

Host Defence Peptides: Harnessing Innate Immunity for Next-Generation Antimicrobial Therapeutics

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Abstract:

Background: Antimicrobial resistance (AMR) is a growing global health threat, with increasing resistance to existing antibiotics and relatively few new antimicrobial agents in development. Host defence peptides (HDPs) are naturally occurring components of the innate immune system with both antimicrobial and immunomodulatory activity. This review explores how HDPs work, their potential role in tackling AMR and the challenges involved in developing them as therapeutic agents.

Methods: A literature review was conducted using MEDLINE and EMBASE, examining evidence on HDP structure and function, mechanisms of antimicrobial activity, immunomodulatory effects, antimicrobial resistance, therapeutic development and potential antiviral applications.

Results: HDPs are predominantly cationic and amphipathic peptides that interact with microbial membranes, leading to membrane disruption and cell death. Their activity is not limited to direct microbial killing; HDPs can also influence inflammatory responses, recruit immune cells and enhance host defence. These multiple mechanisms of action make HDPs particularly interesting in the context of multidrug-resistant organisms and may make the development of resistance more difficult than with some conventional antimicrobials. HDPs have also shown antiviral and immunomodulatory activity. However, their clinical development is limited by several challenges, including cytotoxicity, peptide instability, pharmacokinetic limitations, effective delivery and manufacturing costs.

Conclusion: HDPs have significant potential in the development of new antimicrobial therapies, particularly in the context of rising AMR. However, challenges involving toxicity, stability, delivery and cost need to be addressed before wider clinical use. Further developments in peptide engineering and drug delivery may help overcome these limitations and support the translation of HDPs into clinically useful therapies.

Keywords:

Host defence peptides, antimicrobial resistance, antimicrobial drug discovery, antimicrobial peptides, immunomodulation, multidrug resistance.