### การเตรียมใจบูโปรเฟนไลโปโชมจากเฉซิทินถั่วเหลืองโดยวิธีเมคานิคัลดิสเพอร์ชัน

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วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาเภสัชศาสตรมหาบัณฑิต สาขาวิชาเภสัชกรรม ภาควิชาเภสัชกรรม บัณฑิตวิทยาลัย จุพาลงกรณ์มหาวิทยาลัย ปีการศึกษา 2540

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# PREPARATION OF IBUPROFEN LIPOSOMES USING SOYBEAN LECITHIN BY MECHANICAL DISPERSION METHOD

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#### พิมพ์ตันฉบับบทคัดย่อวิทยานิพนธ์ภายในกรอบสีเขียวนี้เพียงแผ่นเดียว

นฤมถ วังวิทยา: การเตรียมไอบูโปรเฟนไลโปโซมจากเลซิทินถั่วเหลืองโดยวิธีเมกานิคัลดิสเพอร์ชัน (PREPARATION OF IBUPROFEN LIPOSOMES USING SOYBEAN LECITHIN BY MECHANICAL DISPERSION METHOD) อ. ที่ปรึกษา: รส. สุชาคา ประเสริฐวิทยาการ, อ. ที่ปรึกษา: ร่วม: รส. คร. อุบถทิพย์ นิมมานนิตย์; 157 หน้า. ISBN 974-638-556-9.

ไอบูโปรเฟนไลโปโซมเตรียมจากเลชิทินถั่วเหลืองด้วยวิธีเมคานิคัลคิสเพอร์ชัน สภาวะที่เหมาะสมในการ เตรียมเพื่อให้ได้เป็นฟิล์มไขมันบางคือ ใช้คลอโรฟอร์มปริมาณ 20 มิลลิลิตรละลายไอบูโปรเฟนและเลซิทินถั่วเหลือง ที่อุณหภูมิระเหยแห้ง 35 องศาเซลเซียส เป็นเวลา 3 ชั่วโมง สารแขวนลอยใอบูโปรเฟนไลโปโซมเกิดขึ้นหลังจากผสม กับน้ำ 3 มิลถิลิตร นาน 2 ชั่วโมง การศึกษาภายใต้กล้องจุลทรรศน์อิเลคตรอนพบว่า ไลโปโชมที่ได้มีลักษณะกลมและ มีโครงสร้างผนังไลไปโซมหลายชั้น สัคส่วนโดยโมลของเลซิทินถั่วเหลืองต่อใอนูโปรเฟนเท่ากับ 1:0.144 สัดส่วนที่ ใอบู โปรเฟน ใล โปโซมมีอนุภาคใหญ่ที่สุดและใอบู โปรเฟนถูกกักเก็บไว้ในใล โปโซมมากที่สุดอย่างมี นัยสำคัญทางสถิติ (P < 0.05) โดยไม่มีผลึกยาปรากฏ สัคส่วนโดยโมลของเลซิทินถั่วเหลืองต่อโคเลสเตอรอลเท่ากับ 9:1 ทำให้ขนาดอนุภาคของใอบูโปรเฟนใลโปโซมเล็กลงและการกักเก็บขาลคลง เมื่อเดิมสเตียริลเอมีนปริมาณ 2.50 ทำให้ขนาคอนุภาคของใอบูโปรเฟนไลโปโซมเล็กลงและการกักเก็บยาลคลง โมลเปอร์เซ็นต์ อัลฟาโทโกเฟอรอลปริมาณ 0.001-0.025 เปอร์เซ็นต์ ทำให้อนุภาคของใอบูโปรเฟนไลโปโชมใหญ่ขึ้นแต่การกักเก็บชา ไม่เปลี่ยนแปลง ความเข้มข้นของไอบูโปรเฟนมีผลต่อขนาดอนุภาคและการกักเก็บยาของไอบูโปรเฟนไลโปโซม มากกว่าสารชอบไขมันตัวอื่นที่เดิมลงไป การเปรียบเทียบไอบไปรเฟนไลโปโซมที่เตรียมขึ้นใหม่กับที่เก็บไว้ที่ 4 องศา เซลเซียส เป็นเวลา 1 เดือนพบว่า มีใอบูโปรเฟนใลโปโซมเพียง 2 สูตรเท่านั้นที่ขนาคอนุภาคของไลโปโซมและการกัก เก็บยาไม่มีการเปลี่ยนแปลง สูตรแรกประกอบด้วยสัดส่วนโดยในลของเลซิทินถั่วเหลืองต่อโคเลสเตอรอล เท่ากับ 9:1 และสเทียริกเอมีนปริมาณ 2.50 ในกเปอร์เซ็นต์ สูตรที่สองประกอบด้วย สัดส่วนโดยในกของเลซิทินถั่วเหลืองต่อ โกเลสเตอรอลเท่ากับ 9:1 สเตียริลเอมีนปริมาณ 2.50 โมลเปอร์เซ็นต์และอัลฟาโทโคเพ่อรอลปริมาณ 0.0125 เปอร์เซ็นต์ ใอนูโปรเฟนใลโปไซมทั้งสองสูตรยังคงเป็นสารแขวนลอย การศึกษาภายใต้กล้องจุลทรรศน์อิเลคตรอน พบว่า ไลโปโซมไม่เปลี่ยนแปลงยังคงมีลักษณะกลม

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## ทินท์ต้นฉบับบทภัตย์ยวิทยานิพหรักายในกรกบรีเพียงนั่งศีย เม่นนา 🚌

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KEY WORD: IBUPROFEN LIPOSOMES / SOYBEAN LECITHIN / CHOLESTEROL / STEARLYAMINE / (±)α-TOCOPHEROL

NARUMOL VANGVITHYA: PREPARATION OF IBUPROFEN LIPOSOMES USING SOYBEAN LECITHIN BY MECHANICAL DISPERSION METHOD. THESIS ADVISOR: ASSO. PROF. SUCHADA PRASERTVITHYAKARN, THESIS CO-ADVISOR: ASSO. PROF. UBONTHIP NIMMANNIT, Ph. D. 157 pp. ISBN 974-638-556-9.

Ibuprofen liposomes were prepared using soybean lecithin by mechanical dispersion method. The appropriate conditions to prepare such a thin film of lipid were found when 20 ml of chloroform was used to dissolve ibuprofen and soybean lecithin and the evaporation temperature was set at 35°C for 3 hours. Milky suspension was obtained after 2 hours of hydration of the thin film with Electron microscopic analysis showed that the spherical vesicle with 3 ml of sterile water. multilamellar structure was formed. The 1:0.144 molar ratio of soybean lecithin to ibuprofen provided the significantly highest size and percentage drug entrapment without crystal of drug (P < 0.05). The 9:1 molar ratio of soybean lecithin to cholesterol led to decrease in size and the percentage drug entrapment. Addition of 2.50 mole% of stearylamine reduced size and the percentage drug entrapment whilst 0.001-0.025% of (±)-α-tocopherol increased size with no change in the percentage drug entrapment. The concentration of ibuprofen had more influence on size and the percentage drug entrapment of ibuprofen liposomes than other lipophilic components added in the liposomal preparation. The comparison of freshly prepared ibuprofen liposomes and after storage at 4°C for 1 month was found to be only two formulations with no change in size and the percentage drug entrapment. The first one was ibuprofen liposomes containing 9:1 molar ratio of soybean lecithin to cholesterol with 2.50 mole% of stearylamine and the latter was that containing 9:1 molar ratio of soybean lecithin to cholesterol with 2.50 mole% of stearylamine and 0.0125% of (±)-α-tocopherol, They were still as milky suspension. Electron microscopic analysis showed that they were unchanged spherical shapes.

ภาควิชา	เกลัชกรรม	ลายมือชื่อนิสิต	40	4
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#### LIST OF ABBREVIATIONS

ANOVA = analysis of variance

AUCs = serum concentration-time curves

°C = degree Celsius

CHEMS = cholesteryl hemisuccinate

cm = centimeter

conc. = concentration

CV = coefficient of variation

Da = Dalton

DDAB = dimethyl-dioctadecyl ammonium chloride

DMRIE = 1,2-dimyristyloxypropyl-3-dimethyl-

hydroxyethyl ammonium bromide

DNA = deoxyribonucleic acid

DOGS = dioctadecyldimethyl ammonium chloride

DOPE = dioleylphosphatidyl ethanolamine

DORIE = 1,2-dioleyloxypropyl-3-dimethyl-hydroxyethyl

ammonium bromide

DOSPA = 2,3-dioleyloxy-N-(2(spermine carboxamido)-

ethyl)-N,N-dimethyl-l-propanamonium

fluoroacetate

DOTAP = 1,2-dioleyloxy-3-(trimethylammonio) propane

DOTMA = N-{1-(2,3-dioleyloxy)propyl}-N,N,N-trimethyl

ammonium chloride

DRV = dried-reconstituted vesicles

ed. (eds) = editor

EDTA = ethylenedinitrilo tetraacetic acid

EIV = ether injection vesicles

et al = et alii, and others

FPV = french press vesicles

g = gram

g/mol = gram per mole

 $\mu g/ml$  = microgram per milliliter

GM1 = monigenic liposomes

HPI = hydrogenated phosphatidylinositol

IUV = intermediate-size unilamellar vesicles

kg = kilogram

1 = liter

l/mole = liter per mole

 $\mu l = microliter$ 

LUV = large unilamellar vesicles

mg = milligram

mg/kg = milligram per kilogram

mg/ml = milligram per milliliter

min = minute

ml = milliliter

ml/min = milliliter per minute

mm = millimeter

 $\mu m = micrometer$ 

 $\mu$ mol = micromole

 $\mu$ mol/ml = micromole per milliliter

M = molar

MEL =	micro-emulsification liposomes
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MIC = minimum inhibitory concentration

MLV = multilamellar vesicles

MVL = multivesicular liposomes

nm = nanometer

no. = number

OA = oleic acid

OLV = oligo-lamellar vesicles

PBS = phosphate buffer saline

PE = phosphatidylethanolamine

PEG-DSPE = polyethylene glycol conjugated with distearoyl

phosphatidylethanolamine

pH = the negative logarithm of the hydrogen ion

concentration

pp. = page

ppm = part per million

RES = reticuloendothelial system

REV = reverse-phase evaporation vesicles

RNA = ribonucleic acid

rpm = revolutions per minute

SD = standard deviation

SEM = scanning electron microscope

SPLV = stable plurilamellar vesicles

SUV = small unilamellar vesicles

 $T_C$  = phase transition temperature

TEM = transmission electron microscope

ULV = unilamellar vesicles

 UV
 =
 ultraviolet

 v/v
 =
 volume by volume

 w/v
 =
 weight by volume

 w/w
 =
 weight by weight

 %
 =
 percent

 <</td>
 =
 less than

 >
 =
 greater than

 ≤
 =
 less than or equal to

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