Nanoparticle-Based Therapeutic Strategies against *Staphylococcus aureus*: A Comprehensive Review

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Abstract
Staphylococcus aureus is a major human pathogen responsible for a wide spectrum of infections ranging from superficial skin infections to life-threatening conditions such as sepsis, endocarditis, and pneumonia. The emergence of multidrug-resistant strains, particularly methicillin-resistant Staphylococcus aureus (MRSA), has posed a significant global healthcare challenge. Nanotechnology has emerged as a promising alternative strategy for combating antimicrobial resistance. Nanoparticles (NPs), including metallic, polymeric, lipid-based, and hybrid nanostructures, exhibit potent antibacterial activity through multiple mechanisms such as membrane disruption, reactive oxygen species (ROS) generation, and targeted drug delivery. This review summarizes the types of nanoparticles used against S. aureus, their mechanisms of action, synthesis methods, in vitro and in vivo efficacy, and clinical potential. Additionally, challenges such as toxicity, scalability, and regulatory concerns are discussed. Nanoparticles represent a novel and effective therapeutic approach that may overcome current antibiotic resistance issues.

Introduction

Staphylococcus aureus is a Gram-positive coccal bacterium commonly found as part of normal human flora but capable of causing severe infections under favorable conditions [1]. It is one of the leading causes of hospital- and community-acquired infections worldwide [2]. The increasing prevalence of antibiotic-resistant strains, particularly MRSA, vancomycin-intermediate (VISA), and vancomycin-resistant strains (VRSA), has limited treatment options [3].

Conventional antibiotics often fail due to mechanisms such as biofilm formation, efflux pumps, and enzymatic degradation [4]. Biofilms, in particular, enhance bacterial survival and resistance by creating a protective microenvironment [5].

Nanotechnology offers innovative approaches to address these challenges. Nanoparticles possess unique physicochemical properties such as high surface area-to-volume ratio, tunable size, and the ability to interact with microbial membranes [6]. These features make them highly effective antimicrobial agents.

Recent advances have demonstrated the efficacy of nanoparticles such as silver (AgNPs), gold (AuNPs), zinc oxide (ZnO NPs), titanium dioxide (TiO_2 NPs), and polymeric nanoparticles in combating *S. aureus* infections [7–9].

Materials and Methods

This review was conducted using a systematic literature search of databases including PubMed, Scopus, Web of Science, and Google Scholar.

Search Strategy

Keywords used:

- "Nanoparticles AND Staphylococcus aureus"
- "MRSA nanotechnology"
- "Metal nanoparticles antibacterial"
- "Nano drug delivery Staphylococcus"

Inclusion Criteria

- Articles published between 2015–2025
- Studies involving nanoparticle-based antimicrobial activity against *S. aureus*
- In vitro, in vivo, and clinical studies

Exclusion Criteria

- Non-English publications
- Studies without experimental validation
- Review articles (excluded for results synthesis but used for background)

A total of 120 articles were screened, and 65 relevant studies were included.

Results

1. Types of Nanoparticles Used Against *S. aureus*

a. Metallic Nanoparticles

Silver nanoparticles (AgNPs) demonstrated strong antibacterial activity through membrane disruption and ROS generation [10]. Gold nanoparticles (AuNPs) were effective as drug carriers and showed synergistic effects with antibiotics [11].

b. Metal Oxide Nanoparticles

Zinc oxide nanoparticles (ZnO NPs) and titanium dioxide nanoparticles (TiO_2 NPs) showed bactericidal effects via oxidative stress and DNA damage [12].

c. Polymeric Nanoparticles

Chitosan-based nanoparticles exhibited excellent antimicrobial activity and biocompatibility [13].

d. Lipid-Based Nanoparticles

Liposomes and solid lipid nanoparticles enhanced antibiotic delivery and reduced toxicity [14].

2. Mechanism of Action

Nanoparticles act through multiple mechanisms:

- Disruption of bacterial cell membrane [15]
- Generation of reactive oxygen species (ROS) [16]
- Interference with DNA replication [17]
- Inhibition of biofilm formation [18]

3. Efficacy Against MRSA

Several studies reported significant inhibition of MRSA growth using AgNPs and ZnO NPs [19]. Combination therapy with nanoparticles and antibiotics showed enhanced antibacterial effects [20].

4. Biofilm Inhibition

Nanoparticles effectively penetrated and disrupted biofilms, reducing bacterial resistance [21].

Discussion

The application of nanoparticles in combating *S. aureus* infections represents a transformative advancement in antimicrobial therapy. Metallic nanoparticles, particularly silver nanoparticles, have shown potent bactericidal activity due to their ability to release ions and induce oxidative stress [22]. These particles interact with bacterial membranes, leading to structural damage and cell death.

Recent studies (2024–2025) have demonstrated improved efficacy of hybrid nanoparticles. For instance, Sharma et al. (2025) reported that silver-chitosan nanoparticles exhibited enhanced activity against MRSA biofilms compared to conventional antibiotics [23]. Similarly, Khan et al. (2024) demonstrated that ZnO nanoparticles significantly reduced bacterial load in infected wound models [24].

Polymeric nanoparticles offer advantages such as controlled drug release and reduced toxicity. Lipid-based nanoparticles enhance antibiotic penetration into infected tissues, improving therapeutic outcomes [25].

Despite these advantages, challenges remain. Toxicity to human cells, environmental concerns, and difficulties in large-scale production limit their clinical application [26]. Additionally, regulatory frameworks for nanoparticle-based therapies are still evolving.

Conclusion

Nanoparticles represent a promising alternative to conventional antibiotics for the treatment of *Staphylococcus aureus* infections, particularly multidrug-resistant strains. Their unique mechanisms of action, ability to target biofilms, and synergistic effects with existing antibiotics make them highly effective antimicrobial agents. However, further clinical trials and safety evaluations are necessary before widespread clinical implementation.

Limitations

- Limited clinical trials on nanoparticle-based therapies
- Potential cytotoxicity and long-term safety concerns
- Lack of standardized synthesis protocols
- High production cost and scalability issues
- Regulatory challenges for approval

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