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REVIEW

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Bacteriophages of *Mycobacterium tuberculosis*, their diversity, and potential therapeutic uses: a review

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Abstract

Tuberculosis (TB) caused by *Mycobacterium tuberculosis* (*M. tuberculosis*) is a highly infectious disease and worldwide health problem. Based on the WHO TB report, 9 million active TB cases are emerging, leading to 2 million deaths each year. The recent emergence of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) strains emphasizes the necessity to improve novel therapeutic plans. Among the various developing antibacterial approaches, phage therapy is thought to be a precise hopeful resolution. Mycobacteriophages are viruses that infect bacteria such as *Mycobacterium* spp., containing the *M. tuberculosis* complex. Phages and phage-derived proteins can act as promising antimicrobial agents. Also, phage cocktails can broaden the spectrum of lysis activity against bacteria. Recent researches have also shown the effective combination of antibiotics and phages to defeat the infective bacteria. There are limitations and concerns about phage therapy. For example, human immune response to phage therapy, transferring antibiotic resistance genes, emerging resistance to phages, and safety issues. So, in the present study, we introduced mycobacteriophages, their use as therapeutic agents, and their advantages and limitations as therapeutic applications.

Keywords: *Mycobacterium tuberculosis*, Drug resistance, Mycobacteriophages, Phage therapy

Background

Tuberculosis (TB) caused by *Mycobacterium tuberculosis* (*M. tuberculosis*) is a highly infectious disease and worldwide health problem, with a high mortality rate and nearly ~ 1.6 million recognized deaths in 2021. It has harmed humankind for approximately 9000 years, with the first report dating back more than 3000 years ago in India and China [1, 2]. TB had a notable effect on social health owing to decreased influence and a more negligible therapeutic effect with mycobacterial therapy. The quick prevalence of disease and the warning development of drug resistance, particularly the appearance of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) strains, have called the alarm to gain novel effective drugs; thus, finding a substitute line for the controlling and management of TB has become essential. One of the main features of *Mycobacterium* is that it produces highly resistant mutants under selective pressure conditions caused by antibiotics. The following evolutionary achievement of resistant mutants depends mostly on the mutant's resistance rate and ability and selective elimination owing to antibiotic therapy. Among the various developing antibacterial approaches, phage therapy is thought to be a precise hopeful resolution. Bacteriophages (phages) are a type of viruses that infect bacteria and are very widespread in the environment. Bacteriophages can be used clinically

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