leap forward in oral healthcare. By using the unique properties of nanoparticles, bioactive scaffolds, and stimuli-responsive systems, these advanced materials enable more precise, effective, and long-lasting solutions for prevention and treatment. From combating resistant infections and regenerating damaged tissues to providing targeted pain relief and early disease detection. While challenges in clinical translation remain, the remarkable potential of these innovations promises to shift dentistry toward minimally invasive, personalized care.

Declaration of Interest

The authors of this article declared no conflict of interest.

Ethical Considerations

Not applicable.

Authors' Contributions

All authors equally contributed to this study.

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Transparency of Data

In accordance with the principles of transparency and open research, we declare that all data and materials used in this study are available upon request.

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Declaration

In order to correct and improve the academic writing of our paper, we have used the language model ChatGPT.

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