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Harnessing the potential of antimicrobial peptides: current advances and future applications

Abstract

Antimicrobial peptides (AMPs) represent a promising class of naturally occurring molecules with diverse structures and functions, offering a potent defense mechanism against microbial pathogens. This review explores the multifaceted role of AMPs in combating infections and their potential applications in various fields, including medicine, agriculture, and biotechnology. We discuss the mechanisms of action of AMPs, their structural diversity, modes of synthesis, and recent advancements in enhancing their stability and efficacy. Furthermore, we highlight the therapeutic potential of AMPs in treating multidrug-resistant infections, their role as alternatives to conventional antibiotics, and their applications in wound healing, immunomodulation, and drug delivery systems. Additionally, we examine the challenges associated with the clinical translation of AMPs and propose strategies to overcome these hurdles. Overall, this review underscores the importance of AMPs as versatile antimicrobial agents and emphasizes their potential to address the growing threat of antibiotic resistance.

Keywords: antimicrobial peptides, AMPs, mechanisms of action, therapeutic applications, drug resistance, biotechnology

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Introduction

Antimicrobial resistance poses a significant threat to global public health, necessitating the exploration of alternative antimicrobial agents. Antimicrobial peptides (AMPs) have emerged as promising candidates due to their potent antimicrobial activities, broad-spectrum efficacy, and unique mechanisms of action.[1] Antimicrobial peptides represent a promising class of antimicrobial agents with diverse applications in medicine, agriculture, and biotechnology. Their unique properties, broad-spectrum efficacy, and potential for overcoming antimicrobial resistance underscore their significance in addressing global health challenges. As research in this field continues to advance, AMPs are poised to play a pivotal role in shaping the future of antimicrobial therapy and biotechnology.[2] This paper is an introduction to the significance of AMPs in addressing the challenges of antimicrobial resistance and outlines the objectives of this review.

Classification of AMPs

AMPs exhibit remarkable structural diversity, ranging from linear peptides to cyclic peptides, and comprising α-helical, β-sheet, and extended structures.[3] We explores the structural motifs commonly observed in AMPs and discusses the classification schemes based on sequence similarity, secondary structure, and antimicrobial activity.

a) Classification based on sequence motifs

AMPs encompass a myriad of sequence motifs, each contributing to their unique antimicrobial properties and biological functions.[4,5] This section delves into the classification of AMPs based on conserved sequence motifs, such as cathelicidins, defensins, and histatins.[5] We explore the structural characteristics and evolutionary significance of each class of AMPs, shedding light on their diverse roles in host defense mechanisms.

b) Classification based on secondary structures

The secondary structure of AMPs plays a pivotal role in their interactions with microbial membranes and intracellular targets. Here, we elucidate the classification of AMPs based on their predominant secondary structures, including α-helices, β-sheets, extended structures, and cyclic peptides.[6] We discuss the structural determinants of antimicrobial activity and the implications of secondary structure diversity for AMP function and therapeutic applications.

c) Physicochemical properties and classification

The physicochemical properties of AMPs, such as amphipathicity, charge, hydrophobicity, and length, contribute to their antimicrobial efficacy and selectivity.[7] This section examines the classification of AMPs based on their physicochemical properties, highlighting the relationship between structure and function.[8] We discuss how variations in physicochemical properties influence the mode of action, target specificity, and therapeutic potential of AMPs.

d) Classification based on modes of action

AMPs employ diverse mechanisms of action to exert their antimicrobial effects, including membrane disruption, pore formation, and intracellular targeting. Here, we classify AMPs based on their modes of action and discuss the structural features associated with each mechanism.[9] We explore the functional significance of mode-of-action diversity and its implications for developing AMP-based therapeutics.

Mechanisms of action

The antimicrobial activities of AMPs stem from their interactions with microbial membranes and intracellular targets. Here, we elucidate the diverse mechanisms of action employed by AMPs, including direct killing, immune modulation membrane disruption, pore formation, inhibition of cell wall synthesis, and intracellular targeting.[10] Furthermore, we discuss the factors influencing the selectivity and efficacy of AMPs against microbial pathogens (Figure 1).

AMPs' ability to be bactericidal is dependent on two primary mechanisms of action: entering the bacterium to interact with internal

components and causing cell lysis by rupturing bacterial membranes for example; The bovine-derived antimicrobial peptide P3 derivative JH-3 is able to inhibit *Salmonella* and *E. coli* by destroying the cell wall and cell membrane, leading to the leakage of bacterial contents, another example the antimicrobial peptide temporin-GHa-GHd changed the permeability and morphology of the bacterial cell membrane, making it rough and caused shrinkage, thereby inhibiting *S. aureus* (Figure 2).

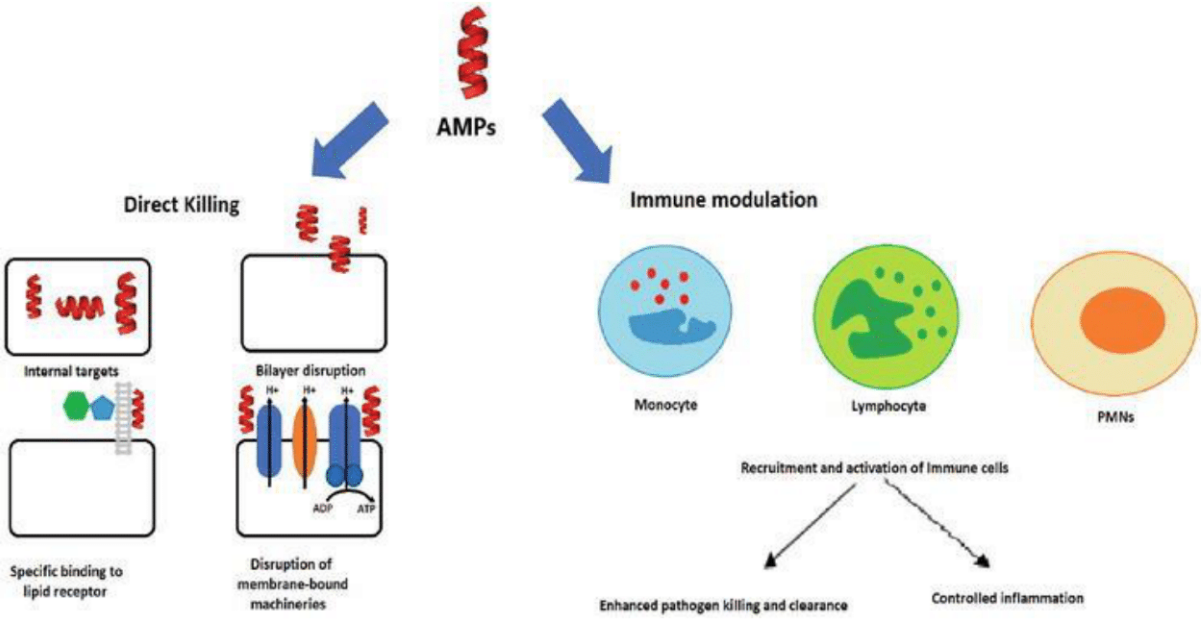

Figure 1 Mechanism of action of antimicrobial peptides.

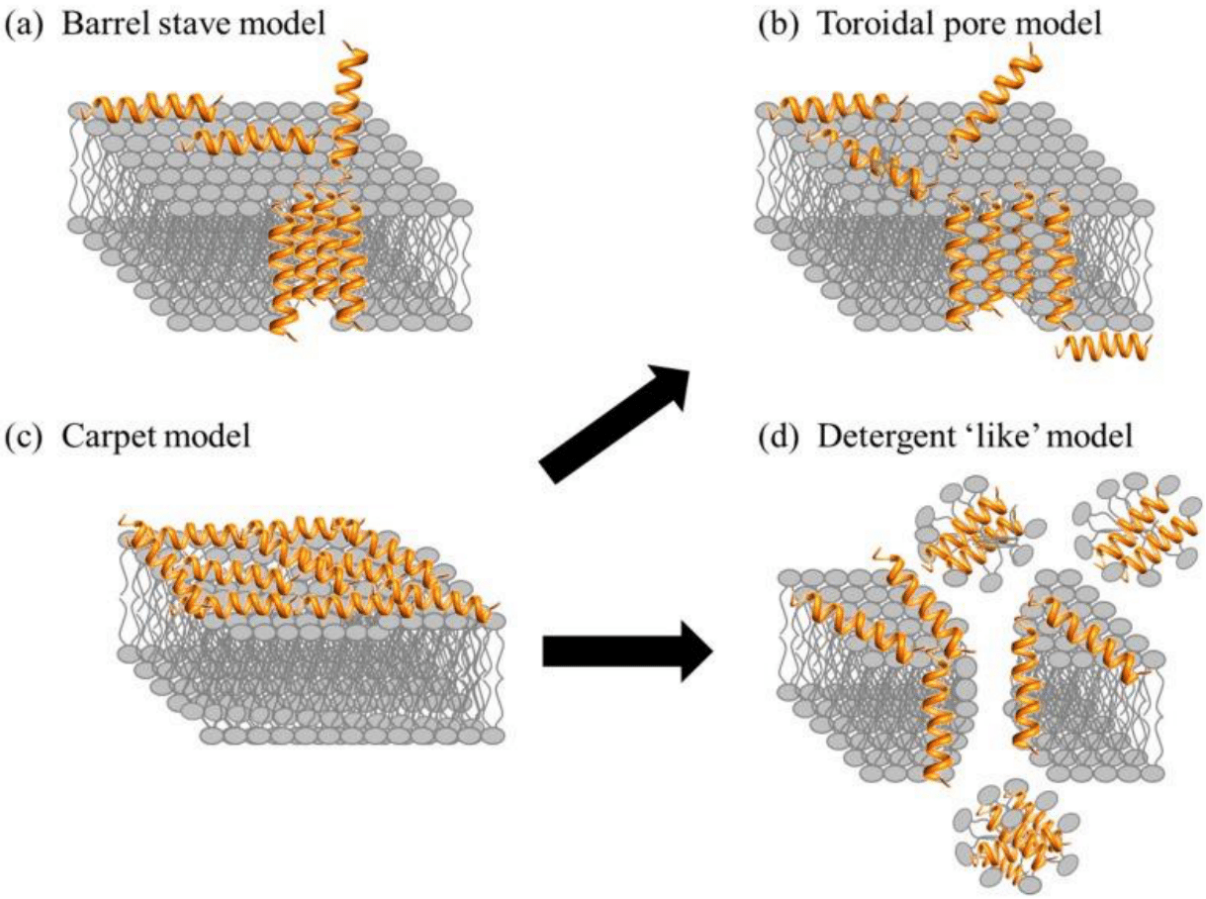

Figure 2 Suggested modes of action for AMPs in bacteria.

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Applications of AMPs

AMPs, or Antimicrobial Peptides, are a diverse class of molecules found in various organisms, including animals, plants, and microorganisms.[11] They play crucial roles in the innate immune systems of these organisms by defending against a wide range of pathogens, including bacteria, fungi, viruses, and even some parasites. Here are some key applications of AMPs:

a) **Therapeutic application:** AMPs hold immense potential for therapeutic applications in combating infectious diseases, including bacterial, fungal, and viral infections. AMPs have wound healing, anti-cancerous activity and immunomodulation activity which have been widely used.[12] This section provides an overview of AMP-based strategies for the treatment of various infectious diseases, highlighting their efficacy, safety profile, and potential synergies with conventional antimicrobial agents (Figure 3). Additionally, we explore the applications of AMPs in wound healing, dermatology, and oral health.

b) **Food preservation:** AMPs can be used to improve the safety and shelf-life of food products by inhibiting the growth of spoilage microorganisms and foodborne pathogens.[13] They can be applied directly to food surfaces or incorporated into packaging materials to prevent microbial contamination.

c) **Biotechnology:** AMPs have potential applications in various biotechnological processes, including the development of antimicrobial coatings for medical devices and implants to prevent infections, as well as in the production of antimicrobial peptides themselves using recombinant DNA technology.[13,14]

d) **Personal care products:** AMPs are increasingly being incorporated into personal care products such as soaps, lotions, and oral care products for their antimicrobial properties. They can help prevent skin infections, acne, and oral diseases caused by pathogenic microorganisms.[15]

e) **Animal health and agriculture:** AMPs can be used in veterinary medicine to treat infections in animals and as alternatives to antibiotics in livestock farming to promote animal health and reduce the risk of antibiotic resistance.[15] They can also be applied topically or added to animal feed to prevent infections and improve overall hygiene.

f) **Biomedical research:** AMPs are valuable tools in biomedical research for studying host-pathogen interactions, antimicrobial mechanisms, and developing new therapeutic strategies against infectious diseases.[16–18] They can also be used as molecular probes for detecting and targeting specific microbial pathogens.

g) **Therapeutic peptide design:** Understanding the structure-function relationships of AMPs can inform the design and development of synthetic peptides with improved antimicrobial activity, stability, and selectivity.[19] These engineered peptides, known as peptidomimetics, hold promise for the development of novel antimicrobial agents with enhanced therapeutic potential.[20]

h) **Emerging trends and future perspectives:** Despite their immense potential, the clinical translation of AMPs faces several challenges, including issues related to stability, toxicity, and manufacturing scalability. In this section, we highlight recent advancements in AMP research, such as the development of synthetic and modified AMPs, novel delivery systems, and combinatorial approaches.[21,22] We also discuss the future directions and potential breakthroughs in AMP-based therapeutics and biotechnological applications.[23]

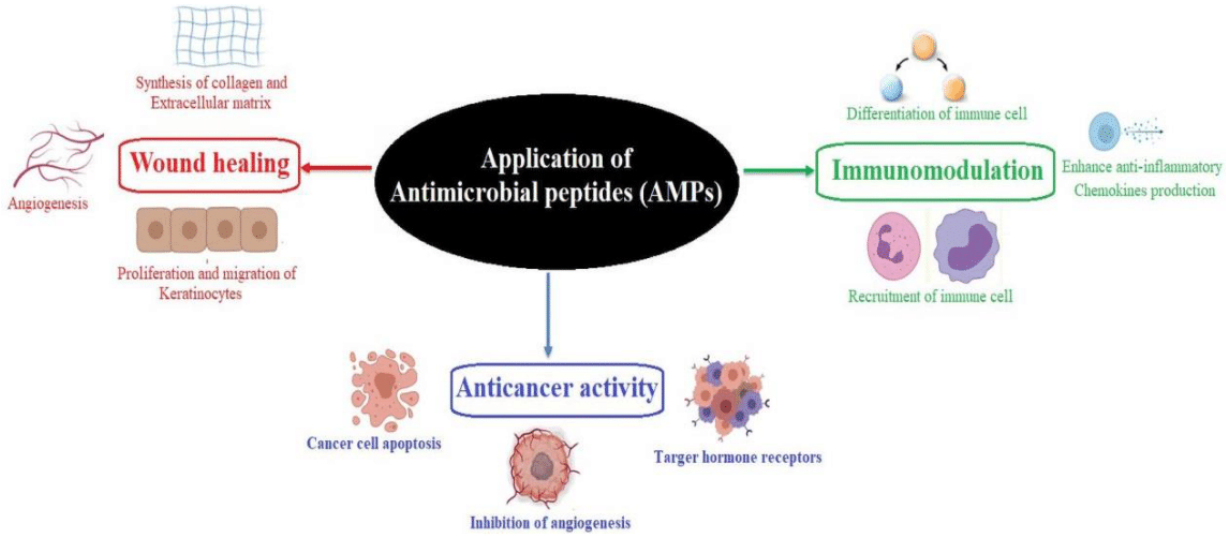

Figure 3 Role of an antimicrobial peptide in immunomodulation, wound healing, and anticancer activity.

Conclusion

Antimicrobial peptides represent a promising class of antimicrobial agents with diverse applications in medicine, agriculture, and biotechnology. Their unique properties, broad-spectrum efficacy, and potential for overcoming antimicrobial resistance underscore their significance in addressing global health challenges. As research in this field continues to advance, AMPs are poised to play a pivotal role in shaping the future of antimicrobial therapy and biotechnology. Antimicrobial peptides represent versatile weapons in nature's microbial warfare, employing diverse mechanisms to combat microbial pathogens. By unravelling the intricate mechanisms of action of AMPs, researchers can harness their potential for therapeutic development and address the growing threat of antimicrobial resistance.

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Data availability

All datasets generated or analysed during this study are included in the manuscript.

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Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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