IRAQI Academic Scientific Journals
Samarra Journal of Pure and Applied Science
SJPAS
مجلة سامراء للعلوم الصرفة والتطبيقية
www.sjpas.com
p ISSN: 2663-7405
e ISSN: 2789-6838

An Overview of Bacteriocins

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https://doi.org/10.54153/sjpas.2022.v4i2.369

Article Information
Received: 05/03/2022
Accepted: 15/05/2022
Keywords:
Bacteriocins, Lactic acid bacteria, Application of bacteriocins, Bacteriocins types, Action of bacteriocin
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Abstract

Bacteriocins are proteinaceous multifunctional compounds, generated by ribosomes and have strong antibacterial activity at specific quantities. some members of archaea and bacteria manufacture bacteriocins which inhibit the nourishment of closely related or similar bacterial strains. Bacteriocins are sorted into three main classes depending on their physiochemical and structural characteristics: bacteriocin class I, bacteriocin class II, and bacteriocin class III. the infections caused by bacteria which is resistant to antibiotic are considered as global health problem. Because of their broad- or narrow-spectrum efficacy towards antibiotic-resistant bacteria, bacteriocins may be a potential solution to this global problem. Bacteriocins prevent the nourishment of aim organisms via affect mainly on the envelope of the cell and via affecting expression of gene as well as production of protein inside the cell. the majority of bacteriocin producers are lactic acid bacteria (LAB), a type of bacterium that may be found normally in nutriment and possess important role since ancient times in the manufacture of dairy product. Bacteriocins regarded antimicrobial peptide which considered safe and nontoxic but When tested using cell culture-based techniques, several bacteriocins have been found to have some cytotoxicity. Bacteriocins have been used for food preservation, a variety of therapeutic applications including peptic ulcer treatment, spermicidal effect, woman care, anticancerous element, use in veterinary, skin and oral care, as well as promotion of plant growth in agriculture.

Introduction:

Bacteriocins are multifunctional protein substances produced by the ribosome with evident effect against bacteria at confirmed concentrate. These compound considered protein toxins secreted by special individual of archaea and bacteria to impede the nourishment of bacterial strains which is closely resembles or identical [1] . Also these compound have the ability to eliminate certain pathogens while maintaining other populations [2].

These particles have antimicrobial affect towards degrading and pathogenic bacteria, which justifies their biotechnological importance. In the case of bacteriocins created via a bacterium will prevent other bacteria belong to same species so is known bacteriocins with narrow-spectrum while if they prevent bacteria belonging to a different genus then is known bacteriocins with broad-spectrum. Bacteriocin secreted via the cells of bacteria had the ability

to resist antimicrobial peptides, which are administered by unique immune proteins generated via host cells [3].

Bacteriocin was initially produced via *Escherichia coli* in 1925, the peptide was given the name "Colicins" which is indicates to its microbial origin [4]. The bacteriocin created by LAB, on the other hand, is of particular importance because the Food and Drug Administration (FDA) have given these bacteria what is called the Generally Regarded as Safe (GRAS) [5]. Nisin, generated via *Lactococcus lactis*, was a first bacteriocin that is widely used commercially. Later a wide range of bacteriocins have been discovered from a different strain of bacteria. Bacteriocin synthesis can be seen as advantageous for the producer since these peptides can inhibit or kill bacteria that compete with the same ecological niche or same nutritional requirements [6].

Bacteriocins classification:

Over years there are various classification methods for sorting bacteriocins, while the bacteriocins for lactic acid bacteria (LAB), have been classified alone in a different method [7], resulting in two to four subcategories[8,9] Soltani and his colleagues suggest renewal bacteriocins classification for both of Gram-negative and Gram-positive bacteria which are sort into two huge parts, the Class I (modified) and Class II(unmodified) bacteriocins [10].

While another study mentioned that Bacteriocins are now classified into major groups depending on their physicochemical and structural properties include Bacteriocins produced by Gram Positive Bacteria which is subdivided into the Class I of Bacteriocins (Lantibiotics)[5]. Lantibiotics are tiny peptides heat stabile with molecular weight less than 5 kDa subject to modified after translation, as well as contains amino acids with polycyclic thioether like methyl-lanthionine and lanthionine, also contain unsaturated amino acids like2-amino isobutyric acid and dehydroalanine. According to the variety in charge, lantibiotics are also divided into two types. Lantibiotics Type A, like lacticin 3147 and nisin which are screw-shaped flexible molecules possess a positive charge and 2–4 kDa that cause pores in the target organism's cell membrane, leading to cytoplasmic membrane depolarization [11]. Lantibiotics Type B are peptides with a molecular weight of 2–3 kDa without net charge or with negative charge, these molecules are globular and effect cellular enzymatic activities, like the formation of cell walls. This category includes mersacidin, which is produced by *Bacillus spp*. [12].

Bacteriocins class II are tiny peptides with molecular weight less than 10 kDa without lanthionine and heat stable as well as this type unmodified after translation, they also possess an amphiphilic structure with helical shape that permit them to infix inside the membrane which in turn leads to depolarization as well as death to the target cell. Bacteriocins class III are proteins possess high molecular mass more than30 kDa and heat labile. several of the megacins secreted by *Bacillus megaterium*, colicins, klebicin secreted by *Klebsiella pneumonia*, enterolysin secreted by *Enterococcus faecalis* and helveticin I secreted by *Lactobacillus helveticus* consider members belong to this class [11], the summary about classification of bacteriocin shows in table 1 with several examples [13].

Table1: Classification of bacteriocins adapted from [9].

Classification	Features	Subcategories	Examples
Class I bacteriocins (lantibiotics)	anthionine or peptides containing β-lanthionine	Type-A(linearmolecules) Type-B(globularmolecules)	Nisin, subtilin, epidermine Mersacidin
Class II bacteriocins	Heterogeneous class of small thermostable peptides	Subclass IIa (antilisterial pediocine bacteriocins type) Subclass IIb (composed of two peptides) Subclass IIc (other bacteriocins)	Pediocin, enterocin, sakacin Plantaricin, lactacin F Lactococcin
Class III bacteriocins	Large thermolabile peptides		HelveticinJ, millericin B

The bacteriocins secreted by gram negative bacteria, can be sorted into two major groups, the bacteriocins contain high molecular weight proteins 30-80-kDa called colicins and peptides with low molecular weight range from 1 -10 kDa known as microcins. *Escherichia coli* strains that possess the colicinogenic plasmid can produce the colicins, while microcins are molecule highly stable and resistance to temperature, proteases and extreme value of pH. they are secreted via enteric bacteria through stress conditions specially when depletion of the nutrient [14].

Bacteriocins and Antibiotics comparison

Bacteriocins, on the other hand, are ribosomally synthesized, whereas antibiotics are produced by several enzyme complexes. Bacteriocins have bacteroistatic and bactericidal activity against determined bacterial number, whereas antibiotics have a considerably wider spectrum. Furthermore, at low concentrations, most of bacteriocins consider more influence towards bacteria in compare with antibiotics. Bacteriocins have long been considered as natural substances due to their presence in various types of foods. The enzymes available inside the gastrointestinal tract like as pepsin and trypsin will inhibit the bacteriocins,for that reason the microorganism of the gastrointestinal tract will not affect by the bacteriocins [15].

Mode of Action

Bacteriocins can inhibit the nourishment of certain organism in different mechanisms, which can be subdivided into various mechanisms that affect primary on the envelope of the cell and mechanisms affect primarily on protein production and expression of gene. Some of bacteriocins affect via attacking primarily on the envelope of the cell, especially those inhibit the gram positive bacteria. Specific bacteriocins type class l effect on the production of peptidoglycan by inhibit the lipid II which found on the membrane of the cell. While some bacteriocins make pores which kill or inhibit the target bacteria (figure1) [8]. Other example, bacteriocins class II like lactococcin A attach to special pore receptor system known as mannose phosphotransferase [8] certain members of lantibiotic or class I bacteriocins like nisin possess action of dual mode, they will attach to the lipid II, which is considered as the major transport of constituent units of peptidoglycan between the cytoplasm and cell wall, so effect on correct synthesis of cell wall finally cause the death of cell. Also they can utilize lipid II like docking

molecule for restart an operation of pore formation and membrane insertion which cause the cell death [16].

Many of bacteriocins which effect on gram negative bacteria can dominate on their aim bacteria via interfering with protein, RNA, DNA metabolism. For example, RNA polymerase inhibit by MccJ25, DNA gyrase inhibit by microcin B17 (MccB17), aspartyl-tRNA synthetase inhibit by MccC7-C51.also there is exception like MccE492 which affect via pores forming (Figure 2) [8].

Some of bacteriocins appear antimicrobial affect through enzymatic activities. Like, colicin E2 appear DNase activity and colicin E3 appear RNase activity toward target organism [17]. On the other hand many of bacteriolytic proteins like lysostaphin which is belongs to bacteriocins class III directly effect on cell wall which is related to specific gram positive bacteria, so cause the death and finally lysis the aim cell [16].

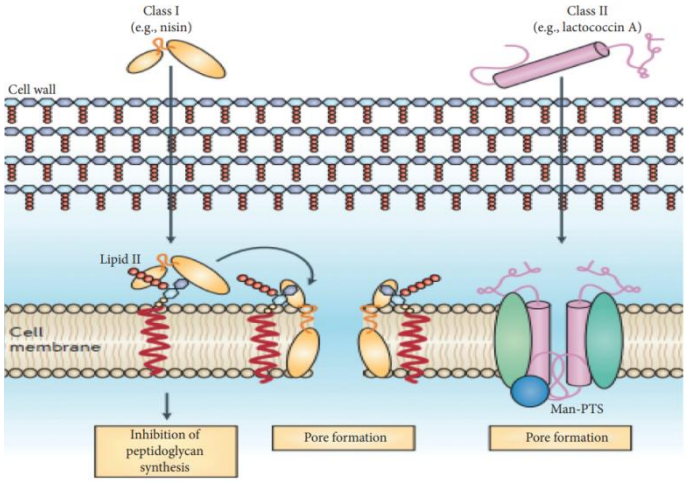

Figure 1: Mechanism of action of bacteriocins on Gram-positive bacteria [16]

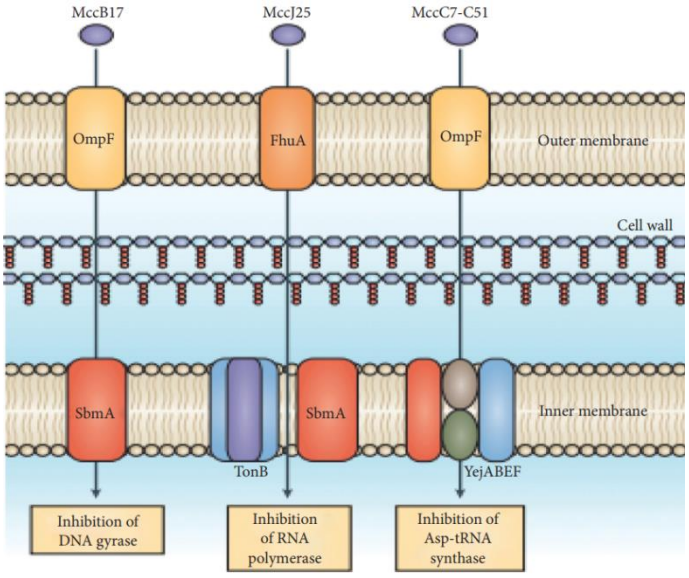

Figure 2: Mechanism of action of bacteriocins on Gram-negative bacteria [16]

Lactic acid bacteria in the dairy manufacture

Bacteriocins are produced by a variety of microorganisms, but those generated by lactic acid bacteria (LAB) have great application in the dairy manufacture. lactic acid bacteria have been utilized for a long time in fermentations of food to convert lactose to lactic acid while also processing other molecules with antimicrobial effect like diacetyl, acetoin, organic acid, antifungal peptides, hydrogen, bacteriocins and peroxide [18]. Most LAB are Generally Regarded as Safe (GRAS) by the American Food and Drug Administration (FDA)due to their widespread utilize in conventional fermented products. majority LAB genera, including *Lactobacillus, Lactococcus Leuconostoc, Pediococcus*, and some *Streptococcus*, the Authority of European Food Safety awarded theses genera the Qualified Presumption of Safety (QPS) status. However, because some *Streptococcus* species and *Enterococcus* consider pathogenic, so they do not awarded GRAS condition or QPS status [19]. Bacteriocins from LAB are efficient through a wide range of pH, resistant to elevation of temperature, also are effective towards a variety of food pathogenic and spoilage bacteria [20]. Bacteriocins produced by(LAB) differ in their spectrum of activities, molecular weight, route of action, genetic origins, biochemical characteristics, as well as resistant to digestive proteases like pancreatin complex, chymotrypsin and trypsin, so they have no negative impact on the gut microbiota [18,21].

Other types of bacteriocins

Researchers demonstrated many other types of bacteriocins which utilize like antimicrobial factor in preservation of food, which comprise leucocin A[22], carnobacteriocin BM[23], mycocin[24]and carnocyclin A. The cooperative utilization of piscicolin 126, carnobacteriocin BM1, and carnocyclin A which is produced via *Carnobacterium maltaromaticum* UAL307 showed antimicrobial affects towards food pathogens, like *Salmonella typhimurium* ATCC 23564, *Pseudomonas aeruginosa* ATCC 14207 and *E. coli* DH5a in the products of meat and milk [23].

On the other hand, for the meat products preservation, sukacin which is secreted via *Lactobacillus sakei* utilized to prevent the nourishment of *Listeria monocytogenes* [25]. In manufacture of full fat and skimmed milk, utilized lactococcin BZ because it shows antimicrobial affect towards *L. monocytogenes* [26]. Also aureocin A70 secreted via *Staphylococcus aureus* shows inhibitory effect towards *L.monocytogenes* in production of skimmed milk[27].

The contamination that happens by molds and yeasts in processed meat, fresh dairy products, beverages and cheese are usually important in industry of food as it causing the spolige of food.to to solve this issue natamycin produced by *Streptomyces gilvo* sporeus or *Streptomyces natalensis* is used because their antimicrobial affects towards molds and yeasts,so prolong the period stage of beverages, processed meat, fresh dairy products and cheese [28].

As well as,mycocin produced via *Debaryomyces hansenii* DSMZ70238 can be utilized in the meat preservation and products of meat via preventing the nourishment of L. monocytogenes [24]. bacteriocin CAMT2 which is produced from *Bacillus amyloliquefaciens* ZJHD3-06 is utilized to preclude the growing of *Vibrio parahaemolyticus*, *E. coli*, *S. aureus* and *L. monocytogenes* [29].

Cytotoxicity against eukaryotic cells

Bacteriocins regarded antimicrobial peptide which considered safe and nontoxic. When tested using cell culture-based techniques, however, several bacteriocins have been found to have some cytotoxicity. It must be noted, for example, that several bacteriocins have been

demonstrated to cause cytotoxicity in mammalian cells at concentrations remarkably greater than the (minimum inhibitory concentrations) required to prevent food deterioration or the existence of bacterial pathogens in processed foods [30].

The following bacteriocins, at minimum inhibitor concentrations, demonstrated no or weak cytotoxicity against several lines of the eukaryotic. Such as enterocin (AS-48, plantaricin (DM5), carnobacteriocins Cbn B2 and Cbn BM1, enterocin (S37), enterocin (DD14), colicin K, E7, E3, E1 and nisin [31-37], in addition the semi-purifed bacteriocins yield by *E. durans* and *Lactococcus lactis* subsp. *Lactis* [38], colicin (E1, E3, E7, K), Nisin and pediocin (PA-1) on the other hand, have been proven to be cytotoxic against lines of the Vero cell at higher concentrations. It's unsurprising that a few of these observations fluctuate in response to concentration [36]. This was demonstrated when a bacteriocin which was semi-purified generated through (Lactobacillus *plantarum* ST8SH) shown extremely cytotoxic at (25 μg mL^{-1}) concentration and not at concentration of (5 μg mL^{-1}) [39]. Furthermore,when healing the wound, some bacteriocins may have considerable antibacterial action at low doses while being toxic to eukaryotic cells at excessive concentrations [40].

According to Cox and his colleagues, certain strains of *E. faecalis* produce cytolysin, a toxin with two-peptide that causes cytotoxicity in a wide range of cells, containing human intestinal epithelial cells, retinal cells, leucocytes and erythrocytes [41]. The cytotoxicity of cationic bacteriocin's thought to be presented through attaching to cells or anionic membranes via hydrophobic bonds so directly destroying them [42]. Even though the bacteriocins' cytotoxic effects have been studied in a variety of lines of the eukaryotic cell, including the epithelial cell lines of human intestinal (9HT29 and Caco-2) [37], the cell line of human embryonic kidney (HEK 293), and cell line belong to cervix epithelial carcinoma of human (HeLa)[32], and It is hard to evaluate their levels of toxicity [39].

According to study the (SV40- HC) cells is more affected to colicin E6, pediocin PA-1, and nisin than normo Vero cells [36]. Furthermore, in the Vero cell line and nisin, the IC50 valure of entrepreneurial nisin (NisaplinR) was observed to be 105 μM. In another study [43], mention that nisin be cytotoxic in concentration of 13.48, 112.25 and 105.46 μM against the cell lines of Vero, HepG2 and MCF-7 respectively. This discrepancy can be attributed to differences in cell membrane composition [38]. Membrane cholesterol or lipid content helps increase the stiffness of the lipid bilayers and prevent antimicrobial peptides like bacteriocins from disrupting them. As a result, increased bacteriocin concentrations are needed to permeate the membrane [44]. Furthermore, changes in cell surface hydrophobicity may alter bacteriocin contact and binding; nevertheless, the specific explanation for the varying cytotoxic effects in various cell types are unknown.

Application of Bacteriocins

Bacteriocins have a variety of uses in the pharmaceutical, food, and agricultural industries.

Preservation of food

Bacteriocins have long been used in the preservation of food to dominate foodborne pathogen [45], also Bacteriocins verbose studied in the field of food industry, especially in dairy merchandise, eggs, meat, and vegetables merchandise [5].

FDA approved used of Nisin in over 48 countries, also NisaplinTM is used as a natural preservative of food. It inhibits the growth of a variety of Gram-positive bacteria containing the

number of significant food-borne pathogenic organisms like *Listeria monocytogenes* in a variety of food systems. It is utilized primarily in the foods products and dairy merchandise also is particularly efficient in the spread and processed cheese production,whereas it prevent the refractory spore-forming organisms, for example, those in the *Clostridium* and *Bacillus* genera. it is especially important in the prevention of *Clostridium botulinum* infection,since the toxin produced by this species can have serious consequences. A number of bacteriocins have been still commercialized, for example lacticin 481 and lacticin 3147, that have shown promise as taste enhancers and natural preservatives [6].

Pediocin PA-1 has a wide ranging lactic acid bacteriocin with a powerful effect on *Listeria monocytogenes*,in addition it is utilized as a food preservative [46]. The addition of Bacteriocins to a portion of food in at least three ways to improve its safety: using a preparation of bacteriocin purified/ semipurified as a component in food, combining an initially fermented component and added a bacteriocin-produced by a strain, or utilizing a bacteriocin-produced by a culture which instead part or all of the starter culture in fermented food to create bacteriocin [6].

Bacteriocins can be utilized to bettering the food sensory and quality character by inhibiting the abnormality blowing of gas in cheese or used excess average of the proteolytic enzymes, biologically active package is Another bacteriocins uses, it is a process use to extend the storage life of food and retain food from exterior contamination [5].

Treatment of Peptic Ulcer

Peptic ulcer is generated via a confrontation between defensive systems of gastroduodenal mucosa as well as destructive effects of pepsin and stomach acid, and also lesions induced by immunological or environmental factors. In cases with duodenal and gastric ulcers, anaerobic *Helicobacter pylori* counts are high. Bacteriocin inhibits *H. pylori*, which cause a peptic ulcer illness.

Bacteriocins generated via *Pediococcus acidilactici* BA28 were recommended for localized personal care treatments aiming to the treatment and prevention of numerous disorders of human, including peptic ulcers, based on antibacterial activity profiles. [47].

Woman Care and Spermicidal Activity

Bacteriocins have the capacity to impact sperm motility, making them potential spermicidal agents [48]. *Lactobacillus fermentum* HV6b MTCC 10770 produces fermenticin HV6b, antimicrobial peptide class II isolated from the human vaginal eco-system. *Mobiluncus*, *Gardnerella vaginalis, Streptococci and Staphylococci*, that cause infections in humans vaginal, can be inhibited by it. Fermenticin HV6b has a unrivalled spermicidal and inhibitory properties.

To protect the human vaginal from microbial pathogens while also functioning as contraceptive approaches, a modern formulation including fermenticin HV6b or *Lactobacillus fermentum* HV6b are used entirely and sometimes in combination with the development creams of vaginal. [49]. Subtilosin is a bacterioicin generates by *Bacillus amyloliquefaciens*, that can inhibit vaginal bacterium *Gardnerella vaginalis* however does not found in a health micro flora as well as vaginal cell surface. Different concentrations of subtilosin (28.3–113.3 g/ml) were tested to see if they could reduce the motility of human spermatozoa. In addition to its antimicrobial properties, as a common spermicide, subtilosin found to limit motility and for

advancement spermatozoa of human in a dose-dependent method. Subtilosin might thus be used in contraception as well as the prevention and treatment of bacterial vaginosis, and in personal care items that are applied to the skin [50].

Anticancer activity

Numerous bacteriocins have been shown anticancer properties by selectively functioning against cancerous cells [11]. Bacteriocins generated through Gram-negative bacteria, for example microcin E492[51] and colicins (A, D, E1, E2, E3) [52], as well as Gram -positive bacteria, such as nisin[20] have been shown cytotoxic effect against malignant human cell. Bacteriocins cause cytotoxicity in cancer cells by inducing apoptosis and/or inhibition the polarization of the cell membrane, which causes permeability changes [11]. Nisin, for example, was shown to increase DNA fragmentation or apoptosis and reduce cell growth in head and neck squamous cell carcinoma cells by inducing cell cycle arrest in the cancer cell, Furthermore, nisin administration lowered tumor size in mice with oral cancer [53]. In other situation, azurin, is a bacteriocin that generated through *P. aeruginosa*, was investigated as possible drug for anticancer because it had specific bound to cancer cells of human also the cytotoxic and effects of apoptotic that resulted, without appearing to affect normal cells [54]. For more information, Kaur and Kaur conducted a comprehensive review of bacteriocin anticancer activity. It is very important to remember that most of the investigations on the anticancer activity of bacteriocins had been conducted in vitro, necessitating the development of in vivo valid studies [11].

Veterinary Use:

In the veterinary industry, the use of nisin as a preventative medication and a treatment for mastitis in cattle has also been examined. [55]. The global dairy industry is greatly affected by the mastitis disease that affects livestock because of its great economic loss among the poor farmers who raise livestock [56]. Injectable drugs based on nisin had been reported and developed to monitoring approximately 99.9% of microorganism that cause mastitis, such as *Streptococcus agalactiae* and *Staphylococcus aureus* next administration of a drug [55].

Skin care

based on scientific and factual research that some probiotics may aid to modifying of the skin's microbiota, lipid barrir,and immune system of the skin, leading in the preservation of homeostasis of the skin[57].

In cases who suffer inflammatory lesions for acne that cause by *Propionibacterium acnes,* bacterocin ESL5, produce from *Enterococcus faecalis* SL-5, was utilize like a lotion, which reduced significantly the pimples and the inflammatory lesions comparing with placebo lotion [58].

Oral Hygiene

Bacteria such as *Streptococcus macedonicus* ACA-DC 198, *Lactobacillus fermentum* ACA-DC 179 and *Lactobacillus plantarun* ACA-DC 269 are known to limit the oral infections growth that produce oral health issues. FTIR spectroscopy demonstrated that macedocin generated from the *S. macedonicus* ACA-DC 198 is effective in eliminating oral infections during lag phase through producing the major modifications in the chemistry of the cell. Macedocin has been found to be an active component in mouthwash and toothpaste formulations [59].

Streptococcus mutans induces dental cavities, which results in tooth decay. according to studies, Both polylysine and nisin effect on the similar microbial flora in the mouth. partial inhibitory doses of polylysine (5 μg/ml) and nisin (200 IU) slow bacterial growth When applied separately. Using both of them at the same time seems to have a synergic activity, suppressing bacterial growth for 24 hours. *S. mutans* was totally inhibited by a formulation containing 50 IU/ml nisin and 10 μg/ml polylysine, whereas completely aerobic flora of the mouth was eliminated by a formulation contain 100 IU/ml nisin and 250 μg/ml polylysine. This is suggested formulation could be used in the manufacture of oral concern items [60]. Halitosis is a type of oral malodor that affects a small percentage of adults. It is a major issue in the working and social environment. In most cases, the growth of undesirable microorganisms is to blame for the odor like *Micromonas micros*, *Streptococcus anginosus*T-29, *Solobacterium moorei* CCUG39336, *Parvimonas micra* ATCC33270, *Eubacterium saburreum* ATCC33271, *Eubacterium sulci* ATCC35585 and *Atopobium parvulum* ATCC33793. In the oral cavity belong to the healthy school student the research can isolate *Streptococcus salivarius* K12. Salivaricin A2 and B are two bacteriocins produced by this bacterium. Salivaricins have been reported to suppress *Streptococcus pyogenes*, a bacterium that can cause pharyngitis [61].Bacteriocins that produced from *S. salivarius* K12 were capable to stop all the bacteria that cause halitosis from growing. The establishing of novel formulas that contain salivaricin and K12 strain or both of them is worth thinking [62].

Promotion of Plant Growth

Bacillus thuringiensis species were tested for their ability to produce bacteriocins. Bacteriocins thuricin 17 and bacthuricin F4 are produced by *B. thuringiensis* NEB17 and BF4, respectively. Bacteriocin C85 is secreted by *Bacillus cereus* UW85. The molecular weights of the above bacteriocins range from 3100 to 3200 Da, and these three bacteriocins may help plants flourish. On, soybean, tomato and corn plants, a formulation containing three bacteriocins and the bacteria that produce them was sprayed. In comparison to controls, the use of this formulation increased leaf area, resulting in a 6 percent improvement in photosynthesis, a 15% increase in plant dry weight, and a 21 percent increase in root nodulation [63].

Conclusion

Bacteriocins have characteristics that allow them to be used in a variety of clinical and food applications and compared to antibiotics, bacteriocins are still less likely to be marketed and permitted for use in food preservation and the treatment of infectious diseases by the WHO and FDA. for that reason, bacteriocin safety needs a lot of attention. Bacteriocin has been shown in numerous investigations to have antibacterial properties against microbial pathogens and has a great potential for usage as an antibiotic alternative due to its proteinaceous characteristic and low toxicity. the research about antimicrobial mode showed that bacteriocins firstly disrupt the cell membrane integrity and pore formation then leakage soluble intracellular substances furthermore bacteriocins affect by inactivation the genetic material of the target bacteria.Furthermore, bacteriocin modulate the microbiota by eliminating the objective pathogens while leaving the rest of the microbial population, making it a better antibacterial agent than antibiotics.

Various tests are necessary to investigate their cytotoxic effects in eukaryotic cells, as well as their potential to produce apoptosis, growth inhibition, hemolytic capabilities, subchronic

and acute toxic effects, and other features. Bacteriocins have long been advocated as a potential solution of food deterioration and food-borne diseases in food industry.Health agencies must approve the use of bacteriocins in industry of food, livestock, or medication, which is lengthy operation requiring clinical tests and trials.

Reference:

[1] Vogel, V., & Spellerberg, B. (2021). Bacteriocin production by beta-hemolytic Streptococci. Pathogens, 10(7), 867.

[2] Cesa-Luna, C., Alatorre-Cruz, J. M., Carreno-Lopez, R., Quintero-Hernandez, V., & Baez, A. (2021). Emerging Applications of Bacteriocins as Antimicrobials, Anticancer Drugs, and Modulators of The Gastrointestinal Microbiota. Polish Journal of Microbiology, 70(2), 143.

[3] Juturu, V., & Wu, J. C. (2018). Microbial production of bacteriocins: Latest research development and applications. *Biotechnology Advances*, *36*(8), 2187-2200.

[4] Gratia A.(1925) "On a remarkable example of antagonism between two strains of hummingbird," Comptes Rendus Biologies (CR BIOL), vol. 93, pp. 1040–1042.

[5] Zacharof, M. P., & Lovitt, R. W. (2012). Bacteriocins produced by lactic acid bacteria a review article. *Apcbee Procedia*, *2*, 50-56.

[6] Deegan, L. H., Cotter, P. D., Hill, C., & Ross, P. (2006). Bacteriocins: biological tools for bio-preservation and shelf-life extension. *International dairy journal*, *16*(9), 1058-1071.

[7] de Freire Bastos, M. D. C., Coelho, M. L. V., & da Silva Santos, O. C. (2015). Resistance to bacteriocins produced by Gram-positive bacteria. *Microbiology*, *161*(4), 683-700.

[8] Cotter, P. D., Ross, R. P., & Hill, C. (2013). Bacteriocins—a viable alternative to antibiotics?. *Nature Reviews Microbiology*, *11*(2), 95-105.

[9] Johnson, E. M., Jung, D. Y. G., Jin, D. Y. Y., Jayabalan, D. R., Yang, D. S. H., & Suh, J. W. (2018). Bacteriocins as food preservatives: Challenges and emerging horizons. *Critical reviews in food science and nutrition*, *58*(16), 2743-2767.

[10] Soltani, S., Hammami, R., Cotter, P. D., Rebuffat, S., Said, L. B., Gaudreau, H., ... & Fliss, I. (2021). Bacteriocins as a new generation of antimicrobials: Toxicity aspects and regulations. FEMS microbiology reviews, 45(1), fuaa039.

[11] Kaur, S., & Kaur, S. (2015). Bacteriocins as potential anticancer agents. *Frontiers in pharmacology*, *6*, 272.

[12] Sahl, H. G., & Bierbaum, G. (1998). Lantibiotics: biosynthesis and biological activities of uniquely modified peptides from gram-positive bacteria. *Annual Reviews in Microbiology*, *52*(1), 41-79.

[13] Güllüce, M., Karadayı, M., & Bariş, Ö. (2013). Bacteriocins: promising natural antimicrobials. *local environment*, *3*, 6.

[14] Blaszczyk, U., & Moczarny, J. (2016). Bacteriocins of gram-negative bacteria—structure, mode of action and potential applications. *Postepy Mikrobiologii*, *55*(2), 157-171.

[15] Walsh, L., Johnson, C. N., Hill, C., & Ross, R. P. (2021). Efficacy of phage-and bacteriocin-based therapies in combatting nosocomial MRSA infections. Frontiers in molecular biosciences, 8, 295.

[16] Cotter, P. D., Hill, C., & Ross, R. P. (2005). Bacteriocins: developing innate immunity for food. *Nature Reviews Microbiology*, *3*(10), 777-788.

[17] Rodali, V. P., Lingala, V. K., Karlapudi, A. P., Indira, M., Venkateswarulu, T. C., & John Babu, D. (2013). Biosynthesis and potential application of bacteriocins. *J Pure Appl Microbiol*, *7*, 2933-2945.

[18] Egan, K., Field, D., Rea, M. C., Ross, R. P., Hill, C., and Cotter, P. D. (2016). Bacteriocins: novel solutions to age old spore-related problems? *Front. Microbiol.* 7:461. doi: 10.3389/fmicb.2016.00461.

[19] EFSA (2007). Scientific committee. introduction of a qualified presumption of safety (QPS) approach for assessment of selected microorganisms referred to EFSA1. Opinion of the Scientific Committee (Question No EFSA-Q-2005-293. *EFSA J.* 587, 1–16.

[20] Ahmad, V., Khan, M. S., Jamal, Q. M. S., Alzohairy, M. A., Al Karaawi, M. A., and Siddiqui, M. U. (2017). Antimicrobial potential of bacteriocins: in therapy, agriculture and food preservation. *Int. J. Antimicrob. Agents* 49, 1–11. doi: 10.1016/j.ijantimicag.2016.08.016.

[21] Sahu, M. M., & Dwivedi, M. V. (2021). Studies on Lactobacillus bacteriocin for production and characterization against some pathogenic and food spoilage bacteria. Journal Homepage: http://mbsresearch. com, 7(4).

[22] Balay, D. R., Dangeti, R. V., Kaur, K., & McMullen, L. M. (2017). Purification of leucocin A for use on wieners to inhibit Listeria monocytogenes in the presence of spoilage organisms. *International journal of food microbiology*, *255*, 25-31.

[23] Martin-Visscher, L. A., Yoganathan, S., Sit, C. S., Lohans, C. T., & Vederas, J. C. (2011). The activity of bacteriocins from Carnobacterium maltaromaticum UAL307 against Gram-negative bacteria in combination with EDTA treatment. *FEMS microbiology letters*, *317*(2), 152-159.

[24] Al-Qaysi, S. A., Al-Haideri, H., Thabit, Z. A., Al-Kubaisy, W. H. A. A. R., & Ibrahim, J. A. A. R. (2017). Production, characterization, and antimicrobial activity of mycocin produced by Debaryomyces hansenii DSMZ70238. *International journal of microbiology*, *2017*.

[25] Saraoui, T., Leroi, F., Chevalier, F., Cappelier, J. M., Passerini, D., & Pilet, M. F. (2018). Bioprotective effect of Lactococcus piscium CNCM I-4031 against Listeria monocytogenes growth and virulence. *Frontiers in microbiology*, *9*, 1564.

[26] Bizani, D., Morrissy, J. A., Dominguez, A. P., & Brandelli, A. (2008). Inhibition of Listeria monocytogenes in dairy products using the bacteriocin-like peptide cerein 8A. *International Journal of Food Microbiology*, *121*(2), 229-233.

[27] de Souza Duarte, A. F., Ceotto, H., Coelho, M. L. V., de Paiva Brito, M. A. V., & de Freire Bastos, M. D. C. (2013). Identification of new staphylococcins with potential application as food biopreservatives. *Food control*, *32*(1), 313-321.

[28] Elsayed, E. A., Farid, M. A., & El-Enshasy, H. A. (2019). Enhanced Natamycin production by Streptomyces natalensis in shake-flasks and stirred tank bioreactor under batch and fed-batch conditions. *BMC biotechnology*, *19*(1), 1-13.

[29] Wu, Y., An, J., Liu, Y., Wang, Y., Ren, W., Fang, Z., ... & Gooneratne, R. (2019). Mode of action of a novel anti-Listeria bacteriocin (CAMT2) produced by Bacillus amyloliquefaciens ZJHD3-06 from Epinephelus areolatus. *Archives of microbiology*, *201*(1), 61-66.

[30] Lohans, C. T., & Vederas, J. C. (2012). Development of class IIa bacteriocins as therapeutic agents. *International journal of microbiology*, *2012*.

[31] Abengózar, M. Á., Cebrián, R., Saugar, J. M., Gárate, T., Valdivia, E., Martínez-Bueno, M., ... & Rivas, L. (2017). Enterocin AS-48 as evidence for the use of bacteriocins as new leishmanicidal agents. *Antimicrobial agents and chemotherapy*, *61*(4), e02288-16.

[32] Das, D., & Goyal, A. (2014). Characterization of a noncytotoxic bacteriocin from probiotic Lactobacillus plantarum DM5 with potential as a food preservative. *Food & Function*, *5*(10), 2453-2462.

[33] Jasniewski, J., Cailliez-Grimal, C., Chevalot, I., Millière, J. B., & Revol-Junelles, A. M. (2009). Interactions between two carnobacteriocins Cbn BM1 and Cbn B2 from Carnobacterium maltaromaticum CP5 on target bacteria and Caco-2 cells. *Food and Chemical Toxicology*, *47*(4), 893-897.

[34] Belguesmia, Y., Madi, A., Sperandio, D., Merieau, A., Feuilloley, M., Prévost, H., ... & Connil, N. (2011). Growing insights into the safety of bacteriocins: the case of enterocin S37. *Research in microbiology*, *162*(2), 159-163.

[35] Caly, D. L., Chevalier, M., Flahaut, C., Cudennec, B., Al Atya, A. K., Chataigné, G., ... & Drider, D. (2017). The safe enterocin DD14 is a leaderless two-peptide bacteriocin with anti-Clostridium perfringens activity. *International journal of antimicrobial agents*, *49*(3), 282-289.

[36] Murinda, S. E., Rashid, K. A., & Roberts, R. F. (2003). In vitro assessment of the cytotoxicity of nisin, pediocin, and selected colicins on simian virus 40–transfected human colon and Vero monkey kidney cells with trypan blue staining viability assays. *Journal of food protection*, *66*(5), 847-853.

[37] Maher, S., & McClean, S. (2006). Investigation of the cytotoxicity of eukaryotic and prokaryotic antimicrobial peptides in intestinal epithelial cells in vitro. *Biochemical pharmacology*, *71*(9), 1289-1298.

[38] Cavicchioli, V. Q., de Carvalho, O. V., de Paiva, J. C., Todorov, S. D., Júnior, A. S., & Nero, L. A. (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. *International Journal of Antimicrobial Agents*, *51*(1), 33-37.

[39] Favaro, L., & Todorov, S. D. (2017). Bacteriocinogenic LAB strains for fermented meat preservation: perspectives, challenges, and limitations. *Probiotics and antimicrobial proteins*, *9*(4), 444-458

[40] Chalekson, C. P., Neumeister, M. W., & Jaynes, J. (2003). Treatment of infected wounds with the antimicrobial peptide D2A21. *Journal of Trauma and Acute Care Surgery*, *54*(4), 770-774.

[41] Cox, C. R., Coburn, P. S., & Gilmore, M. S. (2005). Enterococcal cytolysin: a novel two component peptide system that serves as a bacterial defense against eukaryotic and prokaryotic cells. *Current Protein and Peptide Science*, *6*(1), 77-84.

[42] Pessione, E. (2014). Fighting off human infections: a new role for bacteriocin molecules. In *Interactive Probiotics* (pp. 30-59). CRC Press.

[43] Paiva, A. D., de Oliveira, M. D., de Paula, S. O., Baracat-Pereira, M. C., Breukink, E., & Mantovani, H. C. (2012). Toxicity of bovicin HC5 against mammalian cell lines and the role of cholesterol in bacteriocin activity. *Microbiology*, *158*(11), 2851-2858.

[44] Laverty, G., & Gilmore, B. (2014). Cationic antimicrobial peptide cytotoxicity. *SOJ Microbiol Infect Dis*, *2*(1), 1-8.

[45] Huang, F., Teng, K., Liu, Y., Cao, Y., Wang, T., Ma, C., ... & Zhong, J. (2021). Bacteriocins: potential for human health. *Oxidative Medicine and Cellular Longevity*, *2021*.

[46] Rodríguez, J. M., Martínez, M. I., & Kok, J. (2002). Pediocin PA-1, a wide-spectrum bacteriocin from lactic acid bacteria. *Critical reviews in food science and nutrition*, *42*(2), 91-121.

[47] Kaur, B., Garg, N., Sachdev, A., Kumar, B., Mittu, B., & Chauhan, A. (2012). Isolation and molecular characterization of anti-Helicobacter pylori bacteriocin producing Pediococcus acidilactici BA28. *Open Access Scientific Reports*, *1*(6), 323.

[48] López-Cuellar, M. D. R., Rodríguez-Hernández, A. I., & Chavarría-Hernández, N. (2016). LAB bacteriocin applications in the last decade. *Biotechnology & Biotechnological Equipment*, *30*(6), 1039-1050.

[49] Kaur, B., Balgir, P. P., Mittu, B., Kumar, B., & Garg, N. (2013). Biomedical applications of fermenticin HV6b isolated from Lactobacillus fermentum HV6b MTCC10770. *BioMed research international*, *2013*.

[50] Sutyak, K. E., Anderson, R. A., Dover, S. E., Feathergill, K. A., Aroutcheva, A. A., Faro, S., & Chikindas, M. L. (2008). Spermicidal activity of the safe natural antimicrobial peptide subtilosin. *Infectious diseases in obstetrics and gynecology*, *2008*.

[51] Lagos, R., Tello, M., Mercado, G., García, V., & Monasterio, O. (2009). Antibacterial and antitumorigenic properties of microcin E492, a pore-forming bacteriocin. *Current pharmaceutical biotechnology*, *10*(1), 74-85.

[52] Lancaster, L. E., Wintermeyer, W., & Rodnina, M. V. (2007). Colicins and their potential in cancer treatment. *Blood Cells, Molecules, and Diseases*, *38*(1), 15-18.

[53] Joo, N. E., Ritchie, K., Kamarajan, P., Miao, D., & Kapila, Y. L. (2012). Nisin, an apoptogenic bacteriocin and food preservative, attenuates HNSCC tumorigenesis via CHAC 1. *Cancer medicine*, *1*(3), 295-305.

[54] Yamada, T., Hiraoka, Y., Ikehata, M., Kimbara, K., Avner, B. S., Gupta, T. K. D., & Chakrabarty, A. M. (2004). Apoptosis or growth arrest: Modulation of tumor suppressor p53's specificity by bacterial redox protein azurin. *Proceedings of the National Academy of Sciences*, *101*(14), 4770-4775.

[55] Kitazaki, K., Baba, T., Koga, Y., Kuwano, G., Fukuda, H., Kawada, E., ... & Nagatoshi, K. (2010). The use of nisin A in preventing bovine mastitis infection. *Food and Food Ingredient J Japan*, *215*, 449-456.

[56] Perez, R. H., Zendo, T., & Sonomoto, K. (2014). Novel bacteriocins from lactic acid bacteria (LAB): various structures and applications. *Microbial cell factories*, *13*(1), 1-13.

[57] Cinque, B., Torre, C. L., Melchiorre, E., Marchesani, G., Zoccali, G., Palumbo, P., ... & Cifone, M. G. (2011). Use of probiotics for dermal applications. *Probiotics*, 221-241.

[58] Kang, B. S., Seo, J. G., Lee, G. S., Kim, J. H., Kim, S. Y., Han, Y. W., ... & Park, Y. M. (2009). Antimicrobial activity of enterocins from Enterococcus faecalis SL-5 against Propionibacterium acnes, the causative agent in acne vulgaris, and its therapeutic effect. *The Journal of Microbiology*, *47*(1), 101-109.

[59] Zoumpopoulou, G., Pepelassi, E., Papaioannou, W., Georgalaki, M., Maragkoudakis, P. A., Tarantilis, P. A., ... & Papadimitriou, K. (2013). Incidence of bacteriocins produced by food-related lactic acid bacteria active towards oral pathogens. *International journal of molecular sciences*, *14*(3), 4640-4654.

[60] Badaoui Najjar, M., Kashtanov, D., & Chikindas, M. L. (2009). Natural antimicrobials ε-poly-l-lysine and Nisin A for control of oral microflora. *Probiotics and antimicrobial proteins*, *1*(2), 143-147.

[61] Wescombe, P. A., Hale, J. D., Heng, N. C., & Tagg, J. R. (2012). Developing oral probiotics from Streptococcus salivarius. *Future microbiology*, *7*(12), 1355-1371.

[62] Masdea, L., Kulik, E. M., Hauser-Gerspach, I., Ramseier, A. M., Filippi, A., & Waltimo, T. (2012). Antimicrobial activity of Streptococcus salivarius K12 on bacteria involved in oral malodour. *Archives of oral biology*, *57*(8), 1041-1047.

[63] Smith, D., Lee, K. D., Gray, E., Souleimanov, A., & Zhou, X. (2008). *U.S. Patent Application No. 12/093,779*.

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مجلة سامراء للعلوم الصرفة والتطبيقية
www.sjpas.com
p ISSN: 2663-7405
e ISSN: 2789-6838

لمحة عامة عن البكتريوسينات

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معلومات البحث:

تأريخ الاستلام: 2022/03/05
تأريخ القبـــول: 2022/05/15

الكلمات المفتاحية:
البكتريوسينات, بكتريا حامض اللاكتك, تطبيقات البكتريوسينات, انواع البكتريوسينات, تاثير البكتريوسينات

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الخلاصة:

البكتريوسينات هي مركبات بروتينية متعددة الوظائف يتم إنشاؤها بواسطة الريبوسومات وتمتلك بكميات معينة فعالية قوية مضادة للجراثيم. تقوم بعض أعضاء البكتريا القديمة والبكتيريا بتصنيع البكتريوسينات التي تعمل على تثبيط سلالات بكتيرية وثيقة الصلة أو مشابهة.تقسم البكتريوسينات الى ثلاثة اصناف رئيسية اعتمادا على خصائصها الفيزوكيميائية والتركيبية الى بكتريوسينات الصنف الاول،بكتريوسينات الصنف الثاني و بكتريوسينات الصنف الثالث . تعتبر الالتهابات التي تسببها البكتيريا المقاومة للمضادات الحيوية مشكلة صحية عالمية، وقد تكون البكتريوسينات حلاً محتملاً لهذه المشكلة العالمية بسبب فعاليتها الواسعة أو الضيقة الطيف تجاه البكتيريا المقاومة للمضادات الحيوية. تمنع البكتريوسينات نمو البكتريا الهدف عن طريق تاثيرها بشكل رئيسي على الغلاف الخلوي وبالتاثير ايضا على التعبير الجيني وكذلك عملية صنع البروتين داخل الخلية. غالبية البكتريوسينات تُنتج من قبل بكتيريا حامض اللاكتيك، وهي نوع من البكتيريا التي يمكن العثور عليها بشكل طبيعي في المواد الغذائية ولها دور مهم منذ العصور القديمة في تصنيع منتجات الألبان.تعتبر البكتريوسينات ببتيدات مضادة للمايكروبات بالاضافة لكونها آمنة وغير سامة لكن الدراسات على المزارع الخلوية اظهرت بعض من البكتريوسينات لها نوع من السمية الخلوية. تستخدم البكتريوسينات لحفظ الطعام ، ومجموعة متنوعة من التطبيقات العلاجية بما في ذلك علاج القرحة الهضمية ، مبيدة للحيوانات المنوية ، والعناية بالمرأة ، والعناصر المضادة للسرطان ، والاستخدام في الطب البيطري ، والعناية بالبشرة والفم ، وكذلك تعزيز نمو النبات في الزراعة.