In silico screening of semiarid plant compounds targeting 5-lipooxygenase (LOX)

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5-Lipoxygenase (LOX) are a family of enzymes important in the production of essential chemical mediators in the inflammatory process and allergies. This enzyme is a therapeutic target used in the production of medicaments leukotriene antagonists (LTA) versus obstructive respiratory diseases (asthma, bronchitis, allergic rhinitis). 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 with previous described antiinflammatory potential. Molecular structures of all ligands were prepared in Marvin Sketch (Chemaxon) for verification of the valences and structural errors, and then saved in Mol2 format. AutoDock tools was used for ligand preparation for docking studies and convert them to pdbqt format. Furthermore, it was defined the region of interaction with potential inhibitors (gridbox) and recorded coordinates, based on LOX crystallographic active site described on the literature. The molecular docking calculation was performed using the AutoDock Vina. Ligand docking poses with better energy values were chosen using PyMOL 1.7, and then the complexes were saved in pdb format. The protein-ligand interaction maps for each best energy complex were generated using Discovery Studio 4.0, in order to verifiy if each ligand interacted with the active pocket residues.We selected 26 deposited compound structures, isolated from brazilian semiarid plants, in order to perform virtual screening and molecular docking studies against LOX. After Autodock Vina calculations and pose validations, 16 structures presented affinity energies bellow -7.0 Kcal/Mol interacting with LOX active site residues. The molecule SAM2725 presented the best affinity energy (-9.9 Kcal/Mol) and the best positioning in the pocket (PHE177 and GLN363), in comparison to montelukast® (-8.6 Kcal/Mol), an inhibitor of leukotriene synthesis. Even virtual screening approach using Autodock Vina calculations has a been validated for 190 protein-ligand complexes bellow 2.0 Å, is very important consider free-energy molecular dynamics calculations with solvent accessibility (eg. MMPBS/GBSA) to confirm SAM2725 as a theoretical LOX inhibitor. In addition to molecular dynamics, in a further step we will generate analogues for each best affinity compound found. As a preliminary screening, this study may provide chemical natural compounds to be tested in vitro as new inhibitors of LOX for future drug candidates.