Haptoglobin: The Use of Molecular Modeling Techniques for a Structure-Activity Relationship Study of its Polymorphic Variants

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Haptoglobin (Hp1) is the first line of defense against hemoglobin-mediated oxidative damage during intravascular hemolysis. However its three-dimensional structure has not been experimentally determined. Since molecular modeling computational tools may be used to identify Hp1 3D-structure and the correlation with its biological activity, in this work, we used a homology molecular modeling approach on that purpose. Thus we used Clustal W2, Swiss-model-Deepview/Swiss-PDB Viewer 4.0 and Procheck computational programs for constructing the theoretical models and analyze its structure-activity relationship of HP1 and two variants, Hp1F that present the substitutions N52D and E53K in α-chain, and HpR with an extra arginine in α-chain and other substitutions in β-chain. Our results showed that Hp1 α-chain is similar to system complement proteases (C1r - zimogen catalytic domain and C1s), and apoliprotein-H (24%, 27% and 15% respectively), whereas β-chain is similar the C1r (active catalytic domain) and other serine-proteases (*i.e.* trombin - 29%) with low RMS (0,63 - 1,82 Å) and, similar folding. Despite of that, the volume and the electrostatic potential map analysis of Hp1 revealed a higher electronegativity and area than Hp1F and Hpr. A recent experimental study of our group showed that ecotin, an inhibitor of serine-proteases, is capable of binding to Hp1 in mammary gland involution process. Herein we observed feasible interactions of Hp1 β-chain with ecotin. Thus, Hp1, Hp1F and Hpr homology models may assist in the understanding of the biological role of these molecules in the processes they are involved in (Financial Support: CNPq, FAPERJ, UFF)