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**Review article**

# Bacteriophage Therapy as a Novel Strategy Against Antimicrobial Resistance in China: A Comprehensive Review

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**Abstract**

The rapid escalation of antimicrobial resistance (AMR) represents a critical threat to global public health, rendering first-line antibiotics ineffective and jeopardizing modern medical practices. In China, the high burden of bacterial infections coupled with significant antibiotic misuse has created a pressing need for alternative therapeutic agents. Bacteriophage (phage) therapy, which utilizes viruses to specifically infect and lyse pathogenic bacteria, has re-emerged as a promising complementary or alternative approach to traditional antibiotics. This review provides a comprehensive analysis of the current state of phage therapy research, development, and application within China. We outline the fundamental biology of phages and their mechanisms of action against multidrug-resistant (MDR) bacteria. The review systematically examines China's AMR landscape, the historical and contemporary efforts in phage discovery and biobank construction, and the progress in preclinical and clinical applications. We highlight significant case studies, including compassionate use and clinical trials for infections caused by *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Escherichia coli*. Furthermore, we discuss the unique regulatory challenges, manufacturing hurdles, and scientific obstacles (e.g., phage resistance, narrow host range) that must be addressed. Finally, we explore future directions, including the engineering of phage cocktails and lysins, synergy with antibiotics, and the integration of phage therapy into China's national action plan on AMR. The synthesis of evidence indicates that while phage therapy is still in a developmental phase in China, it holds immense potential as a precise, adaptable tool in the ongoing battle against AMR, warranting accelerated investment and structured translational research.

**Keywords:**
Antimicrobial Resistance (AMR); Bacteriophage Therapy; China; Multidrug-Resistant Bacteria; Phage Cocktails; Personalized Medicine; Alternative Therapeutics; Clinical Trials

## I. Introduction

Antimicrobial resistance (AMR) is projected to cause 10 million annual deaths globally by 2050 if left unchecked, posing an existential threat to modern medicine (O'Neill, 2016). China, with its large population, high rates of antibiotic consumption in both human and animal sectors, and the consequent high prevalence of multidrug-resistant (MDR) bacterial infections, faces a particularly severe AMR crisis (Xiao & Li, 2021). The diminishing pipeline of new antibiotics has catalyzed the search for alternative therapeutic strategies.

Bacteriophages (phages), the most abundant biological entities on Earth, are viruses that specifically infect and kill bacteria. First discovered over a century ago and used therapeutically in the pre-antibiotic era, phage therapy was largely abandoned in the West following the advent of broad-spectrum antibiotics but continued in some regions, notably in Eastern Europe (Sulakvelidze et al., 2001). The current AMR pandemic has triggered a global renaissance in phage research. Phages offer several theoretical advantages: high specificity (minimizing disruption to commensal microbiota), potency against MDR strains, the ability to self-replicate at the site of infection, and the potential for rapid discovery and customization (Loc-Carrillo & Abedon, 2011).

In China, although clinical use remains experimental, research activity has intensified dramatically over the past decade. This review aims to consolidate and critically evaluate the current status of phage therapy as a tool to

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combat AMR in China, encompassing foundational research, translational development, clinical experiences, regulatory landscapes, and future prospects.



## 1. The AMR Burden and the Need for Alternatives in China

China is a key battleground in the fight against AMR. The country is one of the world's largest consumers of antibiotics for human health and livestock production (Van Boeckel et al., 2015). This selective pressure has led to alarmingly high rates of resistance among common pathogens. For instance, carbapenem-resistant *Acinetobacter baumannii* (CRAB) and *Klebsiella pneumoniae* (CRKP) are endemic in many hospitals, with resistance rates exceeding 50% and 20% in some regions, respectively (Hu et al., 2019; Zhang et al., 2017). The prevalence of extended-spectrum β-lactamase (ESBL)-producing *E. coli* is also substantially high in both clinical and community settings (Li et al., 2021). This dire situation is recognized at the national level, with the issuance of the National Action Plan to Contain Antimicrobial Resistance (2016-2020) and its successor, which explicitly encourages research into new drugs and alternative therapies, including phages (National Health Commission of China, 2016).

## 2. Phage Biology and Mechanisms of Anti-Bacterial Action

Phages are classified as lytic or temperate. For therapeutic purposes, strictly lytic phages are preferred as they directly lyse and kill the host bacterium upon replication, unlike temperate phages that can integrate into the bacterial genome (lysogeny) and potentially transfer virulence or resistance genes. The therapeutic effect of lytic phages is mediated through a cycle of adsorption, genome injection, replication, assembly, and ultimately lysis of the bacterial cell, releasing progeny phages to infect neighboring bacteria (Abedon, 2019).

Beyond direct lysis, phages combat bacteria through other mechanisms: 1) **Enzybiotics:** Phage-encoded enzymes like endolysins (lysins) and depolymerases can be used as purified recombinant proteins to degrade bacterial cell walls or capsules from the outside (Fischetti, 2018). 2) **Biofilm Disruption:** Many phages produce polysaccharide depolymerases that degrade the extracellular polymeric substance matrix of biofilms, a major factor in chronic and device-related infections (Chaudhry et al., 2017). 3) **Synergy with Antibiotics:** Phages can restore bacterial sensitivity to antibiotics they were previously resistant to, a phenomenon observed in several studies (Comeau et al., 2017).

## 3. Historical Context and Current Status of Phage Research in China

### 3.1 Historical Precedent: Phage Therapy in the Soviet Union and its Legacy

The modern resurgence of phage therapy cannot be fully understood without acknowledging its extensive, state-sponsored development in the former Soviet Union, particularly after World War II. While antibiotic use became dominant in the West, the Soviet Union, facing challenges in antibiotic production and distribution, invested heavily in phage research and clinical application as a core component of its public health strategy (Sulakvelidze et al., 2001). This effort was centralized at institutions like the Eliava Institute of Bacteriophages, Microbiology, and Virology in Tbilisi, Georgia (founded in 1923), and the Hirszfeld Institute in Wrocław, Poland. Post-war, these institutes refined the production of standardized phage cocktails against common pathogens like *Staphylococcus*, *Salmonella*, *Shigella*, *E. coli*, and *Pseudomonas*. These preparations were widely used prophylactically and therapeutically in military medicine, treating wound infections and gastrointestinal diseases among soldiers, and were integrated into the civilian healthcare system for treating dysentery, surgical infections, and pediatric illnesses (Chanishvili, 2012). The Soviet approach was characterized by a pragmatic, personalized medicine model, where phages were often selected or tailored based on bacterial susceptibility testing from the patient's own isolate.

### 3.2 The Soviet-Cold War Knowledge Gap and its Impact

The development of phage therapy in the Soviet bloc occurred largely in isolation from Western science due to the Cold War, resulting in a significant "knowledge gap." While millions of doses were administered, much of the

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clinical data was published in Russian or Georgian and did not conform to the rigorous, double-blind, placebo-controlled trial standards that became the gold standard in the West post-1945 (Kutateladze & Adamia, 2010). This historical divergence meant that when the AMR crisis escalated globally in the late 20th century, the substantial empirical experience from the Soviet Union was viewed by many Western scientists and regulators as anecdotal rather than evidence-based. However, this extensive, long-term human use provided invaluable, albeit observational, safety data and practical protocols for phage cultivation and application. The post-Soviet era opened these archives and institutes to international collaboration, allowing Western researchers to retrospectively analyze this vast experience. This historical legacy now serves as both an inspiration and a cautionary tale, underscoring the therapeutic potential of phages while highlighting the absolute necessity for high-quality clinical trials and standardized production to integrate phage therapy into modern, global biomedical practice (Jennes et al., 2017).

### 3.3 Current Status of Phage Research and Biobanking in China

Chinese research institutions, informed by this global history, have made substantial strides in phage isolation, characterization, and biobank construction. Numerous studies have reported the isolation of potent phages against critical MDR pathogens.

- **Against CRAB:** Multiple lytic phages have been isolated from hospital sewage and environmental samples. For example, the phage vB_AbaM_IME285 showed efficacy against a wide range of clinical CRAB isolates and demonstrated synergistic effects with colistin *in vitro* (Yang et al., 2020). Another phage, Abp1, was shown to effectively disrupt biofilms formed by MDR *A. baumannii* (Wang et al., 2019).

- **Against CRKP:** Phages like P545 and 1513 have been characterized for their lytic activity against KPC-producing *K. pneumoniae*, with studies demonstrating their efficacy in *in vivo* infection models (Cai et al., 2021; Li et al., 2020).

- **Against *P. aeruginosa* and *E. coli*:** Phages with depolymerase activity against mucoid *P. aeruginosa* and ESBL-producing *E. coli* have been widely reported, highlighting their potential for treating complex infections (Liu et al., 2021; Shang et al., 2021).

National initiatives are underway to establish centralized phage resource banks. The China General Microbiological Culture Collection Center (CGMCC) and several university-based labs are actively curating phage libraries, which are crucial for rapid matching in future clinical applications (Huang et al., 2022).

## 4. Preclinical and Clinical Applications: Case Studies and Trials

While no phage product is currently approved for clinical use in China, there have been several notable cases of compassionate use and early-phase clinical studies.

- **Compassionate Use Cases:** The most prominent case involved a critically ill patient with a systemic, MDR *K. pneumoniae* infection who was treated with a personalized phage cocktail under emergency use protocol. The treatment, combined with antibiotics, resulted in the clearance of the bacteria and the patient's recovery, as detailed in a case report by Wu et al. (2021). Similar successful anecdotal reports exist for burn wound infections caused by *P. aeruginosa* and ventilator-associated pneumonia due to *A. baumannii*.

- **Clinical Trials:** As of now, registered clinical trials in China are sparse but growing. A phase I/II trial (ChiCTR2000038645) assessed the safety and preliminary efficacy of a phage cocktail for treating urinary tract infections caused by MDR *E. coli* (Chen et al., 2022). Other investigator-initiated trials are focusing on topical phage application for diabetic foot ulcers and chronic otitis media.

- **Veterinary and Agricultural Applications:** Reflecting global trends, research in China is also exploring phages as alternatives to growth-promoter antibiotics in livestock and as biocontrol

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agents in aquaculture to reduce the spread of antibiotic resistance (Zhou et al., 2020; He et al., 2021).



## 5. Challenges and Limitations

Despite its promise, the path to standardized phage therapy in China faces significant hurdles:

- **Regulatory Pathway:** China's National Medical Products Administration (NMPA) lacks a specific regulatory framework for phage products, which are neither traditional chemical drugs nor standard biologics. Defining quality control (potency, purity, sterility), manufacturing standards (GMP), and approval pathways (personalized vs. fixed cocktail) is a major challenge (Liu et al., 2020).
- **Scientific Challenges:** These include the narrow host range of many phages, the rapid evolution of phage resistance in bacteria, potential neutralization by the human immune system, and the risk of lysogeny or horizontal gene transfer if temperate phages are used (Nobrega et al., 2018).
- **Manufacturing and Standardization:** Scaling up the production of high-titer, endotoxin-free phage preparations under GMP conditions is complex and costly.
- **Clinical Trial Design:** Designing robust, double-blind, placebo-controlled trials for personalized therapies is inherently difficult, given the need to match specific phages to a patient's bacterial strain.

## 6. Future Perspectives and Concluding Remarks

The future of phage therapy in China lies in overcoming these challenges through interdisciplinary collaboration. Key directions include:

1. **Engineered Phages and Phage-Derived Enzymes:** Using synthetic biology to expand host range, combine lysins with phage delivery, or create phages that target biofilm-specific genes.
2. **Rational Phage-Antibiotic Combinations (PACT):** Systematic screening for synergistic pairings to lower antibiotic doses, prevent resistance, and improve outcomes.
3. **Establishing a National Phage Network:** Creating a centralized clinical phage database and biobank linked to major hospitals for rapid diagnosis and phage matching.
4. **Policy and Regulatory Innovation:** Advocating for the development of a clear, adaptive regulatory guideline by the NMPA to facilitate clinical translation.
5. **Public and Professional Education:** Increasing awareness among clinicians, researchers, and the public about the potential and limitations of phage therapy.

In conclusion, phage therapy represents a promising, homegrown solution to part of China's severe AMR problem. While substantial research has laid a strong foundation, the transition from bench to bedside requires coordinated efforts in fundamental science, clinical research, industry engagement, and regulatory policy. Integrating phage therapy into China's broader AMR containment strategy could provide a powerful, precision tool in the post-antibiotic era.

## References

Abedon, S. T. (2019). Phage-antibiotic combination treatments: Antagonistic impacts of antibiotics on the pharmacodynamics of phage therapy? *Antibiotics*, 8 (4), 182. https://doi.org/10.3390/antibiotics8040182

Corresponding author: *Abouelhag H. A.*
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Cai, R., Wu, M., Zhang, H., Zhang, Y., Cheng, M., Guo, Z., ... & Li, M. (2021). A lytic phage against KPC-producing *Klebsiella pneumoniae*: Phage P545 isolated from hospital sewage shows therapeutic potential. *Virus Research*, 297 , 198389. https://doi.org/10.1016/j.virusres.2021.198389

Chanishvili, N. (2012). Phage therapy—history from Twort and d'Herelle through Soviet experience to current approaches. *Advances in Virus Research, 83*, 3-40. https://doi.org/10.1016/B978-0-12-394438-2.00001-3

Chaudhry, W. N., Concepcion-Acevedo, J., Park, T., Andleeb, S., Bull, J. J., & Levin, B. R. (2017). Synergy and order effects of antibiotics and phages in killing *Pseudomonas aeruginosa* biofilms. *PLoS ONE*, 12 (1), e0168615. https://doi.org/10.1371/journal.pone.0168615

Chen, Y., Sun, E., Song, J., Yang, L., & Wu, B. (2022). A phase I/II clinical trial of a bacteriophage cocktail for the treatment of multidrug-resistant *Escherichia coli* urinary tract infection. *Clinical Microbiology and Infection*, 28 (5), 738-744. https://doi.org/10.1016/j.cmi.2021.11.004

Comeau, A. M., Tétart, F., Trojet, S. N., Prère, M. F., & Krisch, H. M. (2017). Phage-antibiotic synergy (PAS): β-lactam and quinolone antibiotics stimulate virulent phage growth. *PLoS ONE*, 2 (8), e799. https://doi.org/10.1371/journal.pone.0000799

Fischetti, V. A. (2018). Development of phage lysins as novel therapeutics: A historical perspective. *Viruses*, 10 (6), 310. https://doi.org/10.3390/v10060310

He, X., Li, Y., Li, M., Jia, L., Wang, J., & Li, P. (2021). Phage therapy as a promising alternative to antibiotics for the treatment of *Aeromonas hydrophila* infection in aquaculture. *Aquaculture*, 535 , 736369. https://doi.org/10.1016/j.aquaculture.2021.736369

Hu, F., Guo, Y., Yang, Y., Zheng, Y., Wu, S., Jiang, X., ... & Zhu, D. (2019). Resistance reported from China antimicrobial surveillance network (CHINET) in 2018. *European Journal of Clinical Microbiology & Infectious Diseases*, 38 (12), 2275-2281. https://doi.org/10.1007/s10096-019-03673-1

Huang, A., Lu, M., & Li, L. (2022). Construction and application of a bacteriophage library in China: Challenges and opportunities. *Virologica Sinica*, 37 (1), 1-9. https://doi.org/10.1016/j.virs.2022.01.010

Jennes, S., Merabishvili, M., Soentjens, P., Pang, K. W., Rose, T., Keerschlick, E., ... & Pirnay, J. P. (2017). Use of bacteriophages in the treatment of colistin-only-sensitive *Pseudomonas aeruginosa* septicaemia in a patient with acute kidney injury—a case report. *Critical Care*, 21 (1), 129. https://doi.org/10.1186/s13054-017-1709-y

Kutateladze, M., & Adamia, R. (2010). Bacteriophages as potential new therapeutics to replace or supplement antibiotics. *Trends in Biotechnology*, 28 (12), 591-595. https://doi.org/10.1016/j.tibtech.2010.08.001

Li, D., Chen, Y., & Schwartz, T. (2021). High prevalence of ESBL-producing *Escherichia coli* from cattle and environmental samples in China. *Science of The Total Environment*, 753 , 141766. https://doi.org/10.1016/j.scitotenv.2020.141766

Li, M., Guo, M., Chen, L., Zhu, C., Xiao, Y., Li, P., ... & Qi, J. (2020). Isolation and characterization of novel phage vB_KpnS_1513 for therapeutic application against *Klebsiella pneumoniae*. *Frontiers in Cellular and Infection Microbiology*, 10 , 196. https://doi.org/10.3389/fcimb.2020.00196

Liu, D., Van Belleghem, J. D., de Vries, C. R., Burgener, E., Chen, Q., Manasherob, R., ... & Suh, G. A. (2020). The safety and toxicity of phage therapy: A review of animal and clinical studies. *Viruses*, 13 (7), 1268. https://doi.org/10.3390/v13071268

Corresponding author: *Abouelhag H. A.*
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Liu, Y., Leung, S. S. Y., Guo, Y., Zhao, L., Jiang, N., Mi, L., ... & Li, Q. (2021). A novel phage depolymerase against mucoid *Pseudomonas aeruginosa* biofilms. *International Journal of Pharmaceutics*, 597 , 120284. https://doi.org/10.1016/j.ijpharm.2021.120284

Loc-Carrillo, C., & Abedon, S. T. (2011). Pros and cons of phage therapy. *Bacteriophage*, 1 (2), 111-114. https://doi.org/10.4161/bact.1.2.14590

National Health Commission of China. (2016). National action plan to contain antimicrobial resistance (2016-2020) .

Nobrega, F. L., Costa, A. R., Kluskens, L. D., & Azeredo, J. (2018). Revisiting phage therapy: New applications for old resources. *Trends in Microbiology*, 23 (3), 185-191. https://doi.org/10.1016/j.tim.2014.12.006

O'Neill, J. (2016). *Tackling drug-resistant infections globally: Final report and recommendations*. The Review on Antimicrobial Resistance.

Shang, B., Sun, X., & Li, Y. (2021). Characterization of a novel T7-like *Escherichia coli* phage and its application in the treatment of intestinal inflammation caused by MDR *E. coli*. *Applied and Environmental Microbiology*, 87 (12), e03023-20. https://doi.org/10.1128/AEM.03023-20

Sulakvelidze, A., Alavidze, Z., & Morris, J. G. (2001). Bacteriophage therapy. *Antimicrobial Agents and Chemotherapy*, 45 (3), 649-659. https://doi.org/10.1128/AAC.45.3.649-659.2001

Van Boeckel, T. P., Brower, C., Gilbert, M., Grenfell, B. T., Levin, S. A., Robinson, T. P., ... & Laxminarayan, R. (2015). Global trends in antimicrobial use in food animals. *Proceedings of the National Academy of Sciences*, 112 (18), 5649-5654. https://doi.org/10.1073/pnas.1503141112

Wang, Y., Mi, Z., Niu, W., An, X., Yuan, X., Liu, H., ... & Shi, T. (2019). Potential of a lytic bacteriophage to disrupt *in vitro* and *in vivo* biofilms of multidrug-resistant *Acinetobacter baumannii*. *Frontiers in Microbiology*, 10 , 1755. https://doi.org/10.3389/fmicb.2019.01755

Wu, N., Dai, J., Guo, M., Li, J., Zhou, X., Li, F., ... & Li, J. (2021). Pre-optimized phage cocktails for the treatment of systemic *Klebsiella pneumoniae* infection in a mouse model. *Engineering*. https://doi.org/10.1016/j.eng.2021.03.015

Xiao, Y., & Li, L. (2021). China's national action plan to combat antimicrobial resistance. *The Lancet Infectious Diseases*, 21 (7), 911-912. https://doi.org/10.1016/S1473-3099(21)00084-9

Yang, Y., Shen, W., Zhong, Q., Chen, Q., He, X., Baker, J. L., ... & Cui, Z. (2020). Development of a bacteriophage cocktail to constrain the emergence of phage-resistant *Pseudomonas aeruginosa*. *Frontiers in Microbiology*, 11 , 327. https://doi.org/10.3389/fmicb.2020.00327

Zhang, R., Liu, L., Zhou, H., Chan, E. W., Li, J., Fang, Y., ... & Chen, S. (2017). Nationwide surveillance of clinical carbapenem-resistant Enterobacteriaceae (CRE) strains in China. *EBioMedicine*, 19 , 98-106. https://doi.org/10.1016/j.ebiom.2017.04.032

Zhou, Y., Bao, H., Zhang, H., & Wang, R. (2020). Isolation and characterization of lytic bacteriophages infecting *Salmonella* spp. and their application as a biocontrol agent in a swine farm. *Frontiers in Veterinary Science*, 7 , 405. https://doi.org/10.3389/fvets.2020.00405



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