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REVIEW ARTICLE **OPEN ACCESS**

Bacteriocins as a New Generation of Anti Microbials

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ABSTRACTS
Antibiotic-resistant bacteria are alarmingly on the rise as a result of decades of antibiotic misuse in the food industry, animal feed, and clinical settings. Antimicrobial-resistant infections kill 700,000 people annually; if current trends continue, 10 million deaths are predicted from these infections by 2050.Therefore, it is essential to find creative solutions to stop antibiotic resistance. A powerful and remarkably diverse array of pharmaceuticals that are entirely different from the antibiotics used today are produced by bacteria. Strong little antimicrobial peptides called bacteriocins are produced by specific bacteria and can serve as a substitute for conventional antibiotics. Commensals, primarily Firmicutes, use these molecules strategically to colonize and survive in the human gut.
Keyword: *Bacteriocin, Gram positive bacteria, Gram negative bacteria*

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INTRODUCTION

Globalization, the use of numerous broad-spectrum medications, and the overuse of antibiotics in both clinical settings and agriculture have all contributed to the emergence of pathogens resistant to one or more antibiotics, making it more difficult to treat common infectious diseases and increasing rates of morbidity and mortality. Three primary categories comprise the mechanisms of drug resistance:
(1) Drug inactivation through irreversible enzymatic cleavage/modification;
(2) Target modification at the antibiotic binding site;
(3) Decreased drug accumulation as a result of decreased permeability or increased drug efflux.
The CDC (Centers for Disease Control and Prevention) 2019 AR (antibiotic resistance) Threats Report classifies antibiotic-resistant microorganisms as urgent threats (drug-resistant Neisseria gorrhoeae, Clostridium difficile, drug-resistant Acinetobacter, and multidrug-resistant Enterobacteriaceae), serious threats (drug-resistant tuberculosis, and drug-resistant Candida auris), and others based on the urgency and severity of the necessary actions. Drug-resistant Enterobacteriaceae that produce Extended-Spectrum Beta-Lactamase (ESBL) in *Pseudomonas aeruginosa* Drug-resistant Shigella, drug-resistant Campylobacter, drug-resistant Salmonella serotype Typhi, and drug-resistant nontyphoidal Salmonella, resistant to drugs Candida resistant to methicillin Concerning threats (clindamycin-resistant group B, *Streptococcus* erythromycin-resistant group), consider *Staphylococcus aureus,* vancomycin-resistant enterococci, and drug-resistant *Streptococcus pneumoniae*. A Streptococcus, as well as watch list items (azole-resistant Aspergillus fumigatus, drug-resistant *Mycoplasma generitalium*, and drug-resistant *Bordetella pertussis*.

REVIEW OF LITERATURE:

Almost a century ago, bacteriocins were first discovered and are made by a diverse range of bacteria and archaea [1], [2], [3], [4]. Chikindas (2018) states that they are a broad family of tiny proteinaceous compounds that, at certain concentrations, show strong antibacterial action and are created by ribosomal synthesis [5]. According to Kanmani, these substances are mostly produced as precursor peptides that lack physiological activity and have an N-terminal leader sequence [6]. Post-translational modifications (PTMs) may occasionally occur in these precursors prior to the leader region being exported from the cell and cleaved [7]. The main target of these bacteriostatic or bactericidal antimicrobial peptides is bacteria that are closely associated with the strain that produced them [8]. However, on occasion, they can also target a larger range of unrelated species [9]. Bacteriocin-producing cells generally put up defenses against being killed by their own bacteriocins, according to de Freire Bastos, Coelho, and da Silva Santos [10]. These processes may involve the production of self-immunity proteins, the action of efflux pumps, or both. Bacteriocins come in several forms and are widely distributed. To chronicle this diversity, our team

developed the integrated publicly accessible databank (www.hammamilab.org), which comprises structural as well as functional data on over two hundred bacteriocins [11]. Over the years, several classification schemes for bacteriocins have been put forth. Indeed, there are many different ways to categorize bacteriocins of lactic acid bacteria (LAB) alone [12]. Numerous changes have been made to these classification schemes in response to new discoveries about the structures as well as mechanisms of action of bacteriocins [13]. The main criterion used to categorize bacteriocins was whether or not they have post-translationally changed motifs. This classification system was developed by Cotter, Ross, and Hill. Its advantages include being simple, user-friendly, and suitable for bacteriocins derived from both Gram-positive as well as Gram-negative bacteria. Furthermore, only short antimicrobial peptides were taken into account in this classification; larger antimicrobial proteins, including Escherichia coli's colicins, were not taken into account. The modified (class I) and unmodified (class II) bacteriocins are merged into two significant classes in this new classification of bacteriocins from Gram-positive and Gram-negative bacteria. This classification, which takes into account recent developments in the field of ribosomally generated and post-translationally modified peptides (RiPPs), is based on these criteria [14]. Class I peptide PTMs have molecular weights <5kDa and are synthesized with the help of certain enzymes generated in the bacteriocin gene cluster. These class I bacteriocins belong to the RiPPs family as a result. The extensive research on the screening, as well as isolation of bacteriocin-producing bacteria from the LAB genera, is demonstrated by the bacteriocin literature review. The GRAS property of the LAB genera and their immediate applicability in the food sectors are probably what led to this research. An antibacterial compound was first claimed to have been found in 1933 by Whitehead H.R. [15]. It comes from *Lactococcus lactis subsp. lactis.* Later on, NISIN (Group N Streptococcus Inhibitory Substance IN) was the name given to this material [16].

Gram-positive bacteria

Since 1988, *Lactococcus lactis* strains have generated nisin A, the most prevalent class I bacteriocin, ribosomally. Nisin A is authorized for use as a food additive by the FDA (Food and Drug Administration). It's categorized as generally accepted to be safe (GRAS). Through a complicated mechanism that includes the insertion of a membrane that results in the formation of pores (bactericidal) and the masking of lipid II that prevents the formation of cell walls (bacteriostatic), nisin A works. Numerous Gram-positive genera, comprising *Bacillus*, *Enterococcus*, *Clostridium difficile*, *Listeria*, and *Staphylococcus,* are impacted by Lipid II, nisin A. Gram-positive bacteria are particularly vulnerable to the effects of bacteriocins because Gram-negative bacteria's outer barrier prevents them from reaching their goal. On the other hand, data indicates that nisin can effectively treat Gram-negative infections when paired with antibiotics. A recent investigation showed the remarkable efficacy of nisin and polymyxin against *P. aeruginosa* biofilms. It was demonstrated that the quantity of polymyxin needed to break the *P. aeruginosa* biofilm was much lowered in the presence of nisin. It's feasible that polymyxin will make nisin's path to its objective easier. Furthermore, studies show that nisin and clarithromycin work together to combat vancomycin-resistant non-lactam antibiotic bacteria, *P. aeruginosa*, and MRSA.

G**ram-negative bacteria**

The 1st report of bacteriocin-mediated inhibition in antagonistic strains of *Escherichia coli* was published in 1925. On the basis of molecular mass, they were separated into two classes: microcins (1–10 kDa) and colicin-like bacteriocins (30 to 80kDa), which are targeted exclusively at *E. coli.* Chromosome-encoded colicines are present in just a small proportion of plasmids. Three domains comprise “these large proteins: an amino-terminal domain that facilitates the target cell's transport across its outer membrane, a carboxy-terminal cytotoxic domain that displays the inhibitory effect, and a receptor-binding domain that mediates the transport into the periplasm. The” three primary mechanisms by which colicins function are nuclease activity, which involves hydrolyzing the target cell's DNA/RNA, pore formation, which compromises “membrane integrity, and suppression of murein synthesis. The strain that produces colicin-like substances develops an immunity protein to defend against its own bacteriocin. Microcins are a class of very effective antibacterial peptides that combine the colicin absorption mechanism with a variety of forms, self-immunity, and the maturation phases of bacteriocins from Gram-positive bacteria. Their tactic is similar to” that of a "Trojan horse" in that they target internal enzymes involved in the synthesis or structure of DNA and RNA while being recognized as siderophores by the outer membrane receptors of vulnerable bacteria. For example, DNA gyrase GyrB (MccB17) inhibits both ATP synthase (MccH47) and RNA polymerase (MccJ25).

CONCLUSION

Bacteriocins have a variety of applications in both medicine and culinary due to their unique properties. As such, it is imperative to thoroughly examine the safety of bacteriocin. Although bacteriocins' antibacterial efficacy has been thoroughly investigated, little is known regarding their toxicity and safety in vivo and in vitro. To ensure their safety, bacteriocins' immunogenicity as well as in vitro and in vivo toxicity must be

investigated. Numerous tests are required to accurately evaluate their cytotoxicity in eukaryotic cells, acute and subchronic toxicity, growth inhibitory effect, apoptosis-inducing capability, hemolytic activity, etc. Before bacteriocins are used in food, livestock, or medicine, health officials demand thorough testing and clinical studies. By carefully following FDA guidelines, bacteriocins should be legally recognized as trustworthy and safe food preservatives or medicinal agents.

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