International Journal of Biotechnology and Biomedical Sciences
p-ISSN 2454-4582, e-ISSN 2454-7808, Volume 4, Issue 1; January-June, 2018 pp. 9-12

http://www.krishisanskriti.org

An Unexplored Potential Source Tracing for Bacteriocin

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Abstract—*The soil microorganisms have been greatly exploited for their antibiotics to combat and destroy disease causing microbes. The water bodies are unexploited sources of biologically active substances. Given the fact that the about 10 million cubic water reservoirs per NHPC project hold great promise of novel pharmacologically active compounds. It was noted that natural sea water killed 80 percent of the organisms in sewage within half an hour and only 4 to 15 percent bacteria formed colonies on nutrient agar prepared with sea water when compared to a similar medium prepared with distilled water. Lacking the properties of bacteriophage, the bactericidal property of sea water was primarily attributed to its content of antibiotic substances produced by microorganisms. Their efficacy and cost-effectiveness contribute to their popularity. Nevertheless, the continuous use of antibiotics has resulted in the emergence of multidrug-resistant microbial strains that no longer respond to antibiotic therapy. A number of strategies have been explored to control microbial pathogens without the use of antibiotics. Bacteriocins are antimicrobial, proteinaceous compounds with a bactericidal mode of action against bacteria closely related to the producer strains. The present paper describe the use of unexplored source for bacteriocin production and their applications.*

1. INTRODUCTION

NHPC (National Hydroelectric Power Corporation) is an Indian Hydropower generation company that was incorporated in the year 1975 with an objective to plan, promote and organize an integrated and efficient development of hydroelectric power in all aspects. Hydropower or water power. The power is derived from the energy of falling water or fast running water, which may be utilized for useful purposes. Enormous amount of water is stored as water reservoir for the production of electricity. A notable amount of microorganism present in the water bodies [1]. The water reservoirs received the water from different sources such as from domestic and fiels and produced colonies on nutrient agar [2]. The microorganism present in the water bodies play key role in various biological processes such as in the degradation of organic matter into simpler components and in the nitrogen cycle. Due the limited availability of the nutrients required by microbial flora some microorganism produced bactericidal molecules for their survival that kill the related species. These molecules are called bacteriocins [3]. The bacteriocins are very potent antimicrobial components having antibacterial anti cancer properties. As the antibiotics are having many side effects and many resistant microbial strains are also emerging due the misuse of antibiotics. The bacteriocins are very promising alternative to antibiotics. The present paper describe the potential use of the water reservoir which was stored by NHPC for electricity production could be a potential pool for the bacteriocin production that can be an alternative to antibiotics and promising agents as an anticancer agents[4,5]

2. WATER RESERVOIR AND MICROBIAL FLORA

These organisms have a key role in the nitrogen cycle and are involved in biological processes. Bacteria play the central role in natural self-purification by decomposing organic matter into its inorganic components which are then recycled. *Pathogenic organisms, bacteria, and viruses* are of particular concern in lakes and reservoirs used as a source of potable supply or for bathing. In the case of potable supplies, modern water treatment processes, including disinfection, ensure that sources are well protected and that any pathogens present are removed by filtration or killed.

Cyanobacteria are an important group of plants often appearing a dominant part of the phytoplankton of lakes and reservoirs. They tend to form a dense surface bloom rising to the surface and drift to form massive suspensions [6].

3. BACTERIOCINS

Bacteriocins were first identified almost 100 years ago as a heat-labile product present in cultures of *Escherichia coli* V and toxic to *E. coli* S and were given the name of colicin to identify the producing species[7]. Frederick demonstrated that collisions were proteins and that they had a limited range of activity due to the presence or absence of specific receptors on the surface of sensitive cells [8]. Since then, bacteriocins have been found in all major lineages of Bacteria and, more

recently, have been described as universally produced by some members of the Archaea[9]. According to Klaenhammer, 99% of all bacteria may make at least one bacteriocin, and the only reason we have not isolated more is that few researchers have looked for them. Two main features distinguish the majority of bacteriocins from classical antibiotics: bacteriocins are ribosomally synthesized and have a relatively narrow killing spectrum [10].

3. 1Classification of bacteriocins

Bacteriocins are categorized in several ways, including producing strain, common resistance mechanisms, and mechanism of killing. There are several large categories of bacteriocin which are only phenomenologically related. These include the bacteriocins from gram-positive bacteria, the colicins[11] the microcins, and the bacteriocins from Archaea. The bacteriocins from *E. coli* are called *colicins* (formerly called 'colicines,' meaning 'coli killers'). They are the longest studied bacteriocins. They are a diverse group of bacteriocins and do not include all the bacteriocins produced by *E. coli.* In fact, one of the oldest known so-called colicins was called *colicin V* and is now known as *microcin V*. It is much smaller and produced and secreted in a different manner than the classic colicins. Bacteriocins that contain the modified amino acid lanthionine as part of their structure are called lantibiotics. However, efforts to reorganize the nomenclature of the family of ribosomally synthesized and post-translationally modified peptide (RiPP) natural products have led to the differentiation of lantipeptides from bacteriocins based on biosynthetic genes [12].

3.2 Bacteriocins from Gram Negative Bacteria

Gram negative bacteriocins are typically classified by size. Microcins are less than 20 kDa in size; colicin-like bacteriocins are 20 to 90 kDa in size and tailocins or so called high molecular weight bacteriocins which are multi subunit bacteriocins that resemble the tails of bacteriophages. This size classification also coincides with genetic, structural and functional similarities.

3.2.1Microcins

Microcins produced by commensal *E. coli* strains target and eliminate enteric pathogens such as *Salmonella entertica* by mimicking the siderophores the pathogens use for iron scavenging. Microcins also help commensal strains of *E. coli* outcompete pathogenic strains[13,14]

BACTIBASE[15,16] database is an open-access database for bacteriocins including microcins.

3.2.2Colicin-like Bacteriocins

Colocins are bacteriocins (CLBs) found in the Gram-negative *E. coli*. Similar bacteriocins occur in other Gram-negative bacteria. These CLBs are distinct from Gram-positive bacteriocins. They are modular proteins between 20 and 90 kDa in size. They often consist of a receptor binding domain, a translocation domain and a cytotoxic domain. Combinations of these domains between different CLBs occur frequently in nature and can be created in the laboratory. Due to these combinations further subclassifaction can be based on either import mechanism (group A and B) or on cytotoxic mechanism (nucleases, pore forming, M-type, L-type)[17].

3.2.3Tailocins

Most well studied are the tailocins of pseudomonaeroginosa can be further s ubdivided into R-type and F-type pyocins[18].

3.3 Bacteriocins from Gram Positive Bacteria

Bacteriocins from Gram positive bacteria are typically classified into Class I, Class IIa/b/c, and Class III.

3.3.1Class I bacteriocins

The classI bacteriocins are small peptide inhibitors and include nisin and other lantibiotics.

3.3.2Class II bacteriocins

The class II bacteriocins are small (<10 kDa) heat-stable proteins. This class is subdivided into five subclasses. The class IIa bacteriocins (pediocin-like bacteriocins) are the largest subgroup and contain an N terminal consensus sequence -Tyr-Gly-Asn-Gly-Val-Xaa-Cys across this group. The C-terminal is responsible for species-specific activity, causing cell-leakage by permeabilizing the target cell wall. Class IIa bacteriocins have a large potential for use in food preservation as well medical applications due to their strong anti listeria activity and broad range of activity. One example of Class IIa bacteriocin is pediocin *PA-1*[19]. The class IIb bacteriocins (two-peptide bacteriocins) require two different peptides for activity. One such an example is *lactococcin G*, which permeabilizes cell membranes for monovalent sodium and potassium cations, but not for divalent cations. Almost all of these bacteriocins have a GxxxG motifs. This motif is also found in transmembrane, where they are involved in helix-helix interactions. Accordingly, the bacteriocin GxxxG motifs can interact with the motifs in the membranes of the bacterial cells, killing the cells[20]. Class IIc encompasses cyclic peptides in which the N-terminal and c terminal regions are covalentely linked. *Enterocin AS-48* is the prototype of this group. Class IId cover single-peptide bacteriocins, which are not post-translationally modified and do not show the pediocin-like signature. The best example of this group is the highly stable *aureocin A53*. This bacteriocin is stable under highly acidic conditions, high temperatures, and is not affected by proteases[21].

The most recently proposed subclass is the Class IIe, which encompasses those bacteriocins composed by three or four non-pediocin like peptides. The best example is *aureocin A70*, a four-peptide bacteriocin, highly active against Listeria

monocytogenes with potential biotechnological applications [22].

3.3.3Class III bacteriocins

Class III bacteriocins are large, heat-labile (>10 kDa) protein bacteriocins. This class is subdivided in two subclasses: subclass IIIa or bacteriolysins and subclass IIIb. Subclass IIIa comprises those peptides that kill bacterial cells by cell wall degradation, thus causing cell lysis. The best studied bacteriolysin is lysostaphin, a 27 kDa peptide that hydrolises the cell walls of several *Staphylococcus* species, principally *S aureus* [23]. Subclass IIIb, in contrast, comprises those peptides that do not cause cell lysis, killing the target cells by disrupting the membrane potential, which causes ATP efflux.

3.3.4 Class IV bacteriocins

Class IV bacteriocins are defined as complex bacteriocins ontaining lipid or carbohydrates moieties. Confirmation by experimental data was established with the characterisation of sublancin and glycocin F (GccF) by two independent groups[24,25].

4. MODE OF ACTION OF BACTERIOCINS

A widely accepted hypothesis for the mode of action of bacteriocins is that the bacteriocin acts in two steps, involving adsorption of the bacteriocin to specific or nonspecific receptors on the cell surface resulting in cell death[26]. Several other general observations may be made which apply to the antibacterial activities of the low-molecular-weight bacteriocins: (i) within a given species, some strains may be sensitive and others may be resistant to a particular bacteriocin; (ii) a strain that appears to be sensitive to a bacteriocin may also have some cells in the population that are resistant to it; (iii) a strain can be sensitive to one bacteriocin while being resistant to a similar type of bacteriocin; (iv) cells of a strain producing one bacteriocin can besensitive to another bacteriocin;(v) although the spores of a strain whose cells are sensitive to a bacteriocin are resistant to that bacteriocin, they become sensitive following germination; (vi) under normal conditions, gram-negative bacteria are not sensitive to bacteriocins produced by gram-positive bacteria[27].

5. APPLICATION AND FUTURE PROSPECTS

Many, if not most of the presently known bacteriocins were first discovered and studied as antimicrobials. There are also reports on bacteriocins inhibiting quorum sensing in various microorganisms at sub-MIC concentrations [28]. While the primary application of bacteriocins has always been in food preservation[29], antimicrobial resistance to conventional antibiotics presents new opportunities for the exploration of bacteriocins' application in a variety of healthcare products where undesired and potentially resistant microorganisms must be controlled[30]. The National Institute of Health (NIH) recently encour- aged a complementary approach in searching for novel drug formulations, where the activity of conventional antimicrobials can be enhanced when combined with novel and, often naturally derived, antimicrobials[31]. A multipronged approach utilizing synergistically acting antimicrobials with different targets in controlled bacteria has been studied for many years. Different bacteriocins were reported as acting synergistically with various food-grade substances and with bacterio- phages[32,33]. Water reservoir could be utilized as o potential source for the use of microorganism that produce bacteriocins so that health benefits could be provided to mankind.

6. CONCLUSION

Bacteriocins are one of many natural defense mechanisms bacteria use to compete against microorganisms in the same environment. Since the first discovery of nisin, many bacteriocins with unique structures and different modes of activity have been described, and the genes coding for the production, secretion and immunity of most have been reported. During the last decade, many investigators shifted their focus on bacteriocins for food preservation to the treatment of infections and antibiotic-resistant disease-causing bacteria. This exciting new era of bacteriocin research will undoubtedly lead to new inventions and new applications. With the rapid rate at which genome sequences are becoming available, genome mining becomes easier, and with the latest techniques in gene synthesis and protein expression, we can look forward to novel bacteriocins with very dedicated applications.

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