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Bacteriocins and their technological applications: A review

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Abstract
The purpose of this study is to review the various aspects of Bacteriocins and their potential application in food and medicine sector with relevance to the challenges faced in the current era. Various studies done to explore the information on Bacteriocins along with their innate potentials in diverse sectors have been discussed in the review with appropriate examples. The application of Bacteriocins in Food and Medical sector has increased recently owing to their non-toxic and antimicrobial efficacy. Bacteriocins can be produced by both Gram positive and Gram negative bacteria. Evidences of Bacteriocin production in the Archae have also been documented. The Bacteriocins produced by Lactic acid Bacilli are ighly employed as food preservatives. Bacteriocins owing to their high target-specific nature and antimicrobial effectiveness at nanomolar concentrations have been employed in the medicine sector. The current era faces the demand for action of products derived from natural or microbial origin for tacking various challenges like increased antimicrobial resistance, economic losses due to food spoilage. The increase in researches done to explore the diverse calibre of Bacteriocins can help in combating these challenges.

Keywords: Bacteriocins, lactic acid bacteria, antimicrobial resistance, colicins, lantibiotics, *Escherichia coli*

Introduction
The need for scientific recognition is considered to be an essential factor since the significant contributions of Louis Pasteur and Robert Koch and this factor plays an important role in the controlling of microorganisms that are detrimental to the environment. The introduction of antibiotics with the recognition of penicillin discovered in 1929 by Alexander Fleming led to novel avenues that emphasized the therapeutic applications of antibiotics in the battle against disease-causing organisms. The increased exploitation of antibiotics has led to the development of resistance in the micro-organisms resulting in more potent drug resistant infections (Vrancianu *et al*., 2020) [57]. The in such a scenario one such alternative to the conventional antibiotics is the Bacteriocins.

The Bacteriocins are constituted by peptides or proteins that are ribosomally synthesized by the bacteria as a secondary metabolite in its fight for survival. These peptides or proteins are capable of either inhibiting or destroying other microorganismsn (Cotter *et al*., 2005; De Vuyst and Leroy, 2007) [10, 13]. They can possess narrow spectrum or broad spectrum activity and can inhibit taxonomically close bacteria, or a wide range of bacteria based on their corresponding spectrum of activity (Cotter *et al*., 2005; Mills *et al*., 2011) [10, 38].

The past years have brought the Bacteriocins into lime light due to the emergence of considerable interest in their application as food preservatives. This ablity of serving as a safe preservative is due to the fact that they can be easily digested by the human gastrointestinal tract (Mills *et al*., 2011) [38]. The employment of Bacteriocins as a natural food preservative neutralizes the demands for good quality as well as safe food without preservation using chemical substances. Despite the advantages, the application of Bacteriocins as a food additives is limited by various factors like effectiveness elimination of pathogen, expensiveness, etc. (Chen and Hoover, 2006) [7].

The very first bacteriocin to be isolated was achieved in a study employing Gram-negative bacterium *Escherichia coli* and was named as colisin after isolation in 1925. Till date, colisins of *E. coli* remain to be one of the most extensively probed Bacteriocins. Several related studies on Bacteriocins have reported that these molecules constitute a diverse group of antibacterial peptides that are capable of posing significant cidal effects on the taxonomically close bacteria. The various modes of action involved are the inhibition of cell wall synthesis, permeabilization of the target cell membrane leading to its destabilization, or inhibition of

RNase as well as DNase activity (Balciunas *et al*., 2013; Cleveland *et al*., 2001; Nes *et al*., 2007.; Riley and Chavan, 2007; Riley and Wertz, 2002) [5, 9, 41, 45]. Several recent studies have reported that bacteriocin production is not completely restricted to the Gram-negative bacteria and were found to be produced by Gram-positive lactic acid bacteria (LAB). This group constituted by phylogenetically diverse microorganisms were found to be characterized on the basis of their morphological, metabolic as well as physiological properties and were reported to produce Bacteriocins with great application potential in industrial and medicinal sectors due to the GRAS status (generally recognized as safe bacteria) of the LAB (Cintas *et al*., 2001) [8]. In addition, the Bacteriocins from Gram-positive bacteria show a special inhibitory effect that is not directed against only bacteria within the same species as the bacteriocin producer but also against other species and/or genera different from of the producer. Thus, the Bacteriocins produced by Gram-positive bacteria seem to possess a broader range of susceptible organisms and it makes these types of molecules more suitable for technological processes (Cintas *et al*., 2001; Gálvez *et al*., 2007; Nes *et al*., 2007) [8, 16, 41]. This review emphasizes on the various aspects of the Bacteriocins in relevance to the requirements of the current world

Ecological perspectives of Bacteriocins

In the basis of evolutionary pattern, the innate ability to produce one or more Bacteriocins is considered to be a highly advantageous feature. In the study by Riley (1998) [46] that aimed in the examination of Bacteriocins in their natural environment, analysis was carried on *Escherichia coli* in the conjunctiva of guinea pig, *Streptococcus mutans* in the human oral cavity and *Lactobacillus plantarum* in green olive fermentations. The study reported that the competitive advantage was substantially increased in the case of bacteriocin-producing cells when compared to the bacteriocin-sensitive bacteria that existed in the same environment (Riley, 1998) [46]. In another study based on the case of the *L. plantarum*, bacteriocin-producing strain was employed for the fermentation of Spanish-style green olives and it was found that the bacteriocin producer remained at elevated levels over the course of the 12-wk fermentation. In the context of such studies, mathematical models have been devised for the evaluation of the interaction between the bacteriocin producing strain and bacteriocin sensitive strains. Several ecological models of Bacteriocins have been done with focuss on colicins produced by *Escherichia coli* showing activity against other strains of *E. coli* and related members of the *Enterobacteriaceae*. The Colicins differ from Bacteriocins that are produced by the gram-positive bacteria and are capable of three general mechanisms of action that comprises of formation of channel in the cytoplasmic membrane, cellular DNA degradation and protein synthesis inhibition. It is has been estimated that around 30% of the natural population of *E. coli* are capable of producing Bacteriocins (Riley, 1998) [46]. About 25 types of colicin have been identified (Pugsley, 1984). It has also been brought to the limelight that about 70% of the cells an *E. coli* population are capable of exhibiting resistantance to any one type of colicin, and about 30% can demonstrate resistance against all colicins produced in a population (Smarda, 1992) [52].

Classification of bacteriocins

The Bacteriocins have been classified under various classes on the basis of various criteria like the type of producer, physical properties, molecular sizes, chemical structures and their mode of action mechanism. However, there is lack of a definite classification. In the initial years, the Bacteriocins were categorized into four classes by Klaenhammer in the year 1993 [31] (Klaenhammer, 1993) [31]. The class I comprises of lantibiotics that are characterized by very low molecular weight <5kDa and is constituted by lanthionine & its derivatives. The class II comprises of small thermostable peptides that lack lanthionine derivatives and weighs around 10 kDa in molecular weight. The class II is further divided into three subclasses such as IIa, IIb and IIc. The class III is constituted by compounds of high molecular weight >30 kDa with thermostable and the class IV is constituted by large peptides combined with carbohydrates or lipids (Balciunas *et al*., 2013; Klaenhammer, 1993) [5, 31]. As a contradiction to the classification by Klaenhammer, Cleveland *et al*. in 2001 [9] stated that the complex structures of class IV are resultant artifacts obtained due to partial purification and must not be assigned an individual class of Bacteriocins (Cleveland *et al*., 2001) [9]. Cotter *et al*. in 2005 [10] proposed a new classification comprised of two classes: the class I is constituted by lantibiotics and the class II consists of peptides devoid of lanthionine. The High molecular weight thermolabile peptides were separately categorized as bacteriolysins (Cotter *et al*., 2005) [10]. The current classification was proposed by Drider *et al*. in 2006 constituted by three main classes (Table I) that was segregated on the basis of their genetic and biochemical characteristics (Drider *et al*., 2006) [14].

Table 1: Classification of Bacteriocins

Bacteriocin	Producer	Reference
Class I (Lantibiotics) They are Lanthionine or peptides that contain β- lanthionine		
Class I-type A lantibiotics		
nisin	*Lactococcus lactis*	(Microbiol. and 1981, n.d.) [37]
epidermin	*Staphylococcus epidermidis*	(Allgaier *et al*., 1986) [1]
lacticin 481	*L. lactis*	(Piard *et al*., 1992) [42]
Class I-type B lantibiotics		
mersacidin	*Bacillus subtilis*	(Altena *et al*., 2000) [2]
actagardin	*Actinoplanes ssp.*	(Sahl and Bierbaum, 1998) [48]
cinnamycin	*Streptomyces cinnamoneus*	(Sahl and Bierbaum, 1998) [48]
Class II They are a Heterogeneous class of small thermostable peptides.		
Class IIa		
pediocin PA-1/AcH	*Pediococcus acidilactici*	(Motlagh *et al*., 1992) [39]
leucocin A-UAL 187	*Leuconostoc gelidum*	(Hastings *et al*., 1991) [21]

enterocin A	*Enterococcus faecium*	(Aymerich *et al*., 1996) [4]
Class IIb		
lactococcin M	*L. lactis*	(Van Belkum *et al*., 1991) [55]
plantaricin S	*L. plantarum*	(Jimé Nez-di *et al*., 1995) [27]
Class IIc		
divergicin A	*C. divergens*	(Worobo *et al*., 1995) [58]
enterocin P	*E. faecium*	(Cintas *et al*., 2001) [8]
Class III They consist of large thermolabile peptides.		
helveticin J	*Lactobacillus helveticus*	(Joerger and Klaenhammer, 1986) [28]

Table 2: Important bacteriocins produced by Lactic Acid Bacteria.

Bacteriocin	Producer	Reference
Nisin A	Lactococcus lactis	(De Vuyst and Leroy, 2007) [13]
Lactococcin DR	Lactococcus lactis ADRIA 85L030	(Dufour *et al*., 1991) [15]
Estreptococcin A-FF22	Streptococcus pyogenes FF22	(Hynes,' *et al*., 1993) [26]
Lactocin S	Lactobacillus sakei L45	(Nissen-Meyer *et al*., 1992) [42]
Pediocin PA1	Pediococcus acidilactici PAC-1.0	(Henderson *et al*., n.d.) [23]
Leucocin A-UAL187	Leuconostoc gelidum UAL187	(Hastings *et al*., 1991) [21]
Mesentericin Y105	Leuconostoc mesenteroides Y105	(Hechard *et al*., 1992) [22]
Acidocin A	Lactobacillus acidophilus TK9201	(Kanatani *et al*., 1995) [30]
Bavaricin A	Lactobacillus bavaricus MI401	(Larsen *et al*., 1993) [33]
Curvacin A	Lactobacillus curvatus LTH1174	(Tichaczek *et al*., n.d.) [54]
Plantaricin S (Plsα and Plsβ)	Lactobacillus plantarum LCPO10	(Jimé Nez-di *et al*., 1995) [27]
Termophilin 13 (ThmA/ThmB)	Streptococcus thermophilus SPi13	(Marciset *et al*., 1997) [35]
Piscicolin 61	Carnobacterium piscicola LV61	(Holck *et al*., 1994) [25]

Mode of Action

The Bacteriocins possess distinct mechanisms and can be classified as those with bactericidal effect with or without cell lysis and bacteriostatic effect with ability to inhibit cell growth (da Silva Sabo *et al*., 2014) [12]. A maojority of the Bacteriocins that are produced by LAB inhibit the Gram-positive bacteria by targeting the cell envelope-associated mechanisms (Cotter *et al*., 2013) [11]. Several lantibiotics and several Bacteriocins of class II target the Lipid II which occurs an a intermediate in the peptidoglycan biosynthesis machinery that occurs within the bacterial cell envelope and in this inhibition of the peptidoglycan synthesis occurs (Breukink and de Kruijff, 2006) [6]. The Lipid II is employed as a docking molecule by other Bacteriocins for facilitating the formation of pore which results in variation of the cytoplasm membrane potential leading untimely death of the death (Machaidze and Seelig, 2003) [34]. Certain types of Bacteriocins capable of destroying the cells by binding to the cell envelope-associated mannose phosphotransferase system (ManPTS) which results in the formation of formation of pores in cell membrane (Cotter *et al*., 2013) [11]. Certain Bacteriocins are capable of can killing their target cells by the inhibition of gene expression (Parks *et al*., 2007; Vincent and Morero, 2009) [43, 56] and production of protein (Metlitskaya *et al*., 2006) [36].

Microbial Origin of Bacteriocins

The Bacteriocins are fundamentally divided in three groups based on the source from which they are derived:

Bacteriocins of Archaea

The Archaea are a group of bacteria capable of synthesizing their own distinct family of bacteriocin-like antimicrobial peptides and these compounds are named as archaeocins. The halocin S8 derived from halobacteria is a short hydrophobic peptide composed of 36 amino acids and was the first discovered member of the archaeocin family. These proteins are produced during the stationary phase of the cells (Ghanmi *et al*., 2020) [18]. It has been analysed that under the situation of resource scarcity created by microorganisms, the producer strains secrete archaeocins that lyse the target cells and reduces the competition within the local environment (Riley and Chavan, 2007; Riley and Wertz, 2002) [45].

Bacteriocins of Gram-negative Bacteria

The colicin obtained from E. coli was identified by Gratia as an antimicrobial protein in 1925 and this was the first described one in the family of Bacteriocins and since then it has dominated several studies up to the current period. Several Gram-negative bacteria possess ability to produce colicin-like proteins. Marcescins of *Serratia marcescens*, alveicins of *Hafnia alvei*, Klebicins of *Klebsiella pneumonia*, Cloacins of *Enterobacter cloacae* and pyocins of Pseudomonads are important representatives of Bacteriocins produced by other Gram-negative bacteria. Most of the Bacteriocins in this group are relatively enormous and heat-labile peptides. (Balciunas *et al*., 2013; Cleveland *et al*., 2001; Nes *et al*., 2007.; Riley and Chavan, 2007; Riley and Wertz, 2002) [5, 9, 41, 45, 47].

Bacteriocins of Gram-positive Bacteria

Gram-positive bacteria are also renowned producers of a wide variety of Bacteriocins. The non-toxic property on the eukaryotic cells as well as a broad spectrum of bacteriostatic abiltiy makes the Bacteriocins produced by the Gram-positive organism, a unique useful tool potential for industrial as well as medicinal applications. The lactic acid bacteria (LAB) are a group of phylogenetically diverse Gram-positive bacteria that have been characterized by certain common morphological, metabolic as well as physiological properties. These organisms have attracted much interest owing to their GRAS (generally regarded as safe) that is a necessary element for marking the administrable for human consumption (Balciunas *et al*., 2013; Cintas *et al*., 2001; Cleveland *et al*., 2001; Gálvez *et al*., 2007, 2008; Nes *et al*., 2007.; Riley and Chavan, 2007) [5, 8, 9, 16, 17, 41, 45].

The LAB are characterized by their ability to produce lactic acid by their fermentation pathway thereby by conferring them the name "lactic acid bacteria". In the process of fermentation, a member of the LAB converts about 50% of carbon from the sugars into two isomers of lactic acid. Due to their safe nature and valuable metabolic products such as organic acids, diacetyl, acetoin, reuterin, reutericyclin, hydrogen peroxide, antifungal peptides, and Bacteriocins, the LAB have a great importance in medicinal and food applications (Güllüce *et al*., 2013) [19].

Biological features of bacteriocins

All the Bacteriocins are proteinaceous in nature and are synthesized by the ribosomes of the producer microorganisms in accordance to the genetic code that might have been occasionally be placed on plasmids, the parental chromosome or the mobile elements called transposons (Cintas *et al*., 2001; Cleveland *et al*., 2001; Riley and Wertz, 2002) [8, 9, 47]. The Genetic organization of the bacteriocin gene clusters are constituted by a functional operon comprising of the structural gene, the gene encoding immunity protein, the genes responsible for processing as well as transport of the bacteriocin, and, in certain cases, the genes coding posttranscriptional modification enzymes. Moreover, the bacteriocin operons also harbour the gene encoding the gene encoding for response regulator (RR), preinduction factor (IF) and the histidine protein kinase (HPK) gene (Cleveland *et al*., 2001) [9]. The activation of the structural gene marks the initiation of the bacteriocin production and this result in the production of biologically inactive precursors or prepropeptides commonly referred to as the preproBacteriocins. Then, other related segments of the bacteriocin operon sequentially become operational and the process consequently results in the releasing of the mature Bacteriocins possessing antimicrobial activity (Cintas *et al*., 2001) [8].

Recent studies have also pointed out that the induction factors (IF or pheromone) which are a bacteriocin-like peptide composed of 19-26 amino acid residues length with low molecular weight and cationic nature possess great importance in the regulation mechanism (Cintas *et al*., 2001; Cleveland *et al*., 2001; Gálvez *et al*., 2007; Riley and Wertz, 2002) [8, 9, 16, 47]. The immunity of the bacteriocin producer strain to their own product brings out a clear demarcation between the Bacteriocins and antibiotics. In the concept of this phenomenon, a producer strain is capable of protecting itself from the toxicity of its own Bacteriocins. This protective mechanism is dependent on a variety of bacteriocin-specific immune based proteins. These kinds of proteins are encoded by gene sequences of close genetic proximity to the bacteriocin structural/processing genes and are commonly localized on the same operon. The characteristic feature of the immunity proteins are that they have high isoelectric point values in the range of 7-10, small sizes with 51-154 amino acid residues, and putative transmembrane α-helices. This type of characteristic feature facilitates the binding of these immunity conferring proteins to the cytoplasmic membrane of the host cell (Cintas *et al*., 2001; Cleveland *et al*., 2001) [8, 9]. Resistance to Bacteriocins occur in the strains due to spontaneous or induced mutations leading to alterations in the membrane and cell wall. Modifications occur in the bacteriocin receptors, fluidity, membrane lipid composition, electrical potential and load or cell wall thickness as a result of the mutations (Cintas *et al*., 2001; Cleveland *et al*., 2001; Nes *et al*., 2007) [8, 9, 41]. Despite the lack of knowledge on the exact mechanism for resistance to bacteriocin, Van Schaik *et al*. has stated that the mutational changes on the cell surface of the resistant strain can possibly occur due to exposure of cell to low concentrations of Bacteriocins as a part of developing adaptive response to certain internal or external stress factors (Schaik *et al*., n.d.) [49].

Technological applications

The usage of the Bacteriocins in diverse technological applications fundamentally depends on their antimicrobial effects as well as on the value of antimicrobial activity required for the development of novel sophisticated strategies. The rapid emergence and spread of infections caused by multi-resistant bacteria has increased the consideration for research studies aimed in obtaining alternative strategy capable of battling against the infections. Bacteriocins exhibiting broad spectrum antimicrobial activity are a promising natural antimicrobial agent for several industrial applications (Balciunas *et al*., 2013; Cintas *et al*., 2001; Cleveland *et al*., 2001; Gálvez *et al*., 2007, 2008; Mills *et al*., 2011; Riley and Chavan, 2007; Riley and Wertz, 2002) [5, 8, 9, 16, 17, 38, 45].

Bacteriocins in Medicine

The field of Modern medicine has been threatened with the drastic increase in the emergence of antibiotic-resistant pathogens. The undesirable effects of the new-generation antibiotics are due to its high toxicity and therefore the need for alternative strategies is of ultimate importance. Bacteriocins posseses great calibre in serving as candidates for antimicrobial agents in human health and their applications have more advantages in comparison to the traditional antibiotics. The benefits of Bacteriocins are due to low-toxicity, presence of various types in nature, high target-specific mechanism and effectiveness even at nanomolar concentrations (Balciunas *et al*., 2013; Riley and Wertz, 2002) [5, 47].

Bacteriocins in Food sector

The Bacteriocins produced by LAB are currently the only Bacteriocins that are employed in preservation of food and in the production of fermented foods. The LAB has been employed for the fermentation of foods since centuries and are maraked with the GRAS (generally regarded as safe) status according to the U.S. Food and Drug Administration (FDA).The important bacteriocins by LAB are given in Table II. This status permits their usage in the fermentation of foods without the requirement for an additional regulatory approval (Kanatani *et al*., 1995) [30]. Nisin is considered to be the first bacteriocin that was isolated as well as approved for application in the food industry, specifically for the prevention of *Clostridium botulinum* spores in the cheese spreads all over England. Various Attempts have been made for the utilization of Nisin A as an alternative to Nitrite, but these have not been able to produce successful results. Various Bacteriocins like the *Carnobacterium, Pediococcus, Leuconostoc* and *Lacobacillus* sp. have been reported to possess great potential for application in meat products (Stiles *et al*., 1991) [53]. Pediocin is a pure bacteriocin that is derived from *Pediococcus* and this bacteriocin has been utilized for the inhibition of growth of pathogenic bacteria in fully cooked meats subjected to storage refrigeration (Ladha *et al*., 2020) [32]. In a study, Crude forms of bavaricin A extracted from the

Lactobacillus bauaricus was compared with benzoate support solution and controls with no added preservatives and it was found to extend the shelf life of brined shrimp by about 16 days (Hjo¨ *et al*., 1995) [24].

Bacteriocins in packaging film

The application of Bacteriocins in the industries by incorporating them into packaging films has been an area focussed in research for the last decade for the purpose of controlling food spoilage and in fighting against pathogenic organisms. This type of Antimicrobial agent incorporated packaging aids in the prevention of microbial growth on the surface of the food due to direct contact of the package with the surface of foods as in the case of packaged meat and cheese. (Appendini *et al*., 2002) [3].

Bacteriocins against Phytopathogens

The Bacteriocins named carotovoricins and serracin P obtained from *Erwinia carotovora* subsp. *carotovora* and *Serratia plymithicum* respectively were analysed to structurally resemble the phage tails and were said to be induced by the effect of agents capable of damaging DNA (Muriana't And and Klaenhammerl, 1991; Science and 1992) [40, 50]. Glycinicin A produced by *Xanthomonas campestris* is considered to be the best described bacteriocin so far (Nissen-Meyer *et al*., 1992) [42]**.** This bacteriocin is a heterodimer composed of two polypeptides and was found to exhibit potential activity against phytopathogenic bacterial strains of *Xanthomonas* (sciences and 1984, n.d.) [51].

Future perspectives

A considerable interest has risen in the development of diverse combinations of antimicrobial agents available for developing a consortium capable of effective responses. This type of an approach basically involves combining of multiple available antimicrobial factors and is referred to as "hurdle technology". The hurdle technology based on the application of bacteriocin involves the combination of one bacteriocin with another or other types of naturally derived antimicrobials, chemicals agents or admission to particular treatments (Gálvez *et al*., 2007) [16]. The commonly employed components are the combination of Bacteriocins with chemical substances like sodium chloride, organic acids and their salts, chelating agents, natural antimicrobials like essential oils and phenolic compounds comprising of thymol, terpineol, caffeic acid, carvacrol, eugenol, p-coumaric acid, Bacteriocins, non-bacteriocin antimicrobial proteins as well as peptides and physical treatments comprising of pulsed electric fields, heat treatments, high hydrostatic pressure, modified atmosphere packaging and other non-thermal treatments. Moreover, several efforts have provided promising results for the development of novel hurdles with a high efficiency rate for application in the near future (Gálvez *et al*., 2007) [16]. On the other hand, employment of computational methods for research on bacteriocin has drastically risen currently. The BAGEL and BACTIBASE are considered to be the most well-known examples for web-based databases and these facilitate access to computational tools for bacteriocin genome mining, similarity search engines like BLAST, FASTA, SSEARCH; sequence alignment tools like MUSCLE, CLUSTALW, T-COFFEE; physicochemical profile analysis, hidden markov models as well as for structure prediction tools (Gálvez *et al*., 2007; Hammami *et al*., 2010; Jong *et al*., n.d.; Mills *et al*., 2011) [16, 20, 29, 38].

Conclusions

The Bacteriocins serve as excellent candidates for various applications in both the food industry as well as in the medical sector. They are considered to be a diverse group of antimicrobial proteins/peptides produced by different types of bacteria as a secondary metabolite capable of targeting different bacteria to reduce competition by other micro-organisms in a nutrient limited environment. With the increase in the case of drug resistrant pathogen, the Bacteriocins can serve as a potential agent alternative to the conventionally employed antibiotics. Hence the Bacteriocins possess extreme potential in the field of medicine. The Bacteriocins also possess potential in the field of food processing and preservation of foods. The demand for natural and microbiological methods as a satisfactory approach in the food sector is capable of solving economic losses occurring due to microbial spoilage of raw materials and food products, reducing the incidence of food borne illnesses, and also in satisfying the food requirements of the growing world population. However further researches are required to explore the diverse capacities of the bacteriocin which can be suggestive of their application in several sectors.

References

1. Allgaier H, Jung G, Werner RG, Schneider U, Zähner H. Epidermin: sequencing of a heterodet tetracyclic 21-peptide amide antibiotic", European Journal of Biochemistry 1986;160(1):9-22.
2. Altena K, Guder A, Cramer C, Bierbaum G. Biosynthesis of the Lantibiotic Mersacidin: Organization of a Type B Lantibiotic Gene Cluster, Applied And Environmental Microbiology 2000, 66, available at: http://aem.asm.org/ (accessed 30 August 2020).
3. Appendini P, Technologies JHFS, E. undefined. (n.d.). "Review of antimicrobial food packaging", *Elsevier*, available at 2002. https://www.sciencedirect.com/science/article/pii/S1466856402000127 (accessed 30 August 2020).
4. Aymerich T, Holo H, Sigve Håvarstein L, Hugas M, Garriga M, Nes IF. Biochemical and Genetic Characterization of Enterocin A from Enterococcus Faecium, a New Antilisterial Bacteriocin in the Pediocin Family of Bacteriocins, Applied and Environmental Microbiology 1996, Vol. 62, available at: http://aem.asm.org/ (accessed 30 August 2020).
5. Balciunas EM, Castillo Martinez FA, Todorov SD, Franco BDG de M, Converti A, Oliveira RP de S, *et al*. Novel biotechnological applications of bacteriocins: A review, Food Control, July 2013.
6. Breukink E, de Kruijff B, Lipid II as a target for antibiotics, Nature Reviews Drug Discovery, April 2006.
7. Chen H, Hoover DG. Bacteriocins and their Food Applications, Comprehensive Reviews in Food Science and Food Safety, Wiley 2006;2(3):82-100.
8. Cintas LM, Casaus MP, Herranz C, Nes IF, Hernández PE. Review: Bacteriocins of Lactic Acid Bacteria, Food Science and Technology International 2001.
9. Cleveland J, Montville TJ, Nes IF, Chikindas ML. Bacteriocins: Safe, natural antimicrobials for food preservation, International Journal of Food Microbiology, 4 December 2001.
10. Cotter PD, Hill C, Ross RP. Food microbiology: Bacteriocins: Developing innate immunity for food, Nature Reviews Microbiology, October 2005.

11. Cotter PD, Ross RP, Hill C. Bacteriocins-a viable alternative to antibiotics?, Nature Reviews Microbiology, February 2013.
12. Da Silva Sabo S, Vitolo M, González JMD, Oliveira RP de S. Overview of Lactobacillus plantarum as a promising bacteriocin producer among lactic acid bacteria, Food Research International, Elsevier Ltd 2014.
13. De Vuyst L, Leroy F. Bacteriocins from lactic acid bacteria: Production, purification, and food applications, Journal of Molecular Microbiology and Biotechnology 2007;13:194-199.
14. Drider D, Fimland G, Héchard Y, McMullen LM, Prévost H. The Continuing Story of Class IIa Bacteriocins, Microbiology and Molecular Biology Reviews, American Society for Microbiology 2006;70(2):564-582.
15. Dufour A, Thuault D, Boulliou A, Bourgeois CM, Le Pennec JP. Plasmid-encoded determinants for bacteriocin production and immunity in a Lactococcus lactis strain and purification of the inhibitory peptide, Journal of General Microbiology 1991;137(10):2423-2429.
16. Gálvez A, Abriouel H, López RL, Omar N Ben. Bacteriocin-based strategies for food biopreservation, International Journal of Food Microbiology, Int J Food Microbiol 2007;120(1-2):51-70.
17. Gálvez A, López RL, Abriouel H, Valdivia E, Omar N Ben. Application of bacteriocins in the control of foodborne pathogenic and spoilage bacteria, Critical Reviews in Biotechnology, Crit Rev Biotechnol, June 2008.
18. Ghanmi F, Carré-Mlouka A, Zarai Z, Mejdoub H, Peduzzi J, Maalej S, *et al*. The extremely halophilic archaeon Halobacterium salinarum ETD5 from the solar saltern of Sfax (Tunisia) produces multiple halocins, Research in Microbiology, Elsevier Masson SAS 2020;171(2):80-90.
19. Güllüce M, Karadayı M, Barış Ö. Bacteriocins: Promising Natural Antimicrobials, Researchgate.Net, available at 2013. https://doi.org/10.13140/2.1.5014.5606.
20. Hammami R, Zouhir A, Le Lay C, Ben Hamida J, Fliss I. BACTIBASE second release: A database and tool platform for bacteriocin characterization, BMC Microbiology, BioMed Central Ltd 2010, 10. available at:https://doi.org/10.1186/1471-2180-10-22.
21. Hastings JW, Sailer M, Johnson K, Roy KL, Vederas JC, Stiles ME. Characterization of Leucocin A-UAL 187 and Cloning of the Bacteriocin Gene from Leuconostoc Gelidum, Am Soc Microbiol, available at: http://jb.asm.org/ (accessed 30 August 2020) 1991, 173.
22. Hechard Y, Derijard B, Letellier F, Cenatiempo Y. Characterization and purification of mesentericin Y105, an anti-Listeria bacteriocin from Leuconostoc mesenteroides, Journal of General Microbiology 1992;138(12):2725-2731.
23. Henderson J. A.C.-A. of biochemistry and undefined. (n.d.). "Purification and primary structure of pediocin PA-1 produced by Pediococcus acidilactici PAC-1.0", Elsevier, available at 1992. https://www.sciencedirect.com/science/article/pii/000398619290480K (accessed 30 August 2020).
24. Hjo H, Einarsson H, Le`ne HÉ, Le`ne L, Lauzon L. Biopreservation of Brined Shrimp (Pandalus Borealis) by Bacteriocins from Lactic Acid Bacteria, APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Vol. 61, available at: http://aem.asm.org/ (accessed 30 August 2020) 1995.
25. Holck AL, Axelsson L, Schillinger U. Purification and cloning of piscicolin 61, a bacteriocin from Carnobacterium piscicola LV61, Current Microbiology, Springer-Verlag 1994;29(2):63-68.
26. Hynes WL, Ferretti JJ, Tagg JR. Cloning of the Gene Encoding Streptococcin A-FF22, a Novel Lantibiotic Produced by Streptococcus Pyogenes, and Determination of Its Nucleotide Sequence, APPLIED AND ENVIRONMENTAL MICROBIOLOGY, available at: http://aem.asm.org/ (accessed 30 August 2020) 1993.
27. Jimé Nez-di R, Ruiz-barba JL, Cathcart DP, Holo H, Nes IF, Sletten KH, *et al*. Purification and Partial Amino Acid Sequence of Plantaricin S, a Bacteriocin Produced by Lactobacillus Plantarum LPCO10, the Activity of Which Depends on the Complementary Action of Two Peptides Downloaded From, APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Vol. 61, available at: http://aem.asm.org/ (accessed 30 August 2020) 1995.
28. Joerger MC, Klaenhammer TR. Characterization and Purification of Helveticin J and Evidence for a Chromosomally Determined Bacteriocin Produced by Lactobacillus Helveticus 481t Downloaded From, Journal Series of the North Carolina Agri-Cultural Research Service, available at: http://jb.asm.org/ (accessed 30 August 2020) 1986, 167.
29. Jong A de, Hijum S van JBN. acids and undefined. (n.d.). "BAGEL: a web-based bacteriocin genome mining tool", *Academic.Oup.Com*, available at 2006: https://academic.oup.com/nar/article-abstract/34/suppl_2/W273/2505641 (accessed 30 August 2020).
30. Kanatani K, Oshimura M, Sano K. Isolation and Characterization of Acidocin A and Cloning of the Bacteriocin Gene from Lactobacillus Acidophilus Downloaded From, APPLIED AND Environmental Microbiology, Vol. 61, available at: http://aem.asm.org/ (accessed 30 August 2020) 1995, 61.
31. Klaenhammer T.R. Genetics of bacteriocins produced by lactic acid bacteria", *FEMS Microbiology Reviews*, Oxford University Press (OUP) 1993;12(1-3):39-85.
32. Ladha G. K.J.-W.J. of M. and undefined. (n.d.). Characterization of purified antimicrobial peptide produced by Pediococcus pentosaceus LJR1, and its application in preservation of white leg shrimp, Springer, available at 2020: https://link.springer.com/content/pdf/10.1007/s11274-020-02847-w.pdf (accessed 30 August 2020).
33. Larsen AG, Vogensen FK, Josephsen J. Antimicrobial activity of lactic acid bacteria isolated from sour doughs: purification and characterization of bavaricin A, a bacteriocin produced by Lactobacillus bavaricus MI401, Journal of Applied Bacteriology 1993;75(2):113-122.
34. Machaidze G, Seelig J. Specific Binding of Cinnamycin (Ro 09-0198) to Phosphatidylethanolamine. Comparison between Micellar and Membrane Environments, Biochemistry 2003;42(43):12570-12576.
35. Marciset O, Jeronimus-Stratingh MC, Poolman B. Thermophilin 13, a Nontypical Antilisterial Poration Complex Bacteriocin, That Functions without a Receptor*, ASBMB, available at: http://www-

jbc.stanford.edu/jbc/ (accessed 30 August 2020) 1997.
36. Metlitskaya A, Kazakov T, Kommer A, Pavlova O, Praetorius-Ibba M, Ibba M, *et al*. Aspartyl-tRNA Synthetase Is the Target of Peptide Nucleotide Antibiotic Microcin C", Journal of Biological Chemistry 2006;281(26):18033-18042.
37. Microbiol HNA. undefined. (n.d.). "Adv" 1981.
38. Mills S, Stanton C, Hill C, Ross RP. New developments and applications of bacteriocins and peptides in foods. Annual Review of Food Science and Technology 2011.
39. Motlagh AM, Bhunia AK, Szostek F, Hansen TR, Johnson MC, Ray B. Nucleotide and amino acid sequence of pap- gene (pediocin AcH production) in Pediococcus acidilactici H, Letters in Applied Microbiology 1992;15(2):45-48.
40. Muriana't PM, Klaenhammerl TR. Cloning, Phenotypic Expression, and DNA Sequence of the Gene for Lactacin F, an Antimicrobial Peptide Produced by Lactobacillus Spp. T, JOURNAL OF BACTERIOLOGY, available at: http://jb.asm.org/ (accessed 30 August 2020) 1991.
41. Nes I, Yoon S. Biotechnology DDFS undefined. (n.d.). "Ribosomally synthesiszed antimicrobial peptides (bacteriocins) in lactic acid bacteria: a review", *Dbpia.Co.Kr*, available at: http://www.dbpia.co.kr/Journal/articleDetail?nodeId=NODE01728954 (accessed 30 August 2020) 2007.
42. Nissen-Meyer J, Holo H, Havarstein LS. A Novel Lactococcal Bacteriocin Whose Activity Depends on the Complementary Action of Two Peptides, JOURNAL OF BACrERIOLOGY, available at: http://jb.asm.org/ (accessed 30 August 2020) 1992, 174.
43. Parks WM, Bottrill AR, Pierrat OA, Durrant MC, Maxwell A. The action of the bacterial toxin, microcin B17, on DNA gyrase, Biochimie 2007;89(4):500-507.
44. Piard J, Muriana P. M.D.-A. undefined. (1992), Purification and Partial Characterization of Lacticin 481, a Lanthionine-Containing Bacteriocin Produced by Lactococcus Lactis Subsp. Lactis CNRZ 481 Staitioni Dte Re(Cherch(Es Laitihrcs. INRA Downloaded From, Am Soc Microbiol, available at: http://aem.asm.org/ (accessed 30 August 2020) 1992.
45. Riley M, Chavan M. Bacteriocins, available at: https://link.springer.com/content/pdf/10.1007/978-3-540-36604-1.pdf (accessed 30 August 2020) 2007.
46. Riley MA. Molecular mechanisms of bacteriocin evolution, Annual Review of Genetics 1998.
47. Riley MA, Wertz JE. Bacteriocins: Evolution, ecology, and application, Annual Review of Microbiology 2002.
48. Sahl HG, Bierbaum G. Lantibiotics: Biosynthesis and biological activities of uniquely modified peptides from gram-positive bacteria Annual Review of Microbiology 1998.
49. Schaik W, Van CG-J. of food and, undefined. (n.d.). Acid-Adapted Listeria monocytogenes Displays Enhanced Tolerance against the Lantibiotics Nisin and Lacticin 3147, *Meridian.Allenpress.Com*, available at: https://meridian.allenpress.com/jfp/article-abstract/62/5/536/168027 (accessed 30 August 2020) 1999.
50. Science HN. undefined. (n.d.). The crisis in antibiotic resistance, Science. Sciencemag.Org, available at: https://science.sciencemag.org/content/257/5073/1064.abstract (accessed 30 August 2020) 1992.
51. Sciences APM. undefined. (n.d.). The ins and outs of colicins. Part I: Production, and translocation across membranes., Europepmc. Org, available at: https://europepmc.org/article/med/6444117 (accessed 30 August 2020) 1984.
52. Smarda J. Resistance and Tolerance of Bacteria to E Colicins, Bacteriocins, Microcins and Lantibiotics, Springer Berlin Heidelberg 1992, 493-502.
53. Stiles M, Technology JHT. in FS. undefined. (n.d.). Bacteriocin production by lactic acid bacteria: potential for use in meat preservation, *Elsevier*, available at: https://www.sciencedirect.com/science/article/pii/092422449190706O (accessed 30 August 2020) 1991.
54. Tichaczek P, Nissen-Meyer J, Nes I. RVS. A. undefined. (n.d.). "Characterization of the bacteriocins curvacin A from Lactobacillus curvatus LTH1174 and sakacin P from L. sake LTH673", *Elsevier*, available at: https://www.sciencedirect.com/science/article/pii/S0723202011802237 (accessed 30 August 2020) 1992.
55. Van Belkum MJ, Hayema BJ, Jeeninga RE, Kok J, Venema G. Organization and Nucleotide Sequences of Two Lactococcal Bacteriocin Operons, applied and environmental microbiology, Vol. 57, available at: http://aem.asm.org/ (accessed 30 August 2020) 1991.
56. Vincent P, Morero R. The Structure and Biological Aspects of Peptide Antibiotic Microcin J25", Current Medicinal Chemistry 2009;16(5):538-549.
57. Vrancianu CO, Gheorghe I, Czobor IB, Chifiriuc MC. (n.d.). "microorganisms Antibiotic Resistance Profiles, Molecular Mechanisms and Innovative Treatment Strategies of Acinetobacter baumannii, *Mdpi.Com*, available at: https://doi.org/10.3390/microorganisms8060935.
58. Worobo RW, Van Belkum MJ, Sailer M, Roy KL, Vederas JC, Stiles ME. A Signal Peptide Secretion-Dependent Bacteriocin from Carnobacterium Divergens, Journal of Bacteriology, Vol. 177, available at: http://jb.asm.org/ (accessed 30 August 2020) 1995.