Antimicrobial peptides – new emerging antimicrobial drugs?

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Introduction

Over the last decade, the rapid emergence of (multi) drug-resistant bacteria has become a global concern. In the EU alone, resistant bacterial infections are the cause of 33,000 human deaths annually and cause significant production losses in livestock farming. To overcome these problems the need for alternative antibiotics is urgent. A promising alternative group of antibiotics are antimicrobial peptides (AMPs). Some AMPs (*e.g.,* colistin, nisin) are currently applied in food production. A literature study was conducted focusing on the potential use of these compounds in veterinary practice to answer the question: Are AMPs new emerging antimicrobials and growth-promoting agents that should be addressed?

Definition and activity

AMPs are small, positively charged molecules that have been described as evolutionary ancient weapons against microbial infections. AMPs have shown broad-spectrum activity against bacteria, funghi, protozoa, and viruses (figure 1). They are produced by all organisms, from prokaryotes to humans, and serve a fundamental role in innate immunity.

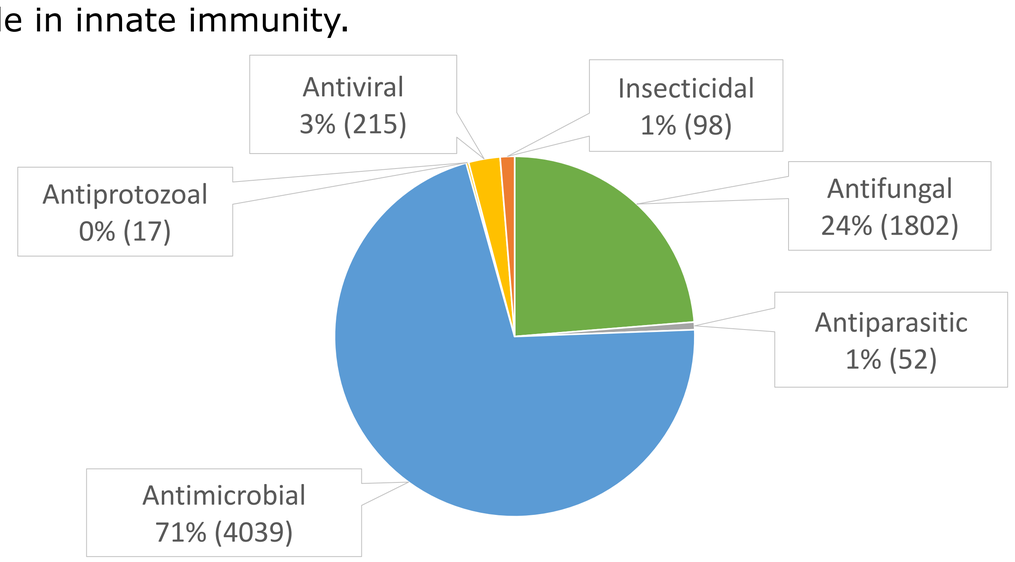

Figure 1. Activity of AMPs that are included in the DRAMP database. Data of the DRAMP database was obtained from Kang et al. (2019) and Fan et al. (2016).

The main characteristic of AMPs is their ability to form secondary structures, namely α-helix, β-sheet, mixed α-helix/β-sheet and extended AMPs (figure 2).

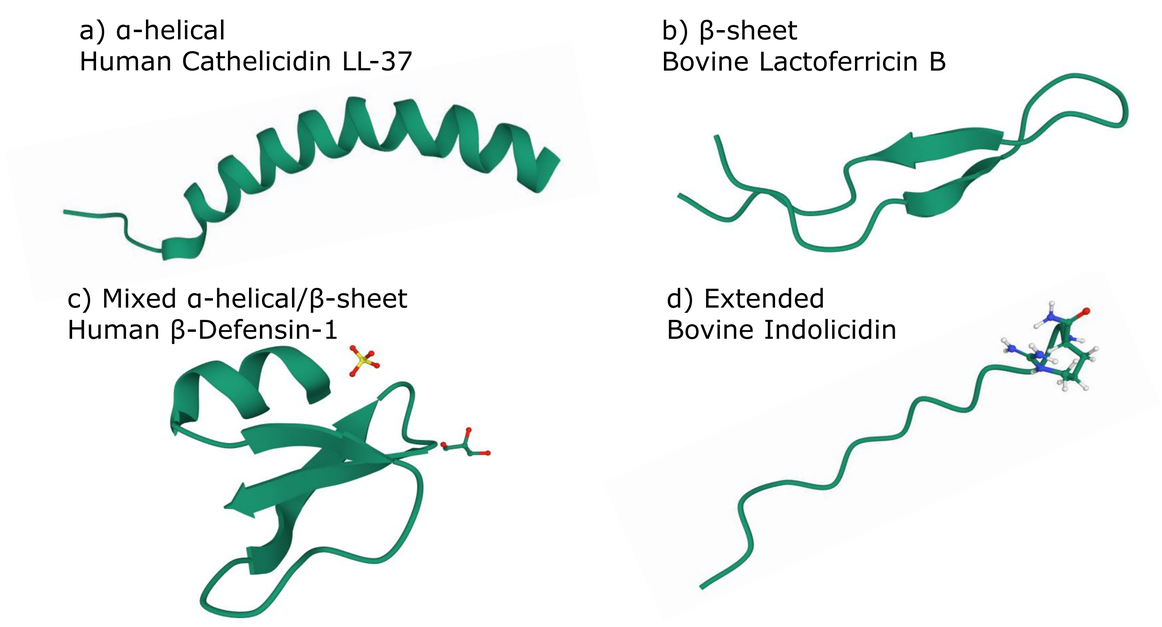

Figure 1. Secondary structure of AMPs: a) LL-37 (α-helix), b) bovine lactoferricin B (β-sheet), c) human β-defensin-1 (mixed α-helix/β-sheet), and d) bovine indolicidin (extended). All structures were obtained freely from the RCSB Protein Data Bank (PDB) (Berman, Westbrook et al. 2000).

Applications

AMP	Animal	Application	Reference
Colistin	Various	Bacterial infections	-
Nisin	Cattle	Food preservative Treatment of mastitis	Hwanhlem et al. (2017) Cao et al. (2017)
Cecropin AD	Weanling pigs	Enhances performance	Wu et al. (2012)
AMP-P5	Weanling pigs Broilers	Improvement of growth performance	Yoon et al. (2013) Choi et al. (2013)
AMP-A3	Weanling pigs Broilers	Improves the performance, nutrient digestibility, intestinal morphology and reduces pathogenic bacteria	Yoon et al. (2014) Choi et al. (2013)
ε-Polylysine	-	Food preservative	Luz et al. (2018)

Advantages and limitations

The advantage of AMPs is that bacteria may have less of a chance to develop drug resistance due to its unique membrane destruction mechanism. Moreover, antimicrobial peptides have broad application prospects including animal and plant disease resistance, food preservatives, and growth-promoting agents.

The main limitation of antimicrobial peptides is cytotoxicity due to their hydrophobic properties. In addition, antimicrobial peptides are prone to biological degradation, loss of activity in serum, differences in *in vitro* and *in vivo* experiments and their complicated structure leads to high research and development costs.

Clinical trials

A limited number of AMPs are currently approved by the EU, although many AMPs are in clinical trials (Figure 3). Currently, 33 AMPs in clinical trials with 33 more AMPs in preclinical stages. It is expected that the number of AMPs in clinical trials increases with the growth of the global peptide market, which is expected to double between 2018 and 2026.

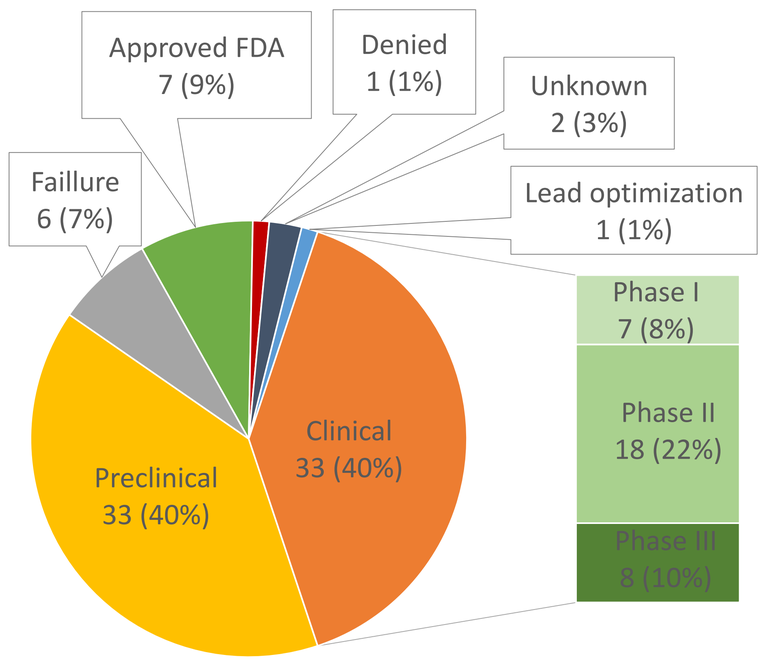

Figure 3. Overview of the number of AMPs that are currently, or have been, in clinical trials. The data was obtained from the DRAMP database from Kang et al. (2019) and Fan et al. (2016).

Conclusion

Research on AMPs has increased significantly in the last 10 years, but their application in food production is currently limited to AMPs such as colistin and nisin. However, because of the increasing number of AMPs in clinical trials, the growing economic value of the peptide drug market, and their growth-promoting properties, an increase in AMP application in food production is expected. It is therefore important to continue to monitor the development and applications of AMPs in food production.

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