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Popular Article

Role of Antimicrobial peptides (AMPs) in control of mastitis

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Abstract

Mastitis is still considered as devastating condition for dairy animals. The management of mastitis involves the use of a wide range of antibiotics. Antimicrobial resistance has a serious challenge in today's era due to the indiscriminate use of antimicrobials. A strong drive towards reducing antibiotic residues in animal food products has led to research in finding new alternatives to antimicrobial agents. There has been a great deal of interest in antimicrobial peptides (AMPs) as potential next-generation antibiotics since they are non-toxic, bioactive small proteins, naturally produced by living organisms that represent the first line of defense against bacteria, viruses, and fungi. As a result of their properties and despite their ancient origin, AMPs should be able to replace antibiotics in the battle against pathogenic microbes in the near future.

Introduction

Mastitis is an economically ruinous condition that causes immense economic losses to the dairy industry. The majority of cases of mastitis are caused by only a few common bacterial pathogens like, *Staphylococcus* spp., *Streptococcus* spp., *Coliforms* spp., and *Actinomyces pyogenes*. Antibiotics are the most effective drugs for the treatment of pathogenic bacteria. However, prolonged and indiscriminate use of antibiotics, especially in developing countries, in agriculture, as well as in both human and veterinary medicine, has contributed to the development of drug-resistant microorganisms (Huan *et al.*,2020). Antimicrobial peptides (AMPs), also known as "host defense peptides (HDP)", are oligopeptides with a varying number of amino acids which are having a broad-spectrum activity against a wide range of microorganisms including mastitis-causing pathogens also. AMPs can be an alternative to antimicrobials in the treatment of mastitis.

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History of AMPs

The first AMP was gramicidin, discovered in 1939 from the soil bacteria *Bacillus brevis*. The first animal-originated AMP defensin, was isolated from leukocytes of rabbits. Afterward, several AMPs have been discovered in both the prokaryotic and eukaryotic kingdoms.

AMPs in mastitis

Antimicrobial peptides (AMPs) are new generation antibiotics that destroy invading microorganisms and play a major role in the innate immune system of body. They showed broad-spectrum activity against several gram-positive and gram-negative bacteria, including some of the drug-resistant strains and can be effectively used in mastitis condition. The therapeutic application of AMPs is very much limited in the present scenario due to their short half-life, enzymatic degradation, high production cost, and cytotoxic effects on eukaryotic cells. The majority of AMPs are still in preclinical studies, while some have been approved for use in treating bovine mastitis.

Bacteriocins

Bacteriocins are secreted by a variety of bacteria for the killing of other bacteria. It acts by cell wall degradation or by disturbing the cytoplasmic membrane through forming pores. They are considered a better alternative to antibiotics, which are currently used for the treatment and prevention of mastitis.

Nisin

It was the first bacteriocin applied to preserve food products. Nisin prevents cell wall synthesis and causes pore formation in bacteria, leading to cell death. Nisin shows variable antimicrobial activity in subclinical mastitis when given intramammary. Nisin-based teat sanitizer (Amibicin N®) and nisin-based products, namely Wipe-Out® Dairy Wipes and Mast Out® were developed and used in initial field trials in subclinical mastitis affected cows.

Lacticin 3147

It is produced by *Lactobacillus lactis* subsp. *lactis* DPC3147 and used as an antimicrobial agent as it inhibited common mastitis-causing micro-organisms, including *S. aureus, S. uberis, S. dysgalactiae,* and *S. agalactiae* (Ryan *et al*., 1998). The bacteriocin lacticin 3147 could be used

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in a teat seal preparation to effectively prevent infection by *Streptococci* and reduce the incidence of infections by *S. aureus*.

Other bacteriocins that could have potential use in mastitis treatment

Lysostaphin

A recombinant mucolytic protein, lysostaphin which is bactericidal in nature, demonstrated as a potential intramammary therapeutic against *S. aureus* producing mastitis in dairy cattle. Lysostaphin, enzymatically degrades the cell wall of *S. aureus*.

Defensins

Defensins are considered as the best-known genetically encoded antimicrobials and act as the first line of defense against intramammary infections occurring in dairy cattle (Gurao *et al.,* 2017). AMPs permeabilize the target cell only when they reach a threshold concentration followed by peptide conformation's transition. The other uncommon models propose the immunomodulatory activity that makes these defensins deserving candidates for replacing conventional antibiotics to treat intramammary infections.

Cathelicidins

These AMPs are produced by neutrophils. In mastitis milk, neutrophils infiltrating the tissue release massive quantities of cathelicidin by degranulation, resulting in high concentrations of AMPs. The AMP cathelicidin is found in the mammary epithelium of animals with IMI but not in healthy udder tissues, making it a highly sensitive and specific indicator of mastitis.

Indolicidin

They belong to the family of cathelicidin AMPs. It was first discovered in bovine neutrophils as a tridecapeptide and showed a bactericidal effect, including its action on *Staphylococcus aureus*. Bovine cathelicidins like BMAP-27 and BMAP-28 can be used in the treatment strategies against bacterial mastitis in dairy cattle.

Mutacins B-Ny266, J-T8 and B-JH1140

AMP Mutacin B-Ny266 has been of importance due to its wide spectrum activity against various pathogenic gram-positive and gram-negative bacteria, including *Staphylococcal* and *Streptococcal* strains resistant to antibiotics. Therefore, it could find application for therapeutic use in mastitis (Mota *et al.,* 2005).

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Lactoferrin

Lactoferrin is an iron-binding glycoprotein that exerts a wide antimicrobial activity against a number of bacterial, viral, and fungal pathogens *in vitro* (Yen *et al.*, 2011). Intramammary treatment with Lactoferrin co-administered with penicillin G increased the cure rate, reducing beta-lactamase activity in resistant *S. aureus* strains.

Lipopeptides

Lipopeptides SLP1, SLP2, SLP3 and SLP4 showed antibacterial activity against *Streptococcus aglactiae* on bacterial mastitis in mice (Peng *et al.*, 2022). These basic amino acids are positively charged in solution, which can react with LPS or lipoteichoic acid.

Polybia MP-1

This AMP was obtained from the venom of the wasp Polybiapaulista. The synthetic polybia MP-1 peptide effectively inhibited *S. aureus*, *E. coli* and *K. pneumoniae*. Polybia MP-1 peptide is safe and can be effectively tried as an alternative to antibiotics for the management of mastitis in cattle (Shah *et al.*, 2022).

Bovine Psoriasin

Bovine Psoriasin plays an important role in providing local defense against bacteria in the udder. It shows antimicrobial activity against *E. coli*, which is an important cause of mastitis among animals (Lee *et al*., 2007).

Esculentin 1–21

Esculentins-1 showed powerful antimicrobial activity against the most diffused mastitis-causing bacteria e.g., *S. agalactiae, P. aeruginosa* and *E. coli* in cattle (Rodrìguez *et al.*, 2009). This peptide rapidly kills microorganisms with a concomitant permeation of the microbial membrane.

Conclusion

AMPs can be considered as unconventional therapeutic small molecules which have attracted great interest in recent years because of their promising potential, as they can be used as alternative or complementary approaches for the treatment of various microbial infections. There is no doubt that synthesized antimicrobials have better competitors already existing in nature since millions of years ago; therefore, the research could be an exploratory step in solving multifactorial issues like mastitis.

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