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Phage therapy for sustainable crop protection: Harnessing bacteriophages for targeted management of bacterial plant pathogens

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Abstract

Bacterial plant diseases are responsible for substantial yield losses and economic damage in global agriculture. Conventional management practices rely heavily on chemical bactericides and antibiotics, which often lead to environmental contamination, disruption of beneficial microbiota, and the emergence of resistant pathogen populations. Phage therapy, which utilizes bacteriophages to specifically infect and lyse bacterial pathogens, has emerged as a promising eco-friendly alternative for crop protection. This review summarizes the biology of bacteriophages, their mechanisms of action, and their application against major phytopathogens, including *Xanthomonas*, *Pseudomonas syringae*, *Erwinia amylovora*, and *Ralstonia solanacearum*. Recent advances in phage isolation, formulation technologies, phage cocktails, and genomic characterization are discussed. The review also highlights challenges related to environmental stability, host specificity, bacterial resistance, and regulatory approval. Integration of phage therapy with microbiome engineering, precision agriculture, and molecular diagnostics offers significant opportunities for developing next-generation biological control strategies capable of supporting sustainable and climate-resilient crop production.

Keywords: Bacteriophages, phage therapy, bacterial plant pathogens, biological control, sustainable agriculture, *Xanthomonas*, *Pseudomonas syringae*, *Ralstonia solanacearum*, crop protection

1. Introduction

Bacterial plant diseases represent one of the most significant constraints on global agricultural productivity, causing substantial economic losses in both field and horticultural crops. Pathogens such as *Xanthomonas*, *Pseudomonas syringae*, *Erwinia amylovora*, and *Ralstonia solanacearum* infect a wide range of hosts and induce symptoms including leaf spots, blights, cankers, wilts, and fruit rots that can drastically reduce marketable yield [1]. The increasing intensification of agriculture, expansion of monoculture systems, and changing climatic conditions have further enhanced the prevalence and geographic spread of many bacterial diseases [2].

Traditional disease management strategies rely heavily on copper-based bactericides, antibiotics, resistant cultivars, and cultural practices. However, prolonged application of chemical bactericides has resulted in the emergence of resistant pathogen populations, accumulation of heavy metals in agricultural soils, and disruption of beneficial microbial communities associated with plants [3]. The use of antibiotics in agriculture has also raised concerns regarding the development of antimicrobial resistance and the potential transfer of resistance determinants to other microbial populations [4]. Consequently, there is an urgent need for environmentally sustainable and highly specific alternatives for bacterial disease management.

Phage therapy has emerged as a promising biological approach that utilizes bacteriophages viruses that specifically infect bacteria to suppress phytopathogenic populations [5]. Unlike broad-spectrum chemical bactericides, bacteriophages exhibit high host specificity and can selectively target pathogenic bacteria while leaving beneficial microorganisms largely unaffected [6]. This specificity is particularly valuable in modern sustainable agriculture, where preservation of the plant microbiome is increasingly recognized as essential for nutrient cycling, stress tolerance, and disease resistance.

Recent advances in phage genomics, high-throughput sequencing, and formulation technologies have accelerated the development of phage-based biocontrol products for agricultural applications [7]. Field studies have demonstrated successful suppression of bacterial spot, fire blight, bacterial wilt, and other important diseases using carefully selected lytic phages or phage cocktails [8]. Furthermore, integration of phage therapy with precision agriculture, microbial consortia, and molecular diagnostics offers new opportunities for targeted and adaptive crop protection strategies.

Given the growing demand for residue-free and eco-friendly crop protection methods, phage therapy is increasingly viewed as a key component of integrated disease management programs. This review examines the biology of bacteriophages, their mechanisms of action, major target pathogens, formulation technologies, challenges in field implementation, and future prospects for sustainable crop protection [1, 2].

2. Biology of Bacteriophages

Bacteriophages are the most abundant biological entities on Earth and are found in virtually all environments where bacteria exist, including soil, water, plant surfaces, and the rhizosphere [9]. They consist of nucleic acid, either DNA or RNA, enclosed within a protein capsid, and some possess a tail structure that facilitates attachment to bacterial cells. Phages are generally classified into lytic and lysogenic groups, although lytic phages are preferred for agricultural biocontrol because they rapidly destroy their bacterial hosts [10].

The lytic infection cycle begins when a phage recognizes and adsorbs to specific receptors on the bacterial surface. After attachment, the phage injects its genetic material into the host cell and hijacks the bacterial metabolic machinery to synthesize viral proteins and replicate phage genomes [11]. Newly assembled phage particles accumulate within the cell until lytic enzymes degrade the bacterial cell wall, releasing progeny phages that can infect neighboring bacterial cells. This self-amplifying process enables phages to multiply in the presence of susceptible pathogens and provides a unique advantage over many conventional bactericides [12].

Host specificity is a defining characteristic of bacteriophages. A particular phage may infect only a single bacterial species or even a subset of strains within a species, depending on the receptors recognized during adsorption [13]. This specificity minimizes non-target effects on beneficial microorganisms but also necessitates careful selection of phages for effective disease control. To broaden the spectrum of activity, researchers often combine multiple phages into cocktails that target different bacterial receptors or strains [14].

Another important aspect of phage biology is their genetic diversity. Modern genomic sequencing allows rapid identification of lytic genes, host recognition proteins, and undesirable elements such as toxin or antibiotic resistance genes [15]. Genomic characterization has become an essential step in phage development to ensure safety, efficacy, and regulatory compliance for agricultural applications. In addition, studies of phage-bacteria coevolution have provided insights into resistance mechanisms and strategies for designing more durable biocontrol systems [16].

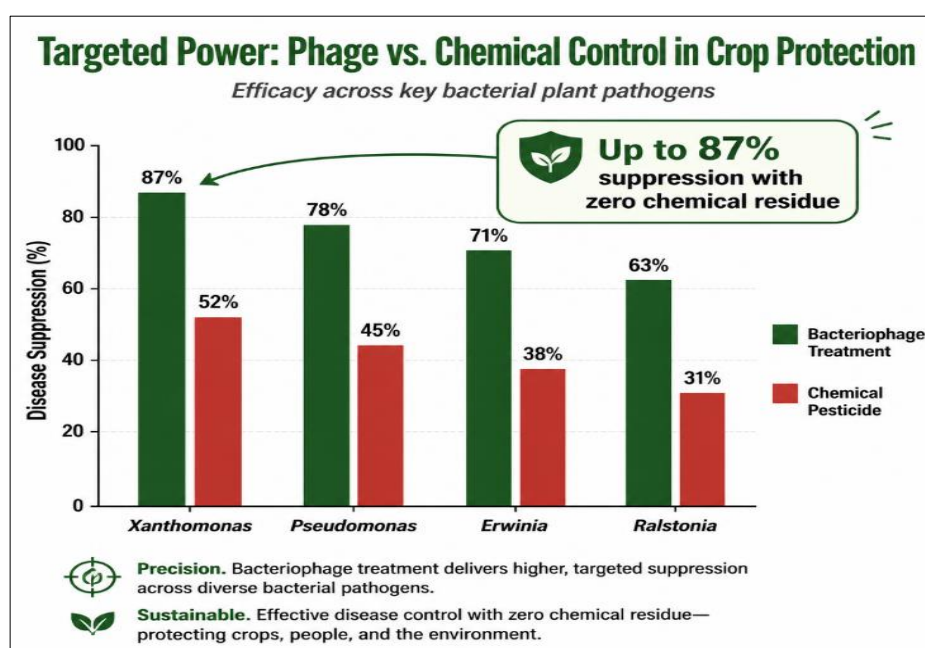


Fig 1: Comparative efficacy of bacteriophage and chemical treatments against bacterial plant pathogens.

3. Mechanisms of Crop Protection

Bacteriophages protect crops through several direct and indirect mechanisms that collectively reduce pathogen populations and limit disease development. The primary mechanism is direct bacterial lysis, in which phages infect susceptible bacterial cells and destroy them during the lytic cycle [5]. As phage particles replicate within infected tissues, they can rapidly amplify and substantially reduce pathogen density in leaves, stems, roots, or vascular tissues [17].

A second important mechanism is the suppression of disease spread. By lowering bacterial populations on plant surfaces and within infected tissues, phages reduce the likelihood of pathogen dissemination through water splash, irrigation, tools, or insect vectors [18]. This is particularly relevant for diseases such as bacterial spot and fire blight, where secondary spread plays a major role in epidemic development.

Many phages also contribute to biofilm disruption. Certain bacteriophages produce depolymerase enzymes that degrade extracellular polysaccharides forming the biofilm matrix ^[19]. Biofilms often protect bacterial pathogens from environmental stress and chemical treatments; therefore, phage-mediated degradation of biofilms can enhance pathogen susceptibility and improve disease control.

Phage therapy may additionally influence the plant-associated microbial community. Because phages are highly specific, they generally spare beneficial rhizosphere and phyllosphere microorganisms, allowing natural microbial antagonists of pathogens to persist ^[6]. This contrasts with broad-spectrum bactericides that can indiscriminately affect both harmful and beneficial bacteria. Preservation of beneficial microbiota may indirectly support plant health through improved nutrient cycling and enhanced natural disease suppression.

Emerging research suggests that combining phages with other biological agents, such as *Bacillus* or *Pseudomonas* species, can produce synergistic effects ^[20]. In such integrated systems, phages reduce pathogen populations while beneficial bacteria compete for ecological niches, produce antimicrobial metabolites, and stimulate plant defense responses. This multifaceted approach has the potential to provide more stable and durable disease management under field conditions.

Overall, the mechanisms of crop protection provided by bacteriophages extend beyond simple bacterial killing and include amplification at infection sites, suppression of pathogen dissemination, disruption of protective biofilms, preservation of beneficial microbiota, and synergistic interactions with other biological control agents ^[17-20]. These properties make phage therapy a promising component of next-generation sustainable crop protection strategies.

Table 1: Major Bacterial Plant Pathogens Targeted by Phage Therapy

Pathogen	Disease	Major host crops	Role of phage therapy
<i>Xanthomonas oryzae</i>	Bacterial leaf blight	Rice	Reduces leaf surface bacterial populations
<i>Xanthomonas campestris</i>	Bacterial leaf spot	Tomato, pepper	Suppresses disease development on foliage
<i>Pseudomonas syringae</i>	Bacterial speck and canker	Tomato, kiwi, stone fruits	Limits epiphytic and pathogenic populations
<i>Erwinia amylovora</i>	Fire blight	Apple, pear	Protects blossoms during infection periods
<i>Ralstonia solanacearum</i>	Bacterial wilt	Tomato, potato, eggplant	Reduces pathogen levels in the rhizosphere and vascular tissues

Table 2: Advantages and Challenges of Agricultural Phage Therapy

Aspect	Advantages	Challenges
Specificity	Targets only pathogenic bacteria	May not infect all pathogen strains
Environmental impact	Biodegradable and residue-free	Reduced persistence under UV exposure
Microbiome effects	Minimal disruption of beneficial microbes	Requires precise pathogen identification
Resistance management	Effective against some antibiotic-resistant bacteria	Pathogens may develop phage resistance
Field application	Compatible with integrated disease management	Variable performance under different environmental conditions
Commercialization	Potential for sustainable crop protection	Regulatory and formulation standardization issues

4. Major Target Pathogens

Bacteriophage therapy has been investigated against several economically important bacterial plant pathogens that affect field crops, vegetables, and fruit trees. Members of the genus *Xanthomonas* are among the most extensively studied targets because they cause bacterial leaf spot and blight diseases in crops such as rice, tomato, pepper, and citrus ^[21]. Phages specific to *Xanthomonas campestris* and *Xanthomonas oryzae* have demonstrated significant reductions in disease severity under greenhouse and field conditions by rapidly lowering bacterial populations on infected foliage ^[22].

Pseudomonas syringae is another important target because it causes bacterial speck, canker, and blossom blight in numerous horticultural crops. Phage applications have shown promising results in tomato and kiwi orchards, where suppression of epiphytic bacterial populations reduced subsequent disease development ^[23]. Similarly, phages targeting *Erwinia amylovora*, the causal agent of fire blight in apple and pear, have provided effective disease control during blossom infection periods when pathogen populations are most vulnerable ^[24].

For soil-borne diseases, *Ralstonia solanacearum* has received considerable attention because of its devastating impact on tomato, potato, eggplant, and several other solanaceous crops. Soil drenching and root-zone

applications of lytic phages have reduced bacterial wilt incidence by decreasing pathogen populations in the rhizosphere and vascular tissues ^[25]. The broad diversity of target pathogens highlights the potential of phage therapy as a versatile tool for managing bacterial diseases across different cropping systems.

5. Phage Isolation and Characterization

Successful phage therapy depends on the identification of highly lytic and environmentally stable bacteriophages. Isolation is typically performed from environments where the target pathogen is abundant, including infected plant tissues, irrigation water, drainage channels, compost, and agricultural soils ^[26]. Enrichment techniques using susceptible bacterial hosts increase the likelihood of recovering effective phages.

After isolation, phages are characterized through a series of microbiological and molecular analyses. Host range determination is used to identify the spectrum of bacterial strains susceptible to infection, while plaque morphology provides preliminary information about lytic activity ^[27]. Electron microscopy enables classification of phages based on capsid and tail structure, and genomic sequencing has become an essential step for confirming the absence of undesirable genes associated with lysogeny, toxin production, or antibiotic resistance ^[28].

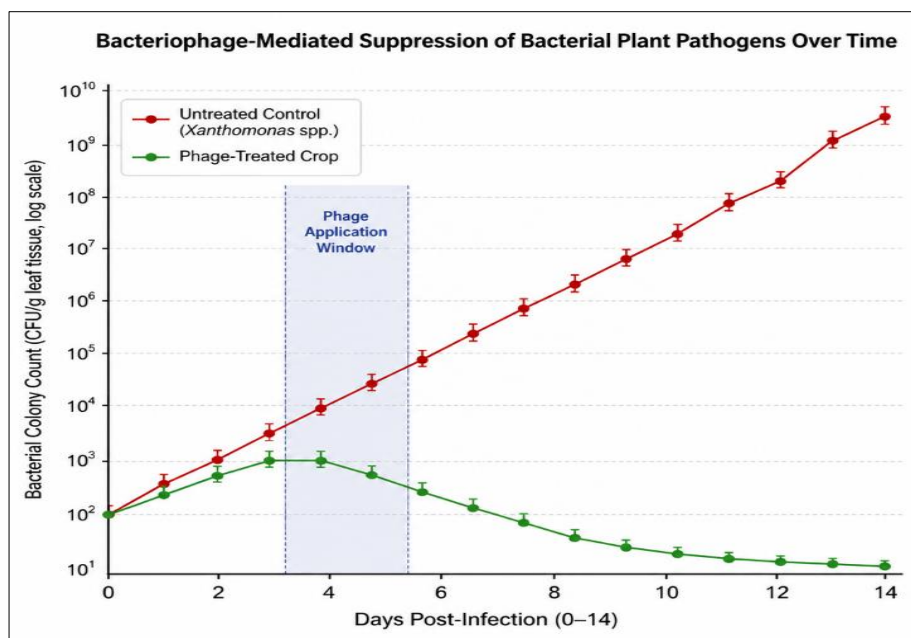


Fig 2: Temporal suppression of *Xanthomonas* infection by bacteriophage treatment compared with untreated control.

Additional characterization includes assessment of adsorption rate, latent period, burst size, thermal tolerance, pH stability, and resistance to ultraviolet radiation. These parameters are critical for selecting phages capable of surviving agricultural environments and maintaining infectivity under field conditions [29]. Comprehensive characterization also facilitates the design of compatible phage cocktails with complementary host ranges and improved biocontrol efficacy.

6. Formulation and Delivery Technologies

Environmental conditions often represent a major limitation for phage performance in agriculture. Exposure to ultraviolet radiation, high temperatures, desiccation, and rainfall can rapidly reduce phage viability on plant surfaces [30]. Consequently, formulation and delivery technologies have become central components of modern phage-based crop protection systems.

Foliar sprays remain the most common method for managing aerial diseases such as bacterial spot and blight. To improve persistence, phages are frequently combined with protective additives including skim milk, sucrose, lignin, or polymer-based UV protectants [31]. Seed treatments allow early establishment of phages around emerging roots and may provide protection during the initial stages of crop development.

For soil-borne pathogens, soil drenching and irrigation-based delivery systems introduce phages directly into the rhizosphere, where they can interact with target bacteria [25]. Encapsulation technologies, particularly those based on alginate, chitosan, or biodegradable polymers, protect phage particles from environmental stress and enable controlled release over time [32]. More recently, nano-enabled formulations have been explored to enhance phage stability, improve adhesion to plant surfaces, and facilitate targeted delivery to infection sites [33]. These advances are substantially improving shelf life, field persistence, and overall biocontrol performance.

7. Phage Cocktails and Resistance Management

A major challenge in phage therapy is the potential development of bacterial resistance to individual phages. Bacteria can alter surface receptors, produce extracellular barriers, or activate defense systems that reduce phage adsorption and replication [34]. To minimize resistance development, researchers increasingly employ phage cocktails containing multiple phages that recognize different bacterial receptors or infect different strains of the same pathogen.

Phage cocktails offer several advantages over single-phage formulations. They broaden the effective host range, reduce the probability that resistant mutants will dominate the population, and often provide more consistent disease suppression under field conditions [35]. In fire blight management, for example, cocktails containing several *Erwinia amylovora* phages have shown superior efficacy compared with individual phages because resistant bacterial variants remained susceptible to other members of the mixture [24].

Integrated resistance management strategies are also being developed by combining phages with beneficial microorganisms such as *Bacillus* and *Pseudomonas* species [36]. In these systems, phages directly lyse pathogenic bacteria, while beneficial microbes compete for ecological niches, produce antimicrobial compounds, and stimulate plant defense responses. Such multifaceted approaches may provide more durable and environmentally resilient disease control than any single intervention alone.

8. Advantages of Phage Therapy

Bacteriophage therapy offers several advantages over conventional chemical bactericides and antibiotics used in agriculture. One of the most significant benefits is high host specificity. Phages infect only susceptible bacterial pathogens, thereby minimizing adverse effects on beneficial microorganisms inhabiting the rhizosphere, phyllosphere, and surrounding soil environment [37]. Preservation of these beneficial microbial communities is important for

maintaining nutrient cycling, plant growth promotion, and natural disease suppression.

Another major advantage is the environmentally friendly nature of phages. Because they are naturally occurring biological entities, phages are biodegradable and do not leave harmful chemical residues on crops, soil, or water bodies [38]. This characteristic makes phage therapy particularly attractive for sustainable agriculture and organic production systems where restrictions on synthetic pesticides are stringent.

Phages also possess a unique self-amplifying capability. After application, lytic phages replicate within susceptible bacterial hosts and increase in number at the site of infection, potentially enhancing their effectiveness without repeated high-dose applications [39]. In contrast, many chemical bactericides gradually lose efficacy as they degrade in the environment.

Importantly, phage therapy may remain effective against antibiotic-resistant bacterial strains. Since phages employ mechanisms distinct from those of antibiotics, bacterial resistance to conventional antimicrobial compounds does not necessarily confer resistance to phage infection [40]. Furthermore, phages can be integrated with other biological control agents and cultural practices, making them compatible with integrated disease management programs.

9. Challenges and Limitations

Despite its considerable promise, phage therapy faces several challenges that currently limit widespread commercial adoption. The most notable limitation is narrow host specificity. While specificity is advantageous for preserving beneficial microbiota, it also means that a phage effective against one strain may not infect other strains of the same pathogen species [41]. Consequently, extensive pathogen characterization and tailored phage selection are often required.

Environmental stability represents another major challenge. Phage particles can be rapidly inactivated by ultraviolet radiation, high temperatures, desiccation, and extreme pH conditions, reducing their persistence on plant surfaces [30]. Although formulation technologies such as encapsulation and UV-protective additives can improve stability, maintaining adequate phage populations under field conditions remains difficult.

Bacterial pathogens may also evolve phage resistance through receptor modification, extracellular polysaccharide production, or activation of defense systems such as restriction-modification and CRISPR-associated mechanisms [34]. The use of phage cocktails and periodic updating of phage formulations can mitigate resistance development, but continuous monitoring is necessary.

Additional obstacles include regulatory approval, large-scale production, quality control, and standardization of phage products [42]. Regulatory frameworks for agricultural phages differ among countries, and the absence of harmonized guidelines can slow commercialization. Moreover, ensuring consistent phage concentration, purity, and stability during manufacturing and storage is essential for reliable field performance.

10. Future Perspectives

The future of agricultural phage therapy is closely linked to advances in genomics, synthetic biology, and precision agriculture. Metagenomic sequencing of crop-associated

microbial communities can facilitate rapid identification of emerging pathogen strains and their susceptibility to available phages [43]. Combined with artificial intelligence and machine-learning algorithms, these data may enable the design of optimized phage cocktails tailored to specific agroecosystems and disease outbreaks.

Synthetic biology and genome engineering offer opportunities to improve phage performance by enhancing environmental stability, expanding host range, or increasing biofilm-degrading activity [44]. Engineered phages could potentially carry additional antimicrobial functions or be modified to evade bacterial resistance mechanisms more effectively.

Integration of phage therapy with precision agriculture technologies is another promising direction. Soil sensors, remote sensing platforms, and geospatial disease mapping can support targeted phage application only where pathogen populations exceed economic thresholds [45]. Such site-specific management could reduce application costs and improve overall efficacy.

Future research is also expected to focus on multifunctional biological systems that combine phages with beneficial microorganisms such as *Bacillus*, *Pseudomonas*, and *Azotobacter*. These integrated approaches may simultaneously provide pathogen suppression, nutrient mobilization, and plant growth promotion, thereby contributing to climate-resilient and environmentally sustainable crop production systems [36].

11. Conclusion

Phage therapy represents a promising and environmentally sustainable strategy for managing bacterial plant diseases. By exploiting the natural ability of bacteriophages to specifically infect and lyse bacterial pathogens, phage-based biocontrol offers a targeted alternative to conventional chemical bactericides. Advances in phage isolation, genomic characterization, formulation technology, and resistance management are steadily improving field performance and commercial feasibility.

Although challenges related to environmental stability, host specificity, and regulatory approval remain, the integration of phage therapy with precision agriculture, molecular diagnostics, and microbiome-based approaches provides substantial opportunities for developing next-generation crop protection systems. Such innovations could play a critical role in reducing chemical inputs, preserving beneficial microbial communities, and supporting sustainable agricultural production under changing environmental conditions.

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