LACTICIN: APPLICATIONS AND FUTURE PERSPECTIVE

Anu

Assistant Professor, Department Of Biotechnology, S.D. College, Hoshiarpur

Kanwardeep Singh Dhaliwal

Assistant Professor, Department Of Biotechnology, S.D. College, Hoshiarpur

Phulan Rani

Assistant Professor, Department Of Agriculture, Ggdsd College, Hariana

ABSTRACT

Bacteriocins have been extensively studied for their potential use in food industries as Biopreservative and pharma companies to be used as an alternative to antibiotics. The bacteriocin, Lacticin produced by Lactococcus lactis has various Biopreservative and biomedical applications. In this review, the future perspectives of Lacticin use as biopreservative, in skin care, as probiotic, as antimicrobial food packaging systems and others has been discussed.

Keywords*: Lactococcus, class II bacteriocins, aschronic gastritis, homeostasis.*

INTRODUCTION

Bacteriocins are natural peptides, secreted by many varieties of bacteria and can be used for killing other bacteria. Thus, bacteriocins 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). There are five classes of bacteriocins. Class I bacteriocins include the lanthionine containing bacteriocins called lantibiotics which include both single peptide (Nisin A, Mersacidin, Lacticin 481) and two peptide (lacticin 3147, Cytolysin) lantibiotics. This class of lantibiotics contain upto 11 subclasses (Cotter *et al.*, 2005). Class II bacteriocins consist of small peptides that do not contain modified residues (Cotter *et al.*, 2005) and these 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 consist of pore forming complexes requiring two peptides for their activity e.g. Enterocin L50A and L50B (Cintas*et al.*, 1998) and Class IIc bacteriocins include all class II bacteriocins that do not fall into other subcategories of classII (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 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.

Lacticins are Class I bacteriocins produced by *Lactococcus lactis*. Lacticin 3147 and Lacticin 481 lantibiotic bacteriocins have been shown to have antimicrobial activity against a wide range of microorganisms. Lacticin 3147, a Class I , two component bacteriocin is produced by *Lactococcus lactis* subsp.*lactis,* isolated from an Irish kefir grain have activity against a broad range of organisms and potentially suitable for several food applications (Mcauliffe O, Ryan MP *et al.*, 1998). A bacteriocin Lacticin Z produced by *Lactococcus lactis* QU14 have been shown to have activity against numerous Gram positive bacteria (Iwatani S *et al.*, 2007). Lacticin 481 is a single peptide lantibiotic that exhibits a medium spectrum of inhibition mainly active against other LAB (O'Sullivan *et al.*, 2003). The mode of action of the two component lantibiotic has also been determined. The lantibiotic Lacticin 3147 exhibits bactericidal activity against a broad range of Gram positive bacteria, which is enhanced when target cells are energised. The pores formed by Lacticin 3147 were shown to be selective for ions and not for larger compounds such as ATP molecules. The resultant loss of ions results in immediate dissipation of the $\Delta\psi$ and hydrolysis of internal ATP, leading to the eventual collapse of the differential pH and ultimately to cell death (McAllife *et al.*, 2001).

BIOPRESERVATIVE POTENTIAL

Biopreservation means to extend the shelf life of the food with the use of microorganisms and their metabolites (Ross *et al*., 2002). Among these bacteriocins, Lacticin is extensively used for biopreservation in dairy products. Lacticin 3147 produced by certain strains of *Lactococcus lactis* was isolated from an Irish Kefir grain used for making buttermilk (Mcauliffe *et al.*, 1998). Lacticin exhibit antimicrobial activity against a variety of food pathogenic and food spoilage bacteria in addition to other LAB (Sobrino-lopez and Martin-Belloso, 2008; Martinez-Cuesta *et al*., 2010). A Lacticin 3147 powder preparation have shown effective against *Listeria* and *Bacillus* in infant milk formulations, cottage cheese and natural yoghurt (Morgan *et al.*, 2001). Lacticin 3147 produced by *Lactococcus lactis* IFPL 3593 was shown to inhibit the germination of clostridia spores and prevent late blowing in semi hard cheese. Thereby, this strain use to prevent late blowing in cheese represents a promising alternative to the addition of lysozyme particularly due the increasing concerns regarding the potential allergenicity of this additive (Carmen *et al.*, 2010). The lytic ability of bacteriocin like Lacticin 3147 might be explored in the acceleration of cheddar cheese ripening and the cell lysis of the starter culture is advantageous for improved flavour development (Guinane *et al.*, 2005).

Lacticin 481 is a single peptide lantibiotic that exhibit antimicrobial activity against other LAB, *Clostridium tyrobutyricum* (O'Sullivan *et al.*, 2003) and *L. monocytogenes* (Ribeiro *et al.*, 2016). The non-purified lacticin 481 was shown mild bacteriostatic activity in milk stored at refrigeration temperatures (Arques *et al.*, 2011). Whereas, the application of semi- purified lacticin 481 to fresh cheeses stored at refrigeration temperatures reduced further the growth of *L. monocytogenes* (Ribeiro *et al.*, 2016).

ANTIMICROBIAL FOOD PACKAGING SYSTEMS

The antimicrobial food packaging increases the shelf life and safety of many food products as they have great potential to reduce the microbial growth in non-sterile foods and also minimize the hazard of post-contamination in the sterile ones (Hotchkiss, 1997). Natural antimicrobial agents such as bacteriocins are of great interest these days. Nisin has been extensively studied bacteriocin for their use in antimicrobial food packaging system, but other bacteriocins are also of interest. These bacteriocins such as Lactocin 705, Enterocins A and B, Sakacin K, Pediocin and Lacticin 3147 are used in the development of antimicrobial food packaging systems (Abreu *et al.*, 2013).

TREATMENT OF PEPTIC ULCERS

Gastric colonization of *Helicobacter pylori* causes upper gastrointestinal disorders such as aschronic gastritis, peptic ulcer diseases, tissue lymphoma and gastric cancer (Correa 1992; Isreal and Peek 2001; Kusters *et al.*, 2006). *Helicobacter pylori* is able to survive the acidic gastric conditions and also able to colonize in these areas (Salama *et al.*, 2001). Proteins CagA and VacA secreted by the bacterium increases its virulence by evoking the immune responses such as inflammatory response, promoting activation and proliferation of T-cells, causing vacuolization in epithelium cells (Cover and Blaser 1992, 2005; Kuiper *et al.,* 1995; Peek *et al.,* 1995; Salama *et al.,* 2001). Nisin and Lacticin BH5 and Lacticin A164 inhibited the growth of *Helicobacter pylori in vitro* and may thus be used in the treatment of peptic ulcers (Delves-Broughton *et al.,* 1996; Kim *et al.,* 2003).

VETERINARY USE

Bovine mastitis is the inflammation of the mammary glands (Turovskiy *et al.,* 2009) and is physical, chemical and bacteriological in milk of the bovine and pathological changes in the glandular tissues of the udder and affects the quantity and quality of the milk (Radostits *et al.,* and Sharma *et al.,* 2012). In dairy animals, Nisin A, Lacticin 3147, Aureoicin A70, Nisin Z and Macedocin ST91KM have tested to control mastitis which causes great economic losses in the dairy industry by affecting the yield of the milk (Ceotto H *et al.,*2012, Pieterse *et al.,* 2010 and Wu J *et al.,* 2007). Lacticin 3147 have proved to be effective in the treatment of bovine mastitis and also shown to have activity against mastitic staphylococci and streptococci (Ryan *et al.,* 1999).

SKIN CARE USE

Bacteriocins for skin care have been marketed by LABs probiotic producers in topical formulations which also have anti-aging benefits (Cinque *et al.,* 2011). There are different commercial options to prevent and treat skin diseases including external signs of aging, acne, bacterial and yeast infections, psoriasis and dermatitis. Current research based on the concerning bacteriocins suggests that they contribute to the modulation of the normal microflora of skin, skin lipids and the immune system which leads to the preservation of natural skin homeostasis (Brown AF, Leech JM, Rogers TR *et al.,* 2014). Salivaricin, Nisin A, Mersacidin, Lacticin 3147 and Leucocin A represent a lead to cure infections caused by multiresistant bacteria. They also have been used against *Propionibacterium acnes* responsible for the pathogenic acne vulgaris and are also used as immune modulators in hospital infections of skin and mucosal wounds (Bowe *et al.,* 2014; Chung WO *et al.,* 2011).

AGAINST SYSTEMIC INFECTIONS

S. aureus, Listeria monocytogenes, and *P. aeruginosa* are often associated with the systemic infections (Czuprynski *et al.,* 2002; Drake and Montie 1988; Harbarth *et al.,* 1998; Klug *et* *al.*, 1997). *Clostridium perfringens*, *Salmonella* spp., *Staphylococcus aureus*, *Helicobacter sp.*, *E. coli,* and *Listeria monocytogenes* are the most prominent bacteria causing gastrointestinal disorders and food poisoning (Tyopponen *et al.*, 2003). Lacticin 3147 acts against *Staphylococcus aureus* and MRSA strains (Galvin *et al.*, 1999, Limbert *et al.*, 1991).

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