1994) **(Figure 1.4)**. Ring hydroxylation that has the share of 42% (range, 27-59%) of PRN metabolism. It is considered as the "first choice" pathway , followed by side chain oxidation with 41% (range, 32-50%), and glucuronidation which accounts for the least percentage of the three pathways of 17% of the dose (range, 10-25%) (Walle *et al.* 1985). Ring hydroxylation process occurs in either position four, five or seven. 7-hydroxy propranolol present in a very small amount in human liver microsomes, whereas 4-hydroxy and 5-hydroxy propranolol are the primary metabolites (Masubuchi *et al.* 1994). However, both of 4-hydroxy and 5-hydroxy propranolol showing a preference for R (+)-PRN stereoselectivity (Marathe *et al.* 1994). The resulted hydroxypropranolol will be either sulphoconjugated favoring the R (+)-PRN enantiomer, whereas conjugation with glucuronic acid favors S (-)-enantiomer. Also, conjugation with glucuronic acid to forming PRN glucuronide, favors the S (-)-enantiomer (Walle *et al.* 1988). N-dealkylation process stereoselectivity is concentration dependent. Therefore, higher concentration accounts for S (-)-enantiomer and the R (+)-enantiomer for lower concentrations (Marathe *et al.* 1994) **(Figure 1.4)**.

As for cytochrome isoforms involved in PRN metabolism, N-desisopropylpropranolol of both S- and R- isomers are highly associated with naphthoflavone and phenacetin o-deethylase (selective inhibitors of CYP1A2), meaning that CYP1A2 is involved in the metabolism of this pathway. On the other hand, quinidine and debrisoquine-4-hydroxylase which are index reaction of CYP2D6 (both are selective inhibitors of CYP2D6) which inhibits both 4 and 5-hydroxypropranolol of both enantiomers (Masubuchi *et al.* 1994; Yoshimoto *et al.* 1995). Furthermore, CYP1A2 has some catalytic activity on 4-hydroxypropranolol because furaphylline, a selective CYP1A2