CONTENTS

| | | page |
|-----------------|---------------------------------|------|
| บทคัด | ย่อ | (3) |
| ABSTI | RACT | (5) |
| ACKN | IOWLEDGEMENT | (7) |
| CONTENTS | | (8) |
| LIST OF TABLES | | (9) |
| LIST OF FIGURES | | (10 |
| ABBREVIATIONS | | (11 |
| CHAP | PTER | |
| 1. IN | TRODUCTION | 1 |
| 2. LI | STERATURE REVIEW | 4 |
| | Introduction to cytochrome P450 | 4 |
| | Human CYPs | 7 |
| | CYP2C19 | 16 |
| | Substrates of CYP2C19 | 17 |
| | Genetic polymorphism of CYP | 24 |
| 3. M | ATERIALS AND METHODS | 33 |
| 4. RI | ESULTS | 37 |
| 5. DI | ISCUSSION | 45 |
| BIBLIOGRAPHY | | 49 |
| APPENDIX | | 66 |
| VITAE | | 71 |

LIST OF TABLES

| Table | page | |
|--|------|--|
| Table 1. Human CYP families, gene and their subfamilies | 8 | |
| Table 2. Human CYP families and their main functions | 10 | |
| Table 3. Inhibitors of some CYP | 13 | |
| Table 4. Inducers of CYP and drug interactions | 16 | |
| Table 5. Allelic Variants of CYP2C19 | | |
| Table 6. Ethnic differences in the frequencies of poor metabolizers of CYP2C19 | | |
| Table 7. The distribution residence of the subjects enrolled in this study | | |
| according to their living places (provinces) | 37 | |
| Table 8. Demographic data of the 162 study subjects | 38 | |
| Table 9. CYP2C19 genotypes of 162 Southern Thai subjects | 41 | |
| Table 10. The allele frequencies of CYP2C19 in Southern Thai subjects | | |
| Table 11. Observed and expected frequency of CYP2C19 genotypes in a | | |
| Southern Thai population | 42 | |
| Table 12. Comparison of the genotype frequency of homozygous EMs, | | |
| heterozygous EMs and homozygous PMs of Southern Thai | | |
| populations with other Asians, Caucasians and Africans populations | 43 | |
| Table 13. Comparative frequencies of CYP2C19 alleles in various Oriental | | |
| Populations | 44 | |

LIST OF FIGURES

| Figure | page |
|--|------|
| Figure 1. Cytochrome P450 cycle in drug oxidations | 6 |
| Figure 2. Metabolic pathway of mephenytoin in human | 19 |
| Figure 3. Metabolic pathway of omeprazole in human | 20 |
| Figure 4. The PCR product amplified for CYP2C19*2 digestion | 38 |
| Figure 5. The PCR-based diagnostic test for CYP2C19*2 mutation | 39 |
| Figure 6. The PCR product amplified for CYP2C19*3 digestion | 40 |
| Figure 7. The PCR-based diagnostic test for CYP2C19*3 mutation | 41 |

LIST OF ABBREVIATIONS

°C degree Celcieus

R trade name

AE acetate- EDTA

AL buffer AL

BMI body mass index

bp base pair

BSA bovine serum albumin

cm centimetre

DNA deoxyribonucleic acid

dNTPs deoxynucleotide triphosphates

gDNA genomic DNA

EDTA ethylene diamine tetraacitic acid

g gram

i.e. id est

mg milligram

ml milliliter

mM milimolar

min minute

P P value

PCR polymerase chain reaction

RFLP restriction fragment length polymorphism

rpm revolution per minute

S.D. standard deviation

SNP single nucleotide polymorphism

Taq polymerase Termus aquaticus polymerase

TBE Tris-borate EDTA

u unit