Uttar Pradesh Journal of Zoology

Volume 44, Issue 16, Page 1-7, 2023; Article no.UPJOZ.2709
ISSN: 0256-971X (P)

A Brief Overview of Bacteriocins and their Potential Applications against Phytopathogenic Bacteria

Shivam Maurya [a++], Gurpreet Kaur [a++*], Chandan Kumar [a++], Shrawan Kumar Sahani [b++], Shashikant Sharma [a++] and Rehan [c++]

[a] Department of Plant Pathology, Lovely Professional University, Phagwara, Punjab, India.
[b] Department of Entomology, Lovely Professional University, Phagwara, Punjab, India.
[c] Department of Horticulture, Lovely Professional University, Phagwara, Punjab, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors made substantial contribution to conception. Took part in drafting of manuscript and agreed to submit to the current journal. Gave final approval of the version to be published and agreed to be accountable for all aspect of the work. All authors read and approved the final manuscript.

Article Information

DOI: 10.56557/UPJOZ/2023/v44i163575

Editor(s):
(1) Prof. Aurora Martínez Romero, Juarez University, Mexico.
Reviewers:
(1) Lisiane de Almeida Martins, FAESB, Brazil.
(2) Sahar Ghazi Imran, Iraq.

Review Article

Received: 24/05/2023
Accepted: 25/07/2023
Published: 31/07/2023

ABSTRACT

Gram-negative phytopathogens severely harm a number of economically significant crop plants. The effectivity of traditional approaches, such as the breeding and introduction of resistant cultivars, is limited by the lack of available sources of genetic resistance. Bacteriocins are small proteinaceous antibiotics produced by bacteria to kill closely related bacteria. Utilization of narrow-spectrum protein antibiotics as biocontrol agents is an effective strategy to shrink losses imposed

[++] Assistant Professor;
**Corresponding author: Email: gurpreet.29529@lpu.co.in;*

due to specific bacterial phytopathogens. Several colicin-like bacteriocins have been found to be active against phytopathogenic bacteria. Bacteriocins frequently affect closely related bacterial strains, making them useful as targeted, low-side-effect, narrow-spectrum antibiotics. Even though using bacteriocins to control plant diseases is a promising strategy, minimal information is there regarding the abundance and functions of these chemicals against pathogenic bacteria and their natural enemies. This review is concerned with the efficient control of economically significant plant pathogenic bacteria using these potent and selective antimicrobial agents.

Keywords: Bacteria; plant disease; phytopathogenic; bacteriocins; antibiotic.

1. INTRODUCTION

Bacteriocins are proteinaceous antimicrobial peptides that are produced by ribosomes [1]. Bacteriocin were first synthesized via *Escherichia coli* in 1925, they were named as "Colicins" because of their microbial origin [2]. Contrarily, the bacteriocin produced by lactic acid bacteria is particularly significant because the Food and Drug Administration (FDA) has designated these bacteria as being "Generally Regarded as Safe [3]. The first commercially generated bacteriocin was nisin, produced by Lactococcus lactis. These substances, which are classified as protein toxins, are released by certain archaea and bacteria in order to prevent the growth of bacterial strains that are similar to or identical to them [4]. Moreover, these substances have the capacity to eradicate certain pathogens while preserving other populations [5]. These compounds have hydrophobic or amphiphilic properties and the bacterial membrane is usually the target of their activities. When a bacteriocin generated by one bacterium is poisonous to other bacteria of the same species, it is referred to as narrow spectrum, and when a bacteriocin inhibits bacteria of different genera, it is referred to as broad spectrum [6]. Typically, bacteriocin-producing cells put up defenses against being destroyed by their own bacteriocins. These defenses may consist of self-immunity proteins, efflux pumps, or a combination of both [7,8]. Bacteriocins' capacity to kill is regarded as an effective tactic for preserving population and lowering the number of rivals to increase the number of resources and living space in habitats. Contrary to the majority of antibiotics, bacteriocins are produced by ribosoms; they are sensitive to proteases and have no harmful effects on either people or the environment. The effectiveness of bacteriocins has been demonstrated to be more than 100 times when compared with number of other traditional antimicrobials [9]. Because of this, bacteria that produce bacteriocins produce self-immunity proteins that shield them from their bacteriocins by scavenging bacteriocins or engaging in antagonist competition for receptor bacteriocin [10].

2. DIFFERENCE BETWEEN BACTERIOCINS AND ANTIBIOTIC

Bacteriocins are generated by ribosomes, whereas several enzyme complexes are involved in the synthesis of antibiotics. Contrary to conventional antibiotics, bacteriocins have bactericidal or bacteriostatic effects on a narrow range of bacteria. Additionally, compared to antibiotics, most bacteriocins are more potent against their target bacteria at lower concentrations Table 1 [11]. Bacteriocins are frequently thought of as being more natural as they have been a part of foods eaten since antiquity. Bacteriocins cannot alter the microbiota of the digestive tract as the trypsin and pepsin enzymes present in the digestive tract inactivate them [12].

Table 1. Difference between bacteriocins and antibiotic [13]

Characteristics	Bacteriocins	Antibiotic
Activity	Reduced spectrum	Variable spectrum
Synthesis	Ribosomally synthesized	Secondary metabolites
Interactive requirement	Non-specific targets	Specific targets
Immunity to host cell	Yes	No
Toxicity	Unknown	Yes
Mode of Action	Pore formation in membrane	Intracellular targets/cell membrane

3. BACTERIOCINS CLASSIFICATION

There are three classes of bacteriocins i.e., Class I, Class II and Class III. Class I bacteriocins are lantibiotics, which are peptides with unusual, post translationally modified amino acids and thioether bridges [14] divided lantibiotics into three categories Type A type B and Type C. Type A lantibiotics are flexible, linear cationic peptides. Type B lantibiotics are spherical rigid peptides and Type C are two-component bacteriocins Table 2 Fig. 1.

Class I bacteriocins exhibits numerous activities including destabilization of membrane and their attachment with particular lipids blocks the synthesis of cell wall [14,16]. Class II bacteriocins constitute an incredibly diverse group of non-modified peptides [17]. Their effects on target cells are comparable to those of class I bacteriocins, but their receptors seem to be proteins rather than lipids [18]. Class III bacteriocins are sensitive to heat and are classified depending on their capacity to lyse cells Table 3.

Table 2. Properties of characterized bacteriocins [15]

Bacteriocins	Producer organism	Properties
Nisin	Lactococcus lactis subsp. lactis	Lantibiotic, broad spectrum, chromosome/plasmid mediated, bactericidal, produced late in the growth cycle
Pediocin A	*Pediococcus pentosaceus* FBB61 and L-7230	
Pediocin AcH	*Pediococus acidilactici* H	Broad spectrum, plasmid mediated
Leucocin	*Leuconostoc gelidum* UAL 187	Broad spectrum, plasmid mediated, bacteriostatic, produced early in the growth cycle
Helveticin J	*L. helveticus* 481	Narrow spectrum, chromosomally mediated, bactericidal
Carnobacteriocin	*Carnobacterium piscicola* LV17	Narrow spectrum, plasmid mediated, produced early in the growth cycle

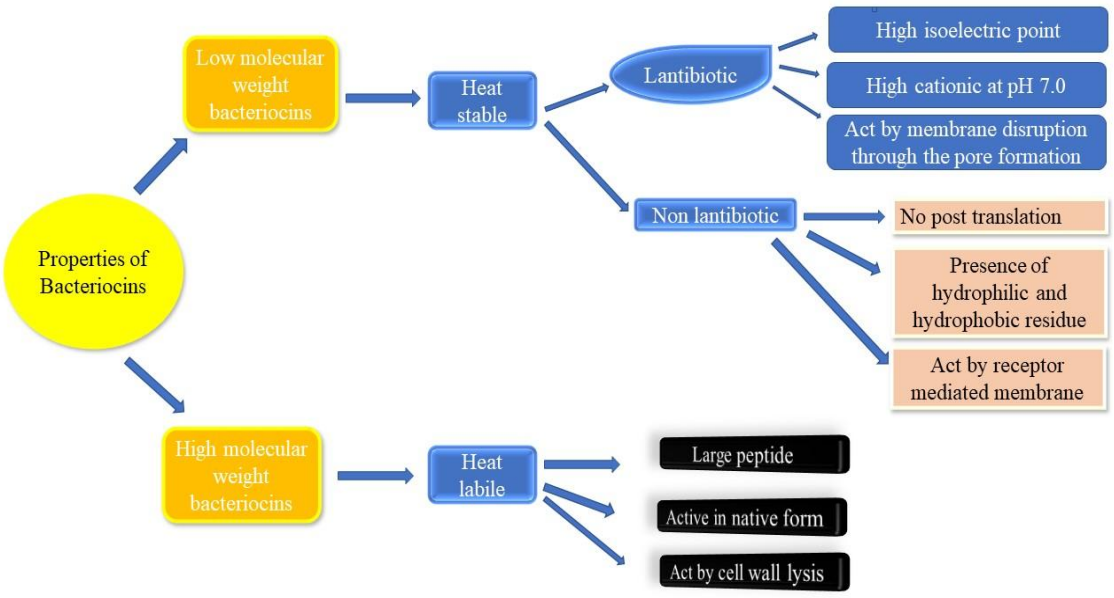

Fig. 1. Properties of bacteriocins

Table 3. Classification of bacteriocins [19]

Classification	Features	Subcategories	Example
Class I Bacteriocins (Lantibiotics)	Anthionine or peptides Containing β-lanthionine	Type- A (Linear molecules) Type-B (Globular molecule)	Nisin, Subtilin, Epidermine, Mersacidin
Class II Bacteriocins	Heterogeneous class of small thermostable peptides	Subclass IIa (Antilisterial pediocine bacteriocins type) Subclass IIa (Composed of two peptides) Subclass IIc (other bacteriocins)	Pediocin, enterocin, sakacin Plantaricin, lactacin F Lactococcin
Class III Bacteriocins	Large thermolabile peptides		Helveticin J, millericin B

Another class of bacteriocins derived from gram-positive bacteria is made up of cyclic peptides, lipid moieties and carbohydrate [20,21]. Colicin bacteriocin produced by gram- negative bacterium *Escherichia coli* is the well known bacteriocin. These bacteriocins primarily target strains of *E. coli* and other closely related enteric organisms [22] by blocking of cell wall synthesis, pore-formation, RNAse and DNAse activities [23]. Proteins from Gram-negative bacteria that attacks the target cell membrane by assembling themselves into particles that resemble bacteriophage tails make up another class of protein bacteriocins [24].

Bacteriocins of Gram-negative bacteria differs from bacteriocins of Gram-positive bacteria. Enterobacteriaceae family members also produce bacteriocins known as microcin's which may or may not possess posttranslational modifications [25]. Trifolitoxins are another class of bacteriocins produced by Gram-negative bacteria, and these bacteria occasionally produce bacteriocins that are "Gram-positive-like" [26].

4. MODE OF ACTION OF BACTERIOCINS

Bacteriocins attacks target organism through a variety of mechanisms. These mechanisms are roughly classified as those that act on the cell envelope and influence expression of genes and production of proteins. Gram positive bacteria inhibiting bacteriocins often attacks the cell envelope.

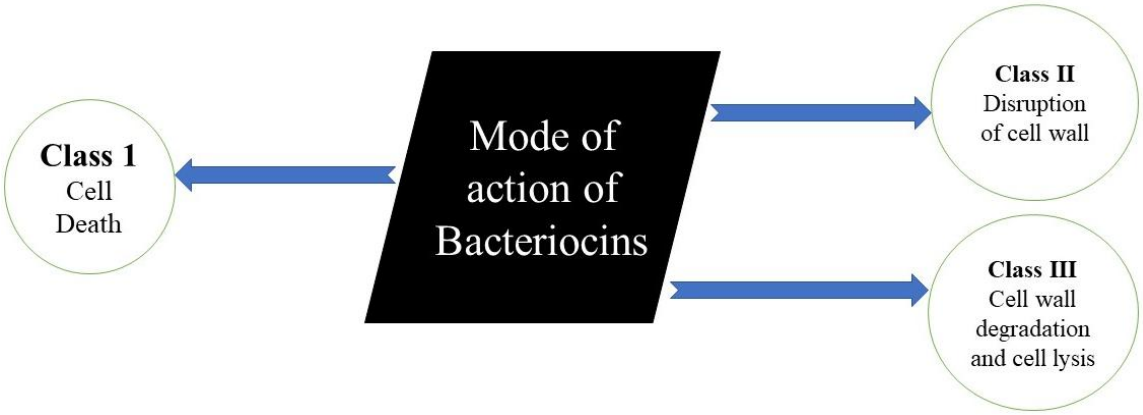

Fig. 2. General mode of action of bacteriocins

Class I bacteriocins prevents the production of lipid-II in cell membrane and alter peptidoglycan synthesis. For their target bacteria to be inhibited or killed, other bacteriocins form pores. Gram-negative inhibiting bacteriocins interferes with RNA, DNA, and protein metabolism. MccJ25, microcin B17 (MccB17) and MccC7-C51 inhibits RNA polymerase, DNA gyrase, and aspartyl-tRNA synthetase, respectively. However, MccE492 functions by forming pores [27]. Few bacteriocins have enzymatic activities. Colicin E3 possess RNase activity, megacin A-216 have phospholipase activity and colicin E2 exhibits DNase activity towards the target organism [28].

Class II bacteriocins gets integrated into target cell membrane by virtue of their amphiphilic helical structure which leads to membrane depolarization and death of the cell. Whereas, class III bacteriocins attacks cell wall of the bacteria and thereby lyse the target cell [29].

5. APPLICATION OF BACTERIOCINS

Management of phytopathogenic bacteria depends on chemicals consisting of antibiotics, mainly streptomycin and copper. These chemicals are harmful to both the environment and human health and the emergence of resistance can limit their efficacy over time [30,31]. Numerous diseases, including citrus greening and fire blight, have been successfully treated with streptomycin.

However, extensive use of antibiotics in agricultural crops might develop reservoirs of resistance that could possibly spread from bacteria that cause plant disease to those that are clinically significant [32,33]. The success of toxin produced by *Bacillus thuringiensis* is largely attributed to both its high level of target selectivity and ease of expression in plants. The properties of bacteriocins are comparable. This is very advantageous in both clinical as well as agricultural systems because it is anticipated that their use will have little impact on the microbiome. Bacteriocins can be directly applied to crops or expressed in plants like Bt toxins. It has been clearly demonstrated by Nomad Biosciences that it is possible to express bacteriocins (LLBs and CLBs) in a number of plant species [34,35,36]. Additionally, bacteriocin toxicity has been found in a variety of animal models [37]. In environment, Bacteriocins are produced naturally and are believed to have low toxicity toward humans and animals. The majority of bacteriocins are thought to be safe to use in preservation of food items [34]. Transgenic plants expressing bacteriocins can be produced to offer resistance against *Pseudomonas syringae.* Non- genetically modified approaches for bacteriocins includes using non-pathogenic bacterial strain for direct application on crop such as Biokeeper and Nogall [38,39]. Alternatively, direct application of bacteriocins have shown great results under in vitro conditions against bacterial leaf spot and olive knot disease of tomato [40,41]. The need for large-scale production of bacteriocin is one potential problem with using bacteriocins as a direct treatment. Production of multi-component bacteriocins is difficult as compare to lectin-like bacteriocin and colicin-like bacteriocin [34,35,42]. Bacteriocins are organized into functional domains, and are easily modifiable, opening up the possibility of producing additional variants through swapping of domains to develop new chimeric bacteriocins with modified functions [43].

6. CONCLUSION AND FUTURE PROSPECTIVES

Overall, important strides have been made in the study of biocontrol agents for the creation of commercial products for the management of bacterial and fungal diseases. However, the lack of readily available, effective BCAs on a large scale prevents the use of biological control. There is great need to identify the novel BCA and methods for screening large numbers of candidates. Additionally, a thorough investigation of model BCA using genomic analysis will offer an essential framework for a thorough analysis of the biological mechanisms of BCA and the development of strategies to increase its positive effects. Additionally, this multi-omics examination will enable analysis of the effects of bacterial field application on the native plant microbiome. This research would make it possible to assess the environmental effects of BCA, assure its biosafety, and learn how to manipulate the microbiome to increase the effectiveness of biocontrol.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. De Vugst L, Vandamme EJ, Bacteriocins of lactic acid bacteria, microbiol, Genet

Appl. London: Blackie Acad and Professional. 1994; ISBN- 75140174-9.
2. Gratia A. On a remarkable example of antagonism between two strains of hummingbird. Comptes Rendus Biologies (CR BIOL). 1925;93:1040–1042.
3. Zacharof MP, Lovitt RW, Bacteriocins produced by lactic acid bacteria a review article. Apcbee Procedia. 2012; 2:50-56.
4. Vogel V, Spellerberg B, Bacteriocin production by beta-hemolytic Streptococci. Pathogens. 2021;10(7):867.
5. Cesa-Luna C, Alatorre-Cruz JM, Carreno-Lopez R, Quintero-Hernandez V, Baez A, et al. Emerging applications of bacteriocins as antimicrobials, anticancer drugs, and modulators of the gastrointestinal microbiota. Polish Journal of Microbiology. 2021;70(2):143.
6. Juturu VJ, Microbial production of bacteriocins: Latest research development and applications. Biotechnol Adv. 2018;36:2187–2194.
7. Bastos MDC, Coelho MLV, da Silva Santos OC, Resistance to bacteriocins produced by Gram-positive bacteria. Microbiol. 2015;161:683–700.
8. Bountra K, Hagelueken G, Choudhury HG, Structural basis for antibacterial peptide self-immunity by the bacterial ABC transporter McjD. EMBO J. 2017;36:3062–79.
9. Bédard F, Biron E. Recent progress in the chemical synthesis of class II and S-Glycosylated Bacteriocins. Front. Microbiol. 2018;9:1048.
10. Lagha A, Haas B, Gottschalk M, Grenier D, et al. Antimicrobial Potential of bacteriocins in poultry and swine production. Veter Res. 2017;48:1–12.
11. Gulluce M, Karaday M, Baris O. Bacteriocins: Promising natural antimicrobials, in Microbial Pathogens and Strategies for Combating Aem: Science, Technology, and Education, A. Mendez-Vilas, Ed., Formatex Research Center, ´ Badajoz, Spain. 2013;1016–1027.
12. Balciunas EM, Martinez FAC, Todorov SD, Franco A, Converti RPDS, et al. Oliveira, “Novel biotechnological applications of bacteriocins: A review,” Food Control. 2013;32(1):134–142.
13. Cleveland J, Montville TJ, Nes IC. Bacteriocins: Safe, natural antimicrobials for food preservation. Int J Food Microbiol. 2001;71:1–20.
14. Chatterjee C, Paul M, Xie L, Van Der Donk WA, et al. Biosynthesis and mode of action of lantibiotics. Chem Rev. 2005;105: 633–684.
15. Soomro AH, Masud T, Anwaar K, Role of lactic acid bacteria (LAB) in Food preservation and Human Health- A Review. Pakistan J Nutr. 2002;1:20-24.
16. Hasper HE, Kramer NE, Smith JL, Hillman JD, Zachariah C, Kuipers OP, de Kruijff B, Breukink E, et al. An alternative bactericidal mechanism of action for lantibiotic peptides that target lipid II. Science. 2016;313:1636–1637.
17. Eijsink VGH, Axelsson L, Diep DB, Havarstein LS, Holo H, Nes F, et al. Production of class II bacteriocins by lactic acid bacteria; an example of biological warfare and communication. Antonie Van Leeuwen. Intl J Gen Mol Microbiol. 2002;81:639–654.
18. Diep DB, Skaugen M, Salehian Z, Holo H, Nes IF, et al. Common mechanisms of target cell recognition and immunity for class II bacteriocins. Proc Natl Acad Sci. 2007;104:2384–2389.
19. Johnson EM, Jung DYG, Jin DYY, Jayabalan DR, Yang DSH, Suh JW, et al. Bacteriocins as food preservatives: Challenges and emerging horizons. Critical reviews in food science and nutrition. 2018;58(16):2743-2767.
20. de Jong A, Hijum SAFT, Bijlsma JJE, Kok J, Kuipers OP, et al. BAGEL: A web-based bacteriocin genome mining tool. Nucleic Acids Res. 2006;34:273–279.
21. Heng NCK, Tagg JR, Class distinction for bacteriocins. Nat Rev Microbiol. 2006;4. DOI: 10.1038/nrmicro 1273-cl
22. Riley MA, Gordon DM, The ecological role of bacteriocins in bacterial competition. Trends Microbiol. 1999;7:129–133.
23. Braun V, Patzer SI, Hantke K, Ton-dependent colicins and microcins: modular design and evolution. Biochimie. 2002; 84:365–380.
24. Michel-Briand Y, Baysse C, The pyocins of Pseudomonas aeruginosa. Biochimie. 2002;84:499–510.
25. Duquesne S, Petit V, Peduzzi J, Rebuffat S, Structural and functional diversity of microcins, gene-encoded antibacterial peptides from enterobacteria. J Mol Microbiol Biotechnol. 2007;13:200–209.
26. Dirix G, Monsieurs P, Marchal K, Vanderleyden J, Michiels J, et al. Screening genomes of Gram-positive

bacteria for double-glycine-motif-containing peptides. Microbiology. 2004;150:1121–1126.
27. Blaszczyk U, Moczarny J, “Bacteriocins of gram-negative bacteria—structure, mode of action and potential applications,” Postepy Mikrobiologii/ 2016;55(2):157–171.
28. Prabhakar KV, Lingala VK, Peelei I, Mikkili, Venkateswarulu, Dulla JB, et al. Biosynthesis and potential application of bacteriocins. Journal of Pure and Applied Microbiology. 2013;7(4):2–13.
29. Cotter PD, Hill C, Ross RP, Bacteriocins: developing innate immunity for food. Nat Rev Microbiol. 2005;3:777–788.
30. Sundin GW, Bender CL, Ecological and genetic analysis of copper and streptomycin resistance in *Pseudomonas syringae* pv. *syringae*. Appl. Environ. Microbiol. 1993;59:1018–1024.
DOI: 10.1128/aem.59.4.1018-1024
31. Damalas CA, Eleftherohorinos IG, Pesticide exposure, safety issues, and risk assessment indicators. Int. J. Environ. Res. Public Health. 2011;8:1402–1419.
DOI: 10.3390/ijerph8051402
32. Norelli JL, Jones AL, Aldwinckle HS, Fire blight management in the twenty-first century: using new technologies that enhance host resistance in apple. Plant Dis. 2003;87:756–765.
DOI: 10.1094/pdis.2003.87.7.756
33. McKenna M, Antibiotics set to flood Florida’s troubled orange orchards. Nature; 2019.
DOI: 10.1038/d41586-019-00878-874
34. Schulz S, Stephan A, Hahn S, Bortesi L, Jarczowski F, Bettmann U, et al. Broad and efficient control of major foodborne pathogenic strains of Escherichia coli by mixtures of plant-produced colicins. Proc Natl Acad Sci U.S.A. 2015;112, E5454–E5460.
35. Paskevicius S, Starkevi CU, Misiunas A, Vitkauskiene A, Gleba Y, Razanskiene A, et al. Plant-expressed pyocins for control of *Pseudomonas aeruginosa*. PLoS One; 2017.
DOI: 10.1371/journal.pone.0185782
36. Schneider T, Hahn-Löbmann S, Stephan, A, Schulz S, Giritch A, Naumann M, et al. Plant-made Salmonella bacteriocins salmocins for control of Salmonella pathovars. Sci Rep. 2018;8:4078.
DOI: 10.1038/s41598-018-22465-9
37. Behrens HM, Six A, Walker D, Kleanthous C, The therapeutic potential of bacteriocins as protein antibiotics. Emerg. Top. Life Sci. 2017;1:65–74.
DOI: 10.1042/etls20160016
38. Jones DA, Ryder MH, Clare BG, Farrand SK, Kerr A, et al. Construction of a Tra - deletion mutant of pAgK84 to safeguard the biological control of crown gall. MGG Mol. Gen. Genet; 1988.
DOI: 10.1007/ bf00334686
39. Chuang DY, Kyeremeh AG, Gunji Y, Takahara Y, Ehara Y, Kikumoto T, et al. Identification and cloning of an Erwinia carotovora subsp. carotovora bacteriocin regulator gene by insertional mutagenesis. J Bacteriol; 1999.
DOI: 10.1128/jb.181.6.1953-1957.1999
40. Lavermicocca P, Lisa Lonigro S, Valerio F, Evidente A, Visconti A, et al. Reduction of olive knot disease by a bacteriocin from Pseudomonas syringae pv. ciccaronei. Appl. Environ Microbiol. 2002;68:1403–1407.
41. Príncipe A, Fernandez M, Torasso M, Godino A, Fischer S, et al. Effectiveness of tailocins produced by prin in controlling the bacterial-spot disease in tomatoes caused by *Xanthomonas vesicatoria*. Microbiol Res. 2018;213:94–102.
42. Rooney W M, Grinter RW, Correia A, Parkhill J, Walker DC, Milner JJ, et al. Engineering bacteriocin-mediated resistance against the plant pathogen *Pseudomonas syringae*. Plant Biotechnol J. 2019;18:1296–1306.
43. Lukacik P, Barnard TJ, Keller PW, Chaturvedi KS, Seddiki N, Fairman JW, et al. Structural engineering of a phage lysin that targets Gramnegative pathogens. Proc Natl Acad Sci U.S.A 2012;109:9857–9862.
DOI: 10.1073/ pnas.1203472109