Molecular Dynamics Simulation and Binding Studies of Ajmalicinine With CDK4

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Cyclin-dependent kinase 4 (CDK4) is an enzyme responsible for the G1 to S phase transition in the cell cycle. CDK4 inhibitor of CDK4 (INK4)-retinoblastoma (Rb) pathway controls cell progression and dysregulation of this pathway lead for initiation and progression of many cancers. Thus, CDK4 inhibitors have the potential to be used as anti-cancer treatments.Ajmalicinine is an alkaloid compound which present in *Petchia ceylanica* (Kukulkaduru), a plant endemic to Sri Lanka. We carried out an in-silico study to investigate whether Ajmalicinine can bind to CDK4 and, if so, its mode of interaction. Molecular docking procedure was employed to predict binding affinity and pose of hypothetical alkaloid compound based on fascaplysin (one of the best inhibitors for CDK4); Carbofascaplysin (as a reference ligand) and Ajmalicinine to CDK4 receptor. Our study revealed that Ajmalicinine successfully docked on to the binding site and with more compatible binding affinity similar to Carbofascaplysin. Molecular dynamic (MD) simulations were performed to investigate the stability of the two complexes in an aqueous medium. The results indicated greater stability and similar behavior in the Ajmalicinine-CDK4 complex in the aqueous medium. The integrity of the complexes was conserved by strong hydrogen bonds formed between the amino acid residues of the proteins and ligands. The findings revealed that Ajmalicinine is a feasible agonist to CDK4 and warrants further investigation of the pharmaceutical potential of Ajmalicininein vitro and in vivo.

Keywords: CDK4, Ajmalicinine, molecular dynamics