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Structure of Antimicrobial Peptide, HP (2-20) and its Analogues Derived from *Helicobacter pylori*, as Determined by 1H NMR Spectroscopy

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HP(2-20) (AKKVFKRLEKLFSKIQNDK) is derived from the N-terminus of *Helicobacter pylori* Ribosomal Protein L1. It shows potent antimicrobial activity against bacterial, fungi and cancer cells without cytotoxic effect. In order to investigate the role of net hydrophobicity on its antimicrobial activity, several analogues have been designed and synthesized. Substitution of Gln and Asp with Trp at position 17 and 19 of HP(2-20) (Anal3) caused a dramatic increase in antibiotic activity without hemolytic effect. In contrast, the decrease of the hydrophobicity by substitution of Leu and Phe with Ser at position 12 and 5 of HP(2-20) showed decrease in their antibiotic activity. The tertiary structures of HP(2-20) and its analogues in SDS micelles have been investigated using NMR spectroscopy. The structures revealed that Anal3 has the longest, well-defined alpha-helix from Val4 to Trp18 and has the largest hydrophobic area in the amphiphilic alpha helix among all analogues. For the HP(2-20) and it' s analogues, most of the amide proton peaks in the α-helical region remained 12 hr after deuterium oxide was added, suggesting that the amide protons in α-helical regions at the mid region involve in intramolecular hydrogen. This hydrophobicity in its amphiphilic helix and the interactions of Trp with cell membrane are the crucial factor for its antimicrobial activities.