

Nanoparticle-Mediated Biofilm Eradication: Overcoming Multidrug Resistance in Clinical Pathogens

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Abstract

Biofilm-associated infections remain a major challenge in healthcare due to biofilms' ability to protect bacteria from antibiotics and host immune responses, contributing significantly to the rise of antimicrobial resistance (AMR). Nanoparticle (NP)-based strategies effectively combat biofilms by improving drug delivery, penetrating biofilm matrices, and exerting antimicrobial activity. Recent advances in metallic, polymeric, and lipid nanoparticles targeting biofilm-forming bacteria show disruption of biofilm structure, reactive oxygen species (ROS) generation, quorum-sensing inhibition, and targeted antimicrobial delivery. These approaches outperform antibiotics in reducing biofilms; optimizing design, safety, and clinical translation is key for MDR treatment.

Keywords: Antimicrobial; Polymeric; Biofilm; Antibiotics; Nanoparticle and Drug Delivery

1. Introduction

Bacterial biofilms are highly organized microbial communities encased in a self-produced extracellular polymeric substance (EPS) matrix composed mainly of polysaccharides, proteins, lipids, and extracellular DNA. This matrix provides structural integrity while enabling cell-cell communication and protection against environmental stresses. Over 80 percent of chronic and persistent infections are due to biofilms which can be colonized in a very broad environment, encompassing human tissues, medical devices alongside industrial equipment. The shift of bacteria to the sessile biofilm-associated lifestyle is accompanied by extensive physiological and genetic alterations, like the drop-in metabolic activity and the changes in gene expression patterns (Rotello, 2023).

The extraordinary resistance to antimicrobial agents (AMAs) is an extremely clinically important aspects of biofilms and it is ubiquitously found to be at least 1000x than their planktonic counterparts. This tolerance roots from various reasons, such as low antimicrobial penetration via the EPS matrix, low evolving rates of biofilm cells, stimulation of stress pathways, and efflux pump overexpression (Chaturvedi and Ranjan, 2025). The thick and structured biofilm habitat also facilitates horizontal gene transfer, especially of antimicrobial resistance (AMR) determinants and enhances the pace of the global AMR crisis and complicates treatment plans, as well.

The traditional antibiotics do not always work against the biofilm-related cases of infections and result in the prolongation of the condition, recurrence, and higher costs of medical care. Such restrictions have necessitated frantic quest of alternative and complementary therapies. Nanotechnology is an effective strategy in fighting biofilms that have been revealed in recent years to be a groundbreaking method. Owing to the ability to penetrate biofilm matrices, disrupt microbial membranes, generate ROS, interfere with quorum sensing pathways, and be effective vectors to deliver drugs to specific cells, nanoparticles (NPs) can be utilized because of the nanoscale size, and high surface area, alongside the possibility to tune physicochemical properties (Imran, et al., 2022; Chia, et al., 2020). This work will critically review

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and synthesize existing literature on nanoparticle-based strategy to eliminate biofilms, with particular emphasis on how these can be utilized to overcome multidrug resistance in clinically relevant bacterial pathogens.

1.1. Biofilm Structure and Antibiotic Resistance

Biofilms are organized microbial communities surrounded by self-produced EPS matrix comprising of polysaccharides, proteins, extracellular DNA (eDNA), and lipids. The EPS is a physical and chemical barrier which restricts diffusion of antibiotics, pH changes inside the microenvironment and resistance determinants' horizontal transfer. Biofilm formation is a process that includes several phases: initial, reversible alongside irreversible adhesion, EPS generation, maturation and finally, dispersion. Slow growing and dormant cells, commonly known as persisters, are especially imbued with antibiotic resistance to antibiotics that act on actively-dividing cells in this matrix (Singh et al., 2025; Rather et al., 2021).

1.2. Nanoparticle Strategies for Biofilm Eradication

1.2.1. Silver (Ag) Nanoparticles

One of the most widely studied NP antibiofilm agents is silver nanoparticles. AgNPs release Ag⁺ ions that damage the bacterial cell membranes, disrupt cellular respiration, and produce ROS, which cause the death of bacteria (More et al., 2023). They are also anti-bacterial adhesive and anti-bacterial EPS. AgNP-antibiotic hybrids which synergistically lower minimum inhibitory concentrations (MICs) and biofilm viability of MDR pathogens such as *Pseudomonas aeruginosa* and *Staphylococcus aureus*, are often less toxic than their constituent high-dose antibiotics (Eyni et al., 2025).

1.2.2. Zinc Oxide (ZnO) and Titanium Dioxide (TiO₂)

ZnO and TiO₂ nanoparticles cause the production of ROS and impair the membrane of bacterial cells. Biosynthesized TiO₂NPs are shown to significantly reduce (up to approximately 94%) biofilm formation by MDR *P. aeruginosa* along with increase antibiotic activity in synergy with antibiotics such as piperacillin (Haji et al., 2024).

1.2.3. Polymeric Nanoparticles and Nanogels

Biodegradable polymeric NPs (e.g., chitosan, polylactic-co-glycolic acid (PLGA), alginate) help in enhancing drug delivery through protecting antibiotics and enhancing pharmacokinetics and releasing the drug over an extended period. They can also interact with the negatively charged bacterial membranes electrostatically on their cationic surfaces to destroy integrity. The targeted delivery of antibiotics in the form of polymeric nanocarriers enhances the availability of antibiotics in biofilms, which lowers the dosage required and, in the process, it could lower systemic toxicity (Feczko, 2021).

1.2.4. Lipid-Based and Hybrid Nanocarriers

Intracellular delivery of AMAs is also mediated by lipid nanocarriers like liposomes and nanophytosomes which can cross biofilm matrices because they have a flexible bilayer structure. Herbal extracts of nanophytosomes have some potential in fighting MDR *Escherichia coli* infections in the urinary tract models and this highlights the versatility of these nanoparticles (Ahsan et al., 2024). Michael Metz and David Teague have presented metal-polymer hybrid materials and dendrimer-based composite materials that improve the efficacy of antibiotics in the treatment of biofilms by growing the activity of these compounds and materials through intrinsic antimicrobial action combined with active delivery of the antibiotics or bioactive molecules, showing high efficacy in even complex biofilms (Zhang et al., 2023).

2. Mechanisms of Nanoparticle Biofilm Disruption

Nanoparticles cause disturbance in the microbial biofilms in various complementary physicochemical and biological processes which exploit the intrinsic resistance of biofilm-based pathogens collectively. Because of their nanoscale size and surface reactivity, nanoparticles can be effectively transported to the EPS matrix and compromise the structural integrity and later, increasing the diffusion of AMAs across the deeper layers of the biofilm (Farah et al., 2026). Metallic nanoparticles and metal oxide NPs can further produce ROS that causes oxidative stress, resulting in lipid peroxidation of bacterial membranes, protein denaturation, and damage to DNA, and hence bacterial cell death. Interaction between positively charged NPs and negatively charged bacterial cell envelope is electrostatic in nature leading to membrane destabilization, increased permeability, and intracellular contents leakage (Munir et al., 2022).

3. Future Perspectives

The advanced nanoparticle platforms that integrate precision targeting, responsiveness and immunomodulation are anticipated to be used by future antibiofilm strategies to address the weaknesses of current therapies. A promising future direction is smart or stimuli-responsive nanoparticles, which can be programmed to release antimicrobial payloads in response to biofilm-specific microenvironmental signals (i.e. acidic pH, bacterial enzymes, redox gradients) to maximize efficacy and reducing off-target toxicity. The other novel strategy is the system of CRISPR-nanoparticle hybrids that allows the targeted delivery of gene-editing vectors to interrupt the antibiotic resistance genes or biofilm-related virulence factors of microbial communities and re-sensitizes multidrug-resistant pathogens to conventional antibiotics, as mentioned in the recent knowledge.

4. Conclusion

The utilization of nanoparticles is a revolutionary line of attack on multidrug-resistant biofilm infections. Their versatile actions- including ROS generation and quorum sensing inhibition and the increased antibiotic delivery- provide significant benefits in comparison with traditional therapy. Despite the limitations of clinical translation, the combination of sophisticated materials science and microbiology can make biofilm-related infection control a paradigm shift and solve the problem of the global AMR crisis.

Disclosure of conflict of interest

No conflict of interest.

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