

Interaction Of Bradykinin And Its TOAC-Containing Derivatives With Model Membranes

Marín, N.¹, Vieira, R.F.F.², Nakaie, C.R.², Schreier, S.¹

¹Department of Biochemistry, Institute of Chemistry, USP, São Paulo, Brazil

²Department of Biophysics, UNIFESP, São Paulo, Brazil

Circular dichroism (CD) and electron paramagnetic resonance (EPR) were employed to investigate the interaction of bradykinin (Arg¹-Pro²-Pro³-Gly⁴-Phe⁵-Ser⁶-Pro⁷-Phe⁸-Arg⁹, BK) and its analogues containing TOAC (2,2,6,6-tetramethylpiperidine-1-oxil-4-amino-4-carboxylic acid) at the N-terminus (TOAC⁰-BK) or replacing Pro³ (TOAC³-BK) with model membranes (large unilamellar vesicles (LUV) of zwitterionic 1-palmitoyl-2-oleoyl phosphatidylcholine (POPC) or 1:1 POPC:POPG (1-palmitoyl-2-oleoyl phosphatidylglycerol, POPG, anionic) and micelles of 1-palmitoyl-2-hydroxy-phosphatidylcholine (LPC) or 1:1 LPC:LPG (1-palmitoyl-2-hydroxy-phosphatidylglycerol, LPG)). In aqueous solution, BK and TOAC⁰-BK displayed similar CD spectra, characteristic of a flexible structure resulting from equilibria between different conformations. In the case of TOAC³-BK, TOAC imposes a bend different from that caused by Pro³. EPR spectra of TOAC-labeled peptides displayed narrow lines, indicating fast tumbling in the time scale of the experiment, the internally-labeled peptide giving rise to broader lines. The peptides bound to a much lesser extent to zwitterionic than to negatively charged model membranes, evincing the importance of electrostatic interactions for binding. The presence of two components in the EPR spectra, one more immobilized, due to membrane-bound peptide, and another due to peptide in solution allowed the calculation of partition coefficients. The more pronounced binding at lower pH (when the peptides carry higher positive charge) corroborated the role of electrostatic interactions for peptide-membrane interaction.

Keywords: Bradykinin, circular dichroism, EPR, model membrane, TOAC.

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