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Review article

APPLICATIONS OF THE BACTERIOCIN, PEDIOCIN

Anu[1] and Harjinder Singh[2]

[1]Department of Biotechnology, S.D. College, Hoshiarpur
[2]Department of Agriculture, Government College, Hoshiarpur

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ABSTRACT

Bacteriocinshave long been studied for their potential use in food industry as biopreservative and in pharma sector to be used as an alternative to antibiotics. The bacteriocin, pediocin produced by *Pediocccus* spp. has various biopreservative and biomedical applications. In this review, the future perspectives of pediocin use as biopreservative, as antineoplastic agent, as antimicrobial food packaging systems, in ulcer treatment and other has been discussed.

INTRODUCTION

Bacteriocins, natural peptides, secreted by many varieties of bacteria can be used for killing other bacteria and thus can be used to treat many types of infections. The bacteriocins have been classified into various classes according to their size, structure and modifications (Klaenhammer, 1993, Nes *et al.,* 1996, and Cotter *et al.,* 2005). Class I bacteriocins include the lantibiotics, which are highly post-translationally modified peptides, whereas class II consists of small peptides that do not contain modified residues (Cotter *et al.,* 2005). The class II bacteriocins are further Subdivided into three categories, Class IIa bacteriocin (Hechard *et al*., 1992) which are pediocin like peptides and are strongly cationic in nature, Class IIb bacteriocin which consist of pore-forming complexes requiring two peptides for their activity e.g. enterocin L50A and L50B (Cintas *et al.,* 1998) and Class IIc bacteriocin include all class II bacteriocins that do not fall into class IIa and IIb (Ennahar *et al.,* 2000). The class III bacteriocins are large bacteriocins e.g. helveticin J, lacticin A and B (Jack *et al.,* 1995). The class IV bacteriocins consist of glycoproteins (lactocin 27), lipoproteins (lacstrepcins) that require non-protein moieties for their activity (Ennahar *et al.,* 2000). The class V bacteriocins consist of circular bacteriocins of 49-108 kDa, carrying two transmembrane segments and have been described in BAGEL database.

Many Lactic acid bacteria produce the pediocin-like bacteriocins (36-48 residues) and share a 40-60% amino acid similarity (Papagianni, 2003). Pediocin are synthesized with a leader peptide attached which is removed by proteolytic cleavage after a double gycine residue in pediocinAcH and pediocin PA-1 (Ray, 1995). These bacteriocins are heat stable and are not post-translationally modified beyond the cleavage of leader peptide (Yamazaki *et al.,* 2005). These bacteriocins are particularly potent inhibitors of *Listeria* sp. showing its activity at low nanomolar concentrations (Cintas *et al.,* 1998). This class of bacteriocins kill susceptible bacteria by forming pores in their membranes, resulting in the loss of the proton motive force (PMF) and depletion of ATP (Ennahar *et al.,* 2000). It is thought that these cationic bacteriocins are first drawn to bacterial cells through an initial electrostatic interaction (Chen *et al.,* 1997). After the initial interaction, the amphiphilic C-terminal α-helix inserts into the membrane, wherein the bacteriocin then induces the formation of hydrophilic pores. This mechanism relies on a mannose phosphotransferase (MPT) protein complex found in the membranes of susceptible organisms, but the exact nature of this mechanism is not clear (Dalet *et al.,* 2001, Diep *et al.,* 2007 and Kjos *et al.,* 2010).

Corresponding author:* **Anu
Department of Biotechnology, S.D. College, Hoshiarpur

Class Class IIa bacteriocin have major applications in biopreservation, but these can also be used as therapeutic agents. These are active against several food-borne pathogens such as *Listeria monocytognes*, *Bacillus cereus, Clostridium botulinum* and *C.perfringens* (Cintas *et al*., 1998). Class IIa bacteriocins are also active against other human pathogens, such as vancomycin-resistant enterococci (Millette *et al.,* 2003) and the opportunistic pathogen *Staphylococci aureus* (Cintas *et al.,* 1998). Some Gram-negative opportunistic pathogen *Aeromonas hydrophila* is also inhibited by these bacteriocins (Elegado *et al.,* 1997). These bacteriocins also show potentially therapeutic properties as antineoplastic (Beaulieu, 2004 and Cornut *et al.,* 2008) and antiviral agents (Todorov*et al.,* 2010).

Biopreservative Potential of Pediocin

Biopreservation refers to the extension of the shelf life and improvent of the safety of foods using microorganisms and their metabolites (Ross *et al.,* 2002). Bacteriocins have a high commercial importance because of their antimicrobial activties. Among these nisin have major applications as biopreservative in food industry. Pediocins have strong inhibitory effect on the growth of *L. monocytogenes* (Hechard *et al.,* 1992). Pediocin produced by *Pediococcus acidilactici* PA-2 has been used as a bacteriocinogenic protective culture in dry fermented sausages (Lahti and others, 2001). Pediocin produced by Pediococcus acidilactici BA 28 has shown to inhibit the growth of microorganisms in different food samples (Garg and Kaur, 2015). PediocinAcH was reported to be inhibitory to several food pathogens like *Staphylococcus aureus, C. perfringens* and *L. monocytogenes* (Bhunia *et al.,* 1988). PediocinAcM (Elegado *et al.,* 1997), Pediocin JD (Berry *et al.,* 1991) and Pediocin L50 (Cintas *et al.,* 1995) have also shown activity against foor borne pathogens.

Antimicrobial Food Packaging Systems

The antimicrobial food packaging increases the shelf life, safety and quality of many food products as they have great potential to reduce microbial growth in non-sterile foods and minimize the hazard of post-contamination in sterile ones (Hotchkiss, 1997). Natural antimicrobial food packaging agents such as bacteriocins are of increased interest these days. Nisin has been extensively studied bacteriocin for their use in antimicrobial food packaging system. Other bacteriocins such as lactocin 705 and lactocin AL 705, enterocins A and B, sakacin K, pediocin produced by *Pediococcus sp.*, lacticin 3147 and nisaplin are used in the development of antimicrobial packaging systems (Abreu *et al.,* 2013).

Antineoplastic Activity of Pediocin

Conventional chemotherapeutic drugs have been used so far. The main concern is that the cancer cells frequently become resistant to chemotherapy due to various factors such as increased expression of drug transporters and the various drug detoxifying enzymes and also due to the increased ability to repair DNA defects in cellular machinery that mediate apoptosis (Raguz and Yague, 2008). Antineoplastic properties of various bacteriocins such as colicins (Chumchalova and Smarda, 2003), microcin (Hertz *et al.,* 2002), pediocin (Beaulieu, 2004) and pyocin (Abdi-Ali *et al.,* 2004) has been established in breast carcinoma, breast adenocarcinoma, ostreosarcoma, leiomyosarcoma, fibrosarcoma, T cell lymphoma, cervix carcinoma, Burkitt lymphoma, pulmonary carcinoma, colon adenocarcinoma, lymphoblastic leukemia and hepatocarcinoma. The cytotoxic effects of bacteriocins on cancerous cells from human origin were also reported earlier (Farkas-Himsley and Cheung, 1975). The bacteriocins interact with the cell surface of the target cells without penetrating into it, yet affecting cell division and DNA synthesis (Jayawardene and Farkas-Himsley, 1969). The membrane interactions between bacteriocin and the target cells are highly specific which is related to the unique receptors (Nomura, 1967). Experiments with Rec-Pediocin CP2 have shown its cytotoxicity against cancerous cell lines which is attributed through the induction of programmed cell death or apoptosis (Kumar *et al.,* 2012).

Immunomodulatory Role of Pediocin And Use As Probiotic

Probiotics are live microorganisms, which when consumed in adequate amounts can provide health benefits to the host (Pineiro and Stanton, 2007). They enhance or maintain the ratio of beneficial to undesirable components in the human gastrointestinal microbiota (O'Hara and Shanahan, 2007). Bacteriocin production has been an important criterion to select the probiotic strain as the impact of bacteriocin production on the ability of a strain to compete within the GI tract and positively influence the health of the host (Corr *et al.,* 2007). A pediocin-producing strain of *Pediococcus acidilactici*, able to survive in the gastrointestinal tract, was found to be an effective inhibitor of several Gram-positive bacterial pathogens, such as *Enterococcus* spp. and *Listeria monocytogenes.* It also inhibited gastric adhesion of opportunistic pathogens from *Klebsiella, Pseudomonas,* and Shigella genera (Speelmans *et al.,* 2006 and Piva *et al.,* 2006). *In vitro* inhibitory activity of pediocin producing probiotic *pediococcus acidilactici* BA28 was evaluated against *Helicobacter pylori* which is the causative agent of peptic ulcers. A probiotic treatment with this pediocin can be used to eliminate *H. pylori* infection and reverse peptic ulcer disease in future (Kaur*et al.,* 2014). *Pediococcus pentosaceus* OZF has also shown immunomodulatory functions *in vivo* and can be used as a probiotic (Osmanagaoglu *et.al.,* 2012).

Spermicidal Action of Pediocin

Various contraceptive chemical spermicides are available, however they have side effects such as vaginal infections due to removal of flora, weakening the natural protection and promoting urinary tract infections (Balzaretti *et al.,* 2015). Bacteriocins have ability to affect the sperm motility and thus can be used as potent spermicidal agents (Kumar *et al.,* 2012). Spermicidal activities of native and recombinant pediocin CP2 have been evaluated (Kumar *et al.,* 2012).

Pediocin in Women Care

Various microorganisms are involved in vaginal infections and bacteriocins can be used against them. Pediocin produced by *Pediococcus pentosaceus* SB83 (Borges *et al.,* 2013), enterocin 62-6, two peptides produced by *E. faecium* (Dezwaan *et al.,* 2007) and lactocin 160 (a peptide like bacteriocin) produced by *Lactobacillus rhamnosus* have exhibited effective action against *G.vaginalis* and *Prevotellabivia, Bacteroides, Peptostreptococcus* and *Mobiluncus* spp.

Pediocin against Bovine Mastitis

Bovine mastitis is defined as the inflammation of the mammary gland (Turovskiy *et al.,* 2009) and is characterized by physical, chemical and usually bacteriological changes in milk and pathological changes in glandular tissues of the udder and affects the quantity and quality of milk (Radostits *et al.,* 2000 and Sharma *et al.,* 2012). Pediocin produced by *Pediococcus pentocaceus* SA131 (isolated from jeotgal) has shown activity against bovine mastitis pathogens, *Streptococcus uberis* E290, *Enterococcus gallinarum* E362, and *Staphylococcus epidermis* ATCC 12228 (Park *et al.,* 2017).

Use of Pediocin in Animal Feedstuff

To improve the performance in the animal feed sector, antibiotics are mainly used, but there is a risk regarding the resistance of bacteria to these antibiotics. Therefore, pediocin can be used with other feed additives according to U.S. Patent no. 0176910A1 which improves the hygienic status and performance in agricultural livestock (Razek, 2002).

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