Molecular Docking and Structural Optimization of Bioactive Compounds from Natural Products Against UAP-1 of *L. braziliensis*

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Leishmaniasis are classified by the World Health Organization (WHO) as a neglected tropical diseases and receive low research investments for developing new methods for treatment and prophylaxis. Molecules derived from natural products are an interesting source for drug synthesis and design, but we little know about their macromolecular targets. Thus, computational methods have high importance to study and analyze the interactions of drug-like molecules, which are candidate to become prototype of new drugs. Assuming that structurally similar molecules exhibit similar biological activity thus, we searched in different public databases for analogs to the essential oil molecules obtained from *Piper marginatum* wichwhich showed good inhibitory activity against *Leishmania* promastigote cultures. These compounds were extracted of leaves from *Piper marginatum* by hydrodistillation and then identified by gas chromatography coupled mass spectrometry. With the molecular structure of the compounds, we then performed structural alignment in Marvin Sketch seeking desired values of Tanimoto similarity. Thereby, we found an interesting structural similarity with inhibitor of N-acetylglucosamine pyrophosphorilase (UAP-1) of *Trypanosoma brucei* with the molecule 3,4-methylenedioxypropiophenone, which constitute 21% of essential oil. Searching in Blastp, we also found 41% of identity between *T. brucei* protein with the homologous UAP-1 from *Leishmania brasiliensis*. Then, we modeled the structure of *Lb*UAP-1 by homology in Modeller, using as reference the homologous protein of *T. Brucei* (PDB ID 4BQH). The model obtained was further evaluated by Ramachandran plot in PROCHECK program, Verify3D, and also by the atomic non-local energy profile in the ANOLEA plot. Analyzing the two cavities, we noted that both shares similar topography and electrostatic potential map.Then, molecular docking simulations of the compound 3,4-methylenedioxypropiophenone, against the modeled UAP-1 protein of *L. brasiliensis* was performed in Molegro program using the MolDock Optimizer algorithm. The cavity of protein was pre-selected in the LbUAP-1 using as reference the spatial coordinates of homolog structure in *T. brucei* and it showed similar biding mode with the crystal inhibitor. Therefore, we designed new inhibitors using the structure with optimized affinity to the biding site and the interactions were analyzed by Biovia Discovery Studio program. This compound from *Piper* essential oil could be used as fragment-based optimization and synthesis of new inhibitors against *Leishmania* species.