CHAPTER I

INTRODUCTION

Recently, successful treatments of peptic ulcer with cimetidine have been reported by several investigators (1-8). Cimetidine has been proven to be effective in the treatment of gastric ulcer (1-3), duodenal ulcer (1,3-6), Zollinger-Ellison Syndrome (1,3,7) and in other conditions where inhibition of gastric acid secretion may be beneficial in numerous clinical studies (8). It is also extensively used intravenously in the treatment of acute gastrointestinal bleeding from various causes (9).

In Thailand, cimetidine is available in both tablet and injection. At least 5 different brands of 400 mg cimetidine tablets are marketed. One is a well known foreign manufactured brand, with high retail price. The others are various local manufactured brands. The methods of production and the final formulation of the drug may markedly affect the bioavailability of the drug (10). Hence, an extensive study was conducted to provide the absolute and relative bioavailabilities of different commercial cimetidine tablets. In addition, it is documented that the degree of inhibition of gastric acid by cimetidine was found to vary with its plasma concentrations (11-13). These observations made it of

interest to evaluate the pharmacokinetics of cimetidine after oral and intravenous administration in healthy volunteers.

Objectives :

1. To provide the absolute bioavailability of cimetidine tablets.

2. To compare the bioavailability of cimetidine tablets marketed in Thailand.

3. To investigate the pharmacokinetics of cimetidine after single oral and intravenous administration of cimetidine tablets and injections in Thai healthy volunteers.

4. To evaluate whether the local manufactured brands of cimetidine tablets are equivalent regarding to the quality and performance to the original brand.

Significance of the Study :

1. This study will provide an information about absolute and relative bioavailability of cimetidine tablets.

2. This study will provide several meaningful information about the pharmacokinetics of cimetidine in Thai healthy volunteers. The results obtained will be compared with previously reported studies which were conducted in other countries. The effects of races and tribes on the pharmacokinetics of this drug could thus be notified.

3. From the pharmacokinetic parameters describing the blood levels versus time profiles obtained from different brands, we would be able to determine whether the local manufactured brand of cimetidine tablets are essentially equivalent to an original formulation. It also enables to evaluate and select the economical products to provide the same biological equivalences.