incidence of the first episode of bleeding from esophageal varices as well as bleeding in patients with cirrhosis (Katzung *et al.* 2004; Watson *et al.* 1987).

1.3.3 Propranolol Pharmacokinetics

1.3.3.1 Absorption and bioavailability

PRN is a highly lipophilic drug that is almost completely absorbed from the GIT following oral administration (Salman *et al.* 2010). PRN peak plasma concentrations occur after 1–3 hours (T_{max}) of ingestion (Ismail *et al.* 2004), and its oral BA is relatively low of 13-23% (Cid *et al.* 1986; Sastry *et al.* 1993). Thus, a major consequence is that oral administration of the drug leads to lower drug concentrations as compared to those achieved after I.V. injection of the same dose. However, its BA could be increased by the concomitant ingestion of food and throughout the long-term administration of the drug (Brunton *et al.* 2006; Katzung *et al.* 2004). PRN is concentrated mainly in the lungs and to a lesser extent in other organs such as the brain, liver, and kidneys. Moreover, it undergoes extensive hepatic metabolism, therefore, the proportion of PRN that reaches the systemic circulation increases as the PRN dose is increased due to saturation of hepatic extraction mechanisms (Craig and Stitzel 2004; Katzung *et al.* 2004). PRN plasma $t_{0.5}$ ranges from 3 to 6 hours (Castleden and George 1979; Ismail *et al.* 2004; Leahey *et al.* 1980). Concentrations of PRN after single oral doses have shown higher concentrations in elderly (2.3 times) than in the young as well as S (-)-PRN enantiomer concentrations are present in higher amounts than R (+)-PRN enantiomer (Walle *et al.* 1988). Moreover, in a study conducted by Johnson et al they demonstrated that area under curve (AUC) for both R (+) and S (-)-PRN