COMPARATIVE STRUCTURAL STUDIES BETWEEN NATIVE PRTX-I AND ITS COMPLEXED FORM WITH a-TOCOPHEROL

dos Santos, J.I[1].; Oliveira, C. Z.[2]; Marcussi, S.[2]; Soares, A. M[2].; Fontes, M. R. M.[1]

[1]Depto. de Física e Biofísica, Instituto de Biociências, UNESP – Botucatu / SP, Brasil
[2]Depto. de Análises Clínicas, Bromatológicas e Toxicológicas, FCFRP, USP – Ribeirão Preto / SP, Brasil

Phospholipases A_2 (PLA_2s) are small calcium–dependent proteins that cause the liberation of fatty acids and lisophospholipids by hydrolysis of membrane phospholipids. These enzymes are largely studied because of the various pharmacological effects they play in envenomation by snake bites. PrTX-I is a basic Lys49-PLA_2 from *Bothrops pirajai* that presents myotoxic activity. This protein was crystallized on its native form and also in associtation with a-tocopherol (aT) and aT acetate under the same crystallization conditions. Comparative studies showed that when the inhibitor is present in the hydrophobic channel of this PLA_2 some residues of this region are dislocated (mainly the ones from de Ca^{2+} binding loop). Other residues from the N-terminal and C-terminal regions also seem to be in different conformations. This fact shows that these residues may play an important role in the inhibition of the myotoxic effect caused by the enzyme. Other native and complexed Lys49-PLA_2s were also compared with the structures obtained. *In vivo* studies were also performed and showed that the aT acetate is able to inhibit 50% of the myotoxic activity presented by PrTX-I.

This work was supported by FAPESP, FUNDUNESP, LNLS and CNPq.