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ด้วยระบบออสโมซิส

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DEVELOPMENT OF OSMOTICALLY CONTROLLED DRUG  
DELIVERY CAPSULES



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ศูนย์วิทยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย

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ณัฐชนันท์ ศิริรัตน์สกุล : การพัฒนาระบบนำส่งยาชนิดแคปซูลที่ควบคุมการปลดปล่อย  
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การพัฒนาระบบออสโมติกของแคปซูลเจลละตินชนิดแข็งเคลือบด้วยฟิล์มชนิดกึ่งซึมผ่าน  
ได้ เคลือบแคปซูลเจลละตินด้วยเครื่องเคลือบฟลูอิดไดซ์เบดโดยมีไฮดรอกซีโพรพิลเมทิล  
เซลลูโลสเป็นชั้นรองและเซลลูโลสอะซีเตตเป็นสารก่อก่อฟิล์มชนิดกึ่งซึมผ่านได้ ใช้โพรปราโนลอล  
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พลาสติกไซเซอร์ ปริมาณสารก่อกแรงดันออสโมติก ความแรงของแรงดันออสโมติกในสารละลายที่  
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พีอีจี400เพิ่มมากขึ้น โดยที่พีอีจี400สามารถละลายออกจากฟิล์มเซลลูโลสอะซีเตตเนื่องด้วย  
คุณสมบัติความชอบน้ำของพีอีจี400ขนาดรูมีอิทธิพลอย่างมากต่อการปลดปล่อยยาเมื่อฟิล์มมีขนาด  
ความหนาแน่น ในทางตรงกันข้ามขนาดรูมีอิทธิพลเพียงเล็กน้อยต่อการปลดปล่อยยาเมื่อฟิล์มมี  
ความหนาแน่นมากขึ้น การปลดปล่อยยาเพิ่มมากขึ้นเมื่อปริมาณโซเดียมคลอไรด์ในตำรับเพิ่มมากขึ้น  
ยกเว้นตำรับที่ประกอบด้วยแลคโตสอย่างเดียวที่มีการปลดปล่อยยามากที่สุด โซเดียมคลอไรด์ใน  
ตำรับอาจจะเหนียวทำให้เกิดการเกาะตัวกันของเจลละตินอันเนื่องมาจากปฏิกริยาระหว่างเจลละติน  
และโซเดียมคลอไรด์เป็นผลให้เกิดการขวางกั้นน้ำที่เข้าระบบดังนั้นการปลดปล่อยยาจึงลดลง แต่  
ทว่าแลคโตสนั้นไม่เหนียวทำให้เกิดการเกาะตัวกันของเจลละตินซึ่งทำให้การปลดปล่อยยามากกว่า  
เมื่อแรงดันออสโมติกของสารละลายที่ใช้ในการทดสอบการปลดปล่อยยาเพิ่มมากขึ้นการ  
ปลดปล่อยยาจะลดลง ความแตกต่างของแรงดันออสโมติกภายในและภายนอกกระบบลดลงอาจเป็น  
สาเหตุหนึ่งในการปลดปล่อยยาลดลง

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NATCHANAN SIRORATSAKUL : THESIS TITLE. DEVELOPMENT OF  
OSMOTICALLY CONTROLLED DRUG DELIVERY CAPSULES

THESIS ADVISOR : ASSOC. PROF. POJ KULVANICH, Ph.D., 247 pp. ISBN  
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Osmotic system of coated hard gelatin capsule was developed. Gelatin capsule shell was coated by fluidized bed coater using hydroxypropylmethylcellulose and cellulose acetate as subcoating layer and semipermeable membrane, respectively. Propranolol hydrochloride was used as a model drug. NaCl, KCl, lactose and sucrose were used as osmotic agents. Various influential factors ie. orifice size, amount of plasticizer, amount of osmotic agent, osmotically active dissolution medium were investigated. PEG400 was used as plasticizer and pore forming agent. SEM photomicrograph shows porous cellulose acetate membrane after coated capsule contacted the water. The drug release increased as amount of PEG400 was increased as PEG400 could leach out from the cellulose acetate film due to hydrophilic property causing porous structure of the membrane. At the low thickness of coating membrane, the orifice size influenced dramatically on drug release. On the contrary, the orifice size influenced slightly on drug release at the high thickness of coating membrane. The drug release rate increased when amount of sodium chloride in formulation was increased. Whereas, the drug release rate of formulation containing lactose was the highest. Sodium chloride in the formulation might induce aggregation of dissolved gelatin shell due to interaction between gelatin and sodium chloride resulting in obstructing water influx into the coated capsule hence less drug release. Whereas, lactose did not induce aggregation of dissolved gelatin shell resulting in higher drug release. When osmotic pressure of dissolution medium was increased, the drug release decreased. Decreased osmotic pressure difference across the membrane might be a cause of slower drug release rate.

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Field of study...Industrial Pharmacy.....Adivisor's signature.....*P. Kulvanich*

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ศูนย์วิทยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย

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## LIST OF ABBREVIATIONS

ANOVA	analysis of variance
CA	cellulose acetate
CV	coefficient of variation
i.e.	example and other
et al	et alli and other
g.	gram(s)
hr.	hour(s)
HCl	hydrochloric acid or hydrochloride
ml.	milliliter (s)
R <sup>2</sup>	coefficient of determination
SD	standard deviation
SEM	scanning electron photomicrograph
UV	ultraviolet
w/w	weight by weight
µm	micrometer(s)
%	percentage
DEP	diethyl phthalate
PEG 400	polyethylene glycol 400
HPMC	hydroxypropylmethylcellulose
PG	propylene glycol
nm.	nanometre
µg.	microgram
M	molarity (mole/litre)
RDT	relative dissolution time
AUC	area under dissolution curve
CV	coefficient variation
mm.	millimetre
rpm.	round per minute
mosm.	milliosmolarity