

NANOCARRIER STRATEGIES TO OVERCOME ANTIMICROBIAL RESISTANCE: A COMPREHENSIVE REVIEW

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ABSTRACT

Antimicrobial resistance (AMR) has emerged as a major global health challenge, substantially reducing the effectiveness of conventional antimicrobial therapy and complicating the management of bacterial infections. The increasing prevalence of multidrug-resistant pathogens has created an urgent need for therapeutic approaches capable of improving antimicrobial efficacy while overcoming biological and microbial barriers to treatment. Nanocarrier-based drug delivery systems have gained considerable attention as promising platforms for addressing these challenges. This review discusses the major mechanisms underlying bacterial antimicrobial resistance, including enzymatic drug inactivation, target modification, reduced membrane permeability, active efflux, biofilm-associated protection, and horizontal transfer of resistance determinants. The principal nanocarrier platforms investigated for antimicrobial applications, including liposomes, polymeric nanoparticles, lipid-based nanoparticles, metallic nanomaterials, dendrimers, and biomimetic systems, are also examined. Particular emphasis is placed on strategies through which nanocarriers can enhance antimicrobial delivery, improve cellular uptake, facilitate biofilm penetration, protect antimicrobial agents from degradation, enable controlled or targeted release, and support combination therapy. Recent preclinical advances and the potential of multifunctional nanocarriers against drug-resistant bacterial infections are further discussed. Despite promising experimental findings, challenges related to nanotoxicity, formulation stability, manufacturing, pharmacokinetics, reproducibility, and clinical translation remain. Overall, nanocarrier-based approaches represent a versatile and potentially complementary strategy for improving antimicrobial therapy and addressing selected barriers associated with AMR.

KEYWORDS: Antimicrobial resistance, Nanocarriers, Antimicrobial drug delivery, Multidrug-resistant bacteria, Biofilms, Targeted drug delivery, Controlled release, Nanoparticles, Antibacterial therapy

1. INTRODUCTION:

Antimicrobial resistance (AMR) has emerged as a major global public health concern, driven largely by the widespread and inappropriate use of antimicrobial agents in human medicine, agriculture, and veterinary practice. [1,2] The increasing prevalence of resistant microorganisms has progressively compromised the effectiveness of several previously reliable antibiotics, contributing to treatment failure, increased morbidity and mortality, and rising healthcare expenditure worldwide. The global burden of AMR is substantial, with bacterial AMR estimated to have been associated with approximately 1.27 million deaths globally in 2019. [3] Projections from the Review on Antimicrobial Resistance have further suggested that, without effective interventions, AMR could contribute to nearly 10 million deaths annually by 2050, accompanied by substantial economic consequences.[4]

The emergence of antibiotic-resistant pathogens, including *Escherichia coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus*, has considerably complicated the management of infectious diseases.[3] The increasing prevalence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) microorganisms represents a serious threat to modern healthcare, as resistant infections can compromise the safety and effectiveness of critical medical interventions, including surgery, organ transplantation, and cancer chemotherapy.[5] Bacteria employ multiple mechanisms to withstand antimicrobial treatment, including enzymatic degradation or modification of antimicrobial agents, alteration of drug targets, reduced membrane permeability, and active efflux of drugs from bacterial cells.[6] In addition, many pathogenic bacteria form biofilms in which microorganisms are embedded within a protective extracellular matrix. Biofilm formation can restrict antimicrobial penetration and promote bacterial persistence under unfavorable conditions, thereby contributing to treatment failure and chronic infection.[7]

The limitations of conventional antimicrobial therapy extend beyond microbial resistance mechanisms. Several antibiotics exhibit unfavorable pharmacokinetic properties, including poor solubility, limited stability, rapid systemic clearance, and inadequate accumulation at infection sites.[8] Consequently, achieving therapeutically

effective drug concentrations may require higher or repeated systemic doses, potentially increasing the risk of toxicity and adverse effects.[9]These limitations highlight the need for innovative delivery approaches capable of improving antimicrobial localization, stability, and therapeutic activity while minimizing unnecessary systemic exposure.

Nanotechnology has emerged as a promising approach for improving the delivery and effectiveness of antimicrobial agents. Nanocarriers are nanoscale delivery platforms capable of encapsulating, entrapping, or associating with antimicrobial compounds and facilitating their transport to specific biological sites. Their tunable physicochemical properties, large surface-area-to-volume ratio, and capacity for surface modification enable improvements in drug solubility and stability and allow controlled or sustained drug release. [10-11]Various nanocarrier platforms have been investigated for antimicrobial applications, including liposomes, polymeric nanoparticles, solid lipid nanoparticles, dendrimers, and metallic nanoparticles.[11-12]These systems can protect antimicrobial agents from premature degradation, enhance their delivery across biological barriers, facilitate penetration into bacterial cells and biofilms, and modify their pharmacokinetic behavior. [11-13] Moreover, certain nanomaterials possess intrinsic antimicrobial properties that may further enhance their activity against resistant microorganisms.[14]

Collectively, these characteristics have positioned nanocarrier-based delivery systems as promising tools for addressing some of the limitations associated with conventional antimicrobial therapy. Integrating nanotechnology with antimicrobial treatment may improve drug delivery, enhance antimicrobial activity, and provide opportunities to counteract multiple mechanisms underlying antimicrobial resistance.[15-17] Accordingly, this review provides a comprehensive overview of nanocarrier-based strategies for combating AMR, with emphasis on major nanocarrier platforms, their mechanisms of action, applications against resistant pathogens, and the current challenges and future prospects associated with their clinical translation.

2. Mechanism of Antimicrobial Resistance:

Antimicrobial resistance in bacteria results from a combination of intrinsic characteristics and acquired genetic or phenotypic adaptations that reduce the activity of antimicrobial agents. Although resistance mechanisms vary among bacterial species and antimicrobial classes, several major processes contribute to treatment failure, including enzymatic drug inactivation, modification of antimicrobial targets, reduced drug uptake, active efflux, biofilm-associated protection, and horizontal transfer of resistance determinants.[18,13]Importantly, individual pathogens may employ multiple mechanisms simultaneously, resulting in multidrug-resistant phenotypes and substantially limiting available therapeutic options.

2.1 Enzymatic Inactivation of Antimicrobial Agents

Enzymatic modification or degradation is one of the most important mechanisms of bacterial resistance. Bacteria can produce enzymes that chemically modify antimicrobial compounds or directly hydrolyze essential structural components of the drug. β -lactamases represent a clinically important example, as these enzymes hydrolyze the β -lactam ring of penicillins, cephalosporins, and related antibiotics, thereby preventing interaction with their bacterial targets. Other resistance-associated enzymes include aminoglycoside-modifying enzymes, which alter antibiotic molecules through acetylation, phosphorylation, or adenylation, reducing their ability to bind ribosomal targets. [19]This mechanism can substantially reduce the concentration of active antimicrobial available to act on the bacterial cell.

2.2 Modification of Antimicrobial Targets

Bacteria may also evade antimicrobial activity by altering the molecular targets recognized by antibiotics. Genetic mutations or acquisition of resistance determinants can modify target proteins, reducing their affinity for antimicrobial molecules while retaining sufficient biological function. Examples include alterations in penicillin-binding proteins that decrease β -lactam susceptibility, modification of ribosomal components affecting macrolides and aminoglycosides, and mutations in DNA gyrase or topoisomerase IV associated with fluoroquinolone resistance.[18,20]Target modification therefore allows bacteria to maintain essential cellular processes despite the presence of an antimicrobial agent.

2.3 Reduced Membrane Permeability

Adequate intracellular or periplasmic accumulation of an antimicrobial is essential for activity against many bacterial targets. In Gram-negative bacteria, changes in outer-membrane permeability, particularly through loss or modification of porins, can restrict the entry of hydrophilic antibiotics. [21]Alterations in membrane composition may further reduce antimicrobial uptake. Consequently, even when an antibiotic remains chemically active, insufficient intracellular accumulation can prevent it from reaching concentrations required for effective bacterial killing.

2.4 Active Efflux of Antimicrobial Agents

Efflux pumps actively transport antimicrobial compounds from bacterial cells and thereby lower their intracellular concentrations. Several transporter families contribute to this process, including resistance-nodulation-division (RND), major facilitator superfamily (MFS), ATP-binding cassette (ABC), small multidrug resistance (SMR), and multidrug and toxic compound extrusion (MATE) systems.[17,20] RND efflux systems are particularly important in Gram-negative pathogens because of their broad substrate specificity and ability to extrude multiple antibiotic classes.[21] Overexpression or structural modification of these pumps can consequently contribute to multidrug resistance.

The major mechanisms through which bacteria evade antimicrobial activity, together with their representative features and consequences for therapeutic efficacy, are summarized in Table 1.

Table 1: Antimicrobial activity with their principle mechanism, and Therapeutic effect

S.No	Resistance mechanism	Principal mechanism	Representative examples	Major consequence
1	Enzymatic inactivation	Degradation or chemical modification of antimicrobial agents [18]	β -lactamases; aminoglycoside-modifying enzymes	Loss or reduction of antimicrobial activity
2	Target Modification	Structural alteration or modification of antimicrobial targets [20]	Altered PBPs; modified ribosomal targets; DNA gyrase/topoisomerase IV mutations	Reduced antimicrobial–target interaction
3	Reduced Membrane Permeability	Decreased uptake of antimicrobial agents through changes in membrane proteins or porins [31]	Porin loss or modification in Gram-negative bacteria	Reduced intracellular antimicrobial concentration
4	Active efflux	Energy-dependent extrusion of antimicrobial compounds from bacterial cells [21]	RND, MFS, MATE, SMR and ABC efflux systems	Subtherapeutic intracellular drug concentration
5	Biofilm-associated resistance	Protection within extracellular polymeric matrix combined with physiological adaptation [22]	EPS matrix; persister cells; altered metabolic activity	Restricted drug penetration and increased antimicrobial tolerance
6	Horizontal gene transfer	Acquisition and dissemination of antimicrobial-resistance genes between bacteria [24]	Conjugation; transformation; transduction	Rapid dissemination and accumulation of resistance determinants

2.5 Biofilm-Associated Resistance

Biofilm formation provides bacteria with an additional level of protection against antimicrobial treatment. Within a biofilm, bacterial cells are embedded in an extracellular polymeric matrix that can restrict antimicrobial penetration and create spatially heterogeneous concentrations of nutrients, oxygen, and drugs. Biofilm-associated cells may also exhibit altered metabolic activity, stress responses, and increased numbers of persister cells, collectively reducing susceptibility to antimicrobial killing.[22] These features make biofilm-associated infections particularly difficult to eradicate and are especially relevant to chronic and device-associated infections.

2.6 Horizontal Transfer of Resistance Determinants

The rapid dissemination of antimicrobial resistance is facilitated by horizontal gene transfer (HGT), through which resistance-associated genetic material can move between bacterial cells. The major mechanisms include conjugation, transformation, and transduction.[23] Conjugation can transfer resistance-bearing plasmids directly between bacterial cells, while transformation involves uptake of extracellular DNA and transduction is mediated by bacteriophages. Mobile genetic elements such as plasmids, transposons, integrons, and insertion sequences can facilitate the movement and accumulation of multiple antimicrobial resistance genes.[23-24] Consequently, HGT can accelerate the emergence of multidrug-resistant bacterial populations across species and ecological niches.

Taken together, these mechanisms demonstrate that antimicrobial resistance is multifactorial and cannot always be overcome simply by increasing the dose of a conventional antibiotic. Strategies capable of improving drug accumulation, bypassing bacterial barriers, disrupting biofilms, protecting antimicrobial cargo, or simultaneously delivering multiple therapeutic agents may therefore provide opportunities to counter several resistance mechanisms. These requirements provide an important rationale for the development of nanocarrier-based antimicrobial delivery systems.

3. Nanocarriers: Types and Key Properties

Nanocarriers are nanoscale delivery systems designed to transport therapeutic agents to specific biological sites while modifying the physicochemical and pharmacokinetic properties of the incorporated drug. In antimicrobial therapy, their application is particularly relevant because conventional antibiotics may exhibit poor solubility, instability, rapid elimination, limited tissue penetration, or inadequate accumulation at the site of infection. Nanocarrier systems can improve drug solubilization and protection, facilitate controlled release, and alter the distribution of antimicrobial agents, thereby providing a more favorable therapeutic profile.[25] The ability to

engineer particle size, surface charge, composition, morphology, and surface functionality further allows these systems to be adapted for different infectious microenvironments.[26]

3.1 Major Types of Nanocarriers

A wide range of organic and inorganic nanocarriers has been investigated for antimicrobial applications. Lipid-based systems, particularly liposomes, are among the most extensively studied platforms. Liposomes consist of phospholipid bilayers surrounding an aqueous core and can accommodate both hydrophilic and hydrophobic antimicrobial agents. Their relatively favorable biocompatibility, versatility in drug loading, and capacity to modify drug biodistribution make them attractive for antimicrobial delivery.[26] Lipid-based nanoparticles also include solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs), which can provide sustained drug release and improve the delivery of poorly soluble antimicrobial agents.[27]

Polymeric nanoparticles represent another important class and can be prepared from biodegradable natural or synthetic polymers. Their composition and surface properties can be tailored to regulate drug loading, release kinetics, cellular uptake, and interaction with bacterial or host-cell membranes.[28] Such flexibility has supported their investigation against a broad range of bacterial infections and as carriers for conventional antibiotics and other antimicrobial compounds.

Metal and metal-oxide nanoparticles, including silver, gold, zinc oxide, and related systems, differ from conventional nanocarriers because the nanoparticle itself may possess antimicrobial activity. Their effects can involve multiple processes, including membrane disruption, oxidative stress, metal-ion release, and interference with essential bacterial functions.[25] However, their therapeutic development requires careful assessment of dose-dependent toxicity, stability, and interactions with host tissues.

Other platforms include dendrimers, nanogels, mesoporous silica nanoparticles, and biomimetic vesicular systems. Dendrimers possess highly branched architectures and multiple surface functional groups, allowing antimicrobial compounds to be incorporated or attached and enabling interactions with bacterial membranes and biofilm matrices.[29] Biomimetic systems, including bacterial outer-membrane vesicles and membrane-coated nanoparticles, have also attracted interest because biological membrane components can facilitate interaction with specific bacterial or host environments and potentially improve delivery across biological barriers.[30]

The major nanocarrier platforms investigated for antimicrobial applications, along with their structural characteristics, principal advantages, limitations, and relevance to antimicrobial delivery, are summarized in Table 2.

Table 2: Major nanocarrier platforms and their properties relevant to antimicrobial delivery

S.No	Nanocarrier	Key structural feature	Major advantage	Important limitation	Antimicrobial relevance
1.	Liposomes	Phospholipid bilayer + aqueous core	Hydrophilic/hydrophobic drug loading; biocompatibility	Stability and leakage issues	Antibiotic delivery and altered biodistribution
2	Polymeric nanoparticles	Biodegradable polymer matrix	Tunable release and surface modification	Formulation complexity	Controlled and targeted antimicrobial delivery
3	SLNs/NLCs	Solid or mixed lipid matrix	Sustained release; improved solubility	Limited drug-loading capacity in some systems	Delivery of poorly soluble antibiotics
4	Metal/metal-oxide nanoparticles	Inorganic nanoscale structure	Intrinsic antimicrobial activity	Potential toxicity	Multimodal antibacterial effects
5	Dendrimers	Highly branched architecture	Multivalent surface functionalization	Toxicity can depend on surface chemistry	Antimicrobial and antibiofilm delivery

3.2 Key Properties Relevant to Antimicrobial Delivery

The therapeutic performance of a nanocarrier depends not only on its composition but also on its physicochemical characteristics. Particle size can influence tissue penetration, cellular uptake, and biodistribution, whereas surface charge affects interactions with bacterial membranes, biological barriers, and

host cells. Surface functionalization can introduce targeting ligands or modify interactions with the surrounding biological environment. In addition, high drug-loading capacity and tunable release kinetics can help maintain effective antimicrobial concentrations over an extended period.[25-28]

An important advantage of nanocarrier engineering is the possibility of integrating several functions within a single platform. A nanocarrier may simultaneously protect an antimicrobial molecule, improve its delivery to the infection site, facilitate interaction with bacterial cells, and provide controlled release. Recent research has increasingly focused on multifunctional and stimuli-responsive systems capable of responding to infection-associated conditions such as pH, enzymes, reactive oxygen species, or other local signals.[31] These developments are particularly relevant to AMR because they provide a platform through which antimicrobial delivery can be adapted to the biological barriers and resistance mechanisms encountered during infection.

Overall, nanocarriers should not be regarded as a single therapeutic category but as a diverse group of engineered platforms with distinct physicochemical and biological properties. Their ability to combine drug delivery with targeting, controlled release, and, in some cases, intrinsic antimicrobial activity provides the foundation for their application in overcoming antimicrobial resistance.

4 Enhancing Antimicrobial Delivery and Cellular Uptake

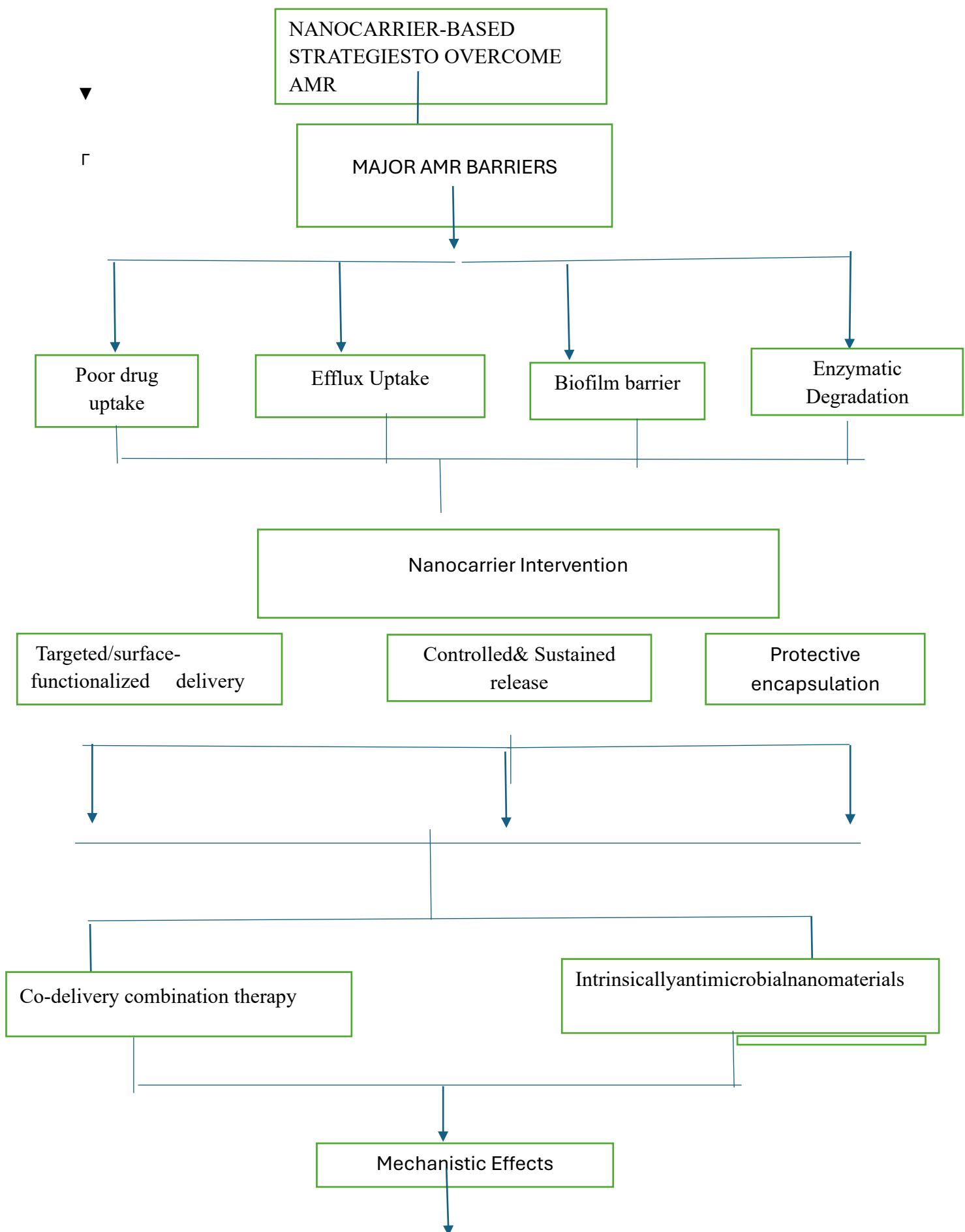
One of the principal advantages of nanocarrier-based antimicrobial therapy is its ability to improve the delivery and intracellular availability of antimicrobial agents. Conventional antibiotics may show limited penetration across bacterial membranes or host-cell barriers, resulting in inadequate drug concentrations at intracellular or difficult-to-reach infection sites. Nanocarriers can modify the physicochemical properties of antimicrobial molecules and facilitate their transport through biological barriers, thereby increasing the amount of active drug reaching the site of infection.[25,32] The nanoscale dimensions and tunable surface characteristics of these systems can also promote interactions with bacterial membranes and enhance cellular uptake, potentially improving antimicrobial activity without requiring proportional increases in systemic drug exposure.

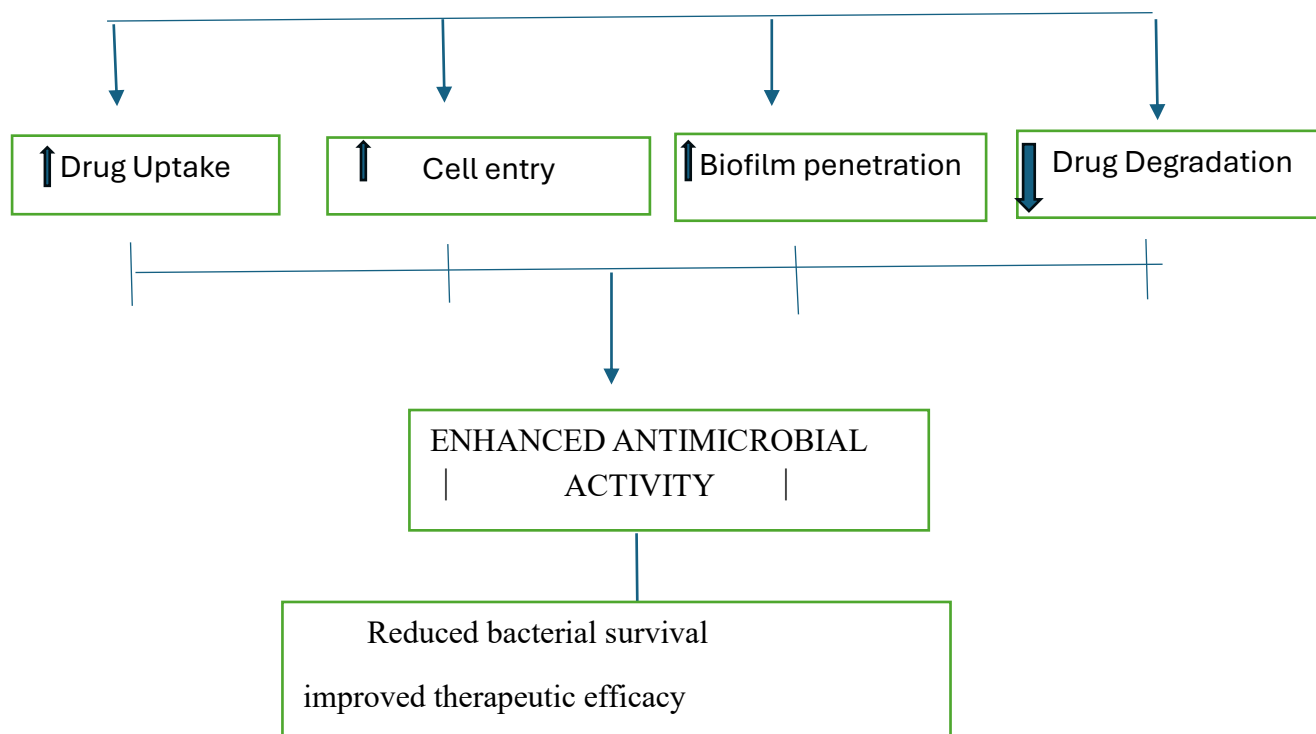
This approach is particularly relevant to intracellular bacterial infections, in which pathogens can persist within macrophages and other host cells, where many conventional antibiotics have limited access. For example, liquid crystalline lipid nanoparticles containing tobramycin or vancomycin have been reported to improve the antibacterial activity of these agents against intracellular *Pseudomonas aeruginosa* and *Staphylococcus aureus*, respectively. The enhanced activity was associated with the ability of the lipid nanoparticles to promote cellular uptake and intracellular delivery of the antimicrobial agents.[33] Similarly, mesoporous organosilica nanoparticles loaded with rifampicin demonstrated enhanced uptake by macrophages and substantially greater intracellular antibiotic delivery compared with free rifampicin, resulting in improved reduction of intracellular *S. aureus*. [34]

Surface engineering provides an additional means of improving bacterial interaction and delivery selectivity. Functionalization with positively charged or bacteria-interacting groups can enhance association with negatively charged bacterial surfaces, while targeting ligands may facilitate preferential accumulation at infected cells or tissues. A recent study using quaternary ammonium chitosan-functionalized mesoporous silica nanoparticles demonstrated enhanced macrophage uptake and targeted delivery of cefoperazone against intracellular methicillin-resistant *S. aureus* (MRSA), illustrating how surface modification can be combined with nanocarrier-mediated drug delivery to address intracellular drug-resistant infections.[35]

Nanocarriers can also improve the delivery of antimicrobial agents to bacteria located within complex infection environments. Their ability to carry relatively high drug payloads, protect encapsulated molecules from premature degradation, and provide controlled release may maintain antimicrobial exposure for longer periods than conventional formulations.[32,36] In addition, nanocarrier architecture can be engineered to influence interactions with bacterial membranes, extracellular matrices, and host cells. Recent work with amphiphilic gold nanoparticles demonstrated that antibiotic-loaded nanoparticles could penetrate bacterial biofilms and reach biofilm-embedded bacteria, while also showing activity against *S. aureus*. [37] Although such findings remain largely preclinical, they illustrate the potential of nanocarrier engineering to overcome spatial and cellular barriers that restrict conventional antimicrobial therapy. Major nanocarrier-based strategies for overcoming antimicrobial resistance, their underlying mechanisms, and the resulting therapeutic benefits are schematically illustrated in **Figure 1**.

Figure 1. Nanocarrier-based strategies for overcoming major barriers associated with antimicrobial resistance.





Importantly, improved delivery does not necessarily imply that nanocarriers directly eliminate genetic resistance. Rather, their therapeutic value may arise from increasing the effective concentration of an antimicrobial at its intended site, improving intracellular access, altering drug distribution, or facilitating interaction with bacterial cells. These effects can potentially restore or enhance the activity of existing antimicrobial agents against difficult-to-treat infections and provide a foundation for more specific strategies targeting efflux, biofilms, enzymatic resistance, and other mechanisms of AMR.

5. Recent Research, Challenges and Clinical Translation

The rapid expansion of nanotechnology research has generated a growing body of preclinical evidence supporting nanocarrier-based approaches against antimicrobial-resistant pathogens. Recent studies have investigated lipid, polymeric, inorganic, and hybrid nanoplatforms for improving antibiotic delivery, enhancing bacterial and biofilm penetration, and enabling combination therapy. Importantly, several recent investigations have moved beyond simple antibiotic encapsulation toward multifunctional systems designed to simultaneously address drug delivery barriers and bacterial resistance mechanisms.[38-39]

5.1 Recent Preclinical Evidence

Recent experimental studies demonstrate that nanocarrier systems can enhance the activity of established antimicrobial agents against resistant bacterial infections. Antibiotic-loaded nanoparticles have shown improved antibacterial effects against clinically important pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA), multidrug-resistant *Pseudomonas aeruginosa*, and resistant Gram-negative bacteria. In several models, nanoscale formulations increased antimicrobial accumulation at the infection site and improved bacterial killing compared with the corresponding free drugs.[40-41]

Particular attention has been directed toward biofilm-associated infections, which represent an important contributor to persistent antimicrobial tolerance. Nanocarriers capable of penetrating the extracellular polymeric matrix may increase antimicrobial exposure within biofilms and facilitate delivery to metabolically heterogeneous bacterial populations. Recent studies using antibiotic-loaded nanoparticles and multifunctional nanomaterials have reported enhanced biofilm disruption and bacterial killing compared with conventional antimicrobial formulations.[42] In addition, combination nanoplatforms incorporating antibiotics with antimicrobial peptides, metal-based components, or other antibacterial agents may provide complementary mechanisms of action and reduce the likelihood that bacteria will survive through a single resistance pathway.[43]

5.2 Challenges and Limitations

Despite encouraging preclinical findings, several barriers continue to limit the clinical translation of antimicrobial nanocarriers. Nanoparticle physicochemical properties—including size, morphology, surface charge, composition, and aggregation state—can substantially influence pharmacokinetics, biodistribution, cellular uptake, and toxicity.⁴⁴ Consequently, apparently similar formulations may produce substantially different biological responses. Establishing standardized characterization methods and reproducible manufacturing processes remains an important requirement for meaningful comparison between studies. Potential toxicity is another major consideration. Some inorganic nanoparticles can generate reactive oxygen

species, release metal ions, or interact nonspecifically with host-cell membranes and proteins. Although these properties may contribute to antimicrobial activity, excessive exposure may result in undesirable effects on mammalian cells.⁴⁵ Long-term accumulation, immunological effects, and interactions with the microbiome also require further investigation before widespread clinical application.

Manufacturing and scale-up represent additional challenges. Formulations developed successfully at laboratory scale may encounter difficulties related to batch-to-batch reproducibility, drug-loading consistency, storage stability, sterilization, and cost-effective production.⁴⁴ Furthermore, differences in experimental design, bacterial strains, infection models, dosing regimens, and nanoparticle characterization make direct comparison across preclinical studies difficult.

5.3 Clinical Translation and Future Perspectives

Although nanomedicine has already produced clinically approved drug-delivery products in several therapeutic areas, translation of nanocarrier-based antimicrobial strategies remains comparatively limited.^[46] Many antimicrobial nanocarriers remain at the in vitro or animal-model stage, and robust clinical evidence demonstrating superiority over optimized conventional antibiotic therapy is still required. Future development should therefore prioritize formulations with clearly defined mechanisms of action, clinically relevant infection models, predictable pharmacokinetics, and well-characterized safety profiles.

The next generation of antimicrobial nanocarriers is likely to focus on multifunctional systems that combine targeted delivery, controlled or stimuli-responsive release, biofilm penetration, and combination therapy within a single platform. Integration with antimicrobial peptides, phage-derived components, immune-modulating agents, or existing antibiotics may further expand therapeutic possibilities.^[47] However, successful translation will depend not only on achieving enhanced antibacterial activity but also on demonstrating reproducible manufacturing, acceptable toxicity, pharmacological advantages, regulatory feasibility, and clinically meaningful improvements in patient outcomes.

Overall, current evidence supports nanocarriers as promising adjuncts to conventional antimicrobial therapy rather than as an immediate replacement for antibiotics. Continued integration of nanomaterial engineering, microbiology, pharmacology, and clinical research will be essential for converting promising laboratory findings into safe and effective therapies for drug-resistant infections.

6 Conclusion

Antimicrobial resistance represents a major and continually evolving threat to the effective management of bacterial infections. The diverse mechanisms employed by resistant bacteria—including antimicrobial inactivation, target modification, reduced permeability, active efflux, biofilm-associated protection, and horizontal dissemination of resistance determinants—substantially limit the effectiveness of conventional antimicrobial therapy. Nanocarrier-based delivery systems have emerged as promising approaches for addressing several of these limitations by improving antimicrobial solubility, stability, cellular uptake, tissue accumulation, and controlled release.

The versatility of nanocarriers enables different therapeutic strategies, ranging from targeted antibiotic delivery and protection of antimicrobial cargo to enhanced biofilm penetration and co-delivery of multiple antimicrobial agents. In addition, certain nanomaterials possess intrinsic antibacterial properties and can act through multiple mechanisms, providing opportunities to reduce dependence on a single antimicrobial target. Recent preclinical research therefore supports the potential of nanocarrier-based systems as complementary approaches for improving treatment against multidrug-resistant and biofilm-associated infections.

Nevertheless, the transition from promising experimental findings to clinically useful therapies remains challenging. Nanotoxicity, formulation stability, manufacturing reproducibility, pharmacokinetic variability, cost, and regulatory requirements must be addressed through systematic investigation. Importantly, enhanced antibacterial activity in laboratory models does not necessarily translate into improved clinical outcomes. Future research should therefore emphasize standardized characterization, clinically relevant infection models, rigorous safety evaluation, and well-designed clinical studies.

Overall, nanocarrier technology offers a versatile platform for enhancing antimicrobial therapy and potentially circumventing several barriers associated with antimicrobial resistance. Continued interdisciplinary research integrating nanotechnology, microbiology, pharmacology, and clinical medicine will be essential for translating these advances into safe, effective, and clinically meaningful strategies against drug-resistant infections.

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