

1.1.2 Distribution

Once a drug enters the bloodstream, it distributes into different body cells and tissues by the influence of tissue hemodynamics and passive diffusion across lipid membranes. The drug binds to plasma proteins such as albumin forming drug-protein complexes. These complexes significantly influence the magnitude or the duration of drug's effect with no effect on the drug's therapeutic activity (Bauer 2001; Caldwell *et al.* 1995; Raffa 2010).

1.1.2.1 Factors affecting drug distribution

Many factors affect drug distribution such as the characteristics of the targeted compartment (bone, fat and muscles) and drug physicochemical properties (Dobesh 2004). Many proteins are involved in drug binding such as albumin, lipoproteins, and acid glycoprotein. Other intracellular proteins including myosin and actin in muscular tissue, melanin in pigmented tissue (particularly the eye) and ligandin that is present in liver, kidney and intestine can also influence drug distribution (Smith *et al.* 2012).

1.1.2.2 Volume of distribution

Volume of distribution (V_d) or the apparent volume of distribution is a theoretical PK parameter. V_d usually relates drug plasma concentrations to the total amount of the drug that is dissolved in the body (Bauer 2001; Dhillon and Gill 2006; Smith *et al.* 2012). The body is not a homogeneous unit, so the concentration of the drug in plasma is not necessarily the same in the liver, kidneys or other tissues. Therefore, V_d relates the total