Structural Studies with a Phospholipase A_2 Homologue Complexed to Mn^{2+} Ions – Possible Role for Myotoxicity Inhibition

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Snakes from *Bothrops* genus are responsible for the great majority of the ophidian accidents that happen in Brazil. Their venom contains many toxins, being of relevance the phospholipases A_2 (PLA_2s). PLA_2s are small, stable and calcium-dependent enzymes that hydrolyze the ester sn-2 bond of phospholipids, liberating lysophospholipids and fatty acids. Otherwise, PLA_2s homologues are non-catalytic but present a wide range of pharmacological activities, such as hypotension, cardiotoxicity, neurotoxicity and myotoxicity. Myotoxic activity has been the focus of many studies, since the serum therapy is not efficient against the muscular injury induced by these PLA_2s. Recent studies show a reduction in myotoxic activity of bothropstoxin-I (BthTX-I, a PLA_2 homologue) in the presence of divalent ions when injected in rats. In order to understand the reason of this reduction and trying to get insights into the mechanisms of phospholipases A_2 homologues action, the co-crystallization of the basic PLA_2 homologue piratoxin-I (PrTX-I) from *Bothrops pirajai* with manganese ions were performed. The crystallographic structure of this complex was determined at 1.9Å and present 92.3% of completeness and R_{merge}=10.1%. Preliminary results indicate electronic densities that may correspond to the manganese ions, deserving to be highlighted the presence of one ion in the hydrophobic channel. This region is known to be the local of interaction of many inhibitors of PLA_2s homologues. Comparative studies are being realized to comprehend the reduction of the myotoxic activity when the manganese ions interact with the toxin.

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