



CLASSIFICATION, MECHANISM OF ACTION AND APPLICATIONS OF BACTERIOCINS FROM LACTIC ACID BACTERIA : A REVIEW

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Abstract

Lactic acid bacteria (LAB) are Gram-positive cocci or rods. They are catalase-negative, non-spore forming, aerotolerant anaerobes. LAB ferment glucose to lactic acid with or without CO₂ and ethanol. LAB may produce a group of potent antimicrobial peptides that exhibit bactericidal activity called bacteriocins, these peptides work against organisms closely related to the bacteriocin producing LAB strain. Certain bacteriocins may prevent the growth of some Gram-positive pathogens, spoilage bacteria, and yeasts. They may even inhibit the growth of some Gram-negative species. These properties caused LAB to be a subject for research as a source of probiotics and as bio-preservatives. The aim of the present review is to delineate the use of lactic acid bacteria and their bacteriocins.

Key words: Bacteriocin; classification; Applications; LAB.

Introduction

Bacteriocins produced by lactic acid bacteria (LAB) are potent antimicrobial peptides or proteins that are active against, closely related bacterial species, Based on its biochemical and genetic properties, bacteriocins are classified into three classes (Nes *et al.*, 1996; Lopetuso *et al.*, 2019). Bacteriocins produced by LAB have antimicrobial activity at concentrations that are lower than antimicrobial peptides from eukaryotic origin, presumably due to their interaction with a specific receptor on target cells (Nissen-Meyer *et al.*, 2001).

Lactic acid bacteria (LAB) are a group of fastidious Gram-positive rods or cocci, with high tolerance for low pH. They are aerotolerant and might be non-aerobic. They cause carbohydrate fermentation for energy. Additionally, they produce lactic acid and are catalase-negative, (De Vuyst and Leroy, 2007; Kaban and Kaya, 2008). The LAB is under the phylum Firmicutes, class Bacilli and order Lactobacillales. LAB classification is based on cell morphology, range of growth temperature, mode of glucose fermentation and patterns of sugar utilization. (Quinto *et al.*, 2014). Lactic acid bacteria include various major genera.

Lactobacillus, *Lactosphaera*, *Leuconostoc*,

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Lactococcus, *Enterococcus*, *Carnobacterium*, *Oenococcus*, *Streptococcus*, *Tetragenococcus*, *Melissococcus*, *Pediococcus*, *Streptococcus*, *Weissella*, *Aerococcus*, *Vagococcus*, *Bifidobacterium*, *Microbacterium* and *Propioni bacterium*. The most common species of Lactic acid bacteria are: *Lactobacillus acidophilus*, *L. Casei*, *L. rhamnosus*, *L. plantarum*, *L. delbrueckii bulgaricus*, *L. reuteri*, *L. fermentum*, *Bifidobacterium bifidum*, *B. adolescentis*, *B. longum*, *B. adolescentis*, *B. breve*, *Enterococcus faecalis*, (Garrity, 1984; Dellaglio *et al.*, 1994; Carr *et al.*, 2002).

There are more than one hundred species under the genus of *Lactobacillus*. Which are largely exist in materials that are rich in carbohydrate. LAB are commonly used in fermentations of food and improvement of texture and test of fermented foods. (Van Geel-Schuttená *et al.*, 1998; Walter, 2008; Khalid, 2011; Hati *et al.*, 2013). *Lactobacilli* are also used in food preservation.

Ecologically, LABs are found naturally in soil, water, sewage, plant silage, decomposing plant materials and fruits. They are part of the microbiota on the intestines, mouth, skin, urinary and genital organs of humans and animals. *Lactobacilli* have a beneficial effect on the ecosystems (Todorov, 2009; König *et al.*, 2009; Djadouni

and Kihal, 2012; Devi *et al.*, 2013; Liu *et al.*, 2014). LAB have been used in different applications such as starter cultures in food and feed fermentations, pharmaceuticals, probiotics and as biological control agents (Leory and De Vuyst, 2004; (Diep & Nes, 2002).

Preservation using various chemicals is associated with serious side effects. (Stevenson, 2010). Therefore, interest in using LAB and their bioproducts bio-preservatives such as bacteriocin and/or other substance for application in non-fermentative preservation. s, and some LAB strains are used as probiotics as natural competitive microbiota. (Fuller, 1989; Parada *et al.*, 2003) LAB may be used to make starter culture using specific conditions. (Cintas *et al.*, 2001).

LAB inhibitory effect on the growth of pathogenic microorganisms has been reported. Additionally, it was demonstrated that extracts from LAB isolates could destroy mycotoxins in addition to probiotic capabilities and antimicrobial activities. (Naidu *et al.*, 1999; Todorov, 2009). Several microorganisms produce antimicrobials or peptide that has exhibit: antibiotics, detrimental effects against fungal species as well as some viruses.. Bacteriocin is one of these extracts. (Klaenhammer *et al.*, 1994; Moreno *et al.*, 2000). Bacteriocins are ribosomally-synthesized bactericidal peptides that are inhibitory to different pathogens (Lopetuso *et al.*, 2019), Fig. 1. It is produced by lactic acid bacteria and have drawn growing attention, as they are active at a nanomolar concentration with no toxicity. Bacteriocins are protein in nature and readily destroyed by digestive tract enzymes.

Bacteriocins are made at the ribosomal sites of the

cell. Therefore it is possible to improve their features to increase their effectiveness and spectrum of action (Saavedra *et al.*, 2004). Lactic acid bacteria (LAB) are known to produce lactic acid from glucose. However their main importance is related to their ability to produce bacteriocins and related substances that have preservative effects through preventing the growth of pathogens and food spoilage bacteria. (Alakomi *et al.*, 2000; De Vuyst and Leroy, 2007).

Sugar fermentation results in a reduction in pH due to the production of lactic and other organic acids that are known for their inhibitory effect of the prolefration of harmful agents. Organic acids are made liposoluble via low PH and that facilitate their passage through cell membrane to reach the cytoplasm of pathogens (Haller *et al.*, 2001). LAB grows optimally at pH 5.5–5.8. LAB have sophisticated needs for growth requirements including vitamins, minerals in addition to several amino acids, fatty acids, peptides, nucleotide bases and carbohydrates (Khalid, 2011). Additionally, it has been applied as a bio-preservative for foods nearly 25 years and in the control of human pathogens (Balciunas *et al.*, 2013; Parada, 2007). Bacteriocins are largely small peptides (<10 kDa) that are amphiphilic cationic, and heat-stable, which are permeable through cell membranes. (Zacharof and Lovitt, 2012). The DNA of LAB has a low G + C content (König and Fröhlich, 2009). Bacteriocins can be categorized into four different groups on the base of based on some common features such as structure, molecular weight, resistance to heat, biochemical and genetic characteristics (Cotter *et al.*,

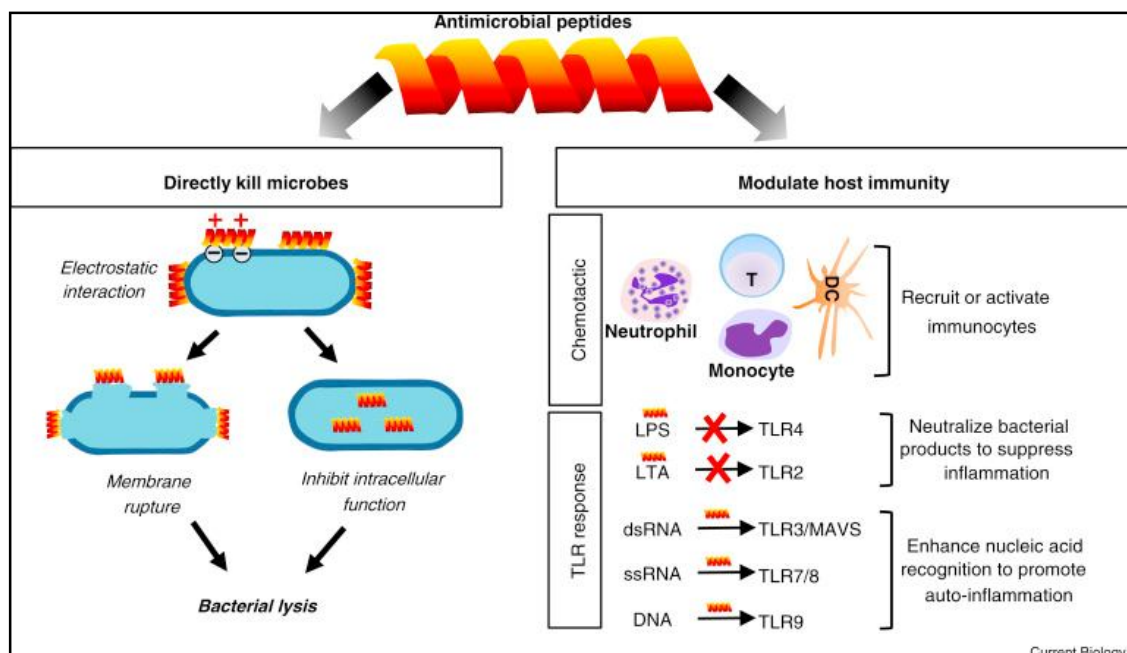


Fig. 1: Diverse mechanisms of action of antimicrobial peptides (Ibrahim, 2019).

2005; González-Martínez *et al.*, 2003; Klaenhammer *et al.*, 1994; Kozak *et al.*, 1978).

Classification of LAB Bacteriocin

Bacteriocins are antimicrobial peptides or proteins produced by some microorganisms including LAB (Nes *et al.*, 2002). Bacteriocins are peptides of small molecular structures consisting of 30-60 amino acids. The structures are amphiphilic helices and are resistant to 100°C for 10 min. They have different spectrum of activity. Their mechanisms of action are also variable. Bacteriocin-producing – Through the expression of a specific immunity protein that is encoded in the bacteriocin operon is expressed by LAB to protect them from their own bacteriocins., (Parada *et al.*, 2007). Recently, four classes of bacteriocins : I; II; III and IV of were described table 1, Their classification is based on producing hosts, molecular weight, physicochemical properties, intrinsic function and amino acid sequence. Genes that control the production of bacteriocins are located on the chromosomes or plasmids. They have minimal genetic machinery that includes immunity proteins which prevent self-toxicity.

Bacteriocins action site are the cytoplasmic membrane of target bacteria targeting the vesicles of energized membrane which leads to disruption of the motive force of protons. (Parada *et al.*, 2007). Through this mechanism, pores are created in the membranes of the targeted cells which leads to dissipation of proton motive force, leakage of nutrients and depletion of ATP and metabolites. This mechanism varies according to the classes of bacteriocins (Driessen *et al.*, 1995; Bennik *et al.*, 1997; Montville and Chen 1998; Herranz *et al.*, 2001). To form a pore, bacteriocins have to interact with the

cytoplasmic membrane of target cells. The disadvantage of site action is due to the fact inhibition affect closely related organisms, and in the process they which may include beneficial bacteria used in creating starter cultures while activity, against Gram-negative contaminants and food spoilers may not be affected whereas specific pathogens might be effectively targeted.... Sensitivity of Gram-negative bacteria to bacteriocins has been improved by adding chelating agents. (Parada *et al.*, 2007).

Class I bacteriocins, the lantibiotics, are peptide that contain the polycyclic thioether amino acids lanthionine or methyllanthionine, in addition to the unsaturated amino acids dehydroalanine and 2 aminoisobutyric acid. The molecular mass, ranges between 2 to 3 kDa with no net charge or a net negative charge (Deegan *et al.*, 2006; Parada *et al.*, 2007). Class II LAB bacteriocins are heat-stable, nonlanthionine-containing peptides that range between 30 to 60 amino acids (Jung and Sahl, 1991). Class III bacteriocins are large heat-labile proteins (Barefoot and Klaenhammer, 1984; Vaughan *et al.*, 1992).

Mode of action of Bacteriocins

Bacteriocins are proteins or peptide molecules that are extracellularly released. These peptides exhibit inhibitory effect against species of microorganisms that are largely related to the LAB. (Tagg *et al.*, 1976). Most LAB bacteriocins are cationic peptides at a neutral pH, hydrophobic in nature and amphiphilic, containing 20 to 60 amino acids (Kuipers *et al.*, 2000). Whether Bacteriocins exhibit bactericidal or bacteriostatic effect to target cells depend on the dose and degree of purity of bacteriocin as well as, physiological state of the indicator cells and experimental conditions (Cintas *et al.*, 2001). Bacteriocin bactericidal effect of bacteriocins causes lysis

Table 1: Various Classes of Bacteriocins.

Classes of bacteriocin	Description	Sub type	Example	Producing bacteria
Class I (Lantibiotics)	Peptides (<5 kDa) that are Heat stable, and contain lanthionine and methyllanthionine	A-Lantibiotics B-Lantibiotics	Nisin, Lacticin, Subtilisin	<i>Lactococcus lactis</i> ; <i>Lactobacillus plantarum</i> LL441; <i>Lactococcus lactis</i> subsp. <i>lactis</i> DPC3147
Class II (Bacteriocins)	Peptides (<10 kDa) that are Heat-stable, do not contain lanthionine	IIa; IIb; IIc	Pediocin, Leucocin	<i>Enterococcus faecium</i> NKR-5-3; <i>Lactobacillus acidophilus</i> ; <i>Lactococcus lactis</i> subsp. <i>cremoris</i> 9 B4
Class III	Peptides (>10 kDa) that are Heat-sensitive and hydrophilic	Subtype IIIa: Bacteriolytic Subtype IIIb: Non bacteriolytic	Helveticin	<i>Lactobacillus helveticus</i> 1829; <i>Lactobacillus helveticus</i> 481
Class IV	complex conjugated proteins (~5.5–7.5 kDa) that are Heat-stable and hydrophobic carbohydrate or lipid		Plantaricin	<i>Enterococcus faecalis</i>

of target cells (Bierbaum and Sahl, 1991). Bacteriocins sites of binding to target cells are teichoic, teichuronic and lipoteichoic, acids that are located on the cell wall of target bacteria which leads to their release causing activation of autolytic enzymes. These enzymes are electrostatically linked to these polymers (Bierbaum and Sahl, 1991; Jack *et al.*, 1995). Additionally, production of bacteriocin is highest at the end of the exponential and early stationary phase (Daba and Simard, 1993; Thomas *et al.*, 2001). Bacteriocin-encoding are organized in operon clusters and may be located on chromosome or in association with transposons or on plasmids (Aymerich *et al.*, 1996; Quadri *et al.*, 1997; Me tivier *et al.*, 1998; Deegan *et al.*, 2006). Several studies reported that detection of bacteriocin gene was approximately 3500-4000 bp in the PCR products which isolated from *Lactobacillus acidophilus* L. lactis subsp. Lactis (Garde *et al.*, 2001; Taale *et al.*, 2013; Abdulla, 2014).

Applications of Bacteriocin

Safety and quality of foods are important to human health. Due to the limitations of the current food preservation methods use of bacteriocins among new methods of food preservation, has been extensively evaluated, (Zacharof and Lovitt, 2012). The application of bacteriocins and bacteriocin-producing microorganisms in food industry is an interesting growing trait as consumer confidence in chemical preservatives has been gradually weakened. Due to the the extensive use of antimicrobials in humans and animals resistance to bacterial antibiotic has emerged as a significant problem. (Lipsitch *et al.*, 2000; Yoneyama and Katsumata, 2006). LAB bacteriocins are natural antimicrobial peptides or proteins with very interesting potential applications in the food industry consistent with, preserving people's health through enhancing the sustainability of food (De Vuyst *et al.*, 1994; Cleveland *et al.*, 2001). Bacteriocins can also be used to improve food quality through protecting from contaminants (Beasley and Saris, 2004).

Conclusion

Bacteriocins that are produced by lactic acid bacteria are increasingly considered as safe alternatives to current reagents in food technology. As current preservatives are chemicals that have harmful effects including cancers and microbial resistance to antibiotics the use of bacteriocins in food industry is an increasing trend to avoid the drawback associated with the current methods for food preservation.

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