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Molecular docking and dynamics of AKT1 and *N*-heterocycles on the search for novel anticancer compounds

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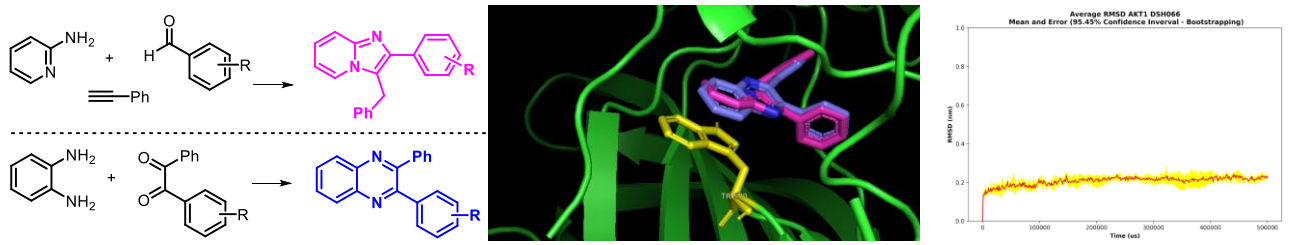
ABSTRACT

The AKT1 human serine/threonine kinase has a main role in the anticancer activity and its inhibition was described by heterocyclic compounds. These allosteric inhibitors effectively bind to tryptophan-80 among other aminoacids in the receptor active site. In this work we have investigated the interaction between modified crystallographic AKT1 (PDB:4EJN) and two classes of *N*-heterocycles (imidazo[1,2-*a*]pyridines and diarylquinoxaline) by *in silico* methods. Model compounds were previously synthesized by cyclization reactions in good yields. Molecular docking (AutoDock software) resulted in high affinity with the active site with free energies between -11.0 and -9.5 kcal/mole for both classes of compounds, with similar π–π interactions between the heteroaromatic rings and Trp-80. Molecular dynamics (GROMACS software) in aqueous solution resulted in high stability of the substrate-receptor complex after 500 ns as depicted by the protein RMSD. From these promising results targeted-oriented design and synthesis of new compounds prior to *in vitro* evaluation are being developed.



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