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Original Article

Applications of Antimicrobial peptides in Veterinary Medicine

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ABSTRACT

Antimicrobial peptides (AMPs) are molecules with a broad-spectrum activity against bacteria, fungi, protozoa and viruses. These peptides are widely distributed in insects, amphibians and mammals. Indeed, they are key molecules of the innate immune system with remarkable antimicrobial and immunomodulatory activity. Besides, these peptides have also shown regulatory activity for gut microbiota and have been considered inductors of growth performance. Livestock production is a sector that has expanded immensely, in an attempt to keep up with meat consumption. According to the FAO, cattle, pigs, and poultry together represent approximately 80% of the meat production. The current review describes the updated findings of antimicrobial peptides in domestic animals, such as bovines, goats, sheep, pigs, horses, canines and felines, analyzing the most relevant aspects of their use as potential therapeutics and their applications in Veterinary medicine.

INTRODUCTION

The innate immune system is the oldest defense mechanism that provides immediate protection against infection and requires different strategies to ensure the elimination of different pathogens. Antimicrobial peptides are essential mechanisms of the innate immune response, these molecules found at strategic sites in animals, mainly in surfaces that are in close contact with pathogens, such as skin, ears, eyes, on epithelial surfaces including the tongue, trachea, lungs and, intestines, and in the bone marrow and testicles. Their role is an essential key for the defense of the host against pathogenic challenges.

To date, more than about 4000 natural antimicrobial peptides (AMPs) have been discovered and about 3000 sequences from animal and plant species have been reported in different databases. These molecules are peptides that contain between 12 and 50 amino acids, they are generally positively charged due to arginine and lysine residues in approximately 50 % of their amino acids, and are called antimicrobial because of the broad- spectrum activity against different microorganisms such as Gram-negative or Gram-positive bacteria, parasites, fungi, and some viruses. Although their antimicrobial properties have been widely studied, in the last decades it has been shown that AMPs play important roles in the modulation of several immune processes such as the activation and recruitment of immune cells, wound healing, angiogenesis, inflammatory and anti-inflammatory activity.

Given the antimicrobial properties and immunological functions, AMPs are being proposed and evaluated as novel antimicrobial agents for treating infectious diseases in different species, representing a hopeful alternative that solves the problem of the increasing number of pathogenic bacteria that have developed resistance to antibiotics due to their indiscriminate use. Furthermore, AMPs can be used as a strategy to modulate the immune response benefiting the host health, but also, interestingly they can regulate another process such as nutrition, since their implementation as a supplement on animal dietary could improve the growth performance in broilers and pigs additionally defensins play an important role in sperm maturation and capacitation, and their adherence to uterine mucosal epithelial cells, thus the AMPs can regulate essential aspects in veterinary medicine in nutrition and reproduction.

SYNTHESIS, PRODUCTION AND MECHANISM OF ACTION

Antimicrobial peptides have been classified into various families according to their amino acid structure, mechanism of function, and organization. Recently, the antimicrobial peptide database has proposed a classification of AMPs based on their three-dimensional structure. According to this classification, there are four families of antimicrobial peptides: α, β, αβ and, non-αβ. The former would correspond to peptides with a helical α structure, which lacks cysteine.

ANTIMICROBIAL EFFECT

Several studies have tested the antimicrobial capacity of animal-derived AMPs on diverse pathogens, including bacteria, viruses, and fungi of different animal species. One of the most attractive antimicrobial aspects of AMPs is that they are effective against multidrug- resistant pathogens, and compared to conventional antibiotics, they kill pathogens extremely fast, using multiple bacterial targets. The most extensively tested AMPs for the antimicrobial effect are defensins and Cathelicidins. Defensins show a broad range of antimicrobial activity against bacteria that have demonstrated resistance to antibiotic treatment (Hoffmann, et al., 1992, Harder, et. al., 2001). Cathelicidins exert antibacterial activity against both Gram-positive and Gram-negative bacteria via electrostatic interactions with the bacterial cell membrane (Turner et. al., 1998).

ANTIMICROBIAL PEPTIDES IN CATTLE

The study of antimicrobial peptides in bovines has been of great interest, since 1980s, at least 38 bovine antimicrobial peptides have been reported. These studies have focused on bovine β-defensins (TAP, LAP, DEFB1, DEFB3, DEFB4 and DEFB5, DEFB10) and cathelicidins (CATHL 1–7, Bactenecins, Indolicidin Bovine and Myeloid Antimicrobial Peptides (BMAPs) (Hsu et al., 2005; Benincasa et al., 2003). These peptides kill bacteria by forming small channels in the membrane resulting in the release of small ions rather than by membrane disruption

APPLICATION IN NON-RUMINANT NUTRITION

In recent years, AMPs have been being extensively evaluated as novel antimicrobial drugs in swine and poultry production. Previous studies have demonstrated the benefits of AMPs on the growth performance of swine and poultry (Liu et al., 2008; Bao et al., 2009). By adding swine

gut intestinal antimicrobial peptides (SGAMP), broilers showed higher average daily gain and feed efficiency under chronic heat stress conditions (Hu et al., 2017). An antimicrobial peptide lactoferrin isolated from milk has been shown to increase the average daily gain (ADG) and the efficiency of gain (G:F) of weaning piglets by 41.80% and 17.20%, respectively (Wang et al., 2006). In addition, the fusion peptide lactoferricin-lactoferrampin (artificial) improved growth performance and decreased diarrhea incidence in weaning pigs. It was also reported that the antimicrobial peptides A3 and P5 had beneficial effects on growth performance in weanling pigs and broilers (Tang et al., 2009).

CONCLUSIONS

Almost 100 years after the discovery of the first antimicrobial peptide (lysozyme), the knowledge regarding AMPs has grown considerably. However, nowadays, there are still important concerns about the security and efficacy of the use of AMPs as therapeutics or alimentary supplements in veterinary medicine, efforts to improve the efficacy and security, should not be abandoned to overcome these obstacles. With the development of technology and evolving knowledge, effective use of AMPs has good potential to improve efficiency of pig and broiler production as they are the major food sources and having a good impact on human health in terms of antibiotics resistance. In veterinary medicine, it is necessary to perform more *in vivo* studies that can be for research evaluating the pharmacokinetics of AMPs.

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