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Review Article

Nanotechnology-Based Strategies against Antimicrobial Resistance: Current Status and Future Prospects

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Abstract

Antimicrobial resistance (AMR) is a rapidly escalating global health crisis that threatens the effective treatment of infectious diseases. The emergence of multidrug-resistant (MDR) pathogens, coupled with the declining discovery of new antibiotics, has necessitated the development of innovative therapeutic strategies. Nanotechnology has emerged as a promising approach owing to its unique physicochemical properties, enabling targeted drug delivery, improved antimicrobial efficacy, enhanced biofilm penetration, and reduced systemic toxicity. This review aims to summarize recent advances in nanotechnology-based strategies for combating AMR, highlighting the mechanisms of action, therapeutic applications, current research progress, and future translational prospects. A comprehensive literature search was performed using PubMed, Scopus, Web of Science, and Google Scholar to identify relevant peer-reviewed articles published in recent years. Studies focusing on nanoparticle-based antimicrobial therapies, drug delivery systems, biofilm-targeting approaches, and clinical advancements were critically evaluated. Various nanoplatforms, including metallic, polymeric, lipid-based, and carbon-based nanoparticles, have demonstrated significant potential in overcoming conventional resistance mechanisms through targeted drug delivery, membrane disruption, reactive oxygen species generation, and controlled drug release. Additionally, nanotechnology enhances antibiotic stability, improves intracellular drug accumulation, and facilitates combination therapies. Despite promising preclinical outcomes, challenges related to toxicity, large-scale manufacturing, regulatory approval, and long-term safety remain barriers to clinical translation. Nanotechnology offers a transformative strategy to address antimicrobial resistance by improving therapeutic efficacy and minimizing resistance development. Continued interdisciplinary research, standardized safety evaluations, and well-designed clinical studies are essential to accelerate the successful clinical implementation of nano-enabled antimicrobial therapies.

Keywords: Antimicrobial resistance; Nanomedicine; Nanoparticle-based drug delivery; Biofilm inhibition; Precision antimicrobial therapy.

1. Introduction

Antimicrobial resistance (AMR) has emerged as one of the most critical global public health threats of the 21st century, undermining decades of progress in the prevention and treatment of infectious diseases. The widespread and often inappropriate use of antibiotics in human medicine, veterinary practice, and agriculture has accelerated the evolution and dissemination of resistant microorganisms, resulting in infections that are increasingly difficult to treat. According to the World Health Organization (WHO), AMR is responsible for prolonged hospitalizations, increased healthcare costs, therapeutic failures, and higher mortality rates. The growing prevalence of multidrug-resistant (MDR), extensively drug-resistant (XDR), and pan drug-resistant (PDR) pathogens poses a significant challenge to modern healthcare systems, necessitating the development of innovative therapeutic strategies beyond conventional antibiotics[1-2].

Nanotechnology has emerged as a promising multidisciplinary approach to overcome the limitations of traditional antimicrobial therapies. Nanomaterials possess unique physicochemical properties, including a high surface area-to-volume ratio, tunable size, enhanced drug-loading capacity, controlled drug release, and targeted delivery, enabling them to effectively combat resistant microorganisms through multiple mechanisms[3]. Unlike conventional antibiotics, nanoparticles can disrupt microbial membranes, generate reactive oxygen species (ROS), inhibit biofilm formation, interfere with quorum sensing, and improve intracellular drug delivery, thereby reducing the likelihood of resistance development. Furthermore, nanotechnology facilitates combination therapies by enhancing the efficacy of existing antibiotics while minimizing systemic toxicity and improving pharmacokinetic profiles[4].

This review provides a comprehensive overview of nanotechnology-based strategies for combating

antimicrobial resistance, emphasizing recent advances in nanomaterial design, mechanisms of antimicrobial action, nano-enabled drug delivery systems, preclinical and clinical progress, current challenges, and future perspectives. By highlighting the potential of nanotechnology as a next-generation antimicrobial platform, this review aims to provide valuable insights into its role in addressing the escalating global burden of antimicrobial resistance[5-6].

1.1 Global Burden of Antimicrobial Resistance

Antimicrobial resistance (AMR) is recognized as one of the greatest threats to global health, food security, and economic development. It occurs when bacteria, fungi, viruses, or parasites evolve mechanisms that reduce or eliminate the effectiveness of antimicrobial agents, rendering standard treatments ineffective. The rapid emergence and dissemination of resistant pathogens have resulted in increasing rates of morbidity, mortality, prolonged hospitalization, and escalating healthcare expenditures worldwide[7]. Recent global estimates indicate that millions of deaths are associated with bacterial AMR annually, with low- and middle-income countries experiencing the highest burden due to inadequate infection control, unrestricted antibiotic use, and limited access to effective therapeutics. The World Health Organization has identified AMR as a priority health challenge requiring urgent international collaboration through surveillance, antimicrobial stewardship, and the development of innovative therapeutic approaches.

1.2 Mechanisms of Antimicrobial Resistance

Microorganisms develop resistance through diverse intrinsic and acquired mechanisms that enable them to survive antimicrobial exposure. Common resistance mechanisms include enzymatic degradation or modification of antibiotics, alteration of drug target sites, reduced membrane permeability, active efflux pump-mediated drug extrusion, and biofilm formation that protects microbial communities from antimicrobial penetration. In addition, horizontal gene transfer through plasmids, transposons, and bacteriophages facilitates the rapid dissemination of resistance genes among bacterial populations[8-9]. These adaptive mechanisms significantly reduce the efficacy of conventional antibiotics and contribute to the emergence of multidrug-resistant pathogens, emphasizing the need for alternative therapeutic strategies.

1.3 Limitations of Conventional Antimicrobial Therapy

Although antibiotics have revolutionized the treatment of infectious diseases, their clinical effectiveness is increasingly compromised by the emergence of resistant microorganisms. Conventional antimicrobial therapy often suffers from poor target specificity, suboptimal bioavailability, limited penetration into infected tissues and biofilms, rapid drug degradation, systemic toxicity, and the development of antimicrobial resistance following prolonged or inappropriate use. Furthermore, the declining rate of novel antibiotic discovery and the lengthy, expensive drug development process have created a significant gap between the emergence of resistant pathogens and the availability of effective therapeutic agents[10]. These limitations underscore the urgent need for innovative antimicrobial approaches capable of overcoming resistance while improving therapeutic outcomes.

1.4 Role of Nanotechnology in Combating AMR

Nanotechnology has emerged as a transformative strategy for addressing antimicrobial resistance by enhancing the efficacy of antimicrobial agents and introducing novel mechanisms of microbial eradication. Nanoparticles can function as drug carriers or intrinsic antimicrobial agents owing to their unique physicochemical characteristics, including nanoscale dimensions, high surface reactivity, and tunable surface functionalization[11]. They improve drug stability, increase targeted delivery, facilitate controlled and sustained drug release, and enhance intracellular accumulation at infection sites. Additionally, nanomaterials exhibit multimodal antimicrobial activities such as membrane disruption, reactive oxygen species generation, inhibition of biofilm formation, efflux pump suppression, and synergistic interactions with conventional antibiotics. These multifunctional properties make nanotechnology a promising platform for combating multidrug-resistant pathogens while minimizing systemic toxicity and reducing the likelihood of resistance development[11-12].

This review aims to provide a comprehensive and up-to-date overview of nanotechnology-based strategies for combating antimicrobial resistance. It discusses the global burden and molecular mechanisms of AMR, the limitations of conventional antimicrobial therapies, and the classification of nanomaterials employed in antimicrobial applications. Furthermore, the review highlights the mechanisms of antimicrobial action of nanomaterials, advances in nano-enabled drug delivery systems, applications against multidrug-resistant pathogens, and recent preclinical and clinical developments. Finally, current challenges, regulatory considerations, and future research directions are critically discussed to provide insights into the translation of nanotechnology-based antimicrobial therapies from laboratory research to clinical practice.

2. NANOTECHNOLOGY PLATFORMS FOR ANTIMICROBIAL THERAPY

Nanotechnology has revolutionized the field of antimicrobial therapy by enabling the development of advanced nanoscale systems capable of overcoming the limitations of conventional antimicrobial agents. Nanocarriers, typically ranging from 1 to 100 nm in size, possess unique physicochemical properties, including a high surface area-to-volume ratio, tunable morphology, controlled drug release, enhanced stability, and the ability to penetrate biological barriers and microbial biofilms[13]. These characteristics facilitate improved drug delivery, increased antimicrobial efficacy, reduced systemic toxicity, and decreased emergence of antimicrobial resistance (AMR). In addition to serving as

carriers for antibiotics, several nanomaterials exhibit intrinsic antimicrobial activity through mechanisms such as membrane disruption, generation of reactive oxygen species (ROS), metal ion release, inhibition of biofilm formation, and modulation of microbial metabolic pathways. Recent advances in nanotechnology have led to the development of diverse nanoplatforms, each offering distinct advantages for combating multidrug-resistant (MDR) pathogens. This section provides an overview of the major nanotechnology platforms currently investigated for antimicrobial therapy.

2.1 Metallic Nanoparticles

Metallic nanoparticles are among the most extensively studied nanomaterials for antimicrobial applications because of their broad-spectrum antimicrobial activity, high stability, ease of synthesis, and multifunctional therapeutic properties. Common metallic nanoparticles include silver (AgNPs), gold (AuNPs), copper (CuNPs), zinc oxide (ZnO NPs), titanium dioxide (TiO_2 NPs), magnesium oxide (MgO NPs), and iron oxide (Fe_3O_4 NPs). These nanoparticles exhibit antimicrobial activity through multiple mechanisms, including disruption of microbial cell membranes, intracellular penetration, generation of reactive oxygen species (ROS), oxidative stress induction, protein denaturation, DNA damage, enzyme inhibition, and release of toxic metal ions. Silver nanoparticles are considered the gold standard among antimicrobial nanomaterials due to their potent activity against Gram-positive bacteria, Gram-negative bacteria, fungi, and certain viruses. Gold nanoparticles primarily function as drug delivery carriers because of their excellent biocompatibility, chemical stability, and ease of surface functionalization. Copper and zinc oxide nanoparticles also demonstrate remarkable antimicrobial efficacy while offering cost-effective alternatives for biomedical applications[14-15]. Moreover, iron oxide nanoparticles possess magnetic properties that enable targeted drug delivery and magnetic hyperthermia, expanding their potential in antimicrobial and theranostic applications.

2.2 Polymeric Nanoparticles

Polymeric nanoparticles are biodegradable and biocompatible nanosystems fabricated from either natural polymers, such as chitosan, alginate, gelatin, dextran, and hyaluronic acid, or synthetic polymers, including poly(lactic-co-glycolic acid) (PLGA), polycaprolactone (PCL), polyethylene glycol (PEG), and polylactic acid (PLA). These nanoparticles are widely employed as drug delivery vehicles because they protect antimicrobial agents from enzymatic degradation, improve aqueous solubility, prolong systemic circulation, and provide controlled and sustained drug release[16]. Polymeric nanoparticles can encapsulate both hydrophilic and hydrophobic antimicrobial agents while allowing surface modification with targeting ligands such as antibodies, peptides, aptamers, or polymers for site-specific drug delivery. Chitosan nanoparticles additionally possess intrinsic antimicrobial activity due to their positively charged amino groups, which interact with negatively charged microbial cell membranes, leading to membrane disruption and leakage of intracellular contents[17]. Owing to their excellent safety profile and versatility, polymeric nanoparticles are extensively explored for treating bacterial infections, fungal diseases, intracellular pathogens, and biofilm-associated infections.

2.3 Lipid-Based Nanocarriers

Lipid-based nanocarriers have emerged as one of the most successful nanotechnology platforms for antimicrobial drug delivery because of their superior biocompatibility, low toxicity, and high drug-loading efficiency. These systems include liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), lipid nanoemulsions, and lipid-polymer hybrid nanoparticles. Liposomes are phospholipid vesicles capable of encapsulating both hydrophilic and hydrophobic antimicrobial agents, thereby improving drug stability, reducing toxicity, and enhancing intracellular delivery. Solid lipid nanoparticles consist of physiologically compatible solid lipids that provide controlled drug release, protect unstable drugs from degradation, and improve pharmacokinetic behavior[18-19]. Nanostructured lipid carriers represent second-generation lipid nanoparticles in which mixtures of solid and liquid lipids increase drug-loading capacity and minimize drug leakage during storage.

Lipid-based nanocarriers demonstrate enhanced penetration into bacterial biofilms and infected tissues while facilitating targeted delivery to intracellular pathogens. Several lipid-based nanoformulations have already progressed into clinical use due to their favorable safety profile and manufacturing feasibility, making them attractive candidates for combating antimicrobial resistance.

2.4 Carbon-Based Nanomaterials

Carbon-based nanomaterials have gained considerable attention because of their exceptional mechanical strength, electrical conductivity, chemical stability, and multifunctional antimicrobial properties. Major carbon nanomaterials include graphene, graphene oxide (GO), reduced graphene oxide (rGO), carbon nanotubes (CNTs), carbon dots (CDs), nanodiamonds, and fullerenes. Graphene oxide possesses oxygen-containing functional groups that facilitate drug loading and surface modification while exerting antimicrobial effects through physical membrane disruption, oxidative stress induction, and extraction of membrane phospholipids. Carbon nanotubes exhibit needle-like structures capable of mechanically penetrating microbial membranes, leading to irreversible cellular damage[20]. Carbon dots have recently emerged as promising antimicrobial nanomaterials owing to their excellent biocompatibility, fluorescence imaging capability, and ROS-mediated antibacterial activity.

In addition to their intrinsic antimicrobial effects, carbon-based nanomaterials serve as efficient carriers for antibiotics, antimicrobial peptides, nucleic acids, and photosensitizers used in photodynamic and photothermal antimicrobial therapies. Their multifunctionality enables simultaneous diagnosis,

imaging, targeted drug delivery, and antimicrobial treatment, making them promising theranostic platforms[20-21].

2.5 Dendrimers, Nanogels, and Hybrid Nanomaterials

Dendrimers are highly branched, monodisperse macromolecules characterized by a well-defined three-dimensional architecture and numerous terminal functional groups that enable high drug-loading capacity and surface functionalization. Poly(amidoamine) (PAMAM) dendrimers are among the most extensively studied dendrimers for antimicrobial applications due to their ability to disrupt bacterial membranes and enhance intracellular drug delivery. Nanogels are nanosized hydrogel particles composed of crosslinked hydrophilic polymers capable of absorbing large amounts of water while maintaining structural stability. Their porous network allows efficient encapsulation of antimicrobial agents and provides stimuli-responsive drug release triggered by changes in pH, temperature, enzyme activity, or redox conditions[22]. Nanogels are particularly advantageous for treating chronic wounds, biofilm-associated infections, and localized bacterial infections because of their prolonged drug retention and excellent biocompatibility.

Hybrid nanomaterials integrate two or more nanoplatforms into a single multifunctional system to achieve synergistic therapeutic effects. Examples include polymer-metal hybrids, lipid-polymer nanoparticles, magnetic-polymeric nanoparticles, graphene-metal composites, and MOF-based hybrid nanostructures. These multifunctional systems combine the advantages of individual nanomaterials, including targeted drug delivery, controlled release, imaging capability, magnetic targeting, and enhanced antimicrobial efficacy, thereby offering promising solutions for multidrug-resistant infections[23].

2.6 Metal-Organic Frameworks (MOFs)

Metal–Organic Frameworks (MOFs) are an emerging class of highly porous crystalline nanomaterials composed of metal ions or metal clusters interconnected by organic ligands. Their exceptionally high surface area, tunable pore size, adjustable chemical composition, and large drug-loading capacity have positioned MOFs as one of the most promising nanoplatforms for antimicrobial therapy. MOFs can efficiently encapsulate antibiotics, antimicrobial peptides, enzymes, nucleic acids, photosensitizers, and metal ions while protecting these therapeutic agents from premature degradation[24]. Controlled release can be achieved through pH-sensitive, enzyme-responsive, or redox-responsive mechanisms, enabling site-specific drug delivery to infected tissues. Certain MOFs also exhibit intrinsic antimicrobial activity through controlled release of antibacterial metal ions, including silver, copper, zinc, cobalt, and iron, which induce oxidative stress, disrupt bacterial membranes, and inhibit essential microbial enzymes.

Furthermore, MOFs have shown considerable promise in photodynamic therapy (PDT), photothermal therapy (PTT), chemodynamic therapy (CDT), and synergistic combination therapies against multidrug-resistant pathogens and biofilm-associated infections. Despite these advantages, challenges related to long-term biocompatibility, biodegradation, toxicity, and large-scale manufacturing remain important considerations for their successful clinical translation[25-26]. Consequently, continued research is focused on developing safe, biodegradable, and multifunctional MOF-based nanoplatforms that can effectively address the growing challenge of antimicrobial resistance.

3. MECHANISMS OF ANTIMICROBIAL ACTION OF NANOMATERIALS

Nanomaterials exhibit potent antimicrobial activity through multiple complementary mechanisms that distinguish them from conventional antibiotics. Unlike traditional antimicrobial agents, which generally target a single cellular process, nanoparticles can simultaneously interact with microbial membranes, intracellular biomolecules, metabolic pathways, and virulence factors. This multimodal mode of action significantly reduces the likelihood of microorganisms developing resistance while enhancing therapeutic efficacy against multidrug-resistant (MDR), extensively drug-resistant (XDR), and biofilm-associated pathogens[27]. The antimicrobial activity of nanomaterials is influenced by their physicochemical properties, including particle size, shape, surface charge, chemical composition, crystallinity, surface functionalization, and concentration. Depending on these characteristics, nanomaterials can directly damage microbial cells, generate oxidative stress, inhibit microbial communication, enhance intracellular drug accumulation, and potentiate the activity of conventional antibiotics. The major antimicrobial mechanisms of nanomaterials are discussed below.

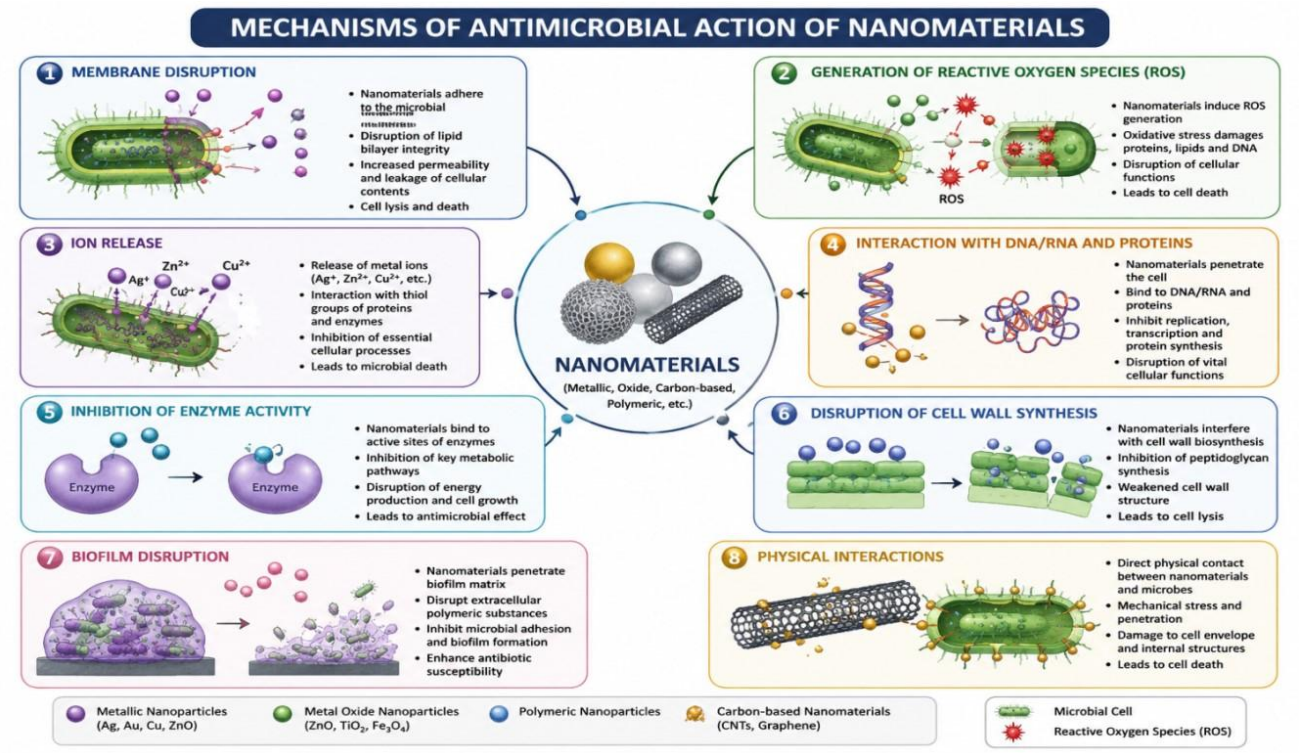

Figure 1: Schematic representation of antimicrobial action of nanomaterials

3.1 Membrane Disruption

Disruption of the microbial cell membrane is one of the primary and most effective antimicrobial mechanisms of nanomaterials. The bacterial cell membrane serves as a protective barrier that regulates nutrient transport, maintains osmotic balance, and preserves cellular integrity. Many nanoparticles, particularly metallic nanoparticles such as silver (AgNPs), zinc oxide (ZnO NPs), copper oxide (CuO NPs), and chitosan-based nanoparticles, possess positively charged surfaces that electrostatically interact with negatively charged bacterial cell envelopes. This interaction destabilizes membrane structure, increases membrane permeability, and causes leakage of intracellular components, including nucleic acids, proteins, ATP, and essential ions. Smaller nanoparticles possess a larger surface area-to-volume ratio, allowing them to penetrate bacterial membranes more efficiently[28-29]. Carbon-based nanomaterials such as graphene oxide and carbon nanotubes can physically pierce or wrap around bacterial membranes, resulting in irreversible structural damage. Membrane disruption also causes depolarization of the cytoplasmic membrane, inhibition of respiratory enzymes, loss of proton motive force, and impairment of ATP synthesis, ultimately leading to bacterial cell death. Since this mechanism targets the physical integrity of the membrane rather than a specific biochemical pathway, the probability of microorganisms developing resistance is considerably reduced[30].

3.2 Reactive Oxygen Species (ROS)-Mediated Killing

Generation of reactive oxygen species (ROS) is another major antimicrobial mechanism responsible for the broad-spectrum activity of numerous nanomaterials. Metallic nanoparticles such as silver, zinc oxide, titanium dioxide, copper oxide, and iron oxide can catalyze the production of highly reactive oxygen species, including hydroxyl radicals (•OH), superoxide anions ($O_2•^-$), hydrogen peroxide (H_2O_2), and singlet oxygen ($^1O_2$). Excessive ROS production overwhelms the microbial antioxidant defense system, resulting in severe oxidative stress. Oxidative damage affects multiple cellular components simultaneously[31]. Lipid peroxidation compromises membrane integrity, oxidation of proteins leads to enzyme inactivation, while DNA oxidation induces strand breaks, mutations, and inhibition of DNA replication. ROS also interfere with electron transport chains, disrupt mitochondrial-like bacterial respiration, and impair essential metabolic pathways. Photocatalytic nanomaterials such as titanium dioxide and zinc oxide further enhance ROS generation under ultraviolet or visible light irradiation, making them highly effective in photodynamic antimicrobial therapy. Because ROS-mediated killing simultaneously damages several cellular targets, microorganisms find it considerably more difficult to develop resistance compared with conventional antibiotics[32-33].

3.3 Biofilm Inhibition and Eradication

Biofilm formation is a major contributor to chronic and recurrent infections and is one of the principal mechanisms responsible for antimicrobial resistance. Biofilms are structured microbial communities enclosed within a self-produced extracellular polymeric substance (EPS) composed of polysaccharides, proteins, extracellular DNA, and lipids. This matrix protects microorganisms from host immune responses and significantly reduces antibiotic penetration, often

making biofilm-associated bacteria up to 1,000 times more resistant than planktonic cells. Nanomaterials offer significant advantages in overcoming biofilm-associated resistance due to their nanoscale dimensions and multifunctional mechanisms of action[34-36]. Their small size enables deeper penetration into the dense biofilm matrix, facilitating direct interaction with embedded bacterial cells. Nanoparticles can degrade extracellular polymeric substances, disrupt biofilm architecture, inhibit microbial adhesion to surfaces, and interfere with biofilm maturation. Furthermore, ROS generation within biofilms damages bacterial membranes and intracellular biomolecules, leading to efficient eradication of persistent microbial populations. Functionalized nanoparticles carrying enzymes such as DNase or dispersin B have also demonstrated enhanced capability to degrade biofilm matrices, improving antibiotic penetration and therapeutic efficacy[36].

3.4 Intracellular Drug Delivery

Many pathogenic microorganisms, including *Mycobacterium tuberculosis*, *Salmonella enterica*, *Listeria monocytogenes*, and *Staphylococcus aureus*, survive and replicate within host cells, where they remain protected from conventional antibiotics and immune surveillance. Nanotechnology-based drug delivery systems provide an effective strategy for targeting these intracellular pathogens by facilitating enhanced cellular uptake and intracellular drug accumulation.

Nanocarriers such as polymeric nanoparticles, liposomes, solid lipid nanoparticles, dendrimers, and metal-organic frameworks (MOFs) efficiently encapsulate antimicrobial agents, protecting them from enzymatic degradation and premature clearance. Following administration, nanoparticles are internalized by host cells through endocytosis or phagocytosis and subsequently release the encapsulated drugs in a controlled manner within intracellular compartments[37]. Surface modification with targeting ligands such as antibodies, peptides, mannose, folic acid, or transferrin further enhances selective delivery to infected macrophages and other immune cells. Improved intracellular drug delivery increases therapeutic concentrations at infection sites while reducing systemic toxicity and minimizing the emergence of antimicrobial resistance.

3.5 Efflux Pump and Quorum Sensing Inhibition

Efflux pumps are membrane-associated transport proteins that actively expel antimicrobial agents from microbial cells, thereby reducing intracellular drug concentrations below therapeutic levels. Overexpression of multidrug efflux pumps is one of the most common mechanisms underlying bacterial multidrug resistance. Certain nanomaterials inhibit efflux pump activity by disrupting membrane integrity, interfering with ATP production required for active transport, or directly blocking transporter proteins. Increased intracellular antibiotic accumulation restores bacterial susceptibility and enhances antimicrobial efficacy[38-39].

In addition to efflux pump inhibition, many nanomaterials interfere with quorum sensing (QS), a cell-to-cell communication system that regulates bacterial virulence, biofilm formation, toxin production, motility, and collective bacterial behavior through signaling molecules known as autoinducers. Nanoparticles can degrade quorum sensing signaling molecules, inhibit their synthesis, or prevent receptor binding, thereby disrupting bacterial communication networks. Suppression of quorum sensing significantly reduces bacterial pathogenicity without directly affecting bacterial viability, thereby decreasing the selective pressure for resistance development[40].

3.6 Synergistic Effects with Conventional Antibiotics

One of the most promising applications of nanotechnology in antimicrobial therapy is its ability to enhance the effectiveness of existing antibiotics through synergistic interactions. Nanoparticles serve as efficient drug carriers that improve antibiotic solubility, stability, bioavailability, pharmacokinetics, and targeted delivery while simultaneously exhibiting intrinsic antimicrobial activity. This dual functionality results in enhanced bacterial killing compared with either nanoparticles or antibiotics administered alone[41].

Nanoparticle–antibiotic combinations improve antibiotic penetration into bacterial cells and biofilms, inhibit resistance mechanisms such as efflux pumps and enzymatic drug degradation, and maintain sustained therapeutic drug concentrations at infection sites. Metallic nanoparticles, particularly silver nanoparticles, have demonstrated synergistic activity with β-lactams, aminoglycosides, fluoroquinolones, glycopeptides, and tetracyclines against multidrug-resistant pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA), carbapenem-resistant *Klebsiella pneumoniae*, multidrug-resistant *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*. Furthermore, multifunctional nanoplatforms combining antimicrobial drugs with photothermal therapy, photodynamic therapy, or chemodynamic therapy have shown remarkable potential for eliminating resistant pathogens and preventing recurrent infections[42-43]. Such synergistic strategies reduce the required antibiotic dosage, minimize systemic toxicity, delay the emergence of resistance, and improve overall therapeutic outcomes, making them a promising approach for future antimicrobial treatment.

4. NANOTECHNOLOGY-BASED DRUG DELIVERY STRATEGIES

Nanotechnology-based drug delivery systems have emerged as a transformative approach for improving the therapeutic efficacy of antimicrobial agents and overcoming the growing challenge of antimicrobial resistance (AMR). Conventional antimicrobial therapies often suffer from poor aqueous solubility, limited bioavailability, rapid degradation, nonspecific tissue distribution, systemic toxicity, and inadequate penetration into infected tissues and microbial biofilms. Moreover, intracellular pathogens and multidrug-resistant (MDR) microorganisms frequently evade

conventional antibiotics through mechanisms such as efflux pump overexpression, enzymatic drug degradation, and reduced membrane permeability. Nanotechnology offers innovative solutions to these limitations by employing nanoscale carriers capable of enhancing drug stability, increasing drug-loading efficiency, facilitating targeted delivery, enabling controlled and sustained drug release, and improving intracellular drug accumulation[44-45].

Nanocarriers-including polymeric nanoparticles, liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), dendrimers, metallic nanoparticles, mesoporous silica nanoparticles, and metal–organic frameworks (MOFs)-provide versatile platforms for encapsulating antimicrobial agents and delivering them directly to infection sites. Surface engineering and functionalization further enable selective targeting of infected tissues while minimizing off-target toxicity. Additionally, multifunctional nanoplatforms integrating diagnosis, imaging, and therapy have opened new avenues for precision antimicrobial treatment[46]. The major nanotechnology-based drug delivery strategies are discussed below.

4.1 Antibiotic-Loaded Nanocarriers

Encapsulation of antibiotics within nanocarriers represents one of the most extensively investigated strategies for enhancing antimicrobial therapy. Antibiotic-loaded nanocarriers protect antimicrobial agents from premature degradation, improve aqueous solubility, prolong systemic circulation, and enhance bioavailability. Furthermore, encapsulation facilitates sustained drug release and increases local drug concentrations at infection sites while reducing systemic toxicity and adverse effects. Various nanocarrier systems have been developed for antibiotic delivery, including polymeric nanoparticles, liposomes, solid lipid nanoparticles, nanostructured lipid carriers, dendrimers, mesoporous silica nanoparticles, metallic nanoparticles, and metal–organic frameworks. These carriers can efficiently encapsulate hydrophilic, hydrophobic, and amphiphilic antimicrobial agents while preserving their biological activity[47]. For example, liposomal formulations of vancomycin, gentamicin, and amphotericin B have demonstrated enhanced antimicrobial efficacy and reduced nephrotoxicity. Similarly, PLGA nanoparticles loaded with ciprofloxacin, doxycycline, rifampicin, or levofloxacin have shown improved intracellular delivery and prolonged therapeutic action against intracellular pathogens.

Nanocarriers also facilitate enhanced penetration into bacterial biofilms, allowing antibiotics to reach bacterial populations that are otherwise inaccessible to conventional formulations. By maintaining therapeutic drug concentrations for extended periods, antibiotic-loaded nanoparticles reduce dosing frequency, improve patient compliance, and decrease the likelihood of resistance development[48-49].

4.2 Targeted Drug Delivery Systems

Targeted drug delivery aims to selectively transport antimicrobial agents to infected tissues or pathogenic microorganisms while minimizing exposure of healthy cells. Nanotechnology has significantly advanced targeted antimicrobial therapy through surface functionalization of nanoparticles with various targeting ligands, including antibodies, peptides, aptamers, carbohydrates, vitamins, polymers, and receptor-specific molecules. Targeting strategies are broadly categorized into passive and active targeting. Passive targeting primarily exploits the enhanced permeability and retention (EPR) effect observed in inflamed and infected tissues, where increased vascular permeability facilitates nanoparticle accumulation. In contrast, active targeting involves conjugating nanocarriers with ligands that specifically recognize bacterial surface molecules, infected macrophages, or receptors overexpressed at infection sites[50]. Examples include mannose-functionalized nanoparticles targeting macrophages infected with *Mycobacterium tuberculosis*, folic acid-modified nanoparticles for inflamed tissues, and antibody-conjugated nanoparticles designed to recognize specific bacterial antigens.

Targeted nanocarriers significantly enhance intracellular drug accumulation, improve therapeutic efficacy against biofilm-associated and intracellular infections, reduce required drug doses, and minimize systemic toxicity. These advantages make targeted drug delivery one of the most promising strategies for treating multidrug-resistant infections.

4.3 Controlled and Stimuli-Responsive Drug Release

Controlled drug release is a key advantage of nanotechnology-based drug delivery systems, allowing sustained therapeutic concentrations over extended periods while reducing dosing frequency and minimizing adverse effects. Conventional antibiotics often exhibit rapid clearance and fluctuating plasma concentrations, leading to suboptimal therapeutic outcomes and promoting resistance. Nanocarriers overcome these limitations by releasing drugs in a predictable and controlled manner. Recent advances have led to the development of stimuli-responsive or "smart" nanocarriers capable of releasing antimicrobial agents in response to specific physiological or pathological stimuli present at infection sites. These stimuli include changes in pH, temperature, enzyme activity, redox potential, magnetic fields, ultrasound, and light irradiation. For instance, pH-responsive nanoparticles release antibiotics selectively within acidic bacterial biofilms or inflamed tissues, whereas enzyme-responsive systems utilize bacterial enzymes to trigger localized drug release. Magnetic nanoparticles enable externally guided drug targeting and controlled release under magnetic field stimulation, while photoresponsive nanoparticles facilitate light-triggered antimicrobial therapy.

Stimuli-responsive nanocarriers improve therapeutic precision by releasing drugs only where needed, thereby enhancing antimicrobial efficacy while

minimizing systemic exposure and adverse effects. Such intelligent drug delivery systems represent an important advancement toward precision antimicrobial therapy[51-52].

4.4 Combination Therapy and Co-delivery Systems

Combination therapy has emerged as an effective strategy for combating multidrug-resistant microorganisms by simultaneously targeting multiple bacterial pathways and reducing the probability of resistance development. Nanotechnology facilitates combination therapy through co-delivery systems capable of encapsulating two or more therapeutic agents within a single nanocarrier. Co-delivery systems may combine different antibiotics, antibiotics with antimicrobial peptides, antibiotics with metal nanoparticles, or antimicrobial agents with anti-inflammatory drugs, quorum sensing inhibitors, biofilm-disrupting enzymes, or nucleic acids such as siRNA and CRISPR-Cas components. Simultaneous delivery ensures synchronized pharmacokinetics and maintains optimal therapeutic ratios of multiple agents at infection sites.

Nanocarriers also enhance synergistic interactions between therapeutic agents by improving drug stability, increasing intracellular accumulation, overcoming bacterial defense mechanisms, and facilitating biofilm penetration. Metallic nanoparticles such as silver and zinc oxide frequently exhibit synergistic antimicrobial activity when combined with conventional antibiotics, enabling dose reduction while enhancing bacterial eradication. Additionally, multifunctional co-delivery systems integrating photodynamic therapy, photothermal therapy, or chemodynamic therapy with antimicrobial drugs have demonstrated remarkable efficacy against resistant pathogens and persistent biofilm-associated infections[53].

4.5 Theranostic Nanoplatforms

Theranostic nanoplatforms integrate diagnostic imaging and therapeutic functions into a single multifunctional nanosystem, enabling simultaneous detection, monitoring, and treatment of infectious diseases. These advanced nanoplatforms represent an emerging frontier in antimicrobial nanomedicine by facilitating real-time assessment of infection progression while delivering targeted antimicrobial therapy. Theranostic nanoparticles often incorporate imaging agents such as fluorescent dyes, magnetic nanoparticles, quantum dots, radionuclides, or contrast agents together with antimicrobial drugs. Iron oxide nanoparticles, for example, possess intrinsic magnetic resonance imaging (MRI) capability while serving as efficient drug carriers. Gold nanoparticles exhibit unique optical properties useful for photothermal therapy and imaging, whereas quantum dots provide fluorescence-based detection of microbial pathogens[54].

Modern theranostic systems are frequently combined with stimuli-responsive drug release, biosensing technologies, artificial intelligence-assisted image analysis, and precision medicine approaches to enable personalized antimicrobial treatment. In addition to monitoring therapeutic response, theranostic nanoplatforms facilitate early diagnosis of resistant infections, optimize treatment regimens, and minimize unnecessary antibiotic exposure. Although challenges related to long-term safety, regulatory approval, manufacturing complexity, and clinical translation remain, theranostic nanotechnology holds significant promise for the future management of antimicrobial resistance through integrated diagnosis and targeted therapy.

5. APPLICATIONS OF NANOTECHNOLOGY AGAINST DRUG-RESISTANT PATHOGENS

Nanotechnology has emerged as a promising strategy for combating multidrug-resistant (MDR) pathogens by enhancing antimicrobial efficacy, overcoming resistance mechanisms, improving targeted drug delivery, and disrupting microbial biofilms. Nanomaterials possess unique physicochemical properties, including a high surface-area-to-volume ratio, tunable surface chemistry, and the ability to penetrate biological barriers. These characteristics enable nanoparticles to act either as antimicrobial agents themselves or as carriers for antibiotics, antifungal drugs, antiviral agents, and antimicrobial peptides[55-56]. Recent advances have demonstrated their effectiveness against resistant Gram-positive and Gram-negative bacteria, pathogenic fungi, viruses, and biofilm-associated infections.

5.1 Gram-Positive Bacterial Infections

Drug-resistant Gram-positive bacteria, particularly **methicillin-resistant *Staphylococcus aureus* (MRSA)**, **vancomycin-resistant *Enterococcus* (VRE)**, and multidrug-resistant *Streptococcus pneumoniae*, remain major causes of hospital- and community-acquired infections. These pathogens exhibit resistance through altered antibiotic targets, biofilm formation, reduced membrane permeability, and efflux pumps, limiting the efficacy of conventional antimicrobial therapy. Nanotechnology offers several innovative approaches to overcome these challenges. Metallic nanoparticles such as silver (AgNPs), zinc oxide (ZnO NPs), copper oxide (CuO NPs), and titanium dioxide (TiO_2 NPs) exhibit intrinsic antibacterial activity by disrupting bacterial membranes, generating reactive oxygen species (ROS), damaging proteins and nucleic acids, and interfering with cellular metabolism. Lipid nanoparticles, polymeric nanoparticles, dendrimers, and mesoporous silica nanoparticles can encapsulate antibiotics such as vancomycin, linezolid, and daptomycin, enhancing drug stability, prolonging circulation time, and facilitating targeted delivery to infection sites[57].

Surface-functionalized nanoparticles can selectively bind bacterial cell walls, increasing intracellular antibiotic concentration while minimizing systemic toxicity. Additionally, nanoparticle-mediated photothermal and photodynamic therapies have shown promising results against persistent Gram-positive infections by producing localized heat or ROS upon external light irradiation, thereby killing bacteria resistant to conventional antibiotics.

Table 1. Applications of Nanotechnology Against Drug-Resistant Pathogens[56-60]

Nanotechnology Application	Nanocarrier/ Nanomaterial	Mechanism of Action	Drug-Resistant Pathogen(s)	Representative Example	Key Advantages
Targeted antibiotic delivery	Liposomes	Enhance intracellular drug delivery, improve bioavailability, reduce toxicity	Methicillin-resistant *Staphylococcus aureus* (MRSA)	Vancomycin-loaded liposomes	Increased antibacterial efficacy, prolonged circulation, reduced systemic toxicity
Controlled drug release	Polymeric nanoparticles (PLGA, Chitosan)	Sustained drug release and enhanced penetration into infected tissues	MRSA, *Pseudomonas aeruginosa*	Ciprofloxacin-loaded PLGA nanoparticles	Reduced dosing frequency and improved patient compliance
Biofilm eradication	Silver nanoparticles (AgNPs)	Disrupt extracellular polymeric substances (EPS), generate reactive oxygen species (ROS)	*P. aeruginosa*, *Escherichia coli*, MRSA	AgNP-coated wound dressings	Effective biofilm disruption and accelerated wound healing
Membrane disruption	Gold nanoparticles (AuNPs)	Damage bacterial membrane integrity and enhance antibiotic uptake	MRSA, *Acinetobacter baumannii*	Vancomycin-conjugated AuNPs	Synergistic antibacterial activity and reduced resistance development
Reactive oxygen species (ROS)-mediated killing	Zinc oxide nanoparticles (ZnO NPs)	ROS generation causing oxidative stress and bacterial death	MRSA, *Klebsiella pneumoniae*	ZnO nanoparticle suspension	Broad-spectrum antimicrobial activity with low resistance potential
Photodynamic antimicrobial therapy	Photosensitizer-loaded nanoparticles	Light-triggered ROS generation destroys bacterial cells	MRSA, multidrug-resistant (MDR) bacteria	Methylene blue-loaded silica nanoparticles	Localized treatment with minimal damage to surrounding tissues
Photothermal therapy	Gold nanorods, graphene oxide	Convert near-infrared (NIR) light into heat, causing bacterial cell death	MRSA, MDR *A. baumannii*	PEGylated gold nanorods	Rapid bacterial elimination and minimal systemic toxicity
Gene delivery and gene silencing	Lipid nanoparticles (LNPs), Polymeric nanoparticles	Deliver siRNA/CRISPR components to inhibit resistance genes	Carbapenem-resistant *Enterobacterales* (CRE), MRSA	siRNA-loaded lipid nanoparticles	Suppression of antimicrobial resistance genes and restoration of antibiotic susceptibility
Combination antimicrobial therapy	Solid lipid nanoparticles (SLNs), Nanostructured	Co-deliver multiple antibiotics or antibiotic–adjuvant combinations	MDR *Mycobacterium tuberculosis*, MRSA	Rifampicin–isoniazid SLNs	Improved synergistic activity and reduced

	lipid carriers (NLCs)				emergence of resistance
Antifungal nanotherapy	Liposomes, Polymeric nanoparticles	Improve antifungal drug delivery and intracellular accumulation	Azole-resistant *Candida auris*	Liposomal amphotericin B	Reduced nephrotoxicity and enhanced antifungal efficacy
Antiviral nanomedicine	Lipid nanoparticles, Dendrimers	Improve antiviral drug delivery and inhibit viral entry	Drug-resistant HIV, Influenza virus	LNP-based antiviral formulations	Enhanced cellular uptake and prolonged antiviral activity
Antimicrobial surface coatings	Silver, Copper, ZnO nanoparticles	Prevent microbial adhesion and biofilm formation on medical devices	MRSA, *P. aeruginosa*, *Enterococcus faecalis*	Silver nanoparticle-coated urinary catheters	Reduced healthcare-associated infections
Diagnostic nanotechnology	Magnetic nanoparticles, Quantum dots	Rapid pathogen detection and antimicrobial resistance profiling	MRSA, MDR *K. pneumoniae*	Magnetic nanoparticle-based biosensors	Early diagnosis and appropriate antimicrobial selection
Vaccine delivery	Lipid nanoparticles, Polymeric nanoparticles	Enhance antigen presentation and stimulate immune responses	Drug-resistant *Mycobacterium tuberculosis*	mRNA lipid nanoparticle vaccines	Improved immunogenicity and targeted immune activation
Stimuli-responsive nanocarriers	pH-responsive polymeric nanoparticles	Release antibiotics selectively at infection sites	MRSA, *P. aeruginosa* biofilms	pH-sensitive chitosan nanoparticles	Site-specific drug release with reduced off-target toxicity

MRSA – Methicillin-resistant *Staphylococcus aureus*, **MDR** – Multidrug-resistant, **ROS** – Reactive oxygen species, **PLGA** – Poly(lactic-co-glycolic acid), **SLNs** – Solid lipid nanoparticles, **NLCs** – Nanostructured lipid carriers, **LNPs** – Lipid nanoparticles, **CRE** – Carbapenem-resistant *Enterobacterales*, **EPS** – Extracellular polymeric substances, **NIR** – Near-infrared

5.2 Gram-Negative Bacterial Infections

Gram-negative bacteria represent one of the greatest challenges in antimicrobial therapy due to their complex outer membrane, lipopolysaccharide (LPS) layer, multidrug efflux pumps, and production of β-lactamases and carbapenemases. Common multidrug-resistant pathogens include *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*. Nanotechnology-based antimicrobial systems improve treatment outcomes by facilitating penetration through the bacterial outer membrane and bypassing conventional resistance mechanisms. Liposomes, polymeric nanoparticles, solid lipid nanoparticles, and nanoemulsions enhance intracellular antibiotic delivery while protecting drugs from enzymatic degradation. Nanocarriers loaded with carbapenems, aminoglycosides, colistin, or fluoroquinolones have demonstrated improved antibacterial efficacy against resistant Gram-negative pathogens[61].

Silver, gold, zinc oxide, and iron oxide nanoparticles also exhibit direct bactericidal activity by inducing oxidative stress, membrane disruption, DNA damage, and metabolic inhibition. Combination nanotherapies involving nanoparticles and conventional antibiotics often demonstrate synergistic antibacterial effects, restoring susceptibility in resistant bacterial strains while allowing lower antibiotic doses and reducing toxicity. Furthermore, stimuli-responsive nanoparticles capable of releasing antibiotics in response to pH, enzymes, or bacterial toxins offer precise infection-site drug delivery and reduced off-target effects.

5.3 Antifungal Nanotherapeutics

The increasing prevalence of antifungal-resistant pathogens, including *Candida auris*, *Candida albicans*, *Aspergillus fumigatus*, and *Cryptococcus neoformans*, has highlighted the need for improved antifungal therapies. Resistance to azoles, echinocandins, and polyenes is driven by alterations in drug targets, increased efflux pump expression, and biofilm formation. Nanotechnology has significantly improved antifungal drug delivery by enhancing drug solubility, stability, tissue penetration, and controlled release. Liposomal formulations of amphotericin B have already demonstrated reduced nephrotoxicity while maintaining potent antifungal activity. Polymeric nanoparticles, lipid nanoparticles, nanoemulsions, and nanostructured lipid carriers have also been

successfully employed for the delivery of itraconazole, fluconazole, voriconazole, and caspofungin.

Metallic nanoparticles, particularly silver nanoparticles, possess intrinsic antifungal activity by disrupting fungal cell membranes, damaging mitochondria, increasing ROS production, and inhibiting fungal biofilm formation. Functionalized nanoparticles carrying antifungal peptides, natural phytochemicals, or RNA-based therapeutics further enhance antifungal efficacy while minimizing host toxicity[62-63]. These advances provide promising alternatives for managing invasive fungal infections caused by multidrug-resistant organisms.

5.4 Antiviral Nanotechnology

Nanotechnology has become an important platform for antiviral therapy, vaccine development, and rapid viral diagnostics. Nanoparticles can inhibit viral infection by preventing viral attachment, blocking host-cell entry, interfering with viral replication, delivering antiviral drugs, or stimulating host immune responses. Lipid nanoparticles (LNPs) have revolutionized nucleic acid delivery by enabling the successful clinical application of mRNA vaccines. Polymeric nanoparticles, liposomes, dendrimers, gold nanoparticles, and silica nanoparticles are also widely investigated as carriers for antiviral agents, small interfering RNA (siRNA), CRISPR-based therapeutics, and immunomodulators.

Metallic nanoparticles such as silver and gold nanoparticles exhibit antiviral activity against influenza virus, human immunodeficiency virus (HIV), herpes simplex virus (HSV), hepatitis viruses, and coronaviruses by binding viral surface proteins and preventing viral entry into host cells. Nanotechnology additionally facilitates targeted drug delivery to infected tissues, sustained drug release, reduced systemic toxicity, and enhanced antiviral efficacy. Multifunctional nanoplatforms combining therapeutic, imaging, and diagnostic capabilities are increasingly being explored for personalized antiviral medicine[64].

5.5 Biofilm-Associated Infections

Biofilm-associated infections are among the most difficult infections to eradicate because microorganisms embedded within extracellular polymeric substances exhibit dramatically increased resistance to antibiotics, host immune responses, and environmental stress. Biofilms commonly develop on chronic wounds, implanted medical devices, urinary catheters, prosthetic joints, and indwelling vascular catheters. Nanotechnology provides effective strategies for biofilm prevention and eradication due to the small size and enhanced penetration capability of nanoparticles. Metallic nanoparticles, polymeric nanoparticles, liposomes, and enzyme-loaded nanocarriers can penetrate the biofilm matrix, disrupt extracellular polymeric substances, and deliver antimicrobial agents directly to embedded microorganisms[65].

Nanoparticles also inhibit bacterial quorum sensing, suppress biofilm maturation, and interfere with microbial communication pathways. Stimuli-responsive nanocarriers capable of releasing antibiotics in response to acidic pH, bacterial enzymes, or ROS further improve treatment specificity. Photothermal and photodynamic nanotherapies have demonstrated excellent biofilm eradication by generating localized heat or ROS, thereby destroying persistent bacterial communities without inducing significant resistance. The integration of nanotechnology with antimicrobial peptides, bacteriophages, enzymes, and conventional antibiotics represents a promising strategy for managing chronic biofilm-associated infections and reducing antimicrobial resistance.

6. CURRENT CHALLENGES, LIMITATIONS AND FUTURE PERSPECTIVES

6.1 Current Challenges

Despite the remarkable progress in nanotechnology-based antimicrobial strategies, several scientific, technical, and regulatory challenges continue to hinder their widespread clinical translation. One of the major obstacles is the incomplete understanding of the interactions between nanomaterials and biological systems. Factors such as nanoparticle size, shape, surface charge, composition, and protein corona formation significantly influence biodistribution, cellular uptake, and therapeutic efficacy, making it difficult to predict in vivo behavior. Furthermore, the heterogeneous nature of multidrug-resistant (MDR) pathogens and biofilms often limits the universal applicability of a single nanoplatform. Another significant challenge is the potential toxicity associated with nanomaterials. Although many nanoparticles exhibit potent antimicrobial activity, excessive production of reactive oxygen species (ROS), accumulation in vital organs, inflammatory responses, and long-term cytotoxicity remain concerns. Environmental safety is also an emerging issue, as large-scale production and disposal of engineered nanoparticles may adversely affect ecosystems and promote unintended microbial adaptation[66-67].

Manufacturing and scalability present additional barriers. Reproducible synthesis of nanoparticles with consistent physicochemical properties under Good Manufacturing Practice (GMP) conditions remains technically demanding and expensive. Moreover, the lack of standardized characterization methods and universally accepted protocols for evaluating antimicrobial efficacy complicates comparison between studies and delays regulatory approval.

6.2 Limitations of Current Nanotechnology-Based Approaches

Although numerous nanocarriers have demonstrated promising preclinical outcomes, only a limited number have progressed to clinical trials. Most published studies are restricted to in vitro experiments or animal models, with insufficient long-term clinical evidence regarding safety, pharmacokinetics, biodistribution, and therapeutic effectiveness in humans. Several nanomaterials also exhibit limitations related to stability, drug-loading efficiency, premature drug leakage, and rapid clearance by the mononuclear phagocyte system (MPS)[68]. Some metallic nanoparticles

may accumulate in organs such as the liver, spleen, kidneys, and lungs, raising concerns regarding chronic toxicity and biodegradability. Additionally, complex synthesis procedures, high production costs, batch-to-batch variability, and difficulties in large-scale manufacturing restrict commercialization.

Another limitation is the absence of harmonized international regulatory guidelines specifically designed for nanomedicines. Conventional pharmaceutical evaluation methods are often inadequate for assessing multifunctional nanoplatforms, creating uncertainty during regulatory review. Ethical considerations, environmental sustainability, and public acceptance also require careful attention before widespread clinical implementation.

6.3 Future Perspectives

Future research should focus on developing next-generation multifunctional nanoplatforms capable of simultaneously diagnosing, targeting, and eradicating multidrug-resistant pathogens while minimizing toxicity to host tissues. Smart and stimuli-responsive nanoparticles that release antimicrobial agents in response to infection-specific triggers such as pH, enzymes, temperature, or bacterial toxins represent a promising direction for precision antimicrobial therapy[69]. Artificial intelligence (AI) and machine learning (ML) are expected to accelerate nanoparticle design by predicting optimal physicochemical characteristics, drug-loading efficiency, toxicity profiles, and therapeutic outcomes. Personalized nanomedicine, tailored according to pathogen genotype, antimicrobial susceptibility, and patient-specific characteristics, may further improve treatment efficacy while reducing unnecessary antibiotic exposure. Combination therapies integrating nanoparticles with antibiotics, antimicrobial peptides, bacteriophages, CRISPR-Cas gene-editing systems, photothermal therapy, photodynamic therapy, or immunomodulatory agents are likely to play an increasingly important role in overcoming complex antimicrobial resistance mechanisms. Biofilm-targeting nanocarriers and infection-site-specific delivery systems also hold great promise for treating chronic and implant-associated infections[70].

From a translational perspective, future efforts should emphasize scalable and environmentally sustainable ("green") nanoparticle synthesis methods, standardized characterization protocols, comprehensive toxicological assessments, and well-designed multicenter clinical trials. International collaboration among researchers, clinicians, regulatory agencies, and pharmaceutical industries will be essential to establish harmonized regulatory frameworks and accelerate commercialization.

Overall, nanotechnology has the potential to transform the management of antimicrobial resistance by providing innovative therapeutic, diagnostic, and preventive strategies. However, realizing its full clinical potential will require overcoming current limitations through interdisciplinary research, technological innovation, regulatory standardization, and rigorous clinical validation. With continued advancements, nanotechnology-based antimicrobial therapies are expected to become an integral component of future precision medicine approaches for combating the global AMR crisis[70].

CONCLUSION

Antimicrobial resistance (AMR) has emerged as one of the most critical global public health challenges, threatening the effectiveness of conventional antibiotics and increasing morbidity, mortality, and healthcare costs. The rapid emergence of multidrug-resistant pathogens, coupled with the slow pace of new antibiotic development, highlights the urgent need for innovative therapeutic strategies. In this context, nanotechnology has demonstrated immense potential as a transformative approach to combat AMR through multiple mechanisms, including direct antimicrobial activity, targeted drug delivery, controlled drug release, biofilm disruption, and synergistic combination therapies. Various nanomaterials, such as metallic nanoparticles, polymeric nanoparticles, lipid-based nanocarriers, dendrimers, carbon-based nanomaterials, and hybrid nanoplatforms, have shown remarkable efficacy against a broad spectrum of drug-resistant bacteria, fungi, and viruses in preclinical studies. Their ability to overcome conventional resistance mechanisms, enhance intracellular drug accumulation, improve pharmacokinetic profiles, and minimize systemic toxicity makes them promising candidates for next-generation antimicrobial therapies. Furthermore, advances in stimuli-responsive and theranostic nanoplatforms have opened new opportunities for simultaneous diagnosis, targeted treatment, and real-time monitoring of infectious diseases. Despite these encouraging developments, several challenges remain before nanotechnology-based antimicrobial systems can be widely adopted in clinical practice. Concerns regarding long-term safety, nanotoxicity, biodegradability, large-scale manufacturing, regulatory approval, and cost-effectiveness must be addressed through standardized evaluation protocols and well-designed clinical trials. Collaborative efforts among researchers, clinicians, industry, and regulatory agencies will be essential to accelerate the translation of laboratory discoveries into safe and effective clinical applications. In conclusion, nanotechnology represents a highly promising and versatile strategy for addressing the growing threat of antimicrobial resistance. Continued interdisciplinary research, technological innovation, sustainable nanoparticle development, and robust clinical validation will be crucial for realizing its full therapeutic potential. With ongoing advancements, nanotechnology-based antimicrobial interventions are expected to play a pivotal role in the future of precision infectious disease management and contribute significantly to global efforts aimed at controlling the AMR crisis.

LIST OF ABBREVIATIONS

AgNPs: Silver nanoparticles; **AMR:** Antimicrobial resistance; **AuNPs:** Gold nanoparticles; **CDs:** Carbon dots; **CDT:** Chemodynamic therapy; **CNTs:** Carbon

nanotubes; **CRE:** Carbapenem-resistant Enterobacterales; **CuNPs:** Copper nanoparticles; **CuO NPs:** Copper oxide nanoparticles; **DNA:** Deoxyribonucleic acid; **EPS:** Extracellular polymeric substances; **EPR:** Enhanced permeability and retention; **Fe_3O_4 NPs:** Iron oxide nanoparticles; **GO:** Graphene oxide; **GMP:** Good Manufacturing Practice; **HIV:** Human immunodeficiency virus; **HSV:** Herpes simplex virus; **LNPs:** Lipid nanoparticles; **LPS:** Lipopolysaccharide; **MDR:** Multidrug-resistant; **MgO NPs:** Magnesium oxide nanoparticles; **ML:** Machine learning; **MOFs:** Metal–organic frameworks; **MRSA:** Methicillin-resistant *Staphylococcus aureus*; **MRI:** Magnetic resonance imaging; **MPS:** Mononuclear phagocyte system; **NIR:** Near-infrared; **NLCs:** Nanostructured lipid carriers; **NPs:** Nanoparticles; **PAMAM:** Poly(amidoamine); **PDT:** Photodynamic therapy; **PEG:** Polyethylene glycol; **PLA:** Polylactic acid; **PLGA:** Poly(lactic-co-glycolic acid); **PDR:** Pan drug-resistant; **PTT:** Photothermal therapy; **QS:** Quorum sensing; **rGO:** Reduced graphene oxide; **ROS:** Reactive oxygen species; **siRNA:** Small interfering RNA; **SLNs:** Solid lipid nanoparticles; **WHO:** World Health Organization; **XDR:** Extensively drug-resistant; **ZnO NPs:** Zinc oxide nanoparticles.

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