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Bacteriocins as Promising Antimicrobial Peptides and Potential Alternatives to Antibiotics: A Comprehensive Review

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Abstract
Bactria have important properties included an ability to adaption of environment by produce antimicrobial peptides, it have bioactivity against for many types of pathogenic bacteria and this character consider the best mechanisms that allow bacteria to defense from delete agent, as while as to compete of nutrient and habitat and space on environment, so these antimicrobial peptides production it call becteriocins. Bacteriocins was producing by many types of bacteria, it producing from Gram + / - bacteria and Arechae and generated by ribosome, classified od bacteriocin deepened of several methods, such as producing bacteria strains, size, structure and functional, mode of actions occurring by pore forming or proteins inhibition synthesis. in last years, there are important attention of bacteriocins application by using it on several field included Food industry as a bio preservative substance using it without needing to addition any of chemical or physical treatments, in addition it using on medical human health care as alternative pathway for treatment many multidrug resistant bacteria and on agriculture for plant growth promotion, these due to properties of bacteriocins as low toxicity, it have strong activity of target pathogenic with low concentration and easily obtain from environment.

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1. Introduction

The misuse of antibiotics during the last century has led to the emergence of antimicrobial resistance in medically important bacteria as well as in commensal ones. Antimicrobial resistance has been recognized as one of the greatest threats to human health. The advent of multi-drug resistant bacteria has augmented the problem to an unimaginable level. Therefore, there is an urgent need to develop alternative therapeutic strategies to combat bacterial infections. (Ahmad *et al*. 2021, Salam *et al*. 2023) [1, 57]. Antimicrobial peptides or bacteriocins are one of the promising alternatives to antibiotics, effective against foodborne and spoilage-causing bacteria as well as biofilm-forming bacteria. (Duraisamy *et al*. 2020) [13].

Antimicrobial peptides are small, cationic, amphipathic peptides that are produced by bacteria and are known to inhibit the growth of similar or closely related bacteria. The growing field of health and medical sciences has laid out their promising role in the treatment and therapies of infectious diseases. The major areas where bacteriocins can be employed as potential candidates are food preservation, food packaging, disinfectants, aquaculture, and more recently as superbugs. (Negash & Tsehai, 2020, Heilbronner *et al*. 2021, Darbandi *et al*. 2022) [42, 21, 11] Their applications in the field of oral care products have significantly increased due to the emergence of resistance and the availability of data related to the beneficial effects on oral microflora. In fact, the role of antibiotics may be taken over by bacteriocins due to their slow-acting and narrow-spectrum nature, thus minimizing their side effects on the human body. In addition, they may replace the chemicals involved in processed food required to inhibit pathogenic infections. Given these promising prospects, many propose to investigate the unique properties and potential applications of bacteriocins as antibacterial peptides.

(Heilbronner *et al*. 2021, Palmer and Foster 2022, Soltani *et al*. 2021) [21, 47, 61].

2. Antimicrobial Peptides: Definition and Classification

Antimicrobial peptides (AMPs) are small peptides produced by a wide variety of species, where they play an important role in various aspects of biology, functioning primarily in host defense against various types of microbes. The diverse sources of these peptides highlight their importance and the biological role they play in vivo. AMPs are present in animals, plants, insects, amphibians, and humans, among others. Based on these findings, it can be inferred that AMPs have made their presence felt during the evolution of living beings and that these peptides play a crucial role in host immune mechanisms. In the pharmaceutical industry, AMPs are classified based on their role in microbial prevention or inhibition. Based on the structural characterization, mechanism of action, and origin of peptides, they could be classified as peptides, which include defensins, cathelicidins, magainins, and cecropins, among others. (Lazzaro *et al*., 2020, Bin *et al*. 2021, Huan *et al*., 2020, Sarkar *et al*., 2021) [31, 4, 22, 58].

These AMPs have been found to be cationic and are widely distributed in nature. They are capable of inducing microbial apoptosis in a calcium-dependent manner. The varied action of the peptides against microbes has also been well documented. AMPs act on the microbe by triggering microbial apoptosis and inhibiting microbial proliferation without showing toxicity to the cells. The structural and functional definition of these peptides is well elucidated. In addition, the pharmacological role and clinical application of these peptides have been dealt with (King *et al*., 2020, Raghavan & Kim, 2024, Zhang & Ning, 2021, Khan *et al*. 2023) [28, 52, 74, 26]. Finally, the comparison of these peptides with other antimicrobial agents showed that these peptides have great potential in therapeutic applications. AMPs have a great pharmacological role and are currently being used in various research fields. Furthermore, the emergence of this field is influenced by recently developing anti-infectious peptides or anti-resistance peptides. These peptides, also known as AMPs, play a pivotal role in presenting a future view of the pharmacological industry factoring infectious diseases that are a challenge in recent evolution. Bacteriocins may also be considered in the view of antimicrobial activity and can be considered as an alternative to antibiotics in the future. Based on the review, recent studies of these topics have been summarized and critically analyzed in depth. (Neves, 2022, Pereira *et al*. 2022, O'Connor *et al*. 2020) [43, 50, 46].

3. Bacteriocins: Nature, Types, and Mechanisms of Action

Since the discovery of penicillin in 1935, the use of antimicrobials, also known as antibiotics, has drastically reduced the fatality and morbidity rates associated with infectious diseases. However, microorganisms have developed several mechanisms of resistance against these molecules. Thus, there is an urgent need for novel antimicrobials, among which bacteriocins can serve as an alternative to assist in mitigating this worldwide issue. Bacteriocins are ribosomally synthesized proteins or toxins produced by various bacterial strains. Formerly, bacteriocins were considered antimicrobial agents against bacteria only. However, ongoing research has opened new perspectives, including the existing potential of these peptides for multidirectional use related to human health, food preservation, protection from infections of plant and animal pathogens, and use in therapeutics and veterinary medicine. (Gupta & Sharma, 2022, Gradisteanu *et al*. 2021, Leite *et al*. 2020, Radaic *et al*., 2020) [19, 18, 32, 51].

Although bacteriocins are known for their antimicrobial properties, they can be toxic to other susceptible host cells as well. Therefore, this review focused on the potential direct use of bacteriocins as antimicrobials. They are reported in prebiotics or probiotic health supplements, and their antimicrobial potency against a variety of pathogens has been demonstrated. Moreover, some bacteriocins, such as lantibiotics, have been approved for use as food additives. A bacteriocin is an antimicrobial protein or peptide produced by many of the lactic acid bacteria and a few of the non-lactic acid bacteria (Darbandi *et al*. 2022, Nebbia *et al*. 2020, Fernandes & Jobby, 2022) [11, 41, 14]. They are recognized based on their specific activity, i.e., interference in cell wall biosynthesis or pore formation. Based on their mode of action, bacteriocins have been divided into different categories. Pore-forming bacteriocins are known for their hydrophobic signal and are actively involved in further disintegration, as well as bacterial cell lysis. This is in addition to the enzymatic mode of action. In nature, these bacteriocins give a selective advantage to the producers in their environmental niche. In this context, bacteriocins are discussed from a detailed mechanism of action perspective, which can be beneficial in finding out there in vitro pharmacokinetic values. Also, the text carries details of novel bacteriocin-like molecules as reported to date. (Zimina *et al*. 2020, Antoshina *et al*., 2022, Yi *et al*. 2022) [75, 2, 72].

4. Comparison of Bacteriocins and Antibiotics

Bacteriocins, as microscopic natural peptides, are produced by bacteria and can kill cells of other organisms, including bacteria. Accordingly, bacteriocins belong to a kind of antibiotics, which are produced by microorganisms. Bacteriocin producers have the inherent ability to override the resistance of target bacteria with a higher minimum inhibitory concentration of antibiotics than that of their directly related pathogenic wild-type strains. Moreover, there are several other species of bacteria that produce peptides or proteins with antimicrobial activity similar to that of bacteriocins (Soltani *et al*. 2021, Negash & Tsehai, 2020, Todorov *et al*., 2022) [42, 61, 67]. Nisin, which is produced by L. lactis, is the only commercial bacteriocin added to foods to date, but more bacteriocins may be used in foods in the future. Usually, bacteriocins are produced after host cells are infected by pathogens, suggesting that bacteriocins are related to immunity against infections caused by pathogenic microorganisms. Additionally, there are some types of antibiotic peptides or proteins in mammals. (Ibarra-Sánchez *et al*. 2020, Soltani *et al*. 2021, Khelissa *et al*., 2021) [24, 61, 27]. Bacteriocin peptides, similar to traditional antibiotics from living microorganisms, are effective against the microorganisms tested. Some, but not all, bacteriocins share some similar characteristics, and some bacteriocins have also been studied for some time. Some bacteriocins have also been discovered that are capable of post-translational modification. No bacteriocin was effective against all microorganisms. Do bacteria, like microorganisms, have some kind of resistance to specific bacteriocins? The role of bacteriophages, the broad or narrow effects of specific bacteriocins on non-target cells, and the broad and narrow effects of naturally occurring or commercial antibiotics, or combinations of these, were dealt with in this study. Remember, only the relative magnitude of these was reviewed. (Darbandi *et al*. 2022, Negash & Tsehai, 2020, Nebbia *et al*. 2020) [11, 42, 41].

5. Advantages and Disadvantages of Bacteriocins as Antimicrobial Agents

Bacteriocins as antimicrobial agents promise several benefits. Their potency to inhibit pathogenic bacteria stands at the forefront of these advantages. A review of different studies elucidates their precise antimicrobial activity with a target spectrum against pathogens, leaving nonpathogenic and beneficial flora at peace. Their natural origin presents a possibility to be applied to food procedures, especially as a bio-preservative. They could also be used in short-chain peptide production to be applied in the medical sector like antibiotics, particularly those used against hospital pathogenic bacteria. Their biodegradable and eco-friendly nature is a great asset for their use as antimicrobial peptides. (Choi *et al*. 2023, Tagg *et al*., 2023, Choeisoongnern *et al*. 2023) [8, 64, 7].

The production of bacteriocins by bacteria is a natural function; therefore, the bacteriocins can be classified as generally recognized as safe. The final acceptance of bacteriocins as food and as an alternative to antibiotics would mainly depend on the global policy enforcing agencies. The stability of bacteriocins could be an issue; however, it could be managed by following encapsulation with suitable materials. Switching between different modes of action along with unique structures might establish one of the key factors as to why bacteria can be resistant to bacteriocins. These antimicrobial peptides share both advantages and disadvantages with regard to conventional antibiotic agents. Considering bacteriocins for pharmaceutical or food applications raises ethical and regulatory concerns. Components outlined provide crucial basic knowledge that is important for future improvements related to the field (Zimina *et al*. 2020, Soltani *et al*. 2021, Todorov *et al*., 2022, Negash & Tsehai, 2020) [42, 61, 75, 67]. These significant advantages, however, are associated with some drawbacks, which limit the range of possible applications of bacteriocins or pose challenges associated with their realistic use. The main disadvantage of these compounds is their high cost of production and stability limitations. Proper storage, as well as diversified cases that influence stability, were outlined. Another limitation of bacteriocins is the regulatory framework that governs the authorization of their use in various sectors. At present, the acceptance and commercial use of bacteriocins are limited due to their small spectrum, unexpected loss of action, and unavailability of clinically important bacteriocins. Bacteriocins have a broad range of applications. Standardized regulations, randomized tests, controlling appropriate concentrations and durations in vitro, in vivo, and in the field of therapeutic applications are necessary. Minimum inhibitory and minimum bacteriolytic concentrations provide significant information about minimal dosage and control the duration of treatment in the food and medical sectors. (Zimina *et al*. 2020, Todorov *et al*., 2022, Soltani *et al*.2021, Yi *et al*.2022) [61, 75, 67, 72].

6. Applications of Bacteriocins in Various Fields

Bacteriocins are antimicrobial peptides produced by bacteria to combat other bacteria. Over the years, bacteriocins have made their mark as promising antimicrobial agents. They can be employed in various fields, such as food preservation to inhibit foodborne pathogenic and spoilage microorganisms, the medical field to thwart infections caused by antibiotic-resistant bacteria, animal diets to improve growth performance and control diseases, and plant protection in sustainable farming practices. The use of bacteriocins in different fields is versatile and is an attractive option compared to other biopreservatives because of the broad spectrum antibacterial activities and the multi-mechanistic modes of action. Extended studies suggest that bacteriocin-producing bacteria could be exploited across a diverse set of fields for the greater good of mankind. (Simons *et al*., 2020, Meade *et al*., 2020, Darbandi *et al*. 2022, Radaic *et al*., 2020) [11, 51, 59, 35].

The use of bacteriocins as biopreservatives in the food industry has shown substantial potential for increasing food safety and shelf life, while also reducing the dependency on chemical preservatives. Adjunctive therapy trials using nisin, as well as muramidase-synthesizing bacteriocins, have indicated that combinations of bacteriocins with clinically relevant antibiotics could show encouraging outcomes. Administration of NUK116 in animal diets resulted in a reduction in pathogen load and mortality (Daba *et al*. 2022, Todorov *et al*., 2022, Lahiri *et al*. 2022) [10, 67, 30]. Reports suggest the possible use of bacteriocins to protect against infected hordes of insects and could potentially be exploited in protected agriculture. Supporting reports indicate that the use of bacteriocins is feasible in areas that include veterinary applications. Consumer preference for cleaner labels in foods bolsters the use of bacteriocin-producing probiotics as substitutes for antibiotic growth promoters in animal diets. Several bacteriocins have been assigned Generally Recognized As Safe status and approved as biopreservatives. However, bacteriocins can be proteinaceous moieties and may require further evaluation. Encapsulation strategies are available for enhancing the activity and stability of bacteriocins, ensuring that they retain their efficacy. Regrettably, there are only a few studies of bacteriocin-producing bacteria available for currently utilized applications (Zimina *et al*. 2020, Soltani *et al*. 2021, Todorov *et al*., 2022, Lahiri *et al*. 2022) [61, 75, 67, 30].

7. Bacteriocins in Food Preservation and Safety

Bacteriocinogeny is studied in a variety of bacteria with different taxonomic and ecological characteristics, belonging to different phyla, such as Firmicutes, Actinobacteria, and Proteobacteria, living in diverse food matrices. The objectives focus on the potential of bacteriocins as natural alternatives to prevent the growth of pathogenic and spoilage microorganisms during the shelf life of different types of foods. Due to increasing consumer awareness and interest in a more natural and clean label diet, the food industry has a growing interest in looking for natural alternatives to synthetic antimicrobials (Nisa *et al*., 2023, Mokoena *et al*., 2021, Yu *et al*., 2023) [45, 37, 73]. The use of bacteriocin-producing strains is considered one of the best options for food preservation and for increasing food safety, with broad application possibilities. Food that is safe to consume is free from pathogenic microorganisms or toxic substances, ensuring that the microbiota present will not pose any health risk to consumers. Metabolism and proteolysis of spoilage microorganisms in food matrices cause organoleptic deterioration that affects consumer wellness, leading to economic losses. Pathogenic microorganisms cause the most foodborne diseases. Therefore, the aim of adding bacteriocin to food is to act on two fronts: increase the shelf life of food by enhancing safety and preventing spoilage. Bacteriocin is integrated into food products in different ways to act on the intentional microbiota that contaminates or alters it (Iseppi *et al*., 2021, Todorov *et al*., 2022) [25, 67]. The regulatory status of bacteriocins and the general regulatory framework to validate the safety of these compounds as food ingredients are also considered. Some of the challenges still to be addressed are related to the absence of synergistic effects in some cases between functional foods and other components, as well as the predominance of antimicrobial effects, storage conditions, food matrices, and synergies of efficacy (Soltani *et al*. 2021, Todorov *et al*., 2022, Yi *et al*. 2022) [61, 67, 72].

8. Bacteriocins in Clinical Medicine

The increasing prevalence of multidrug-resistant (MDR) and pandrug-resistant (PDR) strains of Gram-positive and Gram-negative bacteria underscores the urgent need for alternative drugs that act as potential antimicrobial agents. Bacteriocins have attracted new attention as a potential alternative to conventional antibiotics. A new approach in the field of microbe-based products is to specifically develop tailor-made bacteriocins to treat or prevent certain diseases and infections (Soltani *et al*. 2021, Zimina *et al*. 2020, Ruiz-Pérez *et al*. 2024) [61, 75, 56]. These new strategies are expected to provide new bacteriocin-based commercial products that help protect the health and well-being of humans and animals. Various studies have indicated that bacteriocins can exert bactericidal effects against various resistant and non-resistant bacteria and can successfully be used in a wide variety of fields. The bactericidal mechanisms of bacteriocins also contribute to the effectiveness of other antibiotics by disrupting the bacterial cell envelope. This reveals that bacteriocins have the potential for antibacterial treatment in in vivo systems. Targeting Specific Infections. Direct targeting by adjunctive therapies or direct applications of bacteriocins for topical infections will exhibit high effects to kill bacteria and treat infections in situ (Reinseth *et al*.2020)(Pardhi *et al*.2020)(Yehia *et al*.2022)(Bekiaridou *et al*.2021). Synergism with Other Antibiotics. Bacteriocins can enhance the effectiveness of antibiotics. Their bactericidal mechanisms enable them to disrupt the bacterial cell envelope and offer access to the bacterial cell for antibiotics. Biofilm Disruption. A variety of bacteriocins can act against biofilms, increasing the effectiveness of bacteria killing and decreasing the biofilm removal time. Laboratory research studies have demonstrated the successful use of bacteriocins in killing bacteria resistant to currently available antibiotics. However, to ensure that bacteriocins are safe and effective, rigorously controlled clinical trials are required. Further research results have not yet been published or presented (Gradisteanu *et al*.2021)(Bucheli *et al*., 2022) [18]. To get an investigational medication approved for use in patients, it must undergo a rigorous regulatory review process. The regulatory pathway is the means by which the safety and efficacy of an investigational medication are demonstrated. Many other bacterial bacteriocins have entered various stages of development, either independently or in cooperation with larger pharmaceutical companies. The future will likely include some of these treatments becoming approved therapeutics. Moreover, the unique mode of action of bacterial bacteriocins allows the targeting of deadly human pathogens that have worldwide implications. Focusing on these opportunities may represent nagging, highly resistant, unmet medical needs that will also benefit from the therapeutic application of purified bacteriocins. Bacteriocins can cause resistance in bacteria, but it takes an extended period of time, and the time required for resistance to occur could potentially be valuable when used in a clinical setting. While the production of highly purified bacteriocins and the formulation are still significant issues, the promise holds that one new source of antibiotics can be produced relatively easily and inexpensively in the long term (Simons *et al*., 2020)(Zimina *et al*.2020)(Soltani *et al*.2021)(Antoshina *et al*., 2022) [61, 75, 2, 59].

9. Bacteriocins in Agriculture and Plant Protection

The application of bacteriocins as natural products in agriculture to overcome pathogen control of plants is important as farming practices take an environmental turn towards sustainability. It refers to the production of economically feasible goods in an ecologically compatible way consistent with the conservation of soil, water, and genetic resources, as well as the balance of the ecosystem. Biopesticides are rapidly gaining importance for the promotion of biocontrol agents. Bacteriocins have been shown to be promising antibiotics as biocontrol agents in agriculture against many plant-pathogenic bacteria and fungi. Bacteriocins could potentially be used as a more integrated management strategy for the control of pathogens such as Xanthomonas spp., Ralstonia solanacearum, Pseudomonas spp., Acidovorax spp., and Enterobacter cloacae. (Choi *et al*.2023)(O'Connor *et al*.2020)(Darbandi *et al*.2022)(Cesa-Luna *et al*.2021) [11, 46, 8].

Bacteriocins have great potential for enhancing food production, reducing postharvest losses in fruits, vegetables, and tubers, and promoting human health. It is noteworthy to emphasize that the application of bacteriocins in plants to prevent disease and control plant pathogens has many advantages. In addition to a wide range of enzymatic inhibitory spectra against other plant-pathogenic bacteria or fungi depending on the types of bacteriocins, they have relatively high antibacterial, antifungal, and anticandidal activity, low MIC, and small chemical dissipation as a result. Field and especially close field and glasshouse trials have proven the efficacy and potential of the application of bacteriocins as natural antimicrobials to control infected plant diseases. The success of using bacteriocins to control infected plants as a biocontrol agent has already been examined and reported in some cases. (Hefzy *et al*.2021)(Zimina *et al*.2020)(Leslie *et al*.2021) [75].

Most of the bacteriocins exhibited a good level of antibacterial and antifungal activity and low inhibitory concentration against tested fungi, and as a result, the diseases of several host plants were controlled. The average value of reduction in infection damage depends on the type of tested bacteriocin and the host plant. Enhanced growth after light inoculation with pathogens in bacteriocin solution and control of infected host plants has been reported in some studies. Variation in the efficacy level of various tested bacteriocins against human pathogenic bacteria can be clarified with different compounds according to the source of their production (Darbandi *et al*.2022)(de *et al*.2020) [11]. In short, the use of bacteriocins for the control of disease-causing pathogens in plants in the future is an effective and environmentally friendly management practice that can be recommended for both greenhouse and field applications. This method has been successfully evaluated and found to be effective in controlling plant-pathogenic bacterial diseases. Regulatory guidelines should be considered if investment in bacteriocin development as an agricultural biopesticide for plant control is to be pursued in the future (Rooney *et al*.2020)(Rooney *et al*., 2020).

Based on all published reports, the pathogen host, the source of the bacteriocin-producing bacterium/organism, the type of bacteria, and the economic importance of the crop are crucial factors that have a clear impact on bacteriocin production and release by the plant. Used together with other essential parameters in the control of pests and pathogens, such as temperature, humidity, and the host plant's genetic predisposition to infection, bacteriocins could be ideally integrated into an integrated pest management plan holistically. Further in-depth evaluations and verifications of the investigation are recommended in the overall view. (Peng *et al*.2024)(Heilbronner *et al*.2021) [21].

10. Emerging Trends in Bacteriocin Research

The field of bacteriocin research has already shown advancements that are worth noting, and many exciting and innovative changes are leading future trends. Due to the growing interest in the use of microorganisms for the production of bacteriocins, several genetic engineering and synthetic biology techniques can be implemented to improve the yield and activity of these peptides. Moreover, new technologies, called "-omics", are emerging every day that facilitate the screening of diverse microbial sources and result in the finding of novel and potent bacteriocins. Furthermore, bacteriocins have already been included in nanoparticles and other nanotechnologies for improved delivery to target sites, mucosal surfaces, or certain cell types. Collaboration between academia and industry will significantly help in the development of bacteriocin-based products, helping existing bacteriocin research to reach the market for various applications. (Radaic *et al*., 2020)(Sulthana & Archer, 2021)(Mohanty *et al*.2023)(Naskar & Kim, 2021) [51].

Personalized medicine is a current trend in many medical fields, including cancer and immune-related diseases, and can also be applied to antibiotics or bacteriocins. It is believed that at some point in the near future, a patient will be provided with a medicine that treats bacteria present in the gut while keeping the beneficial ones alive and aiding in recovery. It is also believed that in the upcoming future, a standard antibiotic or a bacteriocin will be clinically prescribed for its specific target only. Moreover, new potential future trends include the combination of bacteriocins either with antibiotics or even with probiotics. Novel and exciting stories have been reported on the discovery of new bacterial effector peptides or proteins, but many fields are open and need to be studied, and a range of scientists from different disciplines should be involved. Indeed, the exploration and increasing popularity of bacteriocin research strongly underline the vibrant, dynamic, and evolving nature of this field. (Choi *et al*.2023)(Heilbronner *et al*.2021)(O'Connor *et al*.2020)(Gradisteanu *et al*.2021) [21, 46, 18, 8].

11. Regulatory Considerations and Challenges in Bacteriocin Development

Bacteria developed resistance to potent antibiotics several decades ago, and this resistance is further percolating to other microorganisms, consequently causing antibiotic resistance in pathogens. Consequently, new antibiotics have to be developed, one of the options being bacteriocins. Bacteriocin development is different, and there are specific requirements for obtaining approval, for example, in food safety versus if applied clinically. Regulatory aspects related to bacteriocin development need an understanding of why it has not been successful. For approval as a food biopreservative, it is necessary to ensure that the compound is selectively toxic. As far as application in humans is concerned, it has to be effective. Unfortunately, it is difficult to ensure it will work effectively while conducting a clinical trial, as bacteria will have already developed resistance to it prior to completion of the study. (Terreni *et al*., 2021)(Cook & Wright, 2022)(Nadeem *et al*.2020)(Uddin *et al*.2021)

Currently, no exhaustive clinical trials are being conducted, and hence approvals are being given more with food preservation in mind. However, the subject of bacteriocin stability and bioavailability is relatively less studied, especially as it involves complex details of establishing the bioefficacy and the effect of each and every constituent of the food matrix in the product. Intellectual property based on naturally occurring bacteriocin derivatives is non-existent. On the contrary, the industry faces patent problems based on mutated or partially characterized bacteriocins, without actual improvement of bioactivity (Soltani *et al*.2022)(Flynn *et al*.2021)(Flynn, 2021) [62]. In our view, a researcher from the industry must develop an invention; specifically, if a particular product shows potential, it can be further taken up for preclinical studies. Additionally, grant funding once bacteriocins are available should also be used for oral awareness and public acceptability of this approach. Overall, a one-size-fits-all market and product would not be appropriate in bacteriocin commercialization (Liang *et al*.2024)(Murray *et al*., 2021)(Wei *et al*., 2024).

Bacteriocins are potential natural options; however, several concerns exist regarding their use in food and marketing. For pharmaceutical or medicinal purposes, the creation of stable products will be at a premium to attract private investment and create ownership of the product. As mentioned, one of the difficult aspects in obtaining approval is that the bacteriocins may have to be systemically available to humans to act. Moderated approval norms require systemic activity, and as such, the bioavailability of the bacteriocin must be demonstrated, which is becoming critical. Broadly, there are several issues, namely, many established clinical criteria to fulfill; however, only moderate trials are done in most cases (Soltani *et al*.2021)(Huang *et al*.2021)(Heilbronner *et al*.2021) [21, 61, 23]. Pre-trial bacteriocin resistance is an enormous possibility, especially if the material is a biopreservative in food. Intellectual property development is also severely encumbered. Commercialization in the field of bacteriocins is a future option; stakeholder discussions have already begun. Treatment of bacteriocins as a biopreservative will be a relatively larger market. Public, governmental, and industrial acceptance of bacteriocins and attracting government funding is necessary because the topic is associated with food safety and clinical safety (Todorov *et al*., 2022)(Zimina *et al*.2020) [75, 67].

12. Future Perspectives and Potential Directions in Bacteriocin Research

Given the varied functional and structural diversity and complexity of bacteriocins, continued research on bacteriocins is warranted. One way to gain a better understanding of bacteriocin function is through the use of multidisciplinary approaches. A combination of methods derived from microbiology, molecular biology, and genomics, together with metabolic, adaptive, and evolutionary studies, should be used to further our knowledge of bacteriocin production and function. Classical methods for the detection and isolation of bacteriocins and their genes are not always efficient. Therefore, we anticipate that developments in these directions will make major contributions to the bacteriocin field. (Meade *et al*., 2020)(Lahiri *et al*.2022)(Krishnamoorthi *et al*.2022)(Śmiałek *et al*.2021) [35, 30].

Investigations of bacteriocin production have increased in recent years, and there is an emphasis on the exploration of innovative methods of producing bacteriocins, including new genomic and biotechnological methods of developing bacteriocin-producing bacteria. Currently, antimicrobial peptides have been directed towards the search for new drugs because of the important challenges represented by multidrug-resistant pathogens. However, the exploration of bacteriocins is not limited to human health but impacts other societal sectors, including food technology and agriculture. The application of bacteriocins can be directed towards the development of new technologies, including the production of new food products. Clearly, the discovery of bacteriocins holds many challenges, and the outcomes are promising. Because of this, a multidisciplinary perspective is important for attaining success. There is a need to address obstacles, including ethical considerations in agriculture and clinical trials, the design of strategies to increase investment in these innovative molecular discoveries, and the promotion of partnerships between academia, industry, and regulatory agencies. Finally, recently isolated bacteriocins belong to a broad spectrum of antimicrobial peptides. This may lead one to envisage a therapy based on the active bacteriocins identified in the microbiome of an individual. (Negash & Tsehai, 2020)(Zimina *et al*.2020)(Trejo-González *et al*.2022)(Todorov *et al*., 2022)(Goh *et al*.2022) [42, 75, 67].

13. Conclusion

In an era where antibiotic resistance seems to be becoming a haunting problem and the antibiotic discovery pipeline is drying out, the discovery of new candidate molecules to replace current antibiotics is desperately warranted. Amidst these challenging times, bacteriocins have emerged as promising alternatives. Bacteriocins are unique in their properties, such as broad-spectrum activity, potency, and mode of action, which make them quite interesting as antimicrobials. They have a wide range of applications, including food biopreservation, veterinary fields, oral hygiene, and medicine. Despite being in the market for quite a long time now, the interest in bacteriocin research has embraced new horizons in recent years. Thus, a comprehensive review discussing bacteriocins at length is certainly timely.

Quite a number of bottlenecks are hindering the full realization of bacteriocins from being mere laboratory novelties. These hurdles can be surmounted by performing more research on bacteriocins to understand their potential and start production on a larger scale. Better regulation should be established and surveillance improved to aid in massive application. In conclusion, new promising research with the aim of developing bacteriocins as future antibiotics is warranted. Production on an industrial scale should be more affordable and less time-consuming to have significant effects. Further work on coupling them with other bacteriocins as potential anti-infective agents or with other synergistic molecules should also be addressed. Given their currently incomplete potency, well-orchestrated approaches in consortia and interdisciplinary units can be conducted for bacteriocins to tap their full potential, including academia, industry, and regulatory bodies.

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