ADVANCE SOCIAL SCIENCE ARCHIVE JOURNAL
Available Online: https://assajournal.com
Vol. 05 No. 02. April-June 2026.Page# 2436-2448
Print ISSN: 3006-2497 Online ISSN: 3006-2500
Platform & Workflow by: Open Journal Systems
https://doi.org/10.5281/zenodo.21130861

Bacteriophage Therapy as A Next-Generation Strategy to Combat Antimicrobial Resistance: Recent Advances and Future Perspectives

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ABSTRACT

Antimicrobial resistance (AMR) is one of the greatest public health problems in the world today and has become a major cause of concern due to its impact on the effectiveness of currently used antimicrobials and the burden of infectious diseases. Multidrug-resistant (MDR), extensively drug-resistant (XDR), and pan-drug-resistant bacterial pathogens are rapidly emerging and spreading and there is an urgent need for alternative therapeutic strategies to *combat them. Bacteriophage therapy is one of the most promising strategies, with the possibility of becoming a new generation of a solution against resistant bacterial infection. Bacteriophages, also known as phages, are viruses that infect and lyse bacterial cells, providing a specific and effective way of controlling bacteria. Phages show high host specificity, do not cause changes in beneficial microbiota and can disrupt bacterial biofilms without harming the phages. Molecular biology, genomics, synthetic biology and bioengineering have greatly improved the therapeutic utility of phages in recent years. Thanks to the development of Phage cocktails, genetically engineered Phages, Phage-derived enzymes and Phage-Antibiotic Combination therapies, the range of clinically relevant pathogens to which they are effective has increased to include members of the ESKAPE group. In addition, progress in genome sequencing and bioinformatics has created a speedy identification and characterization of new potential therapeutic phages. In the case of infections that are refractory or resistant to standard drug treatments, clinical trials and compassionate use cases have shown promising results. Although these are all positive steps, there are a number of challenges that remain in the way of clinical implementation of phage therapy. These include the poor specificity of phages, possible phage resistance, regulatory concerns, manufacturing standardisation concerns and lack of large-scale clinical trials. However, novel technologies like the use of engineered phages, artificial intelligence-driven phage discovery and personalized phage therapy are anticipated to overcome many of these. The review provides a summary of the recent progress, therapeutic applications, challenges and future perspectives on the use of bacteriophages as a sustainable and effective approach in combating the escalating global problem of antimicrobial resistance.*

Keywords: *Antimicrobial Resistance, Bacteriophage Therapy, Enzymes, Genomics, Regulatory Concerns, Artificial Intelligence-Driven*

Introduction

One of the greatest threats to public health in the twenty-first century is Antimicrobial Resistance (AMR) (Ferrara et al., 2024). The prevalence of the use of antibiotics in human medicine, veterinary medicine, agriculture and aquaculture has helped to drive the emergence of resistant bacterial strains that are not responsive to many of the common antimicrobial drugs (Hossain et al., 2022). This has made infections, that have been successfully treated in the past, much more difficult to control and has resulted in a greater number of people suffering from prolonged sickness, rising healthcare expenses, and worsening mortality rates (Hacker, 2024). World health bodies indicate that antimicrobial resistance can undermine decades of medical advances and is a grave concern for treating infectious diseases (Okeke et al., 2024). The proliferation of bacteria with multidrug resistance (MDR), extensively drug resistance (XDR), and pan-drug resistance (PDR) has further necessitated the need for novel therapeutic approaches that can overcome the resistance mechanisms of bacteria (Elshobary et al., 2025).Antibiotics were discovered, which has been a huge impact on modern medicine and drastically lowered the mortality rate for bacterial infections (Muteeb, Rehman, Shahwan, & Aatif, 2023). Yet, due to the amazing effectiveness of antibiotics, bacterial resistance has rapidly emerged (Tarin-Pello, Suay-Garcia, & Perez-Gracia, 2022). Bacteria have evolved a number of mechanisms to resist the action of antimicrobial drugs such as enzymatic inactivation of antibiotics, alteration of drug target, decrease in membrane permeability and active efflux (Zhang et al., 2024). In addition, biofilms form and enable bacterial communities to become more resistant to antimicrobial agents and host immune responses (Almatroudi, 2025).These resistant pathogens include Staphylococcus aureus, Pseudomonas aeruginosa, Acinetobacter baumannii, Klebsiella pneumoniae and Escherichia coli (E. coli). Due to the limited pipeline of new antibiotics and the slow rate of new antimicrobial drug development, other methods to treat bacterial infections are needed (Butler et al., 2022).

One of the potential future solutions that is emerging is bacteriophage therapy, which gets a lot of interest as a next generation antimicrobial therapy (Zalewska-Piątek, 2023). Bacteriophages, commonly known as phages, are viruses that specifically infect and kill bacteria (Kasman & Porter, 2022). They are ubiquitous organisms on earth and found in various environments such as the human microbiome, sewage, soil and water (Awari et al., 2023). In 1915, Frederick Twort and in 1917 Félix d'Hérelle independently found bacteriophages and began studying them as therapeutic agents for bacterial infections before the use of antibiotics became common (Marongiu, Burkard, Lauer, Hoelzle, & Venturelli, 2022). The use of phage therapy faded in many parts of the world, however, after the discovery of highly effective antibiotics in the mid-twentieth century. However, studies on phage therapy continued in other countries, including Georgia, Poland, and Russia, where phages were still an integral part of the treatment of infectious diseases (Summers, 2024).The global problem of antimicrobial resistance is a major reason for the renewed interest for bacteriophage therapy (No & Ekpunobi, 2025). Bacteriophages are highly specific to their target bacteria, which allows them to selectively attack pathogenic bacteria without harming beneficial microorganisms. Bacteriophages are different from broad-spectrum antibiotics because they are highly specific to their target bacteria, allowing them to target pathogenic bacteria while leaving beneficial microbiota unaffected (Soni, Sinha, & Pandey, 2024). This host specificity helps to prevent disruption of normal microbial populations and decreases incidence of secondary infections which can occur with antibiotic use. Moreover, the ability of bacteriophages to multiply at the infection site, provided that susceptible bacterial hosts are present, makes their natural multiplication in the site of infection possible, thus increasing the therapeutic concentration. These have an inherent ability to evolve in conjunction with bacterial populations and are self-amplifying, offering a significant advantage over traditional antimicrobials (Rugarabamu & Mwanyika, 2025).

The lytic cycle is the most important mechanism by which bacteriophages are effective at killing bacteria; in it, the phage binds to a receptor on the surface of the bacterial cell, injects its genetic material into the bacterial cell (Leprince & Mahillon, 2023), replicates and then lyses the bacterial cell to release progeny phages that can infect other nearby bacteria. This mechanism is important for the efficient elimination of bacteria and a possible approach to those infections caused by antibiotic-resistant bacteria. Some phages can also lyse the cell walls and biofilms of bacteria, as well as directly killing bacteria, and have been tested to be effective against a wide range of bacterial species and strains. The development of synthetic biology, genomics and molecular biology in recent years has also opened up the possibilities for phage therapy, as new possibilities can be created by engineering phages with more potent anti-bacterial properties (Zalewska-Piątek, 2023).In the last ten years, many preclinical and clinical trials have shown the efficacy of bacteriophage therapy for various types of multidrug-resistant bacterial infections (Aranaga, Pantoja, Martínez, & Falco, 2022). It is successfully applied in the treatment of chronic infections of the wounds, respiratory tract, urinary tract, gastrointestinal tract and infections of implants associated with biofilm. Furthermore, a synergy effect of phages in combination with conventional antibiotics has been reported, which enhances the elimination of bacteria and minimizes the possibility of emerging resistance. Recent developments in the formulation and delivery of phage cocktails and the introduction of tailored therapeutic applications against individual patients have further bolstered the promise of phages as therapeutic agents (Venkataraman, Shahgolzari, Yavari, & Hefferon, 2025).However, there are still some obstacles that need to be overcome for the increased use of bacteriophage therapy. However, the important obstacles include regulatory uncertainties, limitation of large-scale clinical trials, bacterial resistance to phages, and manufacturing standardization as well as concerns over pharmacokinetics and immune responses. These challenges must be met through joint efforts between researchers, health care providers, regulatory bodies and pharmaceutical companies. The future of phage-based therapeutics looks promising as continued developments in biotechnology, artificial intelligence, and precision medicine are anticipated to further catalyze the development and clinical application of these therapies (Fahim, Hasani, Kabba, & Ragab, 2025).The purpose of this review is to give a complete panorama of the new generation of antimicrobial resistance, bacteriophage therapy (Hitchcock et al., 2023). It explores the biology and mechanisms of bacteriophages, recent developments in the use of phages as therapeutic agents, and clinical trials of phages in treatment against multi-drug-resistant microbes, existing hurdles and prospects for the integration of phage therapy into contemporary antimicrobial treatment strategies.

Biology and Mechanism of Bacteriophages

Phages are viruses that attack only bacterial cells; also known as bacteriophages. They are thought to be the most numerous biological entities in the world, at least 10^{31} particles (Bechelany, 2022). Phages are found everywhere in nature, including soil, fresh water, marine life, sewage, and in the human and animal body's microbiomes (Brown, Charity, & Adriaenssens, 2022). The structure of most bacteriophages is similar to that of a virus: they have a protein capsid enclosing DNA or RNA, and have specific structures like tails and tail-fibers for attaching to the bacterial host (van Raaij, 2024). They are very host specific and are able to detect and infect only a specific kind or strain of bacteria and no other microbes (Soni et al., 2024).There are two broad classes of phages according to their replication strategy: lytic phages and lysogenic (temperate) phages (Rostøl, Chmielowska, Marina, & Penadés, 2026). The lytic phages are used more in therapeutic purposes because they can kill bacterial cells quickly (Hibstu, Belew, Akelew, & Mengist, 2022). Temperate phages, on the other hand, can form a latent (prophase) infection in the bacterial chromosome and persist in this form for long periods (Zhou, Liu, Song, & Chen, 2023). The role of lysogenic phages in the evolution and transfer of bacterial genes is significant, but they cannot be used in clinical therapy because they could carry virulence genes and/or resistance genes (Qin et al., 2022).The antibacterial activity of bacteriophages is mainly mediated through the lytic cycle (Vashisth et al., 2022). The infection process starts with the recognition and attachment of the phage to the bacterial surface by its tail fibres (Leprince & Mahillon, 2023). The viral genome then takes over the host's metabolic system, and the production of phage nucleic acids and structural proteins is directed. Mature phage particles are made by the bacterial cell by assembly of newly synthesized components (Malik et al., 2023).

As the infection develops, the enzymes encoded by the phage break down the cell wall and membrane of the bacteria (Guliy & Evstigneeva, 2025). This eventually results in bacterial lysis, which results in many progeny phages being released into the environment. The newly released phages are able to infect other susceptible bacteria in the area of infection, thereby increasing the antibacterial effect in this region. Other bacteriophages also produce depolymerase enzymes that can break down the biofilm, which is a clump of bacteria that has a structured formation and has an increased antibiotic and immune system resistance. Therefore, lytic phages, due to their specificity, ability to self-replicate and strong bactericidal properties, are attractive substitutes for routine antibiotics (Taati Moghadam et al., 2025). The distinctive nature of these biological properties has reignited the interest in the use of bacteriophage as an innovative approach to fight with multi-drug-resistant bacterial infections in the context of the global problem of antimicrobial resistance.

Antimicrobial Resistance: A Global Health Challenge

Antimicrobial resistance (AMR) is a growing threat to health and one of the greatest public health problems of the 21st century. When microorganisms, like bacteria, viruses, fungi and parasites, develop resistance to an antimicrobial medicine that once worked for them. Consequently, frequent infections are harder to treat, symptoms last longer, health care expenses are higher, and death rates are higher. The uncontrolled and overuse of antibiotics in human medicine, veterinary care and agriculture has contributed massively to the development and dissemination of resistant pathogens around the world (Alara & Alara, 2024).

AMR has a significant and increasing global impact. Resistant infections account for millions of deaths each year and are a heavy burden on the health-care system. There is increasing resistance to multiple drugs in diseases like tuberculosis, pneumonia, urinary tract infections, and bloodstream infections. Besides, AMR is a threat to numerous modern medical procedures, such as organ transplantation, cancer chemotherapy, and major surgeries (So & Walti, 2022), that depend on an effective antimicrobial agent for preventing and treating infection. The complications and mortality rate of these procedures is very high if antibiotics cannot be used effectively (De La Fuente-Nunez, Cesaro, & Hancock, 2023).

AMR is a global problem that needs a coordinated worldwide response from governments, health practitioners, researchers and the public (Tang, Millar, & Moore, 2023). The rational use of antimicrobials, the enhancement of infection prevention and control systems, the strengthening of surveillance systems and investment in the development of new antimicrobial agents and alternative treatments like bacteriophage therapy are key steps (Rahman et al., 2026). Public awareness and education about the importance of correct use and responsible prescribing of antibiotics are also key to minimizing unnecessary antibiotic use. However, there is a need for international cooperation as resistant microorganisms can easily cross borders via travel, trade and environmental channels. Comprehensive and sustainable interventions can help to slow antimicrobial resistance and ensure antimicrobial therapies remain effective for generations to come globally (Salam et al.).

Advantages of Bacteriophage Therapy over Conventional Antibiotics

The use of viruses to specifically target and kill harmful bacteria is known as bacteriophage therapy, and is a potential treatment for bacteria which is emerging as an alternative to traditional antibiotics, particularly in the age of rising antimicrobial resistance (AMR). It’s one of the most important advantages is that it is very specific. (Ranveer et al., 2024)Another advantage is the capacity of phages to evolve with bacteria. If the bacteria become resistant to the phages, the phages can evolve resistance also. This co-evolution is especially beneficial in the treatment of multidrug-resistant (MDR) infections, which are typically resistant to conventional antimicrobial drugs. However, if bacteria resist a particular antibiotic, a new antibiotic needs to be developed, a process that is time consuming and costly. Bacteriophages are also very effective against biofilms, which are clusters of bacteria attached to surfaces, and surrounded by a protective sheath. Biofilms are often associated with chronic infections like diabetic ulcers, CF lung infections, and implant associated infections. Biofilms are typically difficult to treat with antibiotics, while bacteriophages can enter and lyse biofilms to promote bacterial clearance (Liu, Lu, Zhang, Shi, & Chen, 2022).

After entering the target bacteria, bacteriophages replicate within the bacteria at the site of infection as long as the bacteria are present. That is, that a small initial dose can have a cumulative effect which may result in lower frequency of repeated doses than normal antibiotics (Tung & Lawley, 2025).

Bacteriophage therapy is also thought to be not as harmful to humans as it is to bacteria since humans do not have phages (Zalewska-Piątek, 2023). This minimises the risk of toxicity and side effects that may be associated with some of the antimicrobial agents. Moreover, phages are generally present in nature such as soil, water and in humans, showing that they are a natural and likely safe therapeutic agent (Akhila Chandran, 2025).Last but not least, phage therapy may be tailored or individualized for particular infections. Certain phages can be targeted or modified to specifically target the particular bacterial strain that is causing disease. This tailoring approach is beneficial especially in clinical settings, where accurate and effective therapy is essential. To summarise, bacteriophage therapy has the benefits of specificity, adaptability, targeting of biofilms, self-replication, safety and personalization, over traditional antibiotics. The advantages that these properties offer make it an attractive weapon in the battle against antibiotic-resistant infections and an addition to present antimicrobial practices.

Recent Advance in Bacteriophage Therapy

With the rise of antimicrobial resistance (AMR) around the world, there has been a resurgence of scientific and clinical interest in the use of bacteriophage therapy (Hitchcock et al., 2023). Bacteriophages have been increasingly used to treat infectious diseases in the past few years, and their use has become more effective and clinically relevant than ever before, thanks to significant advances in molecular biology, genomics, and biotechnology (Ghaffar, Mustafa, & Salar, 2024).

A key improvement has been the generation of phage genomics and sequencing technologies. High throughput sequencing is now available to rapidly sequence phage genomes and the therapeutic phages will not contain genes encoding toxic products or genes for resistance to antibiotics, etc. This has significantly enhanced the safety of phage therapy and also the time required to identify appropriate therapeutic candidates (Lin, Du, Long, & Li, 2022).

An emerging innovation is the development of engineered and synthetic bacteriophages. Scientists can tailor phages to be more effective against bacteria using genetic engineering techniques such as CRISPR-Cas systems, which could expand their range of action and allow them to target specific bacteria or enter bacterial biofilms more effectively. In some clinical situations, in particular against multidrug resistant bacteria, these engineered phages are more powerful than their natural counterparts (Peng, Chen, & Qimron, 2024).

In addition, the development of phage cocktails has helped to improve treatment outcomes. Combinations of several phages, which recognize various bacterial receptors, are employed, rather than a single phage. This strategy will help decrease the chance of bacteria becoming resistant and enhance the chances of successfully clearing the infection. There are currently a number of clinical trials underway testing phage cocktails for various infections, including respiratory and chronic wounds.

A major breakthrough is the use of phage therapy in combination with antibiotics. Phage and antibiotics have been found to have synergy when used together, showing that the two agents work together to increase the effectiveness of the antibiotic (Xiao, Li, & Sun, 2023). This combination therapy is especially effective for treating infections in the presence of biofilm and persistent infections. The innovations of encapsulation, hydrogels and delivery systems based on nanoparticles help to guarantee the protection of phages from degradation and enhance stability inside the human body, which improves their ability to reach infection sites (Kim, Seo, Kim, Lee, & Jung, 2022).

Last but not least, there are a few countries that have established centres and compassionate-use programmes that enable patients suffering from life-threatening antibiotic-resistant infections to be treated with a personalized phage therapy. It is also being used in ongoing clinical trials in Europe, the USA and Asia, further confirming its safety and effectiveness.

To conclude, the recent developments in the field of genomics, genetic engineering, combination therapy, and delivery systems have been an important boost to the field of bacteriophage therapy, making it an attractive option in the battle against antimicrobial resistance (Rahman et al., 2026).

Table 1: **Bacteriophage therapy as a next-generation**

Aspect	Significance	Key Findings	References
Future Perspectives	It is hoped that it will make treatment with phages more effective and accepted.	Personalized phage therapy, synthetic biology, phage-antibiotic combination therapy and large-scale clinical trials are among the other types of phage therapeutics.	(Sahoo, Meshram, & Sahoo Jr, 2024)
Challenges	Restricts widespread clinical implementation	Narrow host range, possibility of bacterial resistance to phages, regulatory uncertainties and standardization problems	(Kline et al., 2025)
Clinical Applications	Offers other treatment choices when antibiotics are unsuccessful	Treatment of multiple drug-resistant infections caused by Pseudomonas aeruginosa, Staphylococcus aureus, Acinetobacter baumannii and Klebsiella pneumoniae	(Parmanik et al., 2022)
Advantages	Minimises negative impact and reduces the build-up of resistance.	High specificity to target bacteria, self-replication in the site of infection, minimal disruption of normal microbiota, and low toxicity.	(Youssef, Sakr, Shebl, & Aboshanab, 2025)
Recent Advance	Increases the number of therapeutic targets for bacteria	Phage cocktail development, genetic engineering of phages, encapsulation, and improved delivery systems for phages.	(Emencheta et al., 2024)

Clinical Applications of Bacteriophages Against Drug-Resistant Pathogens

There is a renewed interest in the use of bacteriophages as a possible clinical treatment for infections caused by drug resistant microbes (Chung, Nang, & Tang, 2023). There are lots of multidrug-resistant (MDR) and extensively drug-resistant (XDR) bacteria that are becoming more common; standard antibiotics are frequently not effective and the need to find new methods of treatment is critical (Cook & Wright, 2022). There are experimental and clinical trials that have demonstrated the effectiveness of the use of bacteriophages specifically infecting and lysing bacterial cells.

Bacteriophages are also being used clinically in treatment of chronic wound infections, including diabetic foot ulcers, pressure sores, and burn wounds. The infections are often due to resistant bacteria such as Staphylococcus aureus (including MRSA) and Pseudomonas aeruginosa (Nadi, Ahmed, Awad, & Taher, 2024). Phage therapy has proven to be effective in decreasing the number of bacteria in the culture, in breaking up biofilms and in the healing of wounds when antibiotics are not effective. Another important application is for respiratory tract infections, especially in CF patients. Persistent lung infections with antibiotic resistant bacteria occurs in these patients. Phage therapy by inhalation or nebulization has demonstrated efficacy against the inhalation pathogens in the lungs directly, and has led to increased lung function and decreased severity of infection.

Bacteriophages are also being used to treat urinary tract infections (UTIs), particularly recurrent or complicated UTIs with resistant Escherichia coli. Depending on the severity and location of the infection, the phages may be administered orally, intravenously or directly into the urinary tract. There are initial reports of better outcomes in those patients who are not responding to antibiotic therapy.

Also, for implant-associated and device-related infections, including infections of cardiac devices, catheters, and prosthetic joints, there are a few studies looking into the usefulness of phage therapy. The infections are hard to treat because bacteria were able to create protective biofilms on artificial surfaces. Phages can enter into these biofilms and successfully eliminate bacterial colonization, sometimes in conjunction with surgical removal and antibiotics.

Other clinical applications that are emerging are MDR bloodstream infections (sepsis). While this is still in a preliminary phase, there have been some promising results with the use of intravenous phage administration in compassionate-use cases, in which patients with life-threatening infections recovered following phage treatment. Besides, custom-made phage therapy is emerging as a crucial clinical tool, which involves choosing certain phages depending on the infecting bacterial strain of the patient. This customized approach maximizes treatment success and minimizes the risk of resistance (Stracy et al., 2022).To conclude, there is no doubt that bacteriophages are showing a wide range of clinical applications in the treatment of infections that are resistant to drugs, such as those in the wounds, respiratory tract, urinary tract, device infection, and systemic infection. With the expansion of clinical trials, phage therapy has the potential to become an important tool in modern treatment of infectious diseases, alongside antibiotics.

Challenges and Limitations of Bacteriophage Therapy

While bacteriophage therapy holds promise of a new field to combat antibiotic-resistant bacteria, there are a number of challenges and limitations that preclude its broader clinical application. Bacteriophages have a very limited host range. Each phage normally infects only particular strains of bacteria and so a virus that is effective against one strain may not be effective against another, even if both are from the same species. This means that the infecting pathogen must be properly identified before the treatment is initiated and rapid diagnosis is important, but may be challenging in the clinical setting. Another important drawback is the absence of a harmonised regulatory framework. Bacteriophages are biological agents that can be subject to variation according to their origin and manufacturing processes as opposed to conventional antibiotics, which are chemically defined and manufactured in bulk. Guidelines for approval, manufacturing, and quality control of phages are still under development by regulatory agencies in many countries, delaying their clinical use.

The potential for bacterial resistance to phages is another concern. Phages may evolve in parallel to bacteria, but bacteria may evolve defense mechanisms, including modification of receptors or CRISPR-Cas systems, to resist phages. This can lead to reduced long-term efficacy of single-phage and require application of phage cocktails or continuous phage development. Bacteriophages could be recognized and neutralized by the human immune system when administered to humans (especially after repeated doses). This clearance of immunity can diminish the therapeutic outcome and also make treatment decisions more challenging, particularly if long-term treatment is needed for chronic infections (Patel, Huang, & Miliara, 2025).

The other drawback is the difficulty in the large-scale production and purification. The production of phages in a consistent, sterile, high-quality batch is not easy and demands special facilities and quality control. Technically challenging, the removal of bacterial contaminants, endotoxins and unwanted genetic material is essential (Hukic & Hukić, 2025).Moreover, there is a small amount of data from large clinical trials supporting the use of phage therapy on a large scale. The majority of the evidence is derived from compassionate use or small trials or case studies. Finally, there are also challenges regarding storage stability, delivery system, and formulation. The activity of phages might be lost under specific conditions and formulations for oral, topical or intravenous delivery are still under study (Sandhu & Parida, 2026).Finally, although the potential of bacteriophage therapy is great, the therapy is not widely used in the clinic due to specificity, regulatory hurdles, resistance, immune reactions, production hurdles, and limited clinical experience. This is where research and innovation can help meet the challenges in its successful integration with modern medicine (Hua et al., 2025).

Conclusion

The era of antimicrobial resistance (AMR) is one of the most complex healthcare threats of the present, and the usage of bacteriophage therapy seems to be a promising and innovative solution. Rapidly emerging multidrug-resistant (MDR) and extensively drug-resistant (XDR) pathogens have made the use of conventional antibiotics ineffective and other measures are urgently needed. In the context of the present invention, bacteriophage is a biologically precise, flexible and potentially long-term therapeutic approach to bacterial infections. A major advantage of phage therapy is that it is specific to pathogenic bacteria and not harmful to beneficial microbiota. This specificity is important as it minimizes the side effects and it also helps to keep microbial communities in the human body balanced. Furthermore, the power of phages to replicate inside the bacteria in the infected site and adapt to it gives them a dynamic advantage over conventional antibiotics that need development to tackle bacterial resistance. There have been recent advances in scientific research with regard to the application of bacteriophages, such as the safety and efficacy of the treatment, as a result of the discoveries in the fields of genomics, genetic engineering, and formulation technologies. The therapeutic potential has been extended by engineered phages, as well as phage cocktails and combination therapies with antibiotics, especially for the treatment of infections associated with biofilm or chronic infections. The importance of this in today's medical practice is further exemplified by its clinical uses in wound infection, respiratory disease, urinary tract infection, and device-related infections. Although there are these benefits, the use of bacteriophage therapy is still in the developmental and translational phase. Before it can be generally adopted as a treatment, it is important to work through some of the challenges, including its relatively small number of possible hosts, the uncertainty surrounding regulatory approval, interactions with the immune system, challenges to production, and limited large-scale clinical trial data. Ongoing research, funding, and global cooperation are crucial to overcome these challenges and establish a standardized approach to phage therapy. In the future, personalized medicine and bacteriophage therapy could transform the management of infectious diseases. Personalized phage therapy could be a major leap in the treatment of individual bacterial infections, and diminish the need for antibiotics. Additionally, upcoming research and development in biotechnology and synthetic biology can be anticipated to improve the accuracy, stability and availability of phage therapy drugs. To wrap up, bacteriophage therapy is a promising alternative or complementary approach to antibiotics in the future. The future holds promise for phages to significantly contribute to the fight against antimicrobial resistance and public health in the coming years, despite the obstacles that have yet to be overcome.

References

Akhila Chandran, S. (2025). From Soil to Cure: Exploring Nature's Pharmacy.

Alara, J. A., & Alara, O. R. (2024). An overview of the global alarming increase of multiple drug resistant: a major challenge in clinical diagnosis. *Infectious Disorders-Drug TargetsDisorders), 24*(3), 26-42.

Almatroudi, A. (2025). Biofilm resilience: molecular mechanisms driving antibiotic resistance in clinical contexts. *Biology, 14*(2), 165.

Aranaga, C., Pantoja, L. D., Martínez, E. A., & Falco, A. (2022). Phage therapy in the era of multidrug resistance in bacteria: a systematic review. *International Journal of Molecular Sciences, 23*(9), 4577.

Awari, V. G., Umeoduagu, N. D., Agu, K. C., Okonkwo, N. N., Ozuah, C. L., & Victor-Aduloju, A. T. (2023). The ubiquity, importance and harmful effects of microorganisms: An environmental and public health perspective. *International Journal of Progressive Research in Engineering Management and Science, 3*(12), 1-10.

Bechelany, M. (2022). Review on Natural. *Incidental, Bioinspired, and Engineered Nanomaterials: History, Definitions, Classifications, Synthesis, Properties, Market, Toxicities, Risks, and Regulations. Nanomaterials, 12*(2), 177.

Brown, T. L., Charity, O. J., & Adriaenssens, E. M. (2022). Ecological and functional roles of bacteriophages in contrasting environments: marine, terrestrial and human gut. *Current Opinion in Microbiology, 70*, 102229.

Butler, M. S., Gigante, V., Sati, H., Paulin, S., Al-Sulaiman, L., Rex, J. H., . . . Thwaites, G. E. (2022). Analysis of the clinical pipeline of treatments for drug-resistant bacterial infections: despite progress, more action is needed. *Antimicrobial agents and chemotherapy, 66*(3), e01991-01921.

Chung, K. M., Nang, S. C., & Tang, S. S. (2023). The safety of bacteriophages in treatment of diseases caused by multidrug-resistant bacteria. *Pharmaceuticals, 16*(10), 1347.

Cook, M. A., & Wright, G. D. (2022). The past, present, and future of antibiotics. *Science translational medicine, 14*(657), eabo7793.

De La Fuente-Nunez, C., Cesaro, A., & Hancock, R. E. W. (2023). Antibiotic failure: Beyond antimicrobial resistance. *Drug Resistance Updates, 71*, 101012.

Elshobary, M. E., Badawy, N. K., Ashraf, Y., Zatioun, A. A., Masriya, H. H., Ammar, M. M., . . . Assy, A. M. (2025). Combating antibiotic resistance: mechanisms, multidrug-resistant pathogens, and novel therapeutic approaches: an updated review. *Pharmaceuticals, 18*(3), 402.

Emencheta, S. C., Onugwu, A. L., Kalu, C. F., Ezinkwo, P. N., Eze, O. C., Vila, M. M. D. C., . . . Onuigbo, E. B. (2024). Bacteriophages as nanocarriers for targeted drug delivery and enhanced therapeutic effects. *Materials Advances, 5*(3), 986-1016.

Fahim, Y. A., Hasani, I. W., Kabba, S., & Ragab, W. M. (2025). Artificial intelligence in healthcare and medicine: clinical applications, therapeutic advances, and future perspectives. *European Journal of Medical Research, 30*(1), 848.

Ferrara, F., Castagna, T., Pantolini, B., Campanardi, M. C., Roperti, M., Grotto, A., . . . Zambarbieri, G. (2024). The challenge of antimicrobial resistance (AMR): Current status and future prospects. *Naunyn-Schmiedeberg's Archives of Pharmacology, 397*(12), 9603-9615.

Ghaffar, R., Mustafa, G., & Salar, M. Z. (2024). The Role of Molecular Biology in Biotechnology and Medicine. *Zoology: Advancements and Research Trends,(pp: 291-298). FahumSci, Lahore, Pakistan*.

Guliy, O. I., & Evstigneeva, S. S. (2025). Bacteria-and phage-derived proteins in phage infection. *Frontiers in Bioscience-Landmark, 30*(2), 24478.

Hacker, K. (2024). The burden of chronic disease. *Mayo Clinic Proceedings: Innovations, Quality & Outcomes, 8*(1), 112-119.

Hibstu, Z., Belew, H., Akelew, Y., & Mengist, H. M. (2022). Phage therapy: a different approach to fight bacterial infections. *Biologics: Targets and Therapy*, 173-186.

Hitchcock, N. M., Devequi Gomes Nunes, D., Shiach, J., Valeria Saraiva Hodel, K., Dantas Viana Barbosa, J., Alencar Pereira Rodrigues, L., . . . Badaró, R. (2023). Current clinical landscape and global potential of bacteriophage therapy. *Viruses, 15*(4), 1020.

Hossain, A., Habibullah-Al-Mamun, M., Nagano, I., Masunaga, S., Kitazawa, D., & Matsuda, H. (2022). Antibiotics, antibiotic-resistant bacteria, and resistance genes in aquaculture: risks, current concern, and future thinking. *Environmental Science and Pollution Research, 29*(8), 11054-11075.

Hua, H., Tang, J.-Y., Zhao, J.-N., Wang, T., Zhang, J.-H., Yu, J.-Y., . . . Luo, Q.-X. (2025). From traditional medicine to modern medicine: the importance of TCM regulatory science (TCMRS) as an emerging discipline. *Chinese Medicine, 20*(1), 92.

Hukic, M., & Hukić, E. (2025). Ethical and Biosafety Challenges in Modern Microbiology: Navigating the Risks of Emerging Technologies. In *Spectrum of Dual-Use Technologies: Unforeseen Risks Versus Returns* (pp. 163-182): Springer.

Kasman, L. M., & Porter, L. D. (2022). Bacteriophages. In *StatPearls [Internet]*: StatPearls Publishing.

Kim, D.-Y., Seo, Y.-C., Kim, C.-W., Lee, C.-R., & Jung, S.-H. (2022). Factors affecting range of motion following two-stage revision arthroplasty for chronic periprosthetic knee infection. *Knee Surgery & Related Research, 34*(1), 33.

Kline, A., Cobián Güemes, A. G., Yore, J., Ghose, C., Van Tyne, D., Whiteson, K., & Pride, D. T. (2025). Current clinical laboratory challenges to widespread adoption of phage therapy in the united States. *Antibiotics, 14*(6), 553.

Leprince, A., & Mahillon, J. (2023). Phage adsorption to gram-positive bacteria. *Viruses, 15*(1), 196.

Lin, J., Du, F., Long, M., & Li, P. (2022). Limitations of phage therapy and corresponding optimization strategies: a review. *Molecules, 27*(6), 1857.

Liu, S., Lu, H., Zhang, S., Shi, Y., & Chen, Q. (2022). Phages against pathogenic bacterial biofilms and biofilm-based infections: a review. *Pharmaceutics, 14*(2), 427.

Malik, D. J., Goncalves-Ribeiro, H., GoldSchmitt, D., Collin, J., Belkhiri, A., Fernandes, D., . . . Kirpichnikova, A. (2023). Advanced manufacturing, formulation and microencapsulation of therapeutic phages. *Clinical Infectious Diseases, 77*(Supplement_5), S370-S383.

Marongiu, L., Burkard, M., Lauer, U. M., Hoelzle, L. E., & Venturelli, S. (2022). Reassessment of historical clinical trials supports the effectiveness of phage therapy. *Clinical microbiology reviews, 35*(4), e00062-00022.

Muteeb, G., Rehman, M. T., Shahwan, M., & Aatif, M. (2023). Origin of antibiotics and antibiotic resistance, and their impacts on drug development: A narrative review. *Pharmaceuticals, 16*(11), 1615.

Nadi, W. G., Ahmed, L. I., Awad, A. A. N., & Taher, E. M. (2024). Occurrence, antimicrobial resistance, and virulence of Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa isolated from dairy products.

No, O., & Ekpunobi, N. F. (2025). A narrative review exploring phage therapy as a sustainable alternative solution to combat antimicrobial resistance in Africa: Applications, challenges and future directions. *African Journal of Clinical & Experimental Microbiology, 26*(2).

Okeke, I. N., de Kraker, M. E. A., Van Boeckel, T. P., Kumar, C. K., Schmitt, H., Gales, A. C., . . . Laxminarayan, R. (2024). The scope of the antimicrobial resistance challenge. *The Lancet, 403*(10442), 2426-2438.

Parmanik, A., Das, S., Kar, B., Bose, A., Dwivedi, G. R., & Pandey, M. M. (2022). Current treatment strategies against multidrug-resistant bacteria: a review. *Current microbiology, 79*(12), 388.

Patel, S., Huang, M., & Miliara, S. (2025). Understanding treatment adherence in chronic diseases: challenges, consequences, and strategies for improvement. *Journal of Clinical Medicine, 14*(17), 6034.

Peng, H., Chen, I. A., & Qimron, U. (2024). Engineering phages to fight multidrug-resistant bacteria. *Chemical reviews, 125*(2), 933-971.

Qin, S., Xiao, W., Zhou, C., Pu, Q., Deng, X., Lan, L., . . . Wu, M. (2022). Pseudomonas aeruginosa: pathogenesis, virulence factors, antibiotic resistance, interaction with host, technology advances and emerging therapeutics. *Signal transduction and targeted therapy, 7*(1), 199.

Rahman, M. U., Shah, J. A., Khan, M. N., Bilal, H., Zhu, D., Du, Z., & Mu, D.-S. (2026). Innovative approaches to combat antimicrobial resistance: a review of emerging therapies and technologies. *Probiotics and Antimicrobial Proteins, 18*(3), 3597-3614.

Ranveer, S. A., Dasriya, V., Ahmad, M. F., Dhillon, H. S., Samtiya, M., Shama, E., . . . Chaudhary, P. (2024). Positive and negative aspects of bacteriophages and their immense role in the food chain. *npj Science of Food, 8*(1), 1.

Rostøl, J. T., Chmielowska, C., Marina, A., & Penadés, J. R. (2026). Revisiting the life cycle of temperate phages. *Nature Reviews Microbiology*, 1-13.

Rugarabamu, S., & Mwanyika, G. (2025). Biotechnological innovations to combat antimicrobial resistance and advance global health equity. *Bacteria, 4*(3), 46.

Sahoo, K., Meshram, S., & Sahoo Jr, K. (2024). The evolution of phage therapy: a comprehensive review of current applications and future innovations. *Cureus, 16*(9).

Salam, M. A., Al-Amin, M. Y., Salam, M. T., Pawar, J. S., Akhter, N., Rabaan, A. A., & Alqumber, M. A. A. (2023). *Antimicrobial resistance: a growing serious threat for global public health*.

Sandhu, J. S., & Parida, A. (2026). Spot-on phage therapy: stable formulations, smarter dosing for topical phage application. *Frontiers in Cellular and Infection Microbiology, 16*, 1697070.
So, M., & Walti, L. (2022). Challenges of antimicrobial resistance and stewardship in solid organ transplant patients. *Current Infectious Disease Reports, 24*(5), 63-75.
Soni, J., Sinha, S., & Pandey, R. (2024). Understanding bacterial pathogenicity: a closer look at the journey of harmful microbes. *Frontiers in Microbiology, 15*, 1370818.
Stracy, M., Snitser, O., Yelin, I., Amer, Y., Parizade, M., Katz, R., . . . Koren, G. (2022). Minimizing treatment-induced emergence of antibiotic resistance in bacterial infections. *Science, 375*(6583), 889-894.
Summers, W. C. (2024). The cold war and phage therapy: how geopolitics stalled development of viruses as antibacterials. *Annual Review of Virology, 11*(1), 381-393.
Taati Moghadam, M., Mohebi, S., Sheikhi, R., Hasannejad-Bibalan, M., Shahbazi, S., & Nemati, S. (2025). Phage and endolysin therapy against antibiotics resistant bacteria: from bench to bedside. *MedComm, 6*(7), e70280.
Tang, K. W. K., Millar, B. C., & Moore, J. E. (2023). Antimicrobial resistance (AMR). *British journal of biomedical science, 80*, 11387.
Tarin-Pello, A., Suay-Garcia, B., & Perez-Gracia, M.-T. (2022). Antibiotic resistant bacteria: current situation and treatment options to accelerate the development of a new antimicrobial arsenal. *Expert review of anti-infective therapy, 20*(8), 1095-1108.
Tung, H.-R., & Lawley, S. D. (2025). How missed doses of antibiotics affect bacteria growth dynamics. *Bulletin of Mathematical Biology, 87*(5).
van Raaij, M. J. (2024). Bacteriophage receptor recognition and nucleic acid transfer. *Structure and Physics of Viruses: An Integrated Guide*, 593-628.
Vashisth, M., Yashveer, S., Anand, T., Virmani, N., Bera, B. C., & Vaid, R. K. (2022). Antibiotics targeting bacterial protein synthesis reduce the lytic activity of bacteriophages. *Virus research, 321*, 198909.
Venkataraman, S., Shahgolzari, M., Yavari, A., & Hefferon, K. (2025). Bacteriophages as targeted therapeutic vehicles: challenges and opportunities. *Bioengineering, 12*(5), 469.
Xiao, G., Li, J., & Sun, Z. (2023). The combination of antibiotic and non-antibiotic compounds improves antibiotic efficacy against multidrug-resistant bacteria. *International Journal of Molecular Sciences, 24*(20), 15493.
Youssef, R. A., Sakr, M. M., Shebl, R. I., & Aboshanab, K. M. (2025). Recent insights on challenges encountered with phage therapy against gastrointestinal-associated infections. *Gut Pathogens, 17*(1), 60.
Zalewska-Piątek, B. (2023). Phage therapy—challenges, opportunities and future prospects. *Pharmaceuticals, 16*(12), 1638.
Zhang, L., Tian, X., Sun, L., Mi, K., Wang, R., Gong, F., & Huang, L. (2024). Bacterial efflux pump inhibitors reduce antibiotic resistance. *Pharmaceutics, 16*(2), 170.
Zhou, S., Liu, Z., Song, J., & Chen, Y. (2023). Disarm the bacteria: what temperate phages can do. *Current Issues in Molecular Biology, 45*(2), 1149-1167.