Conformational Properties of Peptides from Sticholysin II N-terminus Bound to Lipid Membranes

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Sticholysin II (StII), a cytolysin from de sea anemone *Stichodactyla helianthus*, lyses biological and model membranes *via* pore formation. Sphingomyelin (SM) is considered its putative receptor. Four toxin monomers are proposed to form a toroidal pore, also lined by phospholipids polar headgroups. Studies with StII and another actinoporin, Equinatoxin II, suggest that the proteins N-terminal domain plays an important role in pore formation, since it can move freely, without affecting the general protein fold. To understand the structure and dynamics of pore formation, peptides corresponding to residues 1-30 ($StII_{1-30}$) and 11-30 ($StII_{11-30}$) were synthesized assuming that these fragments can reproduce the N-terminal domain conformation in the whole protein. While the 1-10 sequence contains essentially hydrophobic residues, the remaining residues form an amphipathic a-helix. CD spectroscopy was used to investigate the peptides conformation in the presence of small unilamellar vesicles (SUV) of variable lipid composition. $StII_{1-30}$ bound to a large extent to 1-palmitoyl-2-oleoyl-phosphatidylcholine (POPC): 1-palmitoyl-2-oleoyl-phosphatidic acid (POPA), POPC:SM and POPC:POPA:SM. $StII_{11-30}$ bound to POPC:POPA and POPC:POPA:SM, and to a lesser extent to POPC:SM, probably due to the absence of the first 10 residues, thought to play an important role in peptide-zwitterionic phospholipid interaction. Both peptides remained essentially in solution in the presence of zwitterionic POPC. Upon binding, both peptides acquired a-helical structure. The results suggest that the peptide-membrane interaction involves hydrophobic effects, responsible for $StII_{1-30}$ binding to zwitterionic POPC:SM through residues 1-10, as well as electrostatic effects, that enable the interaction between charged residues (present in both peptides) and negatively charged membranes.
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