**Permeation of model membranes by Peptaibolin mimetics bearing different α,α-dialkylglycines**

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Some peptides are able to interact with the lipid bilayer membrane of bacteria, being able to modify and even permeate the membrane. Such is the case of Peptaibols, a family of natural antimicrobial peptides bearing α,α-dialkylglycines such as Aib, Iva and Deg in their composition. These stereochemically hindered amino acids yield peptides with more defined conformations and more resistant to biodegradation [1], usually adopting highly helical secondary structures that directly correlates to their mechanism of action, and hence antimicrobial properties, which rely on the permeation of the cell membrane and formation of ionic channels [2]. Recent *in silico* studies suggest that membrane affinity might be increased by the substitution of the Aib residues by more structurally constrained and more hydrophobic α,α-dialkylglycines [3].

Bearing these facts in mind, we now report the membrane permeation studies of a model peptide, Peptaibolin (Ac-Leu-Aib-Leu-Aib-Phol), which is the shortest member of the peptaibols family, and several mimetics incorporating unnatural α,α- dialkylglycines (Deg, Dpg, $Ac_6c$) at the native Aib positions [4]. The model membranes were based on small unilamellar vesicles composed of phosphatidylcholines (egg lecithin, DPPC), phosphatidylglycerols (DPPG, DOPG) and cholesterol, at different compositions and ratios, containing a fluorescent probe encapsulated in their aqueous interior, in order to monitor the permeation process by fluorescence spectroscopy. The obtained results revealed a correlation between the length and bulk of the side chain of the unnatural α,α-dialkylglycines and the ability of the corresponding peptide to permeate the model membranes.

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