Feasibility of Phage Therapy as a Targeted Approach Against Periodontal Disease

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Introduction & Background

- **Periodontal disease is a chronic inflammatory condition** caused by bacterial biofilms that damage gum tissue and bone. It's one of the most common oral diseases worldwide and is linked to heart disease, diabetes, Alzheimer's, and poor pregnancy outcomes.

- **Disruptive keystone bacteria like *P. gingivalis, F. nucleatum*, *A. actinomycetemcomitans*, and *S. gordonii*** (and others) destabilize the oral microbiome and maintain chronic inflammation. Their persistent presence prevents healing and fuels ongoing tissue damage.

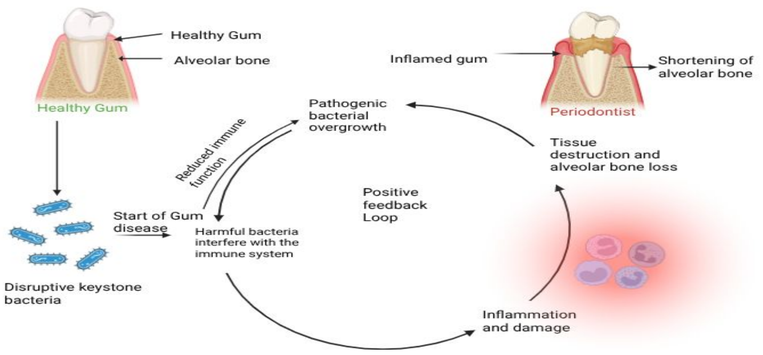


Figure 1: Progression of Periodontal Disease (created with BioRender.)

Standard treatments like subgingival cleaning manage symptoms but don't address the root cause.

- These methods often can't fully remove biofilms, making relapse likely and long term disease control difficult.

Antibiotics are becoming less effective

- Bacteria like *P. gingivalis* and *A. actinomycetemcomitans* develop resistance. This limits treatment options and complicates management of advanced periodontitis. Resistance rates are as high as 55% for doxycycline and 30% for metronidazole have been observed from chronic periodontitis patients in the United States (*Rams et al 2013*)

Bacteriophage therapy offers an alternative precise and effective solution.

- Phages can target specific pathogens without harming beneficial bacteria and are better at penetrating biofilms than antibiotics. Though still in early research and results show strong promise for clinical application.

Materials & Methods

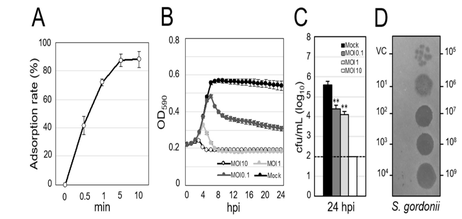
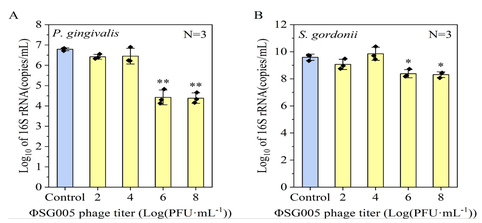
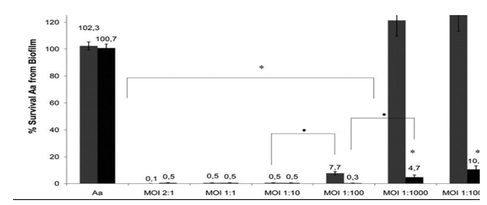
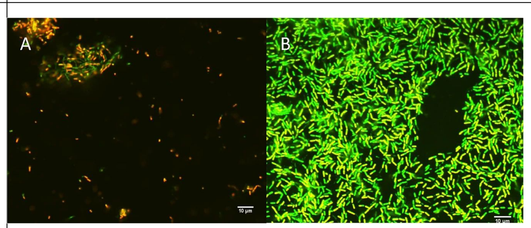
- This project used a structured literature review to evaluate the feasibility of phage therapy as a targeted approach against periodontal disease.

- Research articles came from PubMed, ScienceDirect, and the ASM Journal database. The search used combinations of "bacteriophage therapy," "phage," "periodontal pathogens", and "biofilm".

- There was a variety of primary research articles were reviewed to examine phage performance, assess their impact on periodontal bacteria, and highlight main results reported across studies.

Results

Table 1

Figure 2: *S. gordonii*, phage ΦSG005 Phage ΦSG005 achieved near complete growth suppression within 24 hours at MOI 10, with significant reductions even at lower MOIs (Fujiki et al. 2021).	 *Fujiki et al (2021). Reprinted from original publication.*
Figure 3: ΦSG005 Indirect effect on *P. Gingivalis* ΦSG005 suppressed *S. gordonii* growth within 24 hours and indirectly reduced *P. gingivalis* by over 99 percent by disrupting co-aggregation partners (Fujiki et al. 2021, Wu et al. 2024).	 *Reprinted with permission from Wu et al. (2024)*
Figure 4: *A. actinomycetemcomitans* bacteriophage AabΦ01 High MOI phage treatment greatly decreases *A. actinomycetemcomitans* survival in biofilms with asterisks marking significant drops vs. control (Castillo-Ruiz et al., 2011).	 *Reprinted with permission from Castillo-Ruiz et al. (2011)*
Figure 5: *F. nucleatum* phage FNU1 Kabwe et al. (2019) reported that phage FNU1 cut *F. nucleatum* biofilm biomass by about 70% in 24 hours, and imaging showed a shift from live to dead cells.	 Kabwe et al. (2019) *Reprinted from original publication.*

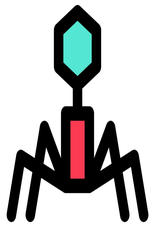
Discussion

- *In vitro* studies show strong phage activity against major periodontal pathogens, even within lab grown biofilms.
- These reductions suggest phages could complement current treatments by targeting species that support biofilm structure and disease progression.
- Phages show narrow host ranges and target specific bacteria while avoiding beneficial ones, which makes them a safe and focused treatment option.
- Overall, bacteriophage therapy appears to be a feasible alternative approach for periodontal care supported by strong *in vitro* results and targeted action.

Limitations

- Clinical trials are expensive and phages have a negative perception
- Immune responses vary unpredictably
- Manufacturing and storing phages is technically difficult
- Phages behave differently in real clinical bacterial strains vs lab strains
- Bacteria evolve resistance to phages. These issues make large trials complicated and costly.

Advantages



- Phages are generally safe and very targeted.
- They can work against antibiotic-resistant bacteria.
- You can engineer bacteriophages to be more effective by helping them last longer, target additional bacterial strains, or break through biofilms more easily.

Future work

- Advance *in vivo* models using rat periodontitis to test phage persistence, biofilm penetration, dosing, and stability in realistic oral environments.
- Develop delivery systems that withstand oral environmental stress, drawing on encapsulation methods used in pulmonary and gastrointestinal phage delivery from previous studies.
- Monitor phage bacteria coevolution to track resistance, guide adaptive phage libraries, and ensure recovery of beneficial oral microbes.
- Design early human trials modeled after successful previous phage studies, using periodontal endpoints like pocket depth, attachment level, and inflammatory markers.

Acknowledgment

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- I also extend my appreciation to Dr. Jutta Heller for supporting me during this project and getting us ready to present.

References