1.3.3.3 Excretion

The kidneys are the primary route of PRN excretion, whereas the liver is the primary route of metabolism (Craig and Stitzel 2004). PRN excretion maybe prolonged and its BA may increase in the presence of liver diseases (e.g., hepatic cirrhosis with portosystemic shunting), hepatic enzyme inhibition, decreased hepatic blood flow or administration of drugs that affect hepatic metabolism (Katzung *et al.* 2004). PRN clearance is enantiomer-selective with preferential removal of the R (+)-enantiomer from the blood. Clearance through naphthalene ring hydroxylation is 2.5 fold greater for the R (+)-enantiomer in comparison to the S (-)-enantiomer due to the differences in the catalytic activities of CYP450 isoenzymes. However, the clearance for both the (+)- and (-)-enantiomers through both glucuronidation and side chain oxidation is identical (Walle *et al.* 1988).

1.3.3.4 Metabolism

PRN is highly extracted by the liver, so it shows marked variations in its BA among patients due to differences in blood flow and hepatic function, and this explains the reason of different concentrations of PRN for patients given the same dose of drug (Ismail *et al.* 2004; Katzung *et al.* 2004). PRN is cleared from the blood at a rate of 16 ml/min per kg. Thus, the liver is able to remove the amount of PRN contained in 1120 ml blood of a 70 kg human in 1 minute (Brunton *et al.* 2006).

Propranolol metabolic pathways

PRN metabolism in man occurs via three primary metabolic pathways namely; naphthalene ring hydroxylation, side chain oxidation, and glucuronidation (Marathe *et al.*