1.2.2 Mechanisms of pharmacokinetic interactions

1.2.2.1 Drug interactions affecting absorption

Absorption mechanisms include active, facilitated, ion-pair transport and passive diffusion. In general, a drug interaction is considered clinically significant if the change in its extent of absorption is more than 20% (Kashuba and Bertino Jr 2001). Small intestine is the largest absorptive site in the GIT. Therefore, drugs that enhance gastric emptying such as metoclopramide accelerate drug absorption, whereas drugs that inhibit gastric emptying including muscarinic acetylcholine receptor antagonists slow absorption (Pleuvry 2005). Drug chelation results in the formation of insoluble compounds due to the formation of ring structure between a metal ion and an organic molecule, an example is the administration of magnesium and aluminum-containing antacids with quinolone antibiotics (Kashuba and Bertino Jr 2001).

1.2.2.2 Drug interactions affecting distribution

Drug interactions affecting distribution are drugs altering protein binding. Albumin is the major protein in the blood which binds acidic and basic drugs. However, acidic drugs are strongly bound to albumin more than basic drugs, whereas the latter binds to α_1-acid glycoprotein (α_1-Agp) (Kashuba and Bertino Jr 2001). Warfarin displacement by erythromycin is an example of protein binding displacement leading to an increased plasma concentration and therapeutic activity of warfarin (Corrie and Hardman 2011; Rolan 1994).