

N-terminal Modifications Modulates the Activity of Hylin a1.

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Antibiotic resistant bacterial strains represent a global health problem. Thus, there is an urgent need for the development of new antibiotics. Castro's group isolated the peptide Hylin a1 (IFGAILPLALGALKNLIK), the first cytolytic peptide isolated from the arboreal South American frog *Hypsiboas albopunctatus*. In this work were evaluated 4 analogues to supply information about the relation regarding structure-biological activity. These analogues contain one Trp at position 6, for fluorescent studies, and different *N*-terminus group: 1)no modification; 2)one acetyl group (no charge); 3)one aspartate (negative charge); 4)one lysine (positive charge). The peptides were synthesized by SPPS using the Fmoc chemical approach and purified by HPLC. The peptide containing Trp in position 6 replacing Leu presented MIC values comparable to wild type sequence: 32 µM, 32 µM, 8 µM and 2 µM for *E. coli*, *P. aeruginosa*, *S. aureus* and *B. subtilis*, respectively. Two peptides containing one acetyl group or an Asp at the *N*-terminus showed MIC values of = 128 µM for *E. coli* and *P. aeruginosa*, although 4 µM for Gram-positive bacteria. Different results were observed when the residue was Lys, the activity against all bacteria was sustained or increased. Conformational properties were investigated by CD technique in water, TFE and in zwitterionic micelles (LPC). These experiments demonstrated that in water the peptides had a random structure, but in TFE and LPC solutions, they acquired a structure composed mainly by α -helix. These results showed that the *N*-terminal region of the peptide *Hy-a1* developed key roles in its antibacterial action in different types of bacteria.

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