Study *in silico* and *in vitro* of PfHT: a Potential Chemotherapy Target

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Introduction: Malaria continues a public health problem. The search for new treatments is required due the parasite resistance to antimalarial drugs. Among transporters identified as potential chemotherapeutic targets, the PfHT has been highlighted. PfHT plays a crucial role in glucose transport during the intraerythrocytic cycle of the parasite. **Objectives:** Thus, this study aims to determine activity in silico and in vitro of PfHT. **Material and Methods:** PfHT models were constructed by homology. Molecular docking simulations between *O*-(undec-10-en)-l-D-glucose and the constructed active site of the PfHT models were performed using Autodock Vina. The complexes were refined by the hybrid QM/MM method. The antimalarial effect of the synthetic glycosides derivatives was measured using traditional method. The cytotoxicity of the compounds was assessed with using MTT colorimetric method. **Results and Discussion:** The model P5 presented a set of 12 α-helix, characteristic of transmembrane proteins. In addition, exhibited 93.2% of residues in favorable regions and negative potential energy according to Ramachandram and ANOLEA, respectively. The O-(undec-10-en-1-yl)-D-glucose derivatives have similar conformations. Consequently, they had similar docking binding energies, differing in only 0.5 Kcal/mol at most, making the biological activity prediction of these compounds difficult. Docking results improved by QM/MM calculations increased the range of bindingenergy in 0.65 Kcal/mol. These data describe the pharmacoforic conformation of potential antimalarial glycosides using *in silico* methodologies. **Conclusions:** PfHT as a potencial chemotherapeutic target. The half maximal inhibitory concentration (IC50) and the lethal drug concentration (LC50) values determined for nine glycosides derivatives **1-9** are given. All compounds showed potency against the *P. falciparum* chloroquine-resistant clone W2, with IC50 values ranging from 0.12 µM to 0.74 µM. In parallel we tested the toxicity of the compounds against the WI-26-VA4 cell line. All the samples presented no cytotoxic activity, with IC50 values >20mM. These data indicate PfHT as a potential chemotherapeutic target.

Key Words: malaria, homology modeling, hexoses.
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