VIRTUAL SCREENING AND PROTEIN-LIGAND DOCKING OF PHOSPHOLIPASES A_2 INHIBITORS

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The knowledge of the three-dimensional structure of a protein is important when the objective is drug design. For this, it was made a survey of complexes of PLA_2 deposited in the PDB and, after that, an alignment pairwise of the 30 sequences of PLA_2 of the complexes using the AMPS package. A pairwise alignment was carried through involving 8 sequences selected by crystallographic criteria, followed of a multiple alignment with the sequence of present the BthTX-I and II toxins in the venom of Bothrops jararacussu, fixing the elements of secondary structure of the templates. MODELLER has been used to yield models with good quality by stereochemical, packing of residues and chemical environment criteria. Docking procedures were performed with rosmarinic acid, a snake venom phospholipase A_2 inhibitor from *Cordia verbenacea*, and 25 phospholipase A_2 inhibitors in order to propose a binding model to them and point out modifications in the structure of rosmarinic acid. All the structures were full optimized by quantum-chemical calculations at B3LYP/6-31G* level. Additionally, a virtual screening by substructure was performed for BthTX-I and II, using a drug-like collection of a 5.5 million compounds commercial database. Results have suggested important structural aspects in the compounds for BthTX inhibition.