1.5 Cimetidine

Cimetidine is the first histamine type 2 (H_2) receptor antagonists. It inhibits gastric acid secretion by reversibly competing with histamine for binding to H_2 receptors on the basolateral membrane of parietal cells. It is used in the treatment of peptic ulcer disease (Brunton *et al.* 2006; Pelkonen and Puurunen 1980; Puurunen and Pelkonen 1979) as well as duodenal ulcers, and uncomplicated gastroesophageal reflex disease (Brunton *et al.* 2006).

1.5.1 Cimetidine drug interactions

Cimetidine is an imidazole-containing drug that binds to CYP450 heme iron and effectively reduce metabolism of endogenous substrates (e.g., testosterone) or other concomitant used drugs metabolized by CYP1A2, CYP2C9, CYP2D6, and CYP3A4 through competitive inhibition. Thus, the half-lives of these drugs will be prolonged (Brunton *et al.* 2006; Katzung *et al.* 2004). As a result, it is used as a control in many of literature studies documenting its role in drug interactions due to its clear effect and role in drug interactions (Piyapolrungroj *et al.* 2000).

Pharmacokinetic drug interaction between PRN and cimetidine may lead to reinforcement of the β-adrenoceptor blocking effects of PRN due to changes in the therapeutic levels of PRN in blood. Such interaction my also lead to pharmacodynamic effects where cimetidine was reported capable of causing dangerous reduction in blood pressure and heart rate in patients receiving PRN for coronary heart disease (Reimann *et al.* 1981).