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STUDIES ON THE STRUCTURE-FUNCTION RELATIONSHIP OF ANTIMICROBIAL PEPTIDES INSOLATED FROM KOREAN FROGS

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Gaegurin 4 (GGN4) is a 37-residue antimicrobial peptide isolated from the skin of a Korean frog, Rana rugosa. This peptide shows a broad range of antimicrobial activity against prokaryotic cells but shows very little hemolytic activity against human red blood cells. The solution structure of GGN4 was studied by using circular dichroism (CD) and NMR spectroscopy. CD investigations revealed that GGN4 adopts mainly an alpha-helical conformation in trifluoroethanol (TFE)/water solution, in dodecylphosphocholine and in sodium dodecyl sulfate micelles, but adopts random structure in aqueous solution. By using both homonuclear and heteronuclear NMR experiments, complete ^{1}H and ^{15}N resonance assignments were obtained for GGN4 in 50% TFE/water solution. The calculated structures of GGN4 consist of two amphipathic alpha-helices extending from residues 2 to 10 and from residues 16 to 32. These two helices are connected by a flexible loop spanning between the residues 11 and 15. By using enzyme digestion and matrix-assisted laser desorption/ionization mass spectroscopy, it was confirmed that GGN4 contains a disulfide bridge formed between the residues Cys31 and Cys37 in its C-terminus. The effect of the disulfide bridge on the structure and the activity of GGN4 was investigated. The reduced form of GGN4 revealed a similar activity and conformation to native GGN4, suggesting that the disulfide bridge does not strongly affect the conformation and the antimicrobial activity of GGN4. As a link of the studies on the structure-function relationship of antimicrobial peptides from Ranidae, we are investigating the structures of various antimicrobial peptides of which sequences are 21 - 46 residues long. TF28 (21-residue), GGN4 derivatives (23-residue), GGN5 (24-residue), and ECN-1c (46-residue) serve as good examples. These studies will not only improve understanding of the mechanism of antimicrobial peptides, but also present new perspectives in the conception of new peptide antibiotics.