Interactions of an alkylated antimicrobial peptide, BP100C$_{16}$, with Phospholipid Vesicles

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Antimicrobial peptides are antimicrobial agents (AMPs) with potential to be used as a therapeutic alternative to the growing antibiotic resistance of microorganisms [1]. BP100, KKLFFKILKYL-NH$_2$, is an AMP hybrid of Cecropin and Melittin. BP100 has high activity against bacteria, low hemolytic effect and high selectivity for negatively charged membranes, characteristic of bacterial membranes [2]. To obtain an analog with a lower minimum inhibitory concentration, MIC, and greater therapeutic potential we synthesized an alkylated BP100 derivative with a hexadecyl alkyl chain, BP100C$_{16}$, C$_{16}$H$_{33}$-AKKLFKKILKYLA-NH$_2$. Here we describe the interactions of BP100C$_{16}$ with large unilamellar vesicles, LUV, prepared by extrusion, with pure 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphatidylcholine (POPC) and mixtures of and 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphatidylglycerol (POPG). LUV leakage by BP100C$_{16}$ was determined using 4,5-carboxyfluoresceine as an internal probe. BP100C$_{16}$ structure and its interaction with LUV were analyzed by CD, NMR, electrophoretic mobility, DLS and optical microscopy with giant vesicles, GUVs. BP100C$_{16}$ increased the permeability of LUV of POPC and different POPC:POPG mixtures. BP100C$_{16}$ was a random coil in water and its structure remained unchanged in the presence of POPC LUV. With PC:PG LUV, BP100C$_{16}$ exhibited a $\alpha$-helix structure. BP100C$_{16}$ aggregated LUV of POPC:POPG 1:1, seen with GUVs, leak the LUV internal content, increased the vesicles hydrodynamic diameter and changed its electrophoretic mobility. We have shown that BP100C$_{16}$ interacts with vesicles through hydrophobic interactions with the alkyl chain and that the peptidic $\alpha$-helix structure is dependent upon the presence of negatively charged phospholipids.

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