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FEASIBILITY STUDY ON PRONIOSOME DEVELOPMENT USING
SAQUINAVIR MESYLATE AS A MODEL DRUG

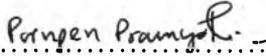
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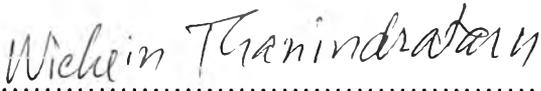
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งานวิจัยนี้มีวัตถุประสงค์เพื่อศึกษาความเป็นไปได้ในการพัฒนาโพรนิโอโซมของชาควินาเวียมีไซเลท และคุณสมบัติทางเคมีกายภาพของโพรนิโอโซมและนิโอโซมที่เตรียมจากโพรนิโอโซม กลุ่มของสารลดแรงตึงผิวโพลีออกซีเอธิลีนอัลคิลอีเธอร์ถูกเลือกนำมาใช้เพื่อศึกษาความสามารถในการก่อกำเนิดนิโอโซมที่อุณหภูมิ 37 องศาเซลเซียสโดยใช้วิธีฟิล์มแห้งในการเตรียมนิโอโซม การเตรียมโพรนิโอโซมของชาควินาเวียมีไซเลททำโดยสองวิธีคือ การผสมสารกระจายตัวของนิโอโซมที่กักเก็บชาควินาเวียมีไซเลท หรือสารละลายของชาควินาเวียมีไซเลทร่วมกับสารลดแรงตึงผิวและไขมัน กับแก๊กโทส หลังจากนั้นนำของผสมมาอบที่อุณหภูมิ 70 องศาเซลเซียสเป็นเวลา 24 ชั่วโมง และผ่านแรงขนาด 30 เมช ทำการศึกษารูปร่าง การกระจายของขนาดอนุภาค คุณสมบัติการไหล และการปลดปล่อยยาออกจากแกรนูล จากการศึกษาพบว่าโพรนิโอโซมของชาควินาเวียมีไซเลทสามารถเตรียมจากทั้งสองวิธีข้างต้นโดยใช้อัตราส่วนโดยโมลระหว่างโพลีออกซิด 4 ลอริลอีเทอร์ คอเลสเทอรอล และโพลีเอธิลีนไกลคอล 40 สเตียเรตเท่ากับ 70:0:30 ในความเข้มข้น 60 มิลลิโมลร่วมกับแก๊กโทส ผลการทดลองพบว่าแกรนูลมีคุณสมบัติการไหลที่ไม่ดี แกรนูลสามารถเปลี่ยนรูปเป็นนิโอโซมได้เองในน้ำ กรดไฮโดรคลอริกเข้มข้น 0.1 นอร์มอล และฟอสเฟตบัฟเฟอร์พีเอช 6.8 ที่อุณหภูมิ 37 องศาเซลเซียส การปลดปล่อยยาจากโพรนิโอโซมเพิ่มขึ้นอย่างมีนัยสำคัญในกรดไฮโดรคลอริกเข้มข้น 0.1 นอร์มอล และฟอสเฟตบัฟเฟอร์พีเอช 6.8 ชาควินาเวียมีไซเลทในโพรนิโอโซมมีความคงตัวนาน 2 เดือนหลังเก็บที่อุณหภูมิ 45 องศาเซลเซียส ความชื้นสัมพัทธ์ $75 \pm 5\%$ ดังนั้นจึงมีความเป็นไปได้ในการพัฒนาโพรนิโอโซมเพื่อเป็นระบบนำส่งยาทางปาก

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สาขาวิชา.....เภสัชอุตสาหกรรม.....
ปีการศึกษา.....2548.....

ลายมือชื่อนิสิต.....รัตนา ศรีชัยศักดิ์.....
ลายมือชื่ออาจารย์ที่ปรึกษา.....จิตติมา ชัชวาลย์สายสินธุ์.....
ลายมือชื่ออาจารย์ที่ปรึกษาร่วม.....พงศกร.....

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KEYWORD: SAQUINAVIR MESYLATE/ NIOSOME / PRONIOSOME

RATTANA SRICHAISAK: FEASIBILITY STUDY ON PRONIOSOME DEVELOPMENT USING SAQUINAVIR MESYLATE AS A MODEL DRUG. THESIS ADVISOR: JITTIMA CHATCHAWALSAISIN, Ph.D., THESIS CO-ADVISOR: PONGSAKORNPAT ARUNOTHAYANUN, Ph. D., 177 pp. ISBN 974-17-4588-5.

In this study, the feasibility to develop proniosomes of saquinavir mesylate was investigated. The physicochemical properties of proniosomes and proniosome-derived niosomes were also studied. A series of polyoxyethylene alkyl ether surfactants were used to study the ability to form niosomes at 37°C in aqueous media by dry film method. Attempts were made to prepare saquinavir mesylate proniosomes by two methods: incorporating dispersion of drug entrapped niosomes or solution of drug and lipid/ surfactants into lactose, then oven-drying at 70°C for 24 h. The dried mass was screened through a 30 mesh sieve. The morphology, size distribution, flowability and drug release of granules were studied. The results showed that both methods could form saquinavir mesylate proniosomes with 60 mM of 70:0:30 mole ratio of polyoxyl 4 lauryl ether: cholesterol: polyethylene glycol 40 stearate and lactose. The granules possessed poor flowability. They could spontaneously transform to niosomes in water, 0.1N hydrochloric acid and phosphate buffer pH 6.8 at 37°C. The drug release from proniosomes in 0.1N hydrochloric acid and phosphate buffer pH 6.8 was significantly increased ($p < 0.05$). Saquinavir mesylate loading proniosomes stored at 45°C and 75±5% relative humidity was stable up to 2 months. In conclusion, proniosomes could be produced and the system could be a candidate for oral drug delivery.

Department....Manufacturing Pharmacy.....Student's signature *Rattana Srichaisak*
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LIST OF ABBREVIATIONS

%	percentage
°C	degree Celsius (centigrade)
µg	microgram (s)
µm	micrometer (s)
λ_{\max}	wavelength of maximum absorption
AUC	area under the curve
CHOL	cholesterol
cm ⁻¹	the reciprocal of centimeters (wave number)
CPP	critical packing parameter
CV	coefficient of variation
DSC	differential scanning calorimetry
e.g.	for example, <i>exempli gratia</i>
EE	entrapment efficiency
et.al.	et alii, and others
g	gram (s)
HLB	hydrophilic lipophilic balance
HPLC	high-performance liquid chromatography
h	hour (s)
HIV	human immunodeficiency virus
HSM	hot stage microscopy
i.e.	id est (that is)
IR	infrared
log	logarithm
log P	n-octanol/ water partition coefficient
mg	milligram (s)
min	minute (s)
ml	milliliter (s)
mM	millimolar (s)
MW	molecular weight
N	normality
NA	not applicable

PBS	phosphate buffer saline
pH	the negative logarithm of the hydrogen ion concentration
pKa	ionization constant
PXRD	powder X-ray diffractometry
r^2	coefficient of determination
rpm	revolution (s) per minute
R-SQV	recrystallized saquinavir mesylate
RT	retention time
SD	standard deviation
SEM	scanning electron microscopy
SF	surfactant
SM52	simulsol [®] M52
SQV	saquinavir mesylate
TEM	transmission electron microscopy
v/v	volume by volume
w/v	weight by volume
w/w	weight by weight