Research & Reviews in Biotechnology & Biosciences

Homepage: www.biotechjournal.in

Volume No: 4, Issue No: 2, Year: 2017 PP: 49-56

Published By: National Press Associates in Association with Lyallpur Khalsa College, Jalandhar, Punjab

ISSN No: 2321-8681

Review Article

Antimicrobial Metabolites of Probiotic Bacteria: Its properties and Diversity

*Swati Srivastava, Ankita Srivastava, Niharika Chandra, Sunil Kumar**

Faculty of Biotechnology, Institute of Bio-Sciences and Technology, Shri Ramswaroop Memorial University, Uttar Pradesh India.

Article History

Received: 10/08/2017
Revised: 02/09/2017
Accepted: 05/10/2017

**Corresponding Author:*
E-Mail: sunil.bio@srmu.ac.in

© Lyallpur Khalsa College, Jalandhar (PB)

Abstract

The antimicrobial activity of lactic acid bacteria and probiotic bacteria are the main aim of this review. In this review, we have compiled the available data on the commonly used preservative and present the current knowledge regarding the antimicrobial compounds, especially bacteriocins, the mechanisms of the action and recent applications of antimicrobial compounds in food. This activity has been attributed to the production of metabolites such as organic acids (lactic and acetic acid), hydrogen peroxide, ethanol, diacetyl, acetaldehyde, acetoine, carbon dioxide, reuterin, reutericyclin and bacteriocins. The potential of using bacteriocins of lactic acid bacteria, primarily used as bio-preservatives, represents a perspective, alternative antimicrobial strategy for continuously increasing problem with antibiotic resistance. Another strategy in resolving this problems is application of probiotics for different gastrointestinal and urogenital infection therapies.

Key words: Antimicrobial activity, bacteriocins, lactic acid bacteria, probiotics, starter cultures

Introduction

Fermentation processes play significant roles in food technology in most of the developing countries. In traditional fermentation processes, the use of natural micro-organisms in the preparation and preservation of different types of food was a regular practice. Now a days, these processes are also concerned with enhancing flavor and other desirable qualities associated with digestibility and edibility [1] and add to the nutritive value of foods as well which helps in the extension of shelf life of food. Since in present scenario, consumers are more concerned about the synthetic chemicals used as preservatives in food, most of them prefer less processed food. These untreated foods can harbor dangerous pathogens which can multiply under refrigeration and without oxygen. The use of antimicrobial metabolites of fermentative microorganisms has proved to be a successful method in controlling these pathogens. These antimicrobial chemicals have been in use for a long time without any known adversative effects. Many of the organic compounds which have stimulated interest are antimicrobial metabolites of bacteria used to produce, or associated with fermented foods [2].Thus fermentative microorganisms are being researched so that it can be improved and used as a potential bio-preservative. Hence fermentative microorganisms are being researched to improve to be used as bio-preservative which will help food industries in the development of effective natural preservation methods.

Lactic acid bacteria (LAB) are a group of gram-positive bacteria together with the genera *Lactobacillus, Lactococcus, Leuconostoc, Pediococcus, and Streptococcus*. The general properties of the bacteria included in the group is gram-positive, non-spore forming, cocci or rods, which produce lactic acid as the major end product during the fermentation of carbohydrates. Lactic acid bacteria are nutritionally particular, and require substrates like carbohydrates, amino acids, peptides, nucleic acids and vitamins. Apart from checking the spoilage of food and preservation of food through natural fermentation, LAB have established commercial applications as starter cultures in the dairy, baking, meat, vegetable, and alcoholic beverages industries. The preservative action of starter culture in food and beverage systems is accredited to the combined action of a range of antimicrobial metabolites produced during the fermentation process. These antimicrobial metabolites include many organic acids such as lactic, acetic and propionic acids produced as end products which offer an acidic environment critical for the growth of many pathogenic and spoilage microorganisms. In addition to acids, other antimicrobial metabolites that can be produced from starter strains are ethanol produced from the hetero-fermentative pathway, H_2O_2 produced during aerobic growth and diacetyl which is generated from excess pyruvate coming from citrate. The use of bacteriocins-producing lactic acid bacteria as protective strains or bacteriocins in form of purified or concentrated compounds as bio-preservatives to control undesirable bacteria remains a primary focus of researches related to food safety and quality [3].

The use of probiotics and their antimicrobial activity in combating different types of diseases is an emerging area of research these days and thus it is necessary for everyone to update their microbial flora time to time and gain knowledge about improving health with the help of probiotics so that we can be protected from various types of illness. When we talk of microbes, our body has different types of microbes which collectively perform different types of functions. The most important of these microbes are those residing in our digestive system. These microbes help to overcome many deficiencies of our digestive system. Alternatively, there are also bad microbes that interfere with our digestive process and will digest food incorrectly which inturn can even add some toxins to our food during the digestive process. Hence we say that we each food cycles our health get deteriorated. In such cases, the use of probiotics in higher dosage is required [4]. When intestine maintains a balance of bacteria such lactobacilli, streptococci, clostridia, coliform and Bacteroides, it remains healthy however factors such as sugar, use of alcohol, genetic disorders chloride and fluoride in drinking water and exposure to environmental toxins can influence the balance of our intestinal flora. It has been observed that useful microflora guarantees good health and they also build our immune system slowly to fight against pathogens [5].

Antimicrobials from Lactic Acid Bacteria

Lactic acid bacteria (LAB) which are commonly used as starter cultures in food are known to produce antimicrobial substances such as bacteriocins, having great potential as food bio-preservative. Lactic acid bacteria produce metabolites such as lactic acid, acetic acid, hydrogen peroxide, bacteriocins and some low molecular weight compounds that are known to have antimicrobial activity. Microbial peptides with molecular masses between 3000 and 6000 DA are small and cationic, have distinct antimicrobial activity and are normally isolated from animals, plants, microbes and in fermented food. In recent years, interest in the antimicrobial compounds has been increasing substantially due to their potential usefulness as natural substitute for chemical food preservatives in the manufacturing of foods with higher shelf life and/or safety. The antimicrobial effect of acids can be observed by interfering with the maintenance of cell membrane potential, inhibiting active transport, reducing intracellular pH and inhibiting a variety of metabolic functions [6]. One good example is propionic acid produced by propionic acid bacteria, which is used for some bio-preservative products, and is known for its antimicrobial action against microorganisms including yeast and moulds.

Low molecular mass antimicrobials

The two main groups in which antimicrobial substances produced by lactic acid bacteria can be divided are: low molecular mass substances with molecular mass <1000 Da and high molecular mass substances with molecular mass >1000 Da such as bacteriocins. All non-bacteriocins antimicrobial substances from LAB are of low molecular mass[7]. The lists of low molecular mass antimicrobial metabolites of LAB are shown in Table 1[8, 9].

Table 1: Low molecular mass antimicrobial metabolites of lactic acid bacteria

S N	Compound	Microorganisms producers	Antimicrobial spectrum
1.	Lactic acid	All lactic acid bacteria	Yeasts, Gram-negative bacteria, gram-positive bacteria
2.	Acetic acid	Hetero fermentative lactic acid bacteria	Yeasts, Gram-negative bacteria, gram-positive bacteria
3.	Hydrogen peroxide	All lactic acid bacteria	Yeasts, Gram-negative bacteria, gram-positive bacteria
4.	Carbon dioxide	Hetero fermentative lactic acid bacteria	Most of the taxonomic groups of microorganisms
5.	Diacetyl acetaldehyde acetoin	variety of genera of lactic acid bacteria including *Lactococcus, Leuconostoc, Lactobacillus* and *Pediococcus*	Yeasts, Gram-negative bacteria, gram-positive bacteria
6.	Reuterin	Lactobacillus reuteri	fungi, protozoa, Gram-positive and Gram-negative bacteria
7.	Reutericyclin	Lactobacillus reuteri	Gram-positive bacteria
8.	3-hydroxy fatty acid	Lactobacillus plantarum	Fungi
9.	Cyclic dipeptides	Lactobacillus plantarum	Fungi

Organic acids

The two important factors i.e. the amount and type of acids produced during fermentation influence the subsequent microbial activity in the fermented material. The two acids that are produced by LAB and are considered to be the best characterized antimicrobials are lactic and acetic acid. Acetic acid, for example, has strong antimicrobial activity against yeasts as compared to lactic acid. Acidification, now a days is preferably used method of preservation during the production of many types of food, such as fermented milk and vegetables, and sausages and the inhibition of pathogenic and spoilage microbiota is carried out through rapid and adequate formation of these organic acids [10]. Different microorganisms display wide-range tolerance to acids. In case of LAB, it has been observed that they are not only tolerant to weak lipophilic acids but also produce them as a by-product of their metabolism.

Hydrogen peroxide

The most common method of producing hydrogen peroxide by most Lactobacilli species is by oxidizing lactate. Production of H_2O_2 by lactic acid bacteria can inhibit the growth of foodborne pathogens and can also be beneficial in food preservation [11]. Hydrogen peroxide production has been considered as the main metabolite of LAB that could protect against urogenital infections, especially in the case of bacterial vaginosis [4]. The bactericidal activity of hydrogen peroxide is mainly dependent on the concentrations applied and on environmental factors such as pH and temperature.

Diacetyl, acetaldehyde and acetoin

The process of formation of active acetaldehyde through decarboxylation of pyruvate follows the hetero-fermentative pathway of lactic acid bacteria. This product when condenses with pyruvate, formsα-acetolactate and with the help of enzymeα-acetolactate synthases, it is further converted into diacetyl. Finally acetoin is formed as a product of decarboxylation of α-acetolactate and reduction of diacetyl [12]. Diacetyl (2,3-butanedione)which is best known for imparting buttery aroma to fermented dairy products, but this property as well as its high concentration necessary to provide preservation of food, limit its use as a food preservative. Similarly, an acetaldehyde, usually present in fermented dairy products in concentrations smaller than necessary for inhibition of undesired microorganisms, also plays a role in controlling the growth of contaminants, together with other antimicrobial metabolites of lactic acid bacteria. Acetoin is widely used in the food and dairy industry as a preservative[13].

Carbon dioxide

Carbon dioxide is mainly produced by hetero-fermentative LAB. The mechanism of action of carbon dioxide as an antimicrobial compound is still unknown. By creating an anaerobic environment, CO_2 inhibits enzymatic decarboxylation and by accumulating in the membrane lipid bilayer, CO_2 helps in the dys-functioning of permeability. It has been found to be very effective in inhibiting the growth of food spoilage microorganisms specifically Gram negative psychotropic bacteria.

Reuterin and reutericyclin

The two compounds reuterin and reutericyclin are known to be isolated from *Lactobacillus reuteri* and are found to be active towards Gram-positive bacteria. Reutericyclin is a tetramic acid derivative and is the first low-molecular-weight antibiotic produced by LAB. Generally, Gram-positive and Gram-negative bacteria as well as several fungi and yeasts are sensitive to reutericyclin. Its mode of action is comparable to weak organic acids for example acetic acid and sorbic acid. Alternatively, reuterin is a mixture of monomeric, hydrated monomeric and cyclic dimeric forms of β-hydroxypropionaldehyde with a broader spectrum of inhibitory activity, including Gram-negative bacteria, fungi and protozoa [14, 15]. In one of the studies against food borne pathogens, it has been reported that reuterin (8 AU/ml) exhibited bacteriostatic activity against *Listeria monocytogenes*, whereas its activity was slightly bactericidal against *Staphylococcus aureus* at 37 °C [16].

Other low molecular mass antimicrobials

Some other new type of antimicrobial compounds were found to be produced by *Lactobacillus plantarum* such as benzoic acid, methylhydantoin and are active against fungi and some Gram negative bacteria[17].

Bacteriocins of lactic acid bacteria

The first bacteriocins production, discovered by Gratia in 1925, has been found in numerous species of bacteria [18]. Bacteriocins are ribosomally synthesized antimicrobial compounds that are produced by many different bacterial species including many members of the lactic acid bacteria [19]. Nisin is a well-known bacteriocins produced by lactic acid bacteria. It inhibits not only closely related species but are also effective against food-borne pathogens and many other gram-positive spoilage microorganisms [20]. A study of 40 wide-type strains of *Lactococcus lactic* showed that 35 produced nisin [21]. Nisin is the only bacteriocins with GRAS (Generally

Regarded as Safe) status for use in specific foods was regarded as safe a result of a history of 25 years and its use in many European countries and was further supported by the preexisting data indicating its nontoxic, nonallergenic nature. Bacteriocins biosynthesis is a necessary characteristic for strain selection as it serves as an important mechanism of pathogen exclusion in fermented foods as well as in the gastrointestinal environment. There are several proposed bacteriocins classifications which divided bacteriocins into 3 or 4 classes: (i) lantibiotics or small, heat-stable, lanthionine-containing, single- and two-peptide bacteriocins (class I), whose biologically inactive prepeptides are subjected to extensive post-translational modification; (ii) small, heat-stable, non-lanthionine-containing bacteriocins (class II), including pediocins like or Listeria-active bacteriocins (class IIa), two-peptide bacteriocins (class IIb) and circular bacteriocins (class IIc); and (iii) bacteriolysins or large, heat-labile, lytic proteins, often murein hydrolases (class III) [22-24]. Some authors [25, 26] also proposed (iv) class IV bacteriocins that require non-proteinaceous moieties (lipid, carbohydrate) for their activity.

Mode of action of bacteriocins

Bacteriocins that are produced by LAB can be of broad or narrow spectrum, but generally their activity is focused against low G+C Gram-positive species [22].The bactericidal mode of action usually acts on the bacterial cytoplasmic membrane, there is no cross-resistance to antibiotics, and their genetic determinants are usually plasmid-encoded, facilitating genetic manipulation. However, generalized membrane disruption models cannot adequately describe the mode of action of bacteriocins. Rather, specific targets seem to be involved in pore formation and other activities.

Immunity to bacteriocins

Two distinct systems of bacteriocins immunity in the producing cell have been identified. Protection can be facilitated by dedicated immunity protein and/or a specialized ABC-transporter system involving two or three subunits that possibly pump the bacteriocins through the producer membrane. The producing cells can be protected from their own bacteriocins when these two immunity systems work synergistically. A check on bacteriocins production and its immunity is most frequently made possible through two-component signal-transduction systems, often as part of the quorum-sensing mechanism [27].A recent advance in this field is the use of immobilized bacteriocins in the development of antimicrobial packaging.

Antimicrobial Activity of Probiotic Bacteria in Prevention and Treatment of Infections

Probiotic is a mono- or mixed culture of live microorganisms which, applied to animal or man, improve the properties of the indigenous microflora at here by benefitting the host, according to broader Fuller's definition. Recently, probiotics have been defined as 'live microorganisms which when administered in adequate amounts helps in the improvement of health of the host' (see reference FAO/WHO).Lactic acid bacteria are considered as the most important probiotic microorganisms because they are indigenous to human gastrointestinal tract of healthy people. Moreover as a probiotic, it shows attractive therapeutic properties and technological applications, such as proteolytic activity; production of polysaccharides; high resistance to freezing and freeze-drying; lactose and citrate fermentation; capacity for adhesion and colonization in digestive mucosa; production of vitamins; and production of antimicrobial compounds. Probiotics are largely administered through functional foods and as dietary supplements (pharmaceuticals) or bio-therapeutics (approved drugs with important therapeutic applications). Studies have shown that probiotics can down regulate inflammation and responses to allergens, and interfere with pathogen infections either directly or through enhancing gut barrier function. The process of antimicrobial activity of the bacteriocins produced by lactic acid bacteria and *Bifidobacterium* are mentioned in Table 2.

Table 2: Spectrum of antimicrobial activity of the bacteriocins produced by LAB and Bifidobacterium

S. No	Genus	Species	Compounds	Inhibitory spectrum	Ref
1.	*Bifidobacterium*	*B. lactis*	Bifilact Bb-12	*Staphylococcus aureus AS 1.72,*	[31]
		B. infantis BCRC	Bifidin I	*Salmonella sps,* *Listeria monocytogenes*	[32, 33]
		*B. bifdum*NCFB	Bifidocin B	*Gram-negative bacteria*	[34]
		Bifidumbacterium spp.	Proteinaceous compounds	*Listeria monocytogenes*	[35]
2.	*Enterococcus*	*E. faecium*WHE 81	Enterocins A and B	*L. monocytogenes*	[36]
		*E. faecalis*A-48-32	Enterocin AS-48	*S. aureus, Bacillus cereus*	[37]
		E. mundi	3944 Da bacteriocin	*Enterococcus faecalis, B. cereus, Clostridium tyrobutyricum, Klebsiella pneumonia, S. aureus*	[38]
3.	*Lactobacillus*	*L. acidophilus*AA11	Acidocin D20079	*Salmonella shigella, Escherichia coli, Staphylococcus aureus,*	[5]
		L. casei	Lactocin 705	*Listeria monocytogenes*	[39]
		L. sake	Sakacin	*Listeria monocytogenes*	[40, 41]
		L. reuteri	Reutericyclin	*Listeria inocua, S. aureus,* *E. faecium*	[42]
		L. plantarum	Plantaricin MG	*L. monocytogenes, S. aureus,* *E. coli, Salmonella* *Typhimurium*	[43]
4.	*Leuconostoc*	*L. gelidum*	Leucocin A	*Listeria monocytogenes*	[39]
		L. mesenteroides	Mesentericin Y105	*Listeria monocytogenes*	[39]
5.	*Pediococcus*	*P. pentosaceous*	Pediocin A	*Staphylococcus sp., Enterococcus sp., Listeria sp., Clostridium sp.*	[39]
		P. acidilacti			[44]
6.	*Lactococcus*	*L. lactis subsp. Lactis*	Nisin	*Lactococcus lactis subsp. lactis, Lactococcus lactis subsp. cremoris, Lacbtobacillusbulgaricus, L. monocytogenes, S. aureus,*	[21, 33, 45]
		L. lactis	Lacticin 481	*Clostridium tyrobutyricum*	[46]

Probiotic Bacteria and Bacteriocins in Human

Probiotics are live microorganisms thought to be healthy for the host organism. According to the currently adopted definition by WHO, probiotics are: "Live microorganisms which when administered in adequate amounts confer a health benefit on the host"[25, 26]. The term "probiotics" was first introduced in 1953 by Kollath [29]. Lactic acid bacteria were referred to as probiotics in scientific literature by Lilley and Stillwell (1965)Most human trials have found that the LAB strains tested may exert anti-carcinogenic effects by decreasing the activity of an enzyme called β-glucuronidase which can generate carcinogens (Heterocyclic amines) in the digestive system [30]Probiotics can also serve a role for stabilizing intestinal microflora. In addition, agents such as bacteriocins have been studied or proposed as potential human and animal therapeutics because they are considered more natural than the currently used antibiotics and are produced by GRAS lactic acid bacteria. Although Gram-negative bacteria do not represent target cells for bacteriocins, additions of chelating agents such as EDTA and detergents such as Tween 80 can broaden their antimicrobial spectrum [30].

Conclusion

The potential application of bacteriocins as consumer friendly bio-preservatives either in the form of protective cultures are as additives is significant. Lactic acid bacteria are typically involved in a large number of spontaneous food fermentations. Food fermentations have a great economic value and it has been accepted that these products contribute in improving human health. LABS have contributed in the increased volume of fermented foods worldwide especially in foods containing probiotics or health promoting bacteria. Bacteriocins produced by LAB are the subject of intense research because of their antibacterial activity against food borne bacteria.

REFRENCES

1. Khetarpaul, N and Chauhan, BM, 1990. Fermentation of pearl millet flour with yeasts and *Lactobacilli*: in vitro digestibility and utilisation of fermented flour for weaning mixtures. Plant Foods Hum Nutr. 40(3): 167-73.
2. Settanni, L and Corsetti, A, 2008. Application of bacteriocins in vegetable food biopreservation. Int J Food Microbiol. 121(2): 123-38.
3. ter Kuile, BH and Hugas, M, 2010. Editorial perspective. Future challenges to microbial food safety. Int J Food Microbiol, 139 Suppl 1: S1-2.
4. Reid, G, 2008. Probiotic *Lactobacilli* for urogenital health in women. J Clin Gastroenterol, 42 Suppl 3 Pt 2: p. S234-6.
5. Mahapatra, S and Banerjee, D, 2010. Diversity and screening for antimicrobial activity of endophytic fungi from Alstonia scholaris. Acta Microbiol Immunol Hung, 57(3): 215-23.
6. Ross, RP, Morgan, S and Hill, C, 2002. Preservation and fermentation: past, present and future. Int J Food Microbiol, 79(1-2): 3-16.
7. Patterson, JA and Burkholder, KM, 2003. Application of prebiotics and probiotics in poultry production. Poult Sci, 82(4): 627-31.
8. Jamalifar, H, 2011. Antimicrobial activity of different *Lactobacillus* species against multi- drug resistant clinical isolates of *Pseudomonas aeruginosa*. Iran J Microbiol, 3(1): 21-5.
9. Azat, R, 2016. Probiotic properties of lactic acid bacteria isolated from traditionally fermented Xinjiang cheese. J Zhejiang Univ Sci B, 17(8): 597-609.
10. Ammor, MS and Mayo, B, 2007. Selection criteria for lactic acid bacteria to be used as functional starter cultures in dry sausage production: An update. Meat Sci, 76(1): 138-46.
11. Dahiya, RS and Speck, ML, 1968. Hydrogen peroxide formation by lactobacilli and its effect on *Staphylococcus aureus*. J Dairy Sci, 51(10): 1568-72.
12. Jyoti, BD, Suresh, AK and Venkatesh, KV, 2004. Effect of preculturing conditions on growth of *Lactobacillus rhamnosus* on medium containing glucose and citrate. Microbiol Res, 159(1): 35-42.
13. Xiao, Z and Xu, P, 2007. Acetoin metabolism in bacteria. Crit Rev Microbiol, 33(2): 127-40.
14. Ganzle, MG and Vogel, RF, 2003. Studies on the mode of action of reutericyclin. Appl Environ Microbiol, 69(2): 1305-7.
15. Leroy, F, Verluyten, J and De Vuyst, L, 2006. Functional meat starter cultures for improved sausage fermentation. Int J Food Microbiol, 106(3): 270-85.
16. Arques, JL, 2004. Antimicrobial activity of reuterin in combination with nisin against food-borne pathogens. Int J Food Microbiol, 95(2): 225-9.
17. Niku-Paavola, ML, 1999. New types of antimicrobial compounds produced by *Lactobacillus plantarum.* J Appl Microbiol, 86(1): 29-35.
18. Garneau, S, Martin, NI and Vederas, JC, 2002. Two-peptide bacteriocins produced by lactic acid bacteria. Biochimie, 84(5-6): 577-92.
19. Jack, RW, Tagg, JR and Ray, B, 1995. Bacteriocins of gram-positive bacteria. Microbiol Rev, 59(2): 171-200.
20. Tagg, JR, Dajani, AS and Wannamaker, LW, 1976. Bacteriocins of gram-positive bacteria. Bacteriol Rev, 40(3): 722-56.
21. Hurst, A, 1978. Nisin: its preservative effect and function in the growth cycle of the producer organism. Soc Appl Bacteriol Symp Ser, 7: 297-314.
22. Cotter, PD, Hill, C and Ross, RP, 2005. Bacteriocins: developing innate immunity for food. Nat Rev Microbiol, 3(10): 777-88.
23. Klaenhammer, TR, 1988. Bacteriocins of lactic acid bacteria. Biochimie, 70(3): 337-49.
24. De Vuyst, L and Leroy, F, 2007. Bacteriocins from lactic acid bacteria: production, purification, and food applications. J Mol Microbiol Biotechnol, 13(4): 194-9.

25. Klaenhammer, TR, 1993. Genetics of bacteriocins produced by lactic acid bacteria. FEMS Microbiol Rev, 12(1-3): 39-85.

26. Nes, IF, 1996. Biosynthesis of bacteriocins in lactic acid bacteria. Antonie Van Leeuwenhoek, 70(2-4): 113-28.

27. Quadri, LE, 2002. Regulation of antimicrobial peptide production by autoinducer-mediated quorum sensing in lactic acid bacteria. Antonie Van Leeuwenhoek, 82(1-4): 133-45.

28. Fuller, R, 1989. Probiotics in man and animals. J Appl Bacteriol, 66(5): 365-78.

29. Hamilton-Miller, JM, 2004. Probiotics and prebiotics in the elderly. Postgrad Med J, 80(946): 447-51.

30. Gillor, O, Nigro, LM and Riley, MA, 2005. Genetically engineered bacteriocins and their potential as the next generation of antimicrobials. Curr Pharm Des, 11(8): p. 1067-75.

31. Jungersen, M, 2014.The Science behind the Probiotic Strain *Bifidobacterium* animalis subsp. lactis BB-12((R)). Microorganisms, 2(2): 92-110.

32. Cui, Y, 2012. Class IIa bacteriocins: diversity and new developments. Int J Mol Sci, 13(12): 16668-707.

33. Yang, E, 2012. Antimicrobial activity of bacteriocin-producing lactic acid bacteria isolated from cheeses and yogurts. AMB Express, 2(1): 48.

34. Guyonnet, D, 2000. Method for rapid purification of class IIa bacteriocins and comparison of their activities. Appl Environ Microbiol, 66(4): 1744-8.

35. Cheikhyoussef, A, 2008. Antimicrobial proteinaceous compounds obtained from bifidobacteria: from production to their application. Int J Food Microbiol, 125(3): 215-22.

36. Izquierdo, E, 2009. Smearing of soft cheese with *Enterococcus faecium* WHE 81, a multi-bacteriocin producer, against *Listeria monocytogenes*. Food Microbiol, 26(1): 16-20.

37. Park, SH, Itoh, K and Fujisawa, T, 2003.Characteristics and identification of enterocins produced by *Enterococcus faecium* JCM 5804T. J Appl Microbiol, 95(2): 294-300.

38. De Kwaadsteniet, M, 2005. Characterization of a 3944 Da bacteriocin, produced by *Enterococcus mundtii* ST15, with activity against Gram-positive and Gram-negative bacteria. Int J Food Microbiol, 105(3): 433-44.

39. Nespolo, CR and Brandelli, A, 2010. Production of bacteriocin-like substances by lactic acid bacteria isolated from regional ovine cheese. Braz J Microbiol, 41(4): 1009-18.

40. Rodriguez, JM, 1995. PCR detection of the lactocin S structural gene in bacteriocin-producing lactobacilli from meat. Appl Environ Microbiol, 61(7): 2802-5.

41. Schillinger, U and Lucke, FK, 1989. Antibacterial activity of *Lactobacillus* sake isolated from meat. Appl Environ Microbiol, 55(8): 1901-6.

42. Ganzle, MG, 2004. Reutericyclin: biological activity, mode of action, and potential applications. Appl Microbiol Biotechnol, 64(3): 326-32.

43. Oldak, A, 2017. Comparison of Antibacterial Activity of Lactobacillus plantarum Strains Isolated from Two Different Kinds of Regional Cheeses from Poland: Oscypek and Korycinski Cheese. Biomed Res Int, 6(8) 0369.

44. Devi, SM and Halami, PM, 2011. Detection and characterization of pediocin PA-1/AcH like bacteriocin producing lactic acid bacteria. Curr Microbiol, 63(2): 181-5.

45. Mokoena, MP, 2017. Lactic Acid Bacteria and Their Bacteriocins: Classification, Biosynthesis and Applications against Uropathogens: A Mini-Review. Molecules, 22(8).

46. Mirkovic, N, 2016. *Lactococcus lactis* LMG2081 Produces Two Bacteriocins, a Nonlantibiotic and a Novel Lantibiotic. Appl Environ Microbiol, 82(8): 2555-62.