Binding of TOAC-Labeled Angiotensin II to Lysophospholipid Micelles

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Angiotensin II (DRVYIHPF, AII) is the main active compound of the renin-angiotensin system, causing vasoconstriction with a resulting increase in blood pressure. In this study we used circular dichroism (CD) and electron paramagnetic resonance (EPR) to examine the interaction between a paramagnetic analogue of Ang II containing the amino acid 2,2,6,6-tetramethylpiperidine-1-oxil-4-amino-4-carboxylic acid (TOAC) at the N-terminus (TOAC[1]-AII) with model membranes. The conformational properties of TOAC[1]-AII were studied in solution and in the presence of variable concentrations of micelles consisting of lysophospholipids - zwitterionic 1-palmitoyl-2-hydroxy-phosphatidylcholine (LPC) or a 1:1 mixture of LPC and anionic 1-palmitoyl-2-hydroxy-phosphatidylglycerol (LPG). The experiments were carried out at pHs 4.0, 7.0, and 10.0. CD spectra showed that TOAC[1]-AII bound to both types of micelles at the three pHs examined, acquiring secondary structure. Upon binding, the peptide gave rise to a ß-turn. The EPR spectra of TOAC[1]-AII also provided evidence for the peptide-micelle interaction. In aqueous solution the spectra of TOAC[1]-AII presented three narrow lines, indicative of fast tumbling. Binding to the micelles caused spectral line broadening. The binding increased with increasing micelle concentration. At intermediate micelle concentrations, two-component spectra were obtained, one due to the peptide in solution and the other to the micelle-bound population. The binding to LPC was low at the three pHs. In the case of LPC:LPG, the binding decreased with increasing pH. These results indicate that, although electrostatic interactions play an important role, other interactions (hydrophobic, hydrogen bonding) also contribute to peptide binding.
Keywords: TOAC, Angiotensin II, circular dichroism, EPR, micelle.

Support: FAPESP, CNPq,