



Bacteriophage Antimicrobial Therapeutics Potential

Abdu Kaif*

Department of Biology, USA

*Corresponding Author's E-mail: kaifabdu@rediff.com

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Abstract

The discovery of antibiotics has trailed substantially behind the emergence of resistant species. Only 8 new antibiotics were authorised by the US Food and Drug Administration between 2010 and 2015. Seven have comparable modes of action to medicines that are presently on the market. However, historical experience with antibiotics such as linezolid, levofloxacin, and ceftaroline should temper optimism as resistant organisms to each of these medications arose within a year or less following their introduction (Anpilov et al., 1984).

INTRODUCTION

New methods of antibiotic treatment must prevent alteration of the gut flora in addition to resistance. It has been established that dysbiosis, or disruption of the gut microbiome, contributes to the development of tumours, multiple sclerosis, obesity, heart disease, and neurological disorders. However, superinfection with *Clostridium difficile*, an organism that causes around 500,000 illnesses and 29,000 fatalities each year in the US, is the most severe and immediate consequence of dysbiosis. The novel antimicrobial drugs that target pathogenic bacterial species without inducing dysbiosis will be the most potent ones. Because of the concurrent rise in immunosuppressed patients, the advent of pathogenic bacteria resistant to the majority, if not all, presently available antimicrobial medicines has become a serious issue in modern medicine (Badran 1994). The fear that humanity is reentering the "preantibiotics" age is now quite serious, and modern medicine and biotechnology now place a high priority on the development of new antiinfection methods.

It was proposed that the injection of bacteriophages may prevent and/or treat bacterial illnesses before the discovery and widespread use of antibiotics. Phage use persisted in the former Soviet Union and Eastern Europe despite the fact that early clinical trials using bacteriophages were not extensively pursued in the United States and Western Europe. The findings of these research were widely disseminated in publications that were not written in English

(mainly Russian, Georgian, and Polish), and as a result, the western scientific community did not easily have access to them. In this minireview, we review the most current literature with a focus on trials done in Poland and the former Soviet Union, and we briefly outline the history of bacteriophage discovery and the early clinical investigations using phages (Adamia et al., 1990). We also go into the reasons why bacteriophage clinical usage failed to catch on in the West and offer our opinions on the possibilities for phage therapeutic research going forward.

BACTERIOPHAGES AS ANTI-MICROBIALS

Other options are required as antimicrobial resistance nears a critical point. Lytic bacteriophage, bacterial viruses that attack and infect a specific type of bacteria, could be a good substitute for antibiotics (Alisky et al., 1998). There has been a thorough assessment of the literature on the use of bacteriophages to treat bacterial illnesses, which dates back approximately 100 years. Researchers reported using phages intravenously to successfully treat typhoid fever, cholera, and *Staphylococcus aureus* bacteremia in the early 1920s. At the Los Angeles County General Hospital, researchers treated 56 patients with type-specific phages throughout the course of a 10-year trial on the use of bacteriophages to treat typhoid fever, and 53 of them fully recovered. In a 1982 research, 48 patients with purulent lung illness who received intravenous *S. aureus* phages were contrasted with an antibiotic-treated control group. Those who got phages

recovered 95% of the time, compared to 64% of those who received antibiotic treatment (Carlton 1999).

Bacteriophages have all the characteristics of a perfect therapeutic agent since they can eliminate a microbial infection while still being safe for the patient. Recently, the effectiveness and safety of bacteriophage treatment have been examined. Although there haven't been any confirmed safety difficulties, the authors listed a number of possible phage therapy-related worries (Chernomordik 1989). First, it's possible that phages won't be there for long enough to completely eradicate the disease. However, Ochs et al. have demonstrated that it takes many days for bacteriophage X174 to be cleared. Researchers have also demonstrated that it is feasible to choose for bacteriophage variants that have a lengthy history of circulating. The potential for anaphylactic responses to injected phage is a second issue. No reports of this happening exist. Early studies reported shock-like reactions to phage injections, but this was caused by impurities in the medium the phage were cultured in (D'Herelle 1917). Therapeutic phages are now thoroughly purified from media constituents and lingering bacterial endotoxin. The potential for a catastrophic release of bacterial exo- and endotoxins during the quick lysis of bacteria by phages is a third area of worry. However, many antibiotics quickly lyse microorganisms, and from a therapeutic viewpoint, the side effects are both negligible and controllable. Single phages or phage mixes must undergo meticulously planned clinical studies in order to receive regulatory approval before they may be used as routine treatments for bacterial illnesses (D'Herelle 1930).

Although there are several reports of clinical uses of phage treatment in the literature, up to this point the study has been fragmented and has lacked both thorough controls and the number of patients necessary to prove its efficacy for a specific application (Hankin 1896). It is time to concentrate on offering the proof required to introduce phage treatment into clinical practise after 95 years of small-scale experiments and debates about its potential. Simple urinary tract infections may soon become frequently lethal if the scientific community does not make a determined effort to identify alternative treatments. The era of antibiotics is coming to an end (Eaton et al., 1934). However, lytic bacteriophage may have already offered the solution in the form of a gift from nature. Phage technology may be developed and understood to provide us the means to combat antibiotic-resistant bacteria.

CONCLUSIONS

In conclusion, bacteriophages have a number of qualities

that might make them desirable therapeutic agents. As evidenced by their extensive clinical use in Eastern Europe and the former Soviet Union as well as the commercial sale of phages in the United States in the 1940s, they are (i) highly specific and very effective in lysing targeted pathogenic bacteria, (ii) safe, and (iii) quickly modifiable to combat the emergence of newly arising bacterial threats. Furthermore, a substantial body of literature—some of which are addressed in this minireview—indicates that phages may function as potent therapeutic agents in specific clinical contexts. Although many of these research do not adhere to the strict requirements now required for clinical trials, there are still several significant issues that need to be resolved before lytic phages may be broadly accepted for therapeutic usage. However, we believe that there is enough evidence—and a pressing need—to pursue more research in the area of phage therapy in order to combat fast growing, antibiotic-resistant bacteria.

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