# BIOMIMETIC LIPOSOMES AS DELIVERY SYSTEMS FOR ANTIMICROBIAL PEPTIDES

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**Background:** Drug-resistant bacterial infections continue to represent one of the biggest public health challenges of our time. There is therefore an ongoing need for both novel anti-infective agents, and innovative strategies for effective delivery of these agents. In the former case, antimicrobial peptides (AMPs) are promising, broad-spectrum anti-infectives that may provide alternatives to conventional antibiotics. In the latter instance, biomimetic nanocarriers, such as liposomes composed of cell membrane-relevant phospholipids, are of considerable current interest. In this work, the synthesis and antimicrobial activity of the ranalexin analog RN7IN6 was investigated. Liposomes composed of bacteria membrane-relevant phospholipids were additionally prepared, and preliminarily investigated as a delivery platform for RN7IN6.

**Methods:** RN7IN6 was synthesised via automated Fmoc-SPPS, characterised and purified. Biomimetic liposomes (LPs) made of POPE (1-hexadecanoyl-2-(9Z-octadecenoyl)-sn-glycero-3-phosphoethanolamine), POPG (1-hexadecanoyl-2-(9Z-octadecenoyl)-sn-glycero-3-phospho-(1′-rac-glycerol)) and CL (cardiolipin) were manufactured using the thin film hydration method followed by extrusion. Preliminary biomimetic LP formulations were also prepared via microfluidic mixing techniques. RN7IN6-adsorbed-LPs were prepared by incubating empty liposomes with a RN7IN6 solution with constant mixing. Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) values of RN7IN6 were determined by broth microdilution, using resazurin dye as a maker of cellular viability.

**Results:** RN7IN6 was successfully synthesised at approximately 90% purity, and noted to be effective against both Gram-positive and Gram-negative bacteria. MBC studies further showed that the AMP had a bactericidal action. Empty biomimetic liposomes prepared via thin film hydration showed a size of 159.75±1.35 nm, a PDI of 0.18±0.01 and a zeta potential of -28.6±1.9 mV. No appreciable difference in size was noted following RN7IN6 incubation; the surface charge of liposomes was however noted to decrease in magnitude, indicative of successful peptide adsorption.

**Conclusions:** Synthesised RN7IN6 showed a promising, broad-spectrum bactericidal activity. Preliminary studies indicated that RN7IN6 could be surface adsorbed to bacteria-relevant liposomes, to produce a biomimetic delivery platform for a novel anti-infective agent. RN7IN6 loading and antibacterial activity of AMP-adsorbed liposomes is currently under investigation.