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A comparison study of binding affinity of charantin to insulin receptor and hypoglycemic potency

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Background: Charantin is a 1:1 mixture of two steroidal saponins 5, 25 – stigmasteryl glucoside (CTA) and β-sitosteryl glucoside (CTB) obtained from *Momordica charantia* which is reputed for its hypoglycemic effect. Abundant pre-clinical studies have documented about the anti-diabetic and hypoglycemic effects of *M. charantia* through various postulated mechanisms. However, not much experimental and/or theoretical studies found in literature about the physiological function and blood glucose lowering effect of charantin.
Objective: Therefore, main objective of the study was to determine the binding stabilities of CTA and CTB in order to initiate further studies to propose its mechanism of action, based on the results.
Method: The molecular docking procedure with DOCK 6 software was employed to predict the binding affinity of CTA, CTB and a mixture of CTA and CTB to insulin receptor (InsR). The same docking procedure was used for insulin and respective grid scores were recorded. Docked ligand-receptor complexes of charantin and insulin with InsR were pursued for molecular dynamic (MD) simulation in Gromacs, for 30 ns time period to investigate the stability of the complexes.
Results: Docking results revealed all the ligands were bonded in the regions of the N-terminus of the A chain and in the B-chain α helix, β turn and β strand of the InsR. CTB showed a comparable binding affinity (-347.3 kJ/mol) to insulin (-387.3 kJ/mol) with InsR ($p \leq 0.05$). The MD results show that the CTB behave significantly similar to insulin ($p \leq 0.05$), with in the same range of 0.3 nm to 0.45 nm in Root Mean Square Deviation (RMSD), ±0.1 nm fluctuation around ~2.1 nm Radius of gyration (Rg) and Solvent Accessible Surface Area (SAS).
Conclusion: Therefore, it could be concluded that the CTB is a suitable candidate to conduct an extensive investigation to find the function and hypoglycemic mechanism and these studies are already underway.