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Nanotechnology-Driven Strategies to Combat Antimicrobial Resistance in the One Health Era

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ABSTRACT

Antimicrobial resistance (AMR) has emerged as one of the greatest global public health threats, compromising the effectiveness of antibiotics and jeopardizing advances in modern medicine. The extensive use and misuse of antimicrobial agents in human medicine, veterinary practice, agriculture, and aquaculture have accelerated the emergence and spread of multidrug-resistant microorganisms. Because resistant pathogens, antibiotic residues, and resistance genes continuously circulate among humans, animals, and the environment, AMR is now recognized as a complex One Health challenge requiring coordinated, multidisciplinary solutions. However, conventional strategies, including the development of new antibiotics and antimicrobial stewardship programs, are increasingly constrained by rapid microbial adaptation, biofilm formation, delayed diagnosis, and the declining antibiotic discovery pipeline. Nanotechnology has emerged as a promising interdisciplinary platform capable of addressing several limitations of conventional antimicrobial approaches. Nanomaterials possess intrinsic broad-spectrum antimicrobial activity, enhance targeted drug delivery, improve biofilm eradication, and enable rapid pathogen detection through advanced nanodiagnostic systems. Furthermore, integrating nanotechnology with artificial intelligence, machine learning, and smart biosensing technologies is accelerating the development of precision antimicrobial therapies and real-time AMR surveillance systems. This review discusses the AMR crisis from a One Health perspective and summarizes recent advances in antimicrobial nanomaterials, nanodrug delivery systems, antibiofilm strategies, and nanodiagnostics. Current translational challenges and future perspectives are also highlighted, emphasizing the potential of nanotechnology to support sustainable AMR management across interconnected human, animal, and environmental sectors.

Keywords: Antimicrobial resistance, artificial intelligence, biofilms, nanodiagnostics, nanodrug delivery, nanoparticles, nanotechnology, One Health.

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INTRODUCTION

Antimicrobial resistance (AMR) has emerged as one of the most serious threats to global public health, modern medicine, food security, and economic stability.[1,2] The extraordinary success of antibiotics during the twentieth century revolutionized healthcare and dramatically reduced mortality from infectious diseases.[3] However, decades of excessive and inappropriate antimicrobial use in human medicine, veterinary practice, agriculture, and aquaculture have accelerated the emergence of resistant microorganisms capable of surviving even the most potent antimicrobial therapies.[4] Today, infections that were once considered easily treatable are becoming increasingly difficult and time-consuming to treat and, in some cases, impossible to cure.

The consequences of AMR extend far beyond individual patient outcomes. Resistant pathogens threaten essential medical procedures, including organ transplantation, cancer chemotherapy, neonatal care, and major surgery, all of which rely heavily on effective infection control.[2] According to global estimates, AMR already contributes to millions of deaths annually and may result in approximately 10 million deaths per year by 2050 unless urgent interventions are implemented.[1] In addition to its devastating health burden, AMR imposes enormous economic costs through prolonged hospitalizations, increased healthcare expenditures, productivity losses, and strain on healthcare infrastructure worldwide.[1,2]

One of the greatest challenges in addressing AMR is that resistance does not emerge or spread within a single, isolated environment. Instead, resistant microorganisms continuously circulate among humans, animals, food products, and environmental reservoirs through highly interconnected transmission pathways.[5] Antibiotics used in livestock production may select for resistant bacteria that enter the food chain, whereas hospital effluents, pharmaceutical waste, and agricultural runoff introduce antimicrobial residues and resistance genes into aquatic and soil ecosystems.[6] Environmental microorganisms further amplify the dissemination of resistance through horizontal gene transfer mechanisms mediated by plasmids, transposons, and other mobile genetic elements. Consequently, AMR has evolved from a purely clinical problem into a complex ecological and global health crisis.

This interconnected pattern of resistance dissemination has emphasized the importance of the One Health concept, which recognizes the close relationships among human, animal, and environmental health. The One Health framework underscores that effective AMR mitigation cannot rely solely on hospital-based antibiotic stewardship programs or the discovery of new antimicrobial drugs. Instead, sustainable control strategies require coordinated, multidisciplinary collaboration among clinicians, microbiologists, veterinarians, environmental scientists, policymakers, and public health authorities. Without integrated surveillance systems and cross-sectoral interventions, resistant pathogens and resistance genes will continue to circulate across ecosystems regardless of local containment efforts.

Despite decades of antimicrobial development, conventional antibiotics are increasingly ineffective against multidrug-resistant pathogens. Microorganisms possess remarkable adaptive capabilities that enable the rapid evolution of resistance mechanisms, including enzymatic antibiotic degradation, target modification, altered membrane permeability, active efflux systems, and biofilm formation.[7] Meanwhile, the antibiotic discovery pipeline has slowed dramatically because of scientific challenges, high development costs, and limited economic incentives for pharmaceutical companies.[3] As resistance evolves more rapidly than new antibiotics are introduced, the effectiveness of conventional antimicrobial therapies continues to decline.

In response to these growing limitations, nanotechnology has emerged as one of the most promising interdisciplinary approaches to combating AMR. Nanomaterials possess unique physicochemical properties, including nanoscale dimensions, high surface-area-to-volume ratios, tunable surface chemistry, and multifunctionality, that enable novel antimicrobial applications.[8] Unlike traditional antibiotics, which often target a single cellular pathway, nanoparticles can attack microorganisms through multiple simultaneous mechanisms, such as reactive oxygen species generation, membrane disruption, protein dysfunction, and nucleic acid damage, thereby reducing the likelihood of resistance development.[9]

Importantly, nanotechnology offers solutions that extend across all One Health domains. In human medicine, nano-enabled systems improve targeted drug delivery, infection control, wound healing, and rapid diagnostics.[10,11] In veterinary and agricultural settings, nanotechnology may reduce excessive dependence on antibiotics through nano-enabled therapeutics, feed additives, vaccines, and biosensors.

Environmental applications, including nanotechnology-based wastewater treatment systems and antimicrobial residue removal technologies, further support AMR mitigation at the ecosystem level.[12] Moreover, the integration of artificial intelligence (AI), smart biosensing systems, and nanoengineering has accelerated the development of advanced precision antimicrobial platforms capable of improving therapeutic efficacy while minimizing toxicity and unnecessary antibiotic exposure.[13]

Therefore, nanotechnology is increasingly recognized as a powerful and versatile strategy capable of addressing AMR from a truly One Health-oriented perspective. However, despite substantial progress, important challenges related to biosafety, toxicity, environmental impact, scalability, regulatory approval, and clinical translation remain unresolved.

This review aims to comprehensively examine the growing AMR crisis through the lens of the One Health framework while critically evaluating the potential of nanotechnology-

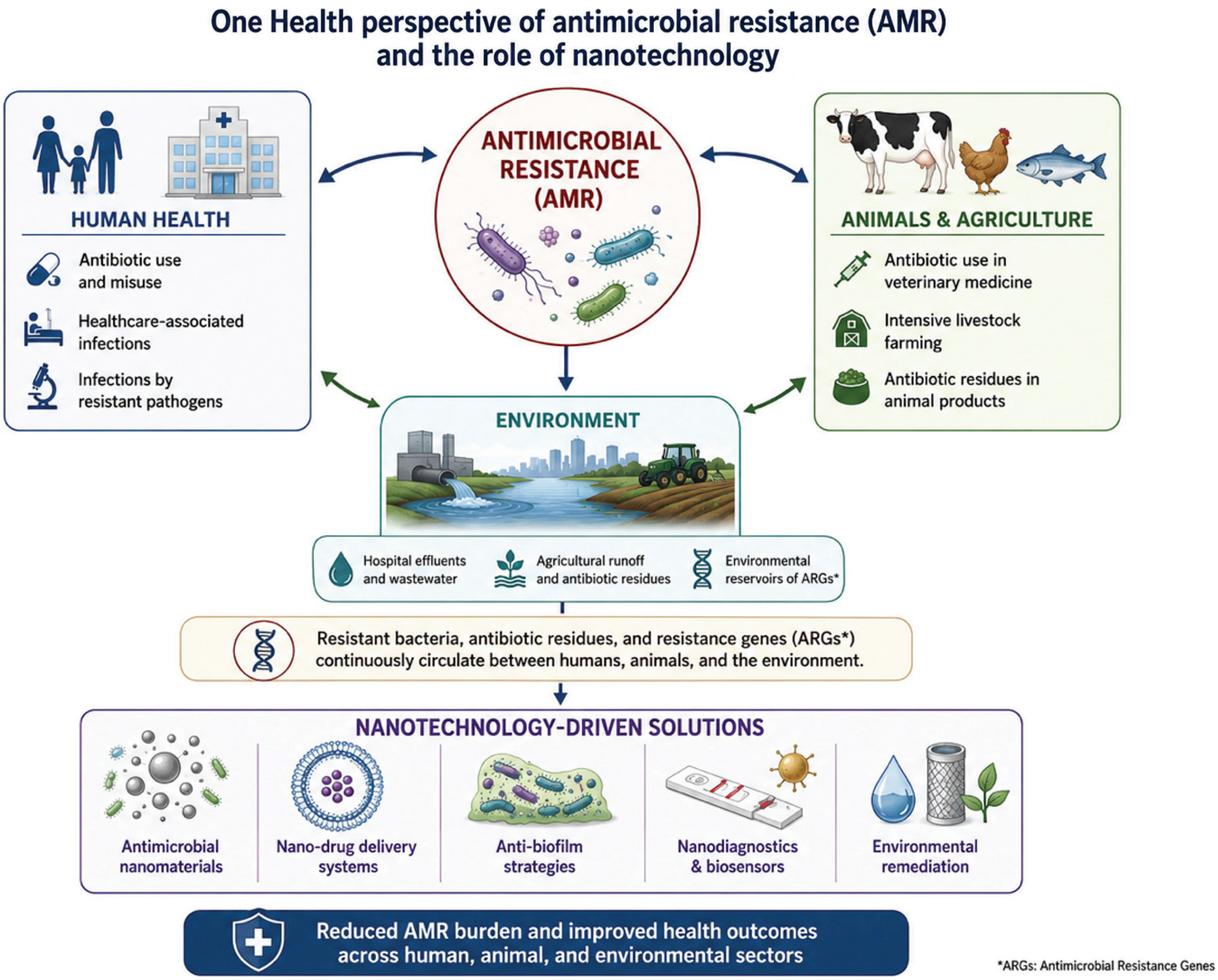

Figure 1. One Health perspective on AMR and the role of nanotechnology. Antimicrobial resistance emerges and spreads through interconnected human, animal, and environmental systems via the circulation of resistant microorganisms, antibiotic residues, and antimicrobial resistance genes (ARGs). A One Health approach integrates these sectors to address AMR through nanotechnology-driven solutions, including antimicrobial nanomaterials, nanodrug delivery systems, antibiofilm strategies, nanodiagnostics and biosensors, and environmental remediation technologies. Together, these approaches contribute to improved antimicrobial stewardship, reduced AMR dissemination, and better health outcomes across human, animal, and environmental domains.

driven strategies as cross-domain solutions. It explores the global burden of AMR, the limitations of conventional antimicrobial approaches, current advances in antimicrobial nanomaterials and nanodrug delivery systems, antibiofilm and nanodiagnostic technologies, applications across human, veterinary, and environmental sectors, integration with emerging technologies such as AI, and future perspectives for sustainable, nano-enabled AMR management.

Figure 1 provides an overview of AMR from a One Health perspective and illustrates how resistant pathogens, antibiotic residues, and antimicrobial resistance genes circulate among humans, animals, and the environment. It also summarizes the major nanotechnology-based strategies discussed throughout this review, highlighting their potential to support integrated AMR prevention, diagnosis, treatment, and environmental remediation within the One Health framework.

THE AMR CRISIS THROUGH THE ONE HEALTH LENS

Human Health Contribution

Human healthcare systems represent one of the primary drivers of the development and dissemination of antimicrobial resistance worldwide. The extensive and frequently inappropriate use of antibiotics in hospitals, outpatient clinics, and community settings has created substantial selective pressure that accelerates the emergence of resistant microorganisms. In many healthcare systems, antibiotics are prescribed unnecessarily for viral infections, such as influenza and the common cold, despite the absence of bacterial pathogens. Empirical broad-spectrum antibiotic therapy, often initiated before a definitive microbiological diagnosis is established, further contributes to resistance selection and microbial adaptation. In addition, self-medication, poor patient adherence, incomplete treatment courses, and unrestricted access to antibiotics in some countries significantly exacerbate the AMR crisis.[14]

The growing prevalence of multidrug-resistant pathogens has become a major challenge in modern clinical practice. Hospital-acquired infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *enterococci* (VRE), and multidrug-resistant *Pseudomonas aeruginosa* are increasingly associated with prolonged hospitalization, increased mortality, and rising healthcare costs.[15] Intensive care units, oncology wards, transplant units, and surgical departments are particularly vulnerable because of the high frequency of invasive procedures, the presence of immunocompromised patients, and extensive antimicrobial exposure.

Another important contributor to AMR in human health is inadequate infection prevention and control. Poor hand hygiene, overcrowded healthcare facilities, insufficient sterilization procedures, and delayed pathogen identification facilitate the transmission of resistant organisms among patients and healthcare workers. International travel and medical tourism further accelerate the global dissemination of resistant pathogens across geographical boundaries.

Biofilm-associated infections constitute another major clinical challenge. Bacterial biofilms protect microorganisms from antibiotics and host immune responses, resulting in persistent infections associated with medical devices, chronic wounds, implanted biomaterials, and indwelling catheters. Within biofilms, microorganisms exhibit altered metabolic states and enhanced resistance to antimicrobial agents, making eradication extremely difficult. Conventional antibiotics often fail to penetrate biofilm matrices effectively, necessitating alternative therapeutic approaches and innovative antimicrobial technologies.[16]

Animal and Agricultural Impact

The animal and agricultural sectors play a major role in the global emergence and dissemination of antimicrobial resistance. Antibiotics are extensively used in livestock production not only for therapeutic purposes but also for disease prevention and growth promotion, particularly in intensive farming systems.[17] Continuous exposure of animals to antimicrobial agents creates strong selective pressure that promotes the survival and proliferation of resistant microorganisms within animal populations. These resistant bacteria may subsequently spread to humans through direct contact with animals, contaminated food products, and environmental pathways.

The large-scale use of medically important antibiotics in the poultry, cattle, swine, and aquaculture industries has raised significant global concern. Resistant pathogens, such as extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and multidrug-resistant *Salmonella* species, have increasingly been detected in food-producing animals.[18] These microorganisms can enter the food chain during slaughter, food processing, transportation, and consumption, thereby facilitating zoonotic transmission and increasing the burden of resistant infections in humans.

Aquaculture systems also contribute substantially to AMR dissemination because of the frequent administration of antibiotics in fish-farming environments. Residual antimicrobial compounds released into aquatic ecosystems may persist for long periods and promote the development of resistance among environmental microorganisms. Similarly, agricultural practices involving manure application and antibiotic-containing fertilizers introduce resistant bacteria and antimicrobial residues into soil ecosystems, creating environmental reservoirs of resistance genes.[19]

Another important concern is the globalization of food trade and animal product distribution, which accelerates the international spread of resistant pathogens across geographical boundaries. Inadequate veterinary oversight, weak antimicrobial stewardship policies, and insufficient surveillance systems in some regions further complicate AMR control efforts in agricultural settings.

Consequently, AMR in animals and agriculture should not be viewed solely as a veterinary issue but rather as a major component of the broader One Health challenge. Effective mitigation strategies require stricter regulations governing antimicrobial use in livestock production, improved farm hygiene and biosecurity measures, enhanced vaccination programs, and the development of sustainable alternatives to antibiotics, including nano-enabled therapeutics, vaccines, and biosensors.

ENVIRONMENTAL RESERVOIRS

Environmental reservoirs play a central role in the persistence, evolution, and dissemination of antimicrobial resistance across ecosystems. Unlike clinical settings, where resistant infections are often detected and monitored, environmental reservoirs allow resistant microorganisms and resistance genes to circulate silently and continuously among humans, animals, water systems, and soil environments. Consequently, the environment functions not only as a passive sink for antimicrobial contaminants but also as an active driver of resistance evolution and transmission.

Wastewater treatment plants, pharmaceutical manufacturing waste, hospital effluents, and agricultural runoff contain antibiotics, resistant bacteria, and resistance determinants that enter natural ecosystems.[20] In many regions, incomplete wastewater treatment processes fail to fully eliminate antimicrobial residues and resistant microorganisms before water is discharged into rivers, lakes, and coastal environments. As a result, aquatic ecosystems become major hotspots for resistance dissemination and microbial adaptation.

Environmental microorganisms may acquire resistance genes through horizontal gene transfer mechanisms, including conjugation, transformation, and transduction. Mobile genetic elements, such as plasmids, transposons, and integrons, facilitate the rapid dissemination of resistance determinants across bacterial populations.[21] Environmental stressors, including heavy metals, disinfectants, and residual antimicrobial compounds, may further increase selective pressure and promote the persistence of resistance genes within microbial communities.

Aquatic systems are particularly vulnerable to AMR dissemination because of contamination from untreated wastewater, industrial discharge, and pharmaceutical pollution. Rivers and surface waters receiving hospital and municipal wastewater often contain high concentrations of resistant bacteria and antimicrobial residues, allowing resistant organisms to spread across large geographical areas. Similarly, groundwater contamination may contribute to the indirect transmission of resistant microorganisms through drinking water systems.

Soil ecosystems also serve as important reservoirs of antimicrobial resistance genes, particularly in areas exposed to intensive agricultural activities, livestock manure application, and antibiotic-containing fertilizers. Resistant bacteria in soil may interact with environmental microorganisms, creating highly dynamic microbial networks that facilitate gene exchange and the long-term persistence of resistance.

Another major concern is the environmental accumulation of antimicrobial compounds and nanoparticles, which may alter natural microbial diversity and ecological balance. The continuous release of antimicrobial agents into ecosystems creates chronic selective pressure that favors resistant microorganisms while suppressing susceptible microbial populations.

Given the complex environmental dimension of AMR, effective mitigation strategies require improved wastewater treatment technologies, stricter pharmaceutical waste management, environmental surveillance systems, and sustainable antimicrobial stewardship practices. Nanotechnology-based environmental remediation systems, advanced filtration membranes, photocatalytic nanoparticles, and nano-enabled biosensors may provide promising tools for reducing antimicrobial contamination and limiting the environmental spread of resistance genes.

WHY CONVENTIONAL STRATEGIES ARE FAILING

Despite decades of scientific progress and the discovery of numerous antimicrobial agents, conventional strategies for combating infectious diseases are becoming increasingly insufficient in the face of rapidly evolving antimicrobial resistance. For many years, the development of new antibiotics was considered the primary solution to resistant infections. However, the extraordinary adaptive capacity of microorganisms has allowed resistance mechanisms to emerge shortly after the introduction of nearly every major antibiotic class. Consequently, resistance is now evolving at a rate that significantly exceeds the pace of novel antibiotic discovery, creating a widening therapeutic gap that threatens the effectiveness of modern healthcare systems.

One of the most critical limitations of conventional antimicrobial approaches is the dramatic slowdown in antibiotic discovery and development. During the golden era of antibiotic discovery in the mid-twentieth century, numerous classes of antibiotics were identified from natural and synthetic sources. In recent decades, however, the development pipeline has declined substantially because of scientific, economic, and regulatory challenges.[4] Pharmaceutical companies have reduced investment in antibiotic research because antimicrobial drugs generally provide lower financial returns than therapies for chronic diseases. Moreover, the rapid emergence of resistance after commercialization often shortens the clinical lifespan of newly introduced antibiotics, further discouraging investment.

At the microbial level, pathogens continuously evolve sophisticated resistance mechanisms that compromise the efficacy of existing drugs. Many antibiotics target specific bacterial structures or metabolic pathways, allowing microorganisms to adapt through spontaneous mutations or the horizontal acquisition of resistance genes.[22] Common resistance mechanisms include enzymatic degradation of antibiotics, modification of drug targets, reduced membrane permeability, overexpression of efflux pumps, and alterations in metabolic pathways. These adaptive responses enable microorganisms to survive antimicrobial exposure and proliferate even in highly selective environments.

Another major challenge is biofilm-associated resistance. Biofilms are highly organized microbial communities enclosed within extracellular polymeric matrices that provide strong protection against antibiotics and host immune defenses.[23] Within biofilms, microorganisms exhibit altered metabolic activity and enhanced resistance to antimicrobial agents, making eradication extremely difficult. Conventional antibiotics often fail to penetrate biofilm structures effectively, resulting in persistent and recurrent infections associated with medical devices, implants, chronic wounds, and indwelling catheters.

Conventional antibiotics also have several pharmacological and therapeutic limitations, including poor bioavailability, systemic toxicity, nonspecific tissue distribution, and rapid degradation in biological environments.[24] Broad-spectrum antimicrobial agents may disrupt the normal microbiota, increasing the risk of secondary infections and further promoting the selection of resistance. Additionally, excessive antibiotic exposure exerts strong selective pressure on microbial populations, accelerating the emergence and dissemination of resistant strains.

Another important weakness of current AMR management strategies is the lack of coordinated global implementation of One Health principles. Human healthcare systems, veterinary sectors, agricultural industries, food production systems, and environmental agencies frequently operate independently, with insufficient communication, integrated surveillance, and data sharing.[25] Consequently, resistant pathogens and resistance genes continue to circulate across interconnected ecosystems despite local containment efforts.

Diagnostic limitations further complicate AMR control. Conventional microbiological diagnostic methods are often time-consuming and may require several days to identify pathogens and determine antimicrobial susceptibility profiles. Delayed diagnosis frequently results in the empirical use of broad-spectrum antibiotics, which contributes substantially to inappropriate antimicrobial exposure and the development of resistance.

In addition, globalization, international travel, urbanization, climate change, and increasing population density facilitate the rapid worldwide dissemination of resistant microorganisms. Resistant pathogens can spread across continents through human migration, food trade, animal transportation, and environmental contamination, making AMR a truly transnational challenge that cannot be effectively controlled through isolated local interventions.

Collectively, these limitations highlight the urgent need for innovative, multidisciplinary approaches capable of overcoming the shortcomings of conventional antimicrobial strategies. The growing failure of traditional antibiotics has therefore accelerated interest in alternative technologies, such as nanotechnology, precision medicine, artificial intelligence-assisted therapeutics, and advanced biosurveillance systems, which may provide more sustainable solutions for combating AMR within the One Health framework.

NANOTECHNOLOGY AS A ONE HEALTH SOLUTION TO AMR

Antimicrobial Nanomaterials

Antimicrobial nanomaterials represent one of the most extensively investigated areas of nanotechnology-based AMR management because of their remarkable ability to inhibit a broad range of pathogenic microorganisms through diverse and often simultaneous mechanisms of action. Unlike conventional antibiotics, which usually target a single bacterial pathway or cellular structure, nanomaterials can interact with microbial cells through multiple physicochemical processes, thereby reducing the likelihood of resistance development and improving antimicrobial efficacy against multidrug-resistant pathogens.

The antimicrobial activity of nanomaterials is strongly influenced by their size, shape, surface charge, chemical composition, and surface functionalization. At the nanoscale, particles possess exceptionally high surface-area-to-volume ratios that enhance their interactions with bacterial membranes and intracellular structures.[26] These unique properties enable nanoparticles to penetrate microbial cell walls more effectively and disrupt critical cellular functions.

A wide variety of nanomaterials have demonstrated promising antimicrobial activity, including metallic nanoparticles, metal oxide nanoparticles, carbon-based nanomaterials, polymeric nanocomposites, and hybrid nanoformulations. Among these, metallic and metal oxide nanoparticles, such as silver nanoparticles (AgNPs), zinc oxide nanoparticles (ZnO NPs), copper oxide nanoparticles (CuO NPs), titanium dioxide nanoparticles (TiO_2 NPs), and gold nanoparticles (AuNPs), have attracted substantial attention because of their potent broad-spectrum antimicrobial properties.[27,28]

Nanomaterials possess unique physicochemical properties that enable potent antimicrobial activity against resistant pathogens. Metallic and metal oxide nanoparticles, including AgNPs, ZnO NPs, CuO NPs, TiO_2 NPs, and AuNPs, have demonstrated broad-spectrum antimicrobial effects.[27]

Silver nanoparticles are among the most extensively investigated antimicrobial nanomaterials because of their potent activity against Gram-positive and Gram-negative bacteria, fungi, and viruses. AgNPs exert antimicrobial effects through multiple mechanisms, including reactive oxygen species (ROS) generation, membrane disruption, protein denaturation, and DNA damage.[29]

Zinc oxide nanoparticles exhibit photocatalytic antimicrobial activity and can induce oxidative stress in bacterial cells. Similarly, titanium dioxide nanoparticles generate ROS upon exposure to ultraviolet light, contributing to microbial inactivation.[28] Gold nanoparticles have gained attention because of their excellent biocompatibility and potential applications in photothermal therapy and biosensing.[27]

The multitarget antimicrobial mechanisms of nanoparticles reduce the likelihood of resistance development compared with conventional antibiotics. In addition, nanoparticle surface modification enables enhanced selectivity and synergistic effects when nanoparticles are combined with antibiotics.

The antimicrobial activity of nanomaterials relies on multiple complementary mechanisms rather than a single molecular target. By simultaneously disrupting bacterial membranes, inducing oxidative stress, interfering with intracellular biomolecules, inhibiting biofilm formation, and enhancing targeted drug delivery, nanotechnology offers a multifaceted strategy for combating multidrug-resistant pathogens. An overview of these principal antimicrobial mechanisms is presented in Figure 2.

Nanodrug Delivery Systems

Nanodrug delivery systems represent one of the most important nanotechnology-based strategies for improving antimicrobial therapy against resistant pathogens. Conventional antibiotics often have poor solubility, limited bioavailability, rapid degradation, nonspecific tissue distribution, and systemic toxicity, all of which reduce therapeutic efficacy and contribute to resistance development. Nano-enabled delivery systems overcome many of these limitations by enhancing drug stability, improving targeted delivery, prolonging circulation time, and enabling controlled or stimuli-responsive drug release directly at infection sites. In addition, nanocarriers can improve intracellular penetration and facilitate antimicrobial accumulation within biofilms and infected tissues, thereby increasing treatment effectiveness while minimizing damage to healthy cells and reducing unnecessary antibiotic exposure.

Nanodrug delivery systems improve antimicrobial therapy by enhancing drug stability, solubility, targeted delivery, and controlled release. Liposomes, polymeric nanoparticles, dendrimers, solid lipid nanoparticles, and nanoemulsions have been widely investigated for antimicrobial applications.[24,30]

Liposomes are phospholipid vesicles capable of encapsulating both hydrophilic and hydrophobic antimicrobial agents. Liposomal formulations improve drug pharmacokinetics, reduce systemic toxicity, and enhance intracellular delivery. Polymeric nanoparticles composed of biodegradable polymers, such as poly(lactic-co-glycolic acid) (PLGA), enable sustained drug release and targeted delivery to infected tissues. Functionalized nanoparticles can specifically target bacterial cells or biofilm environments through ligand-mediated interactions.

Nanodelivery systems may also reduce the required antibiotic dosage and minimize the selective pressure that drives resistance evolution. Combination nanotherapies involving antibiotics and metallic nanoparticles have demonstrated synergistic antimicrobial effects against resistant pathogens.[30]

Nanodiagnostics for AMR Detection

Rapid and accurate detection of resistant pathogens is essential for effective antimicrobial stewardship, early therapeutic intervention, and infection control. Conventional microbiological diagnostic methods often require several days to identify pathogens and determine antimicrobial susceptibility profiles, resulting in delayed treatment decisions and increased empirical use of broad-spectrum antibiotics. Consequently, there is a growing need for rapid, sensitive, cost-effective, and portable diagnostic technologies capable of detecting resistant microorganisms in clinical, veterinary, agricultural, and environmental settings.

Nanotechnology-based diagnostic systems have emerged as highly promising tools for improving AMR detection because of their exceptional sensitivity, rapid response times, and potential for miniaturization. Nanodiagnostic platforms use unique nanoscale properties to detect pathogens, resistance genes, toxins, and antimicrobial susceptibility patterns with high precision. These technologies may significantly reduce diagnostic turnaround times and support more targeted antimicrobial therapy, thereby minimizing unnecessary antibiotic exposure and slowing the development of resistance.[31]

Rapid and accurate pathogen identification is essential for appropriate antimicrobial therapy and antibiotic stewardship. Conventional microbiological methods are often time-consuming and may delay treatment decisions.

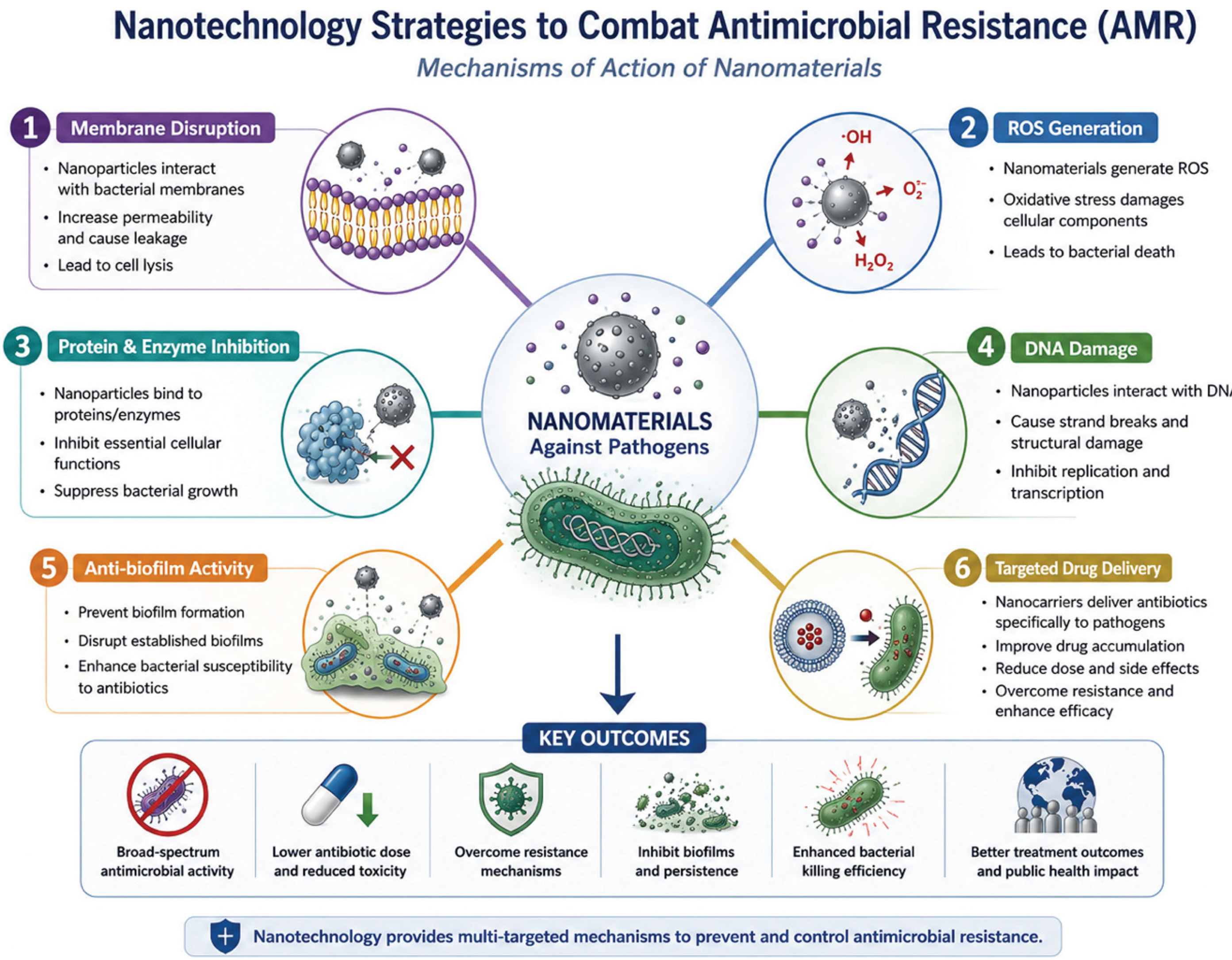

Figure 2. Major antimicrobial mechanisms of nanotechnology-based strategies against antimicrobial-resistant microorganisms. Nanomaterials exert antimicrobial activity through multiple complementary mechanisms, including bacterial membrane disruption, reactive oxygen species (ROS) generation, inhibition of essential proteins and enzymes, nucleic acid damage, biofilm prevention and eradication, and the targeted delivery of antimicrobial agents. Because these mechanisms act simultaneously, nanotechnology can improve bacterial killing efficiency, enhance antibiotic efficacy, reduce the required therapeutic dose, limit toxicity, and decrease the likelihood of resistance development compared with conventional single-target antibiotics.

Nanotechnology-based biosensors and diagnostic systems enable the rapid, sensitive, and portable detection of pathogens and resistance genes.[32] Gold nanoparticles, quantum dots, magnetic nanoparticles, and graphene-based sensors have been used for nucleic acid detection, immunosensing, and surface-enhanced Raman spectroscopy (SERS)-based diagnostics.[11,33–36] These nano-enabled platforms offer several advantages over conventional diagnostic approaches, including high analytical sensitivity, low detection limits, rapid signal amplification, and the ability to detect pathogens directly in complex biological samples. In addition, miniaturized nanobiosensors may support point-of-care testing in hospitals, veterinary clinics, farms, and environmental monitoring systems, thereby improving early detection and facilitating more accurate antimicrobial stewardship strategies.

Point-of-care nanodiagnostic platforms can facilitate the early detection of resistant infections in clinical, veterinary, and environmental settings. Early diagnosis reduces inappropriate antibiotic use and supports precision antimicrobial therapy.

SERS-based nanoplatforms have demonstrated remarkable sensitivity in detecting bacterial fingerprints, resistance biomarkers, and antimicrobial susceptibility patterns.[37–39] These systems use plasmonic nanostructures capable of significantly amplifying Raman scattering signals, thereby enabling ultrasensitive detection or imaging of microbial components even at very low concentrations.[40] SERS-based diagnostics may facilitate the rapid identification of resistant pathogens directly from clinical and environmental samples without requiring lengthy culture procedures.[41] In addition, multiplexed nanoplatforms can simultaneously detect multiple pathogens and resistance genes, improving diagnostic efficiency and supporting more comprehensive surveillance strategies. Integration with artificial intelligence algorithms further enhances diagnostic accuracy, automated data interpretation, and predictive capabilities by enabling the rapid analysis of complex spectral datasets and improving the early detection of emerging resistance patterns.

APPLICATIONS OF NANOTECHNOLOGY ACROSS ONE HEALTH DOMAINS

Human Medicine

Nanotechnology has become an increasingly important tool in human medicine for preventing, diagnosing, and treating infections caused by antimicrobial-resistant pathogens. Unlike conventional antimicrobial therapies, nano-enabled approaches improve therapeutic efficacy by enhancing drug stability, increasing bioavailability, enabling targeted delivery, and reducing systemic toxicity. In addition, many nanomaterials possess intrinsic antimicrobial properties, allowing them to directly inhibit bacterial growth while simultaneously serving as carriers for antibiotics or other therapeutic agents. These multifunctional characteristics make nanotechnology particularly attractive for combating multidrug-resistant (MDR) microorganisms and reducing the excessive use of broad-spectrum antibiotics.[27,30]

One of the most successful clinical applications of nanotechnology is the development of advanced wound dressings and implant coatings containing antimicrobial nanoparticles. Silver nanoparticle-based dressings have demonstrated broad-spectrum antimicrobial activity against Gram-positive and Gram-negative bacteria while promoting wound healing and reducing biofilm formation in chronic wounds.[42] Similarly, nanoengineered coatings applied to orthopedic implants, catheters, prosthetic devices, and cardiovascular implants help prevent bacterial adhesion and significantly reduce the incidence of healthcare-associated infections.[43] Liposomal and polymeric nanoparticle formulations further enhance the intracellular delivery of antimicrobial agents, making them particularly useful for treating persistent infections caused by intracellular pathogens and biofilm-forming bacteria.[44,45]

Recent advances have also expanded the role of nanotechnology in precision medicine. Stimuli-responsive nanocarriers capable of releasing antibiotics in response to pH changes, bacterial enzymes, or inflammatory signals enable localized drug delivery at infection sites while minimizing systemic exposure and adverse effects. In parallel, the integration of nanotechnology with biosensors, molecular diagnostics, and artificial intelligence is facilitating rapid pathogen identification and personalized antimicrobial therapy, thereby supporting antimicrobial stewardship and improving clinical decision-making.[46] These developments highlight the growing potential of nanotechnology to transform the management of resistant infections in modern healthcare systems while aligning with the broader objectives of the One Health approach.

Veterinary Medicine and Agriculture

Nanotechnology offers significant opportunities to reduce antimicrobial use in veterinary medicine and agriculture while maintaining animal health and productivity. Nano-enabled antimicrobial agents, vaccine adjuvants, drug delivery systems, and feed additives have emerged as promising alternatives to the routine use of antibiotics in livestock production.[47] By improving the bioavailability and controlled release of veterinary drugs, nanoformulations can enhance therapeutic efficacy, reduce treatment frequency, and minimize the overall amount of antibiotics administered to food-producing animals.

Nanoparticle-based vaccine delivery systems have also demonstrated considerable potential by improving antigen stability, enhancing immune responses, and providing prolonged protection against infectious diseases.[47] These advances may decrease the incidence of bacterial infections and reduce reliance on prophylactic antibiotic use in intensive farming systems. In addition, nanotechnology has been explored for the development of antimicrobial coatings for animal housing equipment and water systems, which may help reduce pathogen transmission and improve farm biosecurity.

In agriculture, nanotechnology contributes to sustainable food production through the development of nanopesticides, nanofertilizers, and controlled-release agrochemicals that improve resource utilization while reducing environmental contamination.[48] Nano-enabled biosensors can rapidly detect pathogens, toxins, and contaminants on livestock farms and in food production facilities, allowing early intervention before disease outbreaks become widespread. Furthermore, portable nanosensors facilitate real-time monitoring of animal health and food safety, strengthening surveillance programs and supporting the One Health approach to antimicrobial resistance management.[31]

Overall, the integration of nanotechnology into veterinary medicine and agricultural practices has the potential to reduce excessive dependence on antibiotics, improve disease prevention, enhance food safety, and limit the dissemination of resistant microorganisms from animals to humans and the environment. Continued research, regulatory oversight, and field validation will be essential to ensure the safe, effective, and sustainable implementation of these nano-enabled technologies.

Environmental Applications

Environmental remediation represents a critical component of the One Health approach to combating antimicrobial resistance because environmental compartments serve as important reservoirs of antibiotic residues, resistant bacteria, and antimicrobial resistance genes. Nanotechnology-based wastewater treatment systems have shown considerable potential for removing these contaminants from hospital effluents, pharmaceutical wastewater, municipal sewage, and agricultural runoff before they are released into natural ecosystems.[49] By reducing environmental contamination, these technologies help interrupt the transmission cycle of resistant microorganisms among the environment, animals, and humans.

Photocatalytic nanoparticles, such as TiO_2 and ZnO, can generate reactive oxygen species under light irradiation, leading to the degradation of antibiotic residues and effective microbial inactivation. Magnetic nanoparticles facilitate the adsorption and removal of antibiotics, heavy metals, and other environmental pollutants and can be easily recovered using external magnetic fields, making them attractive for large-scale water treatment applications.[50] In addition, nano-enabled filtration membranes, nanocomposite adsorbents, and biosorbent materials have demonstrated promising performance in wastewater purification by improving filtration efficiency, reducing membrane fouling, and enhancing the removal of resistant microorganisms and resistance genes.[51]

Recent advances have also focused on integrating nanotechnology with environmental monitoring systems. Nanotechnology-based biosensors enable the rapid and sensitive detection of antibiotic residues, pathogenic microorganisms, and antimicrobial resistance genes in water, soil, and food production environments. These technologies support continuous environmental surveillance, allowing the early identification of contamination events and facilitating timely interventions. As environmental monitoring becomes increasingly important within the One Health framework, nano-enabled sensing platforms may play a key role in preventing the environmental dissemination of AMR and supporting sustainable ecosystem management.[31]

Integration with Emerging Technologies

The convergence of nanotechnology with emerging digital and computational technologies is transforming AMR management by enabling more precise diagnosis, targeted therapy, predictive surveillance, and personalized treatment strategies. Recent advances in artificial intelligence (AI), machine learning (ML), the Internet of Things (IoT), big data analytics, robotics, and advanced biosensing technologies have significantly expanded the capabilities of nano-enabled antimicrobial platforms. Rather than functioning independently, these innovations increasingly complement one another to create integrated systems capable of addressing AMR across the interconnected human, animal, and environmental sectors within the One Health framework.[52,46]

Artificial intelligence has become a powerful tool for accelerating the design and optimization of antimicrobial nanomaterials. Traditional nanoparticle development often requires extensive laboratory experimentation involving numerous synthesis parameters, making the process time-consuming and costly. AI-driven computational models can analyze large experimental datasets to predict how nanoparticle size, morphology, surface charge, composition, and functionalization influence antimicrobial activity, toxicity, cellular uptake, and biodistribution.[46,53] Machine learning algorithms further assist in identifying optimal nanoparticle formulations by recognizing complex relationships between physicochemical characteristics and biological performance that may not be evident through conventional statistical analyses. Consequently, AI-supported nanoparticle engineering reduces the experimental workload while facilitating the rational development of safer and more effective nanotherapeutics.

Machine learning has also become increasingly important for analyzing complex biological and spectroscopic datasets generated during pathogen identification and antimicrobial susceptibility testing. High-dimensional datasets obtained from genomic sequencing, proteomics, metabolomics, and spectroscopic techniques such as SERS can be rapidly processed using supervised and unsupervised learning algorithms. These computational approaches improve pathogen classification, identify antimicrobial resistance biomarkers, predict resistance phenotypes, and support clinical decision-making with high diagnostic accuracy. As more clinical datasets become available, AI-based predictive models are expected to play an increasingly important role in precision antimicrobial therapy by recommending individualized treatment strategies based on pathogen characteristics and patient-specific factors.[7]

Smart nanodrug delivery systems represent another major advancement resulting from the integration of nanotechnology with materials science and biomedical engineering. Stimuli-responsive nanoparticles can selectively release antimicrobial agents in response to environmental triggers, such as acidic pH, bacterial enzymes, temperature changes, oxidative stress, inflammatory mediators, or bacterial toxins present at infection sites. This controlled drug release minimizes systemic toxicity while maximizing local antimicrobial concentrations, thereby improving therapeutic efficacy and reducing unnecessary antibiotic exposure. Furthermore, multifunctional nanoplatforms capable of simultaneously delivering antibiotics, anti-inflammatory agents, and biofilm-disrupting compounds provide promising opportunities for treating chronic and multidrug-resistant infections more effectively than conventional therapies.[54]

The integration of nanotechnology with advanced biosensing technologies has also revolutionized infectious disease diagnostics. Nano-enabled biosensors incorporating gold nanoparticles, magnetic nanoparticles, quantum dots, graphene, and other nanomaterials provide exceptional analytical sensitivity and enable the rapid detection of pathogens, antimicrobial resistance genes, and microbial toxins.[32] Compared with conventional microbiological culture methods, these platforms substantially reduce diagnostic turnaround times while enabling the multiplex detection of several pathogens in a single assay. Such capabilities are particularly valuable in clinical settings, where early diagnosis supports timely antimicrobial intervention and reduces the inappropriate use of broad-spectrum antibiotics.

Recent advances in SERS further demonstrate the benefits of combining nanotechnology with computational approaches. SERS uses plasmonic nanostructures to amplify Raman scattering signals by several orders of magnitude, enabling ultrasensitive detection of bacterial biochemical fingerprints, resistance biomarkers, and antimicrobial susceptibility profiles.[55] When combined with machine learning algorithms, SERS datasets can be automatically analyzed to classify bacterial species, distinguish resistant isolates from susceptible isolates, and identify subtle molecular changes associated with the evolution of resistance.[7,56] This integration has shown considerable promise for the development of rapid, culture-independent diagnostic systems capable of supporting precision medicine and antimicrobial stewardship.

Beyond clinical applications, IoT-enabled nanosensors are emerging as valuable tools for the continuous monitoring of antimicrobial resistance across multiple One Health environments. Networks of portable nano-enabled sensors can continuously monitor hospitals, livestock farms, food production facilities, wastewater treatment plants, and natural water systems for the presence of antibiotic residues, resistant microorganisms, and resistance genes. The collected data can be transmitted in real time to centralized surveillance systems, where AI algorithms analyze trends, identify emerging outbreaks, and support evidence-based public health interventions. Such integrated surveillance networks may substantially strengthen global AMR preparedness while improving communication among healthcare providers, veterinarians, environmental agencies, and public health authorities.[57]

Despite these promising advances, several important challenges remain before these integrated technologies can be widely implemented. Large, standardized, high-quality datasets are required to train reliable AI models, while data privacy, cybersecurity, algorithmic transparency, and interoperability among digital healthcare systems remain significant concerns. Moreover, regulatory frameworks governing AI-assisted diagnostics and nano-enabled medical devices continue to evolve, requiring international harmonization to facilitate clinical translation. The long-term safety of smart nanomaterials, ethical considerations surrounding AI-assisted decision-making, and equitable access to advanced technologies must also be carefully addressed.

Overall, the integration of nanotechnology with artificial intelligence, machine learning, advanced biosensing technologies, and the IoT represents one of the most promising directions for future AMR management. By combining rapid diagnostics, intelligent therapeutic design, precision drug delivery, and real-time surveillance within a unified One Health framework, these emerging technologies have the potential to fundamentally transform how resistant infections are detected, monitored, and treated worldwide.

The future management of antimicrobial resistance will increasingly rely on the integration of nanotechnology with artificial intelligence, machine learning, biosensors, and digital surveillance systems within the One Health framework. By combining rapid pathogen detection, intelligent data analysis, targeted nanotherapeutics, and coordinated decision-making across human, animal, and environmental sectors, these technologies provide a comprehensive strategy for precision AMR management, as illustrated in Figure 3.

Figure 3. Conceptual framework of AI-enabled nanotechnology for precision AMR management within the One Health framework. Data generated across interconnected human, animal, food, and environmental sectors are collected through nano-enabled biosensors and integrated into artificial intelligence (AI) and machine learning (ML) platforms for rapid analysis, prediction, and decision support. The resulting information guides precision nanotherapeutics, antibiofilm strategies, combination therapies, and environmental remediation while strengthening antimicrobial stewardship, surveillance, and coordinated One Health interventions. This integrated ecosystem supports the earlier detection of resistant pathogens, optimization of treatment strategies, reduction of AMR transmission, and improvement of public health outcomes.

CHALLENGES AND LIMITATIONS

Despite the remarkable progress achieved in nanotechnology-based antimicrobial research, several important scientific, technical, regulatory, economic, and environmental challenges continue to limit the widespread implementation of nano-enabled strategies for combating AMR. Although numerous nanomaterials have demonstrated promising antimicrobial efficacy under laboratory conditions, relatively few have successfully progressed to clinical practice or large-scale environmental applications. Bridging this gap requires a comprehensive understanding of nanoparticle safety, manufacturing, regulatory approval, and long-term performance across diverse One Health settings.

One of the primary concerns is the potential toxicity of nanomaterials. Although nanoparticles can selectively target microbial cells, they also interact with mammalian cells and potentially induce oxidative stress, inflammation, DNA damage, mitochondrial dysfunction, and apoptosis, depending on their size, composition, surface chemistry, concentration, and duration of exposure.[58] Certain metallic nanoparticles may accumulate in organs such as the liver, kidneys, lungs, or spleen following repeated administration, raising concerns about long-term biosafety and chronic toxicity. Furthermore, interactions between nanoparticles and biological systems remain highly complex, making comprehensive toxicological evaluation essential before clinical implementation.

Another significant challenge is the environmental fate and ecotoxicological impact of engineered nanomaterials. The increasing production and use of nanoparticles inevitably lead to their release into wastewater systems, agricultural soils, and aquatic environments. Once released, nanoparticles may persist, aggregate, dissolve, or undergo physicochemical transformations that influence their biological activity and environmental behavior. Their accumulation may alter microbial community composition, affect beneficial microorganisms involved in nutrient cycling, and disrupt ecological balance. Consequently, life-cycle assessment and environmental risk evaluation should become integral components of future nanotechnology development.[59]

The large-scale manufacturing and reproducibility of nanomaterials also remain major obstacles to commercialization. Laboratory-scale synthesis methods often produce nanoparticles with highly controlled physicochemical properties; however, maintaining the same particle size distribution, morphology, surface characteristics, and stability during industrial-scale production remains technically challenging. Batch-to-batch variability can significantly influence antimicrobial activity, pharmacokinetics, and safety profiles, emphasizing the need for standardized manufacturing protocols and rigorous quality-control procedures.

Economic considerations further affect the clinical translation of nanotechnology. The synthesis of high-quality functionalized nanoparticles frequently requires specialized equipment, expensive raw materials, and complex fabrication procedures that increase production costs. In low- and middle-income countries, where the burden of antimicrobial resistance is often greatest, the high cost of nano-enabled therapeutics and diagnostic systems may limit accessibility. Therefore, developing cost-effective, scalable, and sustainable manufacturing strategies remains an important research priority.

Regulatory approval represents another major barrier to widespread implementation. Existing regulatory frameworks were primarily developed for conventional pharmaceuticals and medical devices and are often insufficient to address the unique characteristics of nanomaterials. Regulatory agencies continue to refine guidelines regarding nanoparticle characterization, toxicological assessment, environmental safety, pharmacokinetics, manufacturing quality, and postmarketing surveillance. The lack of internationally harmonized regulatory standards creates uncertainty for manufacturers and slows the translation of promising nanotechnologies into clinical and commercial applications.

Another emerging concern is the possibility that microorganisms may eventually develop adaptive responses to certain nanomaterials. Although nanoparticles generally attack microbial cells through multiple mechanisms, thereby reducing the likelihood of resistance compared with conventional antibiotics, prolonged or inappropriate exposure could still promote microbial adaptation. Changes in membrane composition, activation of oxidative stress defense systems, enhanced biofilm formation, increased efflux pump activity, and altered metabolic pathways have all been proposed as potential adaptive responses to nanoparticle exposure. Continuous surveillance and the rational application of nanomaterials will therefore be necessary to minimize the risk of future nanoresistance.

The clinical evaluation of nano-enabled antimicrobial therapies also remains limited. Most published studies have been conducted under in vitro conditions or in animal models, whereas relatively few large-scale clinical trials have assessed long-term efficacy and safety in human populations. Differences between laboratory conditions and real-world clinical environments may significantly influence therapeutic performance, highlighting the need for multicenter clinical studies involving diverse patient populations before routine medical implementation.

From a One Health perspective, the successful implementation of nanotechnology also requires stronger interdisciplinary collaboration among clinicians, microbiologists, veterinarians, engineers, environmental scientists, toxicologists, regulatory authorities, and policymakers. Effective communication among these disciplines is essential to ensure that nanotechnology-based interventions are not only scientifically effective but also environmentally sustainable, economically feasible, and socially acceptable. International cooperation will further facilitate harmonized regulations, standardized safety assessments, and coordinated surveillance programs for monitoring the long-term impact of nanotechnology on antimicrobial resistance.

Overall, although nanotechnology offers enormous potential for addressing the global AMR crisis, overcoming these scientific and practical limitations will be essential for its successful translation into routine healthcare, veterinary medicine, agriculture, and environmental management. Continued investment in multidisciplinary research, standardized evaluation methods, robust regulatory frameworks, and long-term biosafety studies will play a crucial role in ensuring that nano-enabled technologies can be implemented safely and effectively within the One Health framework.

FUTURE PERSPECTIVES

Future advances in nanotechnology-based strategies for combating AMR will rely on the integration of materials science, biotechnology, artificial intelligence (AI), and precision medicine within the One Health framework. Although numerous nano-enabled antimicrobial platforms have demonstrated promising results under laboratory conditions, their successful translation into clinical practice, veterinary medicine, agriculture, and environmental management requires further improvements in biosafety, scalability, regulatory approval, and cost-effectiveness.

One of the primary research priorities is the development of safer, biodegradable, and environmentally sustainable nanomaterials with enhanced antimicrobial selectivity and reduced toxicity.[60] Future nanoparticle design should focus on optimizing physicochemical properties, such as size, morphology, surface chemistry, and biodegradability, to improve therapeutic efficacy while minimizing adverse effects. Multifunctional nanoplatforms capable of combining targeted drug delivery, antimicrobial activity, biofilm disruption, controlled drug release, and diagnostic functions may provide highly effective theranostic systems for managing resistant infections.

Artificial intelligence and machine learning are expected to further accelerate nanoparticle development by predicting antimicrobial performance, toxicity, and biological interactions before laboratory synthesis.[53] AI-assisted analysis of genomic, proteomic, and spectroscopic datasets will also improve pathogen identification, resistance prediction, and personalized antimicrobial therapy. In parallel, stimuli-responsive nanodrug delivery systems that release antimicrobial agents in response to infection-specific signals may enhance treatment precision while reducing systemic toxicity and unnecessary antibiotic exposure.

Future One Health strategies will increasingly depend on integrating nanotechnology with advanced biosensors, IoT technologies, and AI-driven surveillance systems. Nano-enabled sensors capable of continuously monitoring antibiotic residues, resistant microorganisms, and resistance genes across hospitals, farms, wastewater treatment plants, and environmental ecosystems may strengthen global AMR surveillance and facilitate the early detection of outbreaks.

Despite these promising developments, important challenges remain, including regulatory approval, large-scale manufacturing, quality control, long-term biosafety, and environmental risk assessment. Addressing these limitations through multidisciplinary collaboration, international regulatory harmonization, and continued translational research will be essential for transforming nanotechnology into a practical and sustainable solution for combating AMR. Overall, the integration of nanotechnology with emerging digital technologies offers significant potential to improve antimicrobial therapy, surveillance, and infection control, supporting more effective AMR management across interconnected human, animal, and environmental sectors.

CONCLUSION

Antimicrobial resistance has evolved into a complex global challenge that extends beyond healthcare and affects interconnected human, animal, and environmental systems. The growing failure of conventional antibiotics, driven by rapid microbial adaptation, biofilm formation, and the limited development of new antimicrobial agents, highlights the need for innovative strategies that address AMR from a broader One Health perspective. Nanotechnology offers significant advantages by providing multifunctional platforms capable of enhancing antimicrobial activity, improving targeted drug delivery, disrupting biofilms, and enabling the rapid and sensitive detection of pathogens.

Recent advances in antimicrobial nanomaterials, nanodrug delivery systems, antibiofilm technologies, and nanodiagnostics demonstrate the potential of nanotechnology to complement existing antimicrobial therapies while supporting more effective antimicrobial stewardship. Moreover, the integration of nanotechnology with artificial intelligence, machine learning, and advanced biosensing technologies is creating new opportunities for precision medicine, intelligent diagnostics, and real-time surveillance of resistant pathogens across multiple One Health environments.

Despite these promising developments, several challenges remain, including long-term biosafety, environmental impact, manufacturing scalability, regulatory approval, and clinical translation. Addressing these limitations through interdisciplinary collaboration and continued translational research will be essential for the successful implementation of nano-enabled technologies. Overall, nanotechnology represents a versatile and promising platform that can complement conventional antimicrobial strategies and contribute substantially to sustainable AMR control within the One Health framework.

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