CHAPTER I
INTRODUCTION

1. Rationale and Significance

Kaempferia parviflora (KP) or Krachaidum in Thai is in Zingiberaceae family. It can be found in the upper northeastern regions of Thailand. Its rhizome part has been used in folk medicine as health promotion, stimulation, vitalization, and aphrodisiac effect. It can be generally found in traditional medicine products such as pill and alcohol extract solution dosage forms. It is also available as tea and wine products. Phytochemical investigation found that KP contains several methoxyflavonoids. The major components include 5,7-dimethoxyflavone (DMF), 5,7,4'-trimethoxyflavone (TMF), and 3,5,7,3',4'-pentamethoxyflavone (PMF). Several pharmacological activities of KP and its components have been proved by scientist such as aphrodisiac, anti-peptic ulcer, anti-inflammation, anti-allergic, anti-mutagenicity, anti-depression, antibacterial, anti-fungal, anti-mycobacterium, anti-plasmodium, anti-viral, anti-cholinesterase activity for Alzheimer's disease, anti-cancer, cardioprotection, antiobesity, and inhibition of P-glycoprotein function. Moreover, toxicological study of KP has been reported on its safety. Regarding acute toxicity study in mice, LD_{50} value of KP is more than 13.3 g/kg. A single oral administration of KP ethanolic extract at dose of 2 g/kg was safe in rats. For chronic toxicity study, rats treated with 1 g/kg of KP for six months did not show any abnormality in histopathological examination of organs, behaviors, physical examination, and body weight. According to efficacy and safety of KP, it has the potential to be developed as an alternative medicine from natural source. Nevertheless, it still lacked of pharmacokinetic data of KP that explain what the body does to the herb including absorption, organ distribution, metabolism, and excretion process. These data are important to establish recommended dosage regimen, to support drug labeling, to predict the possible accumulation of drug and/or metabolites in plasma, tissue, feces, and urine drug levels, to estimate the rate and the extent of drug absorption, to determine how changes in physiology or disease affecting the absorption, distribution, metabolism, and excretion of the drug, and to determine the

metabolizing enzymes that metabolize the herb, and to avoid drug-herb interaction of co-administration drugs. Moreover, product development to enhance oral absorption should be developed and characterized to achieve the limitation of low oral bioavailability of KP. The developed formulations result in the effective utilization of KP crude extract.

Consequently, the purpose of this research was to investigate the pharmacokinetic study of KP crude extract in rats including pharmacokinetic parameters, absorption, organ distribution, metabolism, and excretion process. Furthermore, self-microemulsifying drug delivery system (SMEDDS) and cyclodextrin (CD) complex were developed to increase oral bioavailability of methoxyflavones in KP crude extract.

2. Objectives of the study

The aims of this research are the following:

1. To determine the pharmacokinetic parameters of KP crude extract in rats
2. To determine the oral bioavailability value of KP crude extract in rats
3. To investigate the organ distribution of KP crude extract in rats
4. To investigate the excretion of KP crude extract and identify its metabolites in rats
5. To investigate the effect of KP crude extract on cytochrome P450 enzymes (CYP450) in microsomes of mice
6. To develop the product formulations to increase the absorption of KP crude extract including SMEDDS and cyclodextrin complex

3. Research framework

Framework of this research can be summarized in Figure 1.

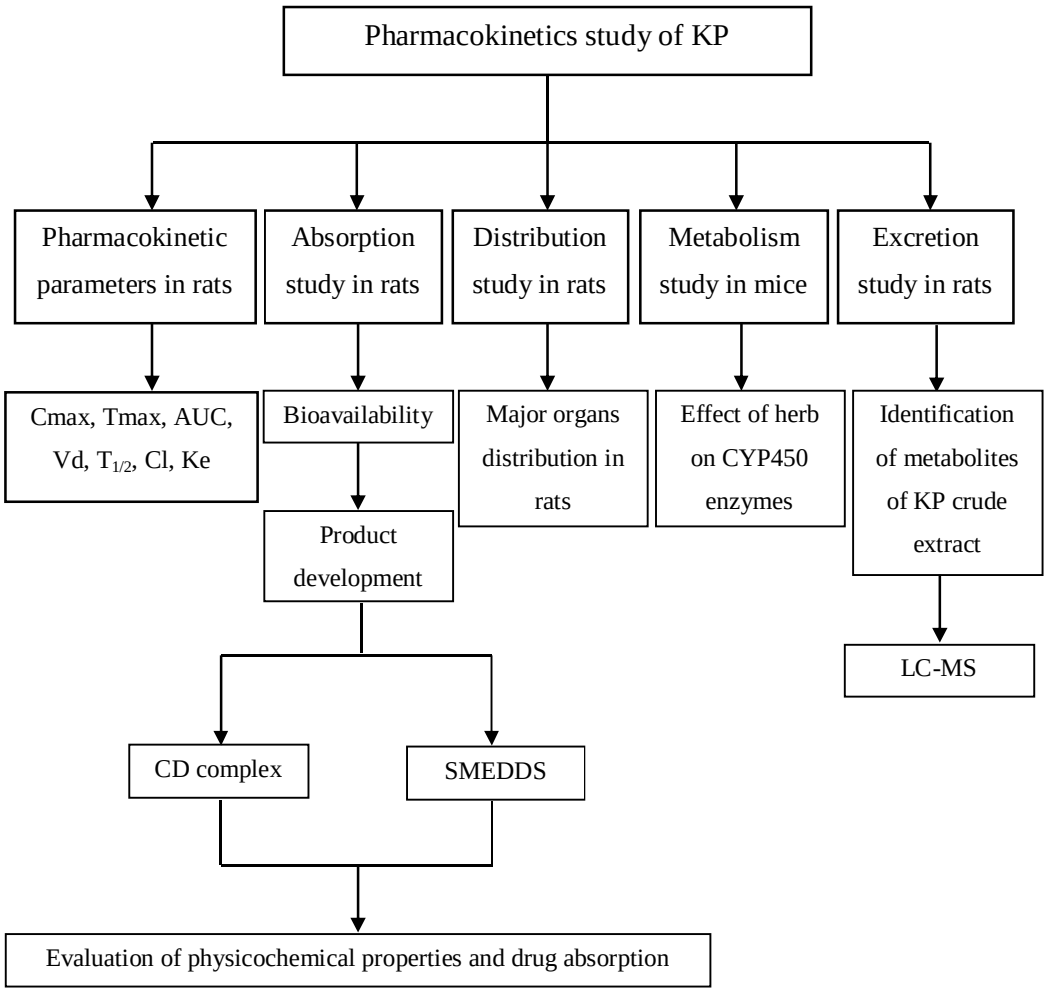

Figure 1 Research framework