

CONTENTS

	page
ABSTRACT (Thai)	(3)
ABSTRACT (English)	(5)
ACKNOWLEDGEMENTS	(8)
CONTENTS	(9)
LIST OF TABLES	(10)
LIST OF FIGURES	(13)
LIST OF ABBREVIATIONS	(15)
CHAPTER	
1 INTRODUCTION	1
2 LITERATURE REVIEW	6
Praziquantel	6
Rifampicin	26
Cytochrome P450	55
3 MATERIALS AND METHODS	67
4 RESULTS	82
5 DISCUSSION AND CONCLUSION	104
BIBLIOGRAPHY	116
APPENDIX	131
VITAE	147

LIST OF TABLES

Table	page
1 Major human liver cytochrome P450 enzymes	12
2 The intra-assay coefficient variation of six different praziquantel concentrations in mobile phase	77
3 The inter-assay coefficient variation of six different praziquantel concentrations in mobile phase	78
4 The intra-assay coefficient variation of six different praziquantel concentrations in human plasma	79
5 The inter-assay coefficient variation of six different praziquantel concentrations in human plasma	80
6 Relative recovery of standard praziquantel in plasma	81
7 Pharmacokinetics parameters of praziquantel in ten subjects after receiving a single oral dose of 40 mg/kg or multiple oral dose of 25 mg/kg praziquantel alone	95
8 Pharmacokinetics parameters of praziquantel in subjects whose praziquantel plasma concentrations could be measured after receiving a single oral dose of 40 mg/kg or multiple oral dose of 25 mg/kg praziquantel alone, and after pretreatment with 600 mg rifampicin orally for 5 days	96

LIST OF TABLES (continued)

Table	page
9 Pharmacokinetics parameters of praziquantel in subjects whose praziquantel plasma concentrations could not be measured after receiving a single oral dose of 40 mg/kg or multiple oral dose of 25 mg/kg praziquantel alone, and after pretreatment with 600 mg rifampicin orally for 5 days	97
10 Pharmacokinetics parameters of praziquantel in ten subjects after receiving a single oral dose of 40 mg/kg or multiple oral dose of 25 mg/kg praziquantel alone, and after pretreatment with 600 mg rifampicin orally for 5 days	98
11 Pharmacokinetics parameters of praziquantel in each of ten subjects receiving a single oral dose of 40 mg/kg praziquantel alone	99
12 Pharmacokinetics parameters of praziquantel in each of ten subjects receiving a single oral dose of 40 mg/kg praziquantel after pretreatment with 600 mg rifampicin orally for 5 days	100
13 Pharmacokinetics parameters of praziquantel in each of ten subjects receiving a multiple oral dose of 25 mg/kg praziquantel alone	101
14 Pharmacokinetics parameters of praziquantel in each of ten subjects receiving a multiple oral dose of 25 mg/kg praziquantel after pretreatment with 600 mg rifampicin orally for 5 days	102

LIST OF TABLES (continued)

Table	page
15 Praziquantel pharmacokinetic data were compared to other published data	103

LIST OF FIGURE

Figure	page
1 Structural formula of praziquantel	6
2 Conjugation of <i>trans</i> - and <i>cis</i> -4-hydroxypraziquantel with uridine-5'-diphosphoglucuronide acid and microsomes containing glucuronyl transferase	12
3 Structural formula of rifampicin	26
4 Principal metabolic derivatives of rifampicin in man, polarity and percentage recovery in bile and urine	31
5 Cytochrome P-450 cycle in drug oxidations	57
6 The standard calibration curve of praziquantel relating drug concentration to peak height ratio of praziquantel to diazepam	89
7 Chromatograms of praziquantel obtained from human plasma blank and spiked with 800 and 1,600 ng/ml of standard praziquantel	90
8 Chromatograms of praziquantel obtained from a representative subject after receiving a single oral dose of 40 mg/kg praziquantel alone and after pretreatment with rifampicin	91
9 Chromatograms of praziquantel obtained from a representative subject after receiving a multiple oral dose of 25 mg/kg praziquantel alone and after pretreatment with rifampicin	92

LIST OF FIGURE (continued)

Figure	page
10 Mean plasma praziquantel concentration after a single oral dose of 40 mg/kg praziquantel administration alone and after rifampicin coadministration	93
11 Mean plasma praziquantel concentration after a multiple oral dose of 25 mg/kg praziquantel administration alone and after rifampicin coadministration	94

LIST OF ABBREVIATIONS

AM	=	ante meridiem
AUC	=	area under the concentration-time curve
° C	=	degree celcius
Cl/f	=	apparent oral clearance
Cl _u /F	=	unbound clearance
cm	=	centimeter
C _{max}	=	maximal plasma concentration
CSF	=	cerebrospinal fluid
C.V.	=	coefficient of variation
d	=	day
e.g.	=	exempli gratia
etc.	=	et cetera
g	=	gram
µg	=	microgram
Hb	=	hemoglobin
Hct	=	hematocrit
hr	=	hour
Ke	=	elimination rate constant
kg	=	kilogram
K _i	=	inhibition rate constant
km	=	kilometer

LIST OF ABBREVIATIONS (Continued)

l	=	litre
μ l	=	microlitre
mg	=	milligram
MIC	=	minimum inhibitory concentration
min	=	minute
ml	=	millilitre
mM	=	millimole
μ M	=	micromole
MRT	=	mean residence time
mV.F.S.	=	millivolt full scale
ng	=	nanogram
P	=	P value
p.m.	=	post meridiem
r	=	correlation coefficient
S.D.	=	standard deviation
SGOT	=	serum glutamic oxaloacetic transaminase
SGPT	=	serum glutamic pyruvic transaminase
$t_{1/2,Z}$	=	elimination half-life
T_{\max}	=	time to maximal plasma concentration
uv	=	ultraviolet
Vd	=	volume of distribution

LIST OF ABBREVIATIONS (Continued)

V_z/f	=	apparent volume of distribution
vs	=	versus
v/v/v	=	volume by volume by volume
WBC	=	white blood cell
\bar{x}	=	mean
yr	=	year
λ_z	=	elimination rate constant
%	=	percent