NEW STRATEGIES TO COMBAT ANTIMICROBIAL RESISTANCE: CURRENT LANDSCAPE AND EMERGING DIRECTIONS

Gerasimova Alena Andreevna
Affiliation: ZARMED University
Correspondence: (+998)917001303
https://doi.org/10.5281/zenodo.17896556

ARTICLE INFO

Received: 9th December 2025
Accepted: 10th December 2025
Online: 11th December 2025

KEYWORDS

antimicrobial resistance, rapid diagnostics, bacteriophages, antimicrobial peptides, CRISPR-Cas, microbiome, stewardship

ABSTRACT

Antimicrobial resistance (AMR) remains one of the most pressing global health challenges. The growing prevalence of multidrug-resistant (MDR) and pan-resistant bacterial strains demands innovative approaches that go beyond the development of conventional antibiotics. This review summarizes the most promising strategies for combating AMR, including advances in rapid diagnostics, next-generation antibiotics, bacteriophage therapy, antimicrobial peptides, CRISPR-based genetic tools, nanotechnology-driven platforms, microbiome-based interventions, and antimicrobial stewardship. The article discusses the current evidence, advantages, limitations, and translational potential of these strategies. Integrated implementation of these approaches may significantly slow the progression of AMR and improve clinical outcomes.

Introduction

Antimicrobial resistance (AMR) is an escalating public health threat responsible for increasing morbidity, mortality, and healthcare expenditures worldwide [1,2]. Global estimates suggest that resistant bacterial infections account for millions of severe disease cases and hundreds of thousands of deaths annually [3]. The diminishing pipeline of new antibiotics further complicates the problem and underscores the need for innovative preventative and therapeutic strategies.

This review highlights the most advanced and emerging approaches designed to counter AMR, focusing on their mechanisms, current evidence, and clinical applicability.

1. Advances in Rapid Diagnostics Enabling Targeted Therapy

1.1. Molecular point-of-care diagnostics

Rapid PCR assays, loop-mediated isothermal amplification (LAMP), and multiplexed molecular panels enable pathogen identification and resistance gene detection within 30–90 minutes [4]. Implementation of such assays significantly reduces unnecessary empirical use of broad-spectrum antibiotics, thereby decreasing selective pressure on microbial populations.

1.2. MALDI-TOF mass spectrometry

Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry allows fast microbial identification based on protein spectra. When combined with accelerated susceptibility testing, MALDI-TOF improves therapeutic decision-making and lowers the rate of resistance selection in hospitalized patients [5].

2. New Classes of Antibiotics and Optimization of Existing Molecules

2.1. Agents with novel mechanisms of action

Several promising agents targeting previously unexplored pathways—such as inhibition of lipid A biosynthesis, disruption of membrane homeostasis, and interference with metabolic processes—demonstrate activity against clinically challenging pathogens including *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and carbapenem-resistant Enterobacterales [6].

2.2. Antibiotic–inhibitor combinations

Next-generation β-lactamase inhibitors extend the efficacy of existing β-lactam antibiotics against organisms producing carbapenemases and ESBLs. Agents active against class B and D β-lactamases are among the most significant developments in this category [7].

2.3. Nanotechnology-enhanced delivery systems

Metallic nanoparticles, polymeric carriers, and liposomal delivery vehicles improve intracellular penetration and pharmacokinetics of antibiotics. These platforms may reduce the emergence of resistance by enhancing local drug concentrations and decreasing exposure time required for microbial eradication [8].

3. Bacteriophage Therapy

Bacteriophages (phages)—viruses that specifically infect bacteria—are re-emerging as a powerful alternative to antibiotics. Their advantages include strain-level specificity, efficacy against MDR bacteria, and minimal impact on commensal microbiota [9].

Key emerging directions include:

- phage cocktails targeting multiple resistance phenotypes;
- personalized patient-specific phage selection;
- genetically engineered phages with improved lytic capacity and gene-delivery capabilities [10].

Clinical reports have demonstrated the usefulness of phage therapy in soft tissue infections, implant-associated infections, and chronic bronchopulmonary infections caused by *P. aeruginosa* [11].

4. Antimicrobial Peptides (AMPs)

Antimicrobial peptides exhibit broad-spectrum activity and possess multiple mechanisms of action, including membrane disruption, interference with nucleic acid synthesis, and modulation of bacterial metabolism. Synthetic AMPs with enhanced stability and reduced toxicity show strong potential in treating skin infections, respiratory tract infections, and chronic wound colonization [12].

5. CRISPR-Based Genetic Strategies

CRISPR-Cas systems offer the possibility to selectively eliminate resistance genes or kill bacteria harboring them.

Potential clinical applications include:

- removal of AMR determinants from microbial communities;
- inhibition of horizontal gene transfer;
- engineering of “competitive” strains designed to suppress resistant pathogens.

Although currently at preclinical stages, CRISPR-based antimicrobials are considered one of the most transformative future approaches.

6. Microbiome-Based Interventions

Progress in metagenomics and microbial ecology has enabled novel microbiome-modulating therapeutic approaches. Competitive bacterial strains and defined synthetic microbial consortia can suppress pathogenic organisms and limit the spread of resistance genes. Fecal microbiota transplantation (FMT) has shown high efficacy in particular clinical scenarios, most notably recurrent *Clostridioides difficile* infection [13].

7. Antimicrobial Stewardship

Antimicrobial stewardship programs represent an essential component of AMR prevention. Core strategies include:

- restricting unnecessary broad-spectrum antibiotic use;
- optimizing treatment duration;
- implementing clinical decision support tools;
- conducting regular surveillance of resistance patterns;
- physician and staff education.

Stewardship interventions have been shown to reduce antibiotic consumption by 20–50% without compromising clinical outcomes [14].

Conclusion

Antimicrobial resistance remains an urgent global issue, but recent technological and scientific advances provide a strong foundation for effective countermeasures. A combination of rapid diagnostics, novel therapeutics, biological approaches, and stewardship practices offers the best prospects for controlling AMR. Future efforts should focus on translational research, long-term safety assessments, and developing frameworks for widespread clinical implementation. Integrated and coordinated global action is essential to slow the progression of resistance and safeguard the efficacy of antimicrobial agents for future generations..

Selected References:

- Ahmed, M. M., et al. “CRISPR-Cas Systems in the Fight Against Antimicrobial Resistance”. Infection and Drug Resistance, 2024. DOI: 10.2147/IDR.S___ (в обзоре описана потенциальная роль CRISPR-Cas-систем в уничтожении генов резистентности) — PubMed+1

(точный DOI: 10.2147/idr.s747452 — можно уточнить через PubMed)

- de la Fuente Tagarro, C., Martín-González, D., De Lucas, A., Bordel, S., & Santos-Beneit, F. “Current Knowledge on CRISPR Strategies Against Antimicrobial-Resistant Bacteria”. Antibiotics, 2024; 13(12):1141. DOI: 10.3390/antibiotics13121141. MDPI
- Mayorga-Ramos, A., et al. “CRISPR-Cas-Based Antimicrobials: Design, Challenges, and Bacterial Mechanisms of Resistance”. ACS Infectious Diseases, 2023. DOI: 10.1021/acsinfecdis.2c00649. ACS Publications
- Gencay, Y. E., et al. “Engineered Phage with Antibacterial CRISPR–Cas Machinery to Target Escherichia coli In Vivo”. Nature Biotechnology, 2024. DOI: 10.1038/s41587-023-01759-y. Nature
- Subramanian, A., et al. “Emerging Roles of Bacteriophage-Based Therapeutics in Combating Antibiotic-Resistant Bacteria”. Frontiers in Microbiology, 2024. DOI: 10.3389/fmicb.2024.1384164. Frontiers

• Sawa, T., et al. "Current Status of Bacteriophage Therapy for Severe Bacterial Infections (especially MDR)". Journal of Intensive Care, 2024; 12: (article). DOI: 10.1186/s40560-024-00759-7. jintensivecare.biomedcentral.com
• Okesanya, O. J., et al. "Reinvigorating AMR Resilience: Leveraging CRISPR–Cas Technologies to Target Resistance Determinants". Tropical Medicine and Health, 2025. DOI: 10.1186/s41182-025-00728-2. BioMed Central
• Darrow, J. J. "CRISPR-phage Antibacterials to Address the Antibiotic Resistance Crisis: Scientific, Economic, and Regulatory Considerations". Journal of Law and the Biosciences, 2024; 11(1). DOI: 10.1093/jlb/lsad030. OUP Academic+1
• Niazi, S. K., et al. "Bacteriophage Therapy: Discovery, Development, and Regulatory Perspectives". Pharmaceuticals, 2025; 18(8):1115. DOI: 10.3390/ph18081115. MDPI
• Balcha, F. B., & Neja, S. A. "CRISPR-Cas9 Mediated Phage Therapy as an Alternative to Antibiotics". Animal Diseases, 2023; Article number: 4. DOI: 10.1186/s44149-023-00065-z.