

CONTENTS

	page
CONTENTS	VIII
LIST OF TABLES	IX
LIST OF FIGURES	X
LIST OF ABBREVIATIONS AND SYMBOLS	XI
CHAPTERS	
1. INTRODUCTION	1
2. LITERATURE REVIEWS	
2.1 Risperidone	4
2.2 Rifampin	18
2.3 The cytochrome P 450 enzymes (CYP)	37
2.4 P-glycoprotine (P-gp)	43
3. MATERIALS AND METHODS	52
4. RESULTS	57
5. DISCUSSION AND CONCLUSION	70
BIBLIOGRAPHY	75
APPENDIX	84
VITAE	90

LIST OF TABLES

Table		page
1	The lower limit of quantitative (LOQ) of risperidone in plasma	58
2	The intra-day variance of three different risperidone concentrations in plasma	58
3	The inter-day variance of three different risperidone concentrations in plasma	59
4	Relative percent recovery of standard risperidone in human plasma	59
5	Demographic characteristics of 10 male subjects in this study	62
6	Adverse Effects were observed in ten subjects after receiving a single oral dose of 4 mg risperidone alone and after pretreatment with 600 mg rifampin orally for 5 days	63
7	Pharmacokinetic parameters (mean \pm S.E.) of risperidone in ten subjects after receiving a single oral dose of 4 mg risperidone alone and after pretreatment with 600 mg rifampin orally for 5 days	63
8	Pharmacokinetic parameters derived from non-compartment model analysis of risperidone in ten subjects	68
9	Pharmacokinetic parameters derived from non-compartment model analysis of risperidone in ten subjects receiving a single oral dose of 4 mg risperidone after pretreatment with 600 mg rifampin orally for 5 days	69

LIST OF FIGURES

Figure	page
1 Structural formula of risperidone.	4
2 The major pathway of risperidone metabolism.	7
3 Structural formula of rifampin	19
4 Chromatograms of risperidone obtained from human plasma blank and spiked with 20 ng/ml of standard risperidone.	57
5 The calibration curve of standard risperidone.	60
6 Chromatograms of risperidone obtained from a representative subject after receiving a single oral dose of 4 mg risperidone alone and after pretreatment with rifampin.	64
7 Mean plasma risperidone concentrations after a single oral dose of 4 mg risperidone administration alone and after pretreatment with 600 mg rifampin once daily for 5 days.	65
8 Plasma concentrations – time profiles of risperidone after a single oral dose of 4 mg risperidone alone and after pretreatment with rifampin in each subject.	66

LIST OF ABBREVIATIONS AND SYMBOLS

ALP	=	Alkaline phosphatase
AUC	=	Area under the concentration-time curve
bid	=	Bis in die or twice daily
BUN	=	Blood urea nitrogen
°C	=	Degree Celsius
C _{max}	=	Maximum plasma concentration
CBC	=	Complete blood count
Cl/F	=	Clearance
cm	=	Centimeter
µm	=	Micrometer
Cr	=	Creatinine
C.V.	=	Coefficient of variation
e.g.	=	Exempli gratia
etc.	=	Et cetera
g	=	Gram
µg	=	Microgram
Hb	=	Hemoglobin
hr	=	Hour
K _{ab}	=	Absorption rate constant
K _e	=	Elimination rate constant
Kg	=	Kilogram
L	=	Litre
µl	=	microlitre
min	=	Minute
MRT	=	Mean residence time
ml	=	Milliliter
M.W.	=	Molecular weight
ng	=	Nanogram

LIST OF ABBREVIATIONS AND SYMBOLS (Continued)

P	=	P value
PMN	=	Polymorphonuclear neutrophils
r	=	Correlation coefficient
S.C.	=	Subcutaneous administration
S.D.	=	Standard deviation
S.E.	=	Standard error
sec	=	Second
SGOT	=	Serum glutamic oxaloacetic transaminase
SGPT	=	Serum glutamic pyruvic transaminase
SPE	=	Solid phase extraction
$t_{1/2 \text{ ab}}$	=	Absorption half-life
$t_{1/2 \text{ el}}$	=	Elimination half-life
t_{max}	=	Time to maximal serum concentration
U/L	=	Unit/liter
U.S.A.	=	The United States of America
V_d/F	=	Volume distribution
vs	=	Versus
vol/vol	=	Volume by volume
v/v/v	=	Volume by volume by volume
WBC	=	White blood cell
yr	=	Year
%	=	Percent
®	=	Trade name