

Bacteriophage therapy: A potentially effective tool in combatting tooth decay

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Caries of dental hard tissues is a multifaceted biofilm illness that spreads easily and occurs because of longstanding low pH in the oral cavity. This causes the teeth to lose net amount of minerals and is the most prevalent health condition worldwide and a significant healthcare issue.¹ Regular carbohydrate intake causes the biofilm microbiota in the mouth to change from its normal condition of preserving equilibrium to one that is acidogenic, aciduric, and cariogenic, which ultimately results in dental cavities.² The biofilm, which is constantly active with low pH changes, boosts the caries process.³ Unbalanced ecology in the stable oral microbiome also leads to the development of caries. Significant variations in protein expression throughout time and under genetic control seem to have an impact on the formation of biofilms.⁴

Since it can be treated with both invasive and non-invasive procedures, existing treatments are insensitive and non-species-specific and kill both pathogenic and commensal species that prevent the formation of pathogenic biofilms. Despite significant scientific advancements, dental caries, driven by various pathogenic bacterial species, remains a costly ailment. A primary bacterium responsible for inducing caries is *Streptococcus mutans*,⁵ although current conventional treatments do not have any specific antibacterial action against the causative agent of caries, *S. mutans*. Therefore, preventing the growth of *S. mutans* and the creation of biofilms may postpone the development of caries.

Many treatment and preventive modalities are proposed in order to prevent and treat dental caries.⁶ One of the contemporary therapies of the innovative technological era is phage (or bacteriophage) therapy, which is a potentially effective substitute strategy. Bacteriophages are viruses that do not infect commensal bacterial cells but only infect a limited strain of bacteria. Phages hijack the cellular machinery of the host bacterium once they recognize it and inject their genetic material, causing cell lysis. Phage targeting cariogenic bacteria also benefits greatly from phages' capacity to break through and disturb biofilms. Therefore, phage therapy is emerging as an alternative approach towards the management of bacterial

infection. Since phages participate in predator-prey interplay with bacteria, a natural check on microbial fluctuations is exerted by their presence. This makes the phage a very potential antibacterial agent with therapeutic value. Special mention has to be given to the plasmid-specific phages that are known to be efficacious in biofilm; they can be easily identified and therefore manipulated easily, thus making them tremendous tools for targeted bacterial therapies.⁷

A rising body of evidence indicates that bacteriophages may play a noteworthy role in the pathogenesis of some oral infections. Here, we review complex evolutionary interactions among bacteriophages, bacteria, and eukaryotic cells within the oral microbiome, with special emphasis on how such interactions lead to the development of anti-phage resistance and the influence on biofilm behaviour. We outline specific bacteriophages and their characteristic targeting pathogens involved in periodontal disease, dental caries, and endodontic infections based on our analysis of different oral diseases. Like other branches of medicine, the field of dentistry with phage therapy looks quite promising for both practical application and scientific study. These viruses are strain-specific against biofilm-forming bacteria, and they are treatable in a wide spectrum of treatment regimens, which makes this therapy probably revolutionary because it could definitely deal with long-standing difficulties of dental care like antibiotics' resistance and biofilm-related infections. Additionally, phage lysins are bacteriophage enzymes that cause lysis of the bacterial cell wall and have novel approaches to combatting antibiotic-resistant pathogens.⁸ These lysins are selective, targeting bacterial cells directly, thus providing an innovative alternative to overcome mechanisms of resistance that compromise conventional antibiotic therapies. Altogether, phage therapy and associated tools, such as lysins, may be a pivot for advancing antibacterial strategies within dentistry and beyond.

The phage therapy is effective against oral bacteria which may be correlated with dental caries, periodontal diseases and bacteria persistently causing infections in the endodontically treated teeth. The bacteriophage provides a promising role against *E. faecalis*, the primary species implicated in secondary, persistent infections subsequent to failed root canal treatments. In the case of Phage

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SMHBZ,⁸ it proved to target the main agent that causes dental caries, thereby reducing biofilm formation, enamel demineralization, and protection of the dentine structure against secondary decay. The lysis of pathogenic *Aggregatibacter actinomycetemcomitans*, which is responsible for resistant periodontal infections, occurred when lysogenic phage S1249 was incubated with human serum. Phage PEf771 presented higher antibacterial activity and substantively against the common agent for secondary infections post root canal treatment, namely, *Enterococcus faecalis*, hence promising a refractory periapical periodontitis treatment in cases where the conventional treatment failed. This altogether concludes the promising perspectives of phage therapy against resistive oral and dental infections.⁹ The efficiency of phages targetting recalcitrant infections situates them as an efficient adjunct or alternative to existing treatments for endodontic care, opening a new horizon for possibilities of more promising clinical outcomes for complex dental infections.

With antibiotic resistance burgeoning so alarmingly, it becomes obvious that alternative therapies like phage therapy, especially the specificity and biosafety profile of this therapy, make it particularly promising. Novel techniques to isolate lytic bacteriophages, purify lysins, and sequence bacterial pathogenicity islands within lysogenic phages have opened a new door, thus showing the way for even more specific and potent therapies. Such phage treatments might probably call for further explorations into the genetic and molecular mechanisms controlling phage-bacteria interactions, particularly for such bacteria as *Streptococcus mutans*, where dental caries is a key disease involved. Such strong empirical evidence might pave the way to far more innovative and tailored therapies for a radical transformation in oral health.¹⁰

The urgent demand for the alternative approach in dentistry underscores the research of phage therapy. Harnessing the power of precision and adaptability, phages could revolutionize dental care, tackle persistence, and curb antibiotic resistance in clinical settings.

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References

1. Kutsch VK. Dental caries: an updated medical model of risk assessment. *J Prosthet Dent.* 2014;111:280-5. doi: 10.1016/j.prosdent.2013.07.014. Epub 2013 Dec 10. PMID: 24331852.
2. Schwendicke F, Frencken JE, Bjørndal L, Maltz M, Manton DJ, Ricketts D, et.al. Managing Carious Lesions: Consensus Recommendations on Carious Tissue Removal. *Adv Dent Res.* 2016;28:58-67. doi: 10.1177/0022034516639271. PMID: 27099358.
3. Kidd EA. Clinical threshold for carious tissue removal. *Dent Clin North Am.* 2010;54:541-9. doi: 10.1016/j.cden.2010.03.001. PMID: 20630195.
4. Struzycka I. The oral microbiome in dental caries. *Pol J Microbiol.* 2014;63:127-35. PMID: 25115106.
5. Kashif M, Ashar A. Important Microbes in Dentistry. 2024. Available at: <https://www.doi.org/10.58532/nbenurmmch22>. Cited on 13. January, 2025
6. Kashif M, Kazmi M. A New Frontier in Oral Health: Unraveling the Efficacy of Probiotic Metabolites vs. Chlorhexidine on *Streptococcus mutans* in Dental Plaque. *J Pak Med Assoc.* 2024;74:430-1.
7. Shlezinger M, Khalifa L, Hourri-Haddad Y, Copenhagen-Glazer S, Resch G, Que YA, et.al. Phage Therapy: A New Horizon in the Antibacterial Treatment of Oral Pathogens. *Curr Top Med Chem.* 2017;17:1199-1211. doi: 10.2174/1568026616666160930145649. PMID: 27770768.
8. Hooshiar MH, Salari S, Nasiri K, Salim US, Saeed LM, Yasamineh S, et.al. The potential use of bacteriophages as antibacterial agents in dental infection. *Virology.* 2024;21:258.
9. Flood M, Patel D, Herring K. The Use of Phage Therapy in Reduction of Oral Cavity Bacteria: A Literature Review. *Dent Rev.* 2024;4:100115.
10. Chen Z, Guo Z, Lin H, Tian Y, Zhang P, Chen H, et.al. The feasibility of phage therapy for periodontitis. *Future Microbiol.* 2021;16:649-56.