

## General Concepts of Bacteriophages to Combat Bacterial Crop Diseases

Luis Amarillas<sup>1</sup>, Ruben León<sup>1</sup>, Mitzi Estrada<sup>2</sup> and Luis Lightbourn<sup>1\*</sup>

<sup>1</sup>*Lightbourn Research Institute, Ciudad Jiménez, Chihuahua, Mexico*

<sup>2</sup>*Faculty of Agronomy, Autonomous University of Sinaloa, Culiacán, Sinaloa, Mexico.*

*Received September 27<sup>th</sup>, 2019; Revised October 07<sup>th</sup>, 2019; Accepted October 09<sup>th</sup>, 2019*

### ABSTRACT

The global problem of antibiotic resistance is one of the greatest public health and food safety threats today. The use of antibiotics in food-producing contributes to the development of antimicrobial resistant bacteria, particularly in settings of intensive food production. In this regard, bacteriophages are one of the most promising alternatives to fighting antibiotic-resistant bacteria. Despite of experimental evidences reported in the several studies demonstrating the successful the effectiveness of phages as biocontrol agents, several practical considerations of finding phages with the desired characteristics to be used as biocontrol agents. The purpose of this review is to provide a comprehensive overview of the progress and challenges for phages as biological control agents against bacterial crop diseases.

**Keywords:** Bacteriophages, Combat, Antibiotic resistance, Diseases

### INTRODUCTION

Annually between 20-40% of global crop production are lost to plant diseases in the world. The economic loss associated with these diseases have been estimated to US\$ 220 billion plus. There is thus a great need to find efficient and sustainable phytopathogenic bacteria management strategies [1,2]. Efforts to reduce these crop losses can indirectly result in an increased crop yields. Pathogens that commonly infect plants are diverse, including viruses, fungi, oomycetes and nematodes. However, phytopathogenic bacteria have a more devastating socioeconomic effect. Antibiotics have been used for the management of bacterial plant diseases, but the extensive use of antibiotic over multiple years accelerates the dramatic increase in the emergence and spread of antibiotic resistant bacterial strains, affecting the control of plant-pathogenic bacteria in crops [3].

The antimicrobial resistance is a significant global threat to public health and food safety, as well as to global economic development. The intensification of agricultural production has led to an inappropriate use of antimicrobials and the application is projected to double by 2030 [4].

In agriculture, the prevention and plant disease management faces ever-growing challenges. The problem is aggravated by the fact that the use of antibiotics to treat crop diseases has been restricted to ensure public health and to limit the emergence and spread of antimicrobial resistance bacteria strains. The use of antibiotics in agriculture is routinely

described as a major contributor in the emerging public health crisis of antibiotic resistance [5,6].

Over the last decades, the intensification of agricultural production and industrialization of land have led to a greatly increase in the use of synthetic agrochemicals include antimicrobials compounds. The antimicrobial play an important role in reducing losses in crop production. However, their misuse can have serious negative impacts on the environment and human health. Therefore, the use of antibiotics in agro-food production should be properly controlled to prevent the spread of antibiotic resistance bacterial strains [7].

The dramatic increase in the emergence of multiple drug-resistant bacterial strains has prompted interest in alternatives approaches to conventional antimicrobials agents [8]. In this regard, a special type of virus known as

**Corresponding author:** Luis Lightbourn, Lightbourn Research Institute, Ciudad Jiménez, Chihuahua, Mexico, Tel: (52) 629 5425101; E-mail: [drlightbourn@institutolightbourn.edu.mx](mailto:drlightbourn@institutolightbourn.edu.mx)

**Citation:** Amarillas L, León R, Estrada M & Lightbourn L. (2020) General Concepts of Bacteriophages to Combat Bacterial Crop Diseases. *J Genomic Med Pharmacogenomics*, 5(1): 422-424.

**Copyright:** ©2020 Amarillas L, León R, Estrada M & Lightbourn L. (2019) Physicochemical Characterization and Pharmacological Properties. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

bacteriophages or phages are one of the most promising alternatives to fighting antibiotic-resistant bacteria [9]. Phages use the intracellular replication machinery of the host cell to produce more copies of the virus, consequently, cell lysis and enable the release of phage progeny from host cells.

These viruses can be considered as natural biological nano machines that integrate multiple functions into one unique metastable structure. Since these viruses are so efficient at killing bacteria, they have emerged as potentially potent tools against multidrug-resistant pathogen bacteria [10].

Like all viruses, majority of the bacteriophages are composed of proteins that encapsulate a DNA or RNA, only a few phage morphotypes have lipid-containing envelopes in the structure of the virion, a morphological characteristic that is probably essential for infection by this type of phage. There are four families of icosahedral bacteriophages that contain lipid membranes: Cystoviridae, Corticoviridae, Plasmaviridae and Tectiviridae. However, only 4% of all known bacterial viruses contains lipids [11,12].

The phages that contains lipids as structural components of the virion are sensitivity to chloroform (or other organic solvents) and detergents, as well as to temperature and pH variations. Further, some phages with lipid-containing are not stable after storage. Therefore, usually these types of viruses are not suitable biological control agents.

Phages are simple organisms that are composed of a core of genetic material (DNA or RNA genome) surrounded by a protein capsid. These biomolecules and consequently the complete virus particle, may lose their stability through damage of its structural elements by different external biochemical, physical and chemical factors, such as temperature, pH, salinity, organic matter, desiccation, UV radiation and enzymes [13,14]. For antibacterial applications, determining the influence of the external factors on bacteriophage particles stability is required to provide a basis for the selection of the most suitable phage for the development of products that can be used in applications for food industries [15]. Thereby, there have been a number of formulations to increase the stability of viral particles.

In this context, scientists have proposed various strategies to increase the stability and protect phages from detrimental environmental conditions. The recent formulation strategies for the phage preparation include: the aqueous formulations are the most applied, oil-in-water emulsion, lyophilized powder, spray-dried powder formulations and microencapsulation may confer resistant properties to phages [16-18].

The phage concentration in the final formulation should be sufficient to ensure that the dose is safe and effective in biocontrol. Formulation should protect phage particles against losing their activity.

In practice, formulation of phages in to cocktails increases the effectiveness of bacteriophages application as potential biological control agents of pathogens. The use of phage cocktails (mixture of multiple phage types possessing a diversity of host ranges) to broaden the spectrum of activity of phage bioformulations for protection against plant pathogenic bacterial.

The main reason for formulation of multiples phages into cocktails is their broader spectra of activity in comparison to individual phage, allow the control of multiple pathogens simultaneously. Phage cocktails incorporating multiples phages reduce the development of phage-resistant mutant's strains (resist phage attack through different mechanisms) as co-evolution resulted.

Some of these phage-based formulations have been designated with a GRAS status (generally recognized as safe) by the U.S. Food and Drug Administration, since they should not induce adverse effects on human health or negative environmental consequences [19]. Research studies should be conducted in order to provide results that allow assessing the biosafety of the bacteriophages for the control the bacterial plant diseases in crop environment.

In the context of global agro-food system, the pathogen control in food using phages can be applied at all stages of production throughout the entire food chain, including the crop production process, handling and packaging of the final product to minimize contamination. Moreover, phage control of spoilage bacteria can result in a significant extension of shelf life of fresh food. In addition, bacteriophages are able to reduce foodborne pathogen levels on food surfaces.

A key factor to consider for using phages as a successful biological control is to improve phage efficacy through appropriate phage selection criteria. Phages selected as biocontrol agents should be strictly lytic (phages that always lyse the infected bacterial cell to release their progeny), have a broad host range against bacterial pathogens (able to infect bacterial genera or closely related species), thus limiting the antibacterial activity of phage on commensal and beneficial bacteria [20]. Preferably, the phages must retain its infectivity under storage at ambient conditions for prolonged periods.

From a biosafety point of view, phages should not possess genes associated with bacterial toxins, pathogenicity, antibiotic resistance or other types of virulence factors. Additionally, phages should also display a low potential to horizontal gene transfer (transduction). Therefore, the complete genome needs to be sequenced to determine whether bacteriophages are suitable to control pathogenic bacteria.

## REFERENCES

1. Chakraborty S, Newton A (2011) Climate change, plant diseases and food security: An overview. *Plant Pathol* 60: 2-14.
2. Worrall E, Hamid A, Mody K, Mitter N, Pappu H (2018) Nanotechnology for plant disease management. *Agronomy* 8: 285.
3. Sundin G, Castiblanco L, Yuan X, Zeng Q, Yang C (2016) Bacterial disease management: Challenges, experience, innovation and future prospects. *Mol Plant Pathol* 17: 1506-1518.
4. Jasovský D, Littmann J, Zorzet A, Cars O (2016) Antimicrobial resistance - A threat to the world's sustainable development. *Ups J Med Sci* 121: 159-164.
5. World Health Organization (WHO) (2015) Global action plan on antimicrobial resistance. ISBN 978 92 4 150976 3.
6. Food and Agriculture Organization of the United Nations (FAO) (2016) The FAO action plan on antimicrobial resistance 2016-2020. ISBN 978-92-5-109392-4.
7. Food and Agriculture Organization of the United Nations (FAO) (2016) The future of food and agriculture – Trends and challenges. ISBN 978-92-5-109551-5.
8. Lopatto E, Choi J, Colina A, Ma L, Howe A, et al. (2019) Characterizing the soil microbiome and quantifying antibiotic resistance gene dynamics in agricultural soil following swine CAFO manure application. *PLoS One* 14: e0220770
9. Mikonranta L, Buckling A, Jalasvuori M, Raymond B (2019) Targeting antibiotic resistant bacteria with phage reduces bacterial density in an insect host. *Biol Lett* 15: 20180895.
10. Ando H, Lemire S, Pires D, Lu T (2015) Engineering modular viral scaffolds for targeted bacterial population editing. *Cell Syst* 1: 187-196.
11. Ackermann HW, Prangishvili D (2012) Prokaryote viruses studied by electron microscopy. *Arch Virol* 157: 1843-1849.
12. Atanasova NS, Senčilo A, Pietilä MK, Roine E, Oksanen HM, et al. (2015) Comparison of lipid-containing bacterial and archaeal viruses. *Adv Virus Res* 92: 1-61.
13. Vandersteegen K, Mattheus W, Ceysens P, Bilocq F, De Vos D, et al. (2011) Microbiological and molecular assessment of bacteriophage ISP for the control of *Staphylococcus aureus*. *PLoS One* 6: 24418.
14. Nap R, Božič A, Szleifer I, Podgornik R (2014) The role of solution conditions in the bacteriophage PP7 capsid charge regulation. *Biophys J* 107: 1970-1979.
15. Ahmadi H, Radford D, Kropinski A, Lim L, Balamurugan S (2017) Thermal-stability and reconstitution ability of *Listeria* phages P100 and A511. *Front Microbiol* 8.
16. Esteban P, Alves D, Enright M, Bean J, Gaudion A, et al. (2014) Enhancement of the antimicrobial properties of bacteriophage-K via stabilization using oil-in-water nano-emulsions. *Biotechnol Prog* 30: 932-944.
17. Zhang Y, Peng X, Zhang H, Watts A, Ghosh D, et al. (2018) Manufacturing and ambient stability of shelf freeze dried bacteriophage powder formulations. *Int J Pharm* 542: 1-7.
18. Vinner G, Rezaie-Yazdi Z, Leppanen M, Stapley A, Leaper M, et al. (2019) Microencapsulation of *Salmonella*-specific bacteriophage Felix O1 using spray-drying in a pH-responsive formulation and direct compression tableting of powders into a solid oral dosage form. *Pharmaceuticals (Basel)* 12: 43.
19. Figueiredo A, Almeida R (2017) Antibacterial efficacy of nisin, bacteriophage P100 and sodium lactate against *Listeria monocytogenes* in ready-to-eat sliced pork ham. *Braz J Microbiol* 48: 724-729.
20. Amarillas L, Rubí-Rangel L, Chaidez C, González-Robles A, Lightbourn-Rojas L, et al. (2017) Isolation and characterization of phillS, a novel phage with potential biocontrol agent against multidrug-resistant *Escherichia coli*. *Front Microbiol* 8.