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An Emerging Approach to Treat the Microbial Infection Based on the Utilization of Bacteriocin's Natural Mode of Action

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Abstract—*Bacteriocins are natural peptides secreted by many varieties of bacteria for the purpose of killing other bacteria. This provides them with a competitive advantage in their environment; eliminating competitors to gain resources. These peptides are ribosomally synthesized. Bacteriocin has been isolated from different habitats like soil, polluted water and various types of food stuffs. They showed antibacterial action against gram positive and gram negative bacteria with different antimicrobial efficacy. The present study aimed to identify the bacteriocin having broad spectrum antimicrobial activity so that these can be used to treat various bacterial infections without any undesirable side effects.*

Keywords*: Bacteriocin, antimicrobial peptides, pathogen,*

1. INTRODUCTION

Bacteriocins are allelopathic, proteinaceous compounds produced by bacteria, which act as anticompetitor toxins against the same or closely related species [1-4]. The term bacteriocin encompasses an array of structurally different molecules produced by a number of phylogenetically distinct Gram-positive and Gram-negative bacterial groups[5]. Bacteriocins may act on cells in a variety of different ways [6]. For example, many bacteriocins, such as mesentericin Y105$ and the B-colicins are membraneactive peptides which act to form pores in the cell membrane of antagonized cells[7]. These compounds cause leakage of ions and other cellular components, and in so doing disrupt the proton motive force, ultimately resulting in cell death [8]. On the basis of structure and mode of action the baceriocins are classified as ClassI, ClassII and clssIII. The Class I exert their effect on cytoplasmic membrane of sensitive cells after binding to specific receptors on outer membrane. They do not lyse cells but inhibit protein synthesis. Example: Pyocin produced by P. aeruginosa. The Class II attack membrane phospholipids, resulting in leakage of intracellular components. Example: Megacin produced by Bacillus megaterium and the Class III bacteriocins are the classic bacteriocins. They are proteins of molecular weight 50000-100000. The structural genes coding for these bacteriocins reside on plasmids. Loss of receptor proteins renders a cell resistant to action by bacteriocin. The cells that produce bacteriocins are immune themselves due to the production of "immunity protein" coded by imm gene. This protein protects itself from its own bacteriocin but also from the bacteriocin produced by related strain or species. Bacteriocin production can be induced in a cell by exposure to certain physical and chemical agents. In contrast to bacteriocins produced by gram negative bacteria, its production cannot be induced in gram positive bacteria. The bacteriocin family includes a diversity of proteins in terms of size, microbial target, mode of action, release, and immunity mechanisms and can be divided into two main groups: those produced by Gram-negative and Gram-positive bacteria [9, 10]

2. BACTERIOCIN OF GRAM -NEGATIVE BACTERIA

Recent surveys of *E. coli*, *Salmonella enterica*, *Hafnia alvei*, *Citrobacter freundii*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, and *Enterobacter cloacae* reveal levels of bacteriocin production ranging from 3 to 26% of environmental isolates [11, 12]. Colicins, bacteriocins produced by *E. coli*, are found in 30–50% of the strains isolated from human hosts and are often referred to as virulence factors [13]. Since their discovery, the colicins of *E. coli* have been the most extensively studied Gram-negative bacteriocins, and they now serve as a model system for investigating the mechanisms of bacteriocin structure/function, genetic organization, ecology, and evolution [14]. Colicins are high molecular weight proteins that kill target cells through a variety of mechanisms. These are usually encoded on one of two types of colicinogenic plasmids. Type A plasmids are small (6 to 10 kb) and present in numerous copies per cell. Type B are monocopy plasmids of about 40 kb, which carry numerous genes in addition to that encoding colicin activity and are able to conjugate. In addition

to colicins, *E. coli* strains produce a second type of bacteriocin, known as microcins, which are smaller than colicins and share more properties with the bacteriocins produced by Gram-positive bacteria, including thermostability, resistance to some proteases, relative hydrophobicity, and resistance to extreme pH [15].

3. BACTERIOCINS OF GRAM –POSITIVE BACTERIA

Bacteriocins of Gram-positive bacteria are as abundant and even more diverse then those found in Gram-negative bacteria. The Gram-positive bacteriocins resemble many of the antimicrobial peptides produced by eukaryotes; they are generally cationic, amphiphilic, membrane-permeabilizing peptides, and range in size from 2 to 6 kDa [16]. They differ from bacteriocins of Gram-negative bacteria in two fundamental ways. First, the bacteriocins produced by Gram-positive bacteria are not necessarily lethal to the producing cell. This critical difference is due to dedicated transport mechanisms Gram-positive bacteria encode to release the bacteriocin toxin. Typically, their biosynthesis is self-regulated with specifically dedicated transport mechanisms facilitating release, although some employ the Sec-dependent export pathway[17]. Second, the Gram-positive bacteria have evolved bacteriocin-specific regulation, whereas bacteriocins of Gram-negative bacteria rely solely on host regulatory networks. Bacteriocins produced by LAB, which have a long history of use in fermentation and meat and milk preservation, are the best characterized of this group. Lactic acid bacteria have been employed for centuries in the fermentation of food, partly due to the fact that they can prevent the growth of spoilage and pathogenic microorganisms[18].

The conventional wisdom about the killing range of Gram-positive bacteriocins is that they are restricted to killing other Gram-positives. The range of killing can vary significantly, from relatively narrow as in the case of lactococcins A, B, and M, which have been found to kill only *Lactococcus*, to extraordinarily broad[19]. For instance, some type A lantibiotics, such as nisin A and mutacin B-Ny266, have been shown to kill a wide range of organisms including *Actinomyces*, *Bacillus*, *Clostridium*, *Corynebacterium*, *Enterococcus*, *Gardnerella*, *Lactococcus*, *Listeria*, *Micrococcus*, *Mycobacterium*, *Propionibacterium*, *Streptococcus*, and *Staphylococcus*[20]. Contrary to conventional wisdom, these particular bacteriocins are also active against a number of medically important Gram-negative bacteria including *Campylobacter*, *Haemophilus*, *Helicobacter*, and *Neisseria*[21].

4. ECOLOGICAL ROLE OF BACTERIOCIN

Early experimental studies on the ecological role of bacteriocins were inconclusive and often contradictory [22]. More recently, a theoretical and empirical base has been established that has defined the conditions that favor maintenance of toxin-producing bacteria in both population and community settings. Almost exclusively, these studies have modeled the action of colicins. Chao and Levins showed that the conditions for invasion of a colicin-producer strain were much broader in a spatially structured environment than in an unstructured one [23]. In an unstructured environment with mass action, a small population of producers cannot invade an established population of sensitive cells. This failure occurs because the producers pay a price for toxin production, the energetic costs of plasmid carriage, and lethality of production, while the benefits, the resources made available by killing sensitive organisms, are distributed at random. Moreover, when producers are rare, the reduction in growth rate experienced by the sensitive strain (owing to extra deaths) is smaller than the reduction felt by the producer (owing to its costs), and the producer population therefore goes extinct [24]. In a physically structured environment, such as on the surface of an agar plate, the strains grow as separate colonies. Toxin diffuses out from a colony of producers, thus killing sensitive neighbors [25]. The resources made available accrue disproportionately to the producing colony owing to its proximity, and therefore, killers can increase in frequency even when initially rare.

5. CONCLUSION

Furthermore, many other bacteriocins may have further as yet undiscovered functions which may increase our understanding of the beneifits of these compounds to the producer. Bacteriocins which exhibit both antimicrobial and other activities represent an efficient use of resources by the cell and a possible reduced burden of their production to the cell. Clearly then, the presence of bacteriocins with multiple functions could result in an overestimation of the fitness costs associated with their production.

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