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Review Article

Bacteriophage Therapy Is an Alternative to Antibiotics

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ABSTRACT

With the increasing problem of antimicrobial resistance, the efficacy of conventional antibiotics has been greatly reduced, necessitating new approaches to manage bacterial infections. Recently, bacteriophage therapy has been re-emphasized as a potential biological strategy because of the ability of bacteriophages to selectively infect and kill pathogenic bacteria with minimal disturbance to the normal microbial community. Recent studies have shown the potential of phages to control the growth of multidrug resistant pathogens, degrade bacterial biofilm and improve treatment outcomes when administered alone or in combination with antibiotics. Recent advances in phage engineering, adaptive evolution and personalized phage formulation have further enhanced their therapeutic potential and widened their spectrum of activity. Despite these promising developments, there are still a number of challenges to be addressed, such as narrow host range, emergence of phage resistance bacterial mutants, standardization of manufacturing processes, regulatory approval and need of strong clinical evidence. In general, the review gives a logical overview of the current development status of phage therapy, discussing mechanisms, therapeutic applications, recent technological advances, limitations, and future prospects. In general, bacteriophage therapy is a promising adjunct or alternative to conventional antibiotics and may make a significant contribution to the global challenges of antimicrobial resistance.

INTRODUCTION

The rise in global spread of antibiotic-resistant bacteria has become a major public health concern. Antimicrobial resistance (AMR) causes more than 1

million deaths globally in 2019 and, if no effective action is taken, could be responsible for about 10 million deaths a year by 2050 [1]. The growing danger of infections that resist antibiotics highlights the pressing

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need for new, sustainable alternatives to traditional antibiotics [2]. Bacteriophage therapy has attracted increasing attention as a promising approach for the control of antibiotic-resistant bacterial infections [3]. Bacteriophages, or phages, are viruses that infect bacteria and archaea and replicate inside their hosts [4]. Phages have either lytic or lysogenic life cycle, depending on their interaction with bacterial hosts. Lytic phages replicate inside bacterial cells and induce cell lysis, whereas lysogenic phages integrate their genetic material into the host genome and stay dormant. For over a century, bacteriophages have been known for their therapeutic potential. One of the earliest observation later linked with bacteriophages was published in 1896 by British chemist Ernest H. Hankin, who observed antibacterial activity in waters from the Ganges and Jumna rivers in India [3]. Some areas, especially Eastern Europe and the former Soviet Union, were still using phage therapy. It was in Georgia and Poland that phage-based treatments were preserved and promoted when their use fell out of favours in Western medicine [5]. Later, specialized institutions were created in these areas for isolation, characterization, development, and production of therapeutic bacteriophages. Their long-standing experience has contributed to the modern understanding of phage therapy and supports its current investigation as an alternative or complementary approach to antibiotic therapy.

MACHANISMS OF PHAGE ACTION AGAINST FOR BACTERIA

The ability of a bacteriophage to infect different bacterial hosts is called the phage host range and is a dynamic property that is affected by the abundance, diversity, and suitability of the available host bacteria [6]. Bacteriophages are thought to be one of the most abundant biological entities on the planet. With an estimated 10^{31} of them on Earth. They can be found in virtually any environment where bacteria can grow, including the intestinal tracts of humans and animals. However, not with standing this enormous diversity, almost half of the complete phages genomes presently deposited in the NCBI database are associated with only seven bacterial genera, namely salmonella, mycobacterium, Gordonia, Escherichia, Streptococcus, pseudomonas, and Lactococcus. This implies that

many phages and phage families are yet to be discovered and characterized [7]. Recently, an active lysogeny lifestyle has been described in which the prophage is not dormant in the bacterial genome but continuously integrated and excised from the host chromosome [8]. Phages may also differ in receptor specificity. Monovalent phages bind to a single receptor while polyvalent phages can bind to more than one receptor. The host range also varies due to differences in receptor recognition. Thus, some bacteriophages have a narrow host range, infecting only certain bacterial strains, but other bacteriophages have a broad host range and infect several strains of the same species or even different bacterial species [6].

BACTERIOPHAGE STRUCTURE AND LIFE CYCLE

Bacteriophage's co-exist with bacterial hosts in nature, and are involved in microbial diversity and bacterial evolution. Biologically they are different from one another in their morphology, their growth requirements, and the pattern of replication. Structurally, most phages are composed of genetic material packaged inside a protein capsid. Lytic phages infect susceptible bacterial cells, multiply within them, and ultimately lyse the cell, releasing newly formed phages [9]. The viral taxonomy now comprise 1 classes, 7 orders, 31 families, 214 genera and 858 species [6]. The phage genome may be single-stranded DNA (ssDNA), double-stranded DNA (dsDNA), double-stranded RNA (dsRNA) or single-stranded RNA (ssRNA) [10]. Lytic phages specifically recognize their bacterial hosts, inject their genetic material, replicate in the host cell and induce bacterial lysis. Temperate phages, in contrast, can integrate their genomes into the bacterial chromosome as prophages or persist as plasmid like elements. These prophages may be induced and enter the lytic cycle under proper conditions [11]. Thus, obligate lytic phages are preferred in phage therapy as they are able to efficiently clear bacterial pathogens while minimizing the risk of horizontal transfer of antibiotic-resistance gene [12].



THERAPEUTIC SIGNIFICANCE OF BACTERIOPHAGE

Bacteriophages are potential candidates for the Treatment of bacterial infections, particularly those from multidrug-resistance pathogens. Their targeting of specific cells make them attractive candidates for antimicrobial therapy [13,14]. Phages are capable of killing susceptible bacteria by infection and lysis, and phage-derived enzymes may also help to degrade bacterial biofilms. This could potentially make them useful against infections that are difficult to treat with conventional antibiotics [14,15]. Combination of phages with antibiotics has been promising for the improvement of bacterial clearance and management of resistance pathogens including *P.aeruginosa*, *A.bau-mannii* and *k.pneumoniae* [15,16]. However, narrow host range, phage resistance and immune elimination are challenges. Further research is needed to develop safe and standardized phage-based therapies for clinical applications [13,16].

ADVANTAGES OF PHAGE THERAPY

Phage therapy offers multiple benefits compared to traditional antibiotics since bacteriophages can specifically target particular bacterial pathogens, encompassing both Gram-positive and Gram-negative bacteria. They are generally found in nature in soil, water, sewage and animal-associated sources, making them relatively easy to isolate[6]. Phage can also replicate at the site of infection, which can reduce the need for repeat doses and increase the effectiveness of treatment [17]. Moreover, their host specificity may help in preservation of beneficial bacteria populations while targeting pathogenic bacteria. In addition, genetic diversity of phages allows to select or develop phages with suitable host specificity and therapeutic activity [18,19].

CHALLENGES AND LIMITATIONS

Different phages have demonstrated promising inhibitory effects on MDR bacteria; however, their clinical applications remains limited due to several challenges. Phages therapy faces numerous challenges, including the potential transfer of antibiotic-resistance gene between bacteria, the lack of standardized protocols for administering phage cocktails, the possibility

of the immune system identifying and neutralizing phages as foreign invaders, limited genomic knowledge for many phages, rapid bacterial lysis releasing endotoxins and superantigens that may trigger inflammatory response, the high specificity of phages complicating treatment preparation for diverse bacterial strains, the dependency on the presence of target bacteria for phage replication, limited recognition of phages as therapeutic agents, and the absence of public health insurance coverage for phage based treatments [20]. Some bacterial pathogens evade phage therapy by residing within eukaryotic cells, making their receptors inaccessible to phages. Although certain phages might have the potential to enter host cells and combat intracellular bacteria, this capability is strain-specific and requires further investigation to fully understand their interaction and therapeutic potential [21,22]. Many of the current problems of patenting phage-based therapeutic preparations may be solved by the future progress of biotechnology and genetic engineering . Such advances could potentially enhance the specificity and accessibility of PT. Modern genome-editing techniques, such as genome sequencing, CRISPR/Cas-mediated engineering, homologous recombination and assembly of phage genomic DNA, can be used to engineer phages with well-defined antibacterial properties. Engineered phages could be potentially engineered to selectively target antibiotics resistant bacterial strains with minimal disruption of the beneficial microorganisms in the patient's normal microbiota. Phage combinations and engineered phages may have more promise for intellectual-property protection, large-scale production and commercialization because of their unique development and maintenance of large phage collections by research laboratories and specialized PT centers in different countries could also improve the availability of therapeutic phages[23]. However, strict quality control procedures are indispensable, regardless of whether phage preparations are produced for specific therapy or broader clinical use. Therapeutic phage products require appropriate testing to ensure sterility, adequate stability and safety. Particularly, preparations should be carefully assessed for the presence of endotoxins, exotoxins, and other potentially harmful contaminants prior to administration to patients [24]. Interest in phages as possible



therapeutic agents has grown but they are unlikely to replace conventional antibiotics. Phage therapy can be used as an adjuvant treatment, particularly in combinations with antibiotic, or as an alternative for patients with severe infections that have not responded to the current available antimicrobial treatments. The growing global problem of multidrug-resistant (MDR) infections, partly related to the widespread and inappropriate use of antibiotics, emphasizes the necessity of studying alternative antimicrobial strategies. In this context, phages therapy is a promising avenue that should be revisited and developed clinically as a potential tool to combat antibiotic-resistance bacterial infections [25].

CONCLUSION

Bacteriophage therapy has become a promising alternative or adjunct to conventional antibiotics especially for multidrug-resistance bacterial infections. Phages have become attractive tools for the management of antimicrobial resistance due to their specific targeting and ability to kill certain bacterial pathogens. Advances in phage isolation, characterization, genetic engineering and phage antibiotic combinations have further increased the therapeutic potential of phages. However, limitations such as narrow host range, bacterial resistance to phages, formulation issues, and regulatory concerns still need to be tackled. Further studies and well designed clinical studies are needed to improve the safety, effectiveness and practical application of phages therapy. In general phages are a promising therapeutic approach that could have a substantial in addressing the escalating global problem of AMR.

REFERENCES

1. Zhang S, Ahn J. Phage therapy as a novel alternative to antibiotics through adaptive evolution and Antibiotics. 2025;14 (10):1040. fitness Doi: 10.3390/antibiotics14101040. trade-offs.
2. Walter N, Mirzaei M, Deng I., Willy C, Alt V, Rupp M. The potential of bacteriophage therapy as an alternative treatment approach for antibiotic-resistant infections. Med Princ Pract. 2024;33 (1):1-9. Doi: 10.1159/000534717.
3. Ogungbe BA, Awoniyi SO, Bolarinde BF, Awotimiro OE. Progress of phage therapy research as an alternative to antibiotics: current status, challenges, and the future of phage therapeutics. Glob Med Interdiscip. 2024;2:100042. Doi:10.1016/j.glmedi.2023.100042.
4. Aswani V, Shukla SK. An early history of phage therapy in the United States: is it time to reconsider? Clin Med Res. 2021;19 (2):82-89. Doi:10.3121/cmr.2021.1605.
5. Essa N, Rossitto M, Fiscarelli E. Phages and phage therapy: past, present and future. Microbiol Med. 2020;35 (1). doi:19 4081/mm.2020.8709.
6. Moghaddam MT, Mohebi S. Sheikhi R, Hasannejad-Bibalan M, Shahbazi S, Nemati S. Phage and endolysin therapy against antibiotics resistant bacteria: from bench to bedside. MedComm. 2025;6 (7):e70280. Doi:10.1002/mco2.70280.
7. Hitchcock NM, Nunes DDG, Shiach J, Hodel KVS, Barbosa JDV, Rodrigues LAP, Coler BS, Soares MBP, Badaró R. Current clinical landscape and global potential of bacteriophage therapy. Viruses. 2023;15 (4): 1020. Doi:10.3390/v15041020.
8. Floccari VA, Dragoš A. Host control by SPB phage regulatory switch as potential manipulation strategy. Curr Opin Microbiol. 2023;71:102260. Doi: 10.1016/j.mib.2022.102260.
9. M. Taati Moghadam, N. Amirmozafari, A. Shariati, M. Hallajzadeh, S. Mirkalantari, A. Khoshbayan, et al., "How Phages Overcome the Challenges of Drug Resistant Bacteria in Clinical Infections," Infection and Drug Resistance 13 (2020): 45-61.
10. G. F. Hatfull and R. W. Hendrix, "Bacteriophages and Their Genomes," Current opinion in virology 1, no. 4 (2011): 298-303.
11. S. Uyttebroek, J. Onsea, W. J. Metsemakers, et al., "The Potential Role of Bacteriophages in the Treatment of Recalcitrant Chronic Rhinosinusitis," Antibiotics (Basel) 10, no. 6 (2021): 675.
12. M. Taati Moghadam, A. Khoshbayan, Z. Chegini, I. Farahani, and A. Shariati, "Bacteriophages, a



- New Therapeutic Solution for Inhibiting Multidrug-resistant Bacteria Causing Wound Infection: Lesson From Animal Models and Clinical Trials.” *Drug Design, Development and Therapy* 14 (2020): 1867-1883.
13. Subramanian A. Emerging roles of bacteriophage-based therapeutics in combating antibiotic resistance. *FrontMicrobiol.* 2024;15:1384164. Doi: 10.3389/fmicb.2024.1384164.
 14. Dicks LMT, Vermeulen W. Bacteriophage-Host Interactions and the Therapeutic Potential of Bacteriophages. *Viruses.* 2024;16 (3):478. Doi: 10.3390/v16030478.
 15. Gordon M, Ramirez P. Efficacy and Experience of Bacteriophages in Biofilm-Related Infections. *Antibiotics.* 2024;13 (2): 125. Doi: 10.3390/antibiotics13020125.
 16. Anastassopoulou C, Ferous S, Petsimeri A, Gioula G, Tsakris A. Phage-Based Therapy in Combination with Antibiotics: A Promising Alternative against Multidrug-Resistant Gram-Negative Pathogens. *Pathogens.* 2024;13 (10):896. Doi: 10.3390/pathogens 13100896.
 17. M. Taati Moghadam, N. Anirmozafari, A. Shariati, M. Hallajzadeh, S. Mirkalantari, A. Khoshbayan, et al., “How Phages Overcome the Challenges of Drug Resistant Bacteria in Clinical Infections,” *Infection and Drug Resistance* 13 (2020): 45-61.
 18. J. R. Meyer, D. T. Dobias, J. S. Weitz, J. E. Barrick, R. T. Quick, and R. E. Lenski, “Repeatability and Contingency in the Evolution of a Key Innovation in phage lambda,” *Science* 335, no. 6067 (2012): 428-432.
 19. M. T. Moghadam, A. Mojtahedi, S. Salamy, et al., “Phage Therapy as a Glimmer of Hope in the Fight Against the Recurrence or Emergence of Surgical Site Bacterial Infections,” *Infection* 52, no. 2 (2024): 385-402.
 20. J. Lin, F. Du, M. Long, and P. Li, “Limitations of Phage Therapy and Corresponding Optimization Strategies: A Review,” *Molecules (Basel, Switzerland)* 27, no. 6 (2022): 1857
 21. 65A. Wernicki, A. Nowaczek, and R. Urban-Chmiel, “Bacteriophage Therapy to Combat Bacterial Infections in Poultry,” *Virology journal* 14, no. 1 (2017): 179.
 22. Jonczyk-Matysiak, E.; Weber-Dabrowska, B.; Owczarek, B.; et al. “Phage-Phagocyte Interactions and Their Implications for Phage Application as Therapeutics.” *Viruses* 2017, 9 (6), 150.
 23. Skurnik, M. “Can Bacteriophage Replace Antibiotics?” *Antibiotics* 2022, 11, 575.
 24. Chen, Y.; Batra, H.; Dong, J.; Chen, C.; Rao, V.B.; Tao, P. “Recent Engineering of Bacteriophages Against Infectious Diseases.” *Frontiers in Microbiology* 2019, 10, 994.
 25. Fur faro, L.; Payne, M.S.; Chang, B.J. “Bacteriophage Therapy: Clinical Trials and Regulatory Hurdles.” *Frontiers in Cellular and Infection Microbiology* 2018, 8, 376.

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