1.2.2.3 Drug interactions affecting excretion

Drugs are excreted by different sites of the body. Lungs are responsible for the excretion of inhalational agents (Corrie and Hardman 2011; Pleuvry 2005). Kidney excretion can be altered by changes in protein binding (Kashuba and Bertino Jr 2001; Pleuvry 2005).

1.2.2.4 Drug interactions affecting metabolism

Liver is the major site responsible for drug metabolism in order to activate or terminate the action of many drugs (Corrie and Hardman 2011). Therefore, a change in drug metabolism is considered as one of the important causes of unexpected drug interactions. Metabolizing enzymes can be inhibited by many drugs resulting in reduced metabolism and prolongation of drug effect (Corrie and Hardman 2011; Craig and Stitzel 2004; Ito *et al.* 1998; Kashuba and Bertino Jr 2001; Snyder *et al.* 2012). On the contrary, numerous drugs and environmental pollutants can induce the P450 system increasing drug metabolism. Enzyme induction has been responsible for failure of therapy for many drugs (Pleuvry 2005).

Enzyme inhibition

Enzyme inhibition is the primary mechanism for drug–drug pharmacokinetic interactions. Enzyme inhibition occurs via four types; competitive, non-competitive, uncompetitive and mechanism based**.** All types of inhibition are affected by the characteristics of CYP isoform and the concentrations of drugs. However, several drugs are metabolized by multiple isozymes where they act as competitive with one CYP and non-competitive with another (Coleman 2010; Ito *et al.* 1998).