Review of Bacteriophages as a Targeted Solution to Antibiotic Resistance and Multidrug Resistant (MDR) Infections

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INTRODUCTION

- Antibiotics are a revolutionary way to treat bacterial infections; however, their widespread use has led to antibiotic resistance due to overuse in healthcare and agricultural industries.
- This resistance leads to the development of multidrug-resistant (MDR) bacteria.
- Bacteriophages are viruses that target and kill bacteria. They can be seen as an alternative to antibiotics with advantages such as specificity and low impact on microbiota. The effectiveness of such treatments can be increased using bacteriophage cocktails or in combination with antibiotics.

OBJECTIVE

- Review research on using bacteriophage therapy as an alternative to antibiotics to treat multidrug-resistant (MDR) bacterial infections. '
- Review the methods and results for combinations of phages and antibiotics, along with bacteriophage cocktails, to see if bacteriophages are a viable alternative.

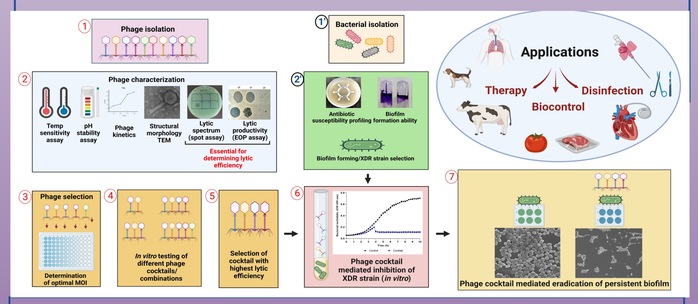

Figure 1: This figure shows the general process used to test the effectiveness of phages. This specific example represents how the first phages are isolated, then characterized using many different methods, and then the phages are selected. The testing of these phages is then done in vitro, where the phage cocktail with the highest lytic efficiency is selected. Separately, bacteria are also isolated, and then the combined phage cocktail is evaluated, and imaging is used to visually assess the biofilms before and after the treatment. (Medhavi Vashisth et al., 2023)

ACKNOWLEDGMENTS

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METHODS AND MATERIALS

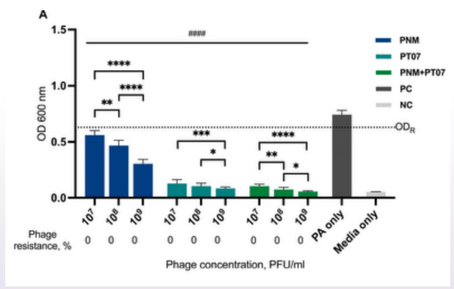
For this literature review, databases such as PubMed, UW library, and ScienceDirect were used to find 20 primary research articles. These articles were all within the last 10 years and included keywords such as "bacteriophage therapy", "antibiotic resistance", and "phage cocktails". The articles were then analyzed for their relevance to using bacteriophages to treat MDR infections.

RESULTS

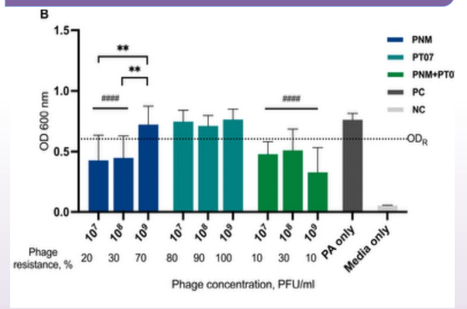
- Bacteriophages are effective against MDR bacteria, for example, *Pseudomonas aeruginosa* and *Staphylococcus aureus* (Banar et. al., 2025; Racenis et al., 2023).
- Phage cocktails can be customized for a wider range of protection to reduce resistance (Banar et al., 2025).
- Using a combination of phages and antibiotics to reduce the development of resistance. It was found that using just phages only reduced bacterial counts by 2.5 log10 CFU; however, with a combination of phages and antibiotics, the reduction was 4.0 log10 CFU over 24 hours (Berryhill et al., 2021).
- Phages can co-evolve with bacteria, which helps prevent antimicrobial resistance.

REFERENCES

A) Bacterial Growth Suppression 12 hrs



B) Bacterial Growth Suppression 24 hrs



- 54-year-old male with *P. aeruginosa* LVAD driveline infection
  - Treated with lytic antipseudomonal phages (PNM and PT07) intravenously and locally.
- Figure 2 shows the bacterial growth suppression of PNM, PT07, and a combination of the two against PAP01 while trying to remove biofilms.
- Positive Control = Untreated PAP01 & Negative Control = Media Only
- Figure 2A: No phage resistance and success in eradication. Phage susceptibility decreased for phages PT07 at 10^8pfu/mL, PNM at 10^7, PT07+PNM at 10^8, and PT07+PNM at 10^8.
- Figure 2B: Furthermore, phage-resistant strains evolved after 24 hours.
- Figure 2C: MBEC or Minimum Biofilm Eradication Concentration was also shown for the three variants. The lowest concentration of the phages that will kill microbial biofilm. None of the phages were successful in preventing biofilm formation

C) Minimum Biofilm Eradication Concentration

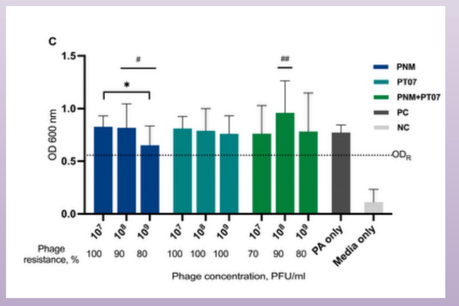


Figure 2: These figure panels show how the phages PNM and PT07 were used to prevent *Pseudomonas aeruginosa* PAP01 growth and remove biofilms. MBEC values, along with statistical differences, were also presented to show treatment effectiveness (phage resistance). (Racenis et al., 2023)

- Planktonic cell growth over 12 hrs decreased for all phages/concentrations, after 24 hrs, only PNM had less growth
- Biofilm eradication was not achieved, as resistance developed 70-100% for PNM, PT07, and their combinations at various concentrations
- The two phages combined with surgical treatment had the best outcome for treating LVAD-associated infections.

FUTURE DIRECTIONS

- Need additional research to focus on the effectiveness, safety, and use of bacteriophage therapy.
- Setting guidelines for clinical applications
- Enhancing phage and cocktail selection for specific infections
- Understand if/how phage resistance occurs so it can be prevented before it becomes widespread
- Understand the effects of phages on the human immune system, although much of the testing is done on animal models.