

Antimicrobial activity of two new peptides (S2-P082090 and S5-P082090) against gram-positive and –negative bacteria: Comparison with Omiganan (OMI)

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Background. The cationic antimicrobial peptides have been shown to have a broad spectrum of antibacterial activity, including gram-positive and gram-negative. These peptides act on the bacterial membrane, permeabilising it selectively, but not targeting a receptor, unlike traditional antibiotics that interact with specific microbial targets. Omiganan Pentahydrochloride® (MBI 226) is a synthetic cationic peptide analogue to indolicidin with activity against bacteria and yeasts and is currently in clinical trials for topical use. The antimicrobial activity of two new *in silico* designed peptides was evaluated against a clinical bacteria panel.

Methods. Antimicrobial activity of peptides S2-P082090 and S5-P082090 was investigated *in vitro* using Omiganan® (OMI) as comparator. MIC was determined by CLSI broth microdilution method (M07-A8) using cation-adjusted Mueller-Hinton broth.

We included 79 previously characterized isolates collected at the National Reference Laboratory (INEI) with different mechanisms of resistance: 38 GP (WT, *vanA*, *vanB*, *vanC*, *mecA*, *ermA*, *ermC*, *msrA*, *lnuA*) and 41 GN (*tem-1*, *cmv*, *cit*, *shv-1*, *ctx-m-2*, *per-2*, *ges-1/3*, *veb-1*, *oxa-9*, *oxa-23*, *oxa-58*, *vim-11*, *imp-1/13/16*, *spm-1*, *kpc-2*). Additionally *P. aeruginosa* ATCC27853, *E. coli* ATCC25922, *S. aureus* ATCC29213 and *E. faecalis* ATCC51299 and ATCC29212 were included as reference strains.

Results.

| Organism (no. Isolates) | MIC ₅₀ /MIC ₉₀ /Range | | |
|-----------------------------|---|-----------------|------------------|
| | S2 | S5 | OMI |
| <i>S. aureus</i> (12) | 32/64/32-128 | 64/64/32-64 | 32/64/32-128 |
| CNS (12) | 8/16/4-32 | 8/8/4-16 | 8/8/4-16 |
| <i>E. faecalis</i> (6) | 128/256/128-256 | 128/256/128-256 | 128/256/128-256 |
| <i>E. non-faecalis</i> (11) | 16/16/8-32 | 16/16/8-16 | 16/16/4-16 |
| <i>K. pneumoniae</i> (12) | 32/64/8-128 | 32/64/8-128 | 128/1024/32-1024 |
| <i>E. coli</i> (9) | 32/64/4-64 | 32/64/16-128 | 64/64/32-64 |
| <i>P. aeruginosa</i> (12) | 64/64/64 | 64/64/32-128 | 512/512/128-512 |
| <i>A. baumannii</i> (10) | 16/32/4-32 | 8/32/4-32 | 64/64/16-128 |

Conclusion. S2-P082090 and S5-P082090 peptides demonstrated comparable MIC₅₀/MIC₉₀/MIC range between them. S2-P082090 and S5-P082090 peptides showed similar activity than OMI against GP isolates but higher against GN. Main differences were observed in *K. pneumoniae* and *P. aeruginosa* with MIC 3-4 dilution lower than OMI.