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Structures of antimicrobial peptides HP (2-20) and interactions between HP(2-20) and membrain studied by NMR spectroscopy

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HP(2-20) (AKKVFKRLEKLFSKIQNDK) derived from the N-terminus of Helicobacter pylori Ribosomal Protein L1 shows potent antimicrobial activity against bacterial, fungi and cancer cells without cytotoxic effect. In order to investigate the relationships between antimicrobial activity and the structures, several analogues have been designed and synthesized. The structures of these peptides in SDS micelles have been investigated using NMR spectroscopy and they revealed that analogue 3 has the longest, well-defined alpha-helix from Val5 to Trp19. NOESY experiments performed on HP and its analogues in nondeuterated SDS micelles show that protons in the indole ring of Trp16 are in close contact with methylene protons of SDS micelles. In order to probe the position of HP and its analogues relative to the SDS micelles, spin-labeled stearate was added. Large effects are observed for the chemical shifts and the intensities of Phe5, Glu9, Phe12, and Trp16 within the helix region by 16-doxylstearate. This result implies that 16-doxylstearate is located in the center of the micelles and the hydrophobic phase of the amphiphilic α-helix is located in contact with the acyl chains of the micelles. Also, Lys3 and Lys4 at N-terminus and Lys20 at C-terminus may produce an optimal arrangement for electrostatic interactions between the sulfate head groups of the SDS and the positively charged lysyl NH_3^+. Interactions between the indole ring of Trp and the membrane, as well as the amphiphilic α-helical structure of HP induced by Trp at the C-terminus may allow HP to span the lipid bilayer. These structural features are crucial for their potent antibiotic activities.