CHAPTER I

INTRODUCTION

Hyperlipidemia is characterized by elevation of serum low-density lipoprotein (LDL). An elevated serum level of LDL is a factor etiologically related to atherosclerotic vascular disease, and in particular to coronary heart disease (Martin, Hulley, Browner, Kuller and Wentworth, 1986; Ross 1986). A protective effect against coronary heart disease of elevated serum high-density lipoprotein (HDL) has been observed in several epidemiologic and clinical studies (Miller and Miller, 1975; Gordon, Castelli, Hjortland, Kannel and Dawber, 1977). A low serum level of HDL appears to be an important risk factor, particularly in population whose serum level of total cholesterol is high.

Clinical trials aimed at reducing elevated serum total cholesterol have demonstrated that whether the reduction is achieved by dietary or pharmacologic means; the incidence of coronary heart disease is reduced. There is a positive correlation between the extent to which LDL is lowered and the incidence of coronary heart disease (Peto, Yusuf and Collins, 1985).

Initially, patients with hyperlipidemia should be treated by dietary control with a low fat and low cholesterol diet. Excess bodyweight and alcohol consumption should be controlled as well as physical excercise is encouraged. Contributory disease, e.g. hypothyroidism or diabetes mellitus, should be sought and treated appropriately. Drug therapy should only be considered when non-drug methods fail to produce satisfactory results. The need for continued dietary control is not reduced when drugs are used.

Gemfibrozil is a drug commonly prescribed for Hyperlipidemia patients. It belongs to the group of fibric acid derivatives. Although there is some structural similarity to clofibrate, preclinically, pharmacological studies in rats, monkeys and dogs indicated that gemfibrozil differed significantly from clofibrate in potency and therapeutic specificity (Hall, Nelson, Russell and Howard, 1981; Jain, Ryan, Lacorte and McMahan, 1981; Tuomilehto et al., 1976).

Gemfibrozil product is available in capsule dosage form. In Thailand, presently, there are four brands of gemfibrozil capsules in the market. One is the innovator's product, with higher retail price, and others are those locally manufactured. As the formulation and production of the dosage form may markedly affect its bioavailability, the bioequivalence of these products,

therefore, should be evaluated. Thus, the present study was conducted to compare the bioavailability of different brands of gemfibrozil capsules commercially available in Thailand.

Objectives

1. To compare the bioavailability of gemfibrozil capsules commercially available in Thailand.
2. To determine the relative bioavailability of gemfibrozil capsules commercially available in Thailand.
3. To calculate the pharmacokinetic parameters of gemfibrozil after single oral administration of gemfibrozil capsules in Thai healthy male volunteers.
4. To investigate the correlation of the in vitro parameters (disintegration time and dissolution rate constant) with the in vivo parameter (C_{max}, t_{max} and AUC)

Significance of the Study

1. This study will provide the information about the bioavailability of gemfibrozil capsules commercially available in Thailand.
2. This study will provide the pharmacokinetic parameter of gemfibrozil in Thai healthy male volunteers.
3. This information of gemfibrozil bioavailability would be very useful in drug-product selection for clinical use.