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Drug interaction studies of Sitagliptin with Diosgenin

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Diosgenin is a naturally occurring steroid saponin found abundantly in yams and legumes. Diosgenin is metabolized by inhibition of the CYP3A4 enzyme. Sitagliptin is an oral antihyperglycemic agent used for the treatment of NIDDM. It belongs to class DPP-4 inhibitor. It is also metabolized by CYP3A4 and CYP2C8 enzymes. We have studied the drug interaction study of diosgenin with sitagliptin in experimental diabetic rats. Diabetes was induced in the albino Wistar rats intraperitoneally using 55 mg/kg streptozotocin (STZ). Then they were divided into four groups of six each. Group I treated with sitagliptin (10 mg/kg), group II treated with diosgenin (20 mg/kg), group III treated with diosgenin followed by sitagliptin and group IV treated with diosgenin for 7 days and on the eighth day followed by sitagliptin. Blood samples were collected from an orbital puncture at time intervals between 0, 1, 2, 4, 8, 12, and 24hrs using heparinized capillaries. Serum was separated by centrifugation and stored at -20°C until further analysis. Different biochemical parameters like total cholesterol, triglycerides, AST, ALT, serum total protein, serum insulin, total antioxidant status and lipid peroxide levels were also estimated by using respective methods for 28 days. The obtained pharmacokinetic data shows an increase in C_{max}, T_{max}, AUC_{total}, AUC_{0-n}, t_{1/2}, MRT and decrease in V_d and CL in both normal and diabetic rats. In pharmacodynamic study group IV shown a decrease in serum glucose levels at all time points. The blood glucose level was decreased more in group IV in diabetic rats when compared to other groups in normal and diabetic rats. In diabetic condition total cholesterol, triglycerides, AST, and ALT levels increases and serum total protein and serum insulin levels decrease. All the serum biochemical parameters were regulated by both diosgenin and sitagliptin. But it was seen more in group IV rats when compared to other groups. After administration of diosgenin and sitagliptin regulates all the biochemical parameters more in group IV when compared to other groups. Diosgenin showed its antioxidant effect and decreased the lipid peroxide levels in a diabetic condition more in group IV than other groups. There was very significant (p<0.001) influence the percentage of glucose reduction in diabetic rats under multiple dose treatment but less significant (p<0.05) influence in normal rats. Thus, the improved pharmacokinetic parameters of sitagliptin were more observed in the multiple dose treatment groups, and the improvement of pharmacodynamics was significant in only diabetic rats under multiple dose treatment, thus showing the significance of the influence of diosgenin in multiple dose exposure under diabetic condition. This may be due to the synergistic effect of diosgenin and sitagliptin by inhibition of CYP3A4 in STZ induced diabetic rats. Hence sitagliptin dose may require special attention if used along with diosgenin or herbal preparations containing diosgenin to avoid complications.

Biography

Dr. Jyothi Penta completed her Ph.D in Pharmaceutical sciences from Kakatiya University. She completed masters and bachelors from Kakatiya University. Her research work was focused on herb-drug interaction studies based on pharmacokinetics and pharmacodynamics in rat models. Biochemical parameters and pk/pd modeling was done to estimate the interaction between anti diabetic drugs and Phyto chemicals.

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