enantiomer in white subjects has shown to be 292 ng.hr/ml versus 394 ng.hr/ml for black subjects (Johnson *et al.* 2000).

1.3.3.2 Distribution

Drug's V_d depends on its free concentration in the blood. As free drug concentration increases, its V_d will also increase because equilibrium is reached between the free drug and body tissues. PRN to plasma protein binding has been found to be 90 to 93.2% in man (Brunton *et al.* 2006; Evans *et al.* 1973; Ismail *et al.* 2004). α_1-AGP and lipoproteins often bind lipophilic and basic drugs like PRN. On the contrary, acidic drugs are bound to albumin. The degree of drug binding to proteins will differ in pathophysiological states due to changes in plasma-protein concentrations (Brunton *et al.* 2006; Katzung *et al.* 2004; Walle *et al.* 1988). For example, α_1-AGP is increased in acute inflammation, hence, total plasma concentration will be changed even though drug elimination is unchanged (Katzung *et al.* 2004). PRN-plasma binding has been found to be enantiomer-selective where R (+)-enantiomer binds to human serum albumin, whereas the opposite S (-)-enantiomer binds to α_1-Agp. Both enantiomers half-lives are identical. However, R (+)-enantiomer V_d is higher than S (-)-enantiomer which could be due to enantiomer selectivity in tissue binding or blood binding or both (Walle *et al.* 1988).

PRN is a lipophilic drug so; it can readily cross the blood-brain barrier. Furthermore, it is rapidly distributed and has large V_d of approximately 4 L/kg (Chidsey *et al.* 1975).