CHAPTER I

INTRODUCTION

Nalidixic acid and the older quinolones are characterised by an unfavorable pharmacokinetic profile (low serum concentrations, short half-lives) (Lode et al., 1987) In addition to the somewhat restricted spectrum of activity of gram-positive organisms and the occasional occurrence of neuropsychiatric adverse experiences (Boreus and Sunstorm, 1967), . their applications have been limited because their clinical uses are often accompanied by the rapid emergence of resistant mutants .

Recent advances and the understanding of the structural activity relationship have led to the synthesis of a number of new and more potent compounds, called fluoroquinolones. These groups readily offer desirable properties such as tissue penetration, broad spectrum of activity and low toxicity.

Norfloxacin is the first of the newer quinolone carboxylic acid which have been first synthesized in Japan (Marble and Bosso, 1986). Its antimicrobial activity in combination with its peroral route of administration and unique mechanism of action, make it an antibiotic that could potentially be used to treat infectious diseases caused by cephalosporin- and

aminoglycoside-resistant organisms. In Thailand, there are more than 6 different brands of norfloxacin 400 mg tablets. One is the innovator's product with high retail price, and the others are locally manufactured products. Due to the formulations and productions of the tablets may affect bioavailability of the drug, the bioequivalence of these drug products should be evaluated (Nordic Council on Medicines, 1987).

Hence , this study is conducted to compare the relative bioavailability of norfloxacin tablets commercially available in Thailand and to investigate the pharmacokinetics of norfloxacin after oral administration of tablet in healthy volunteers.

Objectives:

1. To compare the bioavailability of the local manufactured brands of norfloxacin to that of innovator's product.

2. To investigate the correlation of the in vitro parameters (disintegration time and dissolution rate) with the in vivo parameters (C_{max} , T_{max} and AUC).

3. To investigate the pharmacokinetics of norfloxacin tablet after single oral administration in Thai healthy male volunteers.

Significance of the Study:

1. This study will provide significantly an information about the bioavailability of norfloxacin tablets marketed in Thailand which will enable to select the effective and economical products to provide the same therapeutic efficacy.

2. If relationships between the in vitro tests and the in vivo bioavailability were observed , results obtained from the in vitro studies may be used to predict the in vivo bioavailability of tablets.

3. This study will provide the pharmacokinetics of norfloxacin tablet in Thai healthy volunteers.