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**DEVELOPMENT OF THEOPHYLLINE SUSTAINED RELEASE GRANULES
COATED BY FLUIDIZED BED TECHNIQUE WITH POLY (ETHYLACRYLATE
METHYLMETHACRYLATE) AND ETHYLCELLULOSE
AQUEOUS DISPERSIONS**



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**สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย**

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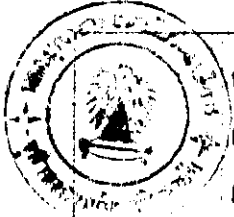
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พิมพ์ต้นฉบับบทคัดย่อวิทยานิพนธ์ภายในกรอบสี่เหลี่ยมนี้เพียงแผ่นเดียว



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การเตรียมธีโอฟิลลีนแกรนูลขนาดต่างๆเคลือบด้วยเอธิลเซลลูโลสเอควีต คีตเพอซัน (ซัวร์ลิส) หรือ โพลีเอธิลอะคริเลต เมธิลเมธาคริเลต เอควีต คีตเพอซัน ซึ่งมีแคปโซลิตผสมอยู่ โดยใช้เทคนิคการพ่นเคลือบแบบฟลูอิดไคซ์เบด เพื่อศึกษาคุณสมบัติทางกายภาพ และ คุณสมบัติการปลดปล่อยตัวยาจากแกรนูลที่ถูกเคลือบแล้วซึ่งบรรจุในแคปซูล เปรียบเทียบกับแกรนูลที่ไม่ได้เคลือบพื้นผิวของแกรนูลที่ไม่ได้เคลือบจะมีลักษณะหยาบ และมีรูปร่างไม่สม่ำเสมอ ส่วนพื้นผิวของแกรนูลที่เคลือบด้วยยูคาจิด เอ็นอี 30ดี จะมีลักษณะหยาบกว่าพื้นผิวของแกรนูลที่เคลือบด้วยซัวร์ลิส การเพิ่มระดับการเคลือบจะทำให้ความหนาของฟิล์มเพิ่มสูงขึ้น ดังนั้นแกรนูลจึงมีขนาดใหญ่ขึ้น รวมทั้งขอบและมุมจะลดต่ำลงด้วยเมื่อมีการเคลือบ ค่าแองเกิล ออฟรีโพส และค่าปริมาณความชื้นของแกรนูลทั้งหมดจะอยู่ในช่วง 30-38 องศา และ 0.74-0.86 เปอร์เซ็นต์ ตามลำดับ การเปรียบเทียบเปอร์เซ็นต์คอมเพรสซิบิลิตี และค่าอัตราการไหลระหว่างแกรนูลที่ไม่ได้เคลือบและแกรนูลที่เคลือบแล้วในแต่ละขนาดของแกรนูล จะให้ผลการทดลองที่มีค่าแปรปรวน เปอร์เซ็นต์อัลองเกชัน แอทแบรค และเปอร์เซ็นต์วอเตอร์ ซอปชันของซัวร์ลิสฟิล์มจะมีค่าเพิ่มสูงขึ้นเมื่อเปอร์เซ็นต์ของไดบิวธิวพาทาเลตที่ใช้เป็นพลาสติกไซเซอร์มีค่าเพิ่มสูงขึ้น ในขณะที่ค่าเท็นซาไซด์ สเทริงของฟิล์มจะลดต่ำลง อัตราการปลดปล่อยตัวยาจากแกรนูลที่ถูกเคลือบแล้วซึ่งบรรจุในแคปซูลจะมีค่าลดต่ำลงเมื่อเพิ่มปริมาณของเอควีต โพลีเมอร์ลิก คีตเพอซัน ชนิดของเอควีตโพลีเมอร์ลิก คีตเพอซัน จะมีผลต่อการปลดปล่อยตัวยา แกรนูลที่มีขนาดใหญ่กว่าซึ่งบรรจุในแคปซูลจะให้การปลดปล่อยตัวยาที่ช้ากว่าแกรนูลที่มีขนาดเล็กกว่า ในปริมาณการปลดปล่อยตัวยาที่ใกล้เคียงกัน จะใช้ปริมาณของยูคาจิด เอ็นอี 30ดี ที่ใช้ในการเคลือบสูงกว่าปริมาณของซัวร์ลิส รูปแบบการปลดปล่อยตัวยาจากแกรนูลที่บรรจุในแคปซูลจะเป็นแบบเฟิร์สออร์เดอร์และแกรนูลที่เคลือบแล้วบางตัวรับจะให้การปลดปล่อยตัวยาที่เข้ามาตรฐานของยูเอสพี

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สาขาวิชา เคมีเภสัชวิทยา
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ลายมือชื่อนิติต ตาพร หริการภักดี
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SARAPORN HARIKARNPAKDEE : DEVELOPMENT OF THEOPHYLLINE SUSTAINED RELEASE GRANULES COATED BY FLUIDIZED BED TECHNIQUE WITH POLY(ETHYLACRYLATE METHYLMETHACRYLATE) AND ETHYLCELLULOSE AQUEOUSE DISPERSION. THESIS ADVISOR : ASSO.PROF.GARNPIMOL C. RITTHIDEJ, Ph.D., THESIS CO-ADVISOR : ASSIS. PROF. WICHEIN THANINDRATARN, 232 pp. ISBN 974-634-999-6

Theophylline granules of different sizes were coated with ethylcellulose aqueous dispersion (Surelease®) or poly(ethylacrylate methacrylate) aqueous dispersion (Eudragit® NE 30D) containing cab-o-sil by fluidized bed technique. The physical properties of coated granules and sustained release characteristics from capsules containing coated granules were evaluated and compared to those of uncoated granules. All uncoated theophylline granules exhibited rough surface and irregular shape. The granules coated with Eudragit® NE 30D exhibited rougher surface than Surelease® coated granules. Increasing the coating level increased the thickness of film, thus granules became slightly larger. Edge and corner were lower when coated.

The angles of repose and the moisture contents of all granules were within the range of 30-38° and 0.74-0.86 % respectively. Comparison of the percent compressibility and the flow rate between uncoated and coated granules of each size showed varied results. For Surelease® film, the percent elongation at break and the percent water sorption were increased with the increasing of the percentage of dibutyl phthalate as plasticizer whereas the tensile strength were decreased. The release rate of the drug from capsules containing granules decreased when increasing the amount of aqueous polymeric dispersion. The type of aqueous polymeric dispersion affected the release of drug. Capsules containing larger granules exhibited slower release of drug than smaller granules. For similar of drug release, the amount of Eudragit® NE 30D used in coating was higher than that of the Surelease®. The drug release model from capsules containing granules fitted mostly to the first-order model. Some formulations of coated granules exhibited drug release conformed to the USP.

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ABBREVIATIONS

bar	N/cm ²
°C	degree celcius
cm	centimeter
Conc.	Concentration
g	gram
HCl	Hydrochloric acid
hr.	hour
mg	milligram
min.	minute
ml	milliliter
ml/min	milliliter per minute
N	Normality
NaOH	Sodium hydroxide
nm	nanometer
SD	Standard deviation
sec.	second
SEM	Scanning Electron Microscope
UV	ultraviolet
wt.	weight
µg/ml	microgram per milliliter
µm (µ)	micrometer