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Review

Antimicrobial potential of bacteriocins: in therapy, agriculture and food preservation

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ABSTRACT

Due to the appearance of antibiotic resistance and the toxicity associated with currently used antibiotics, peptide antibiotics are the need of the hour. Thus, demand for new antimicrobial agents has brought great interest in new technologies to enhance safety. One such antimicrobial molecule is bacteriocin, synthesised by various micro-organisms. Bacteriocins are widely used in agriculture, veterinary medicine as a therapeutic, and as a food preservative agent to control various infectious and food-borne pathogens. In this review, we highlight the potential therapeutic and food preservative applications of bacteriocin.

1. Introduction

Many microbes produce important metabolites such as acids, alcohols, diacetals and various antibiotics such as inhibitory proteinaceous molecules commonly called bacteriocins [1,2]. Bacteriocins are ribosomally synthesised antimicrobial peptides or complex proteins secreted by various Gram-positive and Gram-negative bacteria [3]. The bacteriocins from many bacteria have been reported to be active against human and animal microbial pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE) without showing toxicity [4–12]. The advantages of bacteriocins are their physical stability and non-toxicity [13]. Numerous bacteriocins have been recovered for their remarkable potential as food preservatives [14] or as therapeutic or bio-controlling agents [15–17].

2. Physicochemical classification of bacteriocins

Bacteriocins can be ranked according to their biochemical and genetic characteristics or the presence of disulphide or monosulphide bonds, molecular weight, heat stability, proteolytic enzyme stability, presence or absence of post-translational modification of amino acids, and antimicrobial action [18] (Fig. 1).

2.1. Class I bacteriocins

Class I bacteriocins are small peptides/lantibiotics (<5 kDa, 19–37 amino acids) with the unusual amino acids lanthionine and methyllanthionine in their primary structure. Nearly 60 lantibiotics are known and 30% [19] are purified from lactic acid bacteria [19,20]. These bacteriocins are post-translationally modified, heat-stable peptides and generally act by targeting the skeleton of the cell wall of pathogens, particularly Gram-positive bacteria [21,22].

The enzyme LanC cyclase, encoded by the *lanC* gene, catalyses the formation of lanthionine and methyllanthionine via cyclisation of cysteine onto 2,3-dehydroalanine (Dha) and (*Z*)-2,3-dehydrobutyrine (Dhb) [23,24].

2.1.1. Subclass Ia bacteriocins

These peptides are positively-charged elongated bacteriocins that kill bacteria by pore formation. The prototype antibiotic nisin is a member of this group [24,25].

2.1.2. Subclass Ib bacteriocins

These bacteriocins, including lacticin 481, cytolysin and salivaricin, are characteristically globular, inflexible, with a negative charge or

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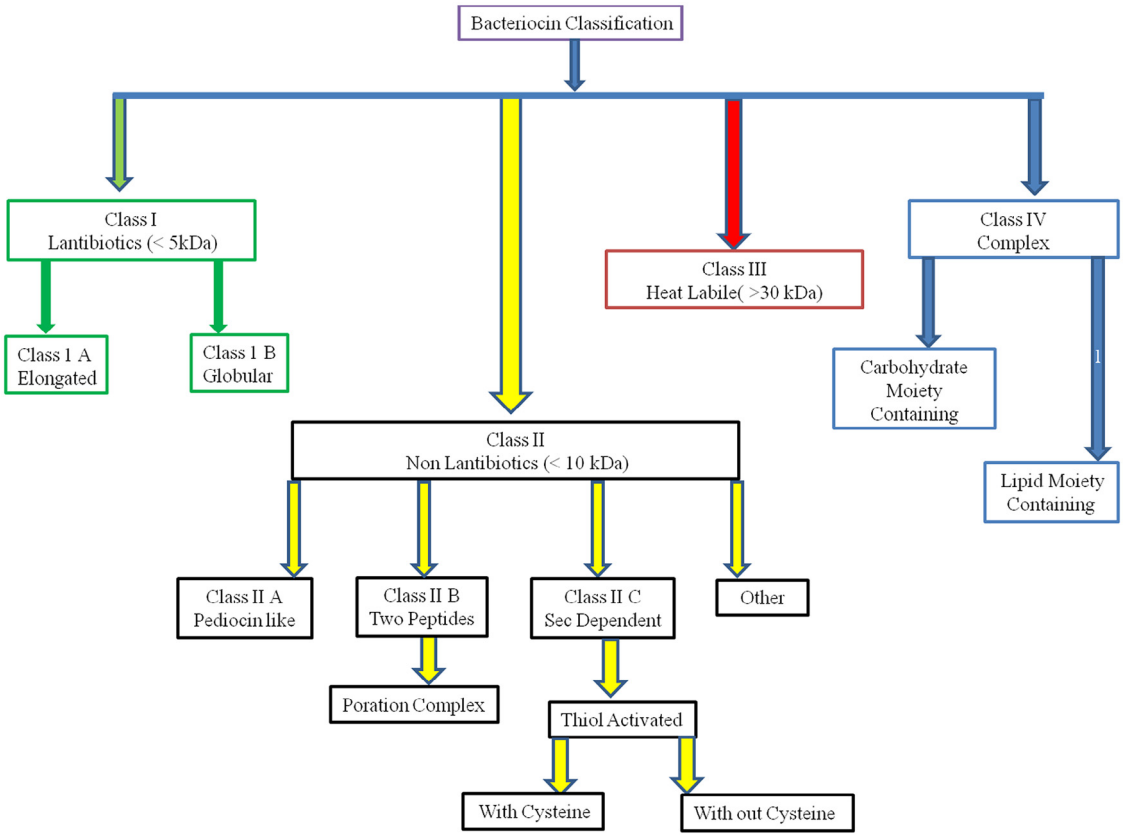

Fig. 1. Classification of bacteriocins based on physicochemical properties.

with no net charge. They inhibit various catalytic enzymes required to complete the life-supporting processes of susceptible bacteria [25].

2.2. Class II bacteriocins

Class II bacteriocins are heat-stable, small (<10 kDa), non-lantibiotics or non-modified or pediocin-like antibiotics, with isoelectric points (pIs) varying from 8.3 to 10.0, characterised by the presence of a hydrophilic N-terminal consensus sequence Tyr-Gly-Asn-Gly-Val-Xaa-Cys [YGNGV(X)C(X)4C(X)V(X)4A] [26,27], transported by ATP-binding cassette (ABC) transport systems [28–30].

2.2.1. Class IIa bacteriocins

The antilisterial bacteriocins are grouped in this class. The representative bacteriocins of this group are leucocin A, acidocin A [30], mesentericin, pediocin PA-1 and sakacin P [31].

2.2.2. Class IIb bacteriocins

Class IIb bacteriocins (two-peptide bacteriocins) require at least two different peptides for activity and thus generally act synergistically. These peptides have little or no activity when tested individually, e.g. lactococcin G and plantaricins [32].

2.2.3. Class IIc bacteriocins

These are small, heat-stable peptides that are carried by leader peptides and are further divided into two groups, the thiolbiotics and cystibiotics. Thiolbiotics are bacteriocins with two cysteine residues, whilst bacteriocins with one cysteine residue are cystibiotics. Lactococcin A, divergicin A and acidocin B are bacteriocins of class IIc [33].

2.3. Class III bacteriocins

Class III bacteriocins are large (>30 kDa) peptides, e.g. zoocin A, lysostaphin, helveticin J [33] and helveticin V [34]. These bacteriocins are classified as heat-labile lytic bacteriocins and heat-labile non-lytic bacteriocins [33,34]. The lytic bacteriocins are generally endopeptidase peptides that lyse the cell wall of bacteria in an enzymatic manner.

Besides lytic bacteriocins, some heat-labile, high-molecular-weight bacteriocins without a lytic mode of action have also been found, e.g. helveticin J from *Lactobacillus helveticus* 481, dysgalacticin from *Streptococcus dysgalactiae* subsp. *equisimilis* W2580, and streptococcin A-M57 [33,34]. The mode of action of dysgalacticin has been studied and it was concluded that this bacteriocin interferes with either glucose transport or metabolism by binding to the phosphoenolpyruvate-dependent glucose and mannose phosphotransferase transport system [33,34].

2.4. Class IV or complex bacteriocins or cyclic bacteriocins

These complex bacteriocins containing lipid or carbohydrate moieties are sensitive to glycolytic or lipolytic enzymes, e.g. plantaricin S and leuconocin S [35]. Recently, a novel, cyclic bacteriocin-like substance, uberolysin, secreted by *Streptococcus uberis* has also been described [36].

3. Structural classification

This system provides a consistent pattern of bacteriocin classification to even classify unclassified bacteriocins on the basis of the presence of extremely conserved amino acid motifs and is helpful in classifying >70% of known bacteriocins to date [37] (Table 1).