intestine with the main absorption site in the colon with the highest permeability (Nagare *et al.* 2010). Therefore, SPIP technique was used in the current investigation to assess how PRN BA would be affected in the presence of GlcN, cimetidine and rifampin using the whole length of the small intestine. The results showed that GlcN increased PRN BA significantly to a higher extent than cimetidine and rifampin **(Figure 3.22).** Everted gut technique has been used due to its ability to evaluate intestinal absorption of drugs without the influence of hepatic first-pass effect (Li *et al.* 2011). In the current study, everted gut model was used to enable the investigation of the effects of SLS as well as GlcN on PRN. The intestinal absorption of PRN or PRN concentration levels in the presence of GlcN was higher than in the presence of SLS **(Figure 3.23)** confirming the previous *in vitro* hepatocyte isolation and culture **(Figure 3.24)** and *in situ* results **(Figure 3.22).**

P-glycoprotein (P-gp) is another factor responsible for drug permeability. PRN is said to be a substrate for the (P-gp) efflux transporter, which decreases PRN oral absorption, thus, reducing its BA. A recent study using the SPIP technique has shown that P-gp affects the intestinal absorption of PRN. Verapamil HCl, a P-gp inhibitor, increased PRN BA when it was co-perfused with PRN more than PRN perfusion alone. This indicated that P-gp is an important contributor for PRN low oral BA (Abushammala *et al.* 2013). D'Emanuele and colleagues have shown that the reduction in PRN BA could be avoided when PRN is administered in conjugation with polyamidoamine (PAMAM) dendrimers (D'Emanuele *et al.* 2004). This complex bypasses P-gp efflux transporter and consequently increases its transport. Another