CHARACTERIZATION OF HEMATIN COMPLEXATION TO A SET OF NEW ANTIMALARIAL AGENTS USING MOLECULAR DYNAMICS SIMULATIONS

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Quinolinic derivatives have been the basis of antimalarial treatment for the past 50 years. It is believed that these compounds act through interaction with hematin in the lysossomal digestive vacuole of the malaria parasite and, consequently, block the hemozoin formation. Such process is mainly guided by the high affinity between antimalarial compounds and the solution forms of protoporphyrin IX. In this context, the current work intends to analyze and properly describe the interactions between hematin and a set of new antimalarial agents in aqueous solution using molecular dynamics (MD) simulations. Therefore, the compounds topologies were built using the Prodrg Server and *ab initio* atomic charges at the 6-31G** basis set. Each compound and hematin molecules were randomly oriented in a box with explicit water molecules and submitted to a 5.0ns MD using GROMACS simulation suite and GROMOS96 force field. Through the simulations, the ligand-hematin complexes were formed spontaneously by diffusion, and the observed interactions allowed us to identify the main interactions responsible for the compounds activity. Additionally, the observation of hemozoin formation from hematin in MD gives important evidence that such process is non-enzymatic, occurring spontaneously in solution. Supported by CNPq, FAPERGS, and CAPES/COFECUB.