## **CONTENTS**

	Page
บทคัดย่อ	(3)
ABSTRACT	(5)
ACKNOWLEDGEMENT	(7)
CONTENTS	(9)
LIST OF TABLES	(10)
LIST OF FIGURES	(11)
ABBREVIATIONS AND SYMBOLS	(13)
1. INTRODUCTION	1
2. LITERATURE REVIEW	4
2.1 LYMPHATIC FILARIASIS	4
2.2 IVERMECTIN	24
3. MATERIALS AND METHODS	44
4. RESULTS	54
5. DISCUSSION AND CONCLUSION	73
BIBLIOGRAPHY	81
APPENDIX	97
VITAE	113

## LIST OF TABLES

	Page
Pharmacokinetic data of ivermectin in animals	37
Intra-day (repeatability) and inter-day (reproducibility)	56
precisions of the HPLC method for ivermectin determination	
Accuracy of the HPLC method for ivermectin determination	56
Recovery of extraction of ivermectin from serum	57
Demographic data of normal and infected cats	60
Pharmacokinetic parameters derived from one-compartment	64
model analysis of ivermectin in eight normal cats receiving a	
single dose of 200 $\mu g/kg$ of ivermectin by subcutaneous	
injection	65
Pharmacokinetic parameters derived from non-compartment	
model analysis of ivermectin in eight normal cats receiving a	
single dose of 200 $\mu g/kg$ of ivermectin by subcutaneous	69
injection Pharmacokinetic parameters derived from one-	
compartment model analysis of ivermectin in an infected cat	
receiving a single dose of 200 $\mu g/kg$ of ivermectin by	
subcutaneous injection	70
Pharmacokinetic parameters derived from non-compartment	
model analysis of ivermectin in an infected cat receiving a	
single dose of 200 $\mu g/kg$ of ivermectin by subcutaneous	
injection	
	Intra-day (repeatability) and inter-day (reproducibility) precisions of the HPLC method for ivermectin determination Accuracy of the HPLC method for ivermectin determination Recovery of extraction of ivermectin from serum Demographic data of normal and infected cats Pharmacokinetic parameters derived from one-compartment model analysis of ivermectin in eight normal cats receiving a single dose of 200 µg/kg of ivermectin by subcutaneous injection  Pharmacokinetic parameters derived from non-compartment model analysis of ivermectin in eight normal cats receiving a single dose of 200 µg/kg of ivermectin by subcutaneous injection Pharmacokinetic parameters derived from one-compartment model analysis of ivermectin in an infected cat receiving a single dose of 200 µg/kg of ivermectin by subcutaneous injection  Pharmacokinetic parameters derived from non-compartment model analysis of ivermectin in an infected cat receiving a single dose of 200 µg/kg of ivermectin by subcutaneous injection

## LIST OF FIGURES

Figure		Page
1	Distribution of lymphatic filariasis	5
2	Endemic areas of lymphatic filariasis by provinces in Thailand	6
3	Prevalence rate of lymphatic filariasis in Thailand	7
4	Life cycles of filarial parasites (Brugia malayi)	10
5	Molecular structure of ivermectin	25
6	Reaction of the formation of the fluorescent derivative of ivermectin	31
	following dehydration	
7	Linearity curve (mean±S.E.) of different concentration of ivermectin	55
	spiked in serum; correlation coefficient $(r) = 0.9991$	
8	Representative chromatograms for comparison of separation of	58
	ivermectin in human serum and cat serum; serum blank (A1, A2),	
	serum spiked with internal standard abamectin (30 ng/ml) (B1, B2),	
	serum spiked with internal standard abamectin (30 ng/ml) and	
	ivermectin (10 ng/ml) (C1, C2)	
9	Representative chromatograms of separation of ivermectin; serum	59
	blank (A), serum spiked with internal standard abamectin (30	
	ng/ml) (B), serum spiked with internal standard abamectin (30	
	ng/ml) and ivermectin (10 ng/ml) in human serum (C), and serum	
	sample collected from a normal cat at 12 hour after ivermectin	
	administration (D)	
10	Concentration-time profiles of ivermectin after a single dose of 200	62
	μg/kg of ivermectin in normal cats; individual animal serum	
	concentrations (A) and mean (± S.E.) (n=8) serum concentrations	
	(B)	

# LIST OF FIGURES (Continued)

Figure		Page
11	Logarithmic concentration-time profiles of ivermectin after a single	63
	dose of 200 µg/kg of ivermectin in normal cats; individual animal	
	serum concentrations (A) and mean (±S.E.) (n=8) serum	
	concentrations (B)	
12	Concentration-time profiles of ivermectin after a single dose of 200 $\mu$	68
	g/kg of ivermectin in a Brugia malayi-naturally infected cat; an	
	arithmetic plot (A) and a logarithmic plot (B)	
13	Periodicity of Brugia malayi microfilariae of the infected cat	71
14	Number of blood microfilariae and serum concentrations in a Brugia	72
	malayi-infected cat receiving a single dose of 200 µg/kg of	
	ivermectin by subcutaneous injection	

#### ABBREVIATIONS AND SYMBOLS

AIC = Akaike's Information Criterion

ALP = Alkaline phosphatase

 $AUC_{0\rightarrow\infty}$  = Area under the concentration-time curve

AUMC  $_{0\rightarrow\infty}$  = Area under the first moment of the concentration-

time curve

BUN = Blood urea nitrogen

CBC = Complete blood count

CNS = Central nervous system

°C = Degree Celsius

 $C_{max}$  = Peak plasma concentration

Cell/mm<sup>3</sup> = Cell per cubic millimeter

CI/F = Clearance

cm = Centimeter

 $\mu m = Micrometer$ 

Cr = Creatinine

C.V. = Coefficient of variation

DEC = Diethylcarbamazine

e.g. = Exampil gratia

etc. = Et cetera

F = Female

 $FeSO_{4}$  = Ferrous sulphate

GABA =  $\gamma$ -aminobutyric acid

g = Gram

μg = Microgram

### ABBREVIATIONS AND SYMBOLS (Continued)

Hb = Hemoglobin

Hct = Hematocrit

HPLC = High performance liquid chromatography

K<sub>ab</sub> = Absorption rate constant

K<sub>e</sub> = Elimination rate constant

 $\lambda_z$  = Elimination rate constant

kg = Kilogram

L = Litre

 $LD_{50}$  = Fifty percent of lethal dose

 $\mu$ I = microlitre

Lymph = Lymphocyte

M = Male

mf = Microfilariae

min = Minute

 $MRT_{0\rightarrow\infty}$  = Mean residence time

ml = Milliliter

mm = Millimeter

mw. = Molecular weight

ng = Nanogram

No. = Number

NMIM = N-methylimidazole

p = p-value

PMN = Polymorphonuclear neutrophils

*r* = Correlation coefficient

### ABBREVIATIONS AND SYMBOLS (Continued)

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

 $t_{1/2 \text{ ab}}$  = Half-life absorption

 $t_{_{1/2\,\,\mathrm{el}}}$  = Half-life elimination

 $t_{1/2}\lambda_z$  = Half-life elimination

TFAA = Trifluoroacetic anhydride

TPE = Tropical pulmonary eosinophilia

 $T_{max}$  = Time to maximal serum concentration

U/L = Unit/liter

U.S.A. = The United States of America

UV = Ultraviolet

 $V_d/F$  = Volume of distribution

V\_/F = Volume of distribution

v.s. = Versus

v/v = Volume by volume

v/v/v = Volume by volume

WBC = White blood cell

WHO = World Health Organization

% = Percent

# ABBREVIATIONS AND SYMBOLS (Continued)