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Biopreservação de alimentos utilizando antimicrobianos de bactérias ácido-láticas

Food biopreservation using antimicrobials produced by lactic acid bacteria

Bioconservación de alimentos utilizando antimicrobianos de bacterias ácido lácticas

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Resumo

Há uma crescente demanda dos consumidores por alimentos naturais, sendo de grande interesse desenvolver e produzir substâncias naturais e eficazes para a conservação de alimentos, que

substituam os conservantes sintéticos. O crescimento de bactérias pode ocorrer nos alimentos devido às condições ambientais durante o manuseio e armazenamento, mesmo que tenham sido observadas as boas práticas de fabricação. Isto pode ocasionar perdas para a indústria, tornando-se também um risco de contaminação ao consumidor, havendo a necessidade de desenvolver novas técnicas de controle dessas fontes de contaminação. As bactérias ácido-láticas são conhecidas por seus benefícios aos organismos de quem os consome e pela capacidade de produzir, em condições adequadas, compostos antimicrobianos naturais, os quais podem ser utilizados como bioconservadores nos alimentos e contribuir para o aumento da sua vida de prateleira. As bacteriocinas são proteínas ou peptídios produzidos nos ribossomos que possuem capacidade de agir contra determinados patógenos, evitando sua multiplicação nos produtos durante os períodos de armazenamento e distribuição. O objetivo desta revisão é apresentar os principais microrganismos produtores de bacteriocinas, as formas de produção, bem como as técnicas pelas quais esses bioprodutos têm sido aplicados na biopreservação de produtos alimentícios e os resultados obtidos. A biopreservação por bacteriocinas vem sendo estudada e estabelecida como um novo e importante método, entretanto é necessária a busca por processos de produção dessas bacteriocinas em maior escala e com redução do custo, para que cada vez mais seu potencial possa ser explorado pela ciência e pela indústria. Estudos relacionados aos mecanismos de ação e às aplicações em alimentos são também necessários, a fim de subsidiar as decisões das agências reguladoras.
Palavras-chave: Bacteriocinas; Conservação; Probióticos.

Abstract

There is a growing consumer demand for natural foods, and it is of great interest to develop and produce natural and effective substances for food preservation, replacing synthetic preservatives. The growth of bacteria can occur in food due to environmental conditions during handling and storage, even if good manufacturing practices have been observed. This can cause losses for the industry, also becoming a risk of contamination to the consumer, being necessary to develop new techniques for controlling these sources of contamination. Lactic acid bacteria are known for their benefits to the organisms of those who consume them and for the ability to produce, under appropriate conditions, natural antimicrobial compounds, which can be used as biopreservatives in food and contribute to the increase of shelf life. Bacteriocins are proteins or peptides produced in ribosomes that have the capacity to act against certain pathogens, preventing their multiplication in products during the periods of storage and distribution. The aim of this review is to present the main bacteriocin-producing microorganisms, the forms of

production, as well as the techniques by which these bioproducts have been applied in the biopreservation of food products and the results obtained. Biopreservation using bacteriocins has been studied and established as a new and important method, however it is necessary to search for production processes of these bacteriocins on a larger scale and with cost reduction, so that their potential can be increasingly explored by science and industry. Studies related to mechanisms of action and applications in food are also necessary in order to support the decisions of regulatory agencies.
Keywords: Bacteriocins; Preservation; Probiotics.

Resumen

Existe una creciente demanda de los consumidores de alimentos naturales, y es de gran interés desarrollar y producir sustancias naturales y efectivas para la conservación de alimentos, que reemplacen a los conservantes sintéticos. El crecimiento de bacterias puede ocurrir en los alimentos debido a las condiciones ambientales durante la manipulación y el almacenamiento, incluso si se han observado buenas prácticas de fabricación. Esto puede causar pérdidas para la industria, y también convertirse en un riesgo de contaminación para el consumidor, con la necesidad de desarrollar nuevas técnicas para controlar estas fuentes de contaminación. Las bacterias del ácido láctico son conocidas por sus beneficios para los organismos de quienes las consumen y por su capacidad para producir, en condiciones apropiadas, compuestos antimicrobianos naturales, que pueden usarse como bioconservadores en los alimentos y contribuyen al aumento de la vida útil de los productos. Las bacteriocinas son proteínas o péptidos producidos en los ribosomas que tienen la capacidad de actuar contra ciertos patógenos, evitando su multiplicación en productos durante los períodos de almacenamiento y distribución. El propósito de esta revisión es presentar los principales microorganismos productores de bacteriocinas, las formas de producción, así como las técnicas por las cuales estos bioproductos se han aplicado en la bioconservación de productos alimenticios y los resultados obtenidos. La biopreservación con bacteriocinas se ha estudiado y establecido como un método nuevo e importante, sin embargo, es necesario buscar procesos de producción de estas bacteriocinas a mayor escala y con reducción de costos, de modo que su potencial pueda ser explorado cada vez más por la ciencia y la industria. Los estudios relacionados con los mecanismos de acción y las aplicaciones en los alimentos también son necesarios para apoyar las decisiones de las agencias reguladoras.
Palabras clave: Bacteriocinas; Conservación; Probióticos.

1. Introduction

Food spoilage is a major concern for the industry and the consumer. Preservation methods emerged along with the development of civilization, being perfected throughout mankind evolution. Emerging methods for food preservation can be classified into three main categories: physical methods (high hydrostatic pressure, membrane processing such as microfiltration, cold plasma, pulsed light, pulsed electric field), chemical methods (antimicrobial disinfectants such as organic acids, ozone and chlorine), biological methods (plant extracts and bacteriocins) (Martínez et al., 2019; Misra et al., 2017; Mukhopadhyay & Ukuku, 2018).

The main alternative used commercially to prevent this deterioration is chemical additives. However, the emergence of a tendency by consumers to avoid such substances in their diets due to the possibility of harmful effects on human health has opened a new area for intensive research to unveil the new range of natural antimicrobial compounds that could efficiently prevent deterioration. These natural additives must be efficient and cannot cause health problems (Kumariya et al., 2019; Shori, 2016; Sidhu & Nehra, 2019).

In the last few decades there has been a growing public and scientific interest in the administration of live microorganisms to prevent or treat diseases (Prabhurajeshwar & Chandrakanth, 2017). Among the existing technologies, biopreservation receives attention due to its minimal impact on the nutritional and sensory properties of food products. This technology is carried out through the use of biocompounds produced in fermentative processes by lactic acid bacteria (LAB) and is based on the fact that these "positive" bacteria kill or prevent the growth of undesirable microorganisms, extending food shelf life (Li et al., 2019; Sabo et al., 2017).

The LAB play important role in the food industry (Wang et al., 2020), preserving fermented foods by producing antifungal metabolites (Le Lay et al., 2016a; Varsha & Nampoothiri, 2016) and antimicrobials (Ahmad et al., 2017; Cruz et al., 2009; Fernandez et al., 2017; Oliveira et al., 2014). That is why the development of natural antimicrobial systems from LAB is of great importance for the food industry (Langa et al., 2018).

The antimicrobial compounds produced by LAB can be organic acids and bacteriocins (Sabo et al., 2017). Among these, bacteriocins are gaining credibility as modulators of the immune and digestive systems, due to their ability to regulate the intestinal microbiota, such as probiotic bacteria (Chugh & Kamal-Eldin, 2020; O'Connor et al., 2020). These bacteria are able to modify alter the composition of the intestinal microbiota and the synthesis of bile acids to obtain health benefits, such as lowering cholesterol, reducing weight and improving insulin sensitivity (Sivamaruthi et al., 2020). Goh et al. (2019) conducted a study in which probiotics were tested on people who had depressive symptoms, and participants treated with probiotics showed significant improvement in symptoms reduction.

Bioactive compounds produced by probiotic bacteria include metabolic bacteriocins, enzymes, amino acids and peptides, short-chain fatty acids, organic acids, vitamins, antioxidants, anti-inflammatory agents, alcoholic compounds, immunomodulators and exopolysaccharides (Ahmad et al., 2017; Chugh & Kamal-Eldin, 2020; Hossain et al., 2017).

Bacteriocins are antibacterial peptides or proteins which consist of amino acids synthesized in the ribosomes of some LAB, being released extracellularly to inhibit the growth of pathogenic microorganisms which are resistant to conventional antimicrobials (Radaic et al., 2020; Wang et al., 2019). Few bacteriocins are released for use in food in the USA and Canada, i.e., nisin produced by *Lactococcus lactis*, pediocin produced by *Pediococcus acidilactici* and Micocin®, a combination of three bacteriocins (carnocycline A, carnobacteriocin BM1 and piscicolin 126) produced by *Carnobacterium maltaromaticum*. Nisin is approved by the FDA and used in more than 48 countries (Zou et al., 2018).

This review describes the use of bacteriocins produced by LAB for use in food biopreservation, addressing aspects of classification, mechanism, methods of production and use in some foods, in order to clarify how these compounds can be safely applied to increase food shelf life.

2. Definition, Classification and Mechanism of Action of Bacteriocins

Bacteriocins are versatile antimicrobials with considerable potential for use as biopreservatives, intestinal modulators and health promoters (O'Connor et al., 2020). Several published reports on bacteriocins state a history of safe use, without any adverse health effects (Ahmad et al., 2017; Barman et al., 2018; Fu et al., 2016; Le Lay et al., 2016b; Varsha & Nampoothiri, 2016), confirming the potential of some cultures of lactic acid bacteria, supernatants or mixtures of active metabolites to be used as antifungal agents. *Lactobacillus* is the most studied genus and the most extensive among lactic acid bacteria (Uroić et al., 2016; Moraes et al., 2018) and certain strains can produce more than one bacteriocin (Mills et al., 2017).

Bacteriocins were first identified in 1925 (Cavera et al., 2015), consisting of small cationic peptides composed of 20 to 60 amino acids, with a high isoelectric point and amphipathic characteristics. They can be spontaneously produced as primary or secondary metabolites (Barbosa et al., 2015; Singh et al., 2015). They are produced by the ribosomes, with pronounced antimicrobial activity in certain concentrations (Chikindas et al., 2018).

With the decrease in the effectiveness of antibiotics to resistant strains, research on antimicrobial peptides is an alternative treatment, since antimicrobial peptides have unique mechanisms of action, due to their relatively simple methods of synthesis and modification, moreover they have not been widely used like conventional antibiotics (Hancock & Sahl, 2006). According to studies carried out against strains resistant to treatments with conventional antibiotics (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii, Pseudomonas aeruginosa* and *Enterobacter*), antimicrobial peptides were characterized as effective against these strains (Menousek et al., 2012; Vila-Farres et al., 2012; Wu et al., 2011).

These substances can be classified based on molecular mass, chemical structure, thermal and enzymatic stability, mechanism of action, antimicrobial activity or presence of modified amino acid residues (Zou et al., 2018).

The most common is to classify them in three major classes. Class I are the peptides <10 kDa and that undergo enzymatic modification, being subdivided into: Ia (I, II, III, IV, and the subdivisions III and IV do not have antimicrobial potential); Ib (peptides capable of forming pores in cell membranes); Ic (peptides capable of forming transient pores in the cell membrane); Id; Ie; If. Class II are the peptides <10 kDa and that do not undergo enzymatic modification, being subdivided into: IIa (peptides presenting a broad antimicrobial spectrum, forming pores in the cell membrane); IIb; IIc; IId (heat-sensitive peptides). Class III are peptides >10 kDa and which do not undergo enzymatic modification, having no subdivisions in their classification (Alvarez-Sieiro et al., 2016).

They have different mechanisms of action: some bacteriocins have the ability to increase the permeability of the cell membrane of the target microorganism through the formation of pores; they can also prevent cell wall synthesis; others manage to penetrate the bacterium's cytoplasm and cleave DNA or RNA; and finally, they can also penetrate the cell membrane and digest the peptidoglycan precursors causing cell death (Radaic et al., 2020; Sun et al., 2018).

Nisin and natamycin (pimaricin) are bacteriocins that are GRAS (g*enerally recognized as safe)* substances. Nisin (GRN n. 65) was discovered by accident in 1920-1930. Natamycin (GRN n. 517), also known as pimaricin, was discovered in 1955 from a culture filtrate of *Streptomyces* in soil sample. These bacteriocins (showed in Table 1) are approved and used worldwide as food additives for preservation (Zou et al., 2018). Regardin toxicity studies, nisin showed no effects on rats (Hagiwara et al., 2010; Reddy et al. 2011) and natamycin showed no effects on rats and rabbits (Levinskas et al. 1966) and on Guinea-pigs (Struyk et al. 1958), confirming that these substances are safe for human health.

Table 1: GRAS bacteriocins and respective producers.

Bacteriocin	Microorganism	Reference
Nisin A	*Lactococcus lactis* 6F3	Kaletta & Entian, 1989
Nisin F	*Lactococcus lactis* F10	Kwaadsteniet et al., 2008
Nisin H	*Streptococcus hyointestinalis* DPC6484	O'Connor et al., 2015
Nisin Q	*Lactococcus lactis* 61-14	Zendo et al., 2003
Nisin U	*Streptococcus uberis* 42	Wirawan et al., 2006
Nisin U2	*Streptococcus agalactiae* D536	Piper et al., 2011
Nisin Z	*Lactococcus lactis* NIZO 22186	Mulders et al., 1991
Natamycin/ Pimaricin	*Streptomyces natalensis*	Struyk et al, 1958

Source:Authors.

The range of bacteriocin inhibitory activity can be narrow, inhibiting only strains that are closely related to the producing organism, or large-scale, inhibiting a wide range of Gram-positive microorganisms (Field et al., 2018).

As a result of the amphiphilic characteristics and the high content of hydrophobic amino acids, the biosynthesis and antimicrobial functionality of bacteriocins can be affected by the components of the food matrix (Barbosa et al., 2018). The general consensus is that the bacteriocin that best adapts to the control of a pathogen will often be found in the same environment (O'Connor et al., 2015).

3. Production and Purification of Bacteriocins

The production of bacteriocins by LAB is generally carried out in complex culture media, such as Man Rogosa and Sharpe (MRS), All Purpose with Tween (APT), Tryptone Glucose Extract (TGE) and Trypticase Soy Broth (TSB), however, their high costs make them unsuitable for large-scale production (Lima et al., 2017). MRS broth is not ideal for commercial production of bacteriocins due to the higher price and the presence of unauthorized ingredients for food applications, such as manganese II sulfate (Juturu & Wu, 2018).

Submerged fermentation is a technique that has been used over the last centuries for having advantageous characteristics such as the ease of sterilization and process control, ease of heat transfer and homogeneity of the media. This technique is more suitable for microorganisms that require high moisture content for growth such as lactic acid bacteria (Sharma et al., 2017; Singh et al., 2017).

Several studies conducted to establish the best conditions for production indicate that bacteriocin biosynthesis is not parallel to bacterial growth. Probiotic bacteria have many nutritional growth requirements, such as amino acids, fatty acids and vitamins (Champagne et al., 2018). Bacteriocin levels are generally higher when temperature, pH and nutrients are lower than required for the growth of probiotic strains (Barbosa et al., 2018; Engelhardt et al., 2018).

Bacteriocin production is currently an active area of research and should ensure that the use of pure bacteriocins is a more viable option in the future (Mills et al., 2017). It is estimated that 30% of the total resources spent in such a process are costs associated with the culture medium and supplements necessary to promote the cellular growth of the microorganism that produces such molecules (Sabo et al., 2017). The production of bacteriocins on a commercial scale is still hampered by high costs and low peptide yield. Cost reduction is being improved by optimizing fermentation processes and bioengineering strains for maximum bacteriocin production (O'Connor et al., 2020).

The use of organic residues as a substrate in fermentation processes can be accepted as one of the solutions to reduce the cost of crops, as well as an environmentally friendly method of removing these residues (Reihani & Khosravi-Darani, 2019). Partially purified bacteriocins produced using food-grade substrates such as milk or whey (Mills et al., 2017), or the use of industrial by-products are being explored as alternative culture substrates (Lima et al., 2017). Agro-industrial waste is a rich source of nutrients, organic and inorganic matter. These residues can be used as alternative substrates of carbon or nitrogen for the production of various microbial products (Singh et al., 2017).

The dairy industry produces a considerable amount of by-products, which can be used in fermentation processes, thus reducing the disposal of these residues and decreasing environmental impacts (Vera et al., 2018), and whey generated during cheese production is the biggest by-product of this industry (Lima et al., 2017). Whey contains lactose (4.5%), salts (1.0%), proteins (0.8%) and lactic acid (0.1-0.8%) (Singh et al., 2017). The high concentration of lactose, the presence of vitamins, minerals, proteins (Sabo et al., 2017) and pH values close to neutral (Lima et al., 2017) make whey an interesting medium for the growth of LAB and meet the objective of promoting the economic production of bioproducts of industrial interest (Sabo et al., 2017). These substrates can be supplemented with sucrose as a carbon source (Vera et al., 2018).

Although several LAB strains have been reported to produce antimicrobial bacteriocins, their production depends on multiple factors, such as: LAB strain, pH, temperature, bacterial growth conditions (Barman et al., 2018; Elayaraja et al., 2014; Lima et al., 2017; Miao et al., 2015) and can also be affected by NaCl concentration. Engelhardt et al. (2018) carried out a study in which they observed that the increasing concentration of NaCl in the fermentation of *Lactobacillus plantarum* ST202Ch resulted in a decrease in antimicrobial activity. This is because the unfavorable effect of NaCl causes osmotic stress in the bacterial cell, which results in a reduction in the ability to produce bacteriocins. In addition, NaCl interferes with the binding of bacteriocins to receptors on the sensitive cell membrane (Barbosa et al., 2018; Verluyten et al., 2004).

Temperature is a critical parameter that must be controlled and varied from organism to organism for maximum cell growth. The pH of the culture also affects the enzymatic processes and transport of various components across the cell membrane, so it is an important parameter to be optimized (Sharma et al., 2017). An example is the study carried out to evaluate the influence of pH and temperature on the growth kinetics of bacteriocin sakacin P by *Lactobacillus sakei* CCUG 42687. Sakacin P production was maximum at 20°C and at higher temperatures (25-30°C) its production decreased, even with similar media and pH, the maximum concentration of sakacin P at 20°C was seven times higher than at 30°C (Aasen et al., 2000).

Another study with a bacteriocin produced by *Pediococcus pentosaceus* ATCC 43200 evaluated the influence of pH and supplements on antimicrobial activity. The cell-free supernatant of the control medium fermented at pH 5.0 was found to exhibit an antimicrobial activity against *Enterococcus* 5.3% higher than at pH 6.0 and up to 20% higher than that of all supplemented media, regardless concentration of supplements. The production of bacteriocin was favored at pH 5.0 or in the absence of additional supplements, which were able to stimulate the growth and production of bacteriocin by *P. pentosaceus* (Azevedo et al., 2019).

After the identification of new bacteriocins, the most critical and complex step is their purification from fermentation broths (Zou et al., 2018). The purification of bacteriocins is a slow process, which consists of several steps such as centrifugation, filtration, precipitation with ammonium sulfate, two steps of solvent extraction and two steps of chromatography (Katharopoulos et al., 2016).

Pei et al. (2020) produced a new bacteriocin SLG10 using *Lactobacillus plantarum* isolated from kombucha that presents antibacterial activity on Gram-positive and Gram-negative bacteria. A method of purification and screening for this bacteriocin was developed through biochromatography coupled with high performance liquid chromatography in reverse phase (RP-HPLC). In another study by Qiao et al. (2020) the bacteriocin enterocin TJUQ1 produced by *Enterococcus faecium* was purified by precipitation with ammonium sulfate, reverse phase chromatography (Sep-Pak C8) and cation exchange chromatography. The results showed that enterocin TJUQ1 was a new bacteriocin class II with broad antibacterial activity against Gram-negative and Gram-positive pathogens from food.

Simpler and more economical purification methods need to be developed compared to chromatography to increase their commercial viability (Wong et al., 2017). A systematic study on the substitution of high-cost media for cheaper alternatives would be the top priority for the promotion of production and application of cost-effective bacteriocins (Juturu & Wu, 2018).

Although there are evidences of the activity that these biocomposites can present as biopreservatives, and of the potential of their use to control contamination in food products, it is necessary to study production methods and purification of lower cost in order to make the technique commercially viable.

4. Applications of Bacteriocins in Food

Antimicrobial compounds are used in foods due to their ability to delay the development of undesirable microorganisms in the product (Barman et al., 2018; Elayaraja et al., 2014). They can be classified into two groups: synthetic and natural antimicrobials (Fu et al., 2016). Among the 36 antimicrobials approved as preservatives by the European Food Safety Authority (EFSA, 2018), 33 are synthetic and only 3 are natural.

The bacteriocins used for biopreservation can be introduced in food in three ways: 1) incorporation of bacteria in the food product, 2) addition of purified or partially purified bacteriocins in the food, 3) addition of a fermented ingredient by bacteriocin-producer strains (Barbosa et al., 2018; Chikindas et al., 2018; O'Connor et al., 2015; Ahmad et al., 2017).

Table 2 summarizes the results obtained in some studies involving the application of bacteriocins produced by LAB in different types of food.

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Table 2: Applications of bacteriocins in food products.

Bacteriocin source	Food	Result	Reference
Lactobacillus plantarum	Raw beef	Increase in the shelf life of meat	Trabelsi et al. (2019)
Lactococcus lactis	Jerky beef	Reduction of the deterioration	Biscola et al. (2014)
Pediococcus pentosaceus *Lactobacillus sakei* *Staphylococcus xylosus*	Pork sausage	Conservation better than with chemical preservatives	Wang et al. (2016)
Lactobacillus curvatus	Cooked pork	Inhibition of *Listeria monocytogenes*	Rivas et al. (2014)
Lactobacillus sakei	Salami	Inhibition of *Listeria monocytogenes*	Barbosa et al. (2018)
Weissella hellenica	Fish fillet	Inhibition of several bacteria	Woraprayote et al. (2018)
Enterococcus mundtii	Fish	Inhibition of Gram-positive bactéria	Schelegueda et al. (2015)
Lactobacillus curvatus	Fish	Inhibition of *Listeria*, coliforms and mesophilic bacteria	Gómez-Sala et al. (2016)
Pediococcus acidilactici *Pediococcus pentosaceus* *Streptococcus thermophilus* *Lactococcus lactis* *Lactobacillus plantarum* *Lactobacillus acidophilus* *Lactobacillus helveticus*	Fish	Increase in the shelf life of fish	Sudalayandi (2011)
Lactobacillus reuteri	Fish fillet	Inhibition of several bacteria	Angiolillo et al. (2018)
Lactobacillus plantarum	Chilled shrimp	Inhibition of *Vibrio parahaemolyticus*	Lv et al. (2017)
Lactobacillus rhamnosus	Goat cheese	Inhibition of *Staphylococcus aureus*, *Salmonella*, *E. coli* and *Listeria*	Rolim et al. (2015)
Lactobacillus casei	Goat cheese	Inhibition of *Staphylococcus aureus* and *Listeria monocytogenes*	Oliveira et al. (2014)
Lactobacillus casei *Lactobacillus plantarum* *Lactobacillus brevis*	Himalayan cheese	Inhibition of deteriorating microorganisms	Mushtaq et al. (2016)
Lactobacillus reuteri	Semi-hard cheese	Inhibition of *Listeria monocytogenes* and *E. coli* O157:H7	Langa et al. (2018)
Pediococcus pentosaceus	Vegetable	Inhibition of *Listeria monocytogenes*	Ramos et al. (2020)
Lactobacillus lactis	Lettuce	Inhibition of *Listeria monocytogenes*	McManamon et al. (2019)
Lactobacillus pentosus	Cut fruit	Inhibition of *Listeria monocytogenes*, *Salmonella* and *E. coli*	Yi et al. (2020)

Source: Authors.

Regardless of the mode of incorporation, the effectiveness of bacteriocins as biopreservers depends on the optimal biosynthesis, level and specificity of antimicrobial activity and interaction with the components of the food matrix (Barbosa et al., 2018). The direct application of antimicrobial compounds in food systems faces challenges such as water insolubility, physical and chemical degradation and impact on the organoleptic properties of food (Fu et al., 2016). It is necessary to evaluate the functionality of bacteriocins added to foods, tested under the same time and temperature conditions in which they are kept before consumption.

4.1. Meat and Meat Products

The use of bacteriocins as a biopreservation agent in meat has been extensively studied in recent years. A study carried out on fermented pork sausages, comparing fermented sausages with inoculated isolated cultures of *Pediococcus pentosaceus, Lactobacillus sakei* and *Staphylococcus xylosus* and those spontaneously fermented. As a result, it was possible to verify that the residual nitrite levels were lower in the inoculated sausages (4.32 mg/kg) compared to the spontaneous fermentation sausages (26.72 mg/kg). This decrease was also present in the values of the tests of substances reactive to thiobarbituric acid, where the inoculated sausages reached 2.64 mg malondialdehyde (MDA)/kg whereas the sausages of spontaneously fermented values reached 13.92 mg MDA/kg. Sausages with inoculation showed nitrite depletion and oxidative stability in fermented sausages and were beneficial for improving the hygienic quality and food safety of fermented sausages (Wang et al., 2016). The use in fermented foods is a great alternative, since the change in flavor caused by fermentation is desired in some foods.

Studies carried out on jerky beef have shown a negative influence on halotolerant microorganisms, reducing the potential for deterioration in this food, during its fermentation, with the use of *Lactococcus lactis* subsp. *lactis* 69 (Biscola et al., 2014). In addition, sakacin Q produced by *Lactobacillus curvatus* ACU-1 demonstrated an important antilisterial action in cooked meat with direct inoculation (protective culture). The microorganism and its bacteriocin showed promising technological characteristics that made it suitable for meat biopreservation (Rivas et al., 2014). The same effect was observed in salami using the inoculation of the starter culture *Lactobacillus sakei* subsp. *sakei* 2a in the pasta (Barbosa et al., 2018).

Woraprayote et al. (2018) developed a study on the production of antimicrobial and biodegradable food packaging to control pathogens in *Pangasius bocourti* fish fillets. The use of packaging impregnated with a new bacteriocin from *Weissella hellenica* BCC 7293 showed inhibition results against Gram-positive bacteria (*Listeria monocytogenes* and *Staphylococcus aureus*) and Gram-negative (*Pseudomonas aeruginosa*, *Aeromonas hydrophila*, *Escherichia* *coli* and *Salmonella* Typhimurium). This antimicrobial film inhibited the growth of target microorganisms by about 2 to 5 log CFU/cm^2.

In another study, the cell culture supernatant of *Enterococcus mundtii* Tw56 was able to inhibit the growth of different genera of Gram-positive bacteria such as *Enterococcus*, *Lactobacillus*, *Leuconostoc*, *Listeria*, *Pediococcus* and *Streptococci*, presenting inhibiting potential against fish spoilage microorganisms, mainly at pH 5.5 (Schelegueda et al., 2015).

Lactobacillus curvatus BCS35 was able to increase the shelf life of four-spot megrim fish (*Lepidorhombus boscii*) by inhibiting the growth of *Listeria*, coliforms and mesophiles without influence in the sensory aspect of these fish (Gómez-Sala et al., 2016). Recently, the action on *Vibrio parahaemolyticus* was demonstrated by Lv et al. (2017), in which the use of purified bacteriocin produced by *Lactobacillus plantarum* in chilled shrimp decreased the development of this pathogenic bacterium by breaking the integrity of the cell membrane with consequent extravasation of the cell content and death of the cells, demonstrating to be an excellent alternative for the biopreservation not only of shrimp, but also of other marine fish. Shirazinejad et al. (2010) used nisin associated with lactic acid in the biopreservation of shrimp. The results indicated action against psychrotrophic microorganisms, such as *Pseudomonas aeruginosa* and other producers of hydrogen sulfite, a gas responsible for the fetid odor of putrefying meat.

Trabelsi et al. (2019) conducted a study using *Lactobacillus plantarum* (10^8 CFU/g) incorporated into raw ground beef in a refrigeration system at 4°C for 10 days. Microbiological, textural, physical-chemical and color parameters were observed. The addition of this probiotic strain as a bioprotective agent was able to extend the shelf life of beef. Considering psychrotrophic microorganisms the treatment with *L. plantarum* conserved the meat for at least 10 days, while the control samples started to deteriorate after 8 days of storage. On day 7 of storage, meat inoculated with 9, 8 and 7 log CFU/g of *L. plantarum* led to a reduction in the psychrotrophic microorganisms, reaching 4.2, 5 and 5.9 log CFU/g, respectively. For the *Enterobacteriaceae* family, the samples with *L. plantarum* showed significantly lower counts compared to the control sample, reaching 1.9, 1.8, 1.78 and 1.1 log CFU/g for control and samples inoculated with 7, 8 and 9 log CFU/g, respectively.

Biopreservation of *Acanthocybium solandri* fish was tested using 7 LAB strains (*Pediococcus acidilactici*, *Pediococcus pentosaceus*, *Streptococcus thermophilus*, *Lactococcus lactis*, *Lactobacillus plantarum*, *Lactobacillus acidophilus* and *Lactobacillus helveticus*). *P. acidilactici* reduced the level of nitrogen trimethylamine to 40 mg%, free fatty acids to 47.66 mg% and peroxides to 97 mg% when compared to the control sample. This study showed that

LAB can be used to preserve fresh fish by controlling bacteria and deteriorating amines for a short period of time (Sudalayandi, 2011).

Another alternative for biopreservation was performed on sea bass (*Centropomus undecimalis*) fillets by Angiolillo et al. (2018), using a protective glycerol film with the addition of *Lactobacillus reuteri*. The protective film decreased the development of aerobic, psychrotrophic and enterobacterial microorganisms in 2 to 3 days compared to sea bass fillets without the protective layer. In addition, it has improved the color and texture of the food due to fermentation, maintaining a compact structure and reducing oxidation reactions.

4.2. Milk and Dairy Products

The biopreservation potential of a bacteriocin produced by *Pediococcus* spp. isolated from milk samples was tested by diffusion tests on food and was compared with two chemical preservatives (sodium sulfite and sodium benzoate). The results showed that 100 µg/L extracted bacteriocin demonstrated antimicrobial potential against *Escherichia coli* and *Shigella* spp. The microbiological quality of food treated with biopreservers was better when compared to chemical preservatives (Skariyachan & Govindarajan, 2019).

During cheese maturation, the microbiota plays an important role in the formation of aromatic compounds, especially in the consumption of lactate, proteolysis, lipolysis and lactose fermentation. Fungi, including yeasts, can play important roles in cheese maturation, with positive or negative effects on flavor formation (Zheng et al., 2018). Molds can also be responsible for cheese deterioration, causing defects such as pigmentation and mycotoxin accumulation (Jurado & Ruiz-Navarro 2018). Deterioration by fungi makes cheese unsuitable for human consumption because they impart unpleasant mold or bitter flavors, leading to huge economic losses for the dairy industry (Fernandez et al., 2017).

Garnier et al. (2017) isolated 105 fungi from dairy products in France, 60% were filamentous fungi, with a great diversity of species (24 species). *Penicillium* was the most abundant genus, followed by *Cladosporium* and *Didymella*.

Cheese is susceptible to fungal deterioration of *Fusarium* species (Varsha & Nampoothiri, 2016), *Cladosporium*, *Mucor*, *Geotrichum* (Fernandez et al., 2017), *Penicillium* and *Aspergillus* (Fernandez et al., 2017; Leggieri et al., 2017; Varsha & Nampoothiri, 2016). A study by Leggieri et al. (2017) with the main fungal species that produce mycotoxins in cheese pointed out that they can grow under conditions comparable to those used for the ripening of cheese and that contamination of the product with multiple mycotoxins is possible.

Cheese deterioration can be reduced by using pasteurization and chemical preservatives, i.e., sorbates and natamycin. However, some microorganisms have acquired the ability to degrade sorbate by decarboxylation into trans-1,3-pentadiene, causing an odor and flavor described as "kerosene-like". Several approaches have been proposed to slow the growth of mold in cheese, being the addition of a protective culture is particularly interesting. Lactic and propionic acid bacteria are the most commonly used microbial groups, since they are naturally present in fermented foods (Fernandez et al., 2017).

Rolim et al. (2015) verified the reduction of the growth of pathogenic agents (*Staphylococcus aureus*, *Salmonella* Enteritidis, *Escherichia coli* and *Listeria monocytogenes*) in goat cheese stored refrigerated for 7, 14 and 21 days when a *Lactobacillus* strain was added during its production. *Lactobacillus rhamnosus* exhibited inhibition rates against *S.* Enteritidis of 4.36%, 5.33% and 5.51% at 7, 14 and 21 days of storage, respectively. The inhibition rates against *S. aureus* were 1.55%, 1.70% and 21.66% at 7, 14 and 21 days of storage, respectively, and against *L. monocytogenes* were 2.62 %, 1.57% and 10.23% at 7, 14 and 21 days of storage, respectively. The inhibition rate against *E. coli* was 7.98% at 7 days of storage and no inhibitory effects at 14 and 21 days. The results indicated that this strain could be used as a protection culture to delay the growth of pathogenic bacteria, mainly *S. aureus* and *L. monocytogenes*.

Oliveira et al. (2014) observed that the probiotic strains added to a goat cheese survived the simulated gastrointestinal digestion and that *Lactobacillus casei* subsp. *paracasei* can be used as a protective culture to retard the growth of *Staphylococcus aureus* by 7.87% and 23.63% and *Listeria monocytogenes* by 12.96% and 32.99% for 14 and 21 days, respectively. From these results, goat cheese may be an important carrier of probiotic strains of *Lactobacillus acidophilus*, *Lactobacillus casei* subsp. *paracasei* and *Bifidobacterium lactis*.

Mushtaq et al. (2016) carried out a study with Himalayan cheese (Kalari), incorporating different probiotic strains *Lactobacillus casei*, *Lactobacillus plantarum* and *Lactobacillus brevis*. The results showed an increase in the antioxidant activity of cheese, a delay in the oxidation of lipids and proteins, an inhibition of the growth of deteriorating microorganisms (psychrotrophic bacteria, yeast and mold), and also, in cheeses with ripening time higher than 30 days, a higher sensory score, with a positive influence on palatability.

Langa et al. (2018) evaluated semi-hard cheeses added with *Lactobacillus reuteri* and glycerol. They obtained positive results in decreasing the count of *Listeria monocytogenes* and *Escherichia coli* O157:H7 in cheeses artificially contaminated with these pathogens. The count of *L. monocytogenes* in the control cheese was 4.31 log CFU/g after 30 days of maturation, whereas in the cheese produced with *L. reuteri* INIA P572 and glycerol, this pathogen was only detectable on the first day, when *L. reuteri* had not yet grown enough to inhibit it. After 7, 15 and 30 days the pathogen was not detectable. After 30 days, *E. coli* O157: H7 counts were 0.85 log CFU/g in the control cheese, but the pathogen was not detected in 25 g of cheese produced with *L. reuteri* and glycerol since day 7.

4.3. Vegetables

Raw vegetables have been identified as a vehicle for the transmission of food-borne outbreaks and play an important role in the epidemiology of listeriosis (Mir et al., 2018). This is a special concern, because this type of food is consumed raw and depends only on cold storage to maintain its safety. In addition, *Listeria* has the ability to survive and multiply at cooling temperatures (McManamon et al., 2019).

Currently, commercial operations use washing treatments with antimicrobials as the only step to reduce microbial populations in fresh products, with chlorine being the most used disinfectant. However, numerous reports indicate that chlorine has limited antimicrobial efficacy at permitted levels and is associated with the production of potentially toxic substances (McManamon et al., 2019).

Ramos et al. (2020) carried out two biopreservation approaches in vegetables. The first evaluated the potential of *Pediococcus pentosaceus* DT016 as a protective culture to limit the growth of *Listeria monocytogenes* in vegetables during storage. The number of pathogens in plants inoculated with *P. pentosaceus* DT016 was significantly lower during the storage period, in which a minimum difference of 1.4 log CFU/g was reported when compared to plants without the protective culture. The second approach was a comparison between pediocin DT016 and chlorine to inactivate and control the proliferation of pathogens in vegetables after washing them with these solutions. Vegetables washed with pediocin showed a significantly lower number of pathogens during storage at a minimum of 3.2 and 2.7 log CFU/g compared to vegetables washed with water and chlorine, respectively.

In another study, carried out by McManamon et al. (2019), it was found that application of nisin A in lettuce was a viable alternative to reduce and delay growth of the pathogen *Listeria monocytogenes*, without affecting the sensory appearance for 2 to 5 days. A reduction of 10 to 100 times in the growth of *L. monocytogenes* was obtained at 4 and 8°C, respectively, during 7 days using 5 mg/kg of nisin A, while lettuce maintained an acceptable sensory appearance for the first 5 days.

Yi et al. (2020) observed that the metabolites of bacteriocin produced by *Lactobacillus pentosus* MS031 controlled the pathogens present in cut fruits during storage. When *L. pentosus* MS031 had contact with pathogens in mixture with the cut fresh fruits, it obtained a 96.3% reduction of *Listeria monocytogenes*, while *Salmonella* Typhi and *Escherichia coli* were reduced to an undetectable level.

5. Final Considerations

Although LAB are the main producers of bacteriocins used in the food industry, the cultivation costs of these microorganisms, as well as the purification and identification of the compounds responsible for biopreservation, still need research. It is necessary to identify cultivation conditions and sources of nutrients for the composition of low-cost culture media, as well as the definition of more accessible techniques for purification and application in food. The use of direct inoculation of LAB in foods to be biopreserved is one of the most used techniques, but it is limited because it does not allow the optimal conditions for growth and obtaining bacteriocins. In addition, the growth of LAB in foods can cause changes in the sensory profiles of products, which may be positive or not.

Biopreservation of food using these compounds has already been studied and established as a new and important method, meeting the needs of consumers, using natural additives. Further studies on different mechanisms of bacteriocins and their effectiveness in food application are necessary, making it possible to increase the interest of government agencies to invest in research and to expand the use of bacteriocins in food.

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