CHAPTER I

INTRODUCTION

Roxithromycin is a derivative of the macrolide antibacterial erythromycin with *in vitro* antibacterial activity resembling that of the parent compound. The pharmacokinetic profile of roxithromycin is characterised by high plasma, tissue and body fluid concentrations and a long half-life permitting an extended dosage interval (Markham and Faulds, 1994).

Mean peak plasma roxithromycin concentrations (C_{max}) ranging between 6.6 and 7.9 mg/L are achieved within two hours after administration of a single oral 150 mg dose. In a direct comparison, C_{max} was 3.3 fold greater than that produced by a single 250 mg dose of erythromycin. The area under the plasma concentration versus time curve (AUC) produced by roxithromycin 150 mg was 16.2 fold greater than that produced by erythromycin (Kees et al., 1988). Multiple doses produced similar differences. The mean elimination half-life of roxithromycin 150 or 300 mg was 8.4 to 15.5 hours in volunteers (Tremblay, Jaeger et al., 1988), considerably longer than that recorded for erythromycin (1.5 to 3 hours) (Nilsen, 1987).

Roxithromycin has proven clinical efficacy in upper and lower respiratory infections, skin and soft tissue infections, urogenital infections and orodental infections, and appears to be as effective as more established treatments including erythromycin, amoxycillin/clavulanic acid and cefaclor (Young, Gonzales, and Sorkin, 1989). Roxithromycin is very well tolerated with an overall incidence of adverse events of approximately 4% (Blanc et al., 1987) and has less potential than erythromycin to produce clinically significant drug interactions (Delaforge, Sartori, and Mansuy, 1988). Thus, roxithromycin is an attractive therapeutic alternative in its established indications, especially when the option of once-daily administration is considered.

Roxithromycin tablets are available in Thailand through a variety of brand names from different manufacturers. At least three brands of roxithromycin tablets are currently marketed, including the innovator's product (Rulid®) with 2-3 times higher retail price than the locally made products. In Thailand where roxithromycin is also widely prescribed, the differences in race and biological behavior may contribute to the bioavailability difference of the drug, the differences in bioavailability always exist among the pharmaceutically equivalent products as well as compliance with official drug standards does not necessarily guarantee bioequivalence. Therefore, the bioequivalence of these roxithromycin tablets should be evaluated.

Therefore, this study was conducted to compare the bioavailability of different brands of roxithromycin tablets commercially available in Thailand in order to facilitate drug products selection, in terms of the drug's efficacy and economic aspect and to investigate the pharmacokinetics of roxithromycin following an oral administration in healthy Thai male volunteers.

Objectives

1. To compare the bioavailability of roxithromycin tablets commercially available in Thailand
2. To investigate the pharmacokinetics of a single dose of roxithromycin tablets in healthy Thai male volunteers.
3. To determine the *in vitro* quality of roxithromycin tablets marketed in Thailand

Significance of the study

1. This study will provide bioavailability data of roxithromycin tablets commercially available in Thailand compared to the innovator's product as a

reference for bioavailability comparisons which would be useful information for any health care institutions in the selection of the most economical products with the same bioavailability as the innovator's product.

2. This study will provide the pharmacokinetics of roxithromycin following an oral administration in healthy Thai male volunteers which would be useful in clinical application including appropriate dosage regimens for the most effective administration.