

## ABSTRACT

The drug-herb combination between metformin and bitter melon frequently showed potential effects such as lowering glucose level. The use of both simultaneously needs to be studied further to find out the benefits and risks. To see whether bitter gourd might affect metformin pharmacokinetics profile and analyse the possible interaction between both. This study aims to analyse metformin in plasma sample using HPLC method and its pharmacokinetic profiles affected by bitter gourd. The study was conducted using an experimental method with post-test randomized controlled group design. Healthy albino rabbits were divided into three groups of 3 rabbits each. They were administered with bitter gourd juice 100% (v/v) and metformin (BM1), bitter gourd juice 50% (v/v) and metformin (BM2), and metformin 26 mg/kg (M). BM1 and BM2 was given bitter gourd juice for 14 days, then a single dose of metformin was given to all groups on the fifteenth day before metformin pharmacokinetic parameters were measured. Blood samples were collected from marginal ear vein puncture using NAF vacutainer at 0, 10, 30, 60, 120, 240, 360, and 480 minutes, centrifuged for 10 minutes at 5000 rpm to isolate plasma. The plasma was analysed using HPLC methods then the concentration versus time used for pharmacokinetic analysis. Bitter gourd fruit juice with 100% (v/v) concentration affected the pharmacokinetic profile of the metformin, decreased the V/F and CL/F, also increased  $K_a$ ,  $T^{1/2}$ ,  $C_{max}$ , MRT, and  $AUC_{0-inf}$ , also significantly increased  $AUC_{0-480}$ , and decreased  $T_{max}$  ( $p < 0.005$ ). Pharmacokinetics parameters of metformin after extravascular input could be analysed with 1-compartmental open model analysis. Bitter gourd fruit juice with 100% (v/v) concentration affected the pharmacokinetic profile of the metformin. It was significantly increased  $AUC_{0-480}$ , and decreased the  $C_{max}$  of metformin. Based on the result, this can be used as consideration to combine metformin and bitter gourd for diabetes mellitus treatment and adjust the metformin dose also resulted in beneficial pharmacokinetics interaction in normal condition.

**Keywords:** Drug-herb interaction; Pharmacokinetic profile; Metformin; Bitter Gourd.