CHAPTER I

INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) are used to treat many rheumatological problems, sprains and strains, dysmenorrhea, and other mildly to moderately painful conditions. The NSAIDs, representing the carboxylic acid and enolic acid classes of medications, are available in Table 1 (Small, 1989).

Table 1 Nonsteroidal Anti-inflammatory Drugs

Carboxylic acids	Enolic acids
Salicylates	Butazones
Aspirin	Phenylbutazone
Nonacetylated salicylates	Oxyphenbutazone
Acetic acids	Oxicams
Indomethacin	Piroxicam
Sulindac	
Phenylacetic acids	
Diclofenac	
Propionic acids	
Ibuprofen	
Naproxen	
Ketoprofen	

Table 1 (Continue)

Carboxylic acids	Enolic acids
Anthranillic acids Mefenamic acid Meclofenamate	

In 1988, the Food and Drug Administration, U.S.A., approved marketing of the NSAID diclofenac sodium for use in the treatment of rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis. Diclofenac is the first NSAID to be approved that is a phenylacetic acid derivative. Diclofenac has been marketed outside U.S.A. since 1973 (Small, 1989).

In Thailand, diclofenac sodium is available in the dosage form of enteric-coated tablet, injection and gel. Presently, at least 10 different brands of 25 mg. diclofenac sodium enteric-coated tablets are marketed. This includes the innovator's product with high retail price. However, there were no any information about the bioequivalence of these products in Thailand. Therefore, the extensive study was conducted to provide the comparative and relative bioavailabilities of different commercially available diclofenac sodium enteric-coated tablets in the market.

Objectives :

1. To compare the bioavailability of the locally manufactured brands of diclofenac sodium enteric-coated tablets to that of the innovator's product.

2. To compare the in vitro quality of the locally manufactured brands of diclofenac sodium enteric-coated to that of the innovator's product according to the general requirements of the Pharmacopoeia.

3. To investigate the correlation between the in vitro parameters (disintegration times and dissolution rate constants) and the in vivo parameters (C_{max}, t_{max} and AUC)

Significance of the Study :

1. This study will provide the information about the bioavailability of diclofenac sodium enteric-coated tablets commercially available in Thailand compared to that of the innovator's product which would be useful in the selection of an effective locally made product.

2. This study will provide the pharmacokinetics of diclofenac sodium in Thai healthy volunteers.

3. If the relationships between the in vitro and the in vivo study were observed, results obtained from the in vitro studies might be used to predict the in vivo bioavailability of the drug.