Next Bioengineering 1 (2025) 100003

Contents lists available at ScienceDirect

Next Bioengineering

journal homepage: www.sciencedirect.com/journal/next-bioengineering

Review article

Emerging technologies and innovative approaches to combat antimicrobial resistance: A narrative review of next-generation therapeutic strategies

Don Eliseo Lucero-Prisno III [a,b,c], Olalekan John Okesanya [d,e], Abdulmajeed Opeyemi Agboola [f], Uthman Okikiola Adebayo [d,g,*], Olaniyi Abideen Adigun [h], Mohamed Mustaf Ahmed [i,j], Noah Olabode Olaleke [k], Tolutope Adebimpe Oso [d,l], Maria Ivy Rochelle S. Tan [m], Jerico Bautista Ogaya [n,o,p], Oluwatobi Babajide Ayelaagbe [d], David Bamidele Olawade [q,r,s]

[a] Department of Global Health and Development, London School of Hygiene and Tropical Medicine, London, United Kingdom
[b] Center for Research and Development, Cebu Normal University, Cebu, Philippines
[c] Research Unit, Bukidnon State University, Malaybalay City, Bukidnon, Philippines
[d] Department of Medical Laboratory Science, Neuropsychiatric Hospital, Aro, Abeokuta, Nigeria
[e] Faculty of Medicine, Department of Public Health and Maritime Transport, University of Thessaly, Volos, Greece
[f] Department of Public Health, Faculty of Allied Health Sciences, Kwara State University, Malete, Kwara State, Nigeria
[g] Department of Medical Laboratory Science, College of Basic Health Sciences, Achievers University, Owo, Ondo State, Nigeria
[h] Department of Medical Laboratory Science, Nigerian Defence Academy, Kaduna, Kaduna State, Nigeria
[i] SIMAD Institute for Global Health, SIMAD University, Mogadishu, Somalia
[j] Faculty of Medicine and Health Sciences, SIMAD University, Mogadishu, Somalia
[k] Department of Medical Laboratory, Osun State College of Health Technology, Ilesa, Nigeria
[l] Department of Medical Laboratory Science, McPherson University, Seriki Sotayo, Ogun State, Nigeria
[m] Department of Nursing, University of the Philippines School of Health Sciences, Manila, Philippines
[n] Department of Medical Technology, Institute of Health Sciences and Nursing, Far Eastern University, Manila, Philippines
[o] Center for University Research, University of Makati, Makati, Philippines
[p] Research and Development Office, Biliran Province State University, Leyte, Naval, Philippines
[q] Department of Allied and Public Health, School of Health, Sport and Bioscience, University of East London, London, United Kingdom
[r] Department of Research and Innovation, Medway NHS Foundation Trust, Gillingham, ME7 5NY, United Kingdom
[s] Department of Public Health, York St John University, London, United Kingdom

ARTICLE INFO

Keywords:
Antimicrobial resistance
CRISPR-Cas systems
Nanotechnology
Bacteriophage therapy
Precision medicine

ABSTRACT

Antimicrobial resistance (AMR) is one of the most pressing global health challenges, with approximately 700,000 deaths annually directly attributable to resistant bacterial infections. This alarming trend threatens to undermine decades of medical progress. The widespread misuse and overuse of antibiotics have accelerated the emergence of multidrug-resistant (MDR) pathogens, leading to increased morbidity, mortality, and healthcare costs. This review examines the intricate mechanisms underlying the development of AMR and discusses innovative next-generation therapeutic strategies and emerging approaches for combating resistant pathogens. CRISPR-based antimicrobials demonstrated over 90 % in vitro efficacy in selectively eliminating MDR pathogens. Nanotechnology-based solutions, such as those utilizing silver and gold nanoparticles, have demonstrated potent bactericidal activity in preclinical settings; however, toxicity and regulatory concerns persist. Bacteriophage therapy and antimicrobial peptides (AMPs) are advancing through early clinical trials, offering targeted activity and immune-modulating effects. Artificial intelligence (AI)-driven drug discovery has already been clinically integrated, accelerating the design of antibiotics and predicting resistance with high efficiency. Comparative analysis reveals that AI tools possess the highest readiness level, while CRISPR and AMPs are promising but remain in early development stages. These emerging strategies collectively present significant potential to

* Corresponding author. Department of Medical Laboratory Science, Neuropsychiatric Hospital, Aro, Abeokuta, Nigeria.
E-mail addresses: don-eliseo.lucero-prisno@lshtm.ac.uk (D.E. Lucero-Prisno), okesanyaolalekanjohn@gmail.com (O.J. Okesanya), abdulmajeedagboola001@gmail.com (A.O. Agboola), uthmanadebayo85@gmail.com (U.O. Adebayo), olaniyiadigun.oa@gmail.com (O.A. Adigun), momustafahmed@simad.edu.so (M.M. Ahmed), noaholaleke@gmail.com (N.O. Olaleke), bimpeadebayo2002@yahoo.com (T.A. Oso), mstan4@up.edu.ph (M.I.R.S. Tan), jericoogaya13@gmail.com (J.B. Ogaya), ayelaagbeoluwatobi461@gmail.com (O.B. Ayelaagbe), d.olawade@uel.ac.uk (D.B. Olawade).

https://doi.org/10.1016/j.nxbio.2025.100003
Received 25 June 2025; Received in revised form 27 August 2025; Accepted 5 September 2025
Available online 9 September 2025

complement or replace conventional antibiotics in addressing AMR. Despite their potential, these technologies face significant implementation challenges, including technical limitations, economic barriers, ethical considerations, and regulatory complexities. This review emphasizes the critical need for multidisciplinary collaboration, sustainable funding models, and global policy frameworks to effectively translate these innovations into clinical practice. The AMR crisis can only be addressed through international collaboration, combining scientific innovation and supportive policy environments.

1. Introduction

Antimicrobial resistance (AMR) refers to the ability of microorganisms, particularly bacteria, to withstand the effects of drugs that kill or inhibit them. This resistance makes many commonly used antibiotics ineffective, making infections more difficult or even impossible to treat, posing a significant threat to public health. This represents a complex and multifaceted challenge that threatens to undermine decades of medical progress in the treatment of infectious diseases [1–6]. AMR is recognized as a global health emergency, with resistance detected in all antibiotics currently in clinical use and only a few novel drugs in the pipeline [7]. The magnitude of the AMR crisis cannot be overstated, as it is responsible for increasing global morbidity and mortality, with antibiotic-resistant bacteria currently causing approximately 700,000 deaths annually [5,6]. Projections suggest that this figure could rise dramatically, reaching an estimated 10 million deaths annually by 2050 if left unchecked. The rise of multidrug-resistant (MDR) pathogens, such as the ESKAPE group (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa*, and *Enterobacter species*), has led to life-threatening infections and a "post-antibiotic era" in which existing antibiotics are often ineffective [3,6,8]. The consequences include longer hospitalization, higher healthcare costs, and limited treatment options [5].

The emergence of resistant bacterial strains is significantly accelerated by the misuse and overuse of antibiotics in both human and veterinary medicine. Inappropriate prescribing, over-the-counter availability, and excessive use in agriculture contribute to the selective pressure that favors resistant organisms [2,5]. In addition to these external factors, bacteria can develop resistance through spontaneous genetic mutations, including point mutations, deletions, and insertions that may modify drug targets or disrupt essential metabolic pathways, rendering antibiotics less effective or entirely ineffective [1,7]. Resistance can also spread rapidly through horizontal gene transfer, which involves the exchange of genetic material via plasmids, transposons, and bacteriophages. This mechanism enables bacteria to acquire and disseminate resistance traits across species and environments, even among distantly related organisms [1,7].

Traditional antibiotics are increasingly ineffective against resistant bacteria, and the development of new antibiotic classes has stagnated over the past two decades [3–8]. This decline in antibiotic development can be attributed to several factors, including the high cost of drug development, lengthy regulatory processes, and limited financial incentives for pharmaceutical companies to develop new antibiotics [9]. Many available antibiotics are now ineffective against drug-resistant strains, and current alternatives often serve only as adjuvants rather than replacements [3,4]. The economic challenges associated with antibiotic development are particularly significant. Unlike other medications that patients may take chronically, antibiotics are typically used for short periods, thereby limiting the potential revenue. Additionally, the goal of antibiotic stewardship is to use new antibiotics sparingly to preserve their effectiveness, further reducing the market incentives. The rapid global spread of AMR and the lack of effective treatments create an urgent need for innovative therapeutic strategies [6,8,10]. Without new solutions, the world faces a future in which minor infections could once again become deadly.

A comprehensive overview of the current understanding of AMR, focusing on the underlying mechanisms and contributing factors that drive its emergence and spread, is necessary. By examining the biological and environmental influences, this review sheds light on the complex interactions that facilitate resistance in microbial populations. It also emphasizes the growing limitations of existing antibiotic therapies and the urgent need for the development of more effective treatment options [11]. To address these challenges, this review explores a range of emerging therapeutic approaches, including bacteriophage therapy, antimicrobial peptides, CRISPR-based interventions, immunomodulators, monoclonal antibodies, and drug repurposing strategies [12]. Each of these methods offers unique advantages in targeting resistant pathogens and represents a promising direction for the development of next-generation antimicrobials. Furthermore, this review discusses the role of advanced technologies such as genomics, artificial intelligence, and nanotechnology that are increasingly integrated into research and clinical practice to improve diagnostics, surveillance, and treatment strategies. These innovations have the potential to revolutionize AMR management globally [13].

This review uniquely integrates diverse next-generation therapies such as CRISPR, nanotechnology, AI, AMPs, and phage therapy within a multidisciplinary context. Unlike prior reviews, it examines technological synergies, translational challenges, regulatory barriers, and public health policy linkages. It also highlights recent clinical advances, synthesizes updated data (2015–2024), and proposes strategic frameworks for future AMR intervention development. Thus, this study aims to explore emerging technologies and innovative approaches for combating AMR by providing a comprehensive narrative review of next-generation therapeutic strategies against AMR.

2. Methodology

This narrative review provides a comprehensive overview of emerging technologies and innovative approaches to combat AMR. A systematic search strategy was employed to identify relevant literature from multiple electronic databases, including PubMed, Web of Science, Scopus, and Google Scholar. The search encompassed publications from January 2015 to December 2024 using a combination of keywords and Medical Subject Headings (MeSH) terms related to antimicrobial resistance, CRISPR-Cas systems, nanotechnology, bacteriophage therapy, antimicrobial peptides, artificial intelligence, and novel therapeutic strategies. Search terms included "antimicrobial resistance," "antibiotic resistance," "CRISPR," "nanotechnology," "bacteriophage therapy," "antimicrobial peptides," "artificial intelligence," "drug discovery," "biofilm disruption," "host-directed therapy," "precision medicine," and "smart drug delivery." Boolean operators (AND, OR) were used to combine the search terms and refine the results. Additional articles were identified through manual screening of the reference lists of relevant reviews and primary research articles.

The inclusion criteria comprised peer-reviewed articles published in English, studies focusing on innovative antimicrobial technologies and strategies, research addressing mechanisms of antimicrobial resistance, clinical trials and preclinical studies of novel antimicrobial approaches, and review articles providing comprehensive overviews of emerging technologies. The exclusion criteria were articles published before 2015, non-English publications, conference abstracts without full-text availability, duplicate publications, and studies focusing solely on traditional antibiotic discovery without innovative approaches. Data extraction involved narrative reviews of the selected articles to identify key

themes, technological approaches, mechanisms of action, clinical applications, challenges, and future perspectives. The extracted information was synthesized to provide a comprehensive summary that highlights the current state of knowledge and identifies gaps for future research. The quality of the included studies was assessed based on the study design, methodology, and relevance to the review objectives.

3. Next-generation antimicrobial technologies

AMR is a global health crisis caused by antibiotic overuse and abuse, resulting in the proliferation of resistant microbes. The convergence of advancing biotechnology and urgent clinical needs has catalyzed the development of innovative antimicrobial strategies. Demographic shifts, including an aging population and increased chronic illnesses, further accelerate resistance. Innovative tools such as CRISPR-Cas, nanotechnology, and lytic bacteriophages are being explored to counteract this growing threat [14].

3.1. CRISPR-based antimicrobials

Clustered regularly interspaced short palindromic repeats (CRISPR) is a groundbreaking genome-editing technique originally derived from a bacterial immune defense mechanism [15]. Its programmable nature enables precise targeting of specific bacteria strains or resistance genes, making it a promising tool for combating AMR [16]. CRISPR–Cas systems allow for the selective elimination of MDR pathogens based on sequence information, offering a highly specific alternative to traditional antimicrobial approaches to disrupt resistance genes with minimal off-target effects [13]. Fig. 1 illustrates the gene editing process with CRISPR/Cas9 technology, demonstrating how guided RNAs direct the Cas9 nuclease to specific target sequences in bacterial genomes, enabling the precise modification or disruption of resistance genes. Direct editing of resistance genes is one of the most exciting applications of CRISPR technology in AMR management. The specificity of CRISPR-based antimicrobials can help preserve the natural microbiome, potentially reducing secondary infections and other complications associated with the use of broad-spectrum antibiotics [17].

Effective delivery of CRISPR systems remains a major challenge, especially when employing bacteriophages as carriers, which poses significant technical difficulties [16]. Nanotechnology-based methods offer promising alternatives by enabling surface modifications that enhance targeting specificity [18]. Despite these advances, the lack of robust in vivo delivery systems continues to hinder the clinical translation of CRISPR-based antimicrobials. In addition to delivery constraints, safety concerns such as immunogenicity and the potential for off-target effects must be addressed. Ethical considerations also surround the clinical application of gene-editing tools [19]. Furthermore, while CRISPR-Cas shows strong promise in targeting resistant bacteria, further research is needed to assess its long-term efficacy and safety. There are also concerns about bacterial adaptation, as some studies report that bacteria expressing resistance genes may exhibit reduced activity of their natural CRISPR-Cas systems, as seen in MDR *Shigella* strains [20]. While CRISPR-Cas systems offer a novel and targeted approach to tackling AMR, overcoming delivery and safety barriers is essential for their advancement from laboratory research to clinical application [21].

3.2. Nanotechnology-based antimicrobials

Nanotechnology is crucial for synthesizing new antibiotics by increasing contact with bacteria and improving bioavailability, absorption, and mucoadhesion. The unique physicochemical properties of nanoparticles (NPs), including their high surface-to-volume ratio and ability to penetrate biological barriers, make them particularly effective against resistant pathogens [23]. Metal nanoparticles such as silver (AgNPs), gold (AuNPs), and copper (CuNPs) have received extensive attention due to their broad-spectrum bactericidal activity. NPs can disrupt bacterial respiration, generate ROS, and induce structural damage to the cell wall, contributing to their antimicrobial activity [24]. These mechanisms differ significantly from those of conventional antibiotics, reducing the likelihood of cross-resistance. In addition, NPs can eradicate bacteria through microbicidal or microbiostatic effects, improve drug solubility, and target viral areas. Nanotechnology-based therapeutics have demonstrated bactericidal effects in vitro and in early animal models, but few have advanced beyond the first phase of trials [25]. Their broad-spectrum efficacy and ability to bypass traditional resistance mechanisms position them as valuable adjuncts, yet toxicity concerns and regulatory gaps limit their clinical adoption. In

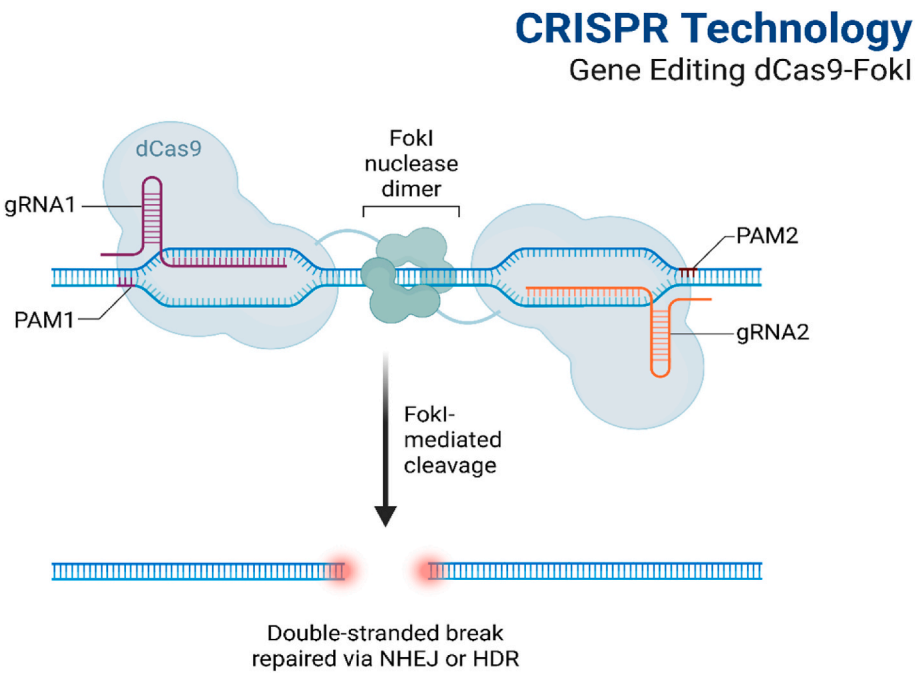

Fig. 1. Gene editing with CRISPR/Cas9, Ahmed, M. (2025). Gene editing with CRISPR/Cas9 [22].

contrast to CRISPR or phage therapy, nanotechnology shows higher technological readiness due to its integration in wound dressings and medical coatings [25].

3.2.1. Synthesis methods and manufacturing of antimicrobial nanoparticles

There are several methods for nanoparticle synthesis, each influencing the resulting particles' properties and biological activities.

3.2.1.1. Physical method.

1 Laser Ablation Methods

Laser ablation is a top-down physical method that produces high-purity, surfactant-free nanoparticles by irradiating a solid metal target in a liquid medium, often water [26]. This process is particularly valuable for biomedical applications due to the absence of chemical contaminants, making the synthesized nanoparticles biocompatible and less cytotoxic. One of its primary benefits is the precise control over particle size and morphology by adjusting laser parameters such as pulse duration, wavelength, and energy [27]. This method is advantageous for AMR control because the clean surfaces of the nanoparticles enhance their interaction with bacterial membranes, leading to improved antimicrobial effectiveness. However, a major limitation is the low yield and relatively high operational cost, which can hinder large-scale production. Moreover, the need for specialized laser equipment reduces its accessibility in resource-constrained environments, and its energy efficiency is lower compared to chemical reduction techniques [23].

2 Irradiation-Based Methods

Irradiation-based methods, such as gamma and microwave irradiation, are advanced physical techniques that facilitate the rapid reduction of metal ions into nanoparticles without relying on toxic chemicals [28]. These methods encourage the formation of nanoparticles with high crystallinity and surface reactivity, traits that enhance antimicrobial effectiveness by improving interactions with bacterial membranes and boosting ROS generation. These techniques are compatible with green synthesis strategies and can be integrated with plant extracts or biopolymers for enhanced biocompatibility [28]. However, limitations include the requirement for specialized equipment and safety protocols, which restricts accessibility in low-resource settings, and the potential for uncontrolled nucleation, leading to polydispersity in nanoparticle size [29,30].

3.2.1.2. Chemical methods.

1 Chemical Reduction

Chemical reduction is widely used for synthesizing antimicrobial nanoparticles due to its ability to produce uniformly distributed particles while minimizing solvent contamination. This method typically involves a metal precursor, a reducing agent, and a capping agent to control nanoparticle size and prevent agglomeration. Among its major advantages are simplicity, low cost, and scalability, making it suitable for both laboratory and industrial production. However, this method often requires precise control of reaction conditions such as pH, temperature, and reagent concentrations to ensure consistency and reproducibility [31,32].

2 Electrochemical Synthesis

Electrochemical synthesis is a scalable and cost-effective technique that enables precise control over nanoparticle size, shape, and composition by modifying factors such as current density, applied voltage, and electrolyte concentration [33]. It is suitable for large-scale production of metal nanoparticles, particularly for antimicrobial coatings and reproducible drug delivery applications, which is essential for consistency in biomedical applications [33]. The method also eliminates the need for chemical reducing agents, thereby minimizing the introduction of toxic residues. This enhances the biocompatibility of the nanoparticles, making them suitable for AMR interventions [34]. However, the technique requires careful optimization, as variations in electrochemical conditions can lead to inconsistent particle properties or undesirable by-products [35].

3.2.1.3. Photochemical methods.

1 UV-Initiated Photoreduction and Photo-Induced Reduction

Photochemical techniques like UV-initiated photoreduction and visible light-induced reduction are bottom-up approaches that utilize light energy to convert metal salts into nanoparticles, typically in the presence of stabilizers or capping agents [36]. These methods are appreciated for their environmental friendliness, as they eliminate the need for toxic chemicals and function under mild reaction conditions [37]. Their effectiveness in combating AMR stems from their capacity to generate ROS and infiltrate bacterial biofilms [38,39]. These materials demonstrate broad-spectrum antimicrobial effects, including against MDR strains [38].

3.2.1.4. Biological methods.

1 Green Synthesis:

Green synthesis approaches are gaining prominence due to their environmental sustainability and cost-effectiveness. Biological nanoparticle synthesis using microbial cells, enzymes, and plant-derived molecules produces nanoparticles with higher stability than those obtained through chemical methods [40].

3.2.2. Types of antimicrobial nanoparticles

Antimicrobial nanoparticles are broadly categorized based on their composition and structural properties.

3.2.2.1. Metal nanoparticles.

i. **Silver Nanoparticles (AgNPs):** Since 1920, the FDA has recognized AgNPs' antibacterial properties, making them the most researched metallic nanoparticles. They can cause electrostatic changes, porosity changes, rupture, cytoplasmic content leakage, bacterial respiratory disruption, enzyme inhibition, and DNA damage [41]. These effects are attributed to multiple mechanisms of action, making it difficult for bacteria to develop resistance. The nanoparticles adhere to bacterial membranes via proteoglycans, causing structural damage and stress through interactions with enzymes and DNA. These effects are thought to result from silver ions released by AgNPs, which negatively impact the respiratory chain and protein synthesis [42].

ii. **Gold nanoparticles (AuNPs):** AuNPs exhibit weak intrinsic antibacterial activity; however, their effectiveness against both Gram-positive and Gram-negative bacteria is well established. Interestingly, size plays a crucial role in antimicrobial efficacy, with AuNPs less than 2 nm demonstrating strong activity. Photothermal therapy (PTT) is a promising approach for enhancing their antimicrobial potential [15].

iii. **Copper nanoparticles (CuNPs):** Owing to their susceptibility to air, CuNPs develop an oxide coating that diminishes their antibacterial effectiveness, which resulted in introducing

stabilization strategies, such as chelates, to maintain metal ion stability. This led to greater antibacterial activity of CuNPs. Their strong antimicrobial properties against various bacterial and yeast species make them suitable for coating medical devices (Fig. 2). However, because it produces hydroxyl radicals, a common problem called agglomeration can be hazardous [43].

iv. **Zinc oxide (ZnO):** ZnONP's primary mode of action involves the generation of ROS, which induce damage to microbial membranes, proteins, and genetic material, and direct interaction with bacterial cell walls, causing membrane disruption and eventual cell lysis. Their antimicrobial effectiveness depends on characteristics such as particle size, morphology, and surface charge [44].

v. **Titanium dioxide (TiO_2):** TiO_2NP exhibit antimicrobial activity mainly through their photocatalytic ability to generate ROS upon exposure to UV or visible light, which creates oxidative stress within microbial cells, leading to membrane disruption and cell death. The anatase form of TiO_2 is particularly effective and has been utilized in applications such as environmental sanitization, self-cleaning surfaces, and medical device coatings. The modification of its properties through metal doping can increase its effectiveness under visible light, expanding its practical uses [45].

3.2.2.2. Carbon-based nanoparticles.

i. **Carbon Nanotubes (CNTs):** CNTs demonstrate antimicrobial activity by inducing oxidative stress and physically piercing bacterial cell membranes. Functionalized CNTs have been reported to disrupt membrane integrity and suppress biofilm formation, even in MDR strains such as *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* [46].

ii. **Nanodiamonds:** These are carbon-based nanoparticles that retain many of the remarkable physical and chemical properties of bulk diamond. They can be synthesized through various methods, including detonation, high-pressure high-temperature processes, and laser-based techniques. Nanodiamonds have been used as carriers for antibiotics and AMPs due to their high surface area and biocompatibility [47]. Similarly, dendrimers and polymeric nanoparticles have emerged as promising platforms for controlled antibiotic delivery [48].

3.2.2.3. Polymeric nanoparticles and nano-carriers.

i. **Poly (lactic-co-glycolic acid) (PLGA) Nanoparticles:** Polymeric nanoparticles such as PLGA have emerged as promising platforms for controlled antibiotic delivery due to their biodegradability, biocompatibility, and sustained drug-release properties. PLGA helps protect antibiotics from rapid degradation and ensures targeted delivery to infection sites [49,50]. PLGA offers several key advantages, including FDA approval, the flexibility to encapsulate both hydrophilic and hydrophobic drugs, and low toxicity [49].

ii. **Dendrimers:** Dendrimers offer a branched structure that allows for high drug-loading capacity and targeted delivery, making them effective nano-carriers for antimicrobials [48]. Dendrimers offer key benefits such as a well-defined molecular structure, multivalence, the capacity to traverse biological barriers, and the potential to minimize AMR. However, challenges, including their intricate and costly synthesis, potential cytotoxicity at higher doses, and the need for surface modification to enhance safety and biocompatibility, persist [51].

In addition to nanoparticle synthesis methods, formulation techniques like nanoemulsions are increasingly used to enhance the delivery and antimicrobial performance of nanoparticulate systems. Nanoemulsions are thermodynamically stable dispersions that can improve the solubility, bioavailability, and membrane penetration of antimicrobial agents. Although not a synthesis method, they play a crucial role in optimizing the functionality of nanoparticles in biomedical applications [52]. Despite the potential of all the synthetic methods, nanotechnology-based antimicrobials face several limitations. The risks underscore the importance of optimizing dosing regimens and exploring

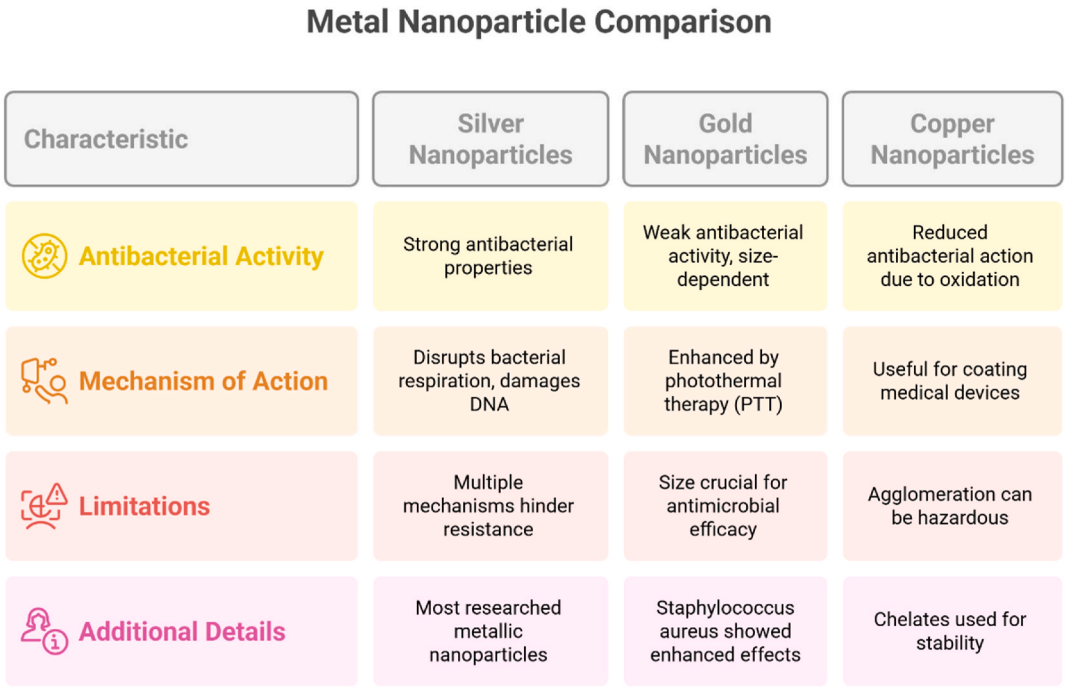

Fig. 2. Metal nanoparticle comparison.

combination therapies. Advances in nanotechnology have led to the development of novel antimicrobial agents, which are being explored for use in both industrial and medical settings. However, further research is required to assess their effects on healthy human tissues before they can be widely applied in biological systems [30,53].

3.3. Bacteriophage therapy

Bacteriophage therapy offers a promising approach to combat AMR infections by selectively attacking harmful bacteria while preserving beneficial ones. Phages are natural predators of bacteria, exhibiting high tissue permeability without disrupting beneficial intestinal microflora. This advantage over broad-spectrum antibiotics helps to maintain normal microbiomes [54]. However, rapid pathogen identification and CRISPR-modified bacteriophages are required to realize their full potential. The resurgence of interest in phage therapy is driven by both the AMR crisis and advances in biotechnology, which have overcome many historical limitations [55]. Phage particles interact with bacteria through outer membrane receptors, with each phage typically targeting specific bacterial species or strains, offering a level of precision unmatched by chemical antimicrobial agents. They accumulate in high concentrations; however, successful therapy requires the isolation of the infection-causing bacterium. While their protein composition can trigger immune recognition and reduce therapeutic efficacy, it also enables bioengineering modifications to improve their performance [56]. To mitigate immune system interference, strategies such as PEGylation, encapsulation in protective carriers, stabilization with nanocarriers, or binding to macroscopic supports have been proposed to enhance their ability to eradicate antibiotic-resistant bacteria [57]. Recent developments in biotechnology have enabled the modification of bacteriophage particles to enhance their ability to penetrate bacterial biofilms, boost efficacy, broaden lytic activity against various bacterial infections, and improve stability and specificity [56]. Bioengineered phages can also be designed to carry additional therapeutic payloads, such as antimicrobial peptides and enzymes that further support biofilm disruption. These advancements significantly strengthen the therapeutic value of phage therapy while preserving the target specificity that distinguishes phages as promising antimicrobial agents [58].

3.4. Antimicrobial peptides (AMPs)

AMPs are cationic host defense peptides found across all kingdoms of life that disrupt membrane structure. These naturally occurring molecules represent one of the most ancient and evolutionarily conserved defense mechanisms against microbial infections. Owing to their charged nature, rapid action, multiple mechanisms of action, difficulty in establishing resistance, and ability to be easily modified and manufactured in silico, AMPs are used to target pathogenic bacteria to prevent AMR [59]. These peptides can also be used as adjuvants to other antibiotics, increasing their effects and eliminating resistance [60]. AMPs employ multiple mechanisms to eliminate pathogens, making it difficult for them to develop resistance. Their action often begins with interaction with negatively charged moieties such as lipopolysaccharides (LPS) in Gram-negative bacteria and lipoteichoic acid (LTA) in Gram-positive bacteria. After passing through or creating pores in the bacterial cell wall or outer membrane, cytoplasmic membrane rupture and subsequent cell lysis occur [61]. Their modes of action are divided into pore-forming and non-pore-forming categories. They can also activate enzymes like autolysins that lead to autolytic death and inhibit the synthesis of cell walls, DNA, RNA, and proteins [62]. In addition to direct antimicrobial effects, AMPs possess immunomodulatory properties that enhance host defense. Peptides present in tissues and mucous membranes can suppress or destroy pathogens, including viruses, protozoans, bacteria, and fungi. They also exhibit anti-biofilm activity by altering membrane permeability, disrupting signaling, degrading polysaccharides and biofilm matrices, inhibiting alarm systems, and reducing gene expression. These characteristics make them a promising approach for eliminating persistent bacterial forms due to their strong inactivation capabilities [63].

3.5. AI-driven drug discovery and Computational approaches

Artificial intelligence (AI) has revolutionized infectious disease management by enhancing pathogen detection, identifying resistant bacteria, and facilitating target identification, dynamic modelling, peptide design, and drug repurposing, which ultimately strengthens antibiotic stewardship and combats AMR (Table 1) [64,65]. The integration of machine learning (ML) algorithms with biological data has accelerated antimicrobial discovery and optimized treatment strategies. AI technology automates learning and improvement without explicit programming by constructing and predicting models using data. ML algorithms can identify patterns in vast datasets that are impossible to detect manually. Deep learning (DL), a component of ML, mimics brain structure through algorithms such as convolutional, recurrent, deep reinforcement, and generative adversarial networks and is widely used in drug discovery [66]. The application of AI in antimicrobial research has shown promise in several key areas, including molecular design, target identification, and resistance prediction. AI is revolutionizing the healthcare sector by aggregating patient data, detecting diseases early, and using advanced imaging technologies. It reduces costs and improves drug prescription precision, resulting in better patient care [67]. Real-time decision support systems powered by AI can help clinicians select optimal antimicrobial therapies based on patient-specific factors and local resistance patterns [68]. AI algorithms can significantly reduce the time required for resistance detection, which is critical for timely and accurate diagnosis of MDR pathogens as well as administration of treatment [69]. Antibiograms aid in identifying high-risk agents, and the creation of customized machine-learning models holds promise for forecasting and mitigating AMR. AI for antimicrobials has the potential to transform clinical care, enhance surveillance systems, and accelerate drug development [70].

The Decision Tree model uses large datasets to capture nonlinear correlations between features and outputs. These models can predict treatment outcomes and resistance development with increasing accuracy as more data become available. Training datasets are used to preprocess the data and extract relevant input characteristics [69,71]. Complex models have greater variance, whereas simpler models have a larger bias. Several AI-powered tools are currently available for AMR surveillance and analysis. Metagenomics and Metadesign of Subways and Urban Biomes (MetaSUB-AMR) monitors and tracks resistance in urban environments by using metagenomic data and algorithms to analyze environmental DNA samples and map AMR genes [72]. DeepAMR and DeepARG employ deep learning to identify resistance genes and mutations in complex microbial communities. Mykrobe Predictor assists clinicians in tailoring antibiotic treatment plans, while AMR FinderPlus detects resistance genes and mutations in bacterial genomes [72].

3.6. Current and well-established therapeutics against AMR

Although next-generation technologies are rapidly advancing, well-established antimicrobial strategies continue to play a significant role in managing resistant infections (Table 2). Notably, immunotherapeutic approaches present a novel direction by enhancing and regulating the host's immune defenses instead of exclusively targeting pathogens. It therefore shows a strong potential to complement traditional antibiotics, reduce reliance on direct bactericidal activity, and improve outcomes in infections caused by MDR organisms.

3.6.1. β-Lactam/β-Lactamase inhibitor combinations

β-lactam antibiotics, including penicillin and cephalosporin, are among the most used antimicrobial agents in clinical practice. However,

Table 1
Comparative evaluation of next-generation AMR therapeutic strategies [19,73].

S/N	Therapeutic Strategy	Developmental Stage	Pros	Limitations	Comparative Effectiveness	Readiness Level
1.	CRISPR-based Antimicrobials	Preclinical/Limited animal trials	Highly specific, gene-targeting, preserves microbiota	Delivery challenges, potential for resistance	Promising against MDR genes	Low
2.	Nanotechnology (Ag, Au, Cu NPs)	Preclinical to limited clinical	Broad spectrum, novel mechanisms, and drug carriers	Toxicity concerns, lack of long-term safety data	Complementary to antibiotics, some synergy	Medium
3.	Bacteriophage Therapy	Phase I/II trials	Specificity, biofilm penetration, and modifiable	Immune clearance, host specificity, and regulatory	Effective in compassionate use cases	Medium
4.	AMPs	Late preclinical to early clinical trial	Fast-acting, multiple mechanisms, immunomodulatory	Toxicity at high doses, stability	Complementary and adjuvant to antibiotics	Medium
5.	AI-Driven Drug Discovery	Active clinical integration (diagnostics)	Fast screening, predictive analytics, and cost-effective	Data bias, limited interpretability	Enhances the speed of drug development and surveillance	High

Table 2
Comparative summary of innovative therapeutic approaches against AMR

S/N	Therapeutic Strategy	Mechanism of Action	Advantages	Limitations	Clinical Stage	Recent Experimental/In Silico Evidence	References
1.	β-lactamase inhibitors	Enzyme inhibition to restore β-lactam efficacy	Effective against β-lactamase-producing strains	Resistance emergence, limited spectrum	Approved/ Clinical	Recent docking studies reveal novel β-lactamase binding sites improving inhibitor potency	(101).
2.	Combination therapies	Synergistic drug action	Broad coverage, reduced resistance	Toxicity, pharmacokinetic mismatches	Clinical/ Standard	Experimental in vitro models confirm synergy of colistin with nanomaterials against MDR *P. aeruginosa*	(78).
3.	Vaccinology	Infection prevention, herd immunity	Long-lasting, reduces antibiotic use	High development cost, strain variability	Approved/ Ongoing	In silico-designed peptide vaccines against *K. pneumoniae* show promising immunogenicity	(11).
4.	Immunotherapies	Boost host immune response	Targeted, less resistance pressure	Limited use in immunocompromised, cost	Clinical/ Preclinical	Experimental monoclonal antibodies against *A. baumannii* tested in murine models with positive outcomes	(102).
5.	Phytotherapy	Disrupt membranes, inhibit efflux/ quorum sensing	Natural, multi-target action, low resistance	Variability, poor bioavailability, and limited trials	Preclinical	In silico studies identify indole alkaloids binding MDR efflux pumps against MDR *E. coli*	(103).
6.	Probiotics/ Microbiome engineering	Competitive exclusion, immune modulation	Safe, preventive, gut microbiota restoration	Strain-specific, limited regulation	Preclinical/ Some Clinical	Recent experimental models show engineered probiotics *E. coli* suppresses P. aeruginosa and gut bacteria	(104).
7.	Photodynamic therapy (PDT)	ROS-mediated microbial killing	Non-antibiotic, biofilm-effective	Light exposure required, local use only	Preclinical	New in silico photosensitizer designs improve ROS yield; in vivo validation in biofilm-infected wounds	(105).
8.	Immunomodulatory therapies	Modulate immune system (e.g., cytokines, checkpoint inhibitors)	Enhances innate immunity; supportive in sepsis or MDR infections	Risk of immune overactivation; unclear long-term effects; limited clinical validation	Preclinical/ Experimental	Experimental cytokine therapy models show improved clearance of MDR *E. coli* in mice	(106).

their effectiveness has been significantly compromised by the widespread bacterial production of β-lactamases, which are enzymes that hydrolyze the β-lactam ring and neutralize the antibiotic's activity [74]. To overcome this resistance mechanism, β-lactamase inhibitors, including clavulanic acid, sulbactam, tazobactam, avibactam, vaborbactam, and relebactam, have been developed to restore the efficacy of β-lactam antibiotics [75]. Several advanced combinations have shown clinical efficacy against extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae and carbapenem-resistant organisms [75]. For instance, avibactam–ceftazidime has demonstrated significant activity against carbapenem-resistant *Klebsiella pneumoniae* in both clinical and experimental studies [76]. These combinations represent an important step in prolonging the utility of β-lactams and restoring activity against resistant strains [77].

3.6.2. Combination antibiotic therapy

Combination antibiotic therapy continues to be a commonly employed strategy in addressing AMR, especially for infections caused by MDR pathogens. This approach aims to enhance therapeutic efficacy through synergistic interactions, extend the spectrum of antimicrobial activity, and reduce the likelihood of resistance development [78]. Commonly used antibiotic combinations include colistin with carbapenems or tigecycline for treating carbapenem-resistant *Acinetobacter baumannii*; vancomycin in combination with ceftaroline or daptomycin for managing persistent *Staphylococcus aureus* bacteremia; and trimethoprim–sulfamethoxazole (TMP–SMX), which is effective against various Gram-positive and Gram-negative pathogens, including community-acquired MRSA [79]. Clinical observations reveal that colistin–rifampin combinations exhibited synergistic activity in vitro and prevented resistance against carbapenemase-producing *Klebsiella pneumoniae*; however, in vivo efficacy was limited and strain-dependent,

highlighting their heterogeneous but potentially beneficial role in specific infections [80]. However, limitations such as increased toxicity, cost, and limited data on optimal combinations highlight the need for continued clinical trials and pharmacodynamic modeling [81].

3.6.3. Advanced immunotherapies

Immunotherapies are emerging as a powerful and increasingly accepted approach in the management of AMR infections. In contrast to conventional antibiotics that target pathogens directly, these therapies focus on enhancing the host's immune defenses, providing a complementary or alternative strategy for infection control. Principal modalities include monoclonal antibodies (mAbs), therapeutic vaccines, and agents that modulate immune responses [82]. For instance, bezlotoxumab, a monoclonal antibody, has been approved for the prevention of recurrent *Clostridioides difficile* infections by neutralizing its toxin [83]. In addition, adjunctive immunotherapies are being explored for their potential to treat infections caused by MDR *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, where conventional antibiotics often fail [84]. Furthermore, cytokine-based treatments and immune checkpoint inhibitors are being repurposed to enhance innate immune function in critical conditions such as sepsis [85].

3.6.4. Vaccinology

Vaccinology serves as an essential and proactive strategy in combating AMR by reducing the incidence of infections that would otherwise require antibiotic treatment, thereby lessen selective pressure and curbing the emergence and spread of resistance. Established vaccines targeting high-burden pathogens such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Mycobacterium tuberculosis* have already demonstrated substantial public health impact and have contributed significantly to lowering global antibiotic use [86]. However, ongoing research is expanding this approach toward the development of vaccines against drug-resistant organisms, including MRSA and MDR *Klebsiella pneumoniae* [50]. These efforts represent a proactive and sustainable approach to reducing the global burden of AMR, especially as effective vaccination can prevent both community- and hospital-acquired infections [87]. The high cost of vaccine research and the lengthy development timelines can delay access, particularly in low- and middle-income countries (LMICs). Antigenic variability among bacterial strains may reduce vaccine efficacy or necessitate frequent reformulations, as seen with pneumococcal vaccines [88]. In addition, suboptimal immune responses in certain populations, along with logistical difficulties related to vaccine distribution and cold chain requirements, can limit real-world impact. Another critical issue is the lack of strong commercial incentives for developing vaccines against some resistant bacteria, particularly those that cause relatively rare or geographically confined infections, making them less attractive to pharmaceutical developers [89]. A notable experimental example is a candidate vaccine against MDR *K. pneumoniae* that generated strong antibody responses in mice and reduced bacterial loads, but strain-specific antigenic differences limited cross-protection [90].

3.6.5. Phytotherapy

Phytotherapy involves the therapeutic application of medicinal plants and their bioactive compounds. This practice has emerged as a promising avenue in AMR management due to its dual antimicrobial and resistance-modifying properties. Plant-derived constituents such as alkaloids, flavonoids, terpenoids, and essential oils have demonstrated diverse mechanisms of action, including disruption of bacterial cell membranes, inhibition of efflux pumps, interference with quorum sensing, and synergistic enhancement of conventional antibiotic efficacy. These naturally occurring compounds offer a rich and largely untapped reservoir of potential anti-infective agents, making phytotherapy a compelling candidate for integration into AMR control strategies, especially in resource-limited settings or in combination with modern therapeutics [91]. The advantages of phytotherapy are notable. It leverages compounds from natural and renewable sources, offering biocompatibility, broad-spectrum potential, and reduced environmental impact. Also, the vast biodiversity of medicinal plants provides an extensive reservoir of novel therapeutic candidates [92]. However, a major concern is the lack of standardization and quality control in the production of plant-based remedies, with variability in chemical composition due to differences in species, cultivation conditions, and extraction methods [92].

3.6.6. Photodynamic therapy (PDT)

PDT is a novel, non-antibiotic strategy that uses light-activated photosensitizing agents to produce ROS, which are toxic to microbial cells. These ROS damage essential cellular components such as membranes, proteins, and nucleic acids. PDT has demonstrated notable effectiveness in managing localized infections, particularly those that are caused by biofilm-forming or drug-resistant pathogens that are typically unresponsive to conventional antibiotics [93]. One major benefit of PDT is its broad-spectrum antimicrobial action, effective against bacteria, fungi, and certain viruses, while posing a low risk of resistance development due to its multi-target oxidative mechanism [94]. PDT offers precise localization, reducing systemic side effects and protecting nearby healthy tissue [93]. However, the clinical application of PDT is currently limited by several factors, which include its reliance on direct light exposure, limiting its application to surface-level or easily accessible infections. There is also a risk of damaging host tissues if light intensity or photosensitizer dosage is not precisely managed [94]. Despite these limitations, PDT remains a promising adjunct or alternative to antibiotic therapy, particularly in managing chronic wounds, oral infections, and device-associated biofilms, and its continued refinement may broaden its clinical utility in the context of AMR [94].

3.6.7. Immunomodulatory therapies

Immunomodulatory therapies are designed to regulate and optimize the host's immune system to enhance infection control. These treatments involve the use of agents like cytokines, immune stimulants, and checkpoint inhibitors to either strengthen weakened immune responses or reduce harmful inflammation. This strategy is especially beneficial for immunocompromised individuals such as those with HIV, cancer, post-transplant conditions and sepsis, where immune system imbalance plays a central role. Immunomodulatory therapies' benefits include their host-targeted mechanism, which reduces selective pressure on pathogens and the likelihood of resistance development. They can also enhance the effectiveness of antibiotics, especially when microbial clearance is dependent on a functional immune system. These therapies also offer potential personalization, which allows immune interventions to be tailored to a patient's immune status [38]. However, these therapies pose some limitations and risks, including overactivation of the immune system. This can lead to harmful inflammatory responses, including cytokine storms, which may exacerbate illness or lead to organ failure. Also, insufficient immune modulation may result in limited or no clinical benefit [95]. More clinical trials are needed to establish efficacy, safety, and long-term outcomes across diverse patient populations [96].

3.6.8. Probiotics and microbiome engineering

Probiotics and microbiome engineering have emerged as promising strategies for both the prevention and restoration of microbial balance in AMR. These interventions focus on supporting or reestablishing healthy microbiota by encouraging the proliferation of beneficial microbes capable of suppressing pathogenic species. Their mechanisms of action include competitive exclusion of harmful bacteria, secretion of antimicrobial compounds, and stimulation of mucosal immune responses [97, 98]. Benefits of probiotics and microbiome-based interventions include their non-invasive administration and their favorable safety profile in the general population. They are relatively cost-effective, easily incorporated into existing treatment regimens, and have shown potential in reducing the frequency and severity of infections, thereby decreasing

antibiotic use and the subsequent development of resistance [99]. The clinical efficacy of probiotics is highly strain-specific, and many commercially available products lack scientific evidence. There is a lack of standardization in formulation, dosing, and regulatory oversight, leading to variability in product quality and effectiveness [100]. Despite these challenges, probiotics and microbiome engineering significantly expand the therapeutic landscape against AMR by leveraging the natural microbiota as a biological barrier to infection. As research progresses, greater precision, regulatory clarity, and clinical validation will be essential to fully integrate these strategies into routine AMR prevention and treatment frameworks.

4. Innovative approaches to combat AMR

AMR is a critical global health threat, and traditional antibiotic development is not keeping pace with the rise of resistant pathogens. Its complexity demands innovative strategies beyond conventional antimicrobial discovery, including biofilm disruption, host-directed therapies, precision medicine, and advanced drug delivery systems (Fig. 3).

4.1. Biofilm-disrupting strategies

Bacterial biofilms represent one of the most challenging aspects of AMR, as they can be up to 1000 times more resistant to antibiotics than planktonic bacteria. Enzyme-based biofilm degradation, quorum-sensing inhibitors, and anti-adhesion molecules are being explored to break down biofilms and disrupt bacterial communication, making pathogens more susceptible to antibiotic treatment and immune system clearance [10,11,107]. The complex architecture of biofilms, characterized by bacterial cells embedded within a self-produced extracellular polymeric matrix, presents multiple physiological and structural barriers that impede effective antimicrobial penetration [11,107]. Novel approaches include the use of dispersin enzymes that degrade biofilm matrix components, small molecules that interfere with quorum-sensing pathways, and surface modifications that prevent initial bacterial adhesion [108]. For example, an experimental study demonstrated that *Nocardiopsis lucentensis* EMB25, an uncommon actinobacteria, inhibited and eradicated *P. aeruginosa* biofilm utilizing its secondary metabolites to target the quorum-sensing pathways and bind to LasR and RhlR, although not validated via in vivo models [109]. Similarly, quorum-sensing inhibitors such as furanones have shown promising in-vitro effects; however, their instability and cytotoxicity remain major limitations for translation into clinical use [110].

4.2. Host-directed therapies

Host-directed therapies prioritize the enhancement of the body's innate defense mechanisms over direct pathogen elimination. Approaches such as immune modulation are being explored as viable alternatives to conventional antimicrobial strategies, with the aim of improving clinical outcomes and reducing dependence on antibiotics [11,107]. They recognize that successful treatment of infections depends on both pathogen elimination and effective host immune function. Probiotics, microbiome engineering, and vaccines targeting resistant pathogens are being investigated to prevent infections and reduce the spread of AMR [10,11,107]. These approaches can attenuate pathogen virulence and enhance the body's natural ability to clear infections [11,107]. Immunomodulatory therapies encompass cytokine modulators, immune checkpoint inhibitors tailored for infectious diseases, and therapeutic vaccines aimed at stimulating the immune system to target specific drug-resistant pathogens [111]. Experimental findings support these strategies: a murine sepsis model treated with IL-7 immunotherapy showed improved 92 % survival and immune recovery yet concerns regarding immune overactivation and cytokine storm remain a critical drawback [112]. Likewise, engineered probiotics reduced colonization of gut inflammatory diseases in vitro, but strain-specific variability and regulatory gaps hinder consistent application in humans [113].

4.3. Precision medicine and personalized therapies

The era of precision medicine offers new opportunities to optimize

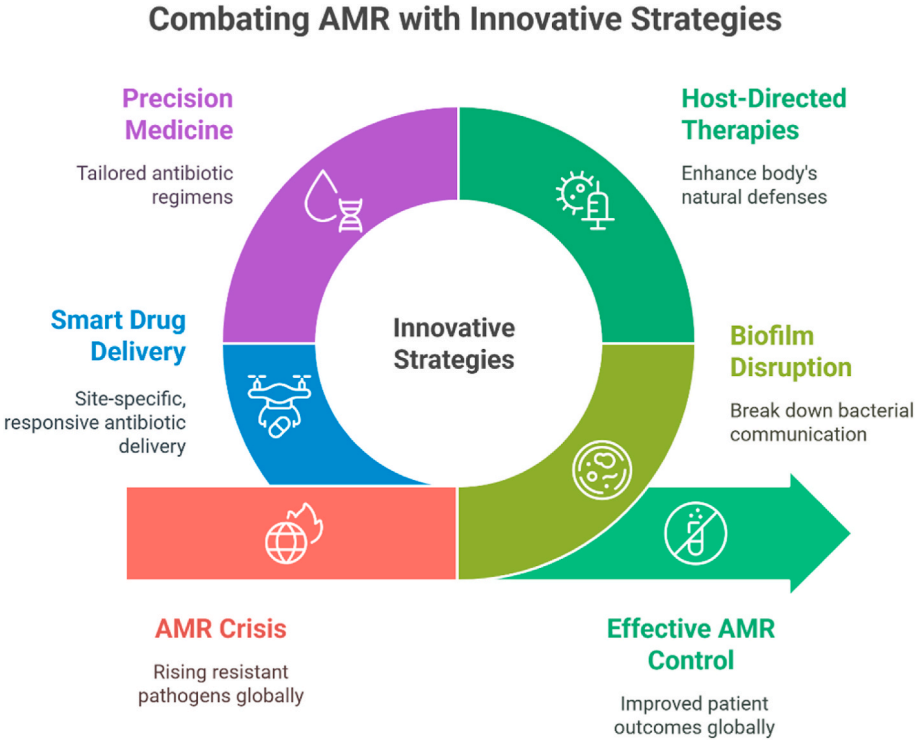

Fig. 3. Combating AMR with innovative strategies.

antimicrobial therapy using individualized treatment approaches. Genomic and metagenomic approaches enable the rapid identification of resistance genes and pathogen strains, supporting tailored antibiotic regimens [107,114,115]. Advances in rapid diagnostic technologies now allow pathogen identification and susceptibility testing within hours rather than days. Rapid diagnostics and AI-driven tools are improving the precision and timeliness of targeted therapy, thereby reducing unnecessary antibiotic use [107,114,115]. Personalized medicine, including clonotyping and patient-specific factors such as pharmacokinetics, immune status, and microbiome composition, is increasingly integrated into clinical decision-making to optimize therapeutic outcomes [107,114]. Recent clinical pilot studies have demonstrated the feasibility of sequencing-based diagnostics, providing same-day resistance profiles, which enable optimized antibiotic therapy in critically ill patients. However, the high cost, limited availability in low-resource settings, and challenges in integrating genomic data into real-time clinical decision-making remain significant limitations [116].

4.4. Smart drug delivery systems

Advanced drug delivery systems represent a paradigm shift in the administration of antimicrobials and targeting of infection sites. Bionanomaterials, hydrogels, and implantable devices are being developed for site-specific, responsive antibiotic delivery. These innovations aim to enhance efficacy, minimize side effects, and address the key limitations of conventional antimicrobial therapy, including poor tissue penetration, systemic toxicity, and suboptimal drug concentrations at infection sites [107,115,117,118]. These systems can be engineered to release drugs in response to infection signals or environmental triggers, thereby improving treatment outcomes [107,118,119]. Examples include pH-responsive nanoparticles that release antibiotics in the acidic environment of infected tissues and magnetic nanocarriers guided to infection sites within the body [55]. For instance, an experimental pH-sensitive chitosan nanoparticle system successfully released ciprofloxacin in acidic abscess environments and reduced bacterial loads in vivo, though inconsistent release kinetics were observed across batches [120]. Similarly, Silver Oxytetracycline Nanostructures (Ag-OTC-Ns) exhibited superior antimicrobial efficacy against *Klebsiella pneumoniae* compared to free oxytetracycline, $AgNO_3$, and AgNPs, effectively eradicated lung infection and reduced inflammation in mice without significant toxicity, and remained stable after gamma sterilization, highlighting their potential as a safe and potent therapeutic option [121].

5. Challenges in implementing next-generation AMR solutions

The implementation of next-generation AMR solutions faces significant challenges in the scientific, economic, ethical, and regulatory domains. Translating promising laboratory discoveries into clinical practice requires overcoming multiple interconnected barriers.

5.1. Clinical and scientific challenges

The rapid pace of technological advancement in AMR research, while promising, has created significant standardization challenges. NGS and associated bioinformatics tools often produce variable results, which can undermine the reliability and clarity of AMR data interpretation. This inconsistency poses challenges in making informed decisions based on the findings. The need to harmonize and validate these technologies for large-scale implementation remains a significant obstacle [119,122]. Interlaboratory variability and the lack of standardized protocols further complicate the implementation of new diagnostic technologies. Establishing consistent protocols for benchmarking and quality control is difficult when tools and techniques are constantly evolving [119,122]. The need to track a wide range of pathogens and evolving resistance mechanisms, along with geographic differences in resistance patterns, makes standardization efforts highly complex. Choosing suitable datasets and defining appropriate evaluation criteria present challenges, as they must account for the extensive variability [119,122].

5.2. Economic and commercialization barriers

The economic landscape of antimicrobial development presents unique challenges that distinguish it from other pharmaceutical sectors. The development, validation, and maintenance of effective platforms for detecting and treating AMR require substantial investment. These efforts require not only advanced research and infrastructure but also a well-trained workforce, all of which places a considerable strain on available resources [119,122]. The anticipated return on investment for antimicrobial development is often insufficient to attract private sector investment, particularly given the emphasized antibiotic overuse or abuse. Compounding these challenges is the issue of sustainability in the development of antimicrobials. Financial incentives and market support for producing and distributing new antimicrobial agents are often lacking, leading to significant market failures and reduced interest in antibiotic innovation [119,123].

5.3. Ethical and social considerations

Ensuring equitable access to advanced AMR solutions remains a critical challenge, particularly in resource-limited settings where healthcare infrastructure and funding are limited [119,123]. The digital divide and technological disparities between developed and developing nations further complicate the implementation of AI-driven and high-tech antimicrobial solutions. In addition, fostering public trust in emerging technologies, such as genetic modification and synthetic biology, is crucial for their successful adoption. Without widespread acceptance, these innovative approaches may face resistance, despite their potential benefits [119,123]. Ethical considerations also arise regarding the use of genetic modification technologies, such as CRISPR, in clinical settings, particularly concerning long-term effects and potential unintended consequences [124].

5.4. Regulatory hurdles

The regulatory landscape for novel antimicrobial technologies is complex and rapidly evolving. The implementation of new technologies to combat AMR necessitates harmonization, thorough validation, and continuous quality assurance. However, these processes are complicated by the rapid pace of technological innovation and the need for coordinated international efforts [119,122]. Traditional regulatory frameworks were not designed to evaluate novel technologies, such as engineered bacteriophages, CRISPR-based therapeutics, or AI-driven diagnostic tools [125]. Furthermore, the development of transparent, community-driven benchmarking platforms and the establishment of standardized datasets are essential for achieving regulatory approval [119,122].

6. Public health policy, global strategy, and stakeholder roles

Effectively addressing AMR requires scientific innovation, strong public health policies, coordinated global strategies, and multisectoral collaboration. Central to both national and international efforts are robust surveillance systems and antimicrobial stewardship programs. The WHO's Global Antimicrobial Resistance Surveillance System (GLASS) supports standardized data collection and facilitates early detection of resistance trends, while national systems adapt these frameworks for local use [126]. Recent advancements, including the integration of AI into surveillance, have further strengthened real-time monitoring and predictive responses to AMR threats [127–129]. Antibiotic stewardship programs (ASPs), implemented in hospitals and community settings, help to optimize antimicrobial prescribing and

prevent misuse. These programs, supported by multidisciplinary teams, including infectious disease specialists, pharmacists, and microbiologists, are instrumental in reducing overprescription and preserving the effectiveness of current treatments [130,131]. However, implementing ASPs remains particularly challenging in LMICs due to resource constraints, limited diagnostic capacity, and workforce shortages [132, 133]. Innovative models, including digital decision-support tools and mobile health platforms, are being developed to address these gaps and expand stewardship capacity in resource-limited settings [133–135].

Regulatory and policy interventions are essential in shaping environments that promote the responsible use of antimicrobials [136]. Measures such as restricting over-the-counter antibiotic sales and regulating the use of antimicrobials in agriculture have proven critical for containment [137]. At the same time, forward-thinking policy approaches are needed to stimulate antimicrobial innovation. Public–private partnerships and financial incentive models such as market entry rewards are being explored to revitalize the stagnating antibiotic development pipeline [138,139].

Public education and awareness campaigns remain key to shifting behavior and encouraging responsible antibiotic use. Through community outreach, schools, and media engagement, such as campaigns, help foster informed decision-making and bolster the societal foundation necessary to contain AMR [140–143]. The broader global response depends on the coordinated action of key stakeholders. The WHO's Global Action Plan on AMR provides a comprehensive framework based on surveillance, awareness, infection prevention, optimal antimicrobial use, and sustainable investment [144]. The Centers for Disease Control and Prevention (CDC) leads national responses by supporting surveillance and stewardship initiatives [145], while the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) regulate the approval and safety of new antimicrobials, including next-generation technologies like phage therapy, nanomaterials, and gene-editing tools [146,147]. The United Nations has elevated AMR as a global political priority, advocating for the One Health approach that recognizes the interconnectedness of human, animal, and environmental health [148]. Non-governmental organizations (NGOs) and private sector initiatives, such as CARB-X and the Global Antibiotic Research and Development Partnership (GARDP), are also instrumental in accelerating innovation and ensuring equitable access to novel treatments [149,150].

Ultimately, addressing AMR requires a coordinated global response grounded in robust public health policies and strategic frameworks. These approaches serve as the backbone for monitoring resistance trends, ensuring rational antibiotic use, and fostering multi-sectoral collaboration (Fig. 4).

7. Future perspectives and research directions

Looking ahead, the fight against AMR must evolve using dynamic and integrative strategies. While current efforts lay a solid foundation, future progress hinges on embracing multidisciplinary innovation, developing alternative therapeutic options, and reinforcing global policy frameworks to sustain momentum and equity in response. A key direction for AMR research is the convergence of multiple scientific disciplines to design effective interventions. Synthetic and systems biology are opening new frontiers in the understanding of microbial behavior, resistance mechanisms, and host-pathogen interactions. These tools enable the construction of tailored genetic circuits, reprogrammed microbes, and novel biosensors for the real-time detection or counteraction of resistance [151,152]. The integration of AI, nanotechnology, and bacteriophage therapy enhances the efficacy and specificity of AMR treatments. AI-driven predictive modelling can optimize drug design and identify resistance patterns, while nanotechnology provides targeted drug delivery systems that minimize side effects and enhance drug bioavailability. Phage therapy, revived with renewed scientific interest, holds promise for the precision eradication of resistant bacteria [153, 154]. The concept of personalized and precision medicine is also gaining traction as a long-term strategy. By incorporating patient-specific data, such as genomic profiles, microbiome analysis, and immune responses, tailored treatment plans can improve outcomes and reduce the likelihood of resistance emergence [155,156]. This individualized approach represents a shift from a one-size-fits-all therapy to a more responsive and data-informed care.

Beyond conventional antibiotics, research is increasingly exploring underutilized natural resources and novel therapeutic targets. Plant- and marine-derived antimicrobial compounds, many of which possess unique structures and modes of action, are being systematically studied for their potential to overcome existing resistance [157,158]. Another area of focus is the development of antivirulence agents and immunomodulating compounds. These therapies aim not to kill pathogens directly but to disarm them or strengthen host defenses, thereby reducing the selective pressure for resistance. Immune-boosting strategies, including probiotics and immunotherapies, are being tested as adjuncts to traditional treatments [159,160]. Simultaneously, advances in biomaterial science are contributing to infection control in both clinical and environmental contexts. Antimicrobial coatings, smart wound dressings, and biofilm-disrupting materials are engineered to prevent infections on medical devices and hospital surfaces, adding a layer of defense [161,162].

Scientific innovation must be matched by a supportive policy environment to ensure that its impact reaches all populations. Strengthening international collaborations remains a top priority. Coordinated surveillance, harmonized regulatory frameworks, and data-sharing initiatives can accelerate the translation of research into actionable strategies [162]. Securing sustainable funding for antibiotic development is critical. Public-private partnerships, market entry rewards, and government-backed innovation funds are being explored as viable mechanisms to incentivize investment in new antimicrobials while mitigating financial risks for developers [161]. Importantly, expanding access to novel therapies in low-resource settings should be a guiding

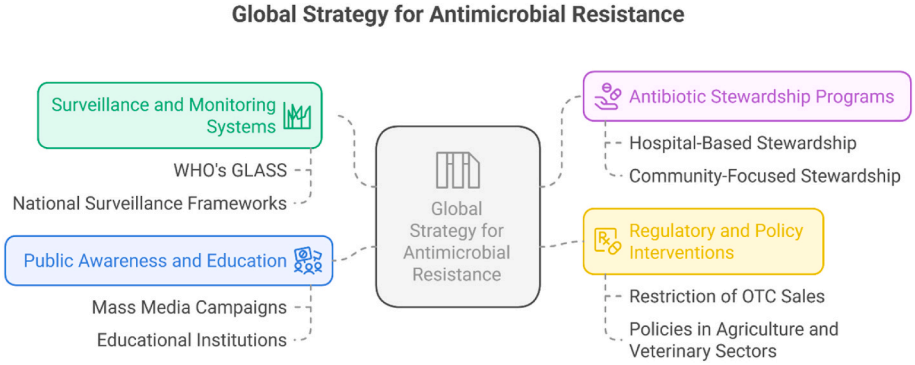

Fig. 4. Global strategy for AMR.

principle. Equitable distribution models, capacity-building programs, and global procurement strategies are essential to prevent the exacerbation of existing health disparities [163]. By integrating scientific progress with inclusive policies, future responses to AMR can be both impactful and sustainable.

8. Limitations of the review

While this narrative review provides a broad overview of emerging technologies and innovative approaches to combat AMR, several limitations were acknowledged. As a narrative review, the methodology does not follow a systematic approach, which may introduce selection bias in the selection and interpretation of literature. Although the search strategy was comprehensive and included multiple databases, it may have inadvertently excluded relevant studies published in non-English languages or indexed in databases not searched. The rapidly evolving nature of AMR research also presents a challenge in ensuring complete coverage. This review focuses primarily on scientific and technological innovations, with less emphasis on the socioeconomic and cultural factors influencing the development, implementation, and accessibility of AMR interventions. These dimensions are critical, as the effectiveness of any antimicrobial strategy depends not only on its scientific validity but also on its real-world applicability and acceptability across different healthcare systems and populations. Also, some of the technologies discussed are still in early stages of research and development. Their long-term safety, efficacy, scalability, and cost-effectiveness remain to be fully established through rigorous preclinical studies, clinical trials, and real-world applications. In addition, certain promising areas of research may have received limited attention due to scope constraints and the need to prioritize the most significant developments. The dynamic nature of AMR means that resistance mechanisms and treatment strategies will continue to evolve, requiring continuous reassessment and updating to maintain the relevance and utility of such reviews.

9. Conclusion

AMR remains one of the most critical global health threats, undermining decades of progress in infectious disease treatment. This narrative offers a multidimensional synthesis of both conventional and emerging therapeutics, critically evaluates their clinical readiness, and highlights underrepresented strategies such as phytotherapy, probiotics, and photodynamic therapy. It underscores the complex nature of AMR, driven by antibiotic misuse, genetic mutations, and horizontal gene transfer. As traditional treatments lose effectiveness, next-generation technologies, such as CRISPR-Cas systems, nanotechnology-based antimicrobials, antimicrobial peptides, bacteriophage therapy, and AI-driven drug discovery, have emerged as promising alternatives that target resistance through novel mechanisms. However, despite these advances, significant implementation challenges persist. These include scientific barriers to data standardization and clinical validation, economic hurdles related to funding and market incentives, ethical and social concerns surrounding equitable access and public trust, and regulatory complexities that hinder timely clinical adoption. Additionally, the vast diversity of pathogens and evolving resistance mechanisms demands flexible and adaptive therapeutic strategies. Future research should focus on improving the safety, scalability, and regulatory integration of innovative antimicrobial therapies. A significant gap in translating laboratory advances into clinically approved solutions, particularly for technologies like CRISPR-Cas antimicrobials, nanomaterials, and bacteriophage-based treatments, persists. Standardized protocols for efficacy testing, toxicity assessment, and long-term safety evaluations are lacking and should be a top research priority. Another critical gap is the limited therapeutic pipeline targeting novel mechanisms of action. Expanding this pipeline through the development of antivirulence agents, immunomodulators, and biologically derived compounds represents a major future direction. These alternatives remain underexplored despite their potential to reduce selective pressure for resistance. On the systems level, policy reforms should prioritize global and regional AMR surveillance systems, equitable access to new treatments, and sustainable financing models that incentivize both innovation and affordability. There is also a need for research into market-shaping strategies that can overcome the economic barriers facing antimicrobial development, particularly in low-resource settings. The development of robust public health policies, international collaboration frameworks, and integrated regulatory pathways is essential for effective implementation. Global organizations such as the WHO, CDC, FDA, and EMA play a significant role in guiding harmonized regulations and accelerating technology adoption, yet gaps in global regulatory coherence and coordination persist.

Furthermore, future progress depends on the active engagement of private sector stakeholders, academic researchers, and non-governmental organizations, which are essential for ensuring sustainable development, commercialization, and distribution of novel therapies. Addressing AMR requires an interdisciplinary and collaborative approach that transcends traditional boundaries. Coordinated efforts among microbiologists, clinicians, bioengineers, data scientists, public health professionals, and policymakers are essential. Only by fostering collective action and maintaining long-term investment in research and development can we close existing knowledge gaps and strengthen health systems to effectively confront the escalating threat of AMR. With the window of opportunity narrowing, prompt, coordinated, and strategic efforts are now more essential than ever.

Informed consent statement

Not applicable.

Author contributions

DELP III conceptualized and designed the study. UOA, OAA, AOA, NOO, TAO, MIRS, JBO and OBA wrote the first draft of the manuscript. OJO, MMA, and DBO critically revised the manuscript for important intellectual content. DELP III supervised the study. All authors have read and approved the final manuscript.

Institutional review board statement

Not applicable.

Data availability statement

Not applicable because no new data or databases were used in the preparation of this work.

Clinical trial

Not Applicable.

Funding

This research received no external funding.

Declaration of competing interest

The authors of this review declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this manuscript.

Acknowledgement

The authors acknowledge the use of Paperpal (https://paperpal.com/), an AI-powered academic tool, for language editing and

academic paraphrasing to enhance the clarity and readability of the manuscript. This assistance was limited to linguistic refinement, and the intellectual content, analysis, and interpretations remain entirely the authors' own.

References

[1] Olalekan Olatunji Aliu, Janet Aderonke Olaboye, Chukwudi Cosmos Maha, Tolulope Olagoke Kolawole, Samira Abdul, Next-Generation strategies to combat antimicrobial resistance: integrating genomics, CRISPR, and novel therapeutics for effective treatment, Eng. Sci. Technol. J. 5 (7) (2024 Jul 24) 2284–2303. Available from: https://fepbl.com/index.php/estj/article/view/1344.

[2] G.M. Ikokwu, I.D. Oseghale, I. Omoregie, O.H. Ralph-Okhiria, E.F. Ighile, Emerging trends in antimicrobial resistance and novel therapeutic strategies, Int. J. Pathog. Res. 12 (3) (2023 Jun 3) 10–26. Available from: https://journalijpr.com/index.php/IJPR/article/view/226.

[3] A. Tarín-Pelló, B. Suay-García, M.T. Pérez-Gracia, Antibiotic resistant bacteria: current situation and treatment options to accelerate the development of a new antimicrobial arsenal, Expert Rev. Anti Infect. Ther. 20 (8) (2022 Aug 3) 1095–1108. Available from: https://www.tandfonline.com/doi/full/10.1080/14787210.2022.2078308.

[4] J. Murugaiyan, P.A. Kumar, G.S. Rao, K. Iskandar, S. Hawser, J.P. Hays, et al., Progress in alternative strategies to combat antimicrobial resistance: focus on antibiotics, Antibiotics 11 (2) (2022 Feb 4) 200. Available from: https://www.mdpi.com/2079-6382/11/2/200.

[5] D. Chinemerem Nwobodo, M.C. Ugwu, C. Oliseloke Anie, M.T.S. Al-Ouqaili, J. Chinedu Ikem, U. Victor Chigozie, et al., Antibiotic resistance: the challenges and some emerging strategies for tackling a global menace, J Clin Lab Anal 36 (9) (2022 Sep 10) [Internet], https://onlinelibrary.wiley.com/doi/10.1002/jcla.24655.

[6] Z. Breijyeh, B. Jubeh, R. Karaman, Resistance of gram-negative bacteria to current antibacterial agents and approaches to resolve it, Molecules [Internet] 25 (6) (2020 Mar 16) 1340. Available from: https://www.mdpi.com/1420-3049/25/6/1340.

[7] E.M. Darby, E. Trampari, P. Siasat, M.S. Gaya, I. Alav, M.A. Webber, et al., Molecular mechanisms of antibiotic resistance revisited, Nat. Rev. Microbiol. 21 (5) (2023 May 21) 280–295. Available from: https://www.nature.com/articles/s41579-022-00820-y.

[8] R.Y.K. Chang, S.C. Nang, H.K. Chan, J. Li, Novel antimicrobial agents for combating antibiotic-resistant bacteria, Adv. Drug Deliv. Rev. 187 (2022 Aug) 114378. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0169409X2200268X.

[9] U.A. Haruna, G. Eshun, O.J. Okesanya, Y.A. Mohammed Elhadi, I.I.I.D.E. Lucero-prisno, Antimicrobial resistance strains the wallet: who pays when we hit the wall? Microbes Infect. Dis. (2024 Nov 5) [cited 2025 Sep 5]; Available from: https://mid.journals.ekb.eg/article_390702.html.

[10] A. Vitiello, M. Sabbatucci, M. Boccellino, A. Ponzo, R. Langella, A. Zovi, Therapeutic and unconventional strategies to contrast antimicrobial resistance: a literature review, Discov. Med. 35 (178) (2023) 750. Available from: https://www.discovmed.com/EN/10.24976/Discov.Med.202335178.70.

[11] M. Oliveira, W. Antunes, S. Mota, Á. Madureira-Carvalho, R.J. Dinis-Oliveira, D. Dias da Silva, An overview of the recent advances in antimicrobial resistance, Microorganisms 12 (9) (2024 Sep 21) 1920 [Internet], https://www.mdpi.com/2076-2607/12/9/1920.

[12] M.E. Elshobary, N.K. Badawy, Y. Ashraf, A.A. Zatioun, H.H. Masriya, M. M. Ammar, et al., Combating antibiotic resistance: mechanisms, multidrug-resistant pathogens, and novel therapeutic approaches: an updated review, Pharmaceuticals 18 (3) (2025 Mar 12) 402 [Internet], https://www.mdpi.com/1424-8247/18/3/402.

[13] D. Yamin, V. Uskoković, A. Wakil, M. Goni, S. Shamsuddin, F. Mustafa, et al., Current and future technologies for the detection of antibiotic-resistant bacteria, Diagnostics 13 (20) (2023 Oct 18) 3246 [Internet], https://www.mdpi.com/2075-4418/13/20/3246.

[14] R. Lima, F.S. Del Fiol, V.M. Balcão, Prospects for the use of new technologies to combat multidrug-resistant bacteria, Front Pharmacol. 10 (2019 Jun 21). Available from: https://www.frontiersin.org/article/10.3389/fphar.2019.00692/full.

[15] R.S. Riley, E.S. Day, Gold nanoparticle-mediated photothermal therapy: applications and opportunities for multimodal cancer treatment, WIREs Nanomed. Nanobiotechnol. 9 (4) (2017 Jul 3). Available from: https://wires.onlinelibrary.wiley.com/doi/10.1002/wnan.1449.

[16] M. Ahmed, H. Kayode, O. Okesanya, B. Ukoaka, G. Eshun, M. Mourid, et al., CRISPR-cas systems in the fight against antimicrobial resistance: current status, potentials, and future directions, Infect. Drug Resist. 17 (2024 Nov) 5229–5245. Available from: https://www.dovepress.com/crispr-cas-systems-in-the-fight-against-antimicrobial-resistance-curre-peer-reviewed-fulltext-article-IDR.

[17] J. Shen, J. Zhou, G.Q. Chen, Z.L. Xiu, in: R.M. Sandri-Goldin, J. Virol (Eds.), Efficient genome engineering of a virulent Klebsiella bacteriophage using CRISPR-cas9, vol. 92, 2018 Sep, 17, https://journals.asm.org/doi/10.1128/JVI.00534-18.

[18] M. Ahmed, G.H. Daoud, A. Mohamed, R. Harati, New insights into the therapeutic applications of CRISPR/Cas9 genome editing in breast cancer, Genes 12 (5) (2021 May 12) 723 [Internet], https://www.mdpi.com/2073-4425/12/5/723.

[19] O.J. Okesanya, M.M. Ahmed, J.B. Ogaya, B.O. Amisu, B.M. Ukoaka, O.A. Adigun, et al., Reinvigorating AMR resilience: leveraging CRISPR–Cas technology potentials to combat the 2024 WHO bacterial priority pathogens for enhanced global health security—a systematic review, Trop Med Health 53 (1) (2025 Apr 2) 43 [Internet], https://tropmedhealth.biomedcentral.com/articles/10.1186/s41182-025-00728-2.

[20] S. Chen, H. Liu, W. Liang, L. Hong, B. Zhang, L. Huang, et al., Insertion sequences in the CRISPR-Cas system regulate horizontal antimicrobial resistance gene transfer in Shigella strains, Int. J. Antimicrob. 53 (2) (2019 Feb) 109–115. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0924857918302796.

[21] T. Boonsiri, S. Watanabe, X.E. Tan, K. Thitiananpakorn, R. Narimatsu, K. Sasaki, et al., Identification and characterization of mutations responsible for the β-lactam resistance in oxacillin-susceptible mecA-positive Staphylococcus aureus, Sci Rep 10 (1) (2020 Oct 9) 16907 [Internet], https://www.nature.com/articles/s41598-020-73796-5.

[22] D. Bikard, C.W. Euler, W. Jiang, P.M. Nussenzweig, G.W. Goldberg, X. Duportet, et al., Exploiting CRISPR-Cas nucleases to produce sequence-specific antimicrobials, Nat Biotechnol 32 (11) (2014 Nov 5) 1146–1150. Available from: https://www.nature.com/articles/nbt.3043.

[23] H.F. Hetta, Y.N. Ramadan, A.I.A. Al-Harbi, E. Ahmed, B. Battah, N.H. Abd Ellah, et al., Nanotechnology as a promising approach to combat multidrug resistant bacteria: a comprehensive review and future perspectives, Biomedicines 11 (2) (2023 Jan 31) 413 [Internet], https://www.mdpi.com/2227-9059/11/2/413.

[24] M. Kumar, A. Curtis, C. Hoskins, Application of nanoparticle technologies in the combat against anti-microbial resistance, Pharmaceutics 10 (1) (2018 Jan 14) 11 [Internet], https://www.mdpi.com/1999-4923/10/1/11.

[25] S. Zaidi, L. Misba, A.U. Khan, Nano-therapeutics: a revolution in infection control in post antibiotic era, Nanomed. Nanotechnol. Biol. Med. 13 (7) (2017 Oct) 2281–2301. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1549963417301235.

[26] E. Fazio, B. Gökce, A. De Giacomo, M. Meneghetti, G. Compagnini, M. Tommasini, et al., Nanoparticles engineering by pulsed laser ablation in liquids: concepts and applications, Nanomaterials 10 (11) (2020 Nov 23) 2317 [Internet], https://www.mdpi.com/2079-4991/10/11/2317.

[27] R. Abbasi, G. Shineh, M. Mobaraki, S. Doughty, L. Tayebi, Structural parameters of nanoparticles affecting their toxicity for biomedical applications: a review, J. Nanoparticle Res. 25 (3) (2023 Mar 27) 43. Available from: https://link.springer.com/10.1007/s11051-023-05690-w.

[28] U.O. Aigbe, O.A. Osibote, Green synthesis of metal oxide nanoparticles, and their various applications, J. Hazard Mater. Adv. 13 (2024 Feb) 100401 [Internet], https://linkinghub.elsevier.com/retrieve/pii/S2772416624000020.

[29] A. Safari, P. Rafie, S. Taeb, M. Najafi, S.M. Mortazavi, Development of lead-free materials for radiation shielding in medical settings: a review, J. Biomed. Phys. Eng. 14 (3) (2024 Jun 1) 229.

[30] D.M. AlQurashi, T.F. AlQurashi, R.I. Alam, S. Shaikh, M.A.M. Tarkistani, Advanced nanoparticles in combating antibiotic resistance: current innovations and future directions, J. Nanotheranostics 6 (2) (2025 Mar 23) 9. Available from: https://www.mdpi.com/2624-845X/6/2/9.

[31] M.K. Peiris, C.P. Gunasekara, P.M. Jayaweera, N.D. Arachchi, N. Fernando, Biosynth. Silver Nanoparticle: are they effective antimicrobials? Mem Inst Oswaldo Cruz 112 (8) (2017 Aug) 537–543. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0074-02762017000800537&lng=en&tlng=en.

[32] P. Szczyglewska, A. Feliczak-Guzik, I. Nowak, Nanotechnology–general aspects: a chemical reduction approach to the synthesis of nanoparticles, Molecules 28 (13) (2023 Jun 22) 4932 [Internet], https://www.mdpi.com/1420-3049/28/13/4932.

[33] O. Lebedeva, D. Kultin, L. Kustov, Electrochemical synthesis of unique nanomaterials in ionic liquids, Nanomaterials 11 (12) (2021 Dec 1) 3270 [Internet], https://www.mdpi.com/2079-4991/11/12/3270.

[34] P.R. More, S. Pandit, A De Filippis, G. Franci, I. Mijakovic, M. Galdiero, Silver nanoparticles: bactericidal and mechanistic approach against drug resistant pathogens, Microorganisms 11 (2) (2023 Feb 1) 369 [Internet], https://www.mdpi.com/2076-2607/11/2/369.

[35] E. Matei, A.A. Ștăulean, M. Râpă, A. Constandache, A.M. Predescu, G. Coman, et al., ZnO nanostructured matrix as nexus catalysts for the removal of emerging pollutants, Environ Sci Pollut Res 30 (54) (2023 Nov 3) 114779–114821. Available from: https://link.springer.com/10.1007/s11356-023-30713-3.

[36] N. Jara, N.S. Milán, A. Rahman, L. Mouheb, D.C. Boffito, C. Jeffryes, et al., Photochemical synthesis of gold and silver nanoparticles—a review, Molecules 26 (15) (2021 Jul 29) 4585. Available from: https://www.mdpi.com/1420-3049/26/15/4585.

[37] A. Zuhrotun, D.J. Oktaviani, A.N. Hasanah, Biosynthesis of gold and silver nanoparticles using phytochemical compounds, Molecules 28 (7) (2023 Apr 5) 3240 [Internet], https://www.mdpi.com/1420-3049/28/7/3240.

[38] G. Muteeb, M.T. Rehman, M. Shahwan, M. Aatif, Origin of antibiotics and antibiotic resistance, and their impacts on drug development: a narrative review, Pharmaceuticals 16 (11) (2023 Nov 15) 1615. https://www.mdpi.com/1424-8247/16/11/1615.

[39] Cristea, A.G. Hohotă, E.L. Lisă, Iacob, S. Ciobotaru, I. Dragostin, C.S. Ștefan, I. Fulga, et al., Antimicrobial smart dressings for combating antibiotic resistance in wound care, Pharmaceuticals 18 (6) (2025 May 30) 825 [Internet], https://www.mdpi.com/1424-8247/18/6/825.

[40] S. kazemi, A. Hosseingholian, S.D. Gohari, F. Feirahi, F. Moammeri, G. Mesbahian, et al., Recent advances in green synthesized nanoparticles: from

production to application, Mater. Today Sustain. 24 (2023 Dec) 100500. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2589234723001860.
[41] Y.G. Yuan, Q.L. Peng, S. Gurunathan, Effects of silver nanoparticles on multiple drug-resistant strains of Staphylococcus aureus and Pseudomonas aeruginosa from mastitis-infected goats: an alternative approach for antimicrobial therapy, Int. J. Mol. Sci. 18 (3) (2017 Mar 6) 569. Available from: https://www.mdpi.com/1422-0067/18/3/569.
[42] X. Liu, J. Li, Y. Qiao, H. Zhu, F. Meng, Existence, release, and antibacterial actions of silver nanoparticles on Ag& ndash;PIII TiO2 films with different nanotopographies, Int. J. Nanomed. 3389 (2014 Jul). Available from: http://www.dovepress.com/existence-release-and-antibacterial-actions-of-silver-nanoparticles-on-peer-reviewed-article-IJN.
[43] A.K. Chatterjee, R. Chakraborty, T. Basu, Mechanism of antibacterial activity of copper nanoparticles, Nanotechnology 25 (13) (2014 Apr 4) 135101. Available from: https://iopscience.iop.org/article/10.1088/0957-4484/25/13/135101.
[44] B. Qu, Z. Xiao, Y. Luo, Sustainable nanotechnology for food preservation: synthesis, mechanisms, and applications of zinc oxide nanoparticles, J. Agric. Food Res. 19 (2025 Mar) 101743. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2666154325001140.
[45] D.A. Serov, A.V. Gritsaeva, F.M. Yanbaev, A.V. Simakin, S.V. Gudkov, Review of antimicrobial properties of titanium dioxide nanoparticles, Int J Mol Sci 25 (19) (2024 Sep 29) 10519 [Internet], https://www.mdpi.com/1422-0067/25/19/10519.
[46] J. Lan, J. Zou, H. Xin, J. Sun, T. Han, M. Sun, et al., Nanomedicines as disruptors or inhibitors of biofilms: opportunities in addressing antimicrobial resistance, J Contr Release 381 (2025 May) 113589 [Internet], https://linkinghub.elsevier.com/retrieve/pii/S0168365925001981.
[47] H. Park, T.V. Patil, C. Mo, K.T. Lim, Nanodiamond: a multifaceted exploration of electrospun nanofibers for antibacterial and wound healing applications, J Nanobiotechnol 23 (1) (2025 Apr 9) 285 [Internet], https://jnanobiotechnology.biomedcentral.com/articles/10.1186/s12951-025-03351-9.
[48] L. Eltaib, Polymeric nanoparticles in targeted drug delivery: unveiling the impact of polymer characterization and fabrication, Polymers 17 (7) (2025 Mar 21) 833. Available from: https://www.mdpi.com/2073-4360/17/7/833.
[49] H.O. Alsaab, F.D. Alharbi, A.S. Alhibs, N.B. Alanazi, B.Y. Alshehri, M.A. Saleh, et al., PLGA-based nanomedicine: history of advancement and development in clinical applications of multiple diseases, Pharmaceutics 14 (12) (2022 Dec 6) 2728 [Internet], https://www.mdpi.com/1999-4923/14/12/2728.
[50] S. Kumar, R.P. Mahato, S. Ch, S. Kumbham, Current strategies against multidrug-resistant Staphylococcus aureus and advances toward future therapy, Microbe 6 (2025 Mar) 100281. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2950194625000494.
[51] C.K. Ezeh, M.E.U. Dibua, Anti-biofilm, drug delivery and cytotoxicity properties of dendrimers, ADMET DMPK [Internet] (2024 Feb 14). Available from: https://pub.iapchem.org/ojs/index.php/admet/article/view/1917.
[52] Sambhakar S. Preeti, R. Malik, S. Bhatia, A. Al Harrasi, C. Rani, et al., Nanoemulsion: an emerging novel technology for improving the bioavailability of drugs, in: P.K. Bolla (Ed.), Scientifica (cairo) [Internet], 2023 Oct 28;2023, pp. 1–25. Available from: https://www.hindawi.com/journals/scientifica/2023/6640103/.
[53] D. Sharma, S. Gautam, S. Singh, N. Srivastava, A.M. Khan, D. Bisht, Unveiling the nanoworld of antimicrobial resistance: integrating nature and nanotechnology, Front Microbiol. (2025 Jan 9) 15. Available from: https://www.frontiersin.org/articles/10.3389/fmicb.2024.1391345/full.
[54] A. Subramanian, Emerging roles of bacteriophage-based therapeutics in combating antibiotic resistance, Front Microbiol. 15 (2024 Jul 5). Available from: https://www.frontiersin.org/articles/10.3389/fmicb.2024.1384164/full.
[55] A.C. Rios, C.G. Moutinho, F.C. Pinto, F.S. Del Fiol, A. Jozala, M.V. Chaud, et al., Alternatives to overcoming bacterial resistances: state-of-the-art, Microbiol. Res. 191 (2016 Oct) 51–80. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0944501316301574.
[56] L.K. Harada, E.C. Silva, W.F. Campos, F.S. Del Fiol, M. Vila, K. Dąbrowska, et al., Biotechnological applications of bacteriophages: state of the art, Microbiol. Res. 212–213 (2018 Jul) 38–58. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0944501318301332.
[57] A.C. Rios, M.M.D.C. Vila, R. Lima, F.S. Del Fiol, M. Tubino, J.A. Teixeira, et al., Structural and functional stabilization of bacteriophage particles within the aqueous core of a W/O/W multiple emulsion: a potential biotherapeutic system for the inhalational treatment of bacterial pneumonia, Proc. Biochem. 64 (2018 Jan) 177–192. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1359511317310954.
[58] L. Cui, S. Watanabe, K. Miyanaga, K. Kiga, T. Sasahara, Y. Aiba, et al., A comprehensive review on phage therapy and phage-based drug development, Antibiotics 13 (9) (2024 Sep 11) 870 [Internet], https://www.mdpi.com/2079-6382/13/9/870.
[59] Q.Y. Zhang, Z.B. Yan, Y.M. Meng, X.Y. Hong, G. Shao, J.J. Ma, et al., Antimicrobial peptides: mechanism of action, activity and clinical potential, Mil. Med. Res. 8 (1) (2021 Sep 9) 48. Available from: https://mmrjournal.biomedcentral.com/articles/10.1186/s40779-021-00343-2.
[60] W.H. Kim, H.S. Lillehoj, W. Min, Evaluation of the immunomodulatory activity of the chicken NK-Lysin-Derived peptide cNK-2, Sci Rep 7 (1) (2017 Mar 23) 45099 [Internet], https://www.nature.com/articles/srep45099.
[61] L. Tajer, J.C. Paillart, H. Dib, J.M. Sabatier, Z. Fajloun, Z. Abi Khattar, Molecular mechanisms of bacterial resistance to antimicrobial peptides in the modern era: an updated review, Microorganisms 12 (7) (2024 Jun 21) 1259 [Internet], https://www.mdpi.com/2076-2607/12/7/1259.
[62] E.F. Haney, S.C. Mansour, R.E.W. Hancock, Antimicrobial peptides: an introduction, 2017, pp. 3–22. Available from: http://link.springer.com/10.1007/978-1-4939-6737-7_1.
[63] M. Yasir, M.D.P. Willcox, D. Dutta, Action of antimicrobial peptides against bacterial biofilms, Materials 11 (12) (2018 Dec 5) 2468. Available from: https://www.mdpi.com/1996-1944/11/12/2468.
[64] A. Cesaro, S.C. Hoffman, P. Das, C. de la Fuente-Nunez, Challenges and applications of artificial intelligence in infectious diseases and antimicrobial resistance, Npj Antimicrob. Resist. 3 (1) (2025 Jan 7) 2. Available from: https://www.nature.com/articles/s44259-024-00068-x.
[65] T. Lluka, J.M. Stokes, Antibiotic discovery in the artificial intelligence era, Ann N Y Acad Sci 1519 (1) (2023 Jan 29) 74–93 [Internet], https://nyaspubs.onlinelibrary.wiley.com/doi/10.1111/nyas.14930.
[66] K.K. Mak, M.R. Pichika, Artificial intelligence in drug development: present status and future prospects, Drug Disscov. Today 24 (3) (2019 Mar) 773–780. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1359644618300916.
[67] F. Pennisi, A. Pinto, G.E. Ricciardi, C. Signorelli, V. Gianfredi, The role of artificial intelligence and machine learning models in antimicrobial stewardship in public health: a narrative review, Antibiotics [Internet] 14 (2) (2025 Jan 30) 134. Available from: https://www.mdpi.com/2079-6382/14/2/134.
[68] S.A. Alowais, S.S. Alghamdi, N. Alsuhebany, T. Alqahtani, A.I. Alshaya, S. N. Almohareb, et al., Revolutionizing healthcare: the role of artificial intelligence in clinical practice, BMC Med. Educat. 23 (1) (2023 Sep 22) 689. Available from: https://bmcmededuc.biomedcentral.com/articles/10.1186/s12909-023-04698-z.
[69] T. Ali, S. Ahmed, M. Aslam, Artificial intelligence for antimicrobial resistance prediction: challenges and opportunities towards practical implementation, Antibiotics [Internet] 12 (3) (2023 Mar 6) 523. Available from: https://www.mdpi.com/2079-6382/12/3/523.
[70] C.K. Corbin, L. Sung, A. Chattopadhyay, M. Noshad, A. Chang, S. Deresinksi, et al., Personalized antibiograms for machine learning driven antibiotic selection, Commun Med 2 (1) (2022 Apr 8) 38 [Internet], https://www.nature.com/articles/s43856-022-00094-8.
[71] P. Mengsiri, R. Ungcharoen, S. Gertphol, A machine learning and neural network approach for classifying multidrug-resistant bacterial infections, Health Anal. 7 (2025 Jun) 100388 [Internet], https://linkinghub.elsevier.com/retrieve/pii/S2772442525000073.
[72] D. Danko, D. Bezdan, E.E. Afshin, S. Ahsanuddin, C. Bhattacharya, D.J. Butler, et al., A global metagenomic map of urban microbiomes and antimicrobial resistance, Cell 184 (13) (2021 Jun) 3376–3393.e17 [Internet], https://linkinghub.elsevier.com/retrieve/pii/S0092867421005857.
[73] A. Saffari Natanzi, M. Poudineh, E. Karimi, A. Khaledi, H. Haddad Kashani, Innovative approaches to combat antibiotic resistance: integrating CRISPR/Cas9 and nanoparticles against biofilm-driven infections, BMC Med. 23 (1) (2025 Aug 20) 486. Available from: https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-025-04323-4.
[74] L. Narendrakumar, M. Chakraborty, S. Kumari, D. Paul, B. Das, β-Lactam potentiators to re-sensitize resistant pathogens: discovery, development, clinical use and the way forward, Front Microbiol. 13 (2023 Mar 10). Available from: https://www.frontiersin.org/articles/10.3389/fmicb.2022.1092556/full.
[75] Y.S. Huang, H. Zhou, Breakthrough advances in beta-lactamase inhibitors: new synthesized compounds and mechanisms of action against drug-resistant bacteria, Pharmaceuticals 18 (2) (2025 Feb 3) 206 [Internet], https://www.mdpi.com/1424-8247/18/2/206.
[76] S.Y. Liu, S.H. Chou, C. Chuang, C.H. Juan, Y.C. Ho, H.L. Ho, et al., Clinical and Microbiological characteristics of patients with ceftazidime/avibactam-resistant Klebsiella pneumoniae carbapenemase (KPC)-producing K. pneumoniae strains, Ann Clin Microbiol Antimicrob 24 (1) (2025 Apr 18) 26 [Internet], https://ann-clinmicrob.biomedcentral.com/articles/10.1186/s12941-025-00797-5.
[77] P. Omosigho, K.R. Odede, O.J. Okesanya, Prevalence, antimicrobial susceptibility, and phenotypic identification of ESBL and carbapenemase-producing Escherichia coli from isolates of patients attending Edo Specialist Hospital, Nigeria, Microbes Infect. Dis. (2024 Nov 9) [cited 2025 Sep 5]; Available from: https://mid.journals.ekb.eg/article_391084.html.
[78] N. Morales-Durán, A. León-Buitimea, J.R. Morones-Ramírez, Unraveling resistance mechanisms in combination therapy: a comprehensive review of recent advances and future directions, Heliyon [Internet] 10 (6) (2024 Mar) e27984. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2405844024040155.
[79] I. Gajic, N. Tomic, B. Lukovic, M. Jovicevic, D. Kekic, M. Petrovic, et al., A comprehensive overview of antibacterial agents for combating multidrug-resistant bacteria: the current landscape, Dev. Future Oppot. Chall. Antibiotics 14 (3) (2025 Feb 21) 221. Available from: https://www.mdpi.com/2079-6382/14/3/221.
[80] M.E. Pachón-Ibáñez, G. Labrador-Herrera, T. Cebrero-Cangueiro, C. Díaz, Y. Smani, J.P. del Palacio, et al., Efficacy of colistin and its combination with rifampin in vitro and in experimental models of infection caused by carbapenemase-producing clinical isolates of Klebsiella pneumoniae, Front Microbiol. 9 (2018 May 15). Available from: http://journal.frontiersin.org/article/10.3389/fmicb.2018.00912/full.
[81] A.M.B. Amorim, L.F. Piochi, A.T. Gaspar, A.J. Preto, N. Rosário-Ferreira, I. S. Moreira, Advancing drug safety in drug development: bridging computational predictions for enhanced toxicity prediction, Chem. Res. Toxicol. 37 (6) (2024

Jun 17) 827–849. Available from: https://pubs.acs.org/doi/10.1021/acs.chemrestox.3c00352.
[82] S. Buchhorn de Freitas, D.D. Hartwig, Promising targets for immunotherapeutic approaches against Acinetobacter baumannii, Microb. Pathog. 173 (2022 Dec) 105855. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0882401022004685.
[83] D.R. Giacobbe, S. Dettori, S. Di Bella, A. Vena, G. Granata, R. Luzzati, et al., Bezlotoxumab for preventing recurrent Clostridioides difficile infection: a narrative review from pathophysiology to clinical studies, Infect Dis. Ther. 9 (3) (2020 Sep 6) 481–494. Available from: https://link.springer.com/10.1007/s40121-020-00314-5.
[84] Coyne AJ. Kunz, A. El Ghali, D. Holger, N. Rebold, M.J. Rybak, Therapeutic strategies for emerging multidrug-resistant Pseudomonas aeruginosa, Infect Dis. Ther. 11 (2) (2022 Apr 12) 661–682. Available from: https://link.springer.com/10.1007/s40121-022-00591-2.
[85] D. Liu, L. Liu, X. Zhao, X. Zhang, X. Chen, X. Che, et al., A comprehensive review on targeting diverse immune cells for anticancer therapy: beyond immune checkpoint inhibitors, Crit. Rev. Oncol. Hematol. 210 (2025 Jun) 104702. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1040842825000903.
[86] K.U. Jansen, W.C. Gruber, R. Simon, J. Wassil, A.S. Anderson, The impact of human vaccines on bacterial antimicrobial resistance. A review, Environ. Chem. Lett. 19 (6) (2021 Dec 29) 4031–4062. Available from: https://link.springer.com/10.1007/s10311-021-01274-z.
[87] M. Hasso-Agopsowicz, E. Sparrow, A.M. Cameron, H. Sati, P. Srikantiah, S. Gottlieb, et al., The role of vaccines in reducing antimicrobial resistance: a review of potential impact of vaccines on AMR and insights across 16 vaccines and pathogens, Vaccine 42 (19) (2024 Jul) S1–S8 [Internet], https://linkinghub.elsevier.com/retrieve/pii/S0264410X24006765.
[88] R.B. Kennedy, I.G. Ovsyannikova, P. Palese, G.A. Poland, Current challenges in vaccinology, Front. Immunol. 11 (2020 Jun 25). Available from: https://www.frontiersin.org/article/10.3389/fimmu.2020.01181/full.
[89] K.U. Jansen, A.S. Anderson, The role of vaccines in fighting antimicrobial resistance (AMR), Hum Vaccines Immunother 14 (9) (2018 Sep 2) 2142–2149 [Internet], https://www.tandfonline.com/doi/full/10.1080/21645515.2018.1476814.
[90] J. Liao, X. Zhang, X. Zeng, Z. Zhao, T. Sun, Z. Xia, et al., A rational designed multi-epitope vaccine elicited robust protective efficacy against Klebsiella pneumoniae lung infection, Biomed. Pharmaco. 174 (2024 May) 116611. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0753332224004955.
[91] T. Khare, U. Anand, A. Dey, Y.G. Assaraf, Z.S. Chen, Z. Liu, et al., Exploring phytochemicals for combating antibiotic resistance in microbial pathogens, Front Pharmacol 12 (2021 Jul 21) [Internet], https://www.frontiersin.org/articles/10.3389/fphar.2021.720726/full.
[92] N. Vaou, C. Voidarou, Chrysa, G. Rozos, C. Saldari, E. Stavropoulou, G. Vrioni, et al., Unraveling nature's pharmacy: transforming medicinal plants into modern therapeutic agents, Pharmaceutics 17 (6) (2025 Jun 7) 754 [Internet], https://www.mdpi.com/1999-4923/17/6/754.
[93] Zhou R. Afrasiyab, K. Raziq, T. Xue, D. Sun, Photodynamic antibacterial therapy by metal complex mediators: a new promise for eliminating drug-Resistant infectious microorganisms, Inorganica. Chim. Acta. 587 (2025 Nov) 122818. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0020169325002841.
[94] N. Suresh, B. Joseph, P. Sathyan, V.K. Sweety, T. Waltimo, S. Anil, Photodynamic therapy: an emerging therapeutic modality in dentistry, Bioor.g Med. Chem. 114 (2024 Nov) 117962. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0968089624003766.
[95] J. Kwak-Kim, C.C. Maier, C.M. Villano, C.J. Bowman, F.R. Brennan, D. Stanislaus, et al., Assessing the impact and risk of immunomodulatory compounds on pregnancy, J. Reprod. Immunol. 169 (2025 Jun) 104453. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0165037825000312.
[96] N.K. Bhol, M.M. Bhanjadeo, A.K. Singh, U.C. Dash, R.R. Ojha, S. Majhi, et al., The interplay between cytokines, inflammation, and antioxidants: mechanistic insights and therapeutic potentials of various antioxidants and anti-cytokine compounds, Biomed. Pharmaco. 178 (2024 Sep) 117177. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0753332224010618.
[97] O.A. Petrariu, I.C. Barbu, A.G. Niculescu, M. Constantin, G.A. Grigore, R. E. Cristian, et al., Role of probiotics in managing various human diseases, from oral pathology to cancer and gastrointestinal diseases, Front Microbiol. 14 (2024 Jan 5). Available from: https://www.frontiersin.org/articles/10.3389/fmicb.2023.1296447/full.
[98] S. Yang, J. Qiao, M. Zhang, L.Y. Kwok, B.B. Matijašić, H. Zhang, et al., Prevention and treatment of antibiotics-associated adverse effects through the use of probiotics: a review, J. Adv. Res. 71 (2025 May) 209–226. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2090123224002303.
[99] T.C.A. Hitch, L.J. Hall, S.K. Walsh, G.E. Leventhal, E. Slack, T. de Wouters, et al., Microbiome-based interventions to modulate gut ecology and the immune system, Mucosal. Immunol. 15 (6) (2022 Nov) 1095–1113. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1933021922017391.
[100] B. Sarita, D. Samadhan, M.Z. Hassan, E.G. Kovaleva, A comprehensive review of probiotics and human health-current prospective and applications, Front Microbiol. 15 (2025 Jan 6). Available from: https://www.frontiersin.org/articles/10.3389/fmicb.2024.1487641/full.
[101] S. Zhang, X. Liao, T. Ding, J. Ahn, Role of β-lactamase inhibitors as potentiators in antimicrobial chemotherapy targeting gram-negative bacteria, Antibiotics 13 (3) (2024 Mar 15) 260. Available from: https://www.mdpi.com/2079-6382/13/3/260.
[102] G. Muteeb, R.N.A. Kazi, M. Aatif, A. Azhar, M El Oirdi, M. Farhan, Antimicrobial resistance: linking molecular mechanisms to public health impact, vol. 33, SLAS Discov, 2025 Jun 100232 [Internet], https://linkinghub.elsevier.com/retrieve/pii/S2472555225000255.
[103] E.U. Alum, B.H. Gulumbe, S.C. Izah, D.E. Uti, P.M. Aja, I.O. Igwenyi, et al., Natural product-based inhibitors of quorum sensing: a novel approach to combat antibiotic resistance, Biochem. Biophys. Rep. 43 (2025 Sep) 102111 [Internet], https://linkinghub.elsevier.com/retrieve/pii/S2405580825001980.
[104] P. Chandrasekaran, S. Weiskirchen, R. Weiskirchen, Effects of probiotics on gut microbiota: an overview, Int. J. Mol. Sci. 25 (11) (2024 May 30) 6022. Available from: https://www.mdpi.com/1422-0067/25/11/6022.
[105] A.K. Surur, A.B. de Oliveira, S.R. De Annunzio, T.M. Ferrisse, C.R. Fontana, Bacterial resistance to antimicrobial photodynamic therapy: a critical update, J. Photochem. Photobiol. B Biol. 255 (2024 Jun) 112905. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1011134424000654.
[106] A. Jain, A. Singam, V.N.K.S. Mudiganti, Newer advancement in immunomodulatory therapy in sepsis: a comprehensive review, Cureus (2024 Mar 31) [cited 2025 Sep 5]; Available from: https://www.cureus.com/articles/241831-newer-advancement-in-immunomodulatory-therapy-in-sepsis-a-comprehensive-review.
[107] E. Anderson, B. Nair, V. Nizet, G. Kumar, Man vs microbes – the race of the century, J. Med. Microbiol. 72 (1) (2023 Jan 9). Available from: https://www.microbiologyresearch.org/content/journal/jmm/10.1099/jmm.0.001646.
[108] S. Sharma, J. Mohler, S.D. Mahajan, S.A. Schwartz, L. Bruggemann, R. Aalinkeel, Microbial biofilm: a review on formation, infection, antibiotic resistance, control measures, and innovative treatment, Microorganisms 11 (6) (2023 Jun 19) 1614 [Internet], https://www.mdpi.com/2076-2607/11/6/1614.
[109] N. Goel, M. Ghosh, D. Jain, R. Sinha, S.K. Khare, Inhibition and eradication of Pseudomonas aeruginosa biofilms by secondary metabolites of Nocardiopsis lucentensis EMB25, RSC Med. Chem. 14 (4) (2023) 745–756. Available from: https://xlink.rsc.org/?DOI=D2MD00439A.
[110] A. Dal, R. Hekimoğlu, B. Sümbül, F.B. Balıbey, Z.Ö. Gökçe, E. Akbulut, et al., Quorum-Sensing inhibition by furanone compounds and therapeutic effects on Pseudomonas aeruginosa keratitis rabbit model, BMC OPhthalmol. 25 (1) (2025 Apr 22) 231. Available from: https://bmcophthalmol.biomedcentral.com/articles/10.1186/s12886-025-04061-4.
[111] A. Nash, S. Aghlara-Fotovat, A. Hernandez, C. Scull, O. Veiseh, Clinical translation of immunomodulatory therapeutics, Adv. Drug Deliv. Rev. 176 (2021 Sep) 113896. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0169409X21002891.
[112] Y. Shindo, A.G. Fuchs, C.G. Davis, T. Eitas, J. Unsinger, C.A.D. Burnham, et al., Interleukin 7 immunotherapy improves host immunity and survival in a two-hit model of Pseudomonas aeruginosa pneumonia, J. Leukoc. Biol. 101 (2) (2017 Feb 1) 543–554. Available from: https://academic.oup.com/jleukbio/article/101/2/543/6932993.
[113] N. Weibel, M. Curcio, A. Schreiber, G. Arriaga, M. Mausy, J. Mehdy, et al., Engineering a novel probiotic toolkit in Escherichia coli nissle 1917 for sensing and mitigating gut inflammatory diseases, ACS SYnth. Biol. 13 (8) (2024 Aug 16) 2376–2390. Available from: https://pubs.acs.org/doi/10.1021/acssynbio.4c00036.
[114] D. Cocker, G. Birgand, N. Zhu, J. Rodriguez-Manzano, R. Ahmad, K. Jambo, et al., Healthcare as a driver, reservoir and amplifier of antimicrobial resistance: opportunities for interventions, Nat. Rev. Microbiol. 22 (10) (2024 Oct 24) 636–649. Available from: https://www.nature.com/articles/s41579-024-01076-4.
[115] S. Parmar, H. Kaur, J. Singh, A.S. Matharu, S. Ramakrishna, M. Bechelany, Recent advances in green synthesis of Ag NPs for extenuating antimicrobial resistance, Nanomaterials 12 (7) (2022 Mar 28) 1115 [Internet], https://www.mdpi.com/2079-4991/12/7/1115.
[116] A.M. Taxt, E. Avershina, S.A. Frye, U. Naseer, R. Ahmad, Rapid identification of pathogens, antibiotic resistance genes and plasmids in blood cultures by nanopore sequencing, Sci Rep 10 (1) (2020 May 6) 7622 [Internet], https://www.nature.com/articles/s41598-020-64616-x.
[117] B. Barsola, S. Saklani, D. Pathania, P. Kumari, S. Sonu, S. Rustagi, et al., Exploring bio-nanomaterials as antibiotic allies to combat antimicrobial resistance, Biofabrication 16 (4) (2024 Oct 1) 042007 [Internet], https://iopscience.iop.org/article/10.1088/1758-5090/ad6b45.
[118] C.L. Moo, S.K. Yang, K. Yusoff, M. Ajat, W. Thomas, A. Abushelaibi, et al., Mechanisms of antimicrobial resistance (AMR) and alternative approaches to overcome AMR, Curr Drug Discov Technol 17 (4) (2020 Sep 8) 430–447 [Internet], https://www.eurekaselect.com/170403/article.
[119] M. Petrillo, M. Fabbri, D.M. Kagkli, M. Querci, G. Van den Eede, E. Alm, et al., A roadmap for the generation of benchmarking resources for antimicrobial resistance detection using next generation sequencing, F1000Research 10 (2022 Mar 16) 80 [Internet], https://f1000research.com/articles/10-80/v2.
[120] A.R. Egorov, A.V. Kurliuk, V.V. Rubanik, A.A. Kirichuk, O. Khubiev, R. Golubev, et al., Chitosan-based ciprofloxacin extended release systems: combined synthetic and pharmacological (in vitro and in vivo) studies, Molecules [Internet] 27 (24) (2022 Dec 13) 8865. Available from: https://www.mdpi.com/1420-3049/27/24/8865.
[121] F.M. Mosallam, R. Elshimy, Eradication of Klebsiella pneumoniae pulmonary infection by silver oxytetracycline nano-structure, AMB Express 14 (1) (2024 May 29) 62 [Internet], https://amb-express.springeropen.com/articles/10.1186/s13568-024-01720-5.

[122] D. Góez, P. Soto, S. Latré, N. Gaviria, M. Camelo, A methodology to design quantized deep neural networks for automatic modulation recognition, Algorithms 15 (12) (2022 Nov 22) 441. Available from: https://www.mdpi.com/1999-4893/15/12/441.
[123] J. Payumo, E. Alocilja, C. Boodoo, K. Luchini-Colbry, P. Ruegg, E. McLamore, et al., Next generation of AMR network, Encyclopedia 1 (3) (2021 Aug 26) 871–892 [Internet], https://www.mdpi.com/2673-8392/1/3/67.
[124] F.B. Ayanoğlu, Bioethical issues in genome editing by CRISPR-Cas9 technology, Turkish J. Biol. 44 (2) (2020 Apr 2) 110–120. Available from: https://journals.tubitak.gov.tr/biology/vol44/iss2/6.
[125] K. Saeed, F. Ayub, M.A. Durrani, M. Mujahid, CRISPR Cas systems: from bacterial defense mechanisms to revolutionary tools reshaping genetic research and translation therapeutics, Microbe 7 (2025 Jun) 100344. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2950194625001128.
[126] W.Y. Belay, M. Getachew, B.A. Tegegne, Z.H. Teffera, A. Dagne, T.K. Zeleke, et al., Antimicrobial resistance with a focus on antibacterial, antifungal, antimalarial, and antiviral drugs resistance, its threat, global priority pathogens, prevention, and control strategies: a review, Ther. Adv. Infect. Dis. 12 (2025 May 23). Available from: https://journals.sagepub.com/doi/10.1177/20499361251340144.
[127] Z.K. Othman, M.M. Ahmed, Y.A. Adebisi, O.J. Okesanya, B.A. Oziama, S. G. Ezedigwe, et al., Leveraging artificial intelligence to combat antimicrobial resistance in geriatric care, Digit. Heal. 11 (2025 May 29). Available from: https://journals.sagepub.com/doi/10.1177/20552076251346612.
[128] H.M. Kajumbula, D.G. Amoako, S.K. Tessema, M.K. Aworh, F. Chikuse, I. N. Okeke, et al., Enhancing clinical microbiology for genomic surveillance of antimicrobial resistance implementation in Africa, Antimicrob Resist Infect Control 13 (1) (2024 Nov 13) 135 [Internet], https://aricjournal.biomedcentral.com/articles/10.1186/s13756-024-01472-8.
[129] B.M. Ukoaka, O.J. Okesanya, F.M. Daniel, M.M. Ahmed, N.G. Udam, P. M. Wagwula, et al., Updated WHO list of emerging pathogens for a potential future pandemic: implications for public health and global preparedness, Le Infez Med [Internet] 32 (4) (2024) 463–477. Available from: http://www.ncbi.nlm.nih.gov/pubmed/39660154.
[130] D. Nathwani, D. Varghese, J. Stephens, W. Ansari, S. Martin, C. Charbonneau, Value of hospital antimicrobial stewardship programs [ASPs]: a systematic review, Antimicrob Resist Infect Control 8 (1) (2019 Dec 12) 35 [Internet], https://aricjournal.biomedcentral.com/articles/10.1186/s13756-019-0471-0.
[131] S. Essack, J. Bell, A. Shephard, Community pharmacists—leaders for antibiotic stewardship in respiratory tract infection, J. Clin. Pharm. Ther. 43 (2) (2018 Apr 4) 302–307. Available from: https://onlinelibrary.wiley.com/doi/10.1111/jcpt.12650.
[132] A. Al Masud, R.L. Walpola, M. Sarker, A. Kabir, M. Asaduzzaman, M.S. Islam, et al., Assessing community antibiotic usage and adherence as per standard treatment guidelines: a potential area to enhance awareness at community pharmacy settings, Explor. Res. Clin. Soc. Pharm/ 17 (2025 Mar) 100552. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2667276624001495.
[133] N. Shamas, E. Stokle, D. Ashiru-Oredope, E. Wesangula, Challenges of implementing antimicrobial stewardship tools in low to middle income countries (LMICs), Infect. Prev. Pract. 5 (4) (2023 Dec) 100315. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2590088923000483.
[134] R. Rolfe, C. Kwobah, F. Muro, A. Ruwanpathirana, F. Lyamuya, C. Bodinayake, et al., Barriers to implementing antimicrobial stewardship programs in three low- and middle-income country tertiary care settings: findings from a multi-site qualitative study, Antimicrob Resist Infect Control 10 (1) (2021 Dec 25) 60 [Internet], https://aricjournal.biomedcentral.com/articles/10.1186/s13756-021-00929-4.
[135] I.O. Qoseem, O.J. Okesanya, N.O. Olaleke, B.M. Ukoaka, B.O. Amisu, J.B. Ogaya, et al., Digital health and health equity: how digital health can address healthcare disparities and improve access to quality care in Africa, Heal Promot. Perspect 14 (1) (2024 Mar 14) 3–8. Available from: https://hpp.tbzmed.ac.ir/Article/hpp-42822.
[136] A. Sharma, A. Singh, M.A. Dar, R.J. Kaur, J. Charan, K. Iskandar, et al., Menace of antimicrobial resistance in LMICs: current surveillance practices and control measures to tackle hostility, J. Infect. Public Health 15 (2) (2022 Feb) 172–181 [Internet], https://linkinghub.elsevier.com/retrieve/pii/S1876034121004251.
[137] C. Llor, R. Benkő, L. Bjerrum, Global restriction of the over-the-counter sale of antimicrobials: does it make sense? Front Public Health 12 (2024 Jul 3) [Internet], https://www.frontiersin.org/articles/10.3389/fpubh.2024.1412644/full.
[138] C. Manyi-Loh, S. Mamphweli, E. Meyer, A. Okoh, Antibiotic use in agriculture and its consequential resistance in environmental sources: potential public health implications, Molecules [Internet] 23 (4) (2018 Mar 30) 795. Available from: https://www.mdpi.com/1420-3049/23/4/795.
[139] M. Anderson, D. Panteli, R. van Kessel, G. Ljungqvist, F. Colombo, E. Mossialos, Challenges and opportunities for incentivising antibiotic research and development in Europe, Lancet Reg. Heal. Eur. 33 (2023 Oct) 100705. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2666776223001242.
[140] P. Mathew, S. Sivaraman, S. Chandy, Communication strategies for improving public awareness on appropriate antibiotic use: bridging a vital gap for action on antibiotic resistance, J. Fam. Med. Prim. Care 8 (6) (2019) 1867. Available from: https://journals.lww.com/10.4103/jfmpc.jfmpc_263_19.
[141] J.L. Cox, M.D. Simpson, Microbiology education and infection control competency: offering a new perspective, J. Microbiol. Biol. Educ. 19 (2) (2018 Jan). Available from: https://journals.asm.org/doi/10.1128/jmbe.v19i2.1475.
[142] J. Mitchell, P. Cooke, C. Ahorlu, A. Arjyal, S. Baral, L. Carter, et al., Community engagement: the key to tackling antimicrobial resistance (AMR) across a one health context? Glob Public Health 17 (11) (2022 Nov 2) 2647–2664 [Internet], https://www.tandfonline.com/doi/full/10.1080/17441692.2021.2003839.
[143] J. Mitchell, H. Hawkings, S. Latham, F. Fieroze, A. Arjyal, D.J. Barrington, et al., Addressing antimicrobial resistance through community engagement: a framework for developing contextually relevant and impactful behaviour change interventions, JAC-Antimicrobial. Resist. 5 (6) (2023 Nov 1) [Internet], https://academic.oup.com/jacamr/article/doi/10.1093/jacamr/dlad124/7449507.
[144] (WHO), WHO. Global action plan on antimicrobial resistance, 2015.
[145] S. Otake, T. Yamagishi, T. Shiomoto, M. Nakashita, H. Kurosu, C. Ikenoue, et al.. What we can and cannot see from the surveillance for drug-resistant Pseudomonas aeruginosa – findings from the evaluation of surveillance system for multidrug-resistant P. aeruginosa infections in Japan, 2024 [cited 2025 Sep 5]; Available from: https://www.researchsquare.com/article/rs-4695483/v1.
[146] R. Joppi, V. Bertele, T. Vannini, S. Garattini, R. Banzi, Food and Drug Administration vs European Medicines Agency: review times and clinical evidence on novel drugs at the time of approval, Br. J. Clin. Pharmacol. 86 (1) (2020 Jan 16) 170–174. Available from: https://bpspubs.onlinelibrary.wiley.com/doi/10.1111/bcp.14130.
[147] Hamburg MA, FDA's approach to regulation of products of nanotechnology, Science 336 (6079) (2012 Apr 20) 299–300 (80-) [Internet], https://www.science.org/doi/10.1126/science.1205441.
[148] United Nations, UN General Assembly's 2016 declaration on AMR [Internet], https://press.un.org/en/2016/ga11825.doc.htm, 2016.
[149] M. Miethke, M. Pieroni, T. Weber, M. Brönstrup, P. Hammann, L. Halby, et al., Towards the sustainable discovery and development of new antibiotics, Nat. Rev. Chem. 5 (10) (2021 Aug 19) 726–749. Available from: https://www.nature.com/articles/s41570-021-00313-1.
[150] V.L. Simpkin, M.J. Renwick, R. Kelly, E. Mossialos, Incentivising innovation in antibiotic drug discovery and development: progress, challenges and next steps, J Antibiot (Tokyo) 70 (12) (2017 Dec 1) 1087–1096 [Internet], https://www.nature.com/articles/ja2017124.
[151] P. Francine, Systems biology: new insight into antibiotic resistance, Microorganisms 10 (12) (2022 Nov 29) 2362 [Internet], https://www.mdpi.com/2076-2607/10/12/2362.
[152] P.A. Aboobacker, L. Ragunathan, T. Sanjeevi, A. Manoharan, A.C. Sasi, V. Chandran, et al., Synthetic biology's latest trends in antimicrobial resistance and biofilm, J. Pure Appl. Microbiol. 17 (1) (2023 Mar 5) 23–34. Available from: https://microbiologyjournal.org/synthetic-biologys-latest-trends-in-antimicrobial-resistance-and-biofilm/.
[153] Ejike Innocent Nwankwo, Ebube Victor Emeihe, Mojeed Dayo Ajegbile, Janet Aderonke Olaboye, Chukwudi Cosmos Maha, Innovative drug delivery methods for combating antimicrobial resistance, Int. Med. Sci. Res. J. 4 (8) (2024 Aug 23) 834–858. Available from: https://fepbl.com/index.php/imsrj/article/view/1454.
[154] G.K. Jena, C.N. Patra, S. Jammula, R. Rana, S. Chand, Artificial intelligence and machine learning implemented drug delivery systems: a paradigm shift in the pharmaceutical industry, J. Bio. X Res. 7 (2024 Jan 23). Available from: https://spj.science.org/doi/10.34133/jbioxresearch.0016.
[155] L.H. Goetz, N.J. Schork, Personalized medicine: motivation, challenges, and progress, Fertil Steril 109 (6) (2018 Jun) 952–963 [Internet], https://linkinghub.elsevier.com/retrieve/pii/S0015028218304072.
[156] Xiaoshu Guo, Precision medicine strategy based on microbiome, Life Stud. 1 (1) (2025 May 31) 87–103. Available from: https://ls.cscholar.com/article/view/45.
[157] P. Angelini, Plant-derived antimicrobials and their crucial role in combating antimicrobial resistance, Antibiotics [Internet] 13 (8) (2024 Aug 9) 746. Available from: https://www.mdpi.com/2079-6382/13/8/746.
[158] D. Bharathi, J. Lee, Recent advances in marine-derived compounds as potent antibacterial and antifungal agents: a comprehensive review, Mar. Drugs 22 (8) (2024 Jul 29) 348. Available from: https://www.mdpi.com/1660-3397/22/8/348.
[159] O. Fleitas Martínez, M.H. Cardoso, S.M. Ribeiro, O.L. Franco, Recent advances in anti-virulence therapeutic strategies with a focus on dismantling bacterial membrane microdomains, toxin neutralization, quorum-sensing interference and biofilm inhibition, Front Cell Infect. Microbiol. 9 (2019 Apr 2). Available from: https://www.frontiersin.org/article/10.3389/fcimb.2019.00074/full.
[160] D.A. Rasko, V. Sperandio, Anti-virulence strategies to combat bacteria-mediated disease, Nat. Rev. Drug Discov. 9 (2) (2010 Feb 18) 117–128. Available from: https://www.nature.com/articles/nrd3013.
[161] S. Hojda, M. Biegun-Żurowska, A. Skórkowska, K. Klesiewicz, M. Ziąbka, A weapon against implant-associated infections: antibacterial and antibiofilm potential of biomaterials with titanium nitride and titanium nitride-silver nanoparticle electrophoretic deposition coatings, Int. J. Mol. Sci. 26 (4) (2025 Feb 14) 1646. Available from: https://www.mdpi.com/1422-0067/26/4/1646.
[162] J. Sahoo, S. Sarkhel, N. Mukherjee, A. Jaiswal, Nanomaterial-based antimicrobial coating for biomedical implants: new age solution for biofilm-associated infections, ACS Omega 7 (50) (2022 Dec 20) 45962–45980. Available from: https://pubs.acs.org/doi/10.1021/acsomega.2c06211.
[163] A. Hoagland, S. Kipping, Challenges in promoting health equity and reducing disparities in access across new and established technologies, Can J Cardiol 40 (6) (2024 Jun) 1154–1167 [Internet], https://linkinghub.elsevier.com/retrieve/pii/S0828282X24001788.