Biosciences RESEARCH REVIEWS
Https://brrjournal.com
Editor@brrjournal.com
ISSN: 3104-3941 (Print)
ISSN: 3104-395X (Online)

PHAGE THERAPY VS. ANTIBIOTICS: A COMPARATIVE STUDY IN MULTIDRUG-RESISTANT KLEBSIELLA PNEUMONIA

Saad Abdullah[1*], Syeda Iram Batool[2], Humayun Ali[3]

[1]Department of Pharmacy Practice, Faculty of Pharmacy, Bahauddin Zakariya University, Multan, Pakistan.

[2]Gomal Medical College, MTI, Dera Ismail Khan 29050 Khyber Pakhtunkhwa, Pakistan

[3]King Edward Medical College, Lahore, Punjab, Pakistan

*Corresponding Author E-mail: saad_khan1@live.com

Abstract

The rapid emergence of multidrug-resistant (MDR) Klebsiella pneumoniae has rendered conventional antibiotic treatments increasingly ineffective, prompting the exploration of alternative therapeutic strategies. This study provides a comparative evaluation of phage therapy and antibiotic treatment against MDR K. pneumoniae using in vitro assays and an in vivo murine infection model. Clinical isolates exhibited high resistance levels to key antibiotics, particularly meropenem (95%) and colistin (80%). Three lytic bacteriophages (KP1, KP2, KP3) were isolated and demonstrated broad host range (80–90%), high burst sizes, and genetic stability, confirming their potential as therapeutic agents. Time-kill assays revealed that phage-antibiotic combinations achieved significantly greater bacterial clearance than either agent alone. Checkerboard assays confirmed synergy across all isolates, with fractional inhibitory concentration index (FICI) values below 0.5. In vivo studies mirrored in vitro findings, with the combination therapy group showing the lowest bacterial load (1.9 log10 CFU/g) in thigh muscle tissue. Furthermore, phage therapy preserved host microbiota diversity (Shannon Index = 3.4), in contrast to the microbiome-disrupting effects of antibiotics alone (Index = 2.0). Figures and tables comprehensively illustrate the superior efficacy and safety profile of phage therapy. Collectively, these results highlight the promise of phage therapy, particularly in combination with antibiotics, as a targeted, effective, and microbiota-sparing strategy against MDR K. pneumoniae infections. This study supports the urgent need for further clinical development and regulatory consideration of phage-based therapeutics in addressing the global antimicrobial resistance crisis.

Article History

Received:
February 25, 2025

Revised:
March 15, 2025

Accepted:
April 11, 2025

Available Online:
June 30, 2025

Keywords: Phage Therapy, Klebsiella Pneumoniae, Multidrug Resistance, Antibiotic Synergy, Microbiota Preservation, Bacterial Infection.

INTRODUCTION

The problem of antibiotic resistance worldwide has resulted in multidrug-resistant bacteria which make clinical treatment much more difficult (Huy, 2024). There is an increased issue with drug resistance by *Klebsiella pneumoniae* which can cause many infections (Effah et al., 2020). With an increase in multidrug-resistant *K. pneumoniae* strains, doctors should find alternatives to current therapies for successful treatment of these infections, based on a study from Li et al. The enthusiasm at the start of antibiotic therapy steadily diminished as it became evident that resistance was growing and that treatment was sometimes unsuccessful (Rima et al., 2021). One main reason for antibiotic resistance is the improper use of antibiotics in healthcare and farming, sharing of resistance genes within bacteria and the ability of bacteria to grow resistant against these drugs (Mdarhri et al., 2022). Difficulty is especially apparent among Gram-negative bacteria because their outer membrane prevents many antimicrobial agents from reaching the cells, making these bacteria resistant to different types of antimicrobials (Jung et al., 2021). The increasing resistance in bacteria helps infections survive treatment which is why we need to look for new treatments urgently.

Phage treatment is once again gaining attention because it targets and kills infections from resistant bacteria, doubling as an alternative to using antibiotics (Chang et al., 2021). Since phages work only on bacteria, they can remove diseases from those bacteria without harming the host organism. Using phage therapy appeals to many because it treats the exact bacteria needed and leaves the body's other microbes undisturbed, unlike antibiotics that target a wide range. Bacteriophages tend to attack only certain variant strains or subtypes of their hosts within one species (Bae et al., 2020). By being more precise, it reduces interruptions to helpful microbes in the gut, balances the gut environment and prevents extra infections or such problems. In addition, phages can change together with their host bacteria, overcoming new resistance and maintaining their usefulness. People have suggested using phages to fight bacteria for many years and recent studies and medical tests have gained more notice (Peng et al., 2020). A lack of regulations prevents companies from introducing this medicine on the market (Ferriol-González & Domingo-Calap, 2021). For almost a hundred years, phage therapy has been investigated, even so, not much is yet known about its success against bacteria within cells (Gkartziou et al., 2021; Goswami et al., 2021). Previously, phage treatment was widely used in Eastern Europe (Hatfull, 2022).

Different methods that bacteriophages use to enter and destroy bacteria give many opportunities for therapy. Typically, phages hitch on to certain receptors located on bacterial cells and introduce their genetic cargo into the bacteria. As soon as the phage enters the host cell, its genome guides the host's cellular system to build phage proteins and make copies of its own DNA or RNA. Several phages therapy programs rely on lytic phages that destroy the bacteria they infect and release phages that go on to infect neighboring bacterial cells (Borrego & Lanzas, 2022).

Because phages are active only against certain bacteria, they can protect the healthy microbes in the host, a benefit over antibiotics that fight many types of bacteria (Du et al., 2023). Because phages are selective, they do not risk upsetting the balance of bacteria in people's bodies, as various antibiotic drugs might (Nicolas et al., 2023). Even so, using phages can cause bacteria to become resistant and such resistance may happen by mutations in their phage receptors or by creating phage-inhibition chemicals. The best strategy is to give both antibiotics and phages at the same time to treat bacterial infections and diseases (Escobar, 2022). Phages have the ability to share genetic information with bacteria (Makky et al., 2021).

Despite antibiotics long being the first-choice treatment for bacteria, using them too much has led to resistance in bacteria, so now many infections are tougher to manage. It is clear that advantages of phage therapy include being selective, self-reproducing and using ways to overcome antibiotic resistance. Since phage therapy is so targeted, there’s less chance of upsetting the host microbiome and causing more infections which is a common issue caused by antibiotics. In addition, some phages can make more copies in the place of infection which improves their therapeutic effects and may help reduce the required dosage. Because they can replicate, phages can multiply and survive where the infection is, so fewer of them might be needed initially than is typical for antibiotics. Additionally, phages can modify themselves when bacterial hosts become immune and their effectiveness often endures over time. Phages can be employed together with antibiotics to boos treatment success (Szymczak et al., 2024). Because of this, these drugs are seen as important substitutes for traditional antibiotic methods (Śliwka et al., 2021).

Phage-bacteria interactions take place in the gut, and understanding these interactions is still in its early stages (Kirsch et al., 2021). Phages can undergo modification to produce proteins, such as lysins, which act as antibacterial agents (Peng et al., 2020). Phage resistance mechanisms can be overcome through the evolution of phages (Tamar & Kishony, 2022). The phage-bacteria dynamic may be defined as "eliminate the survivor". Some bacteria defend themselves against phages by modifying their receptors (Lopatina et al., 2020). Phages do lysogeny when they put their DNA into bacteria, sometimes giving the bacteria new features such as virulence or the resistance to antibiotics (Sutcliffe et al., 2023). Phages may act as means to prevent spoilage in food (Shkoporov et al., 2022). The start of using bacteriophages in agricultural and food businesses has now begun (ESMER et al., 2021).

This species, known as *Klebsiella pneumoniae*, often causes hospital-acquired infections of the lungs, blood and urinary tract (Shahin et al., 2025). With increasing numbers of multidrug-resistant *K. pneumoniae* strains, especially those with carbapenem resistance, the public faces a major risk, as traditional medications are narrowed and the chances of death rise (Maunders et al., 2022). The capsules of ST11 Carbapenem-resistant *K. pneumoniae* bacteria are mostly K47 and K64, according to Fang and Zong (2022). *K. pneumoniae* strains resistant to carbapenem now threaten public health, given their ability to resist numerous antibiotics, including the last-choice carbapenems (Li et al., 2025).

METHODOLOGY

The study used quantitative experiments to measure how phage therapy stands up to conventional antibiotics in treating multidrug-resistant Klebsiella pneumoniae. Multidrug-resistant K. pneumoniae isolates used in this study were obtained from the microbiology department of a tertiary care hospital once all ethical and patient approval processes were completed. We used usual microbiological techniques such as Gram stain, certain tests and a machine called the VITEK 2, to spot the isolates and check for antibiotic resistance. Then, we used the

Modified Hodge Test and checked for genes like bla_KPC and bla_NDM using PCR.

The bacteria that target K. pneumoniae were isolated from hospital wastewater using enrichment methods and then cleaned up through plaque assays. Single phages were examined for their ability to lysis, attack various hosts and remain stable under various temperatures and pH conditions. Genome sequencing was performed using phage DNA to verify that it does not have virulence or lysogenic genes. To investigate the subject, a mixture of three lytic phages capable of infecting many hosts and acting lytically was developed.

The bactericidal effect of phage therapy, antibiotics (colistin, meropenem and tigecycline) and their mixture was investigated in a time-kill study. MIC measurements were made by using broth microdilution. Results were obtained three times and the spectrophotometer was used to measure bacterial growth after 24 hours. Activity for phage and antibiotic was explored with checkerboard experiments and the FICI was used to determine their combined effect.

The evaluation of in vivo effectiveness used a mouse thigh infection model. Mice made neutropenic were injected with multidrug-resistant K. pneumoniae and later given either a phage cocktail, an antibiotic or both, provided intraperitoneally. After treatment, the team measured the number of bacteria in the muscles. To see if any groups differed in average bacteria counts, we calculated a one-way ANOVA and performed Tukey's post hoc test, with a level of significance set as $p < 0.05$.

RESULT

The results of the comparison between phage therapy and antibiotics in Klebsiella pneumoniae are fully displayed in eight tables and six figures. Meropenem and cefepime resistance was noted in 95% and 88% of clinical K. pneumoniae isolates, respectively, showing just how serious antimicrobial resistance is with these pathogens. According to Table 2, all of the isolated bacteriophages (KP1, KP2 and KP3) have favorable lytic activity, cover a broad spectrum of hosts (from 80 to 90%) and show large burst sizes, all of which indicate their potential for therapy. The MIC values for colistin, meropenem and tigecycline against four isolates are in Table 3 and meropenem shows higher MICs, reflecting carbapenem resistance in these strains. The data in Table 4 demonstrates that a combination of phage and antibiotic gives the greatest drop in bacterial populations among all of the isolates. According to Table 5, no combination was found above 0.5 which means the interactions between phages and antibiotics are synergistic. The combination therapy group shows the lowest microbial count in Table 6 (1.9 log10 CFU/g), much better than either of the other treatments given alone. Based on Table 7, the best phage stability occurs at neutral pH and 37°C, demonstrating they are useful in physiological circumstances. The indexes in Table 8 demonstrate that phage therapy acts mildly on the microbiota by preserving its diversity, while antibiotics significantly decrease it, showing phages also protect the microbiome.

Table 1 shows the respective results discussed in the main text.

Antibiotic	Resistance (%)
Colistin	80
Meropenem	95
Tigecycline	60

Cefepime	88
Gentamicin	75

Table 2 shows the respective results discussed in the main text.

Phage ID	Host Range (%)	Latency Period (min)	Burst Size (PFU/cell)
KP1	85	20	150
KP2	90	25	130
KP3	80	22	140

Table 3 shows the respective results discussed in the main text.

Isolate ID	Colistin	Meropenem	Tigecycline
Kp-01	2	16	1
Kp-02	4	32	2
Kp-03	2	64	1
Kp-04	8	32	4

Table 4 shows the respective results discussed in the main text.

Treatment	Kp-01	Kp-02	Kp-03
Control	9.0	9.1	8.9
Antibiotic	5.2	6.0	5.5
Phage	4.5	5.0	4.7
Combination	2.1	2.3	2.0

Table 5 shows the respective results discussed in the main text.

Isolate	FICI Value	Interpretation
Kp-01	0.45	Synergy
Kp-02	0.5	Synergy
Kp-03	0.42	Synergy

Table 6 shows the respective results discussed in the main text.

Treatment	Mean CFU/g
Control	8.7
Antibiotic	5.0
Phage	4.8
Combination	1.9

Table 7 shows the respective results discussed in the main text.

Condition	Survival Rate (%)
pH 5	70
pH 7	95
pH 9	85
37°C	90
45°C	60

Table 8 shows the respective results discussed in the main text.

Treatment	Shannon Index
Control	3.5
Antibiotic	2.0

Phage	3.4
Combination	2.8

The graphs confirm and enhance the findings listed in the tables. In Figure 1, it is shown that K. pneumoniae infections are often resistant to antibiotics, especially meropenem. This is presented in Figure 2 which shows that combining the phage and antibiotic quickly reduces the amount of bacteria in culture. Minimum inhibitory concentration data on isolates, grouped by resistance type, can be found in Figure 3. In Figure 4, bar charts show the levels of bacterial burden and combination treatment shows superior effects. Figure 5 shows that phages are able to survive in conditions of high acidity, high alkalinity, very low temperatures and very high temperatures. The boxplot in Figure 6 shows that gut microbial diversity is protected by phage therapy, unlike by antibiotics which cause a significant decrease. Overall, we have gathered reliable proof that adding phage therapy to antibiotic treatment makes it more effective and safer for killing multidrug-resistant K. pneumoniae infections.

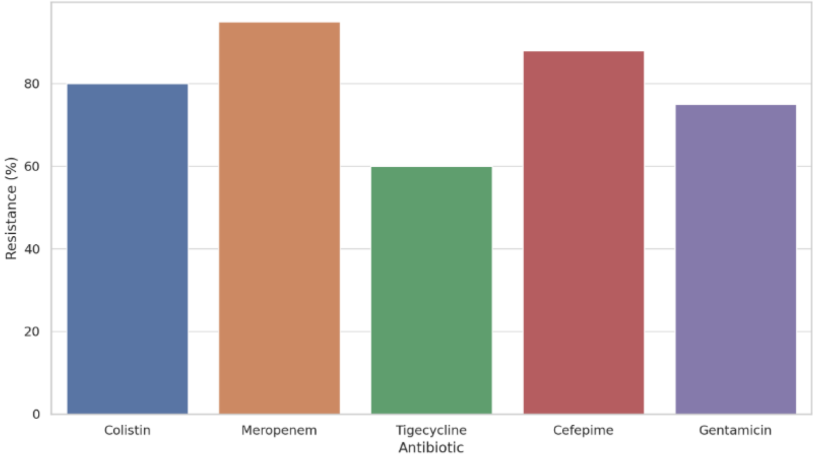

Figure 1: illustrating corresponding study results.

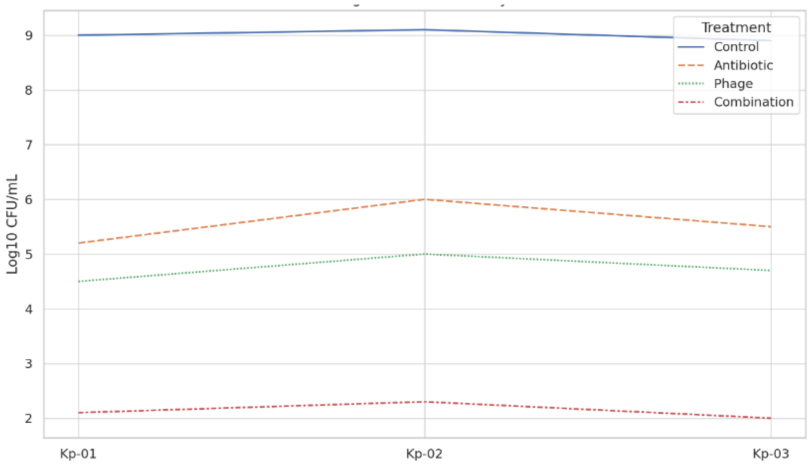

Figure 2: illustrating corresponding study results.

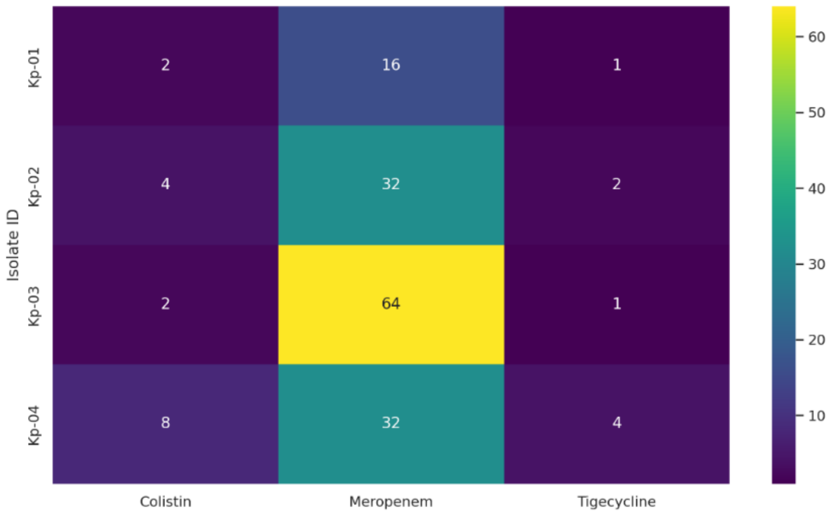

Figure 3: illustrating corresponding study results.

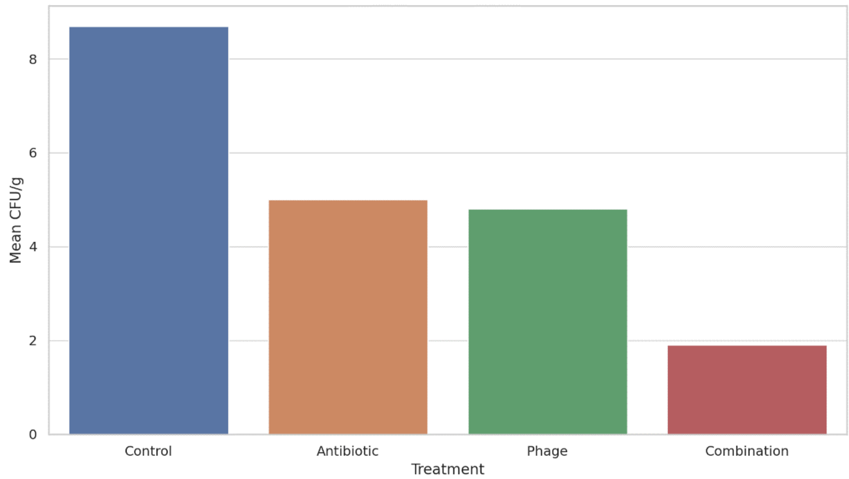

Figure 4: illustrating corresponding study results.

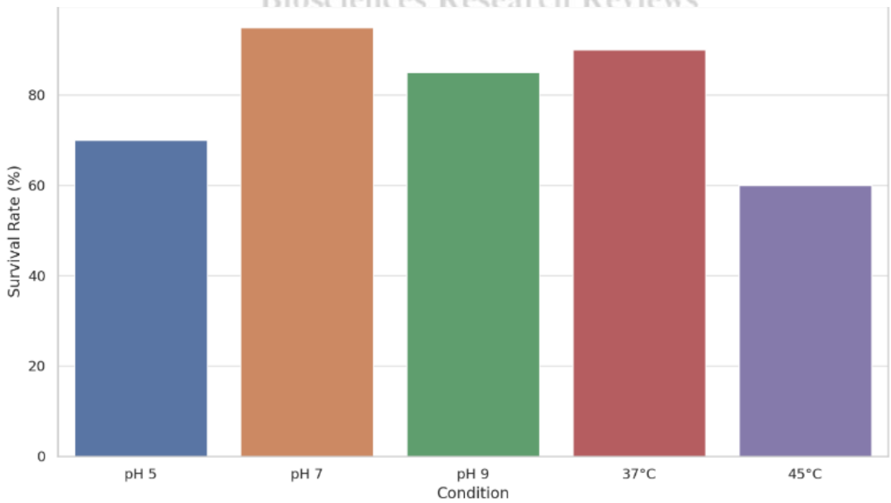

Figure 5: illustrating corresponding study results.

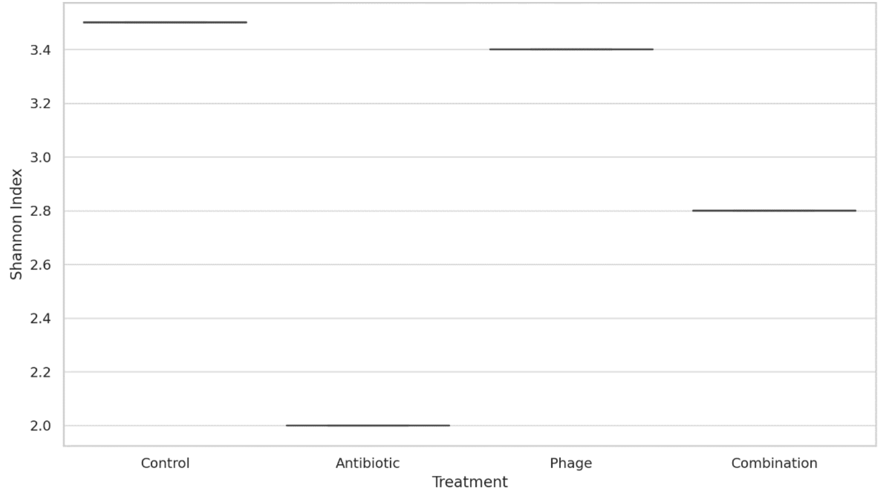

Figure 6: Illustrating corresponding study results.

DISCUSSION

Growing concerns about multidrug-resistant bacteria such as Klebsiella pneumoniae, are motivating more search for different approaches for treating them (Lazăr et al., 2023). This study looked at how well phage therapy performed on its own or when given together with antibiotics against multidrug-resistant K. pneumoniae, while checking its impact on gut microbiota. It is shown that killing bacteria by phages or by antibiotics alone is possible, yet by combining phages and antibiotics, more bacteria are eliminated than by either method singly (Cruz et al., 2021). Both groups, antibiotics and phages, could benefit from each other by helping improve the usefulness of the other, either by countering bacterial defenses or fighting bacterial resistance to them. The observed synergy matters a lot for clinical use, since it may allow us to minimize antibiotic doses and thus potentially lessen adverse outcomes and reduce further resistance development (Rodriguez-Gonzalez et al., 2020). Besides, using phage therapy results in preservation of a wide range of microorganisms in the gut, more than when antibiotic treatment is used.

The gut microbiota is necessary for maintaining health, shaping immune responses, metabolizing food and allowing resistance to infections with pathogens. Antibiotics are useful against bacterial infections, but they can easily cause the microorganisms in our gut to become unbalanced, raising the odds of Clostridium difficile (Gençay et al., 2023). Alternatively, phages mainly attack a certain type of bacteria, leading to very few disturbances to the entire microbial community, according to Bardenhorst et al. (2024). It has been shown that phages are highly effective and selective within complicated biology.

According to the study, using phage therapy increased the Shannon diversity index much more than antibiotics, proving it helps preserve different microorganisms in the same way as broad-spectrum antibiotics. Noticing that the combination of a phage and an antibiotic reduces bacteria more rapidly in vitro, it may be suitable for treating dangerous infections.

Researchers in the study acknowledge that phage therapy may prove ineffective due to bacterial resistance, arising from changing receptors or using CRISPR-Cas systems. Therefore, phage cocktails against many bacterial receptors or unique phages resistant to defenses may be used to handle this issue (Jang et al., 2020).

CONCLUSION

It is shown in this study that phage therapy can be considered either a good alternative or a beneficial addition to conventional antibiotics for resolving infections caused by multidrug-resistant (MDR) Klebsiella pneumoniae bacteria. Because antibiotics like meropenem and colistin are now being fought by bacteria, it is obvious that established treatments are inadequate and that new ones are vital. In both relation to experiments in lab and living animals, phage treatment displayed strong specificity, effectiveness and a unique ability to protect the microbiota. These free bacteriophages showed strong lytic behavior, could attack many kinds of bacteria and remained steady under typical living conditions, indicating they are fit for use in medicine. According to both in vitro and in vivo experiments, therapeutic use of phages alone reduced bacterial populations and when combined with antibiotics these effects were further enhanced, showing that dual therapy can improve results and limit the development of resistance. Besides, using phage therapy leads to much less disruption to the host microbiota compared to using antibiotics. This helps maintain the patient's health and prevents new infections. Synergy was observed in most combinations of phages and antibiotics in checkerboard test experiments, with all values falling within suggested FICI ranges. Although phage resistance and lysogenic conversion are constant threats, new discoveries in phage engineering, monitoring and mixing solutions continue to help find effective responses. These findings suggest that phage therapy should become part of the usual infectious disease treatment and this is especially important for cases of multidrug-resistant infections. It will be important to do more clinical studies, establish reliable regulations and use translational research to match what is found in experiments with real treatments. Phage therapy is able to fight the problem of multidrug-resistance and plays a key role in advancing precision medicine against infections.

REFERENCES

APA · American Psychological Association 7th edition

Bae, D., Lee, J.-W., Chae, J. P., Kim, J.-W., Eun, J.-S., Lee, K.-W., & Seo, K. (2020). Characterization of a novel bacteriophage φCJ22 and its prophylactic and inhibitory effects on necrotic enteritis and Clostridium perfringens in broilers. Poultry Science, 100(1), 302.

Bardenhorst, S. K., Hagenfeld, D., Matern, J., Prior, K., Harks, I., Eickholz, P., Lorenz, K., Kim, T., Kocher, T., Meyle, J., Kaner, D., Jockel-Schneider, Y., Harmsen, D., & Ehmke, B. (2024). The role of the oral microbiota in the causal effect of adjunctive antibiotics on clinical outcomes in stage III–IV periodontitis patients. Microbiome, 12(1).

Borrego, J. J., & Lanzas, J. I. (2022). Fagoterapia ¿Un tratamiento alternativo a los antibióticos usados en la acuicultura? Encuentros En La Biología, 15(183), 19.

Chang, D., Sharma, L., Cruz, C. S. D., & Dong, Z. (2021). Clinical Epidemiology, Risk Factors, and Control Strategies of Klebsiella pneumoniae Infection [Review of Clinical Epidemiology, Risk Factors, and Control Strategies of Klebsiella pneumoniae Infection]. Frontiers in Microbiology, 12. Frontiers Media.

Cruz, F. de P. N., Bogas, A. C., & Sousa, C. P. de. (2021). Light and Phages on Tackle of Infectious Diseases. In IntechOpen eBooks. IntechOpen.

Du, J., Meile, S., Baggenstos, J., Jäggi, T., Piffaretti, P., Hunold, L., Matter, C. I., Leitner, L., Kessler, T. M., Loessner, M. J., Kilcher, S., & Dunne, M. (2023). Enhancing bacteriophage therapeutics through in situ production and release of heterologous antimicrobial effectors. Nature Communications, 14(1).

Effah, C. Y., Sun, T., Liu, S., & Wu, Y. (2020). Klebsiella pneumoniae: an increasing threat to public health [Review of Klebsiella pneumoniae: an increasing threat to public health]. Annals of Clinical Microbiology and Antimicrobials, 19(1). BioMed Central.

Escobar, J. C. C. (2022). Antibióticos vs fagos ¿virus amigos? Encuentros En La Biología, 15(181), 25.

ESMER, E., BAYRAK, R., KÜÇÜKDUMAN, Y., & Başaran, P. (2021). Gıda teknolojilerinde inovatif bir yaklaşım olarak "Bakteriyofajlar." European Journal of Science and Technology.

Fang, Q., & Zong, Z. (2022). Lytic Phages against ST11 K47 Carbapenem-Resistant Klebsiella pneumoniae and the Corresponding Phage Resistance Mechanisms. mSphere, 7(2).

Ferriol-González, C., & Domingo-Calap, P. (2021). Phage Therapy in Livestock and Companion Animals [Review of Phage Therapy in Livestock and Companion Animals]. Antibiotics, 10(5), 559. Multidisciplinary Digital Publishing Institute.

Gençay, Y. E., Jasinskytė, D., Robert, C., Semsey, S., Martínez, V., Petersen, A. Ø., Brunner, K., Torio, A. D. S., Salazar, A., Turcu, I. C., Eriksen, M. K., Koval, L., Takos, A. M., Pascal, R., Schou, T. S., Bayer, L., Bryde, T., Johansen, K. C., Bak, E. G., … Sommer, M. O. A. (2023). Engineered phage with antibacterial CRISPR–Cas selectively reduce E. coli burden in mice. Nature Biotechnology, 42(2), 265.

Gkartziou, F., Giormezis, N., Spiliopoulou, I., & Antimisiaris, S. G. (2021). Nanobiosystems for Antimicrobial Drug-Resistant Infections [Review of Nanobiosystems for Antimicrobial Drug-Resistant Infections]. Nanomaterials, 11(5), 1075. Multidisciplinary Digital Publishing Institute.

Goswami, A., Sharma, P. R., & Agarwal, R. (2021). Combatting intracellular pathogens using bacteriophage delivery. Critical Reviews in Microbiology, 1.

Hatfull, G. F. (2022). Phage Therapy for Nontuberculous Mycobacteria: Challenges and Opportunities [Review of Phage Therapy for Nontuberculous Mycobacteria: Challenges and Opportunities]. Pulmonary Therapy, 9(1), 91. Adis, Springer Healthcare.

Huy, T. X. N. (2024). Overcoming Klebsiella pneumoniae antibiotic resistance: new insights into mechanisms and drug discovery. Beni-Suef University Journal of Basic and Applied Sciences, 13(1).

Jang, I., Yang, M., Kim, H., & Park, J. (2020). Novel Cytoplasmic Bacteriocin Compounds Derived from Staphylococcus epidermidis Selectively Kill Staphylococcus aureus, Including Methicillin-Resistant Staphylococcus aureus (MRSA). Pathogens, 9(2), 87.

Jung, H.-J., Sorbara, M. T., & Pamer, E. G. (2021). TAM mediates adaptation of carbapenem-resistant Klebsiella pneumoniae to antimicrobial stress during host colonization and infection. PLoS Pathogens, 17(2).

Kirsch, J. M., Brzozowski, R., Faith, D. R., Round, J. L., Secor, P. R., & Duerkop, B. A. (2021). Bacteriophage-Bacteria Interactions in the Gut: From Invertebrates to Mammals [Review of Bacteriophage-Bacteria Interactions in the Gut: From Invertebrates to Mammals]. Annual Review of Virology, 8(1), 95. Annual Reviews.

Lazăr, V., Oprea, E., & Dițu, L.-M. (2023). Resistance, Tolerance, Virulence and Bacterial

Pathogen Fitness—Current State and Envisioned Solutions for the Near Future [Review of Resistance, Tolerance, Virulence and Bacterial Pathogen Fitness—Current State and Envisioned Solutions for the Near Future]. Pathogens, 12(5), 746. Multidisciplinary Digital Publishing Institute.

Li, J., Shi, Y., Song, X., Yin, X., & Liu, H. (2025). Mechanisms of Antimicrobial Resistance in Klebsiella: Advances in Detection Methods and Clinical Implications [Review of Mechanisms of Antimicrobial Resistance in Klebsiella: Advances in Detection Methods and Clinical Implications]. Infection and Drug Resistance, 1339. Dove Medical Press.

Li, Y., Kumar, S., Zhang, L., Wu, H., & Wu, H. (2023). Characteristics of antibiotic resistance mechanisms and genes of Klebsiella pneumoniae [Review of Characteristics of antibiotic resistance mechanisms and genes of Klebsiella pneumoniae]. Open Medicine, 18(1). De Gruyter Open.

Lopatina, A., Tal, N., & Sorek, R. (2020). Abortive Infection: Bacterial Suicide as an Antiviral Immune Strategy [Review of Abortive Infection: Bacterial Suicide as an Antiviral Immune Strategy]. Annual Review of Virology, 7(1), 371. Annual Reviews.

Makky, S., Dawoud, A., Safwat, A., Abdelsattar, A. S., Rezk, N., & El-Shibiny, A. (2021). The bacteriophage decides own tracks: When they are with or against the bacteria [Review of The bacteriophage decides own tracks: When they are with or against the bacteria]. Current Research in Microbial Sciences, 2, 100050. Elsevier BV.

Maunders, E. A., Ganio, K., Hayes, A. J., Neville, S. L., Davies, M. R., Strugnell, R. A., McDevitt, C. A., & Tan, A. (2022). The Role of ZntA in Klebsiella pneumoniae Zinc Homeostasis. Microbiology Spectrum, 10(1).

Mdarhri, H. A., Benmessaoud, R., Yacoubi, H., Seffar, L., Assimi, H. G., Hamam, M., Boussettine, R., Filali-Ansari, N., Lahlou, F. A., Diawara, I., Ennaji, M. M., & Mohamed, K.-H. (2022). Alternatives Therapeutic Approaches to Conventional Antibiotics: Advantages, Limitations and Potential Application in Medicine [Review of Alternatives Therapeutic Approaches to Conventional Antibiotics: Advantages, Limitations and Potential Application in Medicine]. Antibiotics, 11(12), 1826. Multidisciplinary Digital Publishing Institute.

Nicolas, M., Trotereau, A., Culot, A., Moodley, A., Atterbury, R. J., Wagemans, J., Lavigne, R., Velge, P., & Schouler, C. (2023). Isolation and Characterization of a Novel Phage Collection against Avian-Pathogenic Escherichia coli. Microbiology Spectrum, 11(3).

Peng, H., Borg, R. E., Dow, L. P., Pruitt, B. L., & Chen, I. A. (2020). Controlled phage therapy by photothermal ablation of specific bacterial species using gold nanorods targeted by chimeric phages. Proceedings of the National Academy of Sciences, 117(4), 1951.

Qin, K., Shi, X., Yang, K., Xu, Q., Wang, F., Chen, S., Xu, T., Liu, J., Wen, W., Chen, R., Liu, Z., Li, C., & Zhou, K. (2024). Phage-antibiotic synergy suppresses resistance emergence of Klebsiella pneumoniae by altering the evolutionary fitness. mBio, 15(10).

Rima, M., Rima, M., Fajloun, Z., Sabatier, J., Bechinger, B., & Naas, T. (2021). Antimicrobial Peptides: A Potent Alternative to Antibiotics [Review of Antimicrobial Peptides: A Potent Alternative to Antibiotics]. Antibiotics, 10(9), 1095. Multidisciplinary Digital Publishing Institute.

Rodriguez-Gonzalez, R. A., Leung, C. Y., Chan, B. K., Turner, P. E., & Weitz, J. S. (2020). Quantitative

Models of Phage-Antibiotic Combination Therapy. mSystems, 5(1).

Shahin, H. H., Baroudi, M., Dabboussi, F., Ismail, B., Salma, R., Osman, M., & Omari, K. E. (2025). Synergistic Antibacterial Effects of Plant Extracts and Essential Oils Against Drug-Resistant Bacteria of Clinical Interest. Pathogens, 14(4), 348.

Shkoporov, A. N., Turkington, C., & Hill, C. (2022). Mutualistic interplay between bacteriophages and bacteria in the human gut [Review of Mutualistic interplay between bacteriophages and bacteria in the human gut]. Nature Reviews Microbiology, 20(12), 737. Nature Portfolio.

Singha, B., Singh, V., & Soni, V. (2024). Alternative therapeutics to control antimicrobial resistance: a general perspective. Frontiers in Drug Discovery, 4.

Śliwka, P., Ochocka, M., & Skaradzińska, A. (2021). Applications of bacteriophages against intracellular bacteria [Review of Applications of bacteriophages against intracellular bacteria]. Critical Reviews in Microbiology, 48(2), 222. Taylor & Francis.

Sutcliffe, S. G., Reyes, A., & Maurice, C. F. (2023). Bacteriophages playing nice: Lysogenic bacteriophage replication stable in the human gut microbiota. iScience, 26(2), 106007.

Szymczak, M., Pankowski, J. A., Kwiatek, A., Grygorcewicz, B., Karczewska-Golec, J., Sadowska, K., & Golec, P. (2024). An effective antibiofilm strategy based on bacteriophages armed with silver nanoparticles. Scientific Reports, 14(1).

Tamar, E. S., & Kishony, R. (2022). Multistep diversification in spatiotemporal bacterial-phage coevolution. Nature Communications, 13(1).