In silico study of Hypoxanthine-guanine Phosphoribosyltransferase inhibitors for drug design against *Leishmania* species

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The hypoxanthine-guanine phosphoribosyltransferase (HGPRT) initiates the metabolism of toxic purine bases of the *Leishmania* species. This enzyme mechanism is specifc for the parasite and is absent in mammalian hosts. This factor allows the HPRT becomes a promising target for drug development on leishmaniasis treatment. The active site of HGPRT presents one guanine monophosphate (GMP) in both chains A and B. The main difference between Leishmania and human enzymes is the interaction between the ribose GMP, which allows a comparison between these enzymes and contributes to the exploration of potential inhibitors. The ligands used in this work are deposited in The SAM Database, hosted at the Laboratory of Bioinformatics and Computational Chemistry from Universidade Estadual do Sudoeste da Bahia, Jequié, Brazil. All compounds were isolated from brazilian semiarid plant species, with active extracts against *Leishmania* species. The molecular structures of the ligands were prepared in Marvin Sketch (Chemaxon) for verification of the valences and structural errors, and then saved in mol2 format. The AutoDock tools was used to prepares the ligands for docking studies and convert them to pdbqt format. Furthermore, it was defined the region of interaction with potential inhibitors (gridbox) and recorded coordinates. The molecular docking calculation was performed using the AutoDock Vina program. Ligand docking poses with better energy values were choosed using PyMOL 1.7, as well as for obtaining the complexes in pdb format. The interaction maps for each best energy complex were generated using Discovery Studio 4.0 program.We selected 82 deposited compound structures, isolated from brazilian semiarid plants, in order to perform virtual screening and molecular docking studies for HGPRT inhibitors, based on previous studies of these plant extracts against *Leishmania* species. Seven structures presented affinity energies bellow -7.0 Kcal/Mol, and all ligands presenting interactions with active site residues of HGPRT. The molecule SAM25442 presented the best affinity energy of -7.8 Kcal/Mol. The next steps of this study are generating analogues for each best affinity compound found, as well as free-energy calculations using molecular dynamics approaches. These chemical constituents can become future drug candidates against *Leishmania* species.