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Pharmaceutical Formulations of Nanotechnology-Based Drug Delivery Systems for Antimicrobial Applications: A Review

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ABSTRACT

Antimicrobial resistance (AMR) is on the rise globally, so creating new tools to combat resistant pathogens is essential. A novel approach that enhances the therapeutic potential of antimicrobial compounds by avoiding resistance mechanisms and reducing systemic side effects is the nanotechnologically based drug delivery system, or Nano-DDS. The preparation and application of pharmaceutical formulations containing nanomaterials, such as liposomes, polymeric nanoparticles, metallic nanoparticles, dendrimers, and carbon-based nanomaterials in antimicrobial therapy, are compiled in this review. Such systems address deadly multidrug-resistant organisms like MRSA and MDR-TB, as well as fungal and viral infections, by overcoming the poor solubility of drugs, enabling site-specific delivery, and promoting drug penetration inside microbial biofilms. Clinical and preclinical studies illustrating the potential of recent developments, such as theragnostic systems and stimuli-responsive nanocarriers, are discussed. Along with examining issues like toxicity, scalability, and regulatory barriers, the review offers solutions for safe clinical translation. Prospects for the future emphasize how nanotechnology can be integrated with artificial intelligence and CRISPR for personalized medicine. This review emphasizes how important nanotechnology is in combating AMR and calls for interdisciplinary cooperation to hasten its clinical adoption and fight the escalating global health emergency.

INTRODUCTION

One of the most urgent issues facing global health is antimicrobial resistance (AMR), which the World Health Organization estimates could kill 10 million people a year by 2050 if left unchecked [1]. The development of multidrug-resistant (MDR) pathogens, including extensively drug-resistant Pseudomonas aeruginosa, multidrug-resistant Mycobacterium tuberculosis (MDR-TB), and methicillin-resistant Staphylococcus aureus (MRSA), has been sped up by the overuse and abuse of antibiotics [2]. These pathogens make treatment outcomes considerably more difficult. Traditional antimicrobial treatments frequently have drawbacks that diminish their therapeutic effectiveness and fuel the emergence of resistance, such as poor drug solubility, quick body clearance, nonspecific biodistribution, and elevated toxicity [3].

These difficulties have prompted research into novel drug delivery methods, and nanotechnology is showing promise as a way to transform antimicrobial treatment. By increasing drug solubility, enabling targeted delivery to infection sites, and facilitating controlled drug release, nanotechnology-based drug delivery system such as liposomes, nanoparticles made of polymers, metallic nanoparticles, dendrimers, and carbon-based nanomaterials offer distinct advantages as they reduce off-target effects and improve therapeutic outcomes [4]. For instance, nanoparticles can deliver high concentrations of antimicrobial agents directly to the target site by penetrating intricate microbial structures like biofilms, which are infamously resistant to traditional treatments. Furthermore, co-delivery of several medications is made possible by nanotechnology, which fosters synergistic effects that can circumvent resistance mechanisms like enzymatic degradation and efflux pumps [5].

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With an emphasis on their design principles, mechanisms of action, and applications against bacterial, fungal, and viral infections, this review attempts to present a thorough analysis of pharmaceutical products of nanotechnology-based drug delivery systems for antimicrobial applications. Along with discussing current issues like toxicity, scalability, and regulatory barriers, it also looks at new developments and potential paths for clinical translation in the future. The transformative potential of nanotechnology in fighting AMR is highlighted in this article by synthesizing findings from recent studies. It also highlights the necessity of interdisciplinary collaboration to close the gap between research and clinical practice [6].

Nanotechnology in Drug Delivery

By modifying materials at the nanoscale (1–100 nm), nanotechnology can develop drug delivery systems with special physicochemical characteristics that overcome the drawbacks of traditional antimicrobial treatments. By increasing drug stability, bioavailability, and the ability to precisely target infection sites, these systems lower systemic toxicity and boost therapeutic efficacy. Many antimicrobial medications have poor solubility and quick clearance, which frequently results in less-than-ideal concentrations at the target site. However, lipid-based vesicles called liposomes, which are nanocarriers, can encapsulate both hydrophilic and hydrophobic medications, making them more soluble and extending their time in the body. Likewise, polymeric nanoparticles, like those derived from poly (lactic-co-glycolic acid) (PLGA), provide tunable characteristics and sustained drug release, enabling infection-specific controlled delivery [7].

Antibiotics can be made more effective against resistant pathogens by combining them with metallic nanoparticles, such as gold and silver, which have inherent antimicrobial activity. Dendrimers are perfect for delivering complex antimicrobial agents because of their branched macromolecular structure, which allows for precise size control and a high drug-loading capacity. In photothermal therapy, where localized heating can further disrupt microbial cells, carbon-based nanomaterials like graphene and carbon nanotubes provide strong platforms for drug delivery [8]. By surface functionalizing with ligands like peptides or antibodies, nanoparticles can target particular microbial cells or infected tissues, ensuring effective drug delivery with the least amount of harm to healthy tissues. In order to guarantee the best possible therapeutic concentrations at the infection site, stimuli-responsive nanoparticles can also release medications in response to environmental cues such as pH, temperature, or enzymes. Clinical applications have been made possible by these developments, which have been proven in multiple preclinical studies to exhibit improved antimicrobial activity against a variety of pathogens [9]. Nanomaterials are a key component of contemporary antimicrobial therapy due to their adaptability and capacity to get past conventional obstacles; research is still being done to optimize their design for particular clinical requirements [10].

Pharmaceutical Formulations for Antimicrobial Applications

Particle size, surface charge, encapsulation effectiveness while stability, and biocompatibility are some of the factors that must be carefully taken into account when developing pharmaceutical formulations based on nanotechnology for antimicrobial applications in order to ensure safe and effective drug delivery. For effective cellular uptake and tissue penetration, especially in the case of infections where deep tissue access is required, particle sizes that are normally smaller than 200 nm are essential [11]. The stability and interaction of nanoparticles with microbial membranes are influenced by their surface charge; cationic nanoparticles exhibit improved binding to the negatively charged surfaces of bacteria, which enhances their antimicrobial efficacy [12].

Therapeutic outcomes are influenced by encapsulation efficiency, which measures how much drug is successfully loaded into the nanocarrier, and high stability, which guarantees that the formulation stays intact during administration and storage. Because of their safety profile, biodegradable materials like PLGA are preferred; biocompatibility is crucial to avoiding toxicity or unfavorable immune reactions [13]. Antibiotics like vancomycin and ciprofloxacin, antifungals like amphotericin B, and antivirals like acyclovir are examples of frequently used antimicrobial agents. Nanoformulation helps each of these drugs get past their intrinsic drawbacks, like poor solubility or fast metabolism. For example, compared to its traditional counterpart, liposomal amphotericin B (AmBisome) has shown improved efficacy and decreased nephrotoxicity, earning approval for clinical use in the treatment of fungal infections [14]. Preclinical models have demonstrated the potential of investigational formulations, such as PLGA-based nanoparticles loaded with antibiotics, to treat MDR infections by improving drug delivery to intracellular pathogens. These formulations are very effective at fighting resistant pathogens because they are made to increase drug stability, decrease systemic toxicity, and guarantee sustained release at the infection site. With continuous attempts to maximize their physicochemical characteristics for particular antimicrobial applications, the development of such formulations keeps progressing [15].

Mechanisms of Antimicrobial Action

Through a variety of mechanisms that target the distinct traits of microbial pathogens, nanotechnology improves the effectiveness of antimicrobial agents. One important mechanism involves the disruption of microbial cell membranes, whereby nanoparticles, especially those with metallic compositions like silver or cationic surfaces, interact physically or electrostatically with the negatively charged bacterial cell wall, causing membrane rupture and cell lysis [16]. Because nanoparticles can pass through biofilms' extracellular matrix and directly deliver high concentrations of antimicrobial agents to the microbial community, they also play a crucial role in inhibiting the formation of biofilms, which are a major cause of chronic infections and resistance [17].

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In order to effectively eradicate pathogens like Mycobacterium tuberculosis, which live inside host macrophages, intracellular delivery is crucial. Nanoparticles can target these cells and release medications in a controlled manner. When antimicrobial medications are combined with nanomaterials, which may have inherent antimicrobial qualities, such as silver nanoparticles, which increase the activity of antibiotics against MDR bacteria by interfering with resistance mechanisms like efflux pumps, synergistic effects are produced [18]. Furthermore, by delivering medications in a way that avoids enzymatic degradation or other resistance pathways, nanoparticles can overcome resistance and guarantee long-lasting therapeutic efficacy. Together, these processes increase the effectiveness of antimicrobial treatments, which makes nanotechnology a potent weapon for combating the problems caused by pathogens that are resistant to antibiotics [19].

Applications in Bacterial Infections

Drug delivery systems based on nanotechnology have demonstrated great promise in the treatment of bacterial infections, especially those brought on by strains of bacteria that are resistant to multiple drugs, such as MRSA, Pseudomonas aeruginosa, and MDR-TB. Because these systems guarantee greater levels of medication at the infection site and lower systemic toxicity, they enhance the delivery of antibiotics like vancomycin, which show improved efficacy against MRSA when encapsulated in liposomes [20]. To improve drug penetration into bacterial cells and get past resistance mechanisms like efflux pumps, polymeric nanoparticles, like those made of PLGA and loaded with ciprofloxacin, have been developed to target Gram-negative bacteria. When combined with antibiotics, gold nanoparticles have demonstrated impressive efficacy in eliminating intracellular bacteria found in macrophages, which is a crucial problem in the treatment of persistent infections such as tuberculosis [21]. By preserving steady drug levels at the infection site, these nanoformulations allow for accurate targeting of bacterial pathogens, lower the necessary therapeutic dose, and lessen the chance of resistance development. Clinical trials to confirm the effectiveness of nanoparticle-based treatments in humans have been made possible by case studies showing that they can dramatically improve outcomes in animal models of bacterial infections. Nanotechnology is a key component of contemporary antimicrobial therapy because of its capacity to tackle the problems caused by bacterial resistance [22].

Applications in Fungal Infections

Due to poor drug penetration, low bioavailability, and growing resistance to antifungal agents, fungal infections caused by pathogens such as Candida albicans and Aspergillus fumigatus are notoriously challenging to treat. By improving the delivery of antifungals like fluconazole and amphotericin B, nanotechnology provides creative solutions. One well-known example is liposomal amphotericin B (AmBisome), which has strong antifungal activity against systemic infections while also dramatically lowering nephrotoxicity [23]. In order to increase fluconazole's effectiveness in treating topical fungal infections like candidiasis, polymeric nanoparticles have been created to better deliver the medication to mucosal surfaces [24].

By overcoming obstacles like thick cell walls and resistance mechanisms, these nanoformulations increase drug solubility, guarantee sustained release, and allow targeted delivery to fungal cells. Additionally, combination therapies in which several antifungal agents are administered simultaneously to produce synergistic effects, especially against resistant fungal strains are made possible by nanotechnology [25]. Recent research has demonstrated that fungal biofilms, a significant obstacle in chronic infections, can be broken down by nanoparticle-based antifungal treatments, improving therapeutic results. The increasing prevalence of resistant fungal infections could be significantly reduced with the continued development of antifungal formulations based on nanotechnology [26].

Applications in Viral Infections

Because viruses are intracellular and undergo rapid mutations that result in resistance, viral infections pose special difficulties. By increasing cellular uptake, enhancing drug stability, and decreasing systemic clearance, drug delivery systems based on nanotechnology increase the effectiveness of antiviral agents. For example, zidovudine and other antiviral medications have been delivered via lipid-based nanoparticles, which have been shown to have better intracellular concentrations and greater effectiveness against viruses such as HIV [27]. In order to combat viral infections, nanoparticles have also demonstrated promise in delivering tiny amounts of interfering RNA (siRNA) to silence viral genes. Furthermore, nanotechnology is being investigated for vaccine delivery, where preclinical studies for influenza and HIV vaccines have shown that nanoparticles improve immune responses by presenting antigens in a controlled way. Nanoparticles are an effective tool in antiviral therapy because of their capacity to precisely deliver antiviral payloads to particular cells, including immune cells. The development of multifunctional nanoparticles that combine therapeutic and diagnostic properties is the subject of ongoing research in order to address the intricate problems associated with viral infections [28].

Nanotechnology in Biofilm-Related Infections

One of the main causes of persistent infections and antibiotic resistance, especially in hospital-acquired infections, is biofilms, which are intricate microbial communities covered in a protective extracellular matrix. Innovative methods for efficiently delivering antimicrobial agents through biofilms are provided by nanotechnology. By interfering with microbial adhesion and quorum sensing, two essential processes in biofilm development, nanoparticles like silver nanoparticles, can prevent the formation of biofilms [29]. Antibiotic-loaded polymeric nanoparticles, like vancomycin, have demonstrated the capacity to pierce the biofilm matrix and release medications in a regulated fashion, eliminating embedded pathogens. The creation of pH-responsive nanocarriers, which release medications in the acidic biofilm microenvironment to improve therapeutic efficacy, is one recent development [30]. There is hope for clinical applications because case studies have shown that

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nanoparticle-based treatments can significantly reduce infections associated with biofilm in preclinical models. Nanotechnology is a vital weapon in the fight against persistent and resistant infections because of its capacity to handle the particular difficulties posed by biofilms [31].

Toxicity and Safety Considerations

The possible toxicity of nanomaterials is still a major concern for their clinical application, despite the fact that nanotechnology has many benefits. Silver and other metallic nanoparticles can build up in organs like the kidneys and liver, causing oxidative stress and possibly long-term toxicity [32]. Likewise, non-biodegradable nanomaterials could cause inflammation or immunological reactions, endangering patient safety. Because they break down into non-toxic byproducts that the body can safely metabolize, biodegradable materials like PLGA are recommended as a solution to these issues [33]. Nanoparticle surface modification, such as polyethylene glycol (PEG) coating, can enhance biocompatibility and decrease immunogenicity. To guarantee the safety of nanoformulations in clinical settings, dose optimization and thorough toxicological research are crucial [34]. In order to make it easier to translate safer nanomaterials into clinical practice, research is still being done on creating standardized procedures for evaluating their toxicity [35].

Manufacturing and Scalability Challenges

Significant obstacles to the large-scale manufacturing of drug delivery systems based on nanotechnology include batch-to-batch reproducibility, drug loading efficiency, and particle size variability. In order to maintain consistent physicochemical properties throughout manufacturing processes, sophisticated methods such as dynamic light scattering and electron microscopy are needed for quality control [36]. Because microfluidic technologies allow for precise control over the synthesis of nanoparticles, they have emerged as a promising method to increase reproducibility and scalability. Another important consideration is cost-effectiveness, since intricate manufacturing procedures can raise production costs and restrict accessibility in environments with limited resources. In order to promote the broad use of antimicrobial treatments based on nanotechnology, ongoing efforts are concentrated on creating scalable and affordable manufacturing techniques [37].

Regulatory and Clinical Translation Hurdles

Due to their distinct physicochemical characteristics that set them apart from traditional medications, the regulatory approval of drug delivery systems based on nanotechnology is a complex process. Clinical translation may be delayed by the need for comprehensive safety, efficacy, and manufacturing consistency data from regulatory bodies such as the FDA and EMA [38]. Since many nanoformulations do not make it past early-stage trials, the process is further complicated by inconsistent preclinical models and high development costs [39]. Although there are still issues with standardizing testing procedures, recent guidelines from regulatory bodies seek to expedite the approval process by offering frameworks for assessing nanomaterials. To overcome these obstacles and hasten the clinical adoption of treatments based on nanotechnology, cooperation between researchers, industry, and regulators is crucial [40].

Recent Advances and Innovations

Novel drug delivery systems with improved functionality have been developed as a result of recent developments in nanotechnology. Temperature-responsive polymeric nanoparticles and pH-sensitive liposomes are examples of stimuli-responsive nanocarriers that improve therapeutic efficacy by enabling targeted drug release at infection sites [41]. By fusing the controlled release capabilities of polymers with the antimicrobial qualities of metals, hybrid nanosystems that combine metallic and polymeric materials offer synergistic effects. Preclinical studies for bacterial infections have shown that theragnostic nanoparticles, which combine therapeutic and diagnostic functions, enable real-time monitoring of treatment efficacy [42]. New approaches to fighting resistant pathogens are being made possible by the combination of nanotechnology and cutting-edge technologies such as artificial intelligence for predictive drug design and CRISPR for gene editing. These developments demonstrate how nanotechnology has the ability to revolutionize antimicrobial treatment and tackle the problems posed by AMR [43].

Clinical and Preclinical Studies

Antimicrobial formulations based on nanotechnology have shown great promise in clinical trials. Clinical studies of liposomal amphotericin B (AmBisome) have demonstrated decreased toxicity and better results for patients with systemic fungal infections. By enhancing drug delivery to intracellular pathogens, preclinical research on PLGA-based nanoparticles loaded with antibiotics, like rifampicin, has demonstrated increased efficacy against MDR-TB [44]. In preclinical models of bacterial infections, gold nanoparticle-antibiotic conjugates have shown promise, completely eliminating pathogens in animal experiments. These studies demonstrate how nanoformulations can enhance therapeutic results and open the door for additional clinical trials to confirm their effectiveness in a range of patient populations [45].

Future Perspectives

The creation of personalized and precision medicine strategies, in which nanoformulations are adapted to patient-specific pathogens and resistance profiles, is where nanotechnology in antimicrobial therapy is headed. The potential for developing extremely successful treatments is enormous when nanotechnology is combined with cutting-edge technologies like CRISPR for targeted gene editing and artificial intelligence for drug design optimization [46]. It will take interdisciplinary cooperation between researchers, clinicians, and industry partners to overcome present obstacles like toxicity, scalability, and regulatory barriers. The clinical adoption of therapies based on nanotechnology will be accelerated by developments in manufacturing methods and regulatory frameworks [47]. The ability of nanotechnology to combat AMR will be further enhanced by ongoing research into novel nanomaterials and combination

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therapies, providing hope for tackling one of the most important global health issues [48].

CONCLUSION

By improving the effectiveness of antimicrobial agents, circumventing resistance mechanisms, and lowering systemic toxicity, drug delivery systems based on nanotechnology offer a revolutionary strategy to combat antimicrobial resistance. The treatment of bacterial, fungal, and viral infections including those brought on by multidrug-resistant pathogens has shown great promise thanks to developments in liposomes, polymeric nanoparticles, metallic nanoparticles, and other nanomaterials. Recent developments in stimuli-responsive and theragnostic systems demonstrate the adaptability of nanotechnology in treating complex infections, despite obstacles in toxicity, scalability, and regulatory approval. Their effectiveness is demonstrated by preclinical and clinical research, opening the door for wider clinical adoption. There are exciting prospects for personalized medicine when nanotechnology is combined with cutting-edge technologies like artificial intelligence and CRISPR. To get past present obstacles and implement these cutting-edge treatments in clinical settings, eventually resolving the global AMR crisis and enhancing patient outcomes, more research and interdisciplinary cooperation are necessary.

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