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Targeted Antimicrobial Nanoparticles to Overcome Multidrug Resistance: Mechanisms, Biofilm Strategies, and Translational Challenges

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ABSTRACT

Antimicrobial resistance is advancing at a concerning ratio, challenging the effectiveness of modern medicine. Pathogens responsible for multidrug resistance are now prevalent in public areas such as healthcare facilities, agricultural environments and community settings, limiting treatment options and contributing to higher illness rate and medical costs. These pathogens have become resistant to traditional antibiotics due to their bacterial defence mechanism including efflux pump amplification, enzymatic inactivation, biofilm establishment and genetic exchange. Antibiotics engineered with nanoparticles offer physiochemical characteristics including unique nano-scale size, high surface-area-to-volume ratio, tunable composition via surface modification with targeting ligands, etc., enabling them to evade or disrupt microbial defence mechanisms. This review presents an in-depth analysis of targeted antimicrobial nanoparticles, discussing their design principles, interaction with microbiological resistance pathways, and recent advancements in biofilm penetration, efflux pump inhibition, and enzyme-triggered drug activation. It also highlights microbiology driven nanoparticle, resistance-limiting antimicrobials, while also addressing challenges in safety, large-scale production, and regulatory approval.

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1. Introduction

In the landscape of global health risks, antimicrobial resistance has emerged as a significant contributor. In the World Health Organization chart, it has been ranked first amongst the top ten global health threats. It is also predicted that by the end of 2050 there will be about ten million deaths due to drug resistance infections [1, 2]. From a microbiologist point of view, resistance to variants is primarily caused due to selective pressure put upon the extensive use of antibiotics. These resistances become survivors and subsequently transmit resistance determinants vertically to progeny or unrelated strains via mobile genetic elements. These multiple drug-resistant pathogens facilitate the proliferation in the ecosystem and renders once – treatable infections potentially fatal. There are two reasons possible for the drawback of the conventional antibiotics. First includes the unavailability of the microbial agents to access the structural behaviour of cell wall and biofilms and secondly includes inactivation of the drug by intrinsic microbial defence system even when the target site is reached. Nanotechnology offers targeted drug delivery system and passive benefits such as augmented penetration, improved structural stability and modulated release kinetics [3, 4]. Through surface modification with ligands, it binds selectively to microbial structures. This dual strategy of nanoparticles (NPs) can surpass the mechanism of multiple drug resistance (MDR), restoring the antimicrobial efficacy [5]. Nanoparticles can also improve drug accumulation at the infection site by increasing local residence time, which is especially useful in biofilm-associated infections. Another advantage is that the physicochemical properties of nanoparticles including size, surface charge, and coating which is tunable leading to enhanced interaction with bacterial membranes. This controlled design approach allows better balance between antimicrobial activity and host safety. Few nano delivery systems can disturb bacterial membranes or metabolic pathways directly, in addition to delivering drugs. This combined physical and pharmacological action may improve treatment response against highly resistant strains. However, the therapeutic outcome depends strongly on formulation quality, targeting efficiency, and biological stability, so rational design and proper characterization are essential for successful translation [6].

This review is motivated by the rapid global escalation of multidrug-resistant infections and the parallel surge in research on targeted antimicrobial nanoparticles as next-generation therapeutic tools. While numerous studies have reported nanoparticle-based antimicrobial systems, the field remains highly fragmented across mechanistic design, biofilm-targeting strategies, and translational development pathways. By systematically connecting mechanisms, targeting strategies, biofilm-directed approaches, and translational barriers, a structured framework is presented to guide future research and streamline the clinical advancement of antimicrobial nanoparticle strategies against multidrug resistance.

2. Microbial Resistance Mechanisms and Their Challenges

Antibiotic actions had been evaded by micro-organisms through multiple strategies. To understand these strategies, it is necessary to design nanoparticle based on the interventions. Such resistance mechanism often functions synergistically, where overcoming a single barrier may be insufficient to fully reinstate antibacterial potency. However. to engineer nanoparticle to bypass MDR it is essential to understand the microbe's physiological genetics and defence networks [7].

2.1. Efflux Pumps

Transmembrane proteins work as efflux pump expelling antibiotic from microbial cell. In gram negative bacteria, tripartite efflux pumps such as Arc AB-ToIC limits the intercellular drug accumulation by spanning both membrane and the periplasm. Similarly in gram positive bacteria Nor A limits fluroquinoline. Efflux owing to their broad substrate specificity presents a major challenge. Thus, it necessitates highly tailored inhibition strategy to avoid the risk of alternate pathway activation [8].

2.2. Enzymatic Drug Degradation

Several bacterial species are known to produce enzymes that degrades or chemically inactivate the antibiotics before it reaches its target site [9, 10]. These enzymes are responsible for the anti-microbial resistance and displays high specificity towards different class of drug.

One such clinical example is β – lactamase enzyme. In many of the antibiotics like Penicillin, Cephalosporins and Carbapenems, these enzymes hydrolyse the β – lactam ring present in them and multiply their capacity to inhibit bacterial cell wall synthesis [11]. Furthermore, extended spectrum of β – lactamase (ESBLs) and carbapenems compromise the efficacy of ESBL and creates a therapeutic challenge in the treatment of acquired infections. Similarly, enzymes like acetyltransferase, phosphotransferase and nucleotide transferase also known as aminoglycoside modifying enzymes are responsible for the alteration of molecular structure of antibiotic. It catalyses the covalent modification of the aminoglycoside via acetylating, phosphorylation and adenylation. After alteration it binds with the 30s ribosome subunit, thereby inhibiting protein synthesis in bacterial.

Localization of plasmid-based genetics play a crucial role in widespread and rapid transmission of enzyme-based resistance factor. Resistance genes spread rapidly within the microbial communities and among various ecological niches. This is caused due to the lateral transfer between different between different bacterial species via conjugation. As a result of this conjugation there is enzymatic versatilities which enhances the spread of multidrug resistance [12].

2.3. Biofilm Formation

Biofilms are multicellular microbial population encased within the extracellular polymeric substance formed from polysaccharides, proteins and extra cellular DNA (eDNA) [13]. This composition of matrix limits drug penetration as it forms a protective barrier for the antibiotics. It reduces susceptibility of anti-microbial by establishing a slow-growth metabolic state as well as makes biofilms difficult towards infections associated to medical devices such as catheters and implants.

2.4. Horizontal Gene Transfer (HGT)

There are three mechanisms responsible for HGT that facilitates the spread of resistance genes between bacterial populations [14]. It includes transformation (uptake od eDNA), transduction (phage-mediated DNA transfer) followed by conjugation (plasmid exchange through direct cell to cell contact). Nanoparticle mediated approach can be engineered to inhibit the mechanism by transporting nucleic acid cargo to degrade the plasmid or suppress the expression of gene essential for conjugative machinery.

3. Nanoparticles (NPs) as Antimicrobial Agents

Nanoparticle has the capacity to adhere directly with microbial surfaces, modulates drug release and penetrate into the biofilm which makes them effective against the MDR. It either functions intrinsically with antimicrobial agents or indirectly as carriers for antimicrobial therapeutics [15, 16].

3.1. Metallic Nanoparticles

Silver Nanoparticles (AgNPs): These nanoparticles are based on broad-spectrum antimicrobial activity. It targets biofilms and drug - resistant strains via ROS (reactive oxygen species) generation, enzyme degradation and membrane damage [17, 18].

Gold Nanoparticles (AuNPs): These comprises of various factors which makes it ideal to fight against MDR. These are biocompatible and modified with peptides, antibiotics or nucleic acid, as well as serve as photothermal activated through infrared radiation to supress bacterial growth [19].

Zinc Oxide Nanoparticles (ZnONPs): These interfere with essential bacterial metabolic pathways by gradually releasing Zn^{2+} ions, which disrupt enzyme activity and impair normal cellular functions. At the same time, the generated ROS induce oxidative stress, leading to damage of proteins, lipids, and nucleic acids, ultimately resulting in bacterial cell death [20].

3.2. Polymeric Nanoparticles

Biodegradable polymer ensures sustained drug release. Polymers such as poly(lactic-co-glycolic) (PLGA) and chitosan through surface modifications are widely used to enhance stability and functionality in antimicrobial formulations. Chitosan contains cationic properties which facilitates electrostatic interactions against the negatively charged bacterial membrane, thereby increase permeability of membrane [21].

3.3. Lipid-Based Nanoparticles

Liposomes: Liposomes combine with the microbial membrane for targeted delivery. It facilitates the encapsulation of both hydrophilic and hydrophobic antibiotics for enhanced drug delivery. It ensures controlled drug release and provides structural stability.

3.4. Hybrid Nanoparticles

Multifunctional system through combination of metallic and polymeric components shows superior antibacterial efficacy. One such typical example is combination of silver – chitosan nanoparticle. It has intrinsic antibacterial activity, inhibiting the growth of various microorganisms. Chitosan a natural biopolymer enhances the activity of silver through micro-adhesive characteristics [22]. It leads to adhesion of nanoparticle to mucosal surfaces, further enhancing their interaction with the bacterial cells.

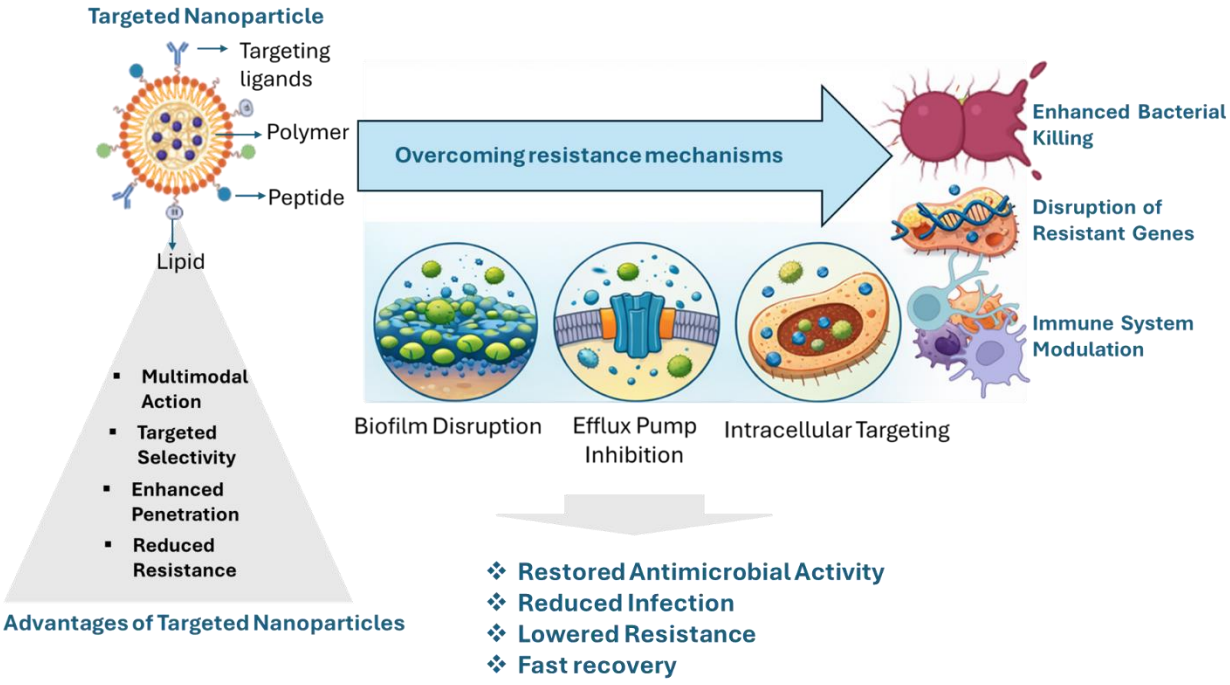

Figure 1: Targeted antimicrobial nanoparticle-based strategies for overcoming microbial resistance mechanisms leading to enhanced therapeutic efficacy.

4. Green-Synthesized Metallic Nanoparticles as Sustainable Antimicrobial Agents

Green synthesis of metallic nanoparticles (NPs) offers sustainable, environmentally friendly and biocompatible alternative towards traditional methods [23]. Natural plant extracts, microorganisms, etc., function as reducing and capping agent. This leads to the green synthesis of NP with tunable physiochemical properties. Furthermore, metallic NPs including AgNPs, AuNPs, ZnoNPs, CuONPs and TioNPs have shown efficacy in broad spectrum anti-bacterial activity against gram positive and gram-negative bacteria along with MDR strains [24].

Green synthesized nanoparticle can enhance the in-built antimicrobial properties of metallic nanostructure through ligand conjugation and surface modification, thus improving specificity and reducing unintended systemic effect. Antibacterial mechanism through these NPs offers an effective means to mitigate resistance phenotype. It includes generation of ROS, bacterial cell membrane disruption, interference with intracellular metabolic pathway and hindrance in biofilm formation (Fig. **1**). Representative examples of such nanoparticles, their origin, size, target microorganisms, and antimicrobial efficacy are summarized in Table **1**, highlighting their promise as sustainable nanoplatforms for combating microbial resistance.

Table 1: Comparative overview of green-synthesized metallic nanoparticles: origin, dimensions, targeted microorganisms, antibacterial efficacy, and key findings.

Nanoparticles (NPs)	Origin	Dimension	Bacterial Isolates were Subjected to Testing	Antibacterial Efficacy (IZD/MIC/MBC) and other Significant Findings	Ref.
AgNPs	Extract from the *Acacia rigidula* plant.	Shape: spherical, Size distribution spans 8–66 nm with a mean of 22.46 nm, while diameter ranges from 15 to 25 nm	*E. coli, P. aeruginosa,* Multidrug-Resistant (MDR*) P. aeruginosa* strain, and *B. subtilis.*	In vitro concentrations of 62.5, 15.6, 7.8, and 0.5 ppm were used for *E. coli*, *P. aeruginosa*, multidrug-resistant *P. aeruginosa*, and *B. subtilis*, respectively.	[17]
AuNPS	Extract from *Euphrasia officinalis* in an aqueous form	Shape: Quasi spherical, Size is 49.72 ±1.2 nm	*P. aeruginosa, E. coli, S. aureus* and *Vibrio parahaemolyticus*	Antibacterial efficacy at concentrations of 15.3 ± 0.5 ppm, 11.7 ± 0.5 ppm, 14.7 ± 0.9 ppm, and 13.7 ± 1.1 ppm. In terms of cytotoxicity, it hinders the growth of human cervical cancer cells (HeLa) at 10 µg/ml but does not impede human lung cancer cells (A549).	[19]
ZnONPs	Extracted from *Cinnamomum verum* bark	Shape: Hexagonal wurtzite. Size is 45 nm	Isolated from *E. coli* MTCC 7443 and *S. aureus* MTCC 7410	Minimum inhibitory concentration is 125 µg/ml for *E. coli* and 62.5 µg/ml for *S. aureus*.	[20]
CuONPs	Extract obtained from the leaves of *Aloe barbadensis.*	Shape: Spherical, Size range is 33.4–64.9 nm	Isolated from *Pseudomonas, Klebsiella, Staphylococcus, E. col*	Zone of inhibition diameters are 11 mm, 12 mm, 8 mm, and 9 mm, respectively.	[25]
TiO_2NPs	Produced through the use of *S. aureus.*	Shape: Spherical, Size range is 20 nm-30 nm	Isolated from *E. coli, B. cereus, S. aureus*	Highly effective against *B. subtilis* (9 mm) and *E. coli* (14 mm), demonstrating antibiofilm activity against these pathogens.	[26]

5. Comparative Translational Perspective of Antimicrobial Nanoparticle Platforms

Although a wide range of antimicrobial nanoparticle platforms has been reported, their translational potential is not equal. Lipid-based and polymeric nanoparticles currently appear more favourable for clinical development compared with many metallic systems. This is mainly because biodegradable carriers show better safety profiles, predictable degradation behaviour, and greater formulation flexibility. Several drug-loaded polymeric and lipid nanocarriers have already reached clinical use in other therapeutic areas, which supports their regulatory acceptability and scale-up feasibility. This prior clinical experience provides indirect but strong translational support for adapting these platforms to antimicrobial applications.

Metal and metal-oxide nanoparticles demonstrate strong intrinsic antimicrobial activity and are highly effective in vitro, particularly against resistant strains and biofilms. However, concerns related to long-term tissue accumulation, oxidative stress, and dose-dependent cytotoxicity remain unresolved. These safety uncertainties

currently limit their systemic clinical use, although they remain promising for localized and surface-associated antimicrobial applications such as coatings and wound care.

Hybrid and stimuli-responsive nanoparticles represent an emerging middle ground. Systems that combine biodegradable carriers with targeting ligands or environment-triggered release mechanisms show improved infection-site selectivity and reduced off-target exposure in animal infection models. Evidence from preclinical studies indicates better bacterial clearance and lower host toxicity compared with non-targeted formulations, suggesting higher translational value if manufacturing complexity can be controlled.

Overall, platforms that integrate biodegradability, controlled release, and reproducible manufacturing presently offer the strongest path toward clinical translation. In contrast, systems that rely solely on high antimicrobial potency without sufficient safety and scalability data are less likely to advance, despite promising laboratory performance

6. Targeting Strategies for Antimicrobial Nanoparticles

Targeting is a central design feature in antimicrobial nanoparticles because it improves local drug concentration at the infection site and reduces collateral damage to host tissues. However, not all targeting approaches show equal translational value. Strategies that combine strong binding selectivity with biological stability and scalable chemistry are currently more promising for real-world use. The following sections compare major targeting routes with respect to mechanism, practicality, and therapeutic performance [27].

6.1. Ligand-Mediated Targeting

Ligand-based targeting relies on decorating nanoparticle surfaces with molecules that can recognize and bind specific bacterial structures. Common ligand classes include antibodies, antimicrobial peptides, aptamers, carbohydrates, and small receptor-binding molecules. These ligands interact with defined surface components such as lipopolysaccharides, teichoic acids, surface adhesins, and membrane proteins.

Among these options, small-molecule ligands and short peptides are often more practical than full antibodies for antimicrobial delivery because they are more stable, less expensive to produce, and easier to attach reproducibly. Antibody-linked nanoparticles offer very high specificity, but their clinical translation is limited by cost, storage sensitivity, and batch variability. Aptamers provide good selectivity and lower immunogenic risk, but their performance can decrease in complex biological fluids due to structural instability.

Performance studies show that ligand density and orientation strongly influence binding efficiency. Simply attaching a ligand is not sufficient — surface presentation and accessibility determine whether bacterial capture actually improves. Therefore, platforms that allow controlled ligand spacing and stable surface anchoring are considered more promising than randomly functionalized systems.

Overall, ligand-mediated targeting is highly effective in controlled models, but its clinical potential depends on ligand stability, manufacturing reproducibility, and retention of binding activity under physiological conditions [28].

6.2. Biofilm-Specific Targeting

Biofilm-associated infections present a different targeting problem because the nanoparticle must first interact with the extracellular polymeric matrix before reaching bacterial cells. Targeting approaches here are designed either to bind matrix components or to actively degrade them. Enzyme-functionalized nanoparticles represent one of the more effective approaches in this category. Enzymes such as DNase and polysaccharide-degrading enzymes can break down extracellular DNA and structural polysaccharides within the matrix. This loosens the biofilm architecture and improves nanoparticle penetration. Systems that combine enzymatic disruption with antimicrobial payload delivery generally show better biofilm reduction than nanoparticles carrying drugs alone. Charge-based targeting is another practical strategy. Many biofilm matrices carry an overall negative charge, so moderately cationic nanoparticles can show enhanced retention and penetration. However, highly positive

surfaces may also increase host cell toxicity, so charge tuning is necessary. Biofilm disrupting enzyme such as dispersin B engineered with NP helps in improved therapeutic delivery leading to the degradation of DNase I and β-1, 6-linked N-acetylglucosamine which catalyses the extracellular DNA via hydrolysis [29]. Thereby it compromises the extracellular polymeric substance (EPS) which leads to diffusion of NP into the inner biofilm layers.

From a translational viewpoint, enzyme-assisted and charge-balanced penetration strategies appear more scalable than complex multi-ligand targeting systems, because they rely on broader matrix properties rather than species-specific markers.

6.3. pH-Responsive and Enzyme-Responsive Release

Stimuli-responsive nanoparticles are designed to release their antimicrobial payload only under infection-associated conditions. Common triggers include acidic pH, bacterial enzymes, and redox gradients. These systems do not depend only on binding selectivity but on environmental selectivity.

In infected tissues and biofilms, localized acidity and elevated enzyme activity are frequently observed. Nanoparticles with pH-sensitive linkers or enzyme-cleavable coatings can remain stable in circulation but release drugs at the target site. This reduces systemic exposure and improves therapeutic index [30].

Among responsive systems, pH-triggered platforms are currently more advanced than enzyme-triggered ones because pH sensitivity is easier to engineer and validate. Enzyme-responsive systems can be highly specific but may suffer from variability across bacterial strains and infection sites.

Stimuli-responsive systems are considered promising for translation when they are built using chemically simple and well-characterized linkers, since regulatory approval favours predictable degradation pathways [31, 32].

7. Disruption of Microbial Resistance Mechanisms Using Nanoparticles

7.1. Efflux Pump Inhibition

Engineered NP can deliver efflux pump inhibitor along with antibiotics. These includes phenylalanine-arginine β-naphthylamide to maintain effective bacterial levels of the antibiotics with the bacterial cells [33].

7.2. Enzyme-Triggered Activation

The concept of NP can also be utilized to encapsulate antibiotic prodrugs. These prodrugs remain inactive until activated by bacterial enzyme such as β lactamase. This enzyme transforms bacterial resistance mechanism by activating drug signals, thus results in increased selectivity.

7.3. Biofilm Penetration

- Metallic NPs like AgNP and ZnONP interferes with extracellular polymeric substances by ion release and reactive oxygen species [34].
- NPs with combination of liposome enzyme hybrids improve penetration precise biofilm disruption.

7.4. Gene Silencing

NPs can target genes responsible for MDR like *blaNDM*, *mecA* through CRISPER-Cas9 and siRNA construct [35]. This strategy involves direct involvement of genes which are responsible for resistance of antibiotics in bacterial system [36].

8. Advantages of Targeted Antimicrobial Nanoparticles

Multimodal Action: These systems can attack microbes through more than one mechanism at the same time, such as physical membrane disruption, chemical toxicity, and controlled drug delivery, making them effective even against MDR strains.

Targeted Selectivity: Minimal effects on host tissues and beneficial microflora.

Reduced Resistance Development: It reduces the chance of adaptive resistance through concurrent targeting of multiple pathways, lowering the probability that microbes can adapt and develop resistance.

Enhanced Penetration: Their small size and surface tunability enhance their potential to penetrate bacterial membranes and biofilm barriers, increasing antimicrobial efficiency.

The Table **2** summarizes the major classes of nanoparticles explored for antimicrobial applications, highlighting their mechanisms of action and the specific resistance pathways they are designed to overcome.

Table 2: Comparative overview of nanoparticle types, mechanisms of action, and antimicrobial resistance pathways targeted.

Nanoparticles (NPs)	Mechanism of Action	Resistance Pathways Targeted	Representative Reference
Silver nanoparticles (AgNPs)	Release of Ag^+ ions causing oxidative stress, protein denaturation, and DNA damage; disruption of bacterial membranes	Overcomes enzymatic degradation and biofilm-mediated resistance by multi-site action	[37]
Gold nanoparticles (AuNPs)	Photothermal effects and conjugation with antibiotics or peptides for enhanced binding to bacterial targets	Evades efflux pumps and reduces intracellular degradation	[38]
Liposomes	Encapsulation of antibiotics for improved solubility, controlled release, and protection from degradation	Circumvents enzymatic inactivation and enhances penetration through biofilms	[39]
Polymeric nanoparticles (e.g., chitosan, PLGA)	Electrostatic interaction with bacterial cell walls, sustained drug release, and immune modulation	Overcomes permeability barriers and biofilm-associated tolerance	[40]
Graphene oxide nanoparticles	Physical disruption of membranes via sharp edges, oxidative stress induction	Targets biofilm integrity and disrupts cell wall synthesis	[41]
Magnetic nanoparticles (Fe_3O_4)	Magnetic field-assisted biofilm disruption and targeted delivery of antibiotics	Bypasses biofilm barriers and enhances local drug concentration	[42]
Antimicrobial peptide-loaded nanoparticles	Membrane permeabilization and interference with intracellular targets	Counters multi-mechanism resistance including efflux and enzymatic degradation	[43]

9. Engineering and Formulation Considerations

From a chemical engineering perspective, the clinical success of targeted antimicrobial nanoparticles depends not only on biological performance but also on fabrication control and process reliability. Nanoparticle synthesis routes such as nanoprecipitation, emulsification, microfluidic mixing, and surface-directed assembly must produce particles with consistent size, surface charge, and ligand density, since small variations can significantly alter antimicrobial activity and targeting behaviour. Process reproducibility across batches is therefore a critical requirement.

Scale-up remains a practical challenge because laboratory preparation methods often rely on tightly controlled small-volume conditions that are difficult to replicate in large reactors. Continuous-flow and microfluidic-assisted fabrication approaches are increasingly considered more scalable because they allow better control over mixing kinetics and particle uniformity. In addition, formulation stability during storage and transport must be ensured, as aggregation, premature drug leakage, or ligand detachment can reduce targeting efficiency and antimicrobial potency. Addressing these engineering and formulation parameters is essential for translating targeted antimicrobial nanoparticle systems from experimental designs to deployable therapeutic products.

10. Challenges

10.1. Safety, Nanotoxicity, and Biocompatibility

Despite promising antimicrobial performance, the safety profile of targeted nanoparticles remains a major concern. Nanoparticles can trigger cellular stress through reactive oxygen species generation, membrane damage, mitochondrial dysfunction, and unintended interactions with intracellular components. These effects may vary with particle size, surface charge, composition, and coating chemistry. Metallic and metal-oxide nanoparticles, in particular, require careful dose optimization and surface modification to reduce host toxicity. Long-term exposure data are still limited, and chronic accumulation risks are not fully understood. Future work must include systematic nanotoxicity mapping across cell types, tissues, and exposure durations, along with standardized safety benchmarks.

10.2. Immune Interactions and Biological Responses

Nanoparticles introduced into the body can interact strongly with the immune system. Protein corona formation, complement activation, and macrophage uptake can alter targeting efficiency and circulation time. In some cases, immune recognition leads to rapid clearance or unintended inflammatory responses. These effects reduce therapeutic consistency and may produce variable outcomes across patient populations. More detailed studies are needed to understand nanoparticle–immune cell interactions, immune tolerance limits, and strategies for immune-stealth surface engineering.

10.3. Biodistribution and Physiological Stability

Targeted antimicrobial nanoparticles often show strong activity in controlled laboratory systems, but their behaviour in complex biological environments is less predictable. Particle aggregation, surface transformation, and premature drug leakage can occur in physiological fluids. Variations in pH, ionic strength, and serum proteins can change nanoparticle stability and targeting performance. In addition, organ-level biodistribution and clearance pathways are not always well defined [44]. Reliable in vivo tracking and standardized biodistribution models are necessary to ensure that nanoparticles reach infection sites at effective concentrations without off-target accumulation [45].

10.4. Scale-Up, Manufacturing, and Reproducibility

Translation beyond laboratory scale is limited by manufacturing challenges. Many nanoparticle systems are produced using multi-step synthesis methods that are difficult to reproduce at industrial scale. Small variations in process parameters can change particle size, surface properties, and drug loading efficiency, which directly affects therapeutic outcome. Batch-to-batch variability remains a key barrier. There is a need for robust, scalable production methods with strict quality control metrics and validated reproducibility standards.

10.5. Regulatory and Translational Pathways

Regulatory approval of antimicrobial nanomedicines is slowed by the lack of harmonized evaluation frameworks. Current drug approval pathways are not fully adapted to nano-enabled systems that combine material, device, and drug characteristics. Comprehensive assessment must include pharmacokinetics, long-term

safety, environmental impact, and interaction with existing therapies [46]. Clear regulatory guidance, validated testing protocols, and cross-disciplinary standards will be required to move targeted antimicrobial nanoparticles from experimental platforms to approved clinical products [47, 48].

11. Conclusion

Targeted antimicrobial NPs address the concern of MDR through an innovative approach [49], aiming to deliver antibiotic directly to infection site by incorporating insights from microbiology and rational nanomaterial design [50]. Despite translational challenges, integration of the domains along with clinical medicine are driving technologies closer towards practical applications, representing a transformative strategy capable of bypassing conventional resistance pathways and redefining the future of efficient therapy against multidrug-resistant infections.

Conflict of Interest

The authors declare no conflict of interest.

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