

P004 Antibacterial lysine-peptoid hybrids with selective cytolytic activity

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Antimicrobial peptides play a key role in innate immunity. These host-defence peptides act very fast and are active against a wide range of pathogenic microorganisms, including, Gram-positive and Gram-negative bacteria, viruses, protozoa, yeasts, and fungi. In recent years, much research within the area of antibacterial resistance has focused on designing short analogues of naturally occurring antimicrobial peptides with increased activity and low cytotoxicity.

Oligomeric *N*-substituted glycines or "peptoids" are structurally similar to peptides and offer several advantages including, stability to proteolysis and biocompatibility. Furthermore, it has also been shown that peptoids display antibacterial activity.

In this study, we report the design, synthesis and characterization of twenty lysine-peptoid hybrids, based on the lead structure [*N*-(1-naphthalenemethyl)glycyl]-[*N*-(4-methylbenzyl)glycyl]-[*N*-(1-naphthalenemethyl)glycyl]-*N*-(butyl)glycine amide. The compounds were tested for antibacterial activity against *S. aureus* ATCC 25923 and *E. coli* ATCC 25922 using a broth microdilution assay.

Finally, the cytotoxicity of the derivatives towards mammalian cells was assessed, using a haemolytic activity assay. Several lysine-peptoid hybrids with potent antibacterial activity and low haemolytic activity were identified. The results presented here suggest that lysine-peptoid hybrids are promising lead structures for developing future therapeutics.