

Metformin interaction with popular Indian herbal remedies, *Boswellia serrata* (Sallaki) and *Withania somnifera* (Ashwagandha) - PK/PD approach with insulin resistant rodent model

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The general perception of herbal medicines as a safer alternative to allopathic drugs often leads to self-medication. Concomitant usage of herbal remedies (by chance or choice) with prescription medicines can lead to un-intended interactions modifying pharmacological properties of either drug, which could lead to potential treatment failure.

We designed a study, where metformin [MET], an extensively prescribed anti-diabetic medication was evaluated with commonly used Indian herbal remedies, Sallaki (SAL) and Ashwagandha (ASH). Pharmacokinetic and pharmacodynamics profiles were determined under normal and insulin resistance conditions in rodents. A sensitive bioanalytical method was developed and validated in-house for the determination of metformin. Pharmacokinetic and pharmacodynamic evaluations were performed by using Winnonlin (v 5.3). The evaluations included estimation of C_{max} , t_{max} , AUC_{0-t} , $AUC_{0-\infty}$, V_d , Cl , $t_{1/2}$ and K_{el} by non-compartmental pharmacokinetic analysis and estimation of plasma glucose concentrations at the scheduled time along with PK sampling. The data assessment involved plotting of response (plasma glucose) vs time and subsequent group wise comparison of the obtained data in both actual and percent-normalized form. The analysis of response vs time data was performed by non-compartmental pharmacodynamics analysis WinNonlin version 5.3.

The PK-PD study demonstrated that increased obesity and associated pathological changes led to increased systemic exposure of metformin. In the absence of herbs, MET glucose profile was stable with a narrow range of plasma glucose variations. ASH does not affect metformin pharmacokinetics. The C_{max} was reduced by 37% and AUC by 47%. Administration of SAL reduces the bioavailability of metformin. In presence of ongoing SAL treatment, higher doses of MET could be required to produce required effect.

This study assumes greater importance considering the fact that the chosen herbal remedies and the drug are used for the treatment of chronic conditions. Not many interactions are reported for metformin owing to its physico-chemical and metabolic characteristics. Our findings demonstrate that concomitant usage of metformin with sallaki may adversely affect the outcome or may result in needless increase in dosage.

Biography

Rekha Shenoy is currently working as an associate professor in the department of pharmacology at Manipal College of Pharmaceutical Sciences, Manipal University. She has been the recipient of three research grants funded by All India Council of Technical Education [AICTE] and Department of Biotechnology [DBT], New Delhi. Her areas of research interest are pharmacology of wound healing and role of antioxidants on healing status, inflammatory disorders and colon cancer. She has fifteen papers in impact factor journals to her credit.

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