


ชีวปริมาณออกฤทธิ์ของของเหลวคิโตโปรเฟนที่บรรจุในแคปซูลเจลาตินชนิดแข็งเคลือบ  
ที่ให้ทางทวารหนักในกระต่าย



นางสาวมัลลิกา เหล่าวีระธรรม

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาเภสัชศาสตรมหาบัณฑิต

สาขาวิชาเภสัชกรรม ภาควิชาเภสัชกรรม  
คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

ปีการศึกษา 2545

ISBN 974-17-2658-9

ลิขสิทธิ์ของจุฬาลงกรณ์มหาวิทยาลัย

BIOAVAILABILITY OF KETOPROFEN LIQUID FILLED IN COATED HARD  
GELATIN CAPSULE FOR RECTAL USE IN RABBITS

Miss Mallika Laoweerathum

A Thesis Submitted in Partial Fulfillment of the Requirements  
for the Degree of Master of Science in Pharmacy

Department of Pharmacy  
Faculty of Pharmaceutical Sciences

Chulalongkorn University

Academic Year 2002

ISBN 974-17-2658-9

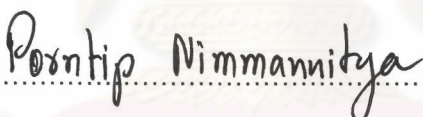
Thesis Title                    Bioavailability of Ketoprofen Liquid Filled in Coated Hard Gelatin Capsule for Rectal Use in Rabbits.  
By                                    Miss Mallika Laoweerathum  
Field of Study                    Pharmacy  
Thesis Advisor                   Associate Professor Uthai Suvanakoot, Ph.D.  
Thesis Co-advisor               Associate Professor Poj Kulvanich, Ph.D.

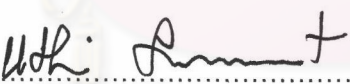
---


Accepted by the Faculty of Pharmaceutical Sciences, Chulalongkorn University  
In Partial Fulfillment of the Requirements for the Master's Degree


  
..... Dean of Faculty of  
Pharmaceutical Sciences  
(Associate Professor Boonyong Tantisira, Ph.D.)


Thesis Committee

  
..... Chairman  
(Associate Professor Porntip Nimmannitya, M.Sc. in Pharm.)

  
..... Thesis Advisor  
(Associate Professor Uthai Suvanakoot, Ph.D.)

  
..... Thesis Co-advisor  
(Associate Professor Poj Kulvanich, Ph.D.)

  
..... Member  
(Associate Professor Parkpoom Tengamnuay, Ph.D.)

  
..... Member  
(Assistant Professor Pol. Lt. Col. Somsong Lawanprasert, Ph.D.)

มัลลิกา เหล่าวีระธรรม : ชีวปริมาณออกฤทธิ์ของของเหลวคีโตโพรเฟนที่บรรจุในแคปซูล  
เจลาตินชนิดแข็งเคลือบที่ให้ทางทวารหนักในกระต่าย (BIOAVAILABILITY OF KETO-  
PROFEN LIQUID FILLED IN COATED HARD GELATIN CAPSULE FOR RECTAL  
USE IN RABBITS) อ.ที่ปรึกษา: รศ.ดร. อุทัย สุวรรณบุญ, อ.ที่ปรึกษาร่วม: รศ.ดร. พจน์  
กุลวานิช, 106 หน้า. ISBN 974-17-2658-9

ศึกษาการตั้งตำรับและชีวปริมาณออกฤทธิ์ของของเหลวคีโตโพรเฟนที่บรรจุในแคปซูลเจลาตินชนิดแข็ง  
เคลือบ การตั้งตำรับคีโตโพรเฟน 100 มิลลิกรัมดำเนินการโดยใช้ตัวทำละลายร่วม 3 ชนิด (PEG 1500 PG  
และ ตัวใดตัวหนึ่งของ Tween 60<sup>®</sup> Tween 80<sup>®</sup> หรือ Dimethyl isosorbide) การปลดปล่อยตัวยาคอกจากทุก  
ตำรับเพิ่มมากขึ้นเมื่อเพิ่มความเข้มข้นของ Tween 60<sup>®</sup> Tween 80<sup>®</sup> หรือ Dimethyl isosorbide จาก 10  
เปอร์เซ็นต์ถึง 30 เปอร์เซ็นต์

ได้คัดเลือกตำรับที่ประกอบด้วย 20 เปอร์เซ็นต์ของ Tween 80<sup>®</sup> และตำรับที่ประกอบด้วย 2 เปอร์เซ็นต์  
ของ Dimethyl isosorbide เพื่อนำมาศึกษาในหลอดทดลองและในสัตว์ทดลอง จากการประเมินผลในหลอด  
ทดลองพบว่าทั้ง 2 ตำรับได้มาตรฐานความสม่ำเสมอของปริมาณตัวยาสัญสำคัญตามข้อกำหนดของเภสัชตำรับ  
อังกฤษ 1993 การเคลือบแคปซูลชนิดแข็งทำให้ใช้เวลาในการละลายและการแตกตัวมากกว่าแคปซูลชนิดแข็งที่  
ไม่ได้เคลือบ สำหรับการศึกษาคงตัวของผลิตภัณฑ์พบว่าผลิตภัณฑ์ที่เก็บไว้ในอุณหภูมิ 40 องศา  
เซลเซียส ความชื้นสัมพัทธ์ 75 เปอร์เซ็นต์เป็นเวลา 3 เดือนมีปริมาณตัวยาสัญสำคัญลดลงและสีของตำรับเหลืองเข้ม  
ขึ้น

ดำเนินการศึกษาชีวปริมาณออกฤทธิ์ของยาเหน็บทวารหนักคีโตโพรเฟน 2 ตำรับที่ได้รับคัดเลือกร่วมกับ  
ยาฉีดเข้ากล้ามเนื้อ Oruvail<sup>®</sup> ในกระต่ายพันธุ์นิวซีแลนด์สีขาวจำนวน 12 ตัว กระต่ายแต่ละตัวได้รับแต่ละตำรับ  
คีโตโพรเฟนเพียงครั้งเดียว เก็บตัวอย่างเลือดตามเวลาที่กำหนดไว้หลังการให้ยาและตรวจหาความเข้มข้นของ  
คีโตโพรเฟนโดยวิธี HPLC พบว่าตัวยาคีโตโพรเฟนที่บรรจุในแคปซูลชนิดแข็งเคลือบที่ให้ทางทวารหนักถูกดูด  
ซึมได้ดีเข้าสู่ระบบไหลเวียนโลหิต ยาเหน็บทวารหนักคีโตโพรเฟนทั้ง 2 ตำรับมีค่าพารามิเตอร์ทางเภสัช  
จลนศาสตร์ที่เกี่ยวข้องไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติยกเว้นค่าความเข้มข้นของยาสูงสุดในพลาสมา  
และมีชีวปริมาณออกฤทธิ์สัมพัทธ์เทียบกับยาฉีดเข้ากล้ามเนื้อ Oruvail<sup>®</sup> เท่ากับ 127 และ 107 เปอร์เซ็นต์ตาม  
ลำดับ

ภาควิชา	เภสัชกรรม	ลายมือชื่อผู้ผลิต..... มัลลิกา เหล่าวีระธรรม.....
สาขาวิชา	เภสัชกรรม	ลายมือชื่ออาจารย์ที่ปรึกษา..... อุทัย สุวรรณบุญ.....
ปีการศึกษา	2545	ลายมือชื่ออาจารย์ที่ปรึกษาร่วม.....

##4376602833 MAJOR: PHARMACY

KEYWORD: BIOAVAILABILITY/ KETOPROFEN/ LIQUID FILLED COATED HARD  
GELATIN CAPSULE/ RECTAL

MALLIKA LAOWEERATHUM: BIOAVAILABILITY OF KETOPROFEN LIQUID FILLED IN  
COATED HARD GELATIN CAPSULE FOR RECTAL USE IN RABBITS. THESIS ADVISOR:  
ASSOC.PROF UTHAI SUVANAKOOT, Ph.D., THESIS CO-ADVISOR: ASSOC.PROF POJ  
KULVANICH, Ph.D. 106 pp. ISBN 974-17-2658-9

Formulation and bioavailability of ketoprofen liquid filled in coated hard gelatin capsule were studied. Formulation of 100 mg ketoprofen was conducted using the combination of three cosolvents (PEG 1500, PG and either Tween 60<sup>®</sup>, Tween 80<sup>®</sup> or Dimethyl isosorbide). The dissolution from all formulations were increased by using higher concentration of Tween 60<sup>®</sup> Tween 80<sup>®</sup> or Dimethyl isosorbide from 10% to 30%.

The formulation with 20% Tween 80<sup>®</sup> and that with 20% Dimethyl isosorbide were subsequently selected for further *in vitro* and *in vivo* studies. *In vitro* evaluation showed that both formulations met the requirement for uniformity of content according to British Pharmacopoeia 1993. Dissolution and disintegration times of coated rectal capsule were longer than those without coating. For stability study, it was found that amount of drug in formulation was decreased after 3 months storage at 40°C with 75% RH and deep yellow formulation was observed.

Bioavailability of the two selected formulations and Oruvail<sup>®</sup> were performed using twelve white New Zealand rabbits. Each rabbit received a single dose of each ketoprofen formulation. Blood samples were collected at predetermined time intervals post dose and determined for ketoprofen concentrations by HPLC. Result demonstrated that ketoprofen was well absorbed from rectal coated capsule into systemic circulation. The relevant pharmacokinetic parameters of both ketoprofen rectal formulations were not statistically significant differences except the C<sub>max</sub> values. Relative bioavailability of each formulation with respect to Oruvail<sup>®</sup> was found to be 127 and 107%, respectively.

Department Pharmacy

Field of study Pharmacy

Academic year 2002

Student's signature..... Mallika Laoweerathum.....

Advisor's signature ..... Uthai Suwanakoot.....

Co-ad Advisor's signature ..... Poj Kulvanich.....

## ACKNOWLEDGEMENTS

First of all, I would like to express my deepest gratitude to my advisor, Associate Professor Dr. Uthai Suvanakoot, for his helpful suggestion of many problems, good guidance, extremely valuable encouragement and understanding throughout course of my study.

I am very grateful to Associate Professor Dr. Poj Kulvanich, my co-advisor for his kindness, helpful comments, and attention to my work for giving valuable advice and correction of this thesis.

Sincere thank goes to all staff members of Pharmacy Department, Faculty of Pharmaceutical Sciences and Graduated School, Chulalongkorn University for granting partly financial support to fulfill this study. I would like to express my thank to those whose names have not been mentioned but their assistance and encouragement firmly deserve acknowledgements.

My grateful appreciation is expressed to Capsule Product Co., Ltd. for supporting hard gelatin capsules and to Rama Production Co., Ltd for providing Methocel<sup>®</sup> E5.

Special thank goes to my lovely friends for their love and cheerfulness. Greatest thank and love go to my family for their love, inspiration, encouragement and continued support throughout these past years.

## CONTENTS

	Page
THAI ABSTRACT.....	iv
ENGLISH ABSTRACT.....	v
ACKNOWLEDGEMENTS.....	vi
CONTENTS.....	vii
LIST OF TABLES.....	viii
LIST OF FIGURES.....	xii
LIST OF ABBREVIATIONS.....	xvi
CHAPTER	
I.    INTRODUCTION.....	1
II.   REVIEW OF LITERATURE .....	3
III.  MATERIALS AND METHODS.....	19
IV.  RESULTS AND DISCUSSION.....	35
V.    CONCLUSIONS.....	80
REFERENCES.....	82
APPENDICES.....	86
VITA.....	106

ศูนย์วิทยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย

## LIST OF TABLES

Table	Page
1 Liquid formulae of 100 mg ketoprofen.....	22
2 Physical appearance of liquid formula of 100 mg ketoprofen in 100 mg of cosolvent.....	37
3 Physical appearance of liquid formula of 100 mg ketoprofen in 150 mg of cosolvent.....	38
4 Physical appearance of liquid formula of 100 mg ketoprofen in 200 mg of cosolvent.....	39
5 The formulation of ketoprofen liquid-filled hard gelatin capsule.....	40
6 Percent released of ketoprofen (Mean $\pm$ S.D.) from three formulations of ketoprofen rectal capsule with Tween 60 <sup>®</sup> .....	42
7 Percent released of ketoprofen (Mean $\pm$ S.D.) from three formulations of ketoprofen rectal capsule with Tween 80 <sup>®</sup> .....	43
8 Percent released of ketoprofen (Mean $\pm$ S.D.) from three formulations of ketoprofen rectal capsule with DMI.....	44
9 Percent released of ketoprofen (Mean $\pm$ S.D.) from 20% Tween 80 <sup>®</sup> formulation.....	50
10 Percent released of ketoprofen (Mean $\pm$ S.D.) from 20% DMI formulation.....	51
11 Disintegration time of uncoated and coated rectal capsule in water at $37 \pm 2^{\circ}\text{C}$ from 20% Tween 80 <sup>®</sup> formulation.....	54
12 Disintegration time of uncoated and coated rectal capsule in water at $37 \pm 2^{\circ}\text{C}$ from 20% DMI formulation.....	54
13 Uniformity of content of ketoprofen (%L.A.) from 20% Tween 80 <sup>®</sup> formulation and 20% DMI formulation.....	56
14 Content of ketoprofen (%L.A.) from 20% Tween 80 <sup>®</sup> formulation at $40^{\circ}\text{C}$ with 75% RH for three months.....	58



## LIST OF TABLES (cont.)

Table	Page	
15	Content of ketoprofen (%L.A.) from 20% DMI formulation at 40°C with 75 % RH, for three months.....	58
16	Plasma ketoprofen concentration ( $\mu\text{g/mL}$ ) of twelve rabbits after administration of 50 mg ketoprofen in coated rectal capsule with 20% Tween 80 <sup>®</sup> .....	62
17	Plasma ketoprofen concentration ( $\mu\text{g/mL}$ ) of twelve rabbits after administration of 100 mg ketoprofen in coated rectal capsule with 20% DMI.....	63
18	Plasma ketoprofen concentration ( $\mu\text{g/mL}$ ) of twelve rabbits after administration of 100 mg Oruvail <sup>®</sup> .....	64
19	Peak plasma concentration ( $C_{\text{max}}$ ) of ketoprofen of twelve rabbits after rectal administration of two formulations of 100 mg ketoprofen and intramuscular administration of 50 mg Oruvail <sup>®</sup> .....	73
20	Analysis of variance for $C_{\text{max}}$ after rectal administration of two formulations of 100 mg ketoprofen ( $\alpha = 0.05$ ) .....	73
21	Time to peak plasma concentration ( $t_{\text{max}}$ ) of ketoprofen of twelve rabbits after rectal administration of two formulations of 100 mg ketoprofen and intramuscular administration of 50 mg Oruvail <sup>®</sup> .....	74
22	Analysis of variance for $t_{\text{max}}$ after rectal administration of two formulations of 100 mg ketoprofen ( $\alpha = 0.05$ ) .....	74
23	Area under the plasma concentration time curve (AUC) of ketoprofen of twelve rabbits after rectal administration of two formulations of 100 mg ketoprofen and intramuscular administration of 50 mg Oruvail <sup>®</sup> .....	76
24	Analysis of variance for AUC after rectal administration of two formulations of 100 mg ketoprofen ( $\alpha = 0.05$ ) .....	76
25	Elimination half-life ( $t_{1/2}$ ) of ketoprofen of twelve rabbits after rectal administration of two formulations of 100 mg ketoprofen and intramuscular administration of 50 mg Oruvail <sup>®</sup> .....	77

## LIST OF TABLES (cont.)

Table	Page	
26	Analysis of variance for $t_{1/2}$ after rectal administration of two formulation of 100 mg ketoprofen ( $\alpha = 0.05$ ).....	77
27	Estimated pharmacokinetic parameters of ketoprofen (Mean $\pm$ S.D.) from twelve rabbits after rectal administration of formulation with 20% Tween 80 <sup>®</sup> rectal coated capsule and formulation with 20% DMI rectal coated capsule and its relative bioavailability.....	79
28	Accuracy of analytical method for determination of ketoprofen in phosphate buffer pH 7.4 at $\lambda = 260$ nm.....	88
29	Accuracy of analytical method for determination of ketoprofen in 75% methanol at $\lambda = 258$ nm.....	88
30	Within run precision of analytical method for determination of ketoprofen in phosphate buffer pH 7.4 at $\lambda = 260$ nm.....	89
31	Within run precision of analytical method for determination of ketoprofen in 75% methanol at $\lambda = 258$ nm.....	89
32	Between run precision of analytical method for determination of ketoprofen in phosphate buffer pH 7.4 at $\lambda = 260$ nm.....	90
33	Between run precision of analytical method for determination of ketoprofen in 75% methanol at $\lambda = 258$ nm.....	90
34	Typical calibration curve data for determination of ketoprofen in phosphate buffer pH 7.4 estimated using linear regression.....	91
35	Typical calibration curve data for determination of ketoprofen in 75% methanol estimated using linear regression.....	93
36	Accuracy of analytical method for determination of ketoprofen in preparation.....	95
37	Within run precision of analytical method for determination of ketoprofen in preparation.....	96
38	Between run precision of analytical method for determination of ketoprofen in preparation.....	96

## LIST OF TABLES (cont.)

Table	Page	
39	Linear regression for determination of ketoprofen in preparation at 0, 0.5, 1, 1.5, 2, 2.5, and 3 months.....	97
40	Accuracy of analytical method for determination of ketoprofen in rabbit plasma.....	98
41	Within run precision of analytical method for determination of ketoprofen in rabbit plasma.....	99
42	Between run precision of analytical method for determination of ketoprofen in rabbit plasma.....	99
43	Typical calibration curve data for determination of ketoprofen in rabbit plasma estimated using linear regression.....	100



ศูนย์วิทยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย

## LIST OF FIGURES

Figure	Page
1. The venous blood system of the rectum.....	5
2. Diagram showing the physical model for transmembrane permeation across a mucosal membrane consisting of lipoidal and aqueous pore pathway.....	7
3. Self-locking type of hard gelatin capsule.....	13
4. The area of sealing of liquid filled hard gelatin capsule.....	15
5. Process of sealing operation.....	15
6. Dissolution profile of ketoprofen from three formulations of ketoprofen rectal capsule with Tween 60 <sup>®</sup> .....	45
7. Dissolution profile of ketoprofen from three formulations of ketoprofen rectal capsule with Tween 80 <sup>®</sup> .....	46
8. Dissolution profile of ketoprofen from three formulations of ketoprofen rectal capsule with DMI.....	47
9. Dissolution profile of ketoprofen from uncoated and coated capsules of 20% Tween 80 <sup>®</sup> formulation.....	52
10. Dissolution profile of ketoprofen from uncoated and coated capsules of 20% DMI formulation.....	53
11. Physical appearance of ketoprofen rectal coated capsule at 40°C with 75% RH.....	57
12. High performance liquid chromatographic peaks of ketoprofen (A) and diclofenac sodium (B).....	61
13. Plasma ketoprofen concentration-time curve of rabbit No.1 after rectal administration of two formulations of 100 mg ketoprofen ( 20% Tween 80 <sup>®</sup> formulation and 20% DMI formulation ) and intramuscular administration of 50 mg Oruvail <sup>®</sup> .....	65

## LIST OF FIGURES (cont.)

Figure	Page
14. Plasma ketoprofen concentration-time curve of rabbit No.2 after rectal administration of two formulations of 100 mg ketoprofen ( 20% Tween 80 <sup>®</sup> formulation and 20% DMI formulation ) and intramuscular administration of 50 mg Oruvail <sup>®</sup> .....	65
15. Plasma ketoprofen concentration-time curve of rabbit No.3 after rectal administration of two formulations of 100 mg ketoprofen ( 20% Tween 80 <sup>®</sup> formulation and 20% DMI formulation ) and intramuscular administration of 50 mg Oruvail <sup>®</sup> .....	66
16. Plasma ketoprofen concentration-time curve of rabbit No.4 after rectal administration of two formulations of 100 mg ketoprofen ( 20% Tween 80 <sup>®</sup> formulation and 20% DMI formulation ) and intramuscular administration of 50 mg Oruvail <sup>®</sup> .....	66
17. Plasma ketoprofen concentration-time curve of rabbit No.5 after rectal administration of two formulations of 100 mg ketoprofen ( 20% Tween 80 <sup>®</sup> formulation and 20% DMI formulation ) and intramuscular administration of 50 mg Oruvail <sup>®</sup> .....	67
18. Plasma ketoprofen concentration-time curve of rabbit No.6 after rectal administration of two formulations of 100 mg ketoprofen ( 20% Tween 80 <sup>®</sup> formulation and 20% DMI formulation ) and intramuscular administration of 50 mg Oruvail <sup>®</sup> .....	67
19. Plasma ketoprofen concentration-time curve of rabbit No.7 after rectal administration of two formulations of 100 mg ketoprofen ( 20% Tween 80 <sup>®</sup> formulation and 20% DMI formulation ) and intramuscular administration of 50 mg Oruvail <sup>®</sup> .....	68

## LIST OF FIGURES (cont.)

Figure	Page
20. Plasma ketoprofen concentration-time curve of rabbit No.8 after rectal administration of two formulations of 100 mg ketoprofen ( 20% Tween 80 <sup>®</sup> formulation and 20% DMI formulation ) and intramuscular administration of 50 mg Oruvail <sup>®</sup> .....	68
21. Plasma ketoprofen concentration-time curve of rabbit No.9 after rectal administration of two formulations of 100 mg ketoprofen ( 20% Tween 80 <sup>®</sup> formulation and 20% DMI formulation ) and intramuscular administration of 50 mg Oruvail <sup>®</sup> .....	69
22. Plasma ketoprofen concentration-time curve of rabbit No.10 after rectal administration of two formulations of 100 mg ketoprofen ( 20% Tween 80 <sup>®</sup> formulation and 20% DMI formulation ) and intramuscular administration of 50 mg Oruvail <sup>®</sup> .....	69
23. Plasma ketoprofen concentration-time curve of rabbit No.11 after rectal administration of two formulations of 100 mg ketoprofen ( 20% Tween 80 <sup>®</sup> formulation and 20% DMI formulation ) and intramuscular administration of 50 mg Oruvail <sup>®</sup> .....	70
24. Plasma ketoprofen concentration-time curve of rabbit No.12 after rectal administration of two formulations of 100 mg ketoprofen ( 20% Tween 80 <sup>®</sup> formulation and 20% DMI formulation ) and intramuscular administration of 50 mg Oruvail <sup>®</sup> .....	70
25. Comparison of plasma ketoprofen concentration-time curve (Mean $\pm$ S.D.) of twelve rabbits after rectal administration of two formulations of 100 mg ketoprofen ( 20% Tween 80 <sup>®</sup> formulation and 20% DMI formulation) and intramuscular administration of 50 mg Oruvail <sup>®</sup> .....	71
26. Typical calibration curve for determination of ketoprofen in phosphate buffer pH 7.4 at $\lambda = 260$ nm.....	92

## LIST OF FIGURES (cont.)

Figure		Page
27	Typical calibration curve for determination of ketoprofen in 75% methanol at $\lambda = 258$ nm.....	94
28.	Typical calibration curve for determination of ketoprofen in formulation at 2 months.....	97
29.	Typical calibration curve for determination of ketoprofen in rabbit plasma.....	101



ศูนย์วิทยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย

## LIST OF ABBREVIATIONS

ANOVA	=	analysis of variance
AUC	=	area under the plasma concentration-time curve
BP	=	British Pharmacopoeia
$C_{\max}$	=	peak plasma concentration
Conc.	=	concentration
C.V.	=	coefficient of variation
$^{\circ}\text{C}$	=	degree Celsius
d.f.	=	degree of freedom
DMI	=	dimethyl isosorbide
$F_{\text{rel}}$	=	relative bioavailability
g	=	gram
GI	=	gastrointestinal tract
HPLC	=	high performance liquid chromatography
HPMC	=	hydroxypropylmethyl cellulose
hr	=	hour
kg	=	kilogram
L	=	liter
L.A.	=	labeled amount
mg	=	milligram
min	=	minute
mL	=	milliliter
MS	=	mean square
$\mu\text{g}$	=	microgram
$\mu\text{L}$	=	microliter
NSAIDs	=	non-steroidal antiinflammatory drugs
PAR	=	peak area ratio
PEG	=	polyethylene glycol
PG	=	propylene glycol



## LIST OF ABBREVIATIONS (cont.)

$r^2$	=	coefficient of determination
S.D.	=	standard deviation
SS	=	sum of square
TEC	=	triethylcitrate
$T_{max}$	=	time to peak plasma concentration
$t_{1/2}$	=	elimination half-life
USP	=	United States Pharmacopoeia
UV	=	ultraviolet
$\lambda$	=	wavelength



ศูนย์วิทยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย