Structural and conformational characterization of human prothrombin

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Prothrombin is an important zymogen of the coagulation cascade since its active form, α-thrombin, is the key enzyme for converting soluble fibrinogen into insoluble fibrin monomers, which in turn organize itself in a proteic clot that establish the platelet plug and, consequently, contribute to control the hemorrhagic processes. The prothrombinase complex (formed by factor Xa, factor Va, Ca^{2+} and anionic phospholipid-containing membranes) is essential in prothrombin activation, in a process that culminates in the generation of α-thrombin and fragment F1.2. As substrate of an enzymatic reaction, prothrombin appears to be a very flexible molecule, fact that may be correlated with the absence of its crystallographic structure. In this context, the current work employs comparative modeling techniques, docking calculations and molecular dynamics simulations in order to construct a theoretical model of the complete human prothrombin, capable to support the structural interpretation of its biological roles at the atomic level and so be potentially employed in further experiments to develop new antithrombotic agents. The so obtained model indicates the presence of hinge movements between prothrombin domains. Also, a high flexibility was able to be observed in a series of regions of the protein, as for its *N*-terminal and some exposed loops, both characteristics that can be associated with its proteolysis susceptibility and specificity.

Key Words: *docking, comparative modeling, molecular dynamics, prothrombin*
Supported by: CNPq IM-INOFAR (420015/05-1), CNPq Universal (472174/2007- 0), CAPES e FAPERGS.