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Review Article

Bacteriocins and lactic acid bacteria

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Abstract

Lactic acid bacteria (LAB) occur naturally in several raw materials like milk, meat and flour used to produce foods. Both gram negative and gram positive bacteria produce bacteriocins. Bacteriocins are proteinaceous antibacterial compounds, which constitute a heterologous subgroup of ribosomally synthesized antimicrobial peptides. Among the Gram positive bacteria, lactic acid bacteria especially, *Lactobacilli* have gained particular attention nowadays, due to the production of bacteriocins. Nisin, the best-known LAB bacteriocin, has been repeatedly shown to be safe and effective for use in foods over the past 30 years. LAB play an important role in food fermentation as the products obtains with their aid are characterized by hygienic safety, storage stability and attractive sensory properties. In this paper the diversity of bacteriocins their appliction and lactic acid bacteria used are probiotics are reviewed.

Keywords: Bacteriocins; Lactic Acid Bacteria; Probiotics

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1. Introduction

Bacterial strains with antimicrobial activity play an important role in the food industry, agriculture and pharmaceutical industry. Many bacterial species inhabit the ecological niches with a limited amount of nutrients. Because of this, many bacterial species produce a variety of antimicrobial substances, such as lactic acid, acetic acid, diacetyl, hydrogen peroxide and the other substances including enzymes, defective phages and lytic agents with potential importance for food fermentation and biopreservation (Table1) [1, 2, 3].

Table 1. Antimicrobial compounds produced by lactic acid bacteria

Metabolic Product	Mode of antagonistic action
Carbon dioxide	**Inhabits decarboxylation reduces membrane permeability**
Diacetyl	**In tracts with arginine -binding proteins**
Hydrogen peroxide	**Oxidize basic proteins**
Lactic acid	**Un dissociated membrane , lowering the intracellular PH.**
Bacteriocins	**Affect membrane, DNA synthesis and protein synthesis.**

Bacteriocins from lactic acid bacteria (LAB) are natural antimicrobial peptides or proteins with interesting potential applications in food preservation and health care [4].
Although bacteriocins could be categorized as antibiotics, they are not. The major difference between bacteriocins and antibiotics is that bacteriocins restrict their activity to strains of species related to the producing species and particularly to strains of the same species, antibiotics on the other hand have a wider activity spectrum and even if their activity is restricted this does not show any preferential effect on closely related strains. In addition, bacteriocins are ribosomally synthesized and produced during the primary phase of growth, though antibiotics are usually secondary metabolites [5, 6, 7]. Both gram negative and gram positive bacteria produce bacteriocins. LAB occur naturally in several raw materials like milk, meat and flour used to produce foods [8, 9]. Lactic acid bacteria (LAB) have traditionally been used in food processing because of their ability to improve the organoleptic characteristics and healthiness of foodstuffs [10]. In this paper the diversity of bacteriocins their appliction and lactic acid bacteria used are probiotics are reviewed.

2. Lactic acid bacteria

Lactic Acid Bacteria are gram-positive, non-sporeforming cocci, coccobacilli or rods with a DNA base composition of less than 35mol% G+C. They ferment glucose primarily to lactic acid, or to lactic acid, CO_2 and ethanol. All LAB grow anaerobically, but unlike most anaerobes, they grow in the presence of O_2 as aerotolerant anaerobes. Although many genera of bacteria produce lactic acid as a primary or secondary end-product of fermentation, the term Lactic Acid Bacteria is conventionally reserved for genera in the order *Lactobacillales*, which includes *Lactobacillus*, *Leuconostoc*, *Pediococcus*, *Lactococcus* and *Streptococcus*, in addition to *Carnobacterium, Enterococcus, Oenococcus, Tetragenococcus, Vagococcus,* and *Weisella. Other genera are: Aerococcus, Microbacterium, Propionibacterium and*

Bifidobacterium [11, 12, 13, 25]. Lactic acid bacteria are among the most important groups of microorganisms used in food fermentations. They contribute to the taste and texture of fermented products and inhibit food spoilage bacteria by producing growth-inhibiting substances and large amounts of lactic acid. As agents of fermentation LAB are involved in making yogurt, cheese, cultured butter, sour cream, sausage, cucumber pickles, olives and sauerkraut, but some species may spoil beer, wine and processed meats [14, 15]. Lactic acid bacteria were referred to as probiotics in scientific literature by Lilley and Stillwell [16]. *Lactobacillus* and *Bifidobacterium* spp. are prominent members of the commensal intestinal flora and are the commoly studied probiotics bacteria. They cause reduced lactose intolerance alleviation of some diarrhoeas, lowered blood cholesterol, increased immune response and prevention of cancer [17, 18]. The selection criteria for probiotic LAB include: human origin, safety, viability/activity in delivery vehicles, resistance to acid and bile, adherence to gut epithelial tissue ability to colonise the gastro intestinal tract, production of antimicrobial substances, ability to stimulate a host immune response and the ability to influence metabolic activities such as vitamin production, cholesterol assimulation and lactose activity [19, 20].

3. Bacteriocins

There is a wide number of bacteriocins produced by different LAB, and they can be classified according to their biochemical and genetic characteristics [10, 14, 20, 21, 22, 23, 24].

3.1. Class I: Lantibiotics

Class I, the lantibiotics, are a class of peptide substances that contain the characteristic polycyclic thioether amino acids lanthionine or methyllanthionine, as well as the unsaturated amino acids dehydroalanine and 2- aminoisobutyric acid. small (< 5 kDa) heat-stable peptides acting on membrane structures. The lantibiotic bacteriocins were initially divided into two subclasses based on structural similarities. Subclass Ia included relatively elongated, flexible and positively charged peptides; they generally act by forming pores in the cytoplasmatic membranes of sensitive target species. The prototypic lantibiotic nisin is a member of this group. Subclass Ib peptides are characteristically globular, more rigid in structure and are either negatively charged or have no net charge. They exert their action by interfering with essential enzymatic reactions of sensitive bacteria. The best example in this group is nisin produced by *Lactococcus lactis* subsp. *Lactis*. All forms of nisin are antimicrobially active against Gram-positive bacteria, such as LAB, *Listeria* sp., *Micrococcus* sp. and sporeforming bacteria like *Bacillus* sp. and *Clostridium* sp.

3.2. Class II: Non-Lantibiotics

Class II bacteriocins are also small (<10 kDa) relatively heat stable, non-lanthionine containing membrane active peptides. This group was divided into three subgroups*: Class IIa:* peptides active against *Listeria*, the characteristic representants are pediocin PA-1and sakacin P. Class IIb: formed by a complex of two distinct peptides. These peptides have little or no activity and it appears to be no sequence similarities between complementary peptides. In this group are lactococcin G and plantaricins EF e JK. Class IIc: Small peptides, heat-stable, which are transported by leader-peptides. In this subclass are found only the bacteriocins divergicin A and acidocin B.

3.3. 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, acidofilicin A and lactacins A and B. The most common bacteriocins produced by LAB are summarized in Table 2 and 3.

Table 2. Most important bacteriocins produced by lactic acid bacteria

Peptide	Species
Lacticin 3147	***Lactococcus lactis* subsp. *lactis***
Nisin	***Lactococcus lactis* subsp. *lactis***
Lactococcin B	***Lactococcus lactis* subsp. *cremoris***
Leucocin A	***Leuconostoc gelidum***
Enterocin A	***Enterococcus faecium***
Pediocin A	***Pediococus pentosaceous***
Pediocin F	***Pediococcus acidilactici***
Pediocin PA-1	***Pediococcus acidilactici***
Pediocin AcH	***Pediococcus acidilactici***
Mesentericin Y105	***Leuconostoc mesenteroides***

Table 3. Antimicrobial peptides produced by *Lactobacilli*

Peptide	Species
Acidolin	***L. acidophilus***
Acidophilin	***L. acidophilus***
Lactacin B	***L. acidophilus***
Lactacin F	***L. acidophilus***
Lactobacillin	***L. brevis***
Lactobrevin	***L. brevis***
Reuterin	***L. Reuteri***
Bulgarin	***L. Bulgaricus***
Plantaricin SIK-83	***L. plantarum***
Plantaricin A	***L. plantarum***
Plantaricin B	***L. plantarum***
Lactolin	***L. plantarum***
Lactolin 27	***L. Helveticus***
Helveticin J	***L. Helveticus***
Lactobin A	***L. amylovorus***
Lactocin 705	***L. casei***
Lactocin S	***L. sake***
Sakacin P	***L. sake***
Curvacin A	***L. curvatus***

4. Most Important Bacteriocins

4.1. Nisin

Nisin was first discovered in England in 1928 as a result of difficulties experienced during cheese making. Nisin is the most widely exploited and applied bacteriocin. Nisin is a peptide formed by 34 amino-acids, with a small molecular weight, below 5 kDa. There are two variants of this bacteriocin: nisin A and Z, which differ from each other only by the amino-acid 27. Histidine in nisin A is replaced by asparagin in nisin Z. Nisin is heat stable at 121ºC but for prolonged heating, becomes less heat stable, especially between pH 5 to 7 [5, 6, 24, 26].

4.2. Plantaricins

L. plantarum has been considered to produce at least 6 distinct bacteriocins. All these peptides were primarily produced as precursors containing a double glycine moiety. *L. plantarum* synthesizes these bacteriocins through the PlnE and PlnF genes. These peptides are then exported and processed by the PlnG and PlnH proteins. The peptide pheromone for this system is encoded by a separate gene (PlnA) 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. plantarum* and other bacteria like *Pediococcus, Carnobacteria, Clostiridia and Propionobacteria* [5, 24, 27].

4.3. Other bacteriocins

acidocin CH5 is produced by *Lactobacillus acidophilus*, and has a restricted activity against Gram-positive bacteria. Leucocin A, produced by *Leuconostoc gelidum*, has a molecular weight of approx. 4 kDa (37 amino-acids), is one of a group of small antibacterial peptides produced by lactic acid bacteria. Plantaricins JK, EF, act as synergetic peptides. They are 30 or 40 residues in length and show little sequence similarity to any other plantaricin approximately. These bacteriocins act with strict specificity and any other combination, except JK or EF results in the complete loss of synergy [5, 27, 28].

5. Applications of Bacteriocins

Nowadays, bacteriocins have been widely utilised especially in the field of food preservation. The use of bacteriocins in food industry especially on dairy, egg, vegetable and meat products has been extensively investigated. Bacteriocins can be applied on a purified or on a crude form or through the use of a product previously fermented with a bacteriocin producing strain as an ingredient in food processing or incorporated through a bacteriocin producing strain (starter culture). Furthermore bacteriocins could be combined with other antimicrobial compounds such as sodium acetate and sodium lactate resulting in enhanced inactivation of bacteria. Bacteriocins can also 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. Another application of bacteriocins is bioactive packaging, a process that can protect the food from external contaminants. For instance the spoilage of refrigerated food commonly begins with microbial growth on the surface that reinforces the attractive use of bacteriocins being used in conjunction with packaging to improve food safety and self-life [5, 10, 24, 30].

6. Conclusion

In recent years bacterial antibiotic 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 resistant strains appeared and spread causing difficulties and the restricted use of antibiotics as growth promoters. So, the continue development of new classes of antimicrobial agents has become of increasing importance for medicine. In order to control their abusive use in food and feed products, one plausible alternative is the application of some bacterial peptides as antimicrobial substances in place of antibiotics of human application. Among them, bacteriocins produced by lactic acid bacteria have attracted increasing attention, since they are active in a nanomolar range and have no toxicity.

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