Chapter Four

4. Discussion

PRN has been used widely to treat hypertension, cardiac arrhythmias, and many other diseases (Routledge and Shand 1978). According to the Biopharmaceutics Classification System (BCS) PRN is classified as class 1 drug with rapid dissolution, high solubility, high permeability and an extensive metabolism (Custodio *et al.* 2008). Dissolution and GIT permeability are fundamental and major parameters controlling the rate and extent of drug absorption (Amidon *et al.* 1995). PRN undergoes extensive first-pass effect by the liver resulting in a relatively low oral BA of 13-23% (Cid *et al.* 1986; Sastry *et al.* 1993) and short plasma $t_{0.5}$ ranging from 3 to 6 hours (Castleden and George 1979; Ismail *et al.* 2004; Leahey *et al.* 1980). As a result, PRN has to be given in high doses to solve this problem, which inevitably increases PRN side effects (Partani *et al.* 2009). Ryu et al. have shown a strategy to overcome PRN low BA by using a route of drug delivery (rectal route) other than oral (Ryu *et al.* 1999). Rectal infusion of PRN induced a 4-5 fold increase in PRN BA. Another study in dogs has shown that PRN oral BA was increased by the administration of PRN laurate salt. This salt is a lipid vehicle containing fatty acids that increases the intestinal absorption of many drugs by various mechanisms (Aungst and Hussain 1992).

A study has shown that GlcN combination with ibuprofen produced a significant antinociceptive synergistic effect; a racemic mixture of GlcN with