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Nanobots: The future of oral infection treatment

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ABSTRACT

Oral diseases such as gingivitis and periodontitis represent significant global health challenges, affecting a substantial portion of the population. These conditions, driven by bacterial biofilms, can cause severe damage to the tooth-supporting tissues, leading to tooth loss and impacting overall well-being. Traditional oral antibiotics face limitations, including broad-spectrum side effects and insufficient concentration at infection sites, often resulting in antimicrobial resistance. This mini-review explores the potential of nanobots for targeted drug delivery in treating oral infections. Nanobots, ranging from 1 to 100 nanometers, can navigate the oral cavity, directly targeting bacterial biofilms and releasing antimicrobial agents in a controlled manner. This targeted approach enhances drug concentration at infection sites, reduces systemic side effects, and minimizes resistance development. Various types of nanobots, such as dentifrobots and pharmacytes, are discussed for their roles in oral healthcare. Recent advancements demonstrate the efficacy of nanobots in vitro and in vivo, highlighting their ability to eradicate biofilms and deliver drugs precisely. However, challenges such as biocompatibility, stability, and regulatory hurdles must be addressed for clinical application. Future directions include integrating multifunctional capabilities for simultaneous infection treatment and tissue repair, real-time monitoring through advanced imaging and biosensing, and personalized therapies tailored to individual microbiomes. By overcoming these challenges, nanobots have the potential to revolutionize oral healthcare, offering innovative solutions to effectively manage and treat oral infections, ultimately improving patient outcomes and overall oral health.

KEYWORDS

Oral health; Biofilms; Nanotechnology; Nanobots; Infection

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Introduction

Oral diseases, particularly gingivitis and periodontitis, pose a significant global health burden, affecting 20-80% of the population, with severe cases accounting for about 11.2% [1]. These infections, driven primarily by bacterial biofilm formation, can damage the tooth-supporting apparatus, including both soft and hard tissues. If left untreated, these conditions can lead to tooth loss, significantly impacting oral health and overall well-being. Furthermore, periodontal diseases have been linked to systemic conditions such as cardiovascular disease, diabetes, and adverse pregnancy outcomes [2].

Conventional oral antibiotics, while revolutionary in their time, present several limitations in treating oral infections. Their broad-spectrum nature often leads to side effects, including allergic reactions, antibiotic-induced colitis, and disruption of beneficial microbial flora. Overuse and misuse of these antibiotics have also contributed to the growing problem of antimicrobial resistance. Additionally, the systemic administration of antibiotics often results in inadequate concentrations at the site of infection, reducing their effectiveness against oral biofilms and necessitating alternative approaches for more efficient treatment [3].

Nanotechnology offers a promising solution to these challenges through the development of nanobots for targeted drug delivery. These nanoscale devices, typically ranging from 1 to 100 nanometers, can be engineered to deliver drugs precisely to the site of infection in the oral cavity, minimizing side effects and enhancing therapeutic efficacy [4]. Nanobots can navigate the complex environment of the mouth, directly targeting bacterial biofilms and releasing antimicrobial agents in a controlled manner, thereby improving treatment outcomes. This targeted approach not only improves the concentration of the drug at the infection site but also reduces the overall dosage required, minimizing potential side effects and resistance development [5].

This review aims to explore the potential of nanobots in combating oral infections, providing an overview of current research and advancements in this innovative field. By examining the latest studies and technological developments, we hope to highlight the promise of nanobots in revolutionizing the treatment of oral diseases.

Oral Biofilms and Challenges in Treatment

Oral biofilms, commonly known as dental plaque, form when oral bacteria adhere to the tooth surface and begin to multiply. This process starts with the initial attachment of planktonic bacteria to the enamel, mediated by specific adhesion molecules and the pellicle, a proteinaceous film derived from saliva. As bacteria colonize, they produce extracellular polymeric substances (EPS) that help bind the cells together and to the tooth surface. Over time, this community of microorganisms matures into a complex, structured biofilm that can include over 500 different bacterial species, creating a robust and persistent bacterial ecosystem on the teeth [6].

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The intricate structure of oral biofilms is maintained by the extracellular matrix (ECM), which consists of polysaccharides, proteins, and extracellular DNA (eDNA). This matrix is crucial for the stability and resilience of the biofilm [7]. It provides a scaffold that holds the bacterial cells in place, facilitating communication and nutrient exchange. Importantly, the ECM acts as a protective barrier, shielding the bacteria from environmental stresses, including antimicrobial agents. The ECM's dense and sticky nature limits the penetration of antibiotics, making it difficult for these drugs to reach and effectively kill the bacteria within the biofilm [8]. This protective feature contributes significantly to the persistence of biofilm-associated infections, as bacteria embedded in the ECM can survive even high concentrations of antibiotics that would typically be lethal to planktonic bacteria. Additionally, the ECM can bind and neutralize antimicrobial compounds, further enhancing the biofilm's defense mechanisms [6].

Biofilms inherently reduce the penetration of antibiotics, significantly contributing to antibiotic resistance. The ECM acts as a physical and biochemical barrier, impeding the diffusion of antibiotic molecules into the deeper layers of the biofilm. Furthermore, the close proximity of bacterial cells within biofilms facilitates the transfer of antibiotic resistance genes through horizontal gene transfer mechanisms. The environment within the biofilm, characterized by nutrient gradients and varied microenvironments, promotes the survival of persister cells—dormant variants of regular cells that are highly tolerant to antibiotics [9]. These factors collectively result in biofilm-associated bacteria being 10 to 1000 times more resistant to antibiotics compared to their planktonic counterparts, posing a significant challenge in clinical treatment [10].

Current treatment methods for oral infections, including scaling and root planing, the use of antibiotics, and antimicrobial rinses face significant limitations [11]. Scaling and root planing are effective at physically disrupting biofilms on accessible surfaces but may not reach bacteria in deeper periodontal pockets [12]. Antibiotics can reduce bacterial load but are often insufficient alone due to limited penetration and the high resistance of biofilm-associated bacteria. Antimicrobial rinses provide temporary relief but cannot eradicate well-established biofilms. These limitations highlight the need for novel therapeutic strategies that effectively target and disrupt biofilms to improve oral health outcomes.

Nanobots: Precision Technology in Drug Delivery

Nanobots, also referred to as nanorobots, represent a groundbreaking advancement in nanorobotics, specifically designed for intricate tasks at the nanoscale within the human body. Typically ranging from 1 to 100 nanometers in size, nanobots are engineered to interact with cells and penetrate cellular structures, enabling targeted applications in medicine [4]. Their ability to navigate biological environments and respond to specific cues, such as detecting and neutralizing pathogens within biofilms, distinguishes them from conventional nanomaterials used in drug delivery [13].

These miniature devices can be constructed from various biocompatible materials, ensuring safe interaction within biological systems. Materials such as diamond or diamondoid/fullerene nanocomposites provide chemical stability and compatibility with bodily environments, thereby minimizing the risk of adverse reactions. Incorporating elements like oxygen and nitrogen further enhances their functionalities, catering to diverse biomedical applications [14].

The fabrication of nanobots involves sophisticated techniques such as physical vapor deposition (PVD) and self-crimping in top-down approaches, and template-assisted electrodeposition and self-assembly in bottom-up methods. These methods offer precise control over material properties and structural design, essential for their effective operation in medical applications, including targeted drug delivery and therapeutic interventions [15].

Nanobots are developed in various types, each tailored for specific functions in drug delivery. Dentifrobots, for example, are designed for oral healthcare, navigating the oral cavity to deliver antimicrobial agents directly to dental plaque and infected gum tissues. This targeted approach minimizes systemic side effects while enhancing treatment outcomes for conditions like periodontal disease and dental caries [16]. Pharmacytes, another type of nanobot, transport drugs precisely to targeted areas within the body, optimizing treatment efficacy and reducing adverse reactions [17].

Microbivores, on the other hand, act as mechanical white blood cells capable of identifying and neutralizing pathogens. In dentistry, they could revolutionize the treatment of oral infections by selectively targeting harmful bacteria, thereby mitigating oral diseases more effectively than traditional methods [18]. Additionally, nanobots like respirocytes and clottocytes offer specialized functionalities such as enhanced tissue oxygenation and rapid hemostatic control, respectively, which are crucial in managing complications during oral surgeries or treatments [19].

Advantages of using nanobots for drug delivery in oral health include enhanced drug bioavailability and localized delivery to infected areas. By navigating complex biological environments, nanobots can deliver therapeutic payloads directly to targeted sites, minimizing off-target effects and reducing the required drug dosage. This precision not only improves treatment efficacy but also enhances patient safety by limiting exposure to healthy tissues, thereby minimizing systemic side effects. Controlled drug release mechanisms further ensure sustained therapeutic action, optimizing treatment outcomes for oral infections and related conditions [20].

In recent advancements, nanobots like chemotaxis-guided hybrid neutrophil micromotors and DNA origami nanorobots have demonstrated exceptional capabilities in delivering drugs precisely within the oral cavity [21]. These innovations, powered by mechanisms such as magnetic fields or chemical reactions, enable precise positioning and controlled drug release, enhancing therapeutic efficacy for oral infections. Moreover, biocompatible and biodegradable materials are integrated into nanobots to ensure safety and efficient degradation post-treatment, addressing concerns regarding long-term accumulation and inflammatory reactions [22].

Nanobots for Oral Infections: Current Research and Applications

Nanobots designed for combating oral infections require meticulous planning to ensure efficacy and safety within the complex oral environment. Biocompatibility and

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biodegradability are critical, with materials like nanophase hydroxyapatite and carbon chosen for their ability to integrate well with oral tissues and degrade naturally [4]. Effective targeting involves programming nanobots to recognize and adhere to specific pathogens embedded in biofilms. For instance, silica-based nanobots loaded with antimicrobial peptides can be catalytically driven to infection sites, demonstrating potent bactericidal activity against various pathogenic strains [20].

Nanobots employ diverse strategies for controlled drug delivery, including self-driven mechanisms using chemical fuels like H2O2 to produce microbubbles that propel them through biofilms. This approach ensures localized release of antimicrobial agents, reducing systemic exposure and enhancing treatment efficacy [23]. Additionally, stimuli-responsive nanobots adjust drug release based on environmental cues such as pH and temperature variations in biofilm microenvironments [20]. For instance, magnetic field-directed nanobots can dynamically alter their shape and produce reactive oxygen species (ROS) to eradicate biofilms while minimizing damage to surrounding tissues. These capabilities make nanobots a promising avenue for targeted oral infection treatment [24].

Research on nanobots for oral infections has made significant strides, showcasing both in-vitro and in-vivo potential. Autonomous biomaterials, like hydrogels and micro/nanobots, have been engineered to sense, respond, and adapt to various stimuli, providing a futuristic alternative for disease treatment. These nanobots can perform tasks such as sensing, diagnostics, delivery, and detoxification through autonomous or externally powered propulsion. The design of micro/nanobots often mimics the behavior of biological organisms, enabling them to integrate seamlessly with biological systems [25].

In-vitro studies have demonstrated the efficacy of nanobots loaded with antibiotics in killing oral pathogens. For instance, silica-based robots loaded with cationic antimicrobial peptides (AMPs) like LL-37 and K7-Pol have shown bactericidal activity against a range of gram-positive and gram-negative bacteria, including S. aureus, P. aeruginosa, E. coli, Acinetobacter baumannii, and Klebsiella pneumoniae. Self-driven microbots, using TiO2 nanoparticles and H2O2, were able to reduce dental biofilm viability by 95%. These microbots produce reactive oxygen species (ROS), such as hydroxyl radicals, which have a potent antimicrobial effect on the dental plaque surface [26].

In-vivo studies, though limited, have shown promising results. Catalytic antimicrobial robots using iron nanoparticles (Fe3O4 NPs) demonstrated the ability to eradicate S. mutans biofilms in a human tooth model. These nanobots, driven by an external magnetic field, not only removed the biofilm but also produced ROS, leading to bacterial cell death. The dynamically assembled magnetic bristles of the nanobots could modify their shape, length, and stiffness to effectively remove the biofilm. Furthermore, the study validated the use of these nanobots for diagnostic sampling of disease-causing biofilms, collecting traces of bacteria, fungi, and extracellular polymeric substances (EPS) [27].

Translating nanobot technology into clinical applications faces several significant challenges. The sensitivity of catalytic nanoparticles to environmental changes, such as pH and temperature, complicates their stability and functionality in biological media. Developing stable coatings to enhance the stability of nanoparticles, ensuring long circulation times in biological environments, and controlling the locomotion of nanobots are critical areas requiring further research. The biocompatibility and safety of nanobots must be rigorously assessed, as any adverse reactions could hinder their clinical use. Additionally, regulatory hurdles must be addressed to ensure the safe and effective use of nanobots in medical settings. The cost and complexity of manufacturing nanobots at a scale suitable for clinical use also pose significant barriers. Ensuring precise control over nanobot movements and actions within the human body is essential for their success in clinical applications. More research and development are needed to overcome these obstacles, including enhancing the stability of nanobots in physiological conditions, improving their targeting accuracy, and ensuring their safe and efficient clearance from the body after completing their therapeutic tasks [4].

By addressing these challenges, nanobots have the potential to revolutionize the treatment of oral infections, offering targeted, non-invasive, and highly effective therapeutic options.

Future Directions and Considerations

The future of nanobots for treating oral infections is promising, with several advancements on the horizon.

Future nanobots are envisioned not only to deliver antibiotics but also to integrate anti-inflammatory drugs and regenerative materials simultaneously. This approach aims to synergistically combat infection, reduce inflammation, and promote tissue repair. For instance, multifunctional nanobots could employ stimuli-responsive mechanisms to release antibiotics upon detecting specific pathogens within oral biofilms. This targeted therapy approach minimizes systemic side effects while maximizing therapeutic efficacy, potentially revolutionizing treatment outcomes in oral healthcare [28].

The incorporation of advanced imaging and biosensing capabilities into nanobots holds promise for real-time monitoring of treatment progress in oral infections. Nanobots equipped with biosensors can detect microbial activities and biomarker concentrations within biofilms, providing clinicians with valuable feedback on treatment efficacy. Real-time monitoring enables timely adjustments in therapeutic strategies, enhancing precision and personalized treatment approaches.

The future of nanobot-based therapies includes personalized approaches tailored to individual oral microbiomes and infection profiles. By leveraging nanotechnology, treatments can be customized to target specific pathogens identified through microbial analysis. This personalized medicine approach ensures precise delivery of therapeutic agents to infection sites, optimizing therapeutic outcomes while minimizing adverse effects on beneficial oral flora [14].

Ethical considerations surrounding nanobot use in oral healthcare encompass potential cytotoxicity, environmental impact, and regulatory challenges. Ensuring nanobots are biocompatible and biodegradable is crucial to mitigate cytotoxic risks and environmental effects upon disposal. Regulatory frameworks must evolve to address safety concerns, standardize testing protocols, and establish

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guidelines for ethical use in clinical settings. Transparency in research and development practices is essential to build public trust and acceptance of nanobot technology. Additionally, ethical discourse should focus on equitable access to nanobot-based therapies, addressing socio-economic disparities in healthcare delivery. Collaborative efforts between researchers, regulatory bodies, and healthcare providers are essential to navigate ethical complexities and ensure responsible innovation in nanobot applications for oral infection treatment [5].

Conclusions

This mini-review highlights the significant potential of nanobots in the treatment of oral infections, offering a targeted and efficient approach to drug delivery. By directly targeting bacterial biofilms in the oral cavity, nanobots can enhance the concentration of therapeutic agents at the infection site, thereby improving treatment efficacy and reducing systemic side effects. Current research underscores their ability to navigate complex oral environments, release drugs in a controlled manner, and effectively combat pathogens. The capability of nanobots to penetrate biofilms and deliver antimicrobial agents precisely where needed addresses the limitations of conventional antibiotics and mechanical treatments. As advancements continue, nanobots hold the promise of transforming oral healthcare, providing innovative solutions to longstanding challenges in managing oral infections. Through continued research and development, nanobots could revolutionize the treatment of gingivitis, periodontitis, and other oral diseases, ultimately improving patient outcomes and enhancing overall oral health.

Disclosure statement

No potential conflict of interest was reported by the author.

References

1. Khabadze Z, Kulikova A, Generalova Y, Abdulkerimova S, Dashtieva M, Bakaev Y, et al. The prevalence of inflammatory periodontal diseases (gingivitis, periodontitis) among the population. J Int Dent Med Res. 2023;16(4):1830-1835.
2. Chatzopoulos GS, Jiang Z, Marka N, Wolff LF. Periodontal disease, tooth loss, and systemic conditions: an exploratory study. Int Dent J. 2024;74(2):207-215. https://doi.org/10.1016/j.identj.2023.08.002
3. Contaldo M, D'Ambrosio F, Ferraro GA, Di Stasio D, Di Palo MP, Serpico R, et al. Antibiotics in dentistry: A narrative review of the evidence beyond the myth. Int J Environ Res Public Health. 2023;20(11):6025. https://doi.org/10.3390/ijerph20116025
4. Viswa Chandra R. Nanorobotics in Dentistry. Nanomat Dent Med. 2023:121-139. https://doi.org/10.1007/978-981-19-8718-2_7
5. Malik S, Waheed Y. Emerging applications of nanotechnology in dentistry. Dent J. 2023;11(11):266. https://doi.org/10.3390/dj11110266
6. Shree P, Singh CK, Sodhi KK, Surya JN, Singh DK. Biofilms: Understanding the structure and contribution towards bacterial resistance in antibiotics. Med Microecol. 2023;16:100084. https://doi.org/10.1016/j.medmic.2023.100084
7. Serrage HJ, Jepson MA, Rostami N, Jakubovics NS, Nobbs AH. Understanding the matrix: the role of extracellular DNA in oral biofilms. Front Oral Health. 2021;2:640129. https://doi.org/10.3389/froh.2021.640129
8. Jakubovics NS, Goodman SD, Mashburn-Warren L, Stafford GP, Cieplik F. The dental plaque biofilm matrix. Periodontol 2000. 2021;86(1):32-56. https://doi.org/10.1111/prd.12361
9. Das A, Patro S, Simnani FZ, Singh D, Sinha A, Kumari K, et al. Biofilm Modifiers: The disparity in paradigm of oral biofilm ecosystem. Biomed Pharmacother. 2023;164:114966. https://doi.org/10.1016/j.biopha.2023.114966
10. Tan P, Wu C, Tang Q, Wang T, Zhou C, Ding Y, et al. pH-triggered size-transformable and bioactivity-switchable self-assembling chimeric peptide nanoassemblies for combating drug-resistant bacteria and biofilms. Adv Mat. 2023;35(29):2210766. https://doi.org/10.1002/adma.202210766
11. Kang Y, Sun B, Chen Y, Lou Y, Zheng M, Li Z. Dental plaque microbial resistomes of periodontal health and disease and their changes after scaling and root planing therapy. Msphere. 2021;6(4):10-128. https://doi.org/10.1128/msphere.00162-21
12. Mahuli SA, Zorair AM, Jafer MA, Sultan A, Sarode G, Baeshen HA, et al. Antibiotics for periodontal infections: Biological and clinical perspectives. J Contemp Dent Pract. 2020;21:372-376. https://doi.org/10.5005/jp-journals-10024-2797
13. Hu M, Ge X, Chen X, Mao W, Qian X, Yuan WE. Micro/nanorobot: A promising targeted drug delivery system. Pharmaceutics. 2020;12(7):665. https://doi.org/10.3390/pharmaceutics12070665
14. Hussain S, Khan MA, Rajan R, Jyoti J, Sharma S, Sahu SK. Nanorobots: The future of healthcare. InAIP Conference Proceedings. AIP Publishing. 2023; 2800(1). https://doi.org/10.1063/5.0162904
15. He T, Yang Y, Chen XB. Preparation, stimulus–response mechanisms and applications of micro/nanorobots. Micromachines. 2023;14(12):2253. https://doi.org/10.3390/mi14122253
16. Thomas S and Baiju RM. Nanotechnology and medicine: The interphase. Nanomat Dent Med 2023:1-31. https://doi.org/10.1007/978-981-19-8718-2_1
17. Panda V, Saindane A, Pandey A. Nanobots: Revolutionising the next generation of biomedical technology and drug therapy. Curr Drug Ther. 2024;19(4):403-412. https://doi.org/10.2174/1574885518666230726123433
18. Patole V, Tupe A, Tanpure S, Swami R, Vitkare V, Jadhav P. Nanorobotic artificial blood components and its therapeutic applications: A minireview. Ir J Med Sci (1971-). 2024:1641-1650. https://doi.org/10.1007/s11845-024-03617-5
19. Neagu AN, Jayaweera T, Weraduwage K, Darie CC. A Nanorobotics-Based Approach of Breast Cancer in the Nanotechnology Era. Int J Mol Sci. 2024;25(9):4981. https://doi.org/10.3390/ijms25094981
20. Montoya C, Roldan L, Yu M, Valliani S, Ta C, Yang M, et al. Smart dental materials for antimicrobial applications. Bioact Mat. 2023;24:1-9. https://doi.org/10.1016/j.bioactmat.2022.12.002
21. Zhou Y, Ye M, Hu C, Qian H, Nelson BJ, Wang X. Stimuli-responsive functional micro-/nanorobots: a review. ACS nano. 2023;17(16):15254-15276. https://doi.org/10.1021/acsnano.3c01942
22. Chen B, Sun H, Zhang J, Xu J, Song Z, Zhan G, et al. Cell-based micro/nano-robots for biomedical applications: A Review. Small. 2024;20(1):2304607. https://doi.org/10.1002/smll.202304607
23. Yin Z, Liu Y, Anniwaer A, You Y, Guo J, Tang Y, et al. Rational designs of biomaterials for combating oral biofilm infections. Adv Mat. 2023:2305633. https://doi.org/10.1002/adma.202305633
24. Nahar L, Sarker SD. Nanotechnology and oral health. Advances in Nanotechnology-Based Drug Delivery Systems. 2022:155-176. https://doi.org/10.1016/B978-0-323-88450-1.00014-4
25. Oral CM and Pumera M. In vivo applications of micro/nanorobots. Nanoscale. 2023;15(19):8491-507. https://doi.org/10.1039/D3NR00502J
26. Arqué X, Torres MD, Patiño T, Boaro A, Sánchez S, de la Fuente-Nunez C. Autonomous treatment of bacterial infections in vivo using antimicrobial micro-and nanomotors. ACS Nano. 2022;16(5):7547-7558. https://doi.org/10.1021/acsnano.1c11013
27. Ray RR, Pattnaik S. Technological advancements for the management of oral biofilm. Biocatal Agric Biotechnol. 2024;56:103017. https://doi.org/10.1016/j.bcab.2023.103017
28. Sachdeva S, Mani A, Mani SA, Vora HR, Gholap SS, Sodhi JK. Nano-robotics: The future of health and dental care. IP Int J Perio Implant. 2021;6:6-10. https://doi.org/10.18231/j.ijpi.2021.002

https://doi.org/10.61577/ohmr.2024.100007