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Review Article

Bacteriocin: the avenues of innovation towards applied microbiology

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Abstract

Microbial adhesion and pathogenesis result in serious problems in world. In case of infectious diseases in human being, there is an epidemiological issue, on another hand, if microbes infect poultry and crops, there is a huge economical and nutritional loss. Antibiotics used to control this microbial pathogenesis but the excess use of antibiotics and other chemical compounds in intensive animal production have several side effects and results in increased antibiotic resistance day by day. Antimicrobial resistance becomes a great problem in the world. Scientists are seeking for the product which can be used as alternative to the antibiotic with less side effects. Bacteriocin is such a type of peptide which works when bacteria become resistant to some antibiotic. It is ribosomaly synthesize antimicrobial peptide by gram positive and gram-negative bacteria. Various types of bacteria produce different type of bacteriocins. They have different antimicrobial spectrum. Spectrum of antimicrobial activity varies from bacteria to bacteria. Due to their proteinaceous nature they are harmless to human gastrointestinal tract. Bacteriocins are used to treat many infectious diseases in animals and human beings. It has wide application in food industry to prevent the growth of pathogenic bacteria. Nisin was the first bacteriocin used in the food as the research advances novel bacteriocins introduced which are being used in food industry for the preservation of food. Moreover, it has wide application in pharmaceutical industry. Bacteriocins are gaining attention in the recent era due to their unique mode of antimicrobial action and wide application in various industries.

Keywords: Antimicrobial activity; Antimicrobial peptide; Bacteriocin and pathogenic bacteria

Introduction

Food spoilage due to microbial adhesion is a great problem. Due to food spoilage there is not only a nutritional loss but also an economical loss **[1]**. Chemical preservatives are not appropriate due to their hazardous effects on human health. It is very important to resolve this problem to fulfill the food requirement of rising world. In this era, natural and microbiological methods are being used to preserve the food **[2]**. To manage the economic loss, use of bacteriocins as preservative in the food industries is a satisfactory approach. In the recent world, bacteriocins application are gaining interest as they are generally regarded as safe (GRAS) by the food authority and World health organization **[3]**.

Moreover, bacteriocins due to its proteinaceous nature implies a putative degradation in gastrointestinal tract of human beings [4] therefore, these bacteriocins aid colonization in the digestive system [5]. Function of peptides can be affected by various factors including proteolytic degradation, non-polar and polar food components and fat contents, sodium chloride concentration and pH [6].

Bacteriocins are not only effective against the closely related organisms but also effective against organisms like mycobacterium, viruses and fungi. Its potential applications have been studied specially in food industry as bio preservative from many years [7], [8]. Moreover, bacteriocin as an antimicrobial agent has been exploited in various fields as their influence against various pathogen related to veterinary and human disease [9], [10], [11].

Background of bacteriocins

It was first reported in 1925, that the antibacterial substance produced by the E. coli have capacity to inhibit the other strains of same species reported by André Gratia [12]. It was thought that the compound produced from bacteria called colicin and are responsible for the inhibitory effect. After that in 1928, it was observed certain *Lactococci* strains ability to inhibit other LAB strains [13]. According to Mattick and Hirsh, studies in 1947 [14], *Lactococcus lactis* subsp. *Lactis* produced an inhibitory substance which called as nisin which has inhibitory effect on prokaryotes [15]. In 1953, nisin was initially marketed, purified and termed as bacteriocin [16] and regarded as safe Food Additives in 1969 by the Joint / World Health Organization Expert Committee/ Food and Agriculture Organization. In the list of food additives, nisin was added in Europe in 1983 and it was used in processed cheese authorized by the American Food and Drug Administration (FDA) in 1988 [17]. Firstly, nisin was approved to be used in food by FDA while as the research advances pediocin have also been used in industrialized foods as preservative obtained from *Pediococcus parvulus*, *Pediococcus acidilactici* and *Lactobacillus plantarum* WHE92 [18]. As reported by Yi [19] *Lactobacillus crustorum* MN047 synthesize a bacteriocin BMP11 which has a rich α-helix confirmation. Bacteriocin was purified through HPLC (high performance liquid chromatography) and ion exchange chromatography and when it tested against food borne pathogen showed minimum inhibitory concentration MIC value of 0.3-38.4 µg/ml. Moreover, it was noted that BMP11 had a bactericidal mode of action. Transmission electron microscope and scanning electron microscope (SEM) results showed that BMP11 destroyed the pathogen cell envelop integrity with cell membrane permeability ad cell wall perforation. Cells envelop integrity destruction further identified through lactic dehydrogenase release and propidium (PI) uptake. Meanwhile, in milk it inhibits the growth of *Listeria monocytogen* and exhibits the antibiofilm formation activity. Therefore, BMP11 has a potential to act as antimicrobial and used as preservative to control the foodborne pathogen in dairy product [19].

Classes of bacteriocins

The heterogenous group which are peptides synthesized ribosomally [3] mainly divided into three classes, I II and III [20] but advanced studies further categories them into further classes and subclasses. They are classified on the basis of their structural and physiochemical properties. Recently bacteriocins have been divided into four categories. Class I bacteriocins, the lentibiotics [21] are broad spectrum peptides like nisin; inhibit the growth of gram-positive spoilage microbes and food borne pathogens. Class II bacteriocins are the small heat stable non lantibiotics which have narrow antimicrobial spectrum. Garviecin LG34 is a class II bacteriocin consisting of 46 amino acid residues which exhibit inhibitory activity against gram negative and gram-positive bacteria. Enterocin CRL35 is another class II bacteriocin with anti-Listerial activity [6], [22]. Class III bacteriocins are large heat labile, break down the cell wall of bacteria in an enzymatic manner and are usually endopeptidase. Class IV bacteriocins are composed of lipids, carbohydrates and an undefined mixture of protein [21]. Class IV bacteriocins are complex bacteriocins and are sensitive to lipolytic and glycolytic enzymes like leuconocin S and plantaricin S.

Mode of action of bacterial bacteriocins

Antimicrobial peptides produced by prokaryotes that kills or inhibit phylogenetic related microorganisms are called bacteriocins [23]. The action of bacteriocins may be as antimicrobial, colonizing or signaling peptides [24]. They mostly form pores on the cell membrane of pathogen whereas their proteinaceous nature let them degrade efficiently and rapidly. Thus, the chance of developing resistance like antibiotics become minimized [22]. Lactic Acid Bacteria (LAB) are studied extensively due to their potential in bio-preservation by producing bacteriocins [8, 24]. It has been predicted that~99% of all bacteria synthesize at least one bacteriocin, with a length of minimum10 amino acids or as long as 688 residues [25]. However, due to multidrug resistance of bacterial clinical strains, the use and application of bacteriocins is gaining more interest [23]. Since the past decade, the reported bacteriocin number has been increased significantly. The high potential of these antimicrobial peptides has expended uses in the pharmaceutical and food industries, in apiculture and agriculture [23, 26]. In recent years, attention is given towards these antimicrobial compounds as they are significant as bio-preservative and substituted for chemical preservatives used in food. They have potential to improve the shelf life of food as well. The equilibrium is attained by their inhibitory activity upon pathogenic bacteria [21].

Different types of bacteria produce different types of bacteriocins that make them distinct from other species of bacteria. Bacteriocins synthesized by LAB (Lactic Acid Bacteria) have variable spectrum of activities. Many bacteriocins are small sized molecules with high isoelectronic points and amphipathic characteristics [27]. The cell produces bacteriocins have specific immunity proteins due to which they are resistant to these antimicrobial peptides [24, 27-29]. LAB (Lactic acid bacteria) are very crucial as they prevent the growth of pathogenic [30] as well as spoilage microbes in food product through the production of acids and antimicrobial agent thus improve the quality and safety of fermented foods [7, 31, 32]. Two LAB species *Lactobacillus sakei* and *Lactobacillus curvatus* plays significant role in the accelerated maturation of fermented meat products and improve flavor. These two species are present in a variety of fermented meat products as their microbiota.

The action of bacteriocin is similar that they replace the structural protein or by bacteriocin antagonistic competition for the receptor [7, 33]. A recent study revealed that the bacteriocin receptor altered with the bacterial membrane structural modifications [34]. Moreover, it was noticed that the additive used with bacteriocin significantly increases it activity [35]. Various classes of bacteriocins have different mode of actions and functions. Functions of class I bacteriocins are to disrupt the membrane of the target (pathogens) by interaction of the peptide with the chiral receptor [36], they are ribosomally produced and post translational peptides (RiPPs), during their biosynthesis they undergo enzymatic modification [3]. In case of class II, cleave the peptide tab. or membrane translocation is facilitated by accessory proteins.

Biosynthesis of bacteriocins

Functional analysis of bacterial genome of bacteriocins producing bacteria revealed that the cluster of genes are located on their chromosomes or carried on plasmids. These encoded proteins are responsible for the biosynthesis of these peptides [37]. Microorganisms synthesize the bacteriocins usually in inactive form (pre-peptides) and they have sequence guide at N-terminal [38]. In class II bactriocin family contain conserved motif 'YGNGVXC' on N-terminal [39]. They have a covalent linkage to form their peptide backbone [37]. The precursor (pre-peptides) synthesized during the bacterial exponential growth phase and transported to cell surface and converted to active form enzymatically. The carrier contains two terminals C and N (peptidic portion), C portion responsible for energy supply and ATP hydrolysis while guide peptide cleavage on N terminal [40]. Accessory proteins facilitate the cleavage of peptide or help in membrane translocation. Three components a response regulator, an inducing peptide (or pheromone-activating factor) and the transmembrane histadine kinase (pheromone receptor) are involved in regulating the bacteriocin production system [41]. The ribosome synthesizes the inducer peptide which is secreted in the external environment, outside the cell and cleaved by the carrier system [7]. Transmembrane histadine kinase is activated when the threshold concentration of compound (inducer peptide) is reached, that leads to the histidine residues autophosphorylation, thus phosphate is transferred to a response regulator protein [7]. Bacteriocin transcription is activated by the phosphorylated regulator (sigma factor sigX) [42]. The positive feedback is initiated by the regulatory system [41] and bacteriocins itself act as pheromone and regulated the production of Lantibiotics like subilin and nisin, at high level [43].

Microbial sources of bacteriocin

Bacteriocin producing bacteria can be isolated from different ecological sources like water, food (yogurt and milk), stool sample (healthy infants), soil and clinical samples. From these samples approximately 54.3% have ability to produce bacteriocin [44]. Furthermore, bacteriocin producing bacteria have been reported to be isolated from malt [45], fermented food products [46], traditional Chinese fermented cucumber [47], meat [48], gastrointestinal tract of chicken [49], traditional Ethiopian fermented beverages [50], chicken ceca [51], Tibetan kefir [52], human, porcine, and avian gastro intestinal tracts (GIT) [53], marine biofilm forming bacteria [54], poultry products [55], fermented meat and fish products [56], molasses [57], fermented fish roe [58], fermented meat [59], fermented food [60], Sturgeon (popular Italian fish), koumiss [61], natural fermented cream [62] and flounder, cutlassfish, sea bass and turbot [30].

Some important species which produce bacteriocin are *Lactobacillus amylovorus* DCE 471 [63], *Lactococcus lactis* subsp. *Lactis* [55], *Lactobacillus plantarum* [64], *Lactobacillus* [50], *Lactobacillus salivarius* [51], *Lactobacillus paracasei* subsp. *Tolerans* [52], *Lactococcus garvieae* LG34 [47], *Lactobacillus crustorum* MN047 [61], *Lactobacillus alimentarius* [48], *Lactobacillus casei* [60] and *Lactobacillus plantarum* [30].

Some bacterial species that have been reported to produce bacteriocins are: *Pediococcus acidilactici* [45], *Enterococcus faecium* C1 [46], *Enterococcus faecalis* [49], *Pediococcus spp* [65], *W. cibaria* N23 [56], *E. faecium* CN-25 [58], *Lactobacillus spp*, *Lactococcus spp*, *Enterococcus spp.* or *Pediococcus spp* [59], *Enterococcus faecalis* LD33 [62], *Bifidobacterium animals* BB04

[66], *Haemophilus haemolyticus* [67] and *Bacillus subtilis* SN7 [68].

Bacteriocins: A natural way to combat with pathogens

Bateriocins are the peptides which interfere with the structural proteins of the target pathogen. The interaction of various classes of bacteriocins with its target is diverse. However, the conjugation of bacteriocins with the incorporation of drug delivery system is recently expanding field [69]. Bacteriocin is considered as "designer's drugs" that means they attack on specific pathogen [70]. Bacteriocins have ability to tolerate acidic condition in acidic environment of gastrointestinal tract GIT. It can be applied to control the growth of lethal microorganisms like *L. monocytogen*. However, in Amado study [71] it was reported that the use of bacteriocin (pediocin SA-1) have ability to inhibit the growth of *L. monocytogen* while enhancing the fermentation quality by promoting the growth of spontaneous fermentation and bacterial communities by their aerobic stability [72]. Some bacterial species displayed high potential of synthesizing bacteriocin like *Staphylococci, Pseudomonas, Proteus* and *Lactobacillus*. Bacteriocin produced by *Pseudomonas aeruginosa* SA 188 named as pyocin not respond to lipolytic and proteolytic enzymes. Moreover, metal salts and organic solvents have no effect on bacteriocin production profile [44].

LAB produced bacteriocins are well known for their efficiency against *Listeria monocytogenes*, which in the last decade is responsible for many food related outbreaks. In current classification of bacteriocins [73], as reported by Vogel [74] a specific class of bacteriocin is dedicated as anti-Listeria activity while there is a serious issue to control *Listeria monocytogenes* in processed food as they have potential to grow in condition like salt concentration, low pH and the presence of nutrients applied during the manufacturing of dry fermented product. According to [75] bacteriocin for preservation of food is increased in food industry as it is the technological alternative to chemical preservative. Lactic acid bacteria (LAB) synthesize a vast variety of antimicrobial peptides (bacteriocins) which have significant contribution towards the safety and preservation of fermented foods [76]. Bacteriocins produced by entomopathogenic *Bacillus thuringiensis* are getting more attention owing to their inhibitory activity against an extensive variety of pathogenic microorganisms [77].

Antibacterial activity

Various bacteriocin producing bacteria have different antimicrobial spectrum as the bacteriocin produce by different bacteria have different properties. The antimicrobial spectrum of bacteriocins depends on the structural and physiochemical properties of bacteriocins. Different kinds of bacteria produce different types of bacteriocins like bacteriocin produced by *Pediococcus acidilactici* strain HW01 have wide antimicrobial activity over a wide range of pH (2-11) as well as to inhibit a wide range of gram-positive bacteria including pathogenic bacteria like, *Streptococcus mutans*, *Staphylococcus aureus*, *L. innocua*, *Listeria monocytogenes* and *Lactobacillus curvatus* [45]. Nisin A inhibits the growth of *Listeria monocytogenes* [3]. Bacterial species producing bacteriocins against pathogens are shown in (Table 1)

Antifungal activity

Bacteriocins not only inhibit the growth of bacteria but also inhibit the growth of fungi [78]. Spoilage of food and agricultural commodities due to molds is very significant for causing economic losses. Molds destroying more than thirty percent crops in developing countries while they produce potentially toxic compounds known as mycotoxins which have ability to cause illness or death in consumers [79]. According to the study of [80], it was observed that *Bacillus subtilis* C9 inhibits the growth of plant pathogen *Rhizoctonia solani* [80]. Furthermore, fungi are ubiquitous in nature and have ability to colonize on various substrates therefore it has high incidence of mycotoxins and molds contamination in food [81]. Lactic acid bacteria (LAB) synthesize a wide variety of secondary metabolites like bacteriocin and organic acids which inhibit microbial growth [82]. Most of Lactic Acid Bacteria reported in past decade as a potential source of antifungal compounds and various studies have showed that various LAB isolates have the significant potential to control the fungi proliferation in many feed and food materials [83-87]. In another study it was reported that the Lactic Acid bacteria have significant potential in preservation of food and used as an antifungal biocontrol agent [88].

Bacteriocin and viruses

Bacteriocins are also active agent against viruses. All living organisms are majorly affected by pathogens like viruses [89]. They may involve in extensive public health problems e.g; polio virus and its eradiation in developing countries is a challenge [90, 91]. Moreover, Herpes simplex viruses (HSV) [92] resistant against available antivirals [93-95]. Isolation of lactic acid bacteria from goat milk (four *Enterococcus durans*: GEn17, GEn09, GEn14 and GEn12 and two *Lactococcus lactis*: GLc05 and GLc03) were tested for cytotoxicity in Vero cells (50% Cytotoxicity Concentration: CC50), and for their antiviral activities against Poliovirus (PV-1) and Herpes simplex virus 1 (HVS-1) strains. Semi-purified bacteriocins presented low cytotoxicity, with CC50 varying from 256.2 μg/mL (GLc05) to 1,084.5 μg/mL (GEn14) [96]. CC10 were determined for all isolates (GLc03: 36.9 μg/mL; GLc05: 51.2 μg/mL; GEn09: 88.1 μg/mL; GEn12: 99.9 μg/mL; GEn14: 275 μg/mL; GEn17: 62.2 μg/mL) and considered for antiviral activity assays. Antiviral activity before virus adsorption was noted against HSV-1 for GEn14 (58.7%), GEn12 (27.9%), and GEn17 (39.2%) and against PV-1 for GLc05 (4.9%), GEn09 (3.4%), GEn12 (24.7%) and GEn17 (23.5%). Antiviral activity after virus adsorption was identified against HSV-1 for GEn17 (71.6%) and against PV-1 for GLc05 (32.7%), GEn09 (91.0%), GEn12 (93.7%) and GEn17 (57.2%). The results indicate that some bacteriocins potential in viral inhibition and their application as new antiviral agent, especially these produced by *E. durans* strains [96].

The potential of cell free supernatant and bacteriocins as antiviral agent is very high. It is effective against influenza A virus A/WSN/33 (H1N1), murine norovirus S99 (MNV), feline herpes virus KS 285 and Newcastle disease virus Montana [97]. According to the study of Lange-Starke [97], cell free supernatant of *Lactobacillus curvatus* strain in 1:10 ratio was effective against H1N1 and MNV. Virus reduction was recorded after incubation of 3 days at 24^{o}C [97]. The efficacy and safety a subtilosin-based nanofibre formulation have also been evaluated against herpes simplex virus type 1 [98]. Furthermore, it was investigated [99] that the inhibitory activity of a bacteriocin synthesized by a strain of *Enterococcus faeciumis* able to inhibit the late stages replication of Herpes Simplex Virus (HSV-1 and 55 HSV-2).

Application of bacteriocins

The applications of bacteriocins increase as the research increases on its structural and functional attributes. With the passage of time the importance of bacteriocin enhanced is due to their significant role in various industries. They have wide application against pathogenic microbes [35], food industry [2, 48] agricultural industry [24, 100] veterinary and pharmaceutical industry [24].

There is significant application of bacteriocins in food industry as they are used to preserve food. In food industry application of bacteriocins can be classified into three categories: dairy, partially purified bacteriocins and others food grade fermented products **[101]**. Nisin is a commonly used bacteriocin for the preservation of food in food industry. It is estimated that the nisin which is commonly used in food industry have lethal dose of 6950 mg/kg **[102].** So, the toxicological studies reveal that the nisin has no toxic effect on human health. It is the bacteriocin applied in food industry and has a wide spectrum of antimicrobial activity against pathogens **[2, 7]**.

Brochothrix thermosphacta is a gram-positive fermenting bacterium. It is a food borne pathogen and decreases the shelf life of packed food **[103]**. As reported by Hu **[48]**, bacteriocin producing bacteria *Lactobacillus alimentarius* FM-MM4 isolated from the fermented meat, exhibited wide range of antimicrobial activity against gram-negative and gram-positive bacteria as well as for yeast **[48]**. It's a novel bacteriocin produced by the *Lactobacillus alimentarius* FM-MM4 which is thermostable while exposed to 121 °C for 15 min with 84.7% residual antimicrobial activity. Moreover, it is stable in pH 2-5. As the properties of lactocin indicated that it has significant potential to be used in food industry for the preservation of food **[48]**.

In seafood industry, marine bacteria have been significantly used as probiotic and antibiotics against *Mycobacterium*, *Pasteurella*, *Streptococcus*, *Cytophaga*, *Vibrio* and *Aeromonas* **[104, 105, 106]**. In food industry, the bacteriocins applied on the surface of sea food in the form of gel and polyethylene film **[107]**. Thus, to retain the synergistic action bacteriocinogenic strains are used in combination with other preservative and they directly incorporated while packed **[108, 109, 110]**. *Carnobacterium divergens* V41 have ability to produce bacteriocin which can be applied on cold-smoked salmon at commercial scale to resist the growth of *L. monocytogenes* **[108]**. The synergistic effect of various bacteriocins has been proved safe for seafood preservation **[111-114]**.

Agriculture

Economically important plants have been lost due to phytopathogens. The traditional method to improve the growth of plants like introduction of resistant cultivars and breeding become limited due to genetic resistance. A bacteriocin like colicin can be used to control the growth of phytopathogenic bacteria having a narrow antimicrobial spectrum and can be used as biocontrol in agriculture **[100]**. Now a days, bacteriocins are also used to preserve the grains **[115]** and also used to control pest in the field. As reported by Tsuda **[116]** lactic acid producing bacteria *Lactobacillus plantarum* strain BY reduced the soft rot disease in Chinese cabbage. This strain is also used to control disease in potato, tomato and onion. After the spray of *Lactobacillus plantarum* strain BY on Chinese cabbage leave it persisted on wound and inhibit the growth of pathogens while it also proliferates in the host tissue **[116]**. The results indicated the application of Lactic Acid Bacteria as a biological control as well as biofertilizer in agriculture. They directly promote the seed germination or plant growth and alleviate numerous abiotic stresses **[117]**.

Pharmaceutical industry

Due to increased antibiotic resistance of pathogens in community there is a need to find out novel antibiotics which are active against multidrug resistance bacteria **[56]**. Various antimicrobial agent has been introduced like bacteriophages, antimicrobial peptides and bacteriocins etc. **[118]**. Phages have an antimicrobial activity but they have narrow host rang and phage resistance limits its application while in case of bacteriocin applications are wide [55]. Bacteriocins are the most natural and appropriate to be used for pharmaceutical industry [7]. It attacks primarily on the lipid which is necessary for biosynthesis of cell wall. Use it as a docking molecule (lipids II) and thus forms a pore in cell wall. Due to its unique mode of action they are significantly used against most of the drug resistant bacteria [119]. Like it has high influence on drug resistance bacteria, for example, (methicillin resistant *Staphylococcus aureus*) MRSA and vancomycin resistant enterococci [120]. Bacteriocin also used to treat skin diseases, as the research reported that the bacteriocin neither allergic nor irritating which has been observed in human patch test. The bacteriocin produced by *Lactococcus spp*. HY 449 is a useful antimicrobial substance to prevent the growth of *Propionibacterium acnea* and to control acne and skin inflammation [121].

Diagnostic applications of bacteriocins

Bacterial drug discovery potential of bacteriocins had been well examined [122]. Specificity and affinity of recognizing of necrotic and apoptotic cell is toward phosphatidyl ethanolamine high by the bacteriocin technetium-99m (99mTc)–duramycin 123. Biomolecules labelling like protein and DNA by fluorescent or radioactive has been defined [123]. In human peripheral blood *Escherichia coli* HSClO produced bacteriocin named as colicin used in the differentiation and detection of leukemic from normal lymphocytes. In flow cytometry studies, bacteriocin affected cell loss the DNA which can be detected by computerized histogram [124]. By labeling of pathogen with nisin, we can study the pathogen mechanisms and pathogen detection has been visualized through fluorescence ratio imaging microscopy [124]. Bacteriocin are also used in the detection of pathogens like bacteria (gram- positive as well as gram-negative), fungi, mycobacterium. Moreover, novel complex bacteriocins in combination with metals used to detect pathogens and other biological analytes [125].

In Pakistan bacteriocins producing bacteria isolated from various indigenous sources like dairy products [126], agricultural soil of Faisalabad [127], fresh and marine water, yoghurt [128]. These antimicrobials were stable at wide range of pH (3-9) and showed stability on boiling 100^{o} C for 3 minutes. They have high potential as a natural preservative [126], biocontrol agent [127], bacteriocinogenic potential against drug resistant bacteria [129] of human and veterinary diseases. Furthermore, bactericidal action of cell wall was observed under electron micrograph [130]. These antagonistic activities of bacteriocins which can be used as a beneficial research tool against pathogenic microorganisms as an antibiotics and useful pharmaceutical products [131].

Table 1. Bacterial species producing bacteriocins against pathogen

Pathogen reported	Bacterial species producing bacteriocin	Reference
Listeria monocytogenes UC8159	pediocin SA-1	[132]
	Pediococcus acidilactici NRRL B-5627,	[72]
	L. plantarum (Lb), *L. plantarum* + *L. lactis* (LbL), *L. plantarum* + *P. acidilactici* (LbP)	[72]
	LAB (Lactic Acid Bacteria)	[59, 72, 127]
	Lactobacillus curvatus 54M16	[132]
	Lactobacillus (L) sakei *Lactobacillus (L) curvatus*	[133]

	Enterococcus (E) faecium	
	Bifidobacterium animals BB04	[66]
	Enterocin CRL35 class IIa bacteriocin	[34]
	Lactobacillus sakei subsp. sakei 2a	[135]
	Lactobacillus crustorum MN047	[19]
L. mono-cytogenes biofilm formation	*bacteriocin fromL. plantarum* ST8SH	[59]
	Lactobacillus paraplantarum FT259	[136]
Escherichia coli	*Lactobacillus crustorum* MN047	[61]
	Weissella hellenica BCC 7239	[61]
	Lactobacillus plantarum (strains ST194BZ, ST414BZ and ST664BZ) *Lactobacillus pentosus* (strain ST712BZ) *Lactobacillus rhamnosus* (strains ST461BZ and ST462BZ) *Lactobacillus paracasei* (strains ST242BZ and ST284BZ)	[61]
	Bifidobacterium animals BB04	[66]
Staphylococcus aureus	*Lactobacillus crustorum* MN047	[61, 134]
	Bifidobacterium animals BB04	[66]
Pseudomonas aeruginosa	*Weissella hellenica* BCC 7239	[137]
Brochotrix thermosphacta	*Lactobacillus curvatus* 54M16	[132]
Salmonella spp	LAB (lactic acid bacteria)	[134]
Salmonella Typhimurium	*Weissella hellenica* BCC 7239	[137]
Enterococcus faecalis	*Lactobacillus plantarum* (strains ST194BZ, ST414BZ and ST664BZ) *Lactobacillus pentosus* (strain ST712BZ) *Lactobacillus rhamnosus* (strains ST461BZ and ST462BZ) *Lactobacillus paracasei* (strains ST242BZ and ST284BZ)	[57]
Aeromonas hydrophila,	*Weissella hellenica* BCC 7239	[137]
Bacillus cerus	*Lactobacillus curvatus* 54M16	[132]
Campylobacter jejuni	*Lactobacillus salivarius*	[51]
Pseudomonas aeruginosa	*Lactobacillus plantarum* (strains ST194BZ, ST414BZ and ST664BZ) *Lactobacillus pentosus* (strain ST712BZ), *Lactobacillus rhamnosus* (strains ST461BZ and ST462BZ) *Lactobacillus paracasei* (strains ST242BZ and ST284BZ)	[57]
Gram positive and gram-negative bacteria	*Lactococcus garvieae,*	[47]
	Bacillus spp	[138]
	Enterococcus faecalis	[49]

	Lactobacillus paracasei subsp. Tolerans	[52]
	Lactobacillus casei (L. casei)	[60]
Lactobacillus casei	*Lactobacillus plantarum* (strains ST194BZ, ST414BZ and ST664BZ), *Lactobacillus pentosus* (strain ST712BZ), *Lactobacillus rhamnosus* (strains ST461BZ and ST462BZ) *and Lactobacillus paracasei* (strains ST242BZ and ST284BZ)	[57]
Weissella hellenica BCC 7293	*(Listeria monocytogenes* and *Staphylococcus aureus) (Pseudomonas aeruginosa, Aeromonas hydrophila Escherichia coli and Salmonella Typhimurium)*	[139]
Fungi	*Lactobacillus paracasei* subsp. *Tolerans*	[52]
Yeast	*Bifidobacterium animals* BB04	[66]
	Bacillus spp	[138]

Conclusion

Bacteriocins are the antimicrobial peptides synthesized by bacteria for their survival. These extracellular peptides are very beneficial on industrial scale. They exhibit the ability to inhibit the wide variety of microorganisms. They not only inhibit the growth of closely related bacteria but also have ability to inhibit the growth of viruses and fungus. The ability of bacteria to produce bacteriocin which have inhibitory spectrum might be used for the welfare of human beings and their efficacy in pharmaceutical industries might be exploited by enhancing its production by bacteriocin engineering. However, shifting the antimicrobial spectrum increases potency and stabilization is still a challenging field. Computational approaches to revolutionize the bacteriocin potency through chemical and biological modification are also on way, but more research is needed to explore the behavior and utility of bacteriocin on commercial scale. Future implications of bacteriocins can led to the avenues of innovation for different industries.

Authors' contributions

Conceived and designed the experiments: Review article idea conceived by: H Hashim, S Sikandar & AW Qurashi, Analyzed the data: H Hashim, S Sikandar & AW Qurashi, Contribution tools: H Hashim, S Sikandar, MA Khan & AW Qurashi, Wrote the paper: H Hashim.

References

1. Abdullah Q, Mahmoud A, & Al-harethi A (2016). Isolation and identification of fungal post-harvest rot of some fruits in Yemen. *PSM Microbiology* 1(1):36-44.
2. Chikindas ML, Weeks R, Drider D, Chistyakov VA, & Dicks LM (2018). Functions and emerging applications of bacteriocins. *Curr Opin Biotechnol*. 49: 23-28.
3. Field D, Ross RP & Hill C (2018). Developing bacteriocins of lactic acid bacteria into next generation biopreservatives. *Curr Opin Food Sci* 20: 1-6.
4. Altuntas EG (2013). Bacteriocins: A natural way to combat with pathogens. *A. Méndez-Vilas, Ed*: 1007-1015.
5. Guinane CM, Piper C, Draper LA, O Connor PM, Hill C, Ross R P & Cotter PD (2015). Impact of environmental factors on bacteriocin promoter activity in gut-derived Lactobacillus salivarius. *Appl Environ Microbiol* 81(22): 7851-7859.
6. Mills S, Ross RP, & Hill C (2017). Bacteriocins and bacteriophage; a narrow-minded approach to food and gut microbiology. *FEMS Microbiol Rev* 41: 129-153.

7. Balciunas EM, Martinez FAC, Todorov SD, de Melo Franco BDG, Converti A, & de Souza ORP (2013). Novel biotechnological applications of bacteriocins: a review. *Food Control* 32(1): 134-142.
8. Alvarez-Sieiro P, Montalbán-Lopez M, Mu D & Kuipers OP (2016). Bacteriocins of lactic acid bacteria: extending the family. *Appl Microbiol Biotechnol* 100(7): 2939-2951.
9. Cotter PD, Ross RP & Hill C (2013). Bacteriocins—a viable alternative to antibiotics?. *Nat Rev Microbiol* 11(2): 95.
10. Saraiva MAF, Nes IF, Baracat-Pereira MC, de Queiroz MV, Mantovani HC, de Moraes 298 CA (2014). Purification and characterization of a bacteriocin produced by Lactococcus lactis subsp. 299 lactis PD6. 9. *J Microbiol Antimicrob* 6: 79-87.
11. Yang SC, Lin CH, Sung CT, & Fang JY (2014). Antibacterial activities of bacteriocins: application in foods and pharmaceuticals. *Front Microbiol* 5: 241.
12. Radha KR, & Padmavathi T (2017). Statistical optimization of bacteriocin produced from *Lactobacillus del brueckii* subsp *bulgaricus* isolated from yoghurt. *Food Res Int*: 24(2).
13. da Silva Sabo S, Vitolo M, Gonzalez JMD & de Souza Oliveira RP (2014). Overview of *Lactobacillus plantarum* as a promising bacteriocin producer among lactic acid bacteria. *Food Res Int* 64: 527-536.
14. Mattick ATR, & Hirsch A (1947). Further observations on an inhibitory substance (nisin) from lactic streptococci. *Lancet* 5: 5-8.
15. Cotter PD, Hill C & Ross RP (2005) Food Microbiology: bacteriocins: developing innate immunity for food. *Nat Rev Microbiol* 3(10): 777.
16. Reeves P (1965). The bacteriocins. *Bacteriol rev* 29(1): 24.
17. AbdelGhany TM (2015). Safe food additives: a review. *J Biol Chem Res* 32(1), 402-437.
18. Enan G, El-Essawy AA, Uyttendaele M & Debevere J (1996). Antibacterial activity of Lactobacillus plantarum UG1 isolated from dry sausage: characterization, production and bactericidal action of plantaricin UG1. *Int J Food Microbiol* 30(3): 189-215.
19. Yi L, Li X., Luo L, Lu Y, Yan H, Qiao Z, & Lü X (2018). A novel bacteriocin BMP11 and its antibacterial mechanism on cell envelope of *Listeria monocytogenes* and *Cronobacter sakazakii*. *Food Control* 91: 160-169.
20. Perez RH, Zendo T, & Sonomoto K (2014). Novel bacteriocins from lactic acid bacteria (LAB): various structures and applications. *Microb Cell Fact*: 13(1).
21. Savadogo A, Ouattara AC, Bassole HI, & Traore SA (2006). Bacteriocins and lactic acid bacteria-a minireview. *Afr J Biotechnol* 5(9).
22. Ahmad V, Khan MS, Jamal QMS, Alzohairy MA, Al Karaawi MA & Siddiqui MU (2017). Antimicrobial potential of bacteriocins: in therapy, agriculture and food preservation. *Int J Antimicrob Agents* 49(1): 1-11.
23. de la Fuente-Salcido NM, Casados-Vázquez LE, & Barboza-Corona JE (2013). Bacteriocins of *Bacillus thuringiensis* can expand the potential of this bacterium to other areas rather than limit its use only as microbial insecticide. *Can J Microbiol* 59(8): 515-522.
24. Dobson A, Cotter PD, Ross RP, & Hill C (2012). Bacteriocin production: a probiotic trait?. *Appl Environ Microbiol* 78(1): 1-6.

25. Hammami R, Zouhir A, Le Lay C, Hamida JB & Fliss I (2010). BACTIBASE second release: a database and tool platform for bacteriocin characterization. *BMC Microbiol* 10(1): 22.
26. Abriouel H, Franz CM, Omar NB, & Gálvez A (2010). Diversity and applications of Bacillus bacteriocins. *Fems Microbiol Rev* 35(1):201-232.
27. Nishie M, Nagao JI, & Sonomoto K (2012). Antibacterial peptides "bacteriocins": an overview of their diverse characteristics and applications. *Biocontrol Sci* 17(1): 1-16.
28. Deegan LH, Cotter PD, Hill C & Ross P (2006). Bacteriocins: biological tools for bio-preservation and shelf-life extension. *Int Dairy J* 16(9): 1058-1071.
29. Mills S, Stanton C, Hill C, & Ross RP (2011). New developments and applications of bacteriocins and peptides in foods. *Annu Rev Food Sci Technol* 2: 299-329.
30. Lv X, Ma H, Sun M, Lin Y, Bai F, Li J & Zhang B (2018). A novel bacteriocin DY4-2 produced by *Lactobacillus plantarum* from cutlassfish and its application as bio-preservative for the control of *Pseudomonas fluorescens* in fresh turbot (*Scophthalmus maximus*) fillets. *Food Control* 89: 22-31.
31. Fadda S, López C & Vignolo, G (2010). Role of lactic acid bacteria during meat conditioning and fermentation: peptides generated as sensorial and hygienic biomarkers. *Meat Sci* 86(1): 66-79.
32. Mangia NP, Trani A, Di Luccia A, Faccia M, Gambacorta G, Fancello F, & Deiana P (2013). Effect of the use of autochthonous *Lactobacillus curvatus, Lactobacillus plantarum* and *Staphylococcus xylosus* strains on microbiological and biochemical properties of the Sardinian fermented sausage. *Eur Food Res Technol* 236(3): 557-566.
33. Hoffmann A, Schneider T, Pag U & Sahl HG (2004). Localization and functional analysis of PepI, the immunity peptide of Pep5-producing *Staphylococcus epidermidis* strain 5. *Appl Environ Microbiol* 70(6): 3263-3271.
34. Masias E, Dupuy FG, da Silva Sanches PR, Farizano JV, Cilli E, Bellomio A, Saavedra L, Minahk C. (2017). Impairment of the class IIa bacteriocin receptor function and membrane structural changes are associated to enterocin CRL35 high resistance in *Listeria monocytogenes*. *Biochim Biophys Acta* 1861(7): 1770-1776.
35. An Y, Wang Y, Liang X, Yi H, Zuo Z, Xu, X Zhang, D, Yu, Changqing, & Han X. (2017). Purification and partial characterization of M1-UVs300, a novel bacteriocin produced by *Lactobacillus plantarum* isolated from fermented sausage. *Food Control* 81: 211-217.
36. Garneau S, Martin NI, & Vederas JC (2002). Two-peptide bacteriocins produced by lactic acid bacteria. *Biochimie* 84(5-6): 577-592.
37. Diep DB, Axelsson L, Grefsli C & Nes IF (2000). The synthesis of the bacteriocin sakacin A is a temperature-sensitive process regulated by a pheromone peptide through a three-component regulatory system. *Microbiol* 146(9):2155-2160.
38. Macwana S & Muriana PM (2012). Spontaneous bacteriocin resistance in *Listeria monocytogenes* as a susceptibility screen for identifying different mechanisms of resistance and modes of action by bacteriocins of lactic acid bacteria. *J Microbiol Methods* 88(1): 7-13.
39. Kaur R & Tiwari SK (2018). Membrane-acting bacteriocin purified from a soil isolate *Pediococcus*

pentosaceus LB44 shows broad host-range. *Biochem Biophys Res Commun* 498(4): 810-816.

40. Aucher W, Lacombe C, Héquet A, Frere J & Berjeaud J M (2005). Influence of amino acid substitutions in the leader peptide on maturation and secretion of mesentericin Y105 by *Leuconostoc mesenteroides*. *Int J Bacteriol* 187(6): 2218-2223.
41. Nes IF, & Eijsink VGH (1999). Regulation of group II peptide bacteriocin synthesis by quorum-sensing mechanisms. Cell-cell signaling in bacteria. ASM Press Washington DC 175.
42. Reck M, Tomasch J, & Wagner-Döbler I (2015). The alternative sigma factor SigX controls bacteriocin synthesis and competence, the two quorum sensing regulated traits in Streptococcus mutans. *PLoS genetics* 11(7): 1005353.
43. Kleerebezem M & Quadri LE (2001). Peptide pheromone-dependent regulation of antimicrobial peptide production in Gram-positive bacteria: a case of multicellular behavior. *Peptides* 22(10): 1579-1596.
44. Naz SA & Rasool SA (2013). Isolation, production and characterization of bacteriocins produced by strains from indigenous environments. *Pak J Bot* 45: 261-267.
45. Ahn H, Kim J & Kim WJ (2017). Isolation and characterization of bacteriocin-producing *Pediococcus acidilactici* HW01 from malt and its potential to control beer spoilage lactic acid bacteria. *Food Control* 80: 59-66.
46. Goh HF & Philip K (2015). Isolation and mode of action of bacteriocin BacC1 produced by nonpathogenic *Enterococcus faecium* C1. *J Dairy Sci* 98(8): 5080-5090.
47. Gao Y, Li D, Liu S, & Zhang L (2015). Garviecin LG34, a novel bacteriocin produced by *Lactococcus garvieae* isolated from traditional Chinese fermented cucumber. *Food Control* 50: 896-900.
48. Hu Y, Liu X, Shan C, Xia X, Wang Y, Dong M & Zhou J (2017). Novel bacteriocin produced by *Lactobacillus alimentarius* FM-MM4 from a traditional Chinese fermented meat Nanx Wudl: Purification, identification and antimicrobial characteristics. *Food Control* 77: 290-297.
49. Hwanhlem N, Ivanova T, Biscola V, Choiset Y & Haertle T (2017). Bacteriocin producing Enterococcus faecalis isolated from chicken gastrointestinal tract originating from Phitsanulok, Thailand: Isolation, screening, safety evaluation and probiotic properties. *Food Control* 78: 187-195.
50. Tadesse G, Ephraim E, & Ashenafi M (2005). Assessment of the antimicrobial activity of lactic acid bacteria isolated from Borde and Shamita, traditional Ethiopian fermented beverages, on some foodborne pathogens and effect of growth medium on the inhibitory activity. *Ital J Food Saf* 5: 13-20.
51. Messaoudi S, Kergourlay G, Dalgalarrondo M, Choiset Y, Ferchichi M, Prevost H, ... & Dousset X (2012). Purification and characterization of a new bacteriocin active against Campylobacter produced by Lactobacillus salivarius SMXD51. *Food Microbiol* 32(1): 129-134.
52. Miao J, Guo H, Ou Y, Liu G, Fang X, Liao Z, Ke, C & Chen, Y & Zhao L & Cao Y (2014). Purification and characterization of bacteriocin F1, a novel bacteriocin produced by Lactobacillus paracasei subsp. tolerans FX-6 from Tibetan kefir, a traditional fermented milk from Tibet, China. *Food Control* 42:48-53.

53. Messaoudi S, Manai M, Kergourlay G, Prévost H, Connil N, Chobert J M, & Dousset X (2013). Lactobacillus salivarius: bacteriocin and probiotic activity. *Food Microbiol* 36(2): 296-304.
54. Palanichamy S, & Subramanian G (2017). Antifouling properties of marine bacteriocin incorporated epoxy based paint. *Prog Org Coat* 103: 33-39.
55. Joerger RD (2003). Alternatives to antibiotics: bacteriocins, antimicrobial peptides and bacteriophages. *Poult Sci* 82(4): 640-647.
56. Pringsulaka O, Thongngam N, Suwannasai N, Atthakor W, Pothivejkul K, & Rangsiruji A (2012). Partial characterisation of bacteriocins produced by lactic acid bacteria isolated from Thai fermented meat and fish products. *Food control* 23(2): 547-551.
57. Todorov SD, & Dicks LMT (2006). Effect of medium components on bacteriocin production by Lactobacillus plantarum strains ST23LD and ST341LD, isolated from spoiled olive brine. *Microbiol Res* 161(2): 102-108.
58. Sonsa-Ard N, Rodtong S, Chikindas ML, & Yongsawatdigul J (2015). Characterization of bacteriocin produced by Enterococcus faecium CN-25 isolated from traditionally Thai fermented fish roe. *Food Control* 54: 308-316.
59. Todorov SD, Perin LM, Carneiro B M, Rahal P, Holzapfel W, & Nero LA (2017). Safety of Lactobacillus plantarum ST8Sh and its bacteriocin. *Probiotics Antimicrob Proteins* 9(3): 334-344.
60. Ullah N, Wang X, Wu J, Guo Y, Ge H, Li T, Saleem K, Zhixi L, & Feng X (2017). Purification and primary characterization of a novel bacteriocin, LiN333, from Lactobacillus casei, an isolate from a Chinese fermented food. *LWT - Food Sci. Technol* 84: 867-875.
61. Yi L, Dang Y, Wu J, Zhang L, Liu X, Liu B, Zhou Y & Lu X (2016). Purification and characterization of a novel bacteriocin produced by Lactobacillus crustorum MN047 isolated from koumiss from Xinjiang. *China J Dairy Sci* 99(9): 7002-7015.
62. Yuehua J, Lanwei Z, Fei L, Huaxi Y, & Xue H (2016). Complete genome sequence of *Enterococcus faecalis* LD33, a bacteriocin-producing strain. *J Biotechnol* 227: 79-80.
63. De Vuyst L, Callewaert R & Pot B (1996). Characterization of the antagonistic activity of Lactobacillus *amylovorus* DCE 471 and large scale isolation of its bacteriocin amylovorin L471. *Syst Appl Microbiol* 19(1): 9-20.
64. Todorov SD, & Dicks LMT (2005). *Lactobacillus plantarum* isolated from molasses produces bacteriocins active against Gram-negative bacteria. *Enzyme Microb Technol* 36(2-3): 318-326.
65. Porto MCW, Kuniyoshi T M, Azevedo P O S, Vitolo M, & Oliveira R P S (2017). Pediococcus spp.: an important genus of lactic acid bacteria and pediocin producers. *Biotechnol Adv* 35(3): 361-374.
66. Liu G, Ren L, Song Z, Wang C, & Sun B (2015). Purification and characteristics of bifidocin A, a novel bacteriocin produced by Bifidobacterium animals BB04 from centenarians' intestine. *Food control* 50: 889-895.
67. Latham RD, Gell DA, Fairbairn RL, Lyons AB, Shukla SD, Cho KY, Jones DA, Harkness NM, Tristram SG. (2017). An isolate of *Haemophilus haemolyticus* produces a bacteriocin-like substance that inhibits the growth of

nontypeable *Haemophilus influenzae*. *Int J Antimicrob Agents* 49(4): 503-506.
68. Lee SG, & Chang HC (2018) Purification and characterization of mejucin, a new bacteriocin produced by Bacillus subtilis SN7. LWT- *Food Sci. Technol* 87: 8-15.
69. Cavera VL, Arthur TD, Kashtanov D & Chikindas ML (2015). Bacteriocins and their position in the next wave of conventional antibiotics. *Int J Antimicrob Agents* 46(5): 494-501.
70. Gillor O, Nigro LM & Riley MA (2005). Genetically engineered bacteriocins and their potential as the next generation of antimicrobials. *Curr Pharm Des* 11(8): 1067-1075.
71. Amado IR, Fuciños C, Fajardo P, Guerra NP & Pastrana L (2012). Evaluation of two bacteriocin-producing probiotic lactic acid bacteria as inoculants for controlling *Listeria monocytogenes* in grass and maize silages. *Anim Feed Sci Technol* 175(3-4): 137-149.
72. Amado IR, Fuciños C, Fajardo P & Pastrana L (2016). Pediocin SA-1: A selective bacteriocin for controlling Listeria monocytogenes in maize silages. *J Dairy Sci* 99(10): 8070-8080.
73. Heng NC, Wescombe PA, Burton JP, Jack RW & Tagg, JR (2007). The diversity of bacteriocins in Gram-positive bacteria. In Bacteriocins. Springer Berlin Heidelberg. pp. 45-92.
74. Vogel BF, Hansen LT, Mordhorst H, & Gram L (2010). The survival of *Listeria monocytogenes* during long term desiccation is facilitated by sodium chloride and organic material. *Int J Food Microbiol* 140(2-3): 192-200.
75. Dickson-Spillmann M, Siegrist M & Keller C (2011). Attitudes toward chemicals are associated with preference for natural food. *Food Qual Prefer* 22(1): 149-156.
76. O'Shea, EF, Cotter PD, Ross RP, & Hill C (2013). Strategies to improve the bacteriocin protection provided by lactic acid bacteria. *Curr Opin Biotechnol* 24(2) 130-134.
77. Pacheco-Cano RD, Norma M, Salcedo-Hernández R, León-Galván M F, Bideshi DK., Hernández-Guzmán G, & Barboza-Corona JE (2014). Characterization, N-terminal sequencing and classification of Tolworthcin 524: a bacteriocin produced by Bacillus thuringiensis subsp. tolworthi. *Microbiol Res* 169(12): 948-953.
78. Katharopoulos E, Touloupi K & Touraki M (2016). Monitoring of multiple bacteriocins through a developed dual extraction protocol and comparison of HPLC-DAD with turbidometry as their quantification system. *J Microbiol Methods* 127: 123-131.
79. Pawlowska AM, Zannini E, Coffey A, & Arendt EK (2012). "Green preservatives": combating fungi in the food and feed industry by applying antifungal lactic acid bacteria. *Adv Food Nutr Res* 66: 217-238.
80. Islam M, Jeong YT, Lee YS & Song CH (2012). Isolation and identification of antifungal compounds from *Bacillus subtilis* C9 inhibiting the growth of plant pathogenic fungi. *Mycobiology* 40(1): 59-66.
81. Hassan YI, Zhou T & Bullerman LB (2016). Sourdough lactic acid bacteria as antifungal and mycotoxin-controlling agents. *Food Sci Technol Int* 22(1): 79-90.
82. Cizeikiene D, Juodeikiene G, Paskevicius A & Bartkiene E (2013). Antimicrobial activity of lactic acid bacteria against pathogenic and spoilage microorganism isolated from food and their control in wheat bread. *Food Control* 31(2): 539-545.

83. Dalié DKD, Deschamps AM, & Richard-Forget F (2010). Lactic acid bacteria–Potential for control of mould growth and mycotoxins: A review. *Food control* 21(4): 370-380.
84. Gerez CL, Torino MI, Rollán G & De Valdez GF (2009). Prevention of bread mould spoilage by using lactic acid bacteria with antifungal properties. *Food control* 20(2): 144-148.
85. Mauch A, Dal Bello F, Coffey A, & Arendt EK (2010). The use of *Lactobacillus brevis* PS1 to in vitro inhibit the outgrowth of *Fusarium culmorum* and other common Fusarium species found on barley. *Int J Food Microbiol* 141(1-2): 116-121.
86. Rouse S, Harnett D, Vaughan A, & Sinderen DV (2008). Lactic acid bacteria with potential to eliminate fungal spoilage in foods. *J Appl Microbiol* 104(3): 915-923.
87. Dal Bello F, Clarke CI, Ryan LAM, Ulmer H, Schober TJ, Ström K J. Sjögrend D.van Sinderenb J. Schnürerc E.K. Arendt (2007). Improvement of the quality and shelf life of wheat bread by fermentation with the antifungal strain *Lactobacillus plantarum* FST 1.7. *J Cereal Sci* 45(3): 309-318.
88. Luz C, Saladino F, Luciano F B, Manes J & Meca G (2017). In vitro antifungal activity of bioactive peptides produced by *Lactobacillus plantarum* against *Aspergillus parasiticus* and *Penicillium expansum*. LWT. *Food Sci. Technol* 81: 128-135.
89. ElSawy KM, Twaroc R, Verma CS & Caves LS (2012). Peptide inhibitors of viral assembly: a novel route to broad-spectrum antivirals. *J Chem Inf Model* 52(3): 770-776.
90. Adekolujo DR, Olayinka SO, Adeniji JA, Oyeyemi OT, & Odaibo AB (2015). Poliovirus and other enteroviruses in children infected with intestinal parasites in Nigeria. *J Infect Dev Ctries* 9(10): 1166-1171.
91. Minor PD (2016). An introduction to poliovirus: pathogenesis, vaccination, and the endgame for global eradication. Poliovirus. *Methods Protoc*: 1-10.
92. James SH, & Prichard MN (2014). Current and future therapies for herpes simplex virus infections: mechanism of action and drug resistance. *Curr Opin Virol* 8:54-61.
93. Arita M (2015). Mechanism of poliovirus resistance to host phosphatidylinositol-4 kinase III β inhibitor. *ACS Infect Dis* 2(2): 140-148.
94. Piret J, & Boivin G (2014). Antiviral drug resistance in herpesviruses other than cytomegalovirus. *Rev Med Virol* 24(3): 186-218.
95. Soumana DI, Ali A, & Schiffer CA (2014). Structural analysis of asunaprevir resistance in HCV NS3/4A protease. *ACS Chem Biol* 9(11): 2485-2490.
96. Cavicchioli VQ, de Carvalho OV, de Paiva JC, Todorov SD, Júnior AS & Nero LA (2018). Inhibition of herpes simplex virus 1 (HSV-1) and poliovirus (PV-1) by bacteriocins from *lactococcus lactis* subsp. lactis and *enterococcus durans* strains isolated from goat milk. *Int J Antimicrob Agents* 51(1): 33-37.
97. Lange-Starke A, Petereit A, Truyen U, Braun P G, Fehlhaber K & Albert T (2014). Antiviral potential of selected starter cultures, bacteriocins and d, l-lactic acid. *Food Environ Virol* 6(1): 42-47.
98. Torres NI, Noll KS, Xu S, Li J, Huang Q, Sinko PJ, Wachsman MB & Chikindas ML (2013). Safety, formulation and in vitro antiviral activity of the antimicrobial peptide subtilosin against herpes simplex virus type 1. *Probiotics Antimicrob Proteins* 5(1): 26-35.

99. Wachsman MB, Farías ME, Takeda E, Sesma F, de Ruiz Holgado AP, de Torres RA, & Coto CE (1999). Antiviral activity of enterocin CRL35 against herpesviruses. *Int J Antimicrob Agents* 12(4): 293-299.
100. Grinter, Rhys, Joel Milner and Daniel Walker (2012). Bacteriocins active against plant pathogenic bacteria. *Biochem Soc Trans* 40 (6): 1498-1502.
101. Makhal S, Kanawjia SK, & Giri A (2015). Effect of microGARD on keeping quality of direct acidified Cottage cheese. *J Food Sci Technol* 52(2): 936-943.
102. Todorov SD, Stojanovski S, Iliev I, Moncheva P, Nero LA, & Ivanova IV (2017). Technology and safety assessment for lactic acid bacteria isolated from traditional Bulgarian fermented meat product "lukanka". *Braz J Microbiol* 48(3): 576-586.
103. Stanborough T, Fegan N, Powell SM, Tamplin M, & Chandry PS (2017). Insight into the genome of *Brochothrix thermosphacta*, a problematic meat spoilage bacterium. *Appl Environ Microbiol* 83(5): 02786-16.
104. Galvez A, Lopez RL, Abriouel H, Valdivia E, & Omar NB (2008). Application of bacteriocins in the control of foodborne pathogenic and spoilage bacteria. *Crit Rev Biotechnol* 28(2): 125-152.
105. Garcia P, Rodriguez L, Rodriguez A, & Martinez B (2010). Food biopreservation: promising strategies using bacteriocins, bacteriophages and endolysins. *Trends Food Sci Technol* 21(8): 373-382.
106. Pilet MF, & Leroi F (2011). Applications of protective cultures, bacteriocins and bacteriophages in fresh seafood and seafood products. In Protective cultures, antimicrobial metabolites and bacteriophages for food and beverage biopreservation: Woodhead Publishing Series in Food Science.Technology and Nutrition. 324-347.
107. Tahiri I, Desbiens M, Kheadr E, Lacroix C, & Fliss I. (2009). Comparison of different application strategies of divergicin M35 for inactivation of Listeria monocytogenes in cold-smoked wild salmon. *Food Microbiol* 26(8), 783-793.
108. Brillet A, Pilet MF, Prevost H, Cardinal M & Leroi F (2005). Effect of inoculation of Carnobacterium divergens V41, a biopreservative strain against Listeria monocytogenes risk, on the microbiological, chemical and sensory quality of cold-smoked salmon. *Int J Food Microbiol* 104(3):309-324.
109. Gebreyohannes G, Moges F, Sahile S & Raja N (2013). Isolation and characterization of potential antibiotic producing *actinomycetes* from water and sediments of Lake Tana, Ethiopia. *Asian Pac J Trop Biomed* 3(6): 426-435.
110. Schöbitz R, Zaror T, León O, & Costa M (1999). A bacteriocin from Carnobacterium piscicola for the control of *Listeria monocytogenes* in vacuum-packaged meat. *Food Microbiol* 16(3): 249-255.
111. Aasen IM, Markussen S, Møretro T, Katla T, Axelsson L & Naterstad K (2003). Interactions of the bacteriocins sakacin P and nisin with food constituents. *Int J Food Microbiol* 87(1-2): 35-43.
112. Al-Holy M, Ruiter J, Lin M, Kang DH, & Rasco B (2004). Inactivation of Listeria innocua in nisin-treated salmon (Oncorhynchus keta) and sturgeon (*Acipenser transmontanus*) caviar heated by radio frequency. *J Food Prot* 67(9): 1848-1854.
113. Neetoo H, Ye M, Chen H, Joerger RD, Hicks DT, & Hoover DG (2008). Use of

nisin-coated plastic films to control *Listera monocytogenes* on vacuum-packaged cold-smoked salmon. *Int J Food Microbiol* 122(1-2): 8-15.

114. Nykänen A, Weckman K, & Lapveteläinen A (2000). Synergistic inhibition of Listeria monocytogenes on cold-smoked rainbow trout by nisin and sodium lactate. *Int J Food Microbiol* 61(1): 63-72.
115. Cherif A, Chehimi S, Limem F, Hansen B M, Hendriksen NB, Daffonchio D & Boudabous A (2003). Detection and characterization of the novel bacteriocin entomocin 9, and safety evaluation of its producer, *Bacillus thuringiensis* ssp. *entomocidus* HD9. *J Appl Microbiol* 95(5): 990-1000.
116. Tsuda K, Tsuji G, Higashiyama M, Ogiyama H, Umemura K, Mitomi M, ... & Kosaka Y (2016). Biological control of bacterial soft rot in Chinese cabbage by Lactobacillus plantarum strain BY under field conditions. *Biol Control* 100: 63-69
117. Lamont JR, Wilkins O, Bywater-Ekegärd M & Smith DL (2017). From yogurt to yield: Potential applications of lactic acid bacteria in plant production. *Soil Biol Biochem* 111: 1-9.
118. Rios AC, Moutinho CG, Pinto FC, Del Fiol FS, Jozala A, Chaud MV, Vila MM, Teixeira JA, & Balcão VM (2016). Alternatives to overcoming bacterial resistances: state-of-the-art. *Microbiol Res Journal* 191: 51-80.
119. Hathaway H, Ajuebor J, Stephens L, Coffey A, Potter U, Sutton JM & Jenkins ATA (2017). Thermally triggered release of the bacteriophage endolysin CHAPK and the bacteriocin lysostaphin for the control of methicillin resistant Staphylococcus aureus (MRSA). *J Control Release* 245: 108-115.
120. Nagao JI (2009). Properties and applications of lantibiotics, a class of bacteriocins produced by Gram-positive bacteria. *J Oral Biosci* 51(3): 158-64.
121. Oh S, Kim SH, Ko Y, Sim JH, Kim K S, Lee S H, Park S & Kim Y J (2006). Effect of bacteriocin produced by *Lactococcus* sp. HY 449 on skin-inflammatory bacteria. *Food Chem Toxicol* 44(4): 552-559.
122. Uzair B, Ahmeda N, Mohammadb FV, Ahmadb VU, & Edwards D (2009). Screening of marine bacteria of Pakistan coast for drug discovery potential. *Proc. Pakistan Acad. Sci* 46(3): 137-144.
123. Imran M, Revol-Junelles AM, de Bruin M, Paris C, Breukink E & Desobry S (2013). Fluorescent labeling of nisin Z and assessment of anti-listerial action. *J Microbiol Methods* 95(2): 107-113.
124. Musclow E & Farkas-Himsley H (1983). Bacteriocin and flow cytometry in laboratory diagnosis of leukemic peripheral blood lymphocytes and bone marrow cells. *Eur J Cancer* 19(2): 163-171.
125. Olstein AD, & Feirtag J (2006). U.S. Patent No. 7,034,113. Washington, DC: U.S. Patent and Trademark Office.
126. Shakeel A, Saeed M, Randhawa MA & Zia MA (2018). Isolation and characterization of bacteriocinogenic lactic acid bacteria from indiginous dairy source and its antimicrobial potential *PAK J AGR Sci* :55(1).
127. Jabeen N, Gul H., Subhan SA, Hussain M, Ajaz M, & Rasool SA. (2009). Biophysicochemical characterization of bacteriocin (s) from indigenously isolated Agrobacterium radiobacterNA 6. *Pak. J. Bot* 41(6): 3227-3237.
128. Rizvi RZ, Wahab A, Pirzada ZA (2014). Screening and identification of aquatic bacteriocinogenic bacillus strains inhibiting clinical methicillin resistant staphylococcus aureus and vancomycin

resistant enterococcus from Pakistan. *Asian J Pharm Clin Res* 7(5):53-56.
129. Zahid M, Ashraf M, Arshad M, Muhammad G, Yasmin A, & Hameed HMA (2015). Antimicrobial activity of bacteriocins isolated from lactic acid bacteria against resistant pathogenic strains. *Int J Nutr Fd Sci* 4: 326-331.
130. Riaz A, Noureen S, Qamar MF, Liaqat I, Arshad M, & Arshad N (2018). Characterization of Bacteriocin like Inhibitory Substances from Enterococcus ratti MF183967. *Pak Vet J.*
131. Siraj W (2015). Antipathic and Non Tenacious Effect of Bacteriocin Producing Strains against Pathogenic Organisms. *RADS Journal of Biological Research & Applied Sciences 6*(2): 01-07.
132. Casaburi A, Di Martino V, Ferranti P, Picariello L, & Villani F (2016). Technological properties and bacteriocins production by Lactobacillus curvatus 54M16 and its use as starter culture for fermented sausage manufacture. *Food Control* 59: 31-45.
133. Fontana C, Cocconcelli PS, Vignolo G & Saavedra L (2015). Occurrence of antilisterial structural bacteriocins genes in meat borne lactic acid bacteria. *Food Control* 47: 53-59.
134. Swetwiwathana A & Visessanguan W (2015). Potential of bacteriocin-producing lactic acid bacteria for safety improvements of traditional Thai fermented meat and human health. *Meat Sci* 109: 101-105.
135. Malheiros PS, Cuccovia IM, & Franco BD (2016). Inhibition of Listeria monocytogenes in vitro and in goat milk by liposomal nanovesicles containing bacteriocins produced by *Lactobacillus sakei* subsp. sakei 2a. *Food Control* 63: 158-164.
136. Winkelströter L K, Tulini F L, & De Martinis EC (2015). Identification of the bacteriocin produced by cheese isolate *Lactobacillus paraplantarum* FT259 and its potential influence on *Listeria monocytogenes* biofilm formation. LWT - *Food Sci. Technol* 64(2): 586-592.
137. Woraprayote W, Pumpuang L, Tosukhowong A, Roytrakul S, Perez RH, Zendo T, ... & Visessanguan W (2015). Two putatively novel bacteriocins active against Gram-negative food borne pathogens produced by *Weissella hellenica* BCC 7293. *Food Control* 55: 176-184.
138. Compaoré CS, Nielsen DS, Ouoba LI, Berner TS, Nielsen KF, Sawadogo-Lingani H et al. (2013). Co-production of surfactin and a novel bacteriocin by Bacillus subtilis subsp. subtilis H4 isolated from Bikalga, an African alkaline Hibiscus sabdariffa seed fermented condiment. *Int J Food Microbiol* 162(3): 297-307.
139. Woraprayote W, Pumpuang L, Tosukhowong A, Zendo T, Sonomoto K, Benjakul S, & Visessanguan W (2018). Antimicrobial biodegradable food packaging impregnated with Bacteriocin 7293 for control of pathogenic bacteria in pangasius fish fillets. *LWT* 89: 427-433.