COMPARATIVE CONFORMATIONAL ANALYSIS OF INDOLICIDIN AND ITS ANALOGUES BY SIMULATED ANNEALING

Balázs Leitgeb[a], Ádám Kerényi[a], and Gábor Rákhely[a,b]

[a]Institute of Biophysics, Biological Research Centre of the Hungarian Academy of Sciences, P.O. Box 521, H-6701 Szeged, Hungary
[b]Department of Biotechnology, University of Szeged, P.O. Box 521, H-6701 Szeged, Hungary

Indolicidin is an antimicrobial tridecapeptide isolated from bovine neutrophils, and it has a remarkable primary structure containing five Trp-s, three Pro-s and three basic residues (Arg, Lys) [1]. This peptide has a broad spectrum of antimicrobial activity against Gram(+) bacteria, Gram(-) bacteria and fungi, as well as it exhibits haemolytic and antiviral activities. The aim of this study was to compare the different structural properties of indolicidin and its *enantio*-, *retro*- and *retroenantio*-analogues, because these analogues showed approximately the same antibacterial activity as the parent peptide [2]. The conformational analysis of the investigated peptides containing *trans* Xxx-Pro peptide bonds were performed using simulated annealing (SA) method. The distributions of the conformers obtained by SA were represented in Ramachandran plots, in which the preferred conformational regions were identified. Furthermore, to characterize the backbone conformations, pseudo-torsion angle maps were constructed, in which the pseudo-torsion angles defined by four consecutive C_α atoms were depicted. The *g(+)*, *g(-)* and *trans* rotamer populations of the amino acid side-chains were also determined. For all peptides, the occurring secondary structural elements were examined, and poly-proline II helical segments were observed along the entire sequence of molecules. Based on the distributions of the values of Φ and Ψ torsion angles, the largest conformer populations were determined. Using the ranges of torsion angles characteristic to the largest populations, the poly-proline II helix-like structures were identified in certain parts of the molecules. In the case of indolicidin and its analogues, the different intramolecular interactions (H-bonds, aromatic-aromatic interactions and proline-aromatic interactions) were also investigated, which can play a role in the stabilization of various conformers.

[1] Selsted, M. E.; Novotny, M. J.; Morris, W. L.; Tang, Y.-Q.; Smith, W.; Cullor, J. S. (1992) *J. Biol. Chem.* **267**, 4292-4295.
[2] Staubitz, P.; Peschel, A.; Nieuwenhuizen, W. F.; Otto, M.; Götz, F.; Jung, G.; Jack, R. W. (2001) *J. Pept. Sci*. **7,** 552-564.