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Influence of *Gymnema sylvestre* on the pharmacokinetics of Glipizide in diabetic and normal rats

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Aim: Diabetes mellitus is associated with oxidative stress induced micro and macro vascular complications. These complications lead to the development of dyslipidemia, hypertension and myocardial infarction. So, these patients are treated with more than two drugs. Herbs are often administered in combination with therapeutic drugs, raising the potential of herb-drug interactions. *Gymnema sylvestre* acts as a destroyer of *Madhumeha* (glycosuria) and other urinary disorders. On account of its property, it might neutralize the excess of sugar present in the body in diabetes mellitus. The sulfonylurea's Glipizide, Glimepiride, and Glibenclamide are metabolized by the CYP2C9 enzyme.

Materials & Methods: *Gymnema sylvestre* leaves were extracted by using solvents (volume ratio of methanol to water was 1:1 ratio). The extract was filtered through 0.45 µm nylon filter (Millipore). The volume was made up to 1000 mL with extracted solvent and clear supernatant was used for HPLC analysis. Glipizide standard curve was plotted by applying different concentrations. The estimation of Glipizide was achieved on HPLC, C18 reverse phase column plate used as stationary phase. The mobile phase consisting of methanol: water: 0.01 M potassium phosphate buffer (60:35:5, v/v/v). Albino male Wistar rats of either sex were randomly divided into four groups of six animals each. The Glipizide was estimated as per ICH guidelines the parameters like the concentration in plasma, C_{max}, AUC(o-t) and AUC(0-∞) (area under the concentration-time curve, AUC) and specificity were determined.

Results: Calibration curve of Glipizide was generated. The maximum peak of plasma concentration of Glipizide (µg/mL) was increased significantly in the presence of *Gymnema sylvestre* leaves extract (GSE), GPZ+GSE, from 0.87±0.08 to 1.42±0.07 in diabetic rats and 0.44±0.06 to 1.23±0.01 in normal rats, respectively. Area under the moment curve of Glipizide (µg/mL) was increased significantly in the presence of extract, GPZ + GSE, from 5.39±0.02 to 10.55±0.18, 2.53±0.08 to 8.52±0.1 in diabetic and normal rats, respectively. The clearance of Glipizide decreased significantly i. e. Glipizide, GPZ + GSE clearances were 6.19±0.12 to 2.57±0.72 in diabetic rats and 9.22±0.02 to 3.62±0.69 in normal rats respectively, but Tmax were same in diabetic and normal rats.

Conclusion: The present study concluded that hydro alcoholic extract of *Gymnema sylvestre* enhanced the bioavailability of Glipizide.

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