showed a trend towards a decrease in PRN concentration levels *in situ* and *in vitro* **(Figure 3.22 and 3.25)** and *in vivo* experiments **(Table 3.49, Figure 3.20)** as compared to the control. Hepatocyte cell isolation and culture technique was used to study drug metabolism and drug-drug interaction between PRN and GlcN in comparison with control drugs (Hewitt *et al.* 2007).

A drug such as PRN is considered highly permeable since the extent of its absorption is greater or equal to 90% of the administered dose based on a mass balance determination or in comparison to an I.V. reference dose (Custodio *et al.* 2008). However, our results indicated that GlcN decreased PRN BA in a dose-dependent manner to a higher extent than that observed when PRN was used alone. This was emphasized by a shorter MRT of PRN with GlcN 200 mg/kg (2.54 h) as compared to PRN alone (2.69 h) meaning that higher clearance of PRN-GlcN 200 mg/kg **(Table 3.48, Figure 3.19)**. Furthermore, PRN was used as powder dissolved in solution and not as tablets. Hence, dissolution parameter would be excluded and permeability is the main factor responsible for PRN BA in the current research. P_{eff} values were optimized by SimCYP program to predict the actual average plasma PRN profile in order to estimate P_{eff}, V_d and clearance. GlcN at 100 mg/kg did not change P_{eff} or clearance of PRN, whereas GlcN at 200 mg/kg decreased P_{eff}, and increased clearance **(Table 3.50)**, which can be related to a dose dependent effect.

Many factors are involved in oral drug delivery, and its BA can be divided into components which reflect intestine delivery (gastric emptying, pH-pK_a), absorption from the lumen (dissolution, lipophilicity), and drug efflux pumps such