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# Molecular modeling a tool for postulating the mechanism of drug interaction: glimepiride alters the pharmacokinetics of sildenafil citrate in diabetic nephropathy animals

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The present study evaluates the possible drug interaction between glimepiride (GLIM) and sildenafil citrate (SIL) in streptozotocin (STZ) induced in diabetic nephropathic (DN) animals and also postulates the possible mechanism of interaction by molecular modeling studies. Diabetic nephropathy was induced by single dose of STZ (60 mg/kg, ip) and confirms it by assessing the blood and urine biochemical parameters on 28th day of its induction. Selected DN animals were used for the drug interaction between GLIM (0.5mg/kg, p.o.) and SIL (2.5 mg/kg, p.o.) after 29th and 70th day of protocol. Drug interaction were assessed by evaluating the plasma drug concentration using HPLC-UV and also determine the change in the biochemical parameter in blood and urine. Mechanism of the interaction was postulated by molecular modeling study using Maestro module of Schrodinger software. DN was confirmed as there was significant alteration in the blood and urine biochemical parameter in STZ treated groups. The concentration of SIL increased significantly ($p<0.001$) in rat plasma when co administered with GLIM after 70th day of protocol. Molecular modelling study revealed few important interactions with rat serum albumin and CYP2C9.GLIM has strong hydrophobic interaction with binding site residues of rat serum albumin compared to SIL. Whereas, for CYP2C9, GLIM has strong hydrogen bond with polar contacts and hydrophobic interactions than SIL. Present study concludes that bioavailability of SIL increases when co-administered chronically with GLIM in the management of DN animals and mechanism has been supported by molecular modeling studies.

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