On the non-canonical structure of peptide derivatives of keratin (KAMPs) through molecular simulations

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Abstract

Antimicrobial resistance constitutes one of the greatest challenges faced by the modern world. The over-prescription and indiscriminate use of antimicrobial agents, especially antibiotics, have led to a significant reduction in their effectiveness against clinically important bacteria, such as *E. coli* and *S. aureus*. Antimicrobial peptides have been increasingly studied over the past two decades as alternative antibacterial agents due to their potential to address antimicrobial resistance through mechanisms involving interactions with both the membrane and intracellular targets, making it harder for resistance to develop compared to conventional antibiotics. In the past decade, computational studies have been conducted that complement experimental observations, offering the opportunity to observe their mechanism of action at the nano- and micro-scale.

Peptides derived from keratin 6A of human corneal epithelial cells (KAMPs) represent a unique class of antimicrobial peptides. Experimental studies have shown that these peptides are active against both Gram-negative and Gram-positive bacteria. However, unlike the majority of candidate antimicrobial peptides, their action is independent of the presence of an α-helix in their structure, and it has been found that some KAMPs form pores in the bacterial membrane.

The present study focuses on the detailed investigation of the structure of seven different peptides from the KAMP family, along with Pw-Antibac12$_3$, which is derived from poultry feather keratin, in both dilute and semi-dilute aqueous solutions. The aim is to explore their secondary structure as well as the specific interactions responsible for their self-organization into aggregates. The predictions of the simulations confirm the experimentally determined non-standard structures of these highly important peptides in dilute solutions and reveal their tendency to form aggregates. This is particularly significant, as this tendency has been correlated with the mechanism of action of antimicrobial peptides in general.