NMR study of short cationic peptides with antimicrobial activity

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Antimicrobial peptides (AMPs) are effective natural antibiotics, easy to produce and without resistance inducing effects.1 Recently, several studies have revealed that short peptide fragments could maintain full antimicrobial activity, with the repeating motif alternating between hydrophobic and positively charged residues.2 Furthermore, it has been shown that the substitution of some hydrogen atoms by fluorine enhances the therapeutic activity of the peptides.3 The exact action mechanism of AMPs is not completely established, but it is generally believed that the positively charged peptide is first electrostatically attracted by the negative bacterial membrane and then disrupts the lipid packing by lipophilic interactions.4 It has been observed that the structure of the peptides is altered when approaching or in contact with the bacterial membrane, normally inducing alpha-helical secondary structure.

In this work, we have studied several pentapeptides, including fluorinated derivatives, by different NMR methods, using SDS and HFIP as membrane mimicking solvents. Our goal was to determine which structural factors affect the antimicrobial activity and how they are related with the mechanism of action of the peptide. We have analyzed the aggregation state of the peptides and the interaction with the SDS micelle by NMR diffusion experiments5. The formation of a complex between the peptide and SDS was further confirmed by transfer NOESY6 and the topology of the binding was determined by water-LOGSY experiments7. Important differences are found between fluorinated and non fluorinated peptides, corresponding to different antimicrobial activities.

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