

CONTENTS

| | Page |
|-----------------------------------|-------------|
| THAI ABSTRACT | iii |
| ENGLISH ABSTRACT | iv |
| ACKNOWLEDGEMENT | v |
| CONTENTS | vi |
| LIST OF TABLES | vii |
| LIST OF FIGURES | ix |
| LIST OF ABBREVIATIONS AND SYMBOLS | xii |
| CHAPTERS | |
| 1 INTRODUCTION | 1 |
| 2 LITERATURE REVIEWS | |
| 2.1 Quetiapine | 4 |
| 2.2 Cytochrome P450 | 25 |
| 2.3 Bioequivalence study | 31 |
| 3 MATERIALS AND METHODS | 41 |
| 4 RESULTS | 49 |
| 5 DISCUSSION AND CONCLUSION | 84 |
| REFERENCE | 88 |
| APPENDIX | 101 |
| VITAE | 108 |

LIST OF TABLES

| Table | | Page |
|--------------|---|-------------|
| 1 | Dopaminergic tracts and effects of dopamine antagonists | 9 |
| 2 | Adverse events in the three treatment groups | 20 |
| 3 | BE study of antipsychotics | 39 |
| 4 | Demographic data of 24 healthy male volunteers enrolled in the study | 51 |
| 5 | Laboratory data of 24 healthy volunteers enrolled in the study | 52 |
| 6 | LLOQ of quetiapine in plasma | 53 |
| 7 | Calibration curve data of quetiapine in plasma | 54 |
| 8 | The intra-day variance of three different quetiapine concentrations in plasma | 55 |
| 9 | The inter-day variance of three different quetiapine concentrations in plasma | 55 |
| 10 | Recovery of quetiapine and IS in plasma | 56 |
| 11 | Freeze-thaw stability of quetiapine in plasma | 60 |
| 12 | Short-term stability of quetiapine in plasma | 60 |
| 13 | Long-term stability of quetiapine in plasma | 61 |
| 14 | Post- preparative stability of quetiapine in plasma | 61 |
| 15 | Stock solution stability of quetiapine and IS | 62 |
| 16 | The plasma concentrations of quetiapine at various sampling times after the administration of Seroquel [®] , 200-mg single dose in 24 subjects | 76 |
| 17 | The plasma concentrations of quetiapine at various sampling times after the administration of Quantia 200 [®] , 200-mg single dose in 24 subjects | 77 |
| 18 | Quetiapine pharmacokinetic parameters of individual subject following a single oral dose of 200-mg of and Seroquel [®] . | 78 |
| 19 | Quetiapine pharmacokinetic parameters of individual subject following a single oral dose of 200-mg of Quantia 200 [®] . | 79 |
| 20 | Comparison of quetiapine pharmacokinetic parameters of individual subject following a single dose of 200 mg of Quantia 200 [®] and Seroquel [®] | 80 |

LIST OF TABLES (Continued)

| Table | | Page |
|--------------|---|-------------|
| 21 | Two-way ANOVA test for ln-transformed data of C_{\max} , AUC_{0-48} and $AUC_{0-\infty}$ of Quantia 200 [®] and Seroquel [®] | 81 |
| 22 | Pharmacokinetic parameters (mean \pm SD) and 90% CI for quetiapine, after the administration of single oral dose of 200 mg of Quantia 200 [®] and Seroquel [®] to 24 healthy volunteers | 82 |
| 23 | Adverse events of 200 mg of Seroquel [®] and Quantia 200 [®] in the 24 subjects | 83 |

LIST OF ABBREVIATIONS AND SYMBOLS

| | | |
|--------------------|---|---|
| % | = | Percent |
| µg | = | Microgram |
| µl | = | Microlitre |
| ® | = | Trade name |
| °C | = | Degree Celsius |
| ALB | = | Albumin |
| ALP | = | Alkaline phosphatase |
| ANOVA | = | Analysis of Variance |
| AUC | = | Area under the plasma concentration-time curve |
| AUC _{0-∞} | = | Area under the plasma concentration-time curve from zero to infinity |
| AUC _{0-t} | = | Area under the plasma concentration-time curve from zero to the last time point |
| BMI | = | Body mass index |
| BUN | = | Blood urea nitrogen |
| CI | = | Confidence interval |
| CL | = | Clearance |
| cm | = | Centimeter |
| C _{max} | = | Maximum concentration |
| Cr | = | Creatinine |
| CV | = | Coefficient of variation |
| DBI | = | Direct bilirubin |
| df | = | Degree of freedom |
| E | = | Eosinophil |
| FBS | = | Fasting blood sugar |
| FDA | = | Food and Drug Administration |
| h | = | Hour |
| Hb | = | Haemoglobin |
| Hct | = | Hematocrit |

LIST OF ABBREVIATIONS AND SYMBOLS (Continued)

| | | |
|-----------|---|---|
| HPLC | = | High performance liquid chromatography |
| i.e. | = | Id est = That is |
| IS | = | Internal standard |
| kg | = | Kilogram |
| L | = | Liter |
| LLOQ | = | Lower limit of quantification |
| Lymph | = | Lymphocyte |
| m | = | Meter |
| min | = | Minute |
| ml | = | Milliliter |
| MS | = | Mean of square |
| ng | = | Nanogram |
| No. | = | Number |
| <i>P</i> | = | <i>p</i> -value |
| PMN | = | Polymorphonuclear neutrophils |
| QC | = | Quality control |
| r^2 | = | Coefficient of determination |
| SD | = | Standard deviation |
| SGOT | = | Serum glutamic oxaloacetic transaminase |
| SGPT | = | Serum glutamic pyruvic transaminase |
| SS | = | Sum of square |
| $T_{1/2}$ | = | Half-life |
| TBL | = | Total bilirubin |
| T_{max} | = | Time to maximum concentration |
| TP | = | Total protein |
| UV | = | Ultraviolet |
| v/v/v | = | Volume by volume by volume |
| Vd | = | Volume of distribution |
| WBC | = | White blood cell |