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**FORMULATION DEVELOPMENT AND EVALUATION OF
HYDROPHOBIC BASE CONTAINING HERBAL EXTRACTS FOR ORAL
ULCERS**

Mr. Chanchit Leesatjakul

**A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science in Pharmacy Program in Industrial Pharmacy**

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ชาญจิต ลิ้มจ๊ะกุล : การพัฒนาสูตรตำรับและการประเมินผลของยาพื้นไม่ชอบน้ำที่บรรจุสารสกัดจากสมุนไพรสำหรับแผลในช่องปาก (FORMULATION DEVELOPMENT AND EVALUATION OF HYDROPHOBIC BASE CONTAINING HERBAL EXTRACTS FOR ORAL ULCERS) อ. ที่ปรึกษา: รศ. ดร. ไกรสิทธิ์ อัมพรายน, 120 หน้า ISBN 974-14-2739-5

การศึกษาวิจัยนี้มุ่งหวังที่จะพัฒนา ยาพื้นไม่ชอบน้ำกับสารก่อเจลที่เหมาะสม ที่ใส่สารเมงโกสดินและหรือเอเชียทีโคไซด์สำหรับบรรเทาแผลแอฟทริส และออร์ล ลิเซน พลานัส ยาพื้นไม่ชอบน้ำที่มีลักษณะทางกายภาพที่ดี เตรียมได้จากกระบวนการหลอมเหลวของพอลิเอธิลีนพอลิเมอร์ (พีอี) และน้ำมันแร่ที่อุณหภูมิประมาณ 80 องศาเซลเซียส พบว่าพีอีพอลิเมอร์ที่อยู่ในน้ำมันแร่ตกตะกอนเป็นผลึกเล็กๆที่ล้อมรอบด้วยส่วนเส้นใยของสัณฐานซึ่งสอดคล้องกันและทำให้มีโครงสร้างคล้ายกับฟองน้ำส่งผลให้เกิดแลคทิกซสามมิติทำให้เจลเบสคงรูปร่างไว้ได้ จากการศึกษาเปอร์เซ็นต์ต่างๆของพีอีที่ใช้ พบว่าปริมาณของ พีอีที่เหมาะสมสำหรับเตรียมเป็นยาพื้นไม่ชอบน้ำ คือ ร้อยละ 4.5 จากการศึกษาทางกระแสวิทยา ที่อุณหภูมิต่างๆพบว่า ยาพื้นไม่ชอบน้ำที่มีปริมาณพีอีร้อยละ 4.5 มีพฤติกรรมการไหลเป็นแบบซูโดพลาสติก พลังงานก่อกัมมันต์ซึ่งคำนวณได้จากการดัดแปลงสมการของอาร์เรเนียสมีก่าเท่ากับ 12.45 กิโลจูล/โมล ประเมินผลเจลาคติน ชานแทน กัม เพคติน คาร์บอกซีเมธิลเซลลูโลส โซเดียม (เอสซีเอ็มซี) และ กลีโกลโคซาน ที่น้ำหนักโมเลกุลต่างๆเพื่อให้ได้สารก่อเจลที่เหมาะสมที่จะนำไปใช้กับยาพื้นไม่ชอบน้ำ สำหรับกลีโกลโคซานที่เตรียมได้จากกระบวนการพ่นแห้ง โดยใช้สภาวะการเตรียมที่เหมาะสม มีลักษณะเป็นผงละเอียดสีเหลืองและมีรูปร่างกลม ส่วนสารก่อเจลชนิดต่างๆที่ผสมกับเบสไม่ชอบน้ำ พบว่า เอสซีเอ็มซี สามารถดูดความชื้นและให้ดัชนีการพองตัวสูงกว่าสารก่อเจลชนิดอื่นๆที่ใช้ในการศึกษานี้ โกลโคซาน กลูตามेट น้ำหนักโมเลกุล 227000 ให้ค่าความทนแรงดึงหรือแรงแอคชัน สูงกว่าสารก่อเจลชนิดอื่นในขณะที่เพคตินแสดงค่าดัชนีการพองตัวสูงกว่าสารก่อเจลชนิดอื่นยกเว้นเอสซีเอ็มซี พบว่า สูตรตำรับยาทาแผลในปากที่เตรียมได้ ประกอบด้วยยาพื้นไม่ชอบน้ำ เอสซีเอ็มซี เพคติน โกลโคซาน กลูตามेट น้ำหนักโมเลกุล 227000 บิวไทเลตต์ไฮดรอกซีโทลูอิน(บีเอชที) และสารออกฤทธิ์ (เมงโกสดินหรือเอเชียทีโคไซด์) ในการศึกษาการเสื่อมสลายด้วยแสงพบว่า เปอร์เซ็นต์ของสารออกฤทธิ์ทั้งเมงโกสดินและเอเชียทีโคไซด์ในสูตรตำรับที่ใช้บีเอชทีเป็นสารต้านออกซิเดชัน มีการเปลี่ยนแปลงเพียงเล็กน้อยซึ่งอยู่ในเกณฑ์ที่ยอมรับได้ หลังจากศึกษาความคงตัวของสูตรตำรับที่อุณหภูมิ 30 องศาเซลเซียส เป็นระยะเวลา 4 เดือน พบว่าเปอร์เซ็นต์ของสารออกฤทธิ์ทั้งเมงโกสดินและเอเชียทีโคไซด์ในสูตรตำรับไม่เปลี่ยนแปลง

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CHANCHIT LEESATJAKUL: FORMULATION DEVELOPMENT AND EVALUATION OF HYDROPHOBIC BASE CONTAINING HERBAL EXTRACTS FOR ORAL ULCERS. THESIS ADVISOR: ASSOC. PROF. KRAISRI UMPRAYN, Ph.D., 120 pp. ISBN 974-14-2739-5

This research study tended to develop hydrophobic base with suitable gelling agents containing mangostin and/or asiaticoside for the relief of oral lichen planus and aphthous ulcer. Hydrophobic base with good physical appearance was prepared from melting process of polyethylene polymer (PE) and mineral oil at about 80 ° C. PE polymer in mineral oil was found to precipitate as small crystallites surrounded by long fibrous amorphous filaments which intermesh and produce a sponge-like structure resulting in a three dimensional lattice responsible for stable gel structure. Among various percentages of PE in this study, it was found that the appropriate amount of PE polymer in hydrophobic base was 4.5 percent. From rheogram at various temperatures, hydrophobic base exhibits pseudoplastic behavior. Activation energy calculated from modified Arrhenius's equation was about 12.45 kJ/mol. Gelatin, xanthan gum, pectin, sodium carboxy methyl cellulose (SCMC) and chitosan salt at various molecular weights were evaluated for suitable gelling agent in hydrophobic base. Chitosan salts prepared by spray-drying process with suitable conditions were fine yellowish powder with round shape. Among these gelling agents mixed with hydrophobic base, SCMC showed the great moisture influx and swelling index while chitosan glutamate molecular weight 227000 showed higher tensile strength or adhesion force than other gelling agents. In addition pectin showed the great value of swelling index than other gelling agents except SCMC. It was found that oral paste formula composed of base, SCMC, pectin, chitosan glutamate molecular weight 227000, butylated hydroxytoluene (BHT) and active ingredient (either mangostin or asiaticoside) was suitable. From photooxidation study the result revealed that the percent contents of both mangostin and asiaticoside in formulation using BHT as antioxidant were slightly changed with in acceptable limit. In addition, after 4 months of stability study at 30 ° C the percent contents of mangostin and asiaticoside in formulation seem to be unchanged at various storage time intervals.

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ABBREVIATIONS

ΔE	=	activation energy
$^{\circ}C$	=	degree Celsius
η	=	viscosity
CV	=	coefficient variation
e.g.	=	<i>exempli gratia</i> , 'for example'
et al.	=	<i>et alii</i> , 'and others'
FDA	=	Food and Drug Administration
g	=	gram
HPLC	=	high performance liquid chromatography
KBr	=	potassium bromide
kJ	=	kilojoule
Kn	=	kilonewton
hrs	=	hours
lm	=	lumen
mg	=	milligram
min	=	minute
ml	=	milliliter
mm	=	millimeter
mm ²	=	square millimeter
mol	=	mole
M.W.	=	molecular weight
N	=	newton
nm	=	nanometer

Pas	=	pascal
pH	=	the negative logarithm of the hydrogen ion concentration
Ph. Eur	=	European Pharmacopoeia
r^2	=	correlation of determination
RH	=	relative humidity
SD	=	standard deviation
sec	=	second
μg	=	microgram
μl	=	microliter
μm	=	micrometer
w/w	=	weight by weight