



Bacteriocins for Food Safety: An Innovative Strategy against Antimicrobial Resistance

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ABSTRACT

Background: To explore the potential of bacteriocins to combat anti-microbial resistance (AMR).

Methods: Different articles on antimicrobial resistance and its possible solutions were reviewed. The critical analysis was done at Parul University, Vadodra and GITAM Deemed to be University, Hyderabad from March 2024 to April 2025. Antimicrobial resistance (AMR) poses a severe global health crisis, characterized by the declining effectiveness of antibiotics, leading to persistent infections and increased mortality rates. In food safety, AMR exacerbates the challenge of controlling pathogens such as *Staphylococcus aureus* and *Listeria monocytogenes*, posing significant risks to public health. Bacteriocins are naturally occurring antimicrobial peptides produced by lactic acid bacteria, present a promising alternative to conventional antibiotics. These peptides selectively inhibit pathogens while preserving beneficial microbiota, making them ideal for food safety systems. As generally recognized as safe (GRAS) substances, bacteriocins offer a sustainable solution to AMR in foodborne pathogens.

Result: This review explores the potential of bacteriocins to combat AMR, highlighting research findings, practical applications and case studies. By incorporating bacteriocins into food safety practices, the global effort to mitigate AMR can be significantly advanced.

Key words: Antimicrobial resistance, Antimicrobials, Bacteriocins, Food pathogens, Foodborne diseases, Nutraceuticals.

Antimicrobial resistance in foodborne pathogens has emerged as a significant global concern, leading to illnesses ranging from mild to life-threatening. Nearly 1.5 million annual deaths, particularly among children, are attributed to infectious diarrhoea. Major foodborne pathogens include *Staphylococcus aureus*, *Listeria monocytogenes* (Sharma *et al.*, 2020; Saeed *et al.*, 2025), *Escherichia coli* (Barathiraja *et al.*, 2015), *Vibrio* spp., *Yersinia enterocolitica*, *Salmonella* spp. and Norwalk-like viruses (Saeed *et al.*, 2025). The rise of AMR complicates disease management and places a significant burden on healthcare systems. Mechanisms like enzymatic modification of antibiotics, biofilm formation and genetic mutations enable pathogens to evade treatments. Resistance is further amplified by environmental factors such as pollution and misuse of antibiotics (Langford *et al.*, 2023).

The emerging anti-microbial resistant strains of food-borne pathogens include the species of Methicillin-resistant *Staphylococcus aureus*, *Pseudomonas aeruginosa* (Escolanoa *et al.*, 2019), *Salmonella* spp., *Salmonella enteritidis*, *Clostridium difficile* and *Listeria monocytogenes*, *Campylobacter jejuni*, *Shigella sonnei*, *Yersinia enterocolitica*, *Escherichia coli* 0157:H7, *Helicobacter pylori*, *Shigella dysenteriae* and *Shigella flexneri* (Umu *et al.*, 2019). The antimicrobial resistance of these pathogens may spread from food producing plants and animals to humans (Oniciuc *et al.*, 2019) posing significant threats to public health and food security.

Bacteriocins are antimicrobial peptides with targeted activity against specific bacteria. They are effective at low concentrations (Soltani *et al.*, 2022) and demonstrate both

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narrow- and broad-spectrum activity. Bacteriocins selectively target and inhibit pathogenic bacteria, minimizing the development of resistance and preserving beneficial microbiota. Bacteriocins recognize pathogens via quorum sensing, a genetic regulation system that ensures high specificity (García-Curiel *et al.*, 2021). Their GRAS designation makes them safe for human consumption and suitable for food safety applications (Ricci *et al.*, 2017).

Different articles on antimicrobial resistance and its possible solutions were reviewed. The critical analysis was done at Parul University, Vadodra and GITAM Deemed to be University, Hyderabad from March 2024 to April 2025.

Classification of bacteriocins

Bacteriocins are secondary metabolites of several bacterial genera. All strains are not capable of their production as it is an energy and nutrient demanding process (García-

Curiel *et al.*, 2021). Bacteriocins can be classified based on their microbial source as Gram positive, Gram negative, archaeal bacteriocins, ribosomal synthesis and post-translation modification of peptides (RiPP nomenclature)

Table 1: Classification of bacteriocins.

Microbial source	Classes	Molecular weight	Features	Subclass	Examples	References
Gram positive bacteriocins (produced by lactic acid bacteria)	Class-I (Lantibiotics)	less than 5 kDa	Thermostable, consists of amino acid structures as lanthionine and methyl l-lanthionine and unsaturated amino groups linked by disulphide bonds. Exhibit high post-translation modifications	Ia- positively charged-polar with net charge-positive Ib- Negatively charged or neutral- with net charge-negative or no charge	Nisin Mersacidin	Todorov, <i>et al.</i> 2019; Negash and Tsehai, 2020
	Class-II (Non-lantibiotic peptides)	less than 10 kDa	Minimal or no post-translation modification	Ila- peptides having activity against <i>Listeria</i> spp. Ilb- peptides in dimeric conformation Ilc- peptides with circular structure Ild- linear peptides	Pediocin PA1, Sakacin A Lactococcin G, Lactacin F Enterocin P Lactococcin A	Negash and Tsehai, 2020 Ricci <i>et al.</i> , 2017; Negash and Tsehai, 2020 Ricci <i>et al.</i> , 2017; Zheng <i>et al.</i> , 2020; Li <i>et al.</i> , 2023
	Class-III (Thermolabile proteins)	More than 30 kDa	Thermolabile		Helveticin J, colicins like klebacin	Negash and Tsehai, 2020; Zheng <i>et al.</i> , 2020
	Colicins	30-80 kDa	Class I (Produced by <i>E. coli</i> consisting of plasmid colicinogenic) Class II (Produced by other members of Enterobacteriaceae)	Ia- consists of plasmid pColE1 Ib- consists of plasmid pColH Non <i>E. coli</i> produced	Colicin E1 Colicin M Megacins	Pérez-Ramos <i>et al.</i> , 2017; Negash and Tsehai, 2020
Gram-negative bacteriocins (<i>E. coli</i> produced or other strains of enterobacteria)	Microcins	1-10 kDa	Stable molecular structure, active at wide pH range, resistant to proteases and temperature change. These are encoded in bacterial genomic DNA	I- molecular weight less than 5 kDa II- molecular weight 5-10 kDa	Microcins L, V, N Microcins E492, M, H47	

(Zimina *et al.*, 2020). The detailed classification of these bacteriocins is shown in the Table 1 and Table 2.

Bacteriocin biosynthesis

Bacteriocins are released as secondary metabolites during microbial fermentation process. The bacteriocin production and release is based on signal transduction systems through a general secretory pathway (GSP) that helps in regulation and secretion of peptides and proteins. There are certain genes that encode the bacteriocin biosynthesis process within the microbe including structural genes, genes encoding secretory accessory proteins, modification genes, regulatory genes and immunity genes. These genes are organised on microbial DNA as operons. The structural genes are located on a leader sequence-MDKLSKFESLSDANLSTIVG. It is a signal peptide consisting of Sec gene that encodes two structural genes-

welY (made up of 42 amino acids) and welM (made up of 43 amino acids). These genes encode pre-pro bacteriocin (premature form of bacteriocin), having N-terminal. The two conserved glycans are present at C-terminus that process the leader sequence and helps in the release of mature bacteriocin. The genes that encode secretory accessory protein helps in processing, transport and secretion of pre-probacteriocin. Modification genes- ComA is ATP binding while ComB encodes permease enzyme that mainly helps in post-translational modification of probacteriocin. The regulatory genes are located on ribosome binding site (RBS) that consist of cellobiose-specific IIC component. The genes mainly encode the regulation of bacteriocin biosynthesis. The immunity gene-Abi gene (made up of 51-154 amino acids) is located on CAAX motif. The gene encodes the protection to bacteriocin producing strain (Todorov *et al.*, 2019) (Fig 1).

Table 2: RIPPs nomenclature of bacteriocins.

RIPPs as bacteriocins	Features	Example
Lanthipeptides	Contain lanthionine group.	Nisin
Linaridins	Lanthipeptides with different pathway for synthesis.	Cypemycin
Proteusins	Complex structured peptides containing D-configured amino acids.	Polytheonamides
Linear azole (in) e-containing peptides (LAPs)	Consist of thiazole and methyl oxazole heterocycles.	Microcin B17
Cyanobactins	Short peptides synthesized by cyanobacteria.	Cyanobactin
Thiopeptides	Synthesized by <i>Bacillus</i> and <i>Staphylococcus</i> spp. The peptides consist consist of thiopeptide macrocycle along with amino acids.	Micrococins
Botromycins	Produced from <i>Streptomyces bottropensis</i> . Peptides consist of macrocyclic amidine and decarboxylated C-terminal thiazole on their structure	Botromycin A2
Lasso peptides	Stable bacteriocins produced by actinobacteria and proteobacteria. Short peptide containing macrolactam ring at the terminal that interacts with C-terminal tail forming a "lasso fold" structure.	Microcin J25
Sactibiotics	Sactipeptides produced from the genus <i>Bacillus</i> . The cysteine residues link to alpha carbon of other amino acids.	Subtilisin A
Bacterial head-to-tail cyclized peptides	Large molecular weight with different synthesis pathway than other RIPPs. Consists of peptide bond in between two amino acids.	Enterocin AS-48
Colicins and microcins	Similar features as mentioned in Table 1.	Colicin M, Microcin L

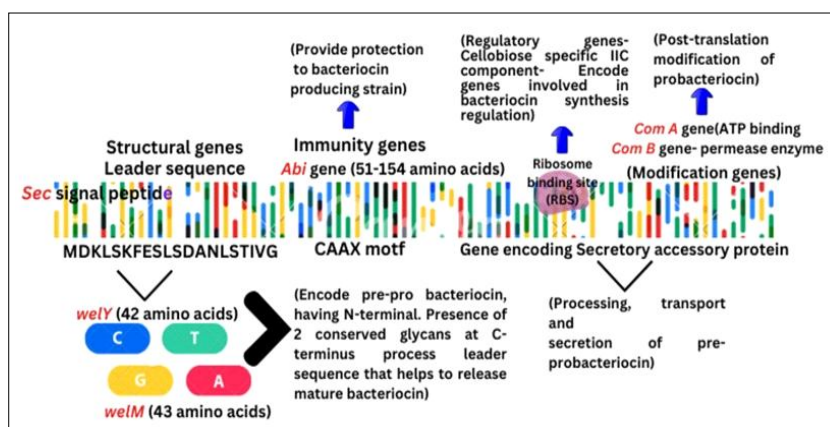


Fig 1: Different genes encoding bacteriocin biosynthesis process.

Bacteriocins as potent proteins in preventing antimicrobial resistance

The successful bacteriocins that demonstrate their potential in preventing antimicrobial resistance in food safety. Below are the details on notable examples (Woo *et al.*, 2021).

AS-48

The circular bacteriocin (Class Ib)-enterocin AS-48 is low toxic and more potent bacteriocin. AS-48 is a 70- amino acid peptide that is produced by different strains of *Enterococcus* spp.

Nisin

The commercially available bacteriocin nisin is a class-Ia lantibiotic produced by the strains of *Lactococcus* and *Streptococcus*. It is a 34 amino acid bacteriocin, made by post-translational modification of lanthionine and dehydroamino acids.

Bac-IB45

A bacteriocin Bac-IB45, class IIa is a highly thermostable, pH stable and broad spectrum bacteriocin isolated from *Lactobacillus plantarum* KIBGE-IB45 strain. The bacteriocin has bactericidal mode of action that inhibits the complete growth of the bacteria.

The bacteriocins AS-48, nisin and Bac-IB45 inhibit the cell wall biosynthesis by creating pores within the membranes of the bacterial cell, therefore increases the permeability of cytoplasmic membrane, thereby releasing the ions and ATP from the bacterial cell and removing the Lipid II (peptidoglycan precursor as docking

molecule) from its main location (Woo *et al.*, 2021) (Fig 2, Table 3). This leads to complete cell inactivation of the pathogens.

ST₁₁₀LD

Bacteriocin produced by *Leuconostoc citreum* strain ST₁₁₀LD is a class IIa bacteriocin. This bacteriocin mainly binds to lipid II present on the membrane of the *Listeria* spp. This high specificity of the bacteriocin for the *Listeria* spp. may be a specific marker or involvement of receptors as a point of contact between bacteriocin and *Listeria* spp. (Table 3).

Modified nisin

The lantibiotic nisin was modified by fusion of peptides (T16 m²). T1 is the tail in the structure consisting of sequence DKPRPYLPRPRPV (Fig 3). It is an anti-microbial peptide that is designed based on statistical analysis to improve the anti-microbial action of nisin against Gram negative antimicrobial resistant food borne pathogens (Table 3) (Li *et al.*, 2023).

Plantaricin A (PlnA)

The species of *Lactiplantibacillus plantarum* produces a cationic bacteriocin called Plantaricin A (PlnA) (Luther *et al.*, 2019; Meng *et al.*, 2021) (Fig 2). The bacteriocin PlnA with a concentration of 25 µg/ml has shown to alter the cellular morphology of multi-drug-resistant strain of food borne pathogen *Escherichia coli* that led to an increase in the outer membrane permeability of *E. coli* at the concentration of 6.25 µg/ml (Table 3) (Meng *et al.*, 2022).

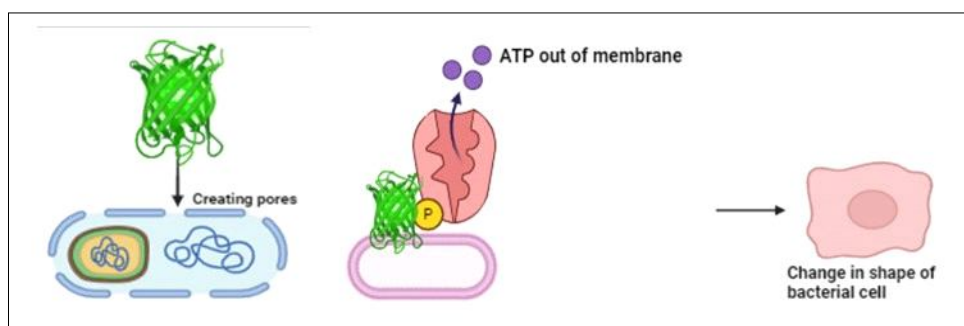


Fig 2: Bacteriocin create pores within bacterial cell wall leading to release of ATP and loss of cellular integrity.

Table 3: MIC of bacteriocins against food bone pathogens.

Multi-drug resistant strains	MIC of Bacteriocins					
	AS-48 (µM)	Nisin	Bac-IB45	ST ₁₁₀ LD	Modified Nisin	PlnA
<i>Staphylococcus aureus</i>	0.23	0.07 µM	160 µg/ml	-	-	-
<i>Staphylococcus chromogenes</i>	0.26	0.04 µM	-	-	-	-
<i>Staphylococcus simulans</i>	0.19	0.12 µM	-	-	-	-
<i>Staphylococcus xylosus</i>	0.25	0.08 µM	-	-	-	-
<i>Listeria monocytogenes</i>	-	0.5-12.5 µg/ml	80 µg/ml	12800 AU/ml	-	-
<i>Pseudomonas aeruginosa</i>	-	-	80 µg/ml	-	32 AU/ml	-
<i>Escherichia coli</i>	-	-	80 µg/ml	-	8 AU/ml	25 µg/ml

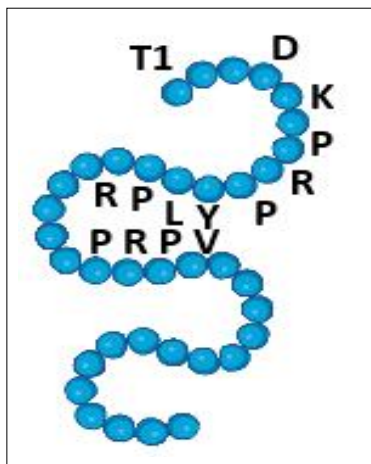


Fig 3: A segment of Nisin peptide.

Regulatory and safety considerations for application of bacteriocins as antimicrobials

Regulatory authorities grant GRAS status to substances deemed safe based on extensive scientific evidence or historical use. For instance, nisin has GRAS approval and is widely applied in food preservation and therapeutics, setting a benchmark for other bacteriocins. The Codex Alimentarius provides internationally recognized guidelines for bacteriocin usage in food. It outlines permissible limits, such as the approved nisin levels (12.5-25 mg/kg) based on the food matrix and application (EFSA, 2021).

Other challenges

The challenges involved for bacteriocin production include -Scaling up requires cost-effective fermentation techniques. Bacteriocins often require encapsulation or specific delivery systems to remain stable and active during food processing and storage. Ensuring compatibility with various food matrices without altering sensory properties presents another significant obstacle. Furthermore, misconceptions about microbial-derived products may hinder consumer acceptance (Lopetuso *et al.*, 2019; Vermeulen *et al.*, 2019).

CONCLUSION

Bacteriocins offer a sustainable, effective solution to the AMR crisis in food safety. Their targeted antimicrobial activity, coupled with safety and regulatory compliance, positions them as a cornerstone in modern food safety systems (Sharma *et al.*, 2021). While nisin serves as a model with established GRAS status and widespread applications, other bacteriocins such as AS-48, Bac-IB45, ST110LD and Plantaricin A show immense potential that requires further research and regulatory consideration (Roemhild and Andersson, 2021). Future exploration into their applications, coupled with advances in production technologies and regulatory alignment, will unlock their full potential in combating AMR globally.

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Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

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Authors' contributions

Parul Thapar and Mohinder Kumar Salooja carried out conception of the work and manuscript preparation. Parul Thapar, Gatadi Srikanth and Mohinder Kumar Salooja carried out data analysis and interpretation. K. Gireesh Babu performed the critical revision and final approval of the version to be published.

Data availability statement

All data generated during the study are included in the manuscript.

Conflict of interest

The authors declare that they have no competing interest.

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