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BACTERIOPHAGE THERAPY: INNOVATIONS, MECHANISM, AND EMERGING APPLICATIONS IN MODERN MEDICINE

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Bacteriophages, viruses that specifically target and kill bacteria, are among the most prevalent organisms on Earth. This paper explores the expanding applications of bacteriophages, particularly in the context of phage therapy, where virulent phages are employed to combat bacterial infections. With the rising threat of antibiotic resistance, bacteriophages offer a promising alternative for treating bacterial diseases in humans and animals. Their use extends beyond healthcare, playing a significant role in biocontrol in health and food safety. Bacteriophages not only eliminate harmful bacteria but also contribute to the natural balance of microbial populations, influencing microbial evolution through horizontal gene transfer. Furthermore, their versatility has led to applications in biotechnology, including vaccine delivery, microbial detection, and the development of systems for protein and antibody display. The ease with which bacteriophages can be manipulated has made them valuable tools in both therapeutic and research settings. This paper also advocates for the growth of phage production companies and the use of phage cocktails, which combine multiple phages, to address diverse bacterial infections at various stages. The promising future of bacteriophage-based therapies and their potential to revolutionize the treatment of bacterial diseases is underscored throughout.

Keywords: Bacteriophage therapy, Antibiotic resistance, Phage cocktails, Biocontrol applications, Microbial evolution, Biotechnology innovation

INTRODUCTION

Viruses are considered intracellular parasites that require a specific host cell for reproduction. A type of virus that exclusively infects and multiplies within bacterial cells is known as a bacteriophage (1). Phages, viruses that are widespread in nature, were independently identified by Frederick Twort and Félix d'Hérelle in 1915 and 1917, respectively (2). These viruses consist mainly of nucleic acids encased in capsid proteins, and can be thought of as protein nanoparticles that carry their genetic material (3). Despite their structural simplicity, exhibit remarkable diversity and are the most abundant organisms on Earth. Found wherever bacteria exist, they are estimated to number around 10^{29}–10^{30} in the biosphere (4). They demonstrate high durability in natural environments and have the potential to reproduce rapidly within suitable hosts, contributing to the destruction of 20% to 40% of bacteria in marine ecosystems every 24 hours (5).

As natural antagonists of their bacterial hosts, bacteriophages are valuable allies in combating bacterial infections (6). Phages can replicate through three primary developmental pathways: lytic, lysogenic, and chronic modes. In the lytic cycle, a phage infects a bacterial cell by attaching to its envelope and injecting its RNA or DNA genome. This leads to phage gene expression, genome replication, and the production and assembly of new virions, which are released when the host cell undergoes lysis due to phage-encoded enzymes. Under metabolically unfavorable conditions like starvation, low energy level of cell some phages may enter a state called "pseudo-lysogeny," pausing their development until host metabolism resumes (7). The lysogenic cycle involves the integration of the phage genome into the host chromosome as a prophage or, less commonly, as a plasmid that replicates independently. If the lysogenic host faces environmental stress, such as DNA damage, the prophage may switch to the lytic mode to propagate. In the chronic, or permanent, infection mode, new virions are released from the host cell without immediate cell lysis; instead, the host eventually dies from energy depletion rather than lysis (8).

The bacteriolytic properties of bacteriophages have been utilized in antibacterial therapy since their discovery in 1917 (9). The post-World War II era, known as the "golden era" of antibiotic discovery, observed the identification of many antibiotic classes still in use today (10). Phages are increasingly recognized for their ability to target antibiotic-resistant bacteria, disrupt biofilms, and penetrate intracellular pathogens, making them promising alternatives to conventional antibiotics (11). As antibiotics are more

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strictly regulated in agriculture, bacteriophages are gaining popularity in some countries like Georgia, Russia and Poland as a viable alternative for controlling bacterial infections due to their unique bactericidal capabilities (12, 13).

Bacteriophage research has seen a resurgence due to the growing global threat of antibiotic resistance to human health (14). This revival has led to significant advancements in areas such as high-resolution microscopy, DNA manipulation, and sequencing technologies (15). In response to these challenges such competing bacteria, bacteriophages, and the presence of antibiotics, bacteria have developed sophisticated defense mechanisms that now also provide protection against antibiotics and other treatments. Horizontal Gene Transfer (HGT) plays a key role in genetic variation within species, with bacteriophages being major contributors to bacterial genome diversification. Other gene transfer processes include integrative plasmids and transposons (15). Phage display technology has been widely used in biotechnology, including immunological and biomedical applications (both in diagnostics and therapy), the creation of novel materials, and several biotechnology companies use phages therapy such as BiomX, PHAXIAM, PHIOGEN, and Bluephage (16, 17). Virus-like nanoparticles, many of which are derived from bacteriophages, are gaining attention due to their environmental ubiquity, abundance, and ability to invade bacteria, making them a promising group of structurally simple viral particles with nanoscale properties (18).

Phages possess unique features, such as their ability to facilitate protein-protein interactions, which make them ideal candidates for a wide range of beneficial applications, including in human and animal health, industry, food science, food safety, and agriculture. To fully harness the potential of phages in these applications, it is crucial to identify and characterize the proteins they produce. This enables their use in various functional processes, such as bacterial detection, drug delivery, vaccine development, and combating multidrug-resistant bacterial infections (15). Bacteriophages, also known as phages, have gained attention as a promising alternative for controlling pathogenic bacteria in food (19). Thus, this paper aims to investigate the role of bacteriophages in both pre-harvest and post-harvest applications, their use in treating bacterial infections, their potential in bacterial diagnostics, and their applications in medicine.

Application of Bacteriophages:

The virus's ability to target specific hosts makes it a promising tool for fighting bacterial infections and cleaning contaminated environments. While research is still ongoing, studies have shown successful use of viruses to treat diseases in humans, plants, animals, and aquatic life (20, 21). The use of bacteriophages to treat bacterial infections is known as bacteriophage therapy. With the rise of antibiotic resistance, there has been renewed interest in phages, natural bacterial predators discovered over a century ago. To be used therapeutically, phages must be lytic, efficiently kill the host bacteria, and be thoroughly characterized to avoid side effects. In the 1930s, phage therapy was widely used to treat bacterial infections in humans and animals, even before the development of penicillin (22).

a) Bacteriophages as Tools to Combat Antimicrobial Resistance (AMR)

The growing problem of antimicrobial resistance (AMR) is now widely acknowledged as a significant public health threat. Traditional antimicrobial drugs are losing their effectiveness, and the development of new antibiotics has slowed considerably. This has led to a surge in interest in alternative treatments for bacterial infections. Among these alternatives, bacteriophages are being rediscovered as a potentially promising option to help address the challenges posed by resistant bacterial infections (23). Before the discovery of antibiotics, bacteriophages were commonly used to treat a variety of bacterial infections, such as cholera, dysentery, typhoid fever, skin and surgical site infections, peritonitis, septicemia, and external otitis (24). Phage therapy began more than two decades before the first antibiotic was used clinically. However, the widespread introduction of broad-spectrum antibiotics in the 1940s quickly overshadowed and largely replaced the use of phages for therapeutic purposes in many parts of the world. Despite this, phage therapy continued to be utilized and developed in the Soviet Union and Eastern Europe, with its use still ongoing in countries such as Poland, Russia, and Georgia (25).

b) Therapeutic Applications of Bacteriophage

Bacteriophages, have been pivotal in advancing our understanding of the immune system, particularly in the context of phage therapy, the use of lytic phages to treat bacterial infections. Their influence extends to biotechnology, where engineered phages are utilized for applications such as epitope identification, antibody production, and the development of phage-based vaccines (26). Phages play a significant role in shaping adaptive immunity, particularly in humoral immunity and the polarization of effector responses. Through their impact on immune signaling, phages can modulate both the innate and adaptive immune responses such as cytokine release, T-cell modulation and significantly affect the course of bacterial infections (27). Initially recognized as small infectious agents capable of killing bacteria, phages have gained attention for their intrinsic antibiotic properties, leading to the development of phage therapy. In this approach, phages or phage cocktails are used to treat patients with bacterial infections. Beyond their direct antibacterial action, phages also activate the human immune system, promoting inflammation as a result of bacterial cell lysis. In this way, phages not only eliminate bacteria directly but also support the immune system's efforts to combat infections (28).

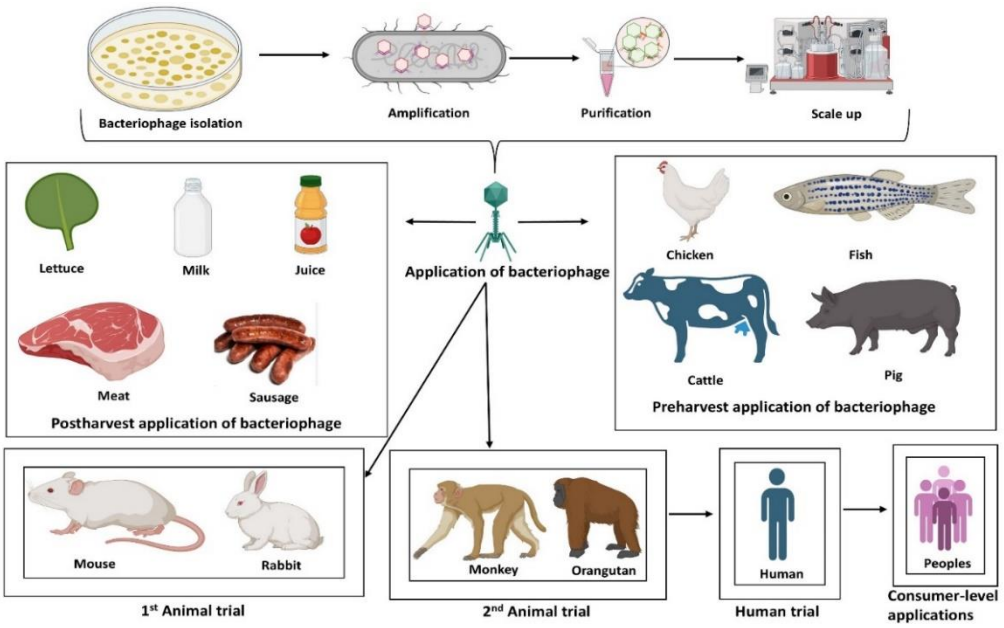

Figure 1: Isolation, enrichment, and preparation of bacteriophages for pre-harvest and post-harvest food safety applications, and for the treatment of infectious diseases.

(c) Advances in Bacteriophage Taxonomy

Bacteriophage genomes are highly diverse that vary greatly in size and type, and may contain genes with unknown functions (29). The proposed approach suggests using the family level as the unit of genomic diversity for phage taxonomy, aligning it with phage genetics, and recommends eliminating the order Caudovirales and the families Myoviridae, Podoviridae, and Siphoviridae as this genome based classifications provide a roadmap for the future (30, 31). These would be replaced by genome-based, monophyletic families, creating a more robust taxonomy to accommodate future research advancements (32). Phages are typically found in environments where their host bacteria thrive. For example, phages that target intestinal bacteria can be isolated from fecal samples, while phages that infect skin bacteria like Staphylococcus aureus are usually found in skin samples or wound exudates. However, identifying a specific phage can be challenging. For instance, phages targeting antibiotic-resistant *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* were easily isolated from sewage samples, but phages against Acinetobacter baumannii were much less common (28). Similarly, bacteriophages that target methicillin-resistant *Staphylococcus aureus* were rarely identified (33). Bacteriophages are gaining popularity as an alternative to antibiotics for managing bacterial infections. Their distinctive ability to kill bacteria makes them a promising option, especially as many countries are starting to limit the use of antibiotics in agriculture (12). Bacteriophages are being investigated for use in both pre-harvest and post-harvest food safety, where they help control bacterial contamination in food products. Furthermore, they are undergoing trials for potential human use in treating infectious diseases, as illustrated in Figure 1.

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Bacteriophages as Biocontrol Agents in Food

Pathogens present in food are widely recognized as a leading cause of foodborne illnesses, posing a significant global public health threat. In recent decades, considerable attention has been focused on identifying the microorganisms responsible for these illnesses and developing new methods for their detection. Foodborne pathogen identification technologies have advanced rapidly, with modern approaches primarily utilizing immunoassays, genome-wide techniques, biosensors, and mass spectrometry. Bacteriophages, along with probiotics and prebiotics, have been known for their ability to combat bacterial infections since the early 20th century (34). The One Health approach, which considers the interconnectedness of human, animal, and environmental health, is particularly relevant in addressing issues such as zoonotic diseases and antibiotic resistance (35). However, tackling these challenges is complex and requires a multi-faceted approach.

In recent years, *Salmonella* spp., pathogenic *Escherichia coli*, and *Listeria monocytogenes* have been implicated in most bacterial outbreaks related to foodborne illnesses, especially those associated with fresh produce (36). These outbreaks have been traced to various sources of contamination, both pre-harvest (e.g., soil, seeds, irrigation water, and animal fecal matter) and post-harvest (e.g., during storage, processing, and packaging). These pathogens possess multiple mechanisms that enable them to effectively attach, survive and colonize, allowing them to adapt to a range of environmental conditions (37, 38). The use of physicochemical methods for food preservation is essential for ensuring food safety, prolonging shelf life, and maintaining the quality of products (39). Ready-to-cook (RTC) foods generally require pre-treatment to

remove contaminants such as dirt and microbial loads, followed by the removal of inedible parts and processing into the desired shapes or cuts. Depending on the specific dish, additional processing steps like marination, frying, or fermentation may be applied before cooking. Due to the perishable nature of most RTC foods, antimicrobial treatments, packaging, and cold storage are critical to maximize shelf life. However, cleaning and sanitation practices often fail to maintain freshness and may even increase the risk of microbial contamination (40).

Heat pasteurization is a common method for disinfecting food products by killing pathogenic bacteria and reducing enzymatic activity (41). Another promising preservation technique is high-pressure processing (HPP), also known as high hydrostatic pressure or ultra-high-pressure processing. HPP is a non-thermal method that applies pressure (100–600 Megapascals) to food products, either solid or liquid, using a liquid medium to transmit the pressure. One of the key benefits of HPP is that it effectively inactivates bacteria and viruses without significantly altering the sensory qualities or nutritional content of the food (42). In recent years, food irradiation has also gained attention for its effectiveness in food preservation, sterilization, and the breakdown of harmful substances, showing great potential for broader application (43). The safety of vegetable based foods is often compromised by various factors, including improper or excessive use of sanitizers. There have been reports of individuals becoming ill after consuming raw vegetables, with outbreaks linked to pathogens on fresh produce becoming more common worldwide. These outbreaks have attracted considerable media attention and have negatively impacted the economic viability of vegetable farming. Efforts to improve food safety in postharvest horticultural products focus on controlling microbial growth and reducing cross-contamination. Sanitizers are used in food safety practices for multiple purposes, such as eliminating pathogens, reducing microbial loads, cleaning hands, tools, and surfaces that come into contact with vegetables, and extending the shelf life of produce (44).

However, methods like pasteurization and high-pressure processing (HPP) are not suitable for fresh produce and certain meat products, as they can alter the sensory characteristics or nutritional content of the foods (45). Similarly, food irradiation, while effective in sterilizing produce, can negatively affect the appearance of some foods and faces low consumer acceptance, compounded by the need for specific labeling of irradiated products (46). As food safety and sustainability remain critical concerns in the global food industry, the increasing demand in Western countries for foods produced through natural processes adds pressure to provide products that are safe, free from chemical preservatives, and meet high consumer quality expectations (47). The widespread use of antibiotics in agriculture and animal farming has led to growing concerns about antibiotic residues in food, which contribute to the natural development of antibiotic resistance in harmful microbial strains. The rise of antibiotic resistance in microbial populations presents a serious global challenge to food safety and security. This issue has been further intensified by the recent identification of new strains of antibiotic-resistant bacteria (ARB) in both plant- and animal-based food products (48). Bacteriophages (phages), natural predators of bacteria, are harmless to humans and animals and are found abundantly in the environment (48). Due to these characteristics, phages have been recognized as promising antimicrobial agents for controlling specific bacterial pathogens in food production. In recent years, several bacteriophage-based products such as ListSheild, EcoSheild, and Salmofresh have been introduced commercially to target major foodborne pathogens, such as Listeria monocytogenes, Escherichia coli, and various Salmonella serovars (49-51). The use of phages is safe and is comparable to antibiotic applications (49). Since the 1980s, phages have been utilized to manage bacterial contamination on food surfaces, control spoilage bacteria, and combat pathogens causing gastrointestinal illnesses (52), as well as to disinfect raw food products. Their specificity makes phages especially effective for sanitizing ready-to-eat (RTE) foods, including milk, vegetables, and meat products (53). Bacteriophages represent a promising tool in the ongoing efforts to enhance food safety and public health. However, like other antimicrobial strategies used in food production, bacteriophages are not a cure all for all food safety issues. While phage-based biocontrol shows potential in addressing foodborne pathogens, their antibacterial spectrum is typically narrower compared to most antibiotics (54). Phages are particularly effective in (i) preventing or reducing bacterial colonization and disease in livestock (phage therapy), (ii) decontaminating carcasses and raw products such as fresh fruits and vegetables, as well as disinfecting equipment and surfaces (bacteriophage sanitation and biocontrol), and (iii) extending the shelf life of perishable processed foods by serving as natural preservatives (biopreservation). Furthermore, phages should be integrated into hurdle technology, working alongside other preservation methods to optimize food safety and consumers also prefer to choose phages treated foods (55, 56).

Clinical Applications of Bacteriophage

Since 2018, research into using bacteriophages to combat multidrug-resistant (MDR) bacterial infections has been growing, reflecting the expanding global bacteriophage market, which is expected to reach USD 1,441.3 million by 2028. The rising prevalence of MDR infections, coupled with the stagnation in novel antibiotic development, has driven significant advancements in exploring various phages as treatments for drug-resistant bacteria. This has made phage therapy a critical innovation for managing challenging drug-resistant infections. Additionally, there is an increasing number of reports on combining phages with antibiotics

for treating patients with severe MDR infections (57). Pathogens such as *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Salmonella*, *Pseudomonas aeruginosa*, *Enterobacter spp., and Escherichia coli* exhibit high to critical levels of drug resistance, contributing to a significant share of hospital-acquired infections globally. Given the declining effectiveness of antibiotics against these pathogens, phage therapy (PT) has emerged as a promising alternative treatment strategy (58, 59).

Phage therapy has been applied in treating *Pseudomonas aeruginosa* induced skin infections, with reporting a significant reduction by four orders of magnitude in *Pseudomonas aeruginosa* 709 levels on human skin following treatment (60). Sewage-derived phages have also shown effectiveness against *Staphylococcus aureus*, a major cause of wound abscesses (61). Research has demonstrated that mice injected intraperitoneally with bacteriophages for *Pseudomonas aeruginosa* infections exhibited lower infection rates (62). Additionally, orally administered bacteriophages have been found to prevent *E. coli*-induced diarrhea in calves and potentially reduce sepsis caused by *Pseudomonas aeruginosa* (63). Phage therapy has also been successfully used in chickens to treat *E. coli*-induced septicemia via intramuscular injection (64). Phages have even been shown to save mice from death caused by vancomycin-resistant *Enterococcus faecium* (65). As antibiotic resistance continues to rise, phage therapy offers a promising alternative to conventional antibiotics. While most of the well-conducted studies on phage therapy have been carried out in animal models, advancing to human clinical trials requires a thorough understanding of these animal studies and insights into how they can be refined to make phage therapy a viable clinical option. Some potential challenges to phage therapy clinical trials, including phage resistance, immune system neutralization, and phage bacteria matching are also mentioned to those studies. The research explores the animal models used in phage therapy research within Western literature and highlights lessons that can help transition phage therapy into practical use as an antibiotic alternative in humans (66). Table 1 summarizes various studies on the development of phage therapy for different bacterial strains.

Table 1: Overview of Phage Therapy Applications for Development Bacterial Strains.

Target bacteria	Bacterial Strain	Phage	Bacteriophage preparation	Model organism and materials used	Follow up Period	Outcome	References
Staphylococcus aureus	Laus102 (MSSA)	vB_SauH_2002 and 66 phages	Injection of 8, 2.10^{10} PFU intravenously 6 hours post-infection	Mice, rats and rabbits	24 hours	Phage treatment accelerated bacterial load clearance at infection sites	(67)
Staphylococcus aureus	*S. aureus* AW7 (MRSA)	2003, 2002, 3A, and K nebulized phages	Administration of 2.10^{10} PFU directly into the lungs at 2, 12, 24, 48 and 72 hours post infection	Mice, rats and rabbits	96 hours	The combination of daptomycin and nebulized phages had saved 55% of the animals, but was not much superior to nebulized phages alone (50%)	(68)
Enterococcus faecalis	Serg	SSsP-1	0.1 mL of phage stock (3×10^8 PFU) was mixed with 0.9 mL of bacterial test culture	Outbred male mice model	24 hours	Phages were able to protect mice from lethal enterococcal infection	(69)
Enterococcus faecalis	CCUG 52538	GVEsP-1	0.1 mL of phage stock (3×10^8 PFU) was mixed with 0.9 mL of bacterial test culture	Outbred male mice model	24 hours	Phages were able to protect mice from lethal enterococcal infection	(69)
Pseudomonas aeruginosa	PCM 2720	F8	0.1 mL of crude phage lysate containing 2.6×10^8 PFU/mL was added	Bacterial lysate	4 hours	Effective biofilm reduction was observed	(70)
Klebsiella pneumoniae	0915	vB_KleM_KB2	Bacteriophage at 10^8 PFU/ml was added with bacterial strain	Clinical Isolates	8 hours	Effective lysis of the bacterium was observed	(71)
Escherichia coli	*E. coli* O157:H7	SPEC13	Phages at 10^9 log PFU/ml was added with bacterial strain	Mice model	6 hours	A notable decrease in the viable counts of bacterial hosts in vivo was observed	(72)
Escherichia coli	K-12 MG1655	T4 phage	Phages at 5.5×10^9 PFU/ml was added with bacterial strain	Membrane Vesicles	5 hours	Lytic phage leads to the formation of MVs through both explosive cell lysis as well as membrane blebbing.	(73)
Salmonella enterica	*S. typhimurium* SA32	ISTP3	Phages at 10^{10} log PFU/ml was added with bacterial strain	Food Samples	12 hours	Demonstrated the capacity to effectively lyse drug-resistant strains of *S. enterica*.	(74)
Aeromonas hydrophila	ZYAH75	ZPAH34	Phages at 10^9 log PFU/ml	Fish and lettuce	12 hours	Phage was able to inhibit the growth of MDR *A. hydrophila* and prevented bacterial biofilm contamination	(75, 76)

Detection of Bacteria Through Phage Typing

Phages are a type of virus that exclusively targets and infects bacteria. Unlike other recognition elements, phages offer several benefits, including their high specificity, ease of acquisition, and strong environmental resilience. These advantages make phages an attractive option for use in the development of biosensors. As a result, phage-based biosensors have gained significant attention in recent years for their potential to detect pathogens (77). Antibody phage display is an effective alternative to hybridoma technology for generating antibodies against specific antigens. This method simplifies the process by substituting the complex procedures that follow animal immunization with straightforward DNA and bacterial manipulations. As a result, it significantly reduces the time required to develop stable antibody-producing clones, making the process more cost-effective. The antibodies produced through phage display undergo multiple affinity selection rounds and can serve as highly selective receptors in biosensors (78).

Because bacteriophages specifically target live bacteria, they allow for quick and precise identification of bacterial cells using detection methods. Phages can be engineered, lysed, isolated, and extracted from their bacterial hosts, making them suitable for various detection techniques. The main types of phage-based detection methods include reporter bacteriophages, bacteriophage amplification, and bacteriophage capture (79).

Bacteriophages are the most abundant biological entities on Earth, harboring vast amounts of untapped genetic information. Since their discovery, phages have attracted significant research interest despite their small size. Advances in genome modification techniques have enabled the creation of engineered phages with tailored characteristics, expanding their potential applications (80). Reporter genes, such as those encoding luciferases or fluorescent proteins, have been incorporated into phage genomes, allowing for gene expression when phages infect living hosts (81, 82). In bacteriophage amplification assays, detection signals arise from the production of new phage particles or the lysis of the bacterial host (77). Plaque formation on a Petri dish typically indicates phage growth, as plaques form when infected bacteria burst, releasing progeny phages that can then infect additional bacteria. Bacteriophage amplification involves infecting bacteria, chemically neutralizing any extracellular phages with virucides, and detecting plaques through a rapidly multiplying "reporter" organism or bacterial lawn. Each plaque corresponds to the initial bacterial infection, and the individual plaques can be isolated and analyzed by PCR for greater specificity (83). In recent years, various biorecognition elements, including antibodies, enzymes, aptamers, and nucleic acids, have been extensively used for pathogen detection in complex samples. However, these molecules often come with high detection limits, require labor-intensive and expensive production, and can exhibit cross-reactivity. Bacteriophage-encoded proteins, particularly the receptor-binding proteins (RBPs) and cell-wall binding domains (CBDs) found in endolysins play a key role in phage attachment to bacterial surface receptors during different stages of the lytic cycle. Due to their exceptional properties such as high specificity, sensitivity, stability, and ease of engineering these proteins are considered promising alternatives to traditional recognition molecules. Their unique characteristics enhance detection methods and offer diverse applications in various detection platforms, including magnetic, optical, and electrochemical systems (84) Phage therapy is being investigated for the treatment of a number of pulmonary infections, including pulmonary arterial hypertension, pneumonia, tuberculosis, cystic fibrosis, and chronic obstructive lung disorders brought on by bacteria resistant to antibiotics (85).

CONCLUSION AND SUGGESTIONS

Bacteriophages are a type of virus that are widely found in nature and have a close association with bacterial cells. Since their discovery, they have been utilized for various applications and continue to play significant roles in modern biotechnology due to the ease with which their genomes can be manipulated. Lytic and lysogenic bacteriophages are present in environments where their host bacteria thrive, making it possible to isolate these viruses from any suitable sample. The potential applications of phages are expanding globally, particularly in Western countries, where they are increasingly recognized as therapeutic agents in hospitals, clinics, and food industries, largely in response to the rise of antimicrobial-resistant bacterial strains. In contrast, the exploration and utilization of phages in developing countries remain limited. While bacteriophages present a promising alternative treatment for bacterial infections, they also serve as valuable tools in vaccine delivery, modulating bacterial populations, and enhancing diagnostic methods. It is advisable to broaden the use of bacteriophage therapy in hospitals, clinics, and food industries to help combat the challenges posed by multi-drug-resistant bacterial pathogens. Establishing various phage production companies to create diverse phage cocktails with therapeutic effects is encouraged. Raising awareness about bacteriophage research is essential for developing monitoring and safety protocols, which will facilitate the wider adoption of bacteriophages across multiple fields, including clinical applications.

CONFLICTS OF INTERESTS

The authors have declared that no competing interests exist.

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