

## Chapter Four: Discussion

In drug development, pharmacokinetics of the chosen chemical entity plays an important role in determining the form of administration, safety and eventually profitability to produce it on an industrial scale. The leading cause of discontinuing further developmental investigations of new chemical entities is problems with pharmacokinetic parameters (Prentis et al., 1988).

Pharmacokinetics is simply known as what the body does to the drug and is divided into Absorption, distribution, metabolism and elimination also known as ADME (Benet, 1984). Metabolism, the primary area of interest in this study, includes all elimination processes which enables the body to remove the drug from the physiological area (Ionescu and Cairra, 2005).

An essential concept associated with pharmacokinetics is bioavailability. It is defined as the rate and extent to which the active pharmaceutical ingredient or its active moiety is absorbed from a pharmaceutical product and becomes available at the site of action (US FDA guideline, 2003). The extent of the active pharmaceutical ingredient or the active moiety that is made available to the target organ depends on (i) its release from the drug formulation, (ii) rate and extent of absorption, (iii) first-pass metabolism, (iv) plasma protein binding and (v) excretion (Ayob and Noordin, 2004).

Hepatic first pass metabolism is the determining factor researched in this study of bioavailability. It is defined as the extent to which a drug is removed by the liver during