CONFORMATIONAL AND FUNCTIONAL STUDIES OF PEPTIDES FROM THE N-TERMINUS OF STICHOLYSINS I AND II

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StI and StII are sea anemone cytolysins whose N-termini are thought to participate in pore formation by penetrating into the bilayer and forming an oligomeric structure. To provide insight into the molecular mechanism of pore formation, we investigated the binding to model membranes of peptides from StI and StII N-termini: residues 1-31 (SELAGTIIDGASLTFEVLDKVLGELGKVSRK) and 12-31 of StI (StI_{1-31}, StI_{12-31}), and 1-30 (ALAGTIIAGASLTFQVLDKVLEE LGKVSRK) and 11-30 of StII ($StII_{1-30}$, $StII_{11-30}$). While residues 1-10 of StII are mostly hydrophobic, this stretch of StI carries some charged residues. The second half of these sequences forms amphipathic α-helices. CD spectra showed that membrane binding promoted an increased α-helical content. EPR spectra of a membrane-incorporated spin label showed the differential effect of the peptides on the packing of bilayers of variable lipid composition. Binding to bilayers of zwitterionic lipids was favored by the presence of the 11 (10) first residues of StI_{1-31} and $StII_{1-30}$, being less pronounced for the former peptide, and pointing to the contribution of hydrophobic interactions. In bilayers containing a negatively charged phospholipid, electrostatic interactions also modulated binding, especially for the shorter peptides, that only bound to these systems. The results agree with studies showing that the hemolytic activity (HA) followed the order: $StII_{1-30}$>StI_{1-31}>shorter peptides. The data were interpreted in terms of $StII_{1-30}$ residues 1-10 being more hydrophobic than the corresponding ones in StI_{1-31}, and of the lack of this stretch in the shorter peptides, evincing the importance of these residues in the mechanism of action of sticholysins.

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