



## Bacteriocins from Lactic Acid Bacteria and Its Potential Applications

Y. Evangelin<sup>1</sup>, T. C. Venkateswarulu<sup>2</sup>, D. John Babu<sup>2</sup>, K. Kasturi<sup>1\*</sup>

<sup>1,1\*</sup>Department of Bio-Technology, Acharya Nagarjuna University, Guntur, India.

<sup>2</sup>Department of Bio-Technology, Vignan's University, Guntur, India.

\*Corresponding author's E-mail: [kasturi.is.kondapalli21@gmail.com](mailto:kasturi.is.kondapalli21@gmail.com)

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### ABSTRACT

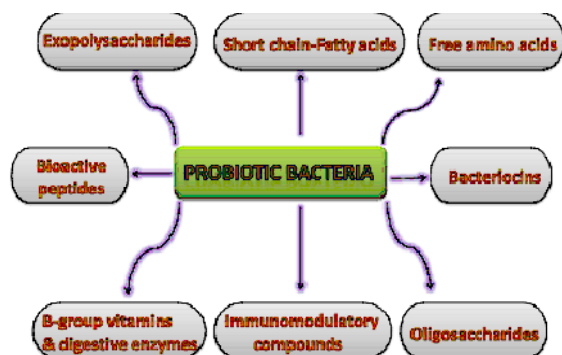
The lactic acid bacteria (LAB) exhibit antimicrobial activity due to production of organic acids, but also of other compounds, such as bacteriocins and antifungal peptides. Bacteriocins are proteinaceous compounds, which are ribosomally synthesized antimicrobial peptides produced by both Gram-positive and Gram-negative bacteria. The bacteria membranes are the target for bacteriocins activity. Bacteriocins classified into several groups in which classes I and II are well studied. The Bacteriocins have been used as biotechnological tools for therapeutic and commercial applications due to their specific modes of actions. Applications of bacteriocins include treatment of infectious diseases of both humans and plants and in fermented sausage (anti-listerial effect), and in cheese (anti-listerial and anti-clostridial effects), and also as preservatives in pharmaceuticals, cosmetics.

**Keywords:** Bacteriocins, LAB (Lactic acid Bacteria), Nisin, Probiotics

### INTRODUCTION

In the recent years probiotic based products have gained a lot of attention due to their health promoting aspects. The probiotics are live microorganisms which when administered in adequate amounts confer to health benefits (or) nutrition of the host by improving the intestinal microbial balance<sup>1</sup>. Moreover certain probiotic bacteria have been respond to produced inhibitory compounds called bacteriocins proven to be antagonistic to various degrees against intestinal pathogens<sup>2</sup>. Because bacteriocins are natural products of many microorganisms associated with foods there is currently enhanced interest in their use as natural food preservatives. Inhibit of the growth of pathogens by producing antimicrobial peptides, so called bacteriocins is considered as the highly appreciated probiotic effect.

The probiotic bacteria generally produce several useful compounds such as bacteriocins, exopoly saccharides, short chain-fatty acids, free amino acids, bioactive peptides, vitamins, digestive enzymes, immunomodulatory compounds and oligosaccharides<sup>1,3</sup> (Figure 1).



**Figure 1:** Overview of compounds produced by probiotic bacteria

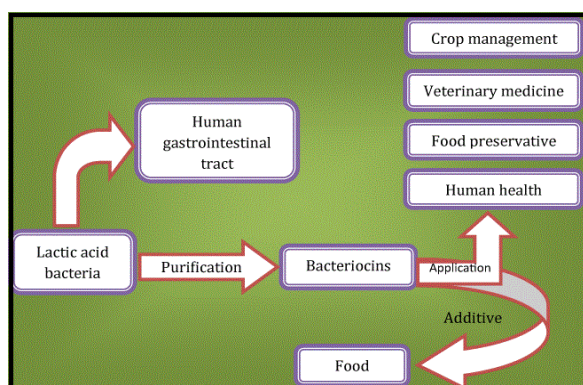
The probiotic bacteria modulate gut flora by the production of different compounds such as organic acids, hydrogen peroxide, carbon dioxide, cyclic dipeptides, fatty acids and proteinaceous toxins<sup>4</sup>.

The most extensively studied and widely used probiotic bacteria are the lactic acid bacteria (LAB), particularly the *Lactobacillus Bifidobacterium* species and *Bacillus* spp. (such as *Bacillus coagulans*, *B. subtilis* and *B. licheniformis*), are "generally regarded as safe" (GRAS) bacteria<sup>5</sup>.

### Lactic Acid Bacteria

Lactic acid bacteria are gram +ve, non-spore forming cocci, coccobacilli (or) rods with a DNA base composition of less than 35 mol % G+C. They ferment glucose primarily to lactic acid, CO<sub>2</sub> and ethanol. Although many genera of bacteria produce lactic acid as a primary (or) secondary end product of fermentation.

The term lactic acid bacteria is conventionally renamed as for genera in the order *lactobacillales*, which includes and streptococcus. The Lactic acid bacteria are the most important groups of microorganisms used in food fermentation. They contribute to the taste and texture of fermented products and inhibit food spoilage bacteria by producing growth inhibiting substances. Lactic acid bacteria were referred as probiotics in scientific literature by Lilly and Stillcuell. *Lactobacillus* and *Bifidobacterium* species are the dominant members of the commensal intestinal flora and are the commonly studied probiotics bacteria<sup>6,7</sup>. Lactic acid bacteria cause rapid acidification of the raw material through the production of organic acids, mainly lactic acid. In addition, their production of acetic acid, ethanol, aroma compounds, bacteriocins exopolysaccharides, and several enzymes is of importance (Figure 2).



**Figure 2:** Overview of the applications of bacteriocin produced by LAB

### Bacteriocins Classification

There are wide number of bacteriocins produced by different LAB and they can be classified accordingly to their biochemical and genetic characteristics.

#### Class I – Lantibiotics

Lantibiotics are class of peptide substances that contain the characteristic polycyclic thioether amino acids lanthionine (or) methylanthionene as well as the unsaturated aminoacids dehydro alanine and aminoisobutyric acid<sup>8</sup>. The small heat-stable peptides (<5KDa) acting on membrane structures. The lantibiotic bacteriocins were initially divided into two sub classes based on structural similarities. Subclass I(a), included relatively elongated, flexible and positively charged peptides, they generally act by forming pores in the cytoplasmic membranes of sensitive target species. The prototypic lantibiotic nisin is a member of this group. Subclass I(b) peptides are characteristically globular, more rigid in structure and are either negatively charged (or) have no net charge. The best example in this group is nisin produced by *Lactococcus lactis*. All forms of nisin are antimicrobially active against Gram +ve bacteria, such as LAB, *Listeria SP*, *Micrococcos SP* and spore forming bacteria like *bacillus SP* and *clostridium SP*.

#### Class II - Non-Lantibiotics

Class II bacteriocins are also small (<10KDa) relatively stable, non-lanthione containing membrane active peptides. This group was divided into three subgroups: Class II(a): Peptides active against *Listeria*, the characteristics represents are pediocin PA-1 and sakacin P. Class II(b); formed by a complex of two distinct peptides. These peptides have little (or) no activity and it appears to be no sequence similarities between complex peptides. In this group are lactocococin G and plantaricis EFJeJK. Class II(c) small peptides heat stable which are transported by leader peptides<sup>9</sup>.

#### Class III - Big Peptides

This group consists of heat labile proteins which are in general of large molecular weight (>30 KDa). In this class are helveticins J and V, acidifilicin A and lactacins A and B.

#### Class IV Bacteriocins

This group consists of either glycoprotein<sup>10,11</sup> or lipoproteins<sup>12,13</sup> that require non-protein moieties for their activity<sup>14</sup>. The most common bacteriocins produced by LAB are summarized in Table 1.

**Table 1:** Bacteriocins produced by lactic acid Bacteria

Bacteriocin Substance	Producing Organism
Lacticin 3147	<i>Lactococcus lactis subsp lactis</i>
Nisin	<i>Lactococcus lactis subsp lactis</i>
Lacto cocain B	<i>Lactococavs lactis subsp lactis cremons</i>
Lencocin A	<i>Lenconostoc gelidium</i>
Entrococin A	<i>Entero coccus faccium</i>
Pediocin A	<i>Pediococcus pentosaccous</i>
Pediocin F	<i>Pediococcus acidilactici</i>
Pediocin PA-1	<i>Pediococcus acidilactics</i>
Pediocin ACH	<i>Pediococcus Acidilactics</i>
Mesertericin Y105	<i>Leuconostoc mgertcroids</i>
Curvalicin	<i>Lactobacillus curvatus</i>
Acidocin J1132 β	<i>Lactobacillus acidophilus</i>
Plantaricin S β	<i>Lactobacillus plantarum</i>
Bacteriocin J46	<i>Lactococcus lactis</i>
Lacticin 481	<i>Lactococcus lactis subsp (Streptococcus lactis)</i>
Lactocin-705	<i>Lactobacillus paracasei</i>
Plantaricin C19	<i>Lactobacillus plantar</i>
Lactocin-S	<i>Lactobacillus sake</i>
Lactocococin MMFII	<i>Lactococcus lactis subsp (Streptococcus lactis)</i>
Curvacin-A	<i>Lactobacillus curvatus</i>
Sakacin-A, Sakacin-P	<i>Lactobacillus sakei</i>
Reuterin	<i>Lactobacillus reuteri</i>
Acidocin B (AcdB)	Plantaricin 1.25 β <i>Lactob</i>

#### Most Important Bacteriocins

##### Nisin

Nisin was first discovered in England in 1928, as a result of difficulties experienced during cheese making. It is the most widely exploited and applied bacteriocin. Nisin is a peptide formed by 34 amino acids with a small molecular weight below 5KDa. The two variants of this bacteriocin are nisin A and Z which differ from each other only by the amino acids 27. The molecule histidine in nisin A is heat stable at 121°C but for prolonged heating, becomes less heat stable, especially between P<sup>H</sup> 5 to 7(7)<sup>15</sup>.

##### Plantaricins

*L. plantarum* has been considered to produce at least 6 distinct bacteriocins. All these peptides are primarily produced as precursors contains a double glycine moiety. The *L. plantanm* synthesizes these bacteriocins through the PlnE and PlnF genes. These peptides are then

exploited and processed by the PlnG and Pln H protics. These peptide pheromone for this system is encoded by a separate gene (Pln A) and is exported by PlnG and PlnH and detected by the histidine protein kinase PlnB which finally phosphorylates two response regulators PlnC and PlnD. Plantaricins inhibit a broad range of LAB including their natural competitor.

*L. Plantarium* and other bacteria like *pediococcus*, *clostridia* and *propionobacteria*<sup>16,17</sup>.

### Applications of Bacteriocins

Bacteriocins have been widely utilized especially in the field of food preservation. The use of Bacteriocins in food industry especially in the dairy, egg, vegetable and meat products has been extensively studied. They can be used to improve food quality and sensory properties, for example increasing the rate of proteolysis (or) in the prevention of gas blowing defect in cheese<sup>18-20</sup>.

Another application of bacteriocins is bioactive packaging, a process that can protect the food from external contaminations, which improves food safety and shelf life<sup>21</sup>.

**Table 2:** Bacteriocins and their Applications

Bacteriocin	Applications	Reference
Nisin	Used as food preservative because it is a natural, toxicologically safe, and broad spectrum antibacterial activity prevented the growth of <i>Listeria monocytogenes</i>	22, 23
Mersacidin	Active against <i>propioni bacterium acnes</i> and may thus be used in the treatment of acne	22
Thuricin	Treat <i>Clostridium difficile</i> -associated disease.	23
Lysostaphin	Used to treat staphylococcal mastitis	24
Subtilosin	Shown to have potent spermicidal activity pediocin PA-1, divergicin 35antilisterial	25
piscicolin 126	Relieved <i>Listeria</i> infection in various tissues	26
Lacticin 3147	Inhibits the growth of <i>S. aureus</i> , MRSA, and vancomycin-resistant strain of <i>Enterococcus faecalis</i>	27
mutacin 1140	Active against tooth decay bacteria	28

### CONCLUSION AND FUTURE DIRECTIONS

The promising application of bacteriocins as biopreservatives either in the form of protective cultures or as additives is significant.

In recent years bacterial resistance has been considered a problem due to the extensive use of classical antibiotics in treatment of human and animal diseases.

As a consequence, multiple resistance strains appeared and spread causing difficulty and the restricted use of antibiotics as growth promoters.

In order to control their abusive use in food and feed

products, one possible alternative is the bacteriocins produced by Lactic acid bacteria which have attracted increasing attention.

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