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Review Article

BACTERIOCIN: A NOVEL APPROACH FOR PRESERVATION OF FOOD

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ABSTRACT

Bacteriocins are antimicrobial peptides which are ribosomally synthesized and produced by Lactic acid bacteria. They play a major role in prevention of human disease such as cancer, inflammatory disease, respiratory infection, systemic infection, intestinal disorder and bacterial infection and also contribute in maintaining the healthy gut microflora. Now day's bacteriocin is emerging as the very promising natural alternative against the antibiotic and chemical preservatives and gaining commercial importance worldwide. The inhibition of pathogenic bacterial strains occurs due to cell permiabilization, but producing strains are protected from it by specific immunity proteins. They are mainly classified in 4 classes: class I, class II, class III, and class IV bacteriocin based on lantibiotics ring. Nisin, Pediocin, Lactococcin B, Acidocin CH5, Curvacin A, and Sakacin are the bacteriocins, which have strong inhibition against pathogenic bacterial strain and used in food preservation. This review article summarizes and focuses on general introduction, classification, ecology and potential applications of bacteriocin as biopreservatives in food industry.

Keywords: Bacteriocin, Lactic Acid Bacteria, Chemical Preservatives, Antibiotics, Biopreservatives.

INTRODUCTION

In the production of food, it is crucial to take proper measures for ensuring its safety and stability during the shelf-life. Food preservation is carried out to maintain the quality of raw material and physicochemical properties as well as the functional quality of the product whilst providing safe and stable products. In general, preservation processes include chemical preservatives to control food spoilage and the outgrowth of pathogenic spore-forming bacteria. Many chemical preservatives are being used for inactivation of food borne pathogens so as to preserve food products for long duration. Long-term intake of these preservatives can affect human health as they reduce all microflora present in the gut either they are healthy bacteria or pathogenic bacteria, causing many diseases like breathing difficulties, obesity and cancer [1, 2]. The resistance of some microorganisms to most commonly used preservatives also has created problems in the food industry. To overcome this problem, there has been an awareness in naturally produced antimicrobial agents such as bacteriocin produced from lactic acid bacteria which have activity against resistant pathogenic strains [3]. Traditionally foods were preserved by lactic acid bacteria, natural constituents of fermented foods used as a starter culture, which confer their preservative effects by the production of lactic acid, hydrogen peroxide and small peptides known as bacteriocins[4, 5]. Bacteriocins produced by LAB have received considerable attention for their possible as biopreservatives in foods [6], with a subsequent reduction in the use of chemical preservatives [7]. The immunity of bacteriocin and how they differ from antibiotics and drawbacks of chemical preservative are discussed in this review.

Chemical preservatives: A silent toxin

Several processed food products available in the market that has different types of preservatives that can help to last longer without becoming contaminated with food-borne illness these are known as artificial preservatives or food additives or chemical preservatives. They can be used alone or in combination with other methods of food preservation. Preservatives may be antimicrobial, which inhibit the growth of bacteria or fungi, including mold, or have antioxidants property which inhibits the oxidation of food constituents. Universal preservatives include calcium propionate, sodium nitrate, sodium nitrite, sulfites (sulfur dioxide, sodium bisulfite, potassium hydrogen sulfite) and disodium. In the United States, all artificial preservatives are "generally recognized as safe" by the U. S. Food and Drug Administration [8]. Not all of these additives are 100-percent safe for everyone sometimes they can give rise to certain health problems. Many people are allergic to certain food additives or colors [9]. ButylatedHydroxytoluene (BHT) and Butylated Hydroxyanisole (BHA) are commonly used preservatives in processed food, can induce allergic reactions in the skin [10]. According to UNEP and OECD, (2002)Long-term contact to high amounts of BHT is toxic in animals, causing liver, thyroid and kidney problems and affecting lung function and blood coagulation [11].

When someone has a reaction after eating certain foods, such an allergy is suspected. Unfortunately, some people do not have a reaction until a day or two later, so it is difficult to know what is causing the problem. When a certain food additive is believed to cause an allergic reaction, the blood is mixed with materials known to trigger allergies. They are associated with adverse effects, which can involve an unpleasant reaction in people sensitive to a particular additive or a potential increased risk for cancer. It is best to eat a preservative-free diet if at all possible. The reaction from these additives can be very mild to life-threatening. They can be immediate or build up in the body over time. In table 1 we are given the name of the chemical which are used in various food products and their side effects on human health.

Lactic acid bacteria

Lacticacid bacteria are a group of Gram-positive, nonmotile, non-spore forming, rod-and coccus-shape bacteria have low proportions of G+C in their DNA (<55%); produce lactic acid either through homofermentative or heterofermentative pathway. The genera comprise in this group are *Lactococcus*, *Lactobacillus*, *Leuconostoc*, *Enterococcus*, *Carnobacterium, Aerococcus, Pediococcus*, *Oenococcus, Streptococcus*, *Tetragenococcus, Vagococcus*, and *Weisella.* LAB isolated from many food and animal sources, showing inhibitory activity against *L. monocytogenes*, *Staphylococcus aureus*, and *Enterococcus faecalis*, and *Salmonella Typhimurium*[28-30]. They are the most widely used bacteria as starter cultures for the industrial processing of fermented dairy, meat, vegetable and cereal products they are beneficial bacteria because they have their ability to break down proteins, carbohydrates and fats in food and help in the absorption of necessary elements and nutrients such as minerals, amino acids and vitamins and increasing health profits [31, 32].

Bacteriocin: Inhibitory peptide

Bacteriocins are narrow range of inhibitory peptide have been found in all major lineages of Bacteria and some members of the Archaea [33]. Theses peptides are ribosomally synthesized inhibit the closely related microorganism [34]. The genes that code for bacteriocins

can be either chromosomally or plasmid coded. Bacteriocins, such as Nisin is accepted safe for use as a food preservative in vegetables, dairy, cheese, meats, and other food products, as they inhibit microorganisms contamination during the production process [35-37].

Table 1: Name of chemical preservatives and their side effect on human health

Chemical preservatives	Occurrence	Side effects
ButylatedHydroxytoluene (BHT) and ButylatedHydroxyanisole (BHA)	Processed foods[12]	BHT induces tumors in the stomach and liver in animals when used at high levels[13]
Sulfites	Processed foods[14]	Aggravate asthma in children and adults[15]
Organophosphates, Organochlorines, Thiocarbamates and Organoarsenic compounds.	Organic foods [16]	Potentially carcinogenic and therefore able to cause genetic damage leading to the development of cancer[17]
Trans-Fats	Found in margarine, vegetable shortenings, crackers, cookies, snack, processed food[[18]	Increased risk for heart disease [19,20]
Sodium Nitrate	Preservation/curing of hotdogs, sausages and other cured foods[21, 22,]	Pancreatic and lung cancer [23]
Propyl Gallate	Used in packaged meals, dry milk, baked goodsgoods to inhibit food bore microbial growth[24]	Cause prostate inflammation and tumors in the brain, pancreas and thyroid[25]
Potassium Bromate	Used to strengthen bread dough[26]	Causing tumors in the kidneys and thyroid[27]

The history of bacteriocins extends to the early 1920s. While their antimicrobial activity was first discovered in 1928, colicin is a first bacteriocins produced from *Escherichia coli* V and show inhibitory activity against *E. coli* S [38]. Bacteriocins were not used in food products until 1951. In the 1960s, the first bacteriocin, called nisin, which is produced by *Lactococcus lactis* subsp. *lactis*, was purified and recognized as a food preservative by FAO/WHO in 1969[39]. In 1988, the FDA approved the use of nisin as an additive in canned products in the United States to inhibit the growth of *Clostridium botulinum*. Moreover, evidence from research studies indicates that the resistance of *L. monocytogenes* to nisin does not appear to be stable, providing additional support for the use of nisin and other bacteriocins over other chemical agents [40].

Bacteriocins may be bactericidal eliminate certain microorganisms, or they may be bacteriostatic, i.e. inhibit the growth of certain microorganisms. The bactericidal or bacteriostatic activity is directed against certain species close to the producer strain [41]. Most of the scientists work on isolation, identification, characterization and purification of bacteriocin of LAB from different natural sources [42].

Henning*et al.* (2015) identify several bacteriocins from *Enterococcus* spp. by using an Enterococcus-Specific Bacteriocin PCR Array; they have strong antimicrobial activity against *L. monocytogenes.* Combinations of different bacteriocins show activity against food borne pathogens and also used as food preservatives [43]. Hu *et al.* (2013) purified plantaricin 163 a bacteriocin, produced by *Lactobacillus plantarum* 163. Plantaricin 163 was stable at high temperature (20 min, 121 °C), active in the presence of acidic pH (3-5), sensitive to protease, and exhibited broad-spectrum antimicrobial activity against closely related bacteria; propose that plantaricin 163 may be employed as a biopreservative in the food industry [44].

According to Chassaing*et al.* (2015) gut microflora play an important role in metabolism and development of immunity in host. Many metabolic syndromes like chronic inflammatory diseases, including inflammatory bowel disease and the group of obesity-associated diseases are caused by disturbance in microflora–host relationship. Suez *et al.*(2014) reported the changes in intestinal microbiota (compositional and functional) by using Non-caloric Artificial Sweeteners (NAS) a food additives may cause glucose intolerance [45, 46].

Mechanism of action

The general killing mechanisms of bacteriocin produced from gram positive bacteria include pore formation and modulation of enzyme activity or by Quorum sensing[47,48]. The bacteriocins are highly cationic such as Lacticin; they are quickly bound to the negatively charged phospholipid bilayer membrane. The interaction between the hydrophobic part of Lacticin and the bacterial target membrane generates unspecific ionic channels, the formation of pore which is aided by the presence of high transmembrane potentials and by the presence of anionic lipids and the absence of cationic lipids that would cause leakage of intracellular components, including ions, ATP, and small proteins, after which, the bacteriocin molecules translocate into the membrane as the pore closes (fig. 1). The type B lantibiotics inhibit the enzyme modulation in the target bacteria. For example, mersacidin interferes with bacterial cell wall biosynthesis [49].

The class IIa bacteriocins act through the formation of pores in the cytoplasmic membrane like type A lantibiotics. The current mechanistic hypothesis to explain the mode of action of bacteriocins belonging to this class involves electrostatic binding of the antibiotic to the target membrane mediated by a putative membrane-bound receptor molecule. However, the existence of a specific receptor is still controversial.

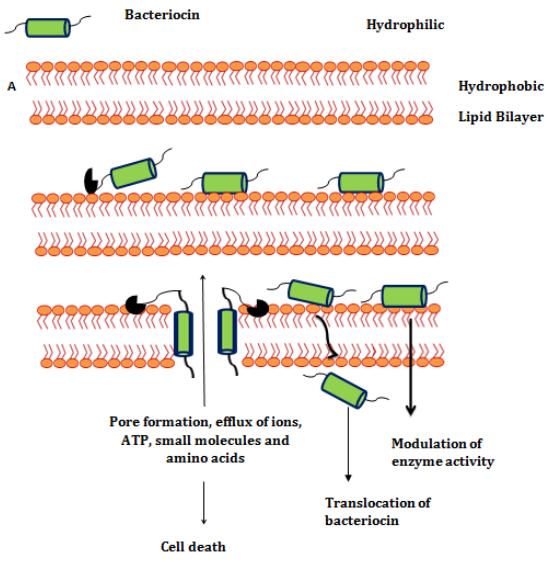

Fig. 1: The general killing mechanisms of bacteriocin including binding of bacteriocin with receptors (A, B), cytoplasmic membrane pore formation, translocation of bacteriocin and modulation of enzyme activity (C) [50]

Classification of bacteriocin

Defensins a Bacteriocins produced by Gram-positive bacteria (resemble antimicrobial peptides produced by eukaryotes) they are approximately 2-6 kDa in size, generally cationic, amphiphilic,

membrane-permeabilizing peptides [51]. Typically, bacteriocin biosynthesis of Gram-positive bacteria is self-regulated with specifically dedicated transport mechanisms facilitating its release. Four main groups of bacteriocin have been identified: Class I modified bacteriocins, known as lantibiotics; Class II, heat stable minimally modified bacteriocins; class III, larger heat labile bacteriocins and Class IV, complex bacteriocins carrying lipid or carbohydrate moieties [47]. The classification of bacteriocins has been reviewed by several authors [52-54]. Settanni and Corsetti, (2008) classified bacteriocin in three classes on the basis of structural, characteristics (fig. 2, table: 2) [36]. Klaenhammer's classification of bacteriocins classifies them into four well-defined classes based on common elements, as follows

Class I bacteriocins (Lantibiotics)

Among four classes of Bacteriocin, lantibiotics classes I Bacteriocin are currently attracting considerable attention because of their biosynthesis and their wide antimicrobial spectra. Members of this class are post-translationally modified to contain amino acids, such as lanthionine and B-methyllanthionine, and several dehydrated amino acids. lanthionine and B-methyllanthionine are formed by dehydration of a serine and a threonine to form dehydroalanine and dehydrobutyrine, respectively, followed by addition of the thiol group of a cysteine to the unsaturated amino acids residues [55]. Lanthionine and dehydroamino acids have been suggested to confer stability on the active conformation of the lantibiotics against heat and acids against proteinease present in the producers' cells. Lantibiotics are further divided into two subgroups, A and B, based on their biosynthetic peculiarities; structural properties, and biological activities, lantibiotics can be classified in to two types. Type A and Type B lantibiotics.

Type A lantibiotics: are linear and larger than type B lantibiotics, ranging in size from 21 to 38 amino acids. The bacteriocins belonging to this class kill the target cell by depolarising the cytoplasmic membrane. Nisin is the best-known and best-studied gram-positive bacteriocin.

Type B lantibiotics*:* Type B lantibiotics have a more globular secondary structure and are smaller (the largest is 19 amino acids in length) than type A. In this class, leader peptides are cleaved by an ABC-transporter. For example, mersacidin.

Class II Bacteriocins

These bacteriocins are small, heat-stable, nonlanthionine-containing, not post-translationally modified peptides, ranging in size from 30 to 60 amino acids, and are usually positively charged at a neutral pH. These bacteriocins are divided into 4 subgroups as follows:

Class IIa

Class IIa (pediocin-like bacteriocins with a strong antilisterial effect) is the largest group, and their members are characterized by a conserved amino-terminal sequence (YGNGVXaaC),shared strong inhibitory activity against *Listeria.* Because of their effectiveness against this food borne pathogen, class IIa bacteriocins are currently of interest as potential natural and non-toxic food preservatives. Some example are pediocin PA-1 and pediocin AcH*(Pediococcus acidilactici),* sakacins A and P *(Lactobacillus sakei),* leucocin A *(Leuconostoc gelidum),* enterocins A and P *(Enterococcus faecium),* and carnobacteriocin *(Carnobacterium sp.).* Pediocin-like bacteriocins are of considerable commercial interest because they are small, heat-resistant peptides that are not post-translationally modified. All of the pediocin-like bacteriocins share certain features, including a seven amino acid conserved region at the N-terminus of the active peptide (–Tyr–Gly–Asn–Gly–Val–Xaa–Cys–) [57].

These class IIa bacteriocins are active against other LAB but are particularly effective against *Listeria monocytogenes.* Perhaps the best-known bacteriocin is pediocin PA-1, which is produced by *P. acidilactici.*

Class IIb

The activity of Class IIb bacteriocin depends on the complementary activity of two peptides. The primary structures of the peptides are notably different and are subdivided into type E (enhanced) and type S (synergistic) peptides. This group includes lacticin F and lactococcin G. The mechanism of action of this class is the formation of pores in the membranes of their target cells. Bacteriocin-induced leakage of various ions dissipates the trans-membrane electrical potential or the trans-membrane pH gradient and thereby also dissipates the proton motive force, which eventually leads to cell death by decreasing the intracellular ATP concentration [58].

Class IIc

Class IIc cyclic bacteriocins, the N-and C-termini of which are covalently linked, are placed in class-IIc or in class-III. These bacteriocins are all cationic (except for subtilisin A) and relatively hydrophobic, size from 3400 to 7200 Da. All cyclic bacteriocin with mode of action that has been characterized render their target-cell membrane permeable to small molecules and thereby disrupt the proton motive force, which eventually results in cell death. The advantage of the cyclic structure of these bacteriocins is not entirely clear, but it has probably stabilized the three-dimensional structure that is required for their antibacterial activity. The cyclic structure, presumably also causes these bacteriocins to be more resistant to proteolysis [58].

Class IId

This class includes other bacteriocins, such as lactocin A and B, which require lipid or carbohydrate moieties for their activity.

Class III Bacteriocins

This group consists of heat-labile peptide antibiotics with a molecular mass larger than 30 kDa. Most of these bacteriocin are produced by bacteria belonging to the genus *Lactobacillus,* including helveticin J produced by *L. helveticus* 481 and lactacin B produced by *Lactobacillus acidophilus.* Their mechanism of action involves the lysis of sensitive cells by catalyzing cell wall hydrolysis. These proteins have a catalytic domain at the N-terminus, while the C-terminus probably represents the target recognition site [59].

Class IV bacteriocins (Cyclic peptides)

Little is known about the structure and function of this class. Characteristics of this group have yet to be determined by purification and biochemical characterization. These bacteriocins include leuconocin S and lactocin 27.

Bacteriocin immunity: Bacteriocin-producing bacteria protect itself from its similar bacteriocin by immunity proteins. When these proteins expressed in sensitive cells, they strongly protect against externally added similar bacteriocin. The immunity protein display strong specificity with respect to the bacteriocins to which they confer resistance. The Producing cell has two different systems for bacteriocin immunity. These two immune system can work synergistically to protect the producing cells from their own Bacteriocin [68]. Near about 20 immunity proteins have been identified from DNA sequences, most of them containing 25 to 35% charged residues. Proteins are highly charged and present towards each other, such that their hydrophobic faces interact and form a hydrophobic core in the center of the protein, whereas the hydrophilic and charged faces of the helices constitute the protein surface. This distribution of residues gives rise to a structurally stable and hydrophilic cytosolic protein. Carnobacteriocin B2 and enterocin A is a class IIa immunity proteins, like cytosolic proteins, loosely associated with the inside of the cell membrane (fig. 3).

According to hybrid immunity proteins model the N-and C-terminal halves of immunity proteins from the same immunity protein subgroup have been interchanged. The bacteriocin and immunity proteins are located on opposite sides of the cell membrane, and there seems to be no direct contact between the two molecules. Thus, the membrane itself or a specific component embedded in, it seems to play a crucial role as a mediator in the recognition between the bacteriocin and the immunity protein. When cross-protection was observed, it was most often directed against closely related bacteriocins. For example, sakacin P and pediocin PA-1/AcH are two very similar bacteriocin, and thus the immunity proteins for sakacin P and pediocin PA-1/AcH protected against sakacin P and pediocin PA-1/AcH, despite the fact that these two immunity proteins display only 28% similarity and are placed in different subgroups.

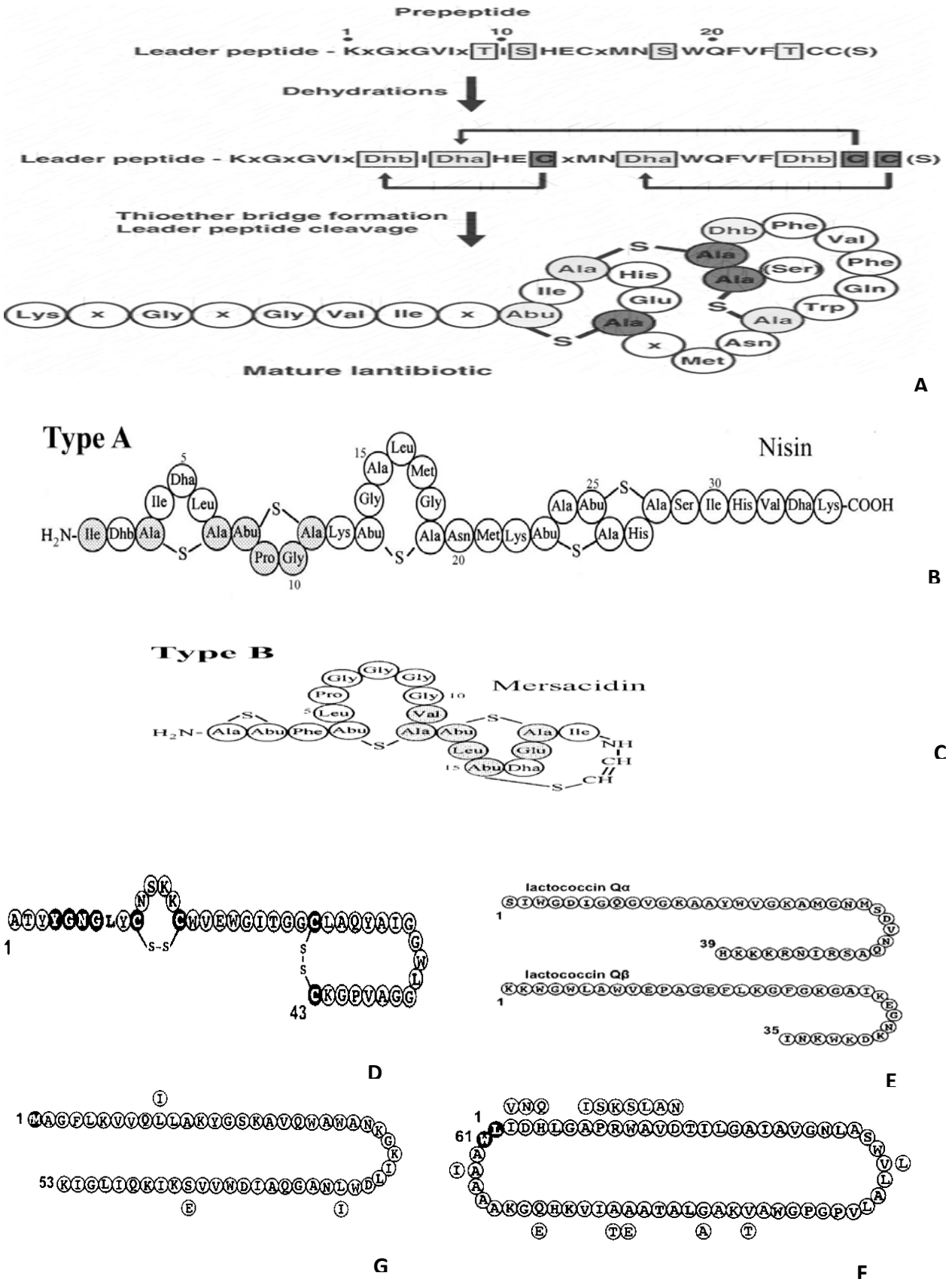

Fig. 2: Formation of mature Lantibiotics from prepeptide after dehydration and cleavage of leader peptide and formation of thioether bridge formation (A), Primary structures of nisin-Type A Lantibiotics (B), Mersacidin–basic structure of Type B Lantibiotics (C), Primary structures of class II bacteriocins, Enterocin-novel class IIa bacteriocin (D), Lactococcin-class IIb (two-peptide) bacteriocin (E), Lactocyclicin Q and leucocyclicin-class IIc (circular) bacteriocins (F). Lacticin Q and lacticin Z-A leaderless class IId bacteriocins (G) (structure of bacteriocin adopted from Perez *et al.*(2014) Microbial Cell Factories [56]

Table 2: Classification of bacteriocin produced from Lactic acid bacteria [59]

Class	Subclass	Characteristics	Example	MW (Da)	Producing species
Class I		Post-translationally modified, linear or globular peptides containing lanthionine, β-methyl lanthionine and dehydrated amino acids	Nisin A[60]	3352	*Lactococcus lactis subsp. lactic* [60]
			Nisin U	3029	*Streptococcus uberis* [61]
			Nisin Z	3493	*Lactococcus lactis subsp. lactic* [60]
Class II	Class IIa	Heat stable, unmodified, non-lanthionine-containing bacteriocins, heterogeneous class of small peptides, Pediocin PA-1like bacteriocins	Pediocin PA-1[62]	4629	*Pediococcus acidilactici* PAC-1.0 [62]
	Class IIb	Composed of two peptide	Lactacin F[63]	4755	*Lactobacillus spp.*[63]
	Class IIc	Circular peptide	Enterocin AS-48[64]	7149	*Enterococcus faecalis* [64]
	Class IId	Linear, non-pediocin like, single-peptide	Lactococcin A [65]	5778	*Lactococcus lactis subsp. Cremoris* [65]
Class III		Large, heat unstable proteins [67]	Caseicin 80[66]	42000	*Lacto bacillus casei* B80 [66]
			Helveticin J[67]	37511	*Lactobacillus helveticus*481[67]

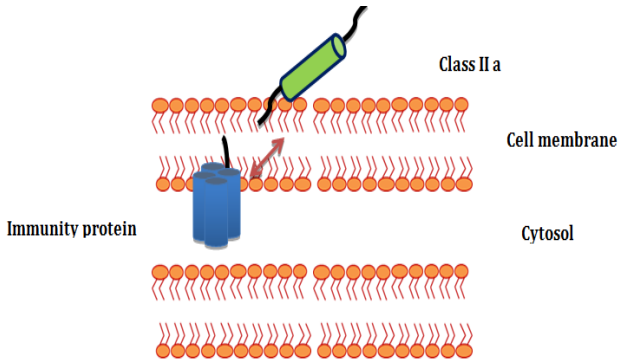

Fig. 3: The class IIa bacteriocin present on the upper side of the outer cell membrane in slanting position and the immunity protein on the cytosolic side. The immunity protein recognizes the bacteriocin and protects the cell against own bacteriocin (fig. adopted and modified [69]

Alternative of antibiotics

Bacteriocins have potency against antibiotic-resistant bacteria like antibiotics. The in situ production of bacteriocin improves gut intestinal flora and struggle against intestinal infections [70, 71]. For medical purposese, bacteriocin is used as viable antibiotics against pathogenic bacteria due to high specificity and multi-antibiotic resistant. Bacteriocin is ribosomal peptides that differ from other non-ribosomal peptides with antimicrobial activity in one critical feature: the protein or peptide nature of bacteriocins and the fact that they are characterized by a narrow target range, the mode of inhibition of bacteriocins has wide spectrum i.e. from enzymatic action to pore formation of the target cell. [72]. The main differences between bacteriocins and antibiotics are summarized in table 3.

Example of bacteriocin those are mostly used as preservatives

Enterocins

Enterocins a group of bacteriocin produced by *Enterococci* species belongs to the group of Gram-positive lactic acid bacteria (LAB), isolated from different food sources i.e. cheese, meat, fish and sausages. They are mainly cocci, pairs or short chains in shape, non-spore forming, facultative anaerobic, oxidase and catalase negative. Enterocins show bactericidal activity against pathogens and food spoilage microorganisms, including *Listeria monocytogenes*, *Clostridium* sp., *E. coli*, *Vibrio cholerae*, *Staphylococcus aureus* and *Bacillus cereus* and work as a natural food preservative [95]. Characterize the functional, safety, and probiotic properties of *Enterococcus faecalis* UGRA10 a new enterocin AS-48-producer strain [96]. *E. faecium* or its enterocins have been used as a starter culture in the production of fermented meat products. *E. faecium* RZS C13 and *E. faecium* CCM 4231 have been used as starter cultures in the production of Spanish sausages [97]. Enterocin AS-48 produced by *E. faecalis* to control an enterotoxic strain of *S. aureus*. Ennahar and Deschamps (2000) found a high activity of enterocin A produced by *E. faecium* against 13 strains of *L. monocytogenes* [98]. It is widely used as starter cultures in the fermentation process. Table 4 contains selected enterocins used as food biopreservatives.

Table 3: Difference between bacteriocin and antibiotics [70]

Characteristic	Bacteriocin	Antibiotics
Application	Food or Clinical [73]	Clinical[74]
Synthesis	Ribosomal[75]	Secondary metabolite[76]
Intensity of bioactivity	Active at nano or micro molar range[77]	Active at micro or milli molar range[78]
Activity spectra	Narrow spectrum[79]	Varying spectrum[80]
Host cell immunity	Yes[81]	No[82,83]
Mechanism of target cell	Usually adaptation affecting cell[84]	Usually a genetically transferable[85]
Proteolytic degradability	High[86]	Low [87]
Interaction requirements	Mostly pore formation, but in a few[88]	Depending on Specific target[89]
Mode of action	Pore cell formation, Cell wall biosynthesis[90]	Cell membrane or intracellular targets[91]
Toxicity towards eukaryotic cells	Note known[92, 93]	Yes[94]

Nisin

The World Health Organization (WHO), Food and Drug Administration (FDA), In 1988 accepted Nisin as GRAS for use as a food preservative and disclosed into the European food additive list, where it was assigned the number E234 [111, 112]. Nisin is classified as a class-Ia bacteriocin peptide consists of 34 amino acid residues (3.5 kDa) produced from *Lactococcus lactis* subsp. *lactis*

strain [113]. Nisin has been shown to be effective in the microbial control of a number of dairy products and its use has been widely assessed in cheese manufacturing at low pH.

The use of nisin-producing starter cultures appears to be a viable means of incorporating and maintaining this bacteriocin, through the cheese-making process, to control food-borne pathogenic and spoilage bacteria. Nisin has the wide spectrum of activity against Gram-negative and Gram-positive bacteria. Identify and characterize nisin A produced by *Lactococcus lactis* subsp. *lactis* LL27. Nisin A shows activity against pathogenic bacteria with the heating and freezing processes which are commonly used in the food processing [114].

Table 4: Application of enterocin produced by bacteria and their antimicrobial spectrum against pathogenic strain

Enterocin	Producer strain	Application	Antimicrobial spectrum against	Reference
Enterocin A	*Lactococcus lactis* MG1614	Cottage cheese	*L. monocytogenes*	[99,100]
Enterocin A and B	E. faecium WHE 81	Munster cheese	*L. monocytogenes*	[101,102]
Enterocin L50A and B	E. faecium F58	Goat milk and Jben (Moroccan Goat cheese)	*L. monocytogenes*	[103]
Enterocin AS-48	*E. faecalis*A-48-32	Fat-free hard cheese	*B. cereus*	[104]
Enterocin AS-48	*E. faecalis*A-48-32	Skim milk and unripe soft cheese	*S. aureus*	[105]
Enterocin CCM 4231	*E. faecium*CCM 4231	Spanish fermented dry sausage	*Listeria. spp.*	[106,107]
Enterocin 13	*E. faecium*RZS C13	Spanish fermented dry sausage	*Listeria. spp*	[108,109]
Enterocin A and B	*E. faecium*CTC492	Fermented dry sausage	*L. innocua*	[110]
Enterocin A and B	*E. faecium*CTC492	Cooked pork	*L. sakei CTC746*	[111]

Pediocins

Pediocins are categorized in the Class II of unmodified antimicrobial peptides (36–48 residues), also known as "antilisterial" or "Listeria-active" bacteriocins produced by *Pediococcus* spp. Pediocins-like bacteriocin are small (<5 kDa), have a 40–60% amino acid sequence similarity, and characterized by a-Y-G-N-G-V-N-amino terminus. Recently, a pediocin by *P.acidilactici* containing formulation is marketed under the commercial name Alta 2341®. The important feature of pediocin is they are stable in the complex environment of food when it's used as a food additive. Pediocin F, one of the bacteriocins produced by *P. acidilactici* isolated from fermented sausage, is a small peptide, with a molecular weight of approximately 4-5 kDa that has shown to be effective against many bacteria associated with food spoilage and food related health hazards. Pediocin F is reported to be sensitive to proteolytic enzymes, resistant to heat and organic solvents, and active over a wide range of pH [115]. In table 5 we listed name of commonly used pediocin and their application in the food industry. Papagianni and Anastasiadou 2009, review and discuss on characteristics of known pediocins molecules biosynthesis and production in fermentation systems [116].

The application of Pediocins in Food can offer a good alternative means of protecting food against food borne pathogens, also provide natural means of preservation and can be accepted by the consumers in the way nisin became accepted. Pediocin produced from *L. plantarum* used in preservation of cheese, inhibit the growth of *Listeria monocytogenes* [117]. Being mild antimicrobials, pediocins are also expected in the future to find more applications in both human and veterinary medicine.

Table 5: List of pediocin producer strain and their application in food industry

Name of strain	Sugar ferment	Application	References
P.acidilactici	Glucose, ribose, xylose, fructose and galactose to DL-lactate	Sauerkraut Fermentations, dry sausages	[118-121]
Pediococcus pentosaceus	Glucose, ribose, galactose, arabinose, and fructose to DL-lactate	Starter cultures in sausage fermentations, brewing industry and, silage fermentations	[122-124]
Pediococcus damnosus	Glucose, sucrose and galactose	Exopolysaccharide production and bacteriocin production	[125,126]

Lacticin 3147

Lacticin 3147 a class I, two-component bacteriocin produced by *Lactococcus lactis* subsp. *lactis,* isolated from an Irish kefir grain has been used for making buttermilk. Numerous research works have recommended that Lacticin 3147 have activity against a broad range of organisms and potentially suitable for several food applications [127]. A bacteriocin, lacticin Zproduced by *L. lactis* QU 14 showed a nano molecular range of MICs against numerous Gram positive bacteria, and the bacteriocin was stable at 100 °C under alkaline conditions[128].

Lasta *et al.* (2015) isolated and characterized the new bacteriocin, lacticin LC14 from *Lactococcus lactis* have bactericidal-type antimicrobial activity against several lactic acid bacteria and pathogenic strains including *Listeria monocytogenes* [129]. As lacticin 3147 inhibits a large number of food pathogenic organisms it would appear to be particularly suited to use as a biopreservatives.

Lactococcin B

The genus *Lactococci* are used in a large variety of industrial food fermentations for the formation of lactic acid from the available carbon source, which results in rapid acidification of food, a critical parameter for the preservation of these food products. Lactococcin B (LcnB) is a small, hydrophobic, positively charged bacteriocin produced by *Lactococcus lactis* subsp. *Cremoris*. *L. lactis* subsp. *cremoris* 9B4 produces at least three bacteriocin named lactococcin A, B, and M [130]. Isolates and characterize *Lactococci* from natural sources and suggest that could be used as starter cultures [131].

Acidocin

The bacteriocin Acidocin B, is plasmid encoded (2.4 kDa) produced by *Lactobacillus acidophilus* strain M46 has an inhibitory spectrum against pathogenic bacteria *Listeria monocytogenes, Clostridium sporogenes, Brochothrixthermo sphacta, Lactobacillus fermentum* and *Lactobacillus delbrueckii* [132].

Leucocin A

Leucocin A is a group of small antibacterial peptides produced by *Leuconostoc pseudomesenteroides , Leuconostoc carnosum* QU15 has a molecular weight 4 kDa (37 amino-acids). This group may include lactacin F (6.3 kDa, 57 amino acids) and leucocin B from *Leuconostoccarnosum* cloned bacteriocin [133].

Lactobacillus acidophilus produced bacteriocin lactacin F, which is a proteinaceous heat-stable component and inhibitory for other lactobacilli as well as *Enterococcus faecalis* [134, 135].

Mesentericin Y105

Mesentericin Y105 is a 37-amino acids residue containg bacteriocin produced by *Leuconostocmesenteroides* Y105 that displays antagonistic activity against Gram-positive bacteria such as *Enterococcus faecalis* and *Listeria monocytogenes* [136].

Sakacin P

Sakacin P is one of the most extensively studied bacteriocin has been found to be very potent against *L. monocytogenes*[137]. The addition of sakacin P in vacuum-packed cold smoked salmon, a lightly processed high-fat (15–20%) product inhibited the growth of *L. monocytogenes* [138]. According *Listeria monocytogenes* L182 grew rapidly on vacuum packed chicken cold the addition of sakacin P completely inhibited the growth of *L. monocytogenes* L182 for 4 weeks. Sakacin A is a bacteriocin produced by *Lactobacillus sakei* Lb706 inhibits the growth of *L. monocytogenes* on cold smoked salmon [138, 139]. Moreover, some research article reported the use of bacteriocin producing cultures in the preservation of meat products ensure that the inhibition of *Listeria* is due to production of Sakacin A [140].

Curvacin A

Curvacin A were produced in the late exponential growth phase of *Lactobacillus curvatus* and active against closely related species,food pathogens *Listeria monocytogenes* and *Enterococcus faecalis*. The bacteriocin curvacin A are small peptides of 38–41 amino acid residues. No unusual amino acids were detected. In the N-terminal region curvacin A and sakacin P shares the similar segment — Tyr-Gly-Asn-Gly-Val. No sequence similarity was detected to previously characterized bacteriocins indicating that these bacteriocins are novel [141].

Reutericyclin

Reutericyclin is the first low-molecular-weight,extremely hydrophobic inhibitory compound inhibits the cytoplasmic membrane of target organisms produced by *Lactobacillus reuteri.* Largely,Gram-positive and negative bacteria as well as numerous fungi and yeasts are sensitive to reutericyclin. Many pathogenic bacteria *S. aureus, L. innocua*, and*E. faecium* are inhibited by reutericyclin. The minimum inhibitory concentrations(MICs) range from 0.06 to 2.5 mg/l [142]. The application of reutericyclin is possible through the addition of a purified compound to food or pharmaceutical products,by fermentation with reutericyclin-producing strains, orthrough the addition of metabolically inactive cells to foods where the product composition allows desorption of reutericyclin associated with the cells [143].

Limitation of bacteriocin activity

The presence of bacteriocins in most of the food used from ancient times makes them to be considered more natural as compared to the currently used antibiotics [144]. A limitation of using bacteriocin in food is that most bacteriocins are moderately small and can diffuse simply through the aqueous phase of food products. However, bacteriocin are hydrophobic molecules and bind to the hydrophobic phase of foods, such as emulsions or food surfaces, which notably reduces the bacteriocin activity. For this reason, many researchers suggest that bacteriocin use is limited to non-emulsified products. However, the bacteriocin production or activity is affected by sensitivity to food enzymes, food environment, poor solubility, uneven distribution in the food matrix and inactivation by other additives [145].

Current and future developments

Much is currently known about bacteriocins, allowing for development of a huge variety of bacteriocins as protective cultures for food preservation. While a wide number of publications and patents have demonstrated relevant results about direct food and antimicrobial applications of LAB[146], but many countries still do not allow the use of purified bacteriocins other than nisin [147]. This problem has been circumvented with approved food-grade bacteriocin-producing strains or their extracellular extracts in many processed foods. In most cases, bacteriocin production and activity has been demonstrated only in the laboratory.

CONCLUSION AND DISCUSSION

The use of bacteriocins in food preservation was started approximately 20 years ago, considered to be part of a barrier mechanism and not the only preserving agent, unless all of the characteristics of the bacteriocin are known. One of the advantages of using bacteriocins in food is that these peptides can be part of human and animal diets because meat and dairy products are natural sources of LAB. Now day's research is concentrated on inhibition of food spoilage or human disease causing bacteria present in vegetables, dairy products and beverages with the use of bacteriocin in place of antibiotics. Bacteriocins have inhibitory potency against antibiotic-resistant bacteria like antibiotics. The in situ production of bacteriocin improves gut intestinal flora and fight against intestinal infections. Their main advantage over chemical preservatives is their ability to preserve without affecting the sensory qualities of the food while adhering to the demand for natural preservatives. The ideal bacteriocin should be potent at low concentrations, active against a range of spoilage and pathogenic organisms, innocuous to the host and economical to produce. These antimicrobials can be introduced into a food through incorporation of the bacteriocin-producing strain into the food product (most common in fermented foods), the generation and use of a bacteriocin-containing fermentate or as a more concentrate bacteriocin-containing food preservative.

CONFLICT OF INTERESTS

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article. The authors are thankful for university grant commission, New Delhi,India forproviding financial support.

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