

**การพัฒนาเทคโนโลยีควบคุมการปลดปล่อยของดีไลท์อะเซมไฮโดรคอลลอยด์ :
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ต่อจลนศาสตร์และการปลดปล่อย**

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**DEVELOPMENT OF DILTIAZEM HYDROCHLORIDE CONTROLLED RELEASE
PELLETS: EFFECT OF DRUG CONCENTRATIONS AND ENCAPSULATING
POLYMERS ON KINETIC AND RELEASE**



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การศึกษาค่าการละลายเทคโนโลยีขนาดยาเคลือบที่ระดับ 7.5 เปรอร์เซ็นต์น้ำหนัก/น้ำหนัก และผสมกับเทคโนโลยีที่ไม่ได้เคลือบเพื่อเป็นขนาดยาค้างคั้งในอัตราส่วน 4:1 ให้การปลดปล่อยที่ไม่แตกต่างกับ เซอร์เบตเซอร์® 90 เอสอาร์ อย่างมีนัยสำคัญในตัวกลางที่ระบุในยูเอสพี 23 และ ตัวกลางเปลี่ยนพีเอช การศึกษาผลของการปลดปล่อยใช้คิลโทอะเซม ไฮโดรคลอไรด์เทคโนโลยีขนาดยาตั้งแต่ 30 45 60 และ 90 มิลลิกรัม รูปแบบการปลดปล่อยของตัวยา 30 และ 45 มิลลิกรัม/ขนาดยา สามารถแบ่งได้เป็น 3 เฟสคือ ช่วงเวลาปรับสมดุลก่อนการปลดปล่อย ช่วงการปลดปล่อยคงที่ และช่วงอัตราการปลดปล่อยลดลง ส่วนระดับยาที่ 60 และ 90 มิลลิกรัม/ขนาดยาพบเฉพาะช่วงเวลาปรับสมดุลก่อนการปลดปล่อย และช่วงของการปลดปล่อยคงที่ ดังนั้นสามารถสรุปได้จากกลไกการปลดปล่อยว่าการแพร่อาจเกี่ยวข้องในช่วงเวลาปรับสมดุลก่อนการปลดปล่อย และแรงขับเคลื่อนในช่วงการปลดปล่อยคงที่อาจมาจากแรงพอง อะวีเซล® ทีเอช 101 กับเอชพีซี-เอ็ม® 0.5 เปรอร์เซ็นต์ และแรงดันออสโมติกที่เกิดจากตัวยาคิลโทอะเซม ไฮโดรคลอไรด์ ซึ่งทำหน้าที่เป็นสารก่อกออสโมติก

สถาบันวิทยบริการ
 จุฬาลงกรณ์มหาวิทยาลัย

ภาควิชา.....เภสัชอุตสาหกรรม.....ลายมือชื่อนิสิต.....ศุรเชษฐ วัฒนา.....
 สาขาวิชา.....เภสัชอุตสาหกรรม.....ลายมือชื่ออาจารย์ที่ปรึกษา.....ไกรสิทธิ์ อัมพรายน.....
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4076532233: MAJOR MANUFACTURING PHARMACY

KEY WORD: DILTIAZEM HYDROCHLORIDE/ ENCAPSULATING POLYMER/ PELLETS/ RELEASE MECHANISM/ SPHERICITY/ TENSILE STRENGTH/ TOUGHNESS

SURACHET WATTANA : DEVELOPMENT OF DILTIAZEM HYDROCHLORIDE CONTROLLED RELEASE PELLETS: EFFECT OF DRUG CONCENTRATIONS AND ENCAPSULATING POLYMERS ON KINETIC AND RELEASE. THESIS ADVISOR : ASSO. PROF. KAISRI UMPRYN, Ph.D. 206 pp. ISBN 974-332-901-3

The high dose (90 mg/150 mg) of diltiazem hydrochloride (DTZ HCl) pellets were prepared by extrusion-spheronization process. Core pellets which provided the most spherical shape containing DTZ HCl and Avicel[®] PH 101 60 : 40 percent w/w and using HPC-M[®] 0.5 percent by weight on dry substance as binder solution were selected. The other doses of DTZ HCl pellets were also prepared and found that rough surface pellets occurred in low dose (30 mg/150 mg), due to the shrinking property of high level of Avicel[®] PH 101. Triethyl citrate 20 percent based on weight of ethylcellulose polymer was used as plasticizer in coating film due to the results of optimum film strength, flexibility, toughness and good drug release characteristic with simple using in coating process.

For dissolution study, the drug pellets were coated with 7.5 percent w/w coating level and mixed with uncoated pellets as an initial dose at the ratio of 4:1 gave an insignificant release to Herbesser[®] 90 SR in medium as described by USP 23 and pH changed medium. The release mechanism was studied with various doses of DTZ HCl coated pellets range from 30, 45, 60 and 90 mg. The release profiles of 30 and 45 mg/doses can be divided into three phases as lag time, constant release and declining rate period. However, at 60 and 90 mg/dose, only lag time and constant release periods occurred. Thus, it can be concluded from the release mechanism that diffusion may be involved during lag time period and the driving force in constant release period probably comes from the swelling force of Avicel[®] PH 101 with 0.5 percent HPC-M[®] and osmotic pressure produced from DTZ HCl which acts as osmotic inducing agent.

ภาควิชา.....เภสัชอุตสาหกรรม.....ลายมือชื่อนิสิต.....
สาขาวิชา.....เภสัชอุตสาหกรรม.....ลายมือชื่ออาจารย์ที่ปรึกษา.....
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LIST OF ABBREVIATIONS

bar	kg/cm ²
°C	degree celsius (centigrade)
cm	centimetre(s)
cps	centipoises
CO	castor oil
e.g.	exempli gratia,for example
et al.	Et alii, and others
DEP	diethyl phthalate
DTZ	diltazem
EC	ethylcellulose
Eqn	equation (s)
g	gram (s)
HCl	hydrochloric acid
HPC-M	hydroxypropylcellulose medium grade
hr	hour (s)
i.e.	id est, that is
kg	kilogram (s)
kJ	kilojule (s)
Mpa	megapascal
mg	miligram (s)
min.	minute (s)
ml	mililitre (s)
mm	milimetre (s)
mm ²	square milimetre (s)

LIST OF ABBREVIATIONS (Cont.)

No.	number
nm	nanometre (s)
PEG	polyethylene glycol
pH	the negative logarithm of hydrogen ion concentration
q.s.	make to volume
r^2	coefficient of determination
rpm	revolution per minute
SD	standard deviation
SEM	scanning electron microscope
TEC	triethyl citrate
USP	The United State Pharmacopoeia
UV	ultraviolet
w/v	weight by volume
w/w	weight by weight
μg	microgram (s)
μl	microlitre (s)
μm	micrometre (s), micron (s)
SR	sustained release
%	percentage
°	degree