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**FORMULATIONS AND PHARMACOKINETICS OF PROLONGED
RELEASE KETOPROFEN RECTAL SUPPOSITORIES**

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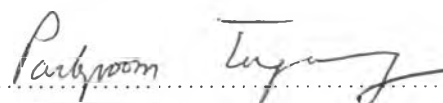
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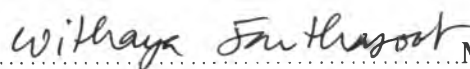
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พิมพ์ต้นฉบับบทคัดย่อวิทยานิพนธ์ภายในกรอบสี่เหลี่ยมนี้เพียงแผ่นเดียว

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ศึกษาการดั่งตำรับและเภสัชจลนพลศาสตร์ของยาเหน็บทวารหนักออกฤทธิ์นานคีโตโพรเฟน การดั่งตำรับดำเนินการโดยใช้ยาพื้นชนิดขบหน้า 3 สูตรร่วมกับสารทำให้ยาออกฤทธิ์นาน 2 ชนิด (ยูเครจิต เอส 100 และ เอส ที 55) ปริมาณสารแต่ละชนิดที่ใช้ขึ้นอยู่กับสัดส่วนของยาต่อสารนั้น ๆ ยาพื้นแต่ละสูตรจะใช้หลายสัดส่วนของยาต่อยูเครจิต เอส 100 หรือ เอส ที 55 นอกจากนี้ใช้ยาพื้นชนิดไม่ขบหน้าที่ผลิตจำหน่ายทั่วไป (ซัพโพซิทอรี เอ เอ็ม) ร่วมด้วยเพื่อการเปรียบเทียบ ทุกตำรับประกอบด้วยคีโตโพรเฟน 100 มิลลิกรัมและเตรียมโดยใช้วิธีการหลอมละลาย การประเมินผลในหลอดทดลองพบว่ายาเหน็บทุกตำรับได้มาตรฐานความสม่ำเสมอของน้ำหนักและปริมาณตัวยาสำคัญตามข้อกำหนดของเภสัชตำรับอังกฤษ 1993 การปลดปล่อยตัวยานอกจากยาพื้นซ้และใช้เวลานานเมื่อเทียบกับตำรับที่เตรียมจากยาพื้นที่ปราศจากยูเครจิต เอส 100 และ เอส ที 55 ตำรับที่ประกอบด้วยสัดส่วนของยาต่อยูเครจิต เอส 100, 1:1 ในยาพื้นสูตรที่ 1 และตำรับที่มีสัดส่วนของยาต่อเอส ที 55, 1:4 ในยาพื้นสูตรที่ 3 ผ่านการพิจารณาคัดเลือกนำไปศึกษาในสัตว์ทดลอง

ดำเนินการศึกษาเภสัชจลนพลศาสตร์ของยาเหน็บทวารหนักชนิดออกฤทธิ์นานคีโตโพรเฟน 2 ตำรับที่ได้รับการคัดเลือกร่วมกับอีก 1 ตำรับที่เตรียมโดยใช้ซัพโพซิทอรี เอ เอ็ม ในกระต่ายพันธุ์นิวซีแลนด์สีขาวจำนวน 9 ตัว กระต่ายแต่ละตัวได้รับยาเหน็บทวารหนักออกฤทธิ์นานคีโตโพรเฟน 100 มิลลิกรัมเพียงครั้งเดียว ตามวิธีการทดลองข้ามสลับ เก็บตัวอย่างเลือดตามเวลาที่กำหนดไว้หลังการให้ยาและตรวจหาความเข้มข้นของคีโตโพรเฟนโดยใช้เอชพีแอลซี ผลปรากฏว่าเภสัชจลนพลศาสตร์ของคีโตโพรเฟนจากยาเหน็บทั้ง 3 ตำรับมีลักษณะเหมือนกันเป็นแบบจำลองชนิดมัลติคอมพาร์ตเมนต์ การวิเคราะห์ความแปรปรวนตามวิธีการทดลองข้ามสลับแบบ 3 ทางพบว่าค่าพารามิเตอร์เภสัชจลนพลศาสตร์ไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติที่ระดับความเชื่อมั่นร้อยละ 95 ยาเหน็บทวารหนักออกฤทธิ์นานคีโตโพรเฟนทั้ง 2 สูตรตำรับมีชีวสมมูลกับตำรับอ้างอิงทั้งในเชิงอัตราเร็วและปริมาณยาที่ถูกดูดซึมเข้าสู่ร่างกาย สารทำให้ยาออกฤทธิ์นานทั้ง 2 ชนิดที่นำมาใช้มีประสิทธิผลเท่าเทียมกันแต่ยูเครจิต เอส 100 มีคุณสมบัติเหนือกว่าเล็กน้อยพิจารณาจากปริมาณที่ใช้ในตำรับมีจำนวนน้อยกว่า และความง่ายในการเตรียมตำรับยาเหน็บ

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สาขาวิชาเภสัชกรรม.....
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ลายมือชื่อนิสิต นวรรตน์ อมรชวิน
ลายมือชื่ออาจารย์ที่ปรึกษาอุทัย สุวรรณภู.....
ลายมือชื่ออาจารย์ที่ปรึกษาร่วม.....

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KEY WORD: FORMULATIONS / PHARMACOKINETICS / PROLONGED RELEASE / KETOPROFEN/ RECTAL SUPPOSITORIES

NAWARUT AMONCHEWIN: FORMULATIONS AND PHARMACOKINETICS OF PROLONGED RELEASE KETOPROFEN RECTAL SUPPOSITORIES. THESIS ADVISOR: ASSOC. PROF. UTHAI SUVANAKOOT, Ph.D. 154 pp. ISBN 974-331-954-9.

Formulations and pharmacokinetics of prolonged release ketoprofen rectal suppositories were studied. Formulations were conducted using three hydrophilic suppository bases and two prolonged release carriers (Eudragit S-100 and HP55). The amount of each carrier used was dependent on the drug to carrier ratios. Various ratios of the drug to Eudragit S-100 or HP55 were individually assigned to each base. A commercially available hydrophobic base (Suppocire[®] AM) was also used for comparison. All formulations with 100 mg ketoprofen were prepared by fusion method. *In vitro* evaluations showed that they met the requirements for uniformity of weight and uniformity of content according to the British Pharmacopoeia 1993. All release profiles were slow and prolonged compared to those without the two carriers. The formulation with Eudragit S-100 at the ratio of 1:1 in Base 1 and that with HP55 at the ratio of 1:4 in Base 3 were subsequently selected for *in vivo* studies.

Pharmacokinetics of the two selected formulations and the one with Suppocire[®] AM were performed using nine New Zealand White rabbits. Each rabbit received a single rectal dose of 100 mg prolonged release ketoprofen rectal suppository in a crossover manner. Blood samples were collected at predetermined time intervals post dose and determined for ketoprofen concentrations by HPLC. Results demonstrated that the pharmacokinetic patterns of ketoprofen from all three formulations were similar and appeared to be multicompartment model. Analysis of variance for three way crossover design revealed that there were no significant differences ($p > 0.05$) among all the corresponding relevant pharmacokinetic parameters obtained. Both formulated products were bioequivalent with the reference formulation with respect to the rate and the extent of drug absorption. The two carriers produced the same efficacies but Eudragit S-100 was slightly superior based on the amount being used was lesser and the ease of preparation.

ภาควิชา.....เภสัชกรรม.....

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CONTENTS

	Page
THAI ABSTRACT.....	iv
ENGLISH ABSTRACT.....	v
ACKNOWLEDGEMENTS.....	vi
CONTENTS.....	vii
LIST OF TABLES.....	viii
LIST OF FIGURES.....	xiv
LIST OF ABBREVIATIONS.....	xvii
CHAPTER	
I. INTRODUCTION.....	1
II. REVIEW OF LITERATURES.....	4
III. MATERIALS AND METHODS.....	42
IV. RESULTS AND DISCUSSION.....	57
V. CONCLUSIONS.....	115
REFERENCES.....	117
APPENDICES.....	123
VITA.....	154

LIST OF TABLES

Table		Page
1	Specifications of standard quality of Suppocire®	20
2	Classification of hydroxypropyl methylcellulose phthalate.....	40
3	A three way crossover design for <i>in vivo</i> study.....	52
4	The displacement values of each compositions in suppository bases.....	57
5	Weight of each suppository (g) from three formulations of conventional hydrophilic and one conventional hydrophobic ketoprofen rectal suppositories.....	61
6	Uniformity of content of ketoprofen (%L.A.) from four formulations of conventional ketoprofen rectal suppositories.....	62
7	Weight of each suppository (g) from three formulations of prolonged release ketoprofen rectal suppositories using Eudragit S-100 as prolonged release carrier.. ..	64
8	Uniformity of content of ketoprofen (%L.A.) from three formulations of prolonged release ketoprofen rectal suppositories using Eudragit S-100 as prolonged release carrier	65
9	Weight of each suppository (g) from two formulations of prolonged release ketoprofen rectal suppositories using HP 55 as prolonged release carrier	66
10	Uniformity of content of ketoprofen (%L.A.) from two formulations of prolonged release ketoprofen rectal suppositories using HP 55 as prolonged release carrier	67
11	Percent released of ketoprofen (Mean \pm S.D.) from three formulations of conventional hydrophilic ketoprofen rectal suppositories.....	69

Table (cont.)	Page
12 Release rate constant of ketoprofen (hr^{-1}) from three formulations of conventional ketoprofen rectal suppositories.....	71
13 Percent released of ketoprofen (Mean \pm S.D.) from conventional hydrophobic ketoprofen rectal suppositories.....	72
14 Percent released of ketoprofen (Mean \pm S.D.) from three formulations of prolonged release ketoprofen rectal suppositories using Eudragit S-100 as prolonged release carrier.....	75
15 Release rate constant of ketoprofen (hr^{-1}) from three formulations of prolonged release ketoprofen rectal suppositories using Eudragit S-100 as prolonged release carrier.....	79
16 Percent released of ketoprofen (Mean \pm S.D.) from two formulations of prolonged release ketoprofen rectal suppositories using HP55 as prolonged release carrier.....	81
17 Release rate constant of ketoprofen (hr^{-1}) from two formulations of prolonged release ketoprofen rectal suppositories using HP55 as prolonged release carrier.....	84
18 Summary of <i>in vitro</i> studies of all formulations of ketoprofen rectal suppositories.....	85
19 Plasma ketoprofen concentration ($\mu\text{g/mL}$) of nine rabbits after administration of 100 mg prolonged release ketoprofen rectal suppositories using Eudragit S-100 as prolonged release carrier.....	89
20 Plasma ketoprofen concentration ($\mu\text{g/mL}$) of nine rabbits after administration of 100 mg prolonged release ketoprofen rectal suppositories using HP55 as prolonged release carrier.....	90
21 Plasma ketoprofen concentration ($\mu\text{g/mL}$) of nine rabbits after administration of 100 mg prolonged release ketoprofen rectal suppositories using Suppocire [®] AM as base.....	91

Table (cont.)	Page
22 Log of peak plasma ketoprofen concentration ($\log C_{\max}$) of nine rabbits after administration of three formulations of 100 mg prolonged release ketoprofen rectal suppositories.....	102
23 Analysis of variance for three way crossover design of $\log C_{\max}$ of nine rabbits after administration of three formulations of 100 mg prolonged release ketoprofen rectal suppositories ($\alpha = 0.05$) and 90 percent confidence interval for the difference of C_{\max} means.....	102
24 The time to peak plasma ketoprofen concentrations (t_{\max}) of nine rabbits after administration of three formulations of 100 mg prolonged release ketoprofen rectal suppositories.....	105
25 Analysis of variance for three way crossover design of time to peak plasma ketoprofen concentrations (t_{\max}) of nine rabbits after administration of three formulations of 100 mg prolonged release ketoprofen rectal suppositories ($\alpha = 0.05$).....	105
26 Log of area under plasma ketoprofen concentration-time curves ($\log \text{AUC}$) of nine rabbits after administration of three formulations of 100 mg prolonged release ketoprofen rectal suppositories.....	106
27 Analysis of variance for three way crossover design of $\log \text{AUC}$ of nine rabbits after administration of three formulations of 100 mg prolonged release ketoprofen rectal suppositories ($\alpha = 0.05$) and 90 percent confidence interval for the difference of AUC means.....	106
28 Elimination rate constant (K_{el}) of ketoprofen of nine rabbits after administration of three formulations of 100 mg prolonged release ketoprofen rectal suppositories.....	107
29 Analysis of variance for three way crossover design of elimination rate constant (K_{el}) of nine rabbits after administration of three formulations of 100 mg prolonged release ketoprofen rectal suppositories ($\alpha = 0.05$).....	107

Table (cont.)	Page
30 Elimination half-lives ($t_{1/2}$) of ketoprofen of nine rabbits after administration of three formulations of 100 mg prolonged release ketoprofen rectal suppositories.....	108
31 Analysis of variance for three way crossover design of elimination half-lives ($t_{1/2}$) of nine rabbits after administration of three formulations of 100 mg prolonged release ketoprofen rectal suppositories ($\alpha = 0.05$).....	108
32 Mean residence time (MRT) of ketoprofen of nine rabbits after administration of three formulations of 100 mg prolonged release ketoprofen rectal suppositories.....	109
33 Analysis of variance for three way crossover design of mean residence time (MRT) of nine rabbits after administration of three formulations of 100 mg prolonged release ketoprofen rectal suppositories ($\alpha = 0.05$).....	109
34 Volume of distribution (V_d / F) of ketoprofen of nine rabbits after administration of three formulations of 100 mg prolonged release ketoprofen rectal suppositories.....	110
35 Analysis of variance for three way crossover design of volume of distribution (V_d / F) of nine rabbits after administration of three formulations of 100 mg prolonged release ketoprofen rectal suppositories ($\alpha = 0.05$).....	110
36 Total plasma clearance (CL / F) of ketoprofen of nine rabbits after administration of three formulations of 100 mg prolonged release ketoprofen rectal suppositories.....	112
37 Analysis of variance for three way crossover design of total plasma clearance (CL / F) of nine rabbits after administration of three formulations of 100 mg prolonged release ketoprofen rectal suppositories ($\alpha = 0.05$).....	112

Table (cont.)	Page
38 Estimated pharmacokinetic parameters of ketoprofen (Mean \pm S.D.) from nine rabbits after administration of three formulations of 100 mg prolonged release ketoprofen rectal suppositories.....	113
39 Accuracy of analytical method for determination of ketoprofen in phosphate buffer pH 7.2 at $\lambda = 260$ nm.....	127
40 Accuracy of analytical method for determination of ketoprofen in chloroform at $\lambda = 255$ nm.....	128
41 Accuracy of analytical method for determination of ketoprofen in methanol at $\lambda = 255$ nm.....	128
42 Within run precision of analytical method for determination of ketoprofen in phosphate buffer pH 7.2 at $\lambda = 260$ nm.....	129
43 Within run precision of analytical method for determination of ketoprofen in chloroform at $\lambda = 255$ nm.....	130
44 Within run precision of analytical method for determination of ketoprofen in methanol at $\lambda = 255$ nm.....	130
45 Between run precision of analytical method for determination of ketoprofen in phosphate buffer pH 7.2 at $\lambda = 260$ nm.....	131
46 Between run precision of analytical method for determination of ketoprofen in chloroform at $\lambda = 255$ nm.....	132
47 Between run precision of analytical method for determination of ketoprofen in methanol at $\lambda = 255$ nm.....	132
48 Typical calibration curve data for determination of ketoprofen in phosphate buffer pH 7.2 estimated using linear regression.....	133
49 Typical calibration curve data for determination of ketoprofen in chloroform estimated using linear regression.....	135
50 Typical calibration curve data for determination of ketoprofen in methanol estimated using linear regression.....	137

Table (cont.)		Page
51	Typical data for determination of the release rate constant according to sigma-minus method.....	140
52	Accuracy of analytical method for determination of ketoprofen in rabbit plasma.....	141
53	Within run precision of analytical method for determination of ketoprofen in rabbit plasma.....	142
54	Between run precision of analytical method for determination of ketoprofen in rabbit plasma.....	143
55	Typical calibration curve data for determination of ketoprofen in rabbit plasma estimated using linear regression.....	144

LIST OF FIGURES

Figure		Page
1	Veinous drainage of the human rectum.....	8
2	The apparatus for the disintegration of suppositories.....	30
3	Cross-sectional diagram of the <i>in vitro</i> release and diffusion rate apparatus.....	33
4	Diagram of the apparatus used in the modified dialysis membrane method.....	34
5	Percent released of ketoprofen from three formulations of conventional hydrophilic ketoprofen rectal suppositories.....	70
6	Percent released of ketoprofen from conventional hydrophobic ketoprofen rectal suppositories.....	73
7	Percent released of ketoprofen from three formulations of prolonged release ketoprofen rectal suppositories using ketoprofen : Eudragit S-100 = 1:1.....	76
8	Percent released of ketoprofen from three formulations of prolonged release ketoprofen rectal suppositories using ketoprofen : Eudragit S-100 = 1:1.5.....	77
9	Percent released of ketoprofen from three formulations of prolonged release ketoprofen rectal suppositories using ketoprofen : Eudragit S-100 = 1:2.....	78
10	Percent released of ketoprofen from three formulations of prolonged release ketoprofen rectal suppositories using ketoprofen : HP55 = 1:3.....	82
11	Percent released of ketoprofen from three formulations of prolonged release ketoprofen rectal suppositories using ketoprofen : HP55 = 1:4.....	83

Figure(cont.)	Page
12 High performance liquid chromatograms of ketoprofen (A) and diclofenac sodium (B).....	88
13 Plasma ketoprofen concentration-time curves of rabbit No. 1 after administration of three formulations of prolonged release ketoprofen rectal suppositories.....	92
14 Plasma ketoprofen concentration-time curves of rabbit No. 2 after administration of three formulations of prolonged release ketoprofen rectal suppositories.....	93
15 Plasma ketoprofen concentration-time curves of rabbit No. 3 after administration of three formulations of prolonged release ketoprofen rectal suppositories.....	94
16 Plasma ketoprofen concentration-time curves of rabbit No. 4 after administration of three formulations of prolonged release ketoprofen rectal suppositories.....	95
17 Plasma ketoprofen concentration-time curves of rabbit No. 5 after administration of three formulations of prolonged release ketoprofen rectal suppositories.....	96
18 Plasma ketoprofen concentration-time curves of rabbit No. 6 after administration of three formulations of prolonged release ketoprofen rectal suppositories.....	97
19 Plasma ketoprofen concentration-time curves of rabbit No. 7 after administration of three formulations of prolonged release ketoprofen rectal suppositories.....	98
20 Plasma ketoprofen concentration-time curves of rabbit No. 8 after administration of three formulations of prolonged release ketoprofen rectal suppositories.....	99

Figure(cont.)	Page
21 Plasma ketoprofen concentration-time curves of rabbit No. 9 after administration of three formulations of prolonged release ketoprofen rectal suppositories.....	100
22 Comparison of plasma ketoprofen concentration-time curves of nine rabbits after administration of three formulations of prolonged release ketoprofen rectal suppositories.....	101
23 Typical calibration curve for determination of ketoprofen in phosphate buffer pH 7.2 at $\lambda = 260$ nm.....	134
24 Typical calibration curve for determination of ketoprofen in chloroform at $\lambda = 255$ nm.....	136
25 Typical calibration curve for determination of ketoprofen in methanol at $\lambda = 255$ nm.....	138
26 Typical calibration curve for determination of ketoprofen in rabbit plasma.....	145

LIST OF ABBREVIATIONS

NSAIDs	=	non-steroidal antiinflammatory drugs
PEG	=	polyethylene glycol
GI	=	gastrointestinal tract
°C	=	degree Celsius
°F	=	degree Fahrenheit
nm	=	nanometer
L.A.	=	labeled amount
μg	=	microgram
mg	=	milligram
g	=	gram
Kg	=	kilogram
μL	=	microliter
mL	=	milliliter
L	=	liter
Conc.	=	concentration
min	=	minute
hr	=	hour
BP	=	British Pharmacopoeia
USP	=	United States Pharmacopoeia
HPLC	=	high performance liquid chromatography
UV	=	ultraviolet
λ	=	wavelength
PAR	=	peak area ratio
ANOVA	=	analysis of variance
d.f.	=	degree of freedom
SS	=	sum of squares
MS	=	mean square
S.D.	=	standard deviation

LIST OF ABBREVIATIONS (cont.)

C.V.	=	coefficient of variation
r^2	=	coefficient of determination
C_{\max}	=	peak plasma concentration
t_{\max}	=	time to peak plasma concentration
AUC	=	area under the plasma concentration-time curve
AUMC	=	area under the moment curve
K_{el}	=	elimination rate constant
$t_{1/2}$	=	elimination half-life
MRT	=	mean residence time
F	=	fraction of drug absorbed
V_d/F	=	volume of distribution divided by fraction of drug absorbed
CL/F	=	total plasma clearance divided by fraction of drug absorbed