

การประยุกต์ใช้สารไขมันและซีดีร่วมกับเอธิลเซลลูโลสเป็นสารเคลือบสำหรับควบคุม
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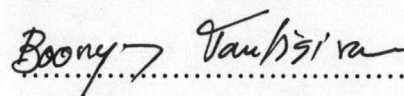
**APPLICATION OF FATS AND WAXES IN COMBINATION WITH
ETHYLCELLULOSE AS COATING MATERIALS FOR CONTROLLED
RELEASE OF DILTIAZEM HYDROCHLORIDE PELLETS USING FLUIDIZED
BED TECHNIQUE**

Miss Warapun Lekrut


**A Thesis Submitted in Partial Fulfillment of the Requirements
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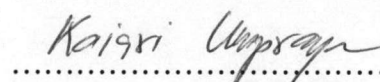
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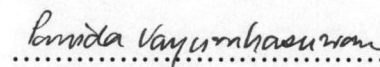
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วราพรรณ เล็กรัตน์ : การประยุกต์ใช้สารไขมันและซีผึ้งร่วมกับเอธิลเซลลูโลส เป็นสารเคลือบสำหรับควบคุมการปลดปล่อยดิลไทอะเซม ไฮโดรคลอไรด์เฟลเลทโดยใช้เทคนิคฟลูอิดไดซ์เบด (APPLICATION OF FATS AND WAXES IN COMBINATION WITH ETHYLCELLULOSE AS COATING MATERIALS FOR CONTROLLED RELEASE OF DILTIAZEM HYDROCHLORIDE PELLETS USING FLUIDIZED BED TECHNIQUE) อ.ที่ปรึกษา : รศ.ดร.โกรสีห์ อัมพรายน, 167 หน้า. ISBN 974-03-1380-9

การเตรียมดิลไทอะเซม ไฮโดรคลอไรด์เฟลเลทขนาดยาสูง (90 มิลลิกรัม) ประกอบด้วยอะซิเตล พีเอช101 และเอชพีซี-เอ็มเตรียมด้วยกระบวนการเอกซ์ทรูชัน-สเฟียโรไนเซชัน พบว่าได้เฟลเลทที่มีรูปร่างกลมผิวเรียบและมีการกระจายขนาดที่แคบ แล้วนำมาเคลือบด้วยตัวทำละลายอินทรีย์ของสารไขมันเดี่ยว (คาร์บูบาแวกซ์ กลีเซอรอลโมโนสเตียเรทและคอมไพรตอล 888 เอทีโอ) หรือเอธิลเซลลูโลสบริสุทธิ์จากนั้นคัดเลือกสารไขมันที่มีความเหมาะสมเพื่อนำมาใช้ศึกษาต่อไป จากการศึกษาพบว่าคอมไพรตอล 888 เอทีโอ เป็นสารไขมันที่มีความน่าสนใจ มีความเหมาะสมที่สุด ศึกษาการเคลือบดิลไทอะเซม ไฮโดรคลอไรด์โดยใช้สารผสมของคอมไพรตอล 888 เอทีโอต่อเอธิลเซลลูโลสในอัตราส่วน 1:1 เคลือบที่ระดับ 10 เปอร์เซ็นต์โดยน้ำหนัก พบว่าให้การปลดปล่อยตัวยาจากเฟลเลทที่มีลักษณะตรงตามข้อกำหนดตามยูเอสพี 24 ศึกษาการเกิดอันตรกริยาทางเคมีระหว่างสารทั้งสองตัว โดยใช้เอกซเรย์ดิฟแฟรกโทเมทรี อินฟราเรดสเปกโทรสโกปี และดิฟเฟอเรนเชียลสแกนนิ่งคาลอริเมทรี พบว่าเป็นเพียงการผสมกันทางกายภาพระหว่างสารทั้งสองเท่านั้น กลไกการปลดปล่อยตัวยาดิลไทอะเซม ไฮโดรคลอไรด์จากเฟลเลทเคลือบพบว่าประกอบด้วย การแพร่ของตัวยาผ่านฟิล์มผสมและปลดปล่อยผ่านทางช่องว่างที่น้ำผ่านได้ของฟิล์ม การทดสอบความเค้นแมคานิกของชั้นเคลือบฟิล์มดิลไทอะเซม ไฮโดรคลอไรด์เฟลเลทโดยใช้เม็ดพอลิสไตรีน แสดงความต้านทานของฟิล์มภายใต้ความเค้นในระบบทางเดินอาหาร

การศึกษาค่าการละลายของดิลไทอะเซม ไฮโดรคลอไรด์เฟลเลทในตัวอย่างเปลี่ยนพีเอช เปรียบเทียบกับตัวอย่างที่ระบุในยูเอสพี 24 โดยใช้น้ำเป็นตัวอย่าง การทดสอบพบว่า การปลดปล่อยตัวยาช่วงต้นของวิธีกติและการเปลี่ยนแปลงพีเอช (พีเอช 1.2) ไม่แตกต่างกัน ($P > 0.05$) ในทางกลับกันการปลดปล่อยในช่วงหลังของการเปลี่ยนแปลงพีเอช (พีเอช 6.8) มีค่าสูงกว่า ($P < 0.05$)

ภาควิชา.....เภสัชอุตสาหกรรม.....ลายมือชื่อนิสิต..... วราพรรณ เล็กรัตน์
สาขาวิชา.....เภสัชอุตสาหกรรม.....ลายมือชื่ออาจารย์ที่ปรึกษา..... โอรสสิน อัมพรายน
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KEY WORDS: DILTIAZEM HYDROCHLORIDE / CARNAUBA WAX / GLYCERYL MONOSTEARATE / COMPRITOL 888 ATO®/ ETHYLCELLULOSE / RELEASE MECHANISM

WARAPUN LEKRUT : APPLICATION OF FATS AND WAXES IN COMBINATION WITH ETHYLCELLULOSE AS COATING MATERIALS FOR CONTROLLED RELEASE OF DILTIAZEM HYDROCHLORIDE PELLETS USING FLUIDIZED BED TECHNIQUE. THESIS ADVISOR: ASSOC. PROF. KAISRI UMPRAYN, Ph.D.,167pp. ISBN 974-03-1380-9

The high dose (90 mg) of diltiazem hydrochloride pellets with Avicel PH101® and HPC-M® were prepared by extrusion-spheronization process and found to possess spherical shape, smooth surface and narrow size distribution. They were coated with organic solvent base solutions of either pure waxes(carnauba wax, glyceryl monostearate and Compritol 888 ATO®) or pure ethylcellulose. Therefore, the suitable wax type was selected for the next studies. The experiments shown that Compritol 888 ATO®, one of the interested wax coating material, is the most optimal coating agent. Further studies revealed that the DTZ HCl coated pellets with the mixtures of Compritol 888 ATO® and ethylcellulose (1:1) at 10% weight gain provided drug release profile in accordance with the USP 24 requirement. The interaction of Compritol 888 ATO® and ethylcellulose were evaluated and observed for chemical interaction. Various methods were used such as X-ray Diffractometry, Infrared Spectroscopy, and Differential Scanning Calorimetry. They indicated that only physical mixture was the best answer of the blended materials. The release mechanism of DTZ HCl from coated pellets was found to compose of diffusion of drug through mix films and release through an aqueous channel of coating membrane. The mechanical stress test of the film coated DTZ HCl pellets via polystyrene beads showed resistant of the film under GI stress conditions.

The in vitro pH change dissolution study of DTZ HCl pellets were conducted and compared with typical dissolution study following the requirement of USP 24 that utilized deionized water as dissolution medium. The studies indicated that the initial period of both normal and pH change (pH 1.2) dissolution test, DTZ HCl was released at equal amount at both conditions (P > 0.05). Conversely, on the later period of pH change (pH 6.8), the higher drug release was observed (P < 0.05).

Department.....Manufacturing Pharmacy...Student's signature.....
Field of study...Industrial Pharmacy.....Advisor's signature.....
Academic year.....2001.....Co-advisor's signature.....

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LIST OF ABBREVIATIONS

°C	degree Celsius
cm	centrimetre
cps	centripoises
e.g.	exempli gratia, for example
DSC	differential scanning calorimetry
DTZ	diltiazem
EC	ethyl cellulose
g	gram
HCl	hydrochloric acid
HPC-M	hydroxypropylcellulose medium grade
hr	hour (s)
kg	kilogram (s)
mg	milligram (s)
min	minute (s)
ml	mililitre (s)
mm	milimetre (s)
pH	the negative logarithm of hydrogen ion concentration
r ²	coefficient of determination
rpm	revolution per minute
SD	standard deviation
SEM	scanning electron microscope
TEC	triethyl citrate

LIST OF ABBREVIATIONS (cont.)

USP	The United State Pharmacopoeia
UV-VIS	ultraviolet-visible
w/w	weight by weight
μg	microgram (s)
μl	microlitre (s)
μm	micrometer (s), micron (s)
%	percentage