



CHAPTER I

INTRODUCTION

Doxycycline, a structural isomer of tetracycline, has been the most widely used among tetracycline derivatives (1). It became available in 1966 (2). The molecule, obtained semi-synthetically from oxytetracycline or methacycline, is highly lipophilic permitting excellent penetration into tissues. In vitro antimicrobial activity of doxycycline is superior to that of the older tetracyclines (chlortetracycline, oxytetracycline, tetracycline) (3). Furthermore it shows far more advantageous pharmacokinetic characteristics. The serum half-life in adult man is between 15 and 22 hours so that a single daily dose is sufficient for therapy. There is only minimal depression of absorption when doxycycline is administered with food, and the drug may be used safely in patients with renal insufficiency (4).

In Thailand, doxycycline is one of the drugs in the National Essential Drug List of Thailand (5) which must be used by generic name in all government hospitals.

At present, more than eight different brands of 100-mg doxycycline capsules are available in the market. One is a well-known original brand, with high retail price. The others are various local manufactured brands. Although it has been used for many years, there appeared to be no available bioavailability data and pharmacokinetic characteristics of these products for verifying whether the local manufactured brands were bioequivalent to that of the original brand. It is known that the manufacturing process and the final formulation

of the drug may markedly affect the bioavailability of the drug (6). Hence, an extensive study was conducted to provide the bioavailability of different commercially doxycycline capsules and to assess the pharmacokinetics of doxycycline after oral administration to Thai healthy volunteers.

Objectives:

1. To compare the bioavailability of doxycycline capsules marketed in Thailand.
2. To investigate the pharmacokinetics of doxycycline after single oral administration of doxycycline capsule to Thai healthy male volunteers.
3. To compare the disintegration time and the dissolution rate of doxycycline capsules marketed in Thailand.
4. To determine statistically the relationship between the in vitro study parameters and the in vivo parameters.

Significance of the study

1. This study will provide significantly an information about the bioavailability of doxycycline capsules.
2. This study will provide meaningful information about the pharmacokinetics of doxycycline in Thai healthy volunteers. The results obtained will be compared with previously studies conducted in other countries.
3. According to the pharmacokinetic parameters obtained from the different brands, we shall be able to justify whether the local manufactured brands of doxycycline capsules are essentially equivalent to an original formulation. It also enables us to select

the most economical products which produce equivalent therapeutic effect and to determine an optimum dosage regimen.