

การเตรียมตัวรับและการประเมินผลทางอินวิโทรของลิโดเคนไฮโดรคลอไรด์
ชนิดแผ่นแปะเยื่อเมือกในช่องปาก



นางสาว เรณู ทวีคุณธรรม

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วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาเภสัชศาสตรมหาบัณฑิต

สาขาวิชาเภสัชอุตสาหกรรม ภาควิชาเภสัชอุตสาหกรรม

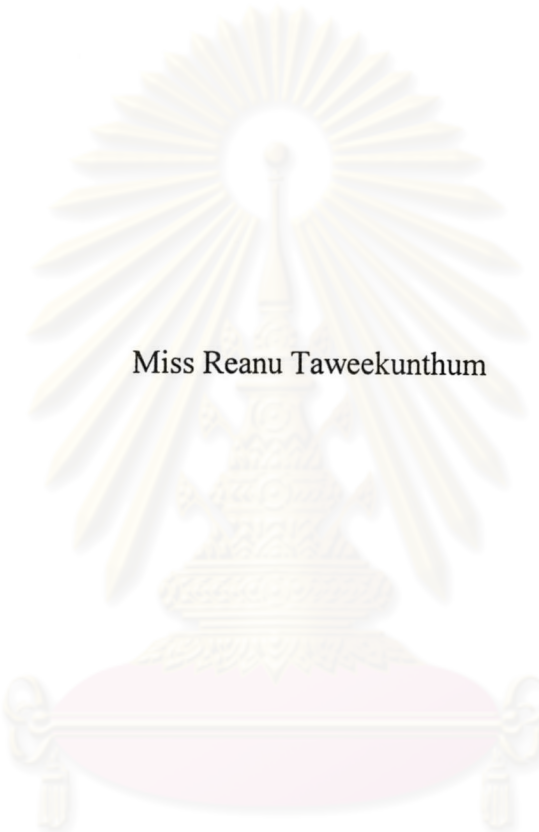
คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

ปีการศึกษา 2544

ISBN 974-03-1381-7

ลิขสิทธิ์ของจุฬาลงกรณ์มหาวิทยาลัย

PREPARATION AND IN-VITRO EVALUATION OF LIDOCAINE
HYDROCHLORIDE ORAL MUCOADHESIVE FILMS



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ศูนย์วิทยทรัพยากร
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A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science in Pharmacy

Department of Manufacturing Pharmacy

Faculty of Pharmaceutical Sciences

Chulalongkorn University

Academic Year 2001


ISBN 974-03-1381-7


Thesis Title Preparation and in-vitro evaluation of lidocaine hydrochloride
 oral mucoadhesive films
By Miss Reanu Taweekunthum
Field of Study Industrial Pharmacy
Thesis Advisor Associate Professor Garnpimol C. Ritthidej, Ph.D.

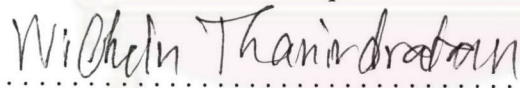
Accepted by the Faculty of Pharmaceutical Sciences, Chulalongkorn
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เรณู ทวีคุณธรรม : การเตรียมตัวรับและการประเมินผลทางอินวิโทรของลิโดเคนไฮโดรคลอไรด์ชนิดแผ่นแปะเยื่อเมือกในช่องปาก (PREPARATION AND IN-VITRO EVALUATION OF LIDOCAINE HYDROCHLORIDE ORAL MUCOADHESIVE FILMS) อ.ที่ปรึกษา : รศ.ดร.กาญจน์พิมล ฤทธิเดช, 220 หน้า. ISBN 974-03-1381-7.

วัตถุประสงค์ของงานวิจัยนี้เพื่อ เตรียมตัวรับลิโดเคนไฮโดรคลอไรด์ชนิดแผ่นแปะเยื่อเมือกในช่องปาก อันจะเป็นทางเลือกใหม่เพื่อทดแทนการบริหารยาในรูปแบบการฉีดในด้านทันตกรรม โดยแผ่นแปะนี้เตรียมจากพอลิเมอร์ที่มีคุณสมบัติในการเกาะติด ได้แก่ ไฮดรอกซีโพรพิลเมธิลเซลลูโลส อี 15 และ อี 4 เอ็ม, ไฮดรอกซีโพรพิลเซลลูโลส, โซเดียม คาร์บอกซีเมธิลเซลลูโลส, และไคโตซาน โดยใช้กรดซิตริกและเมนทอลในการปรับปรุงรสชาติ ศึกษาคุณสมบัติการเกาะติด, คุณสมบัติการยึด, ลักษณะพื้นผิว, คุณสมบัติทางเคมีกายภาพ และการปลดปล่อยยาทางอินวิโทร จากผลการทดลองพบว่า ฟิล์มที่เตรียมจากโซเดียมคาร์บอกซีเมธิลเซลลูโลสมีการตกผลึก ฟิล์มที่เตรียมจากไคโตซานมีสีเหลือง ขณะที่ฟิล์มที่เตรียมจากไฮดรอกซีโพรพิลเมธิลเซลลูโลส และไฮดรอกซีโพรพิลเซลลูโลสไม่มีสี ฟิล์มที่เตรียมได้มีความบางและความยืดหยุ่นเพียงพอที่จะแปะในช่องปากที่มีความโค้งได้ โดยไฮดรอกซีโพรพิลเมธิลเซลลูโลส อี 15 ให้ฟิล์มที่มีคุณสมบัติในการเกาะติดสูงสุด จากการประเมินคุณสมบัติทางเคมีกายภาพ พบว่าลิโดเคนไฮโดรคลอไรด์กระจายตัวอยู่ในรูปโมเลกุล หรือรูปอนุพันธ์ เมื่อเพิ่มปริมาณยาพบว่ามีความหนืดที่ฟิล์มที่เตรียมได้ จะไม่เป็นเนื้อเดียวกัน การผสมไฮดรอกซีโพรพิลเซลลูโลสเข้ากับไฮดรอกซีโพรพิลเมธิลเซลลูโลส อี 15 ให้แผ่นฟิล์มที่มีพื้นผิวไม่เรียบและมีรูพรุน ฟิล์มไฮดรอกซีโพรพิลเมธิลเซลลูโลส อี 4 เอ็ม มีความแข็งและแข็งแรงมากกว่าฟิล์มที่เตรียมจากไฮดรอกซีโพรพิลเมธิลเซลลูโลส อี 15 ฟิล์มที่เตรียมจากไคโตซานมีลักษณะแข็งและเปราะ ขณะที่ฟิล์มที่เตรียมจากไฮดรอกซีโพรพิลเซลลูโลสมีลักษณะอ่อนและเหนียว การผสมไฮดรอกซีโพรพิลเซลลูโลสเข้ากับไฮดรอกซีโพรพิลเมธิลเซลลูโลส อี 15 จะช่วยลดความแข็งของไฮดรอกซีโพรพิลเมธิลเซลลูโลสลง ร้อยละปลดปล่อยของยาจะถูกปลดปล่อยจากฟิล์มที่เตรียมจากไฮดรอกซีโพรพิลเมธิลเซลลูโลส, ไฮดรอกซีโพรพิลเซลลูโลส และส่วนผสมของไฮดรอกซีโพรพิลเมธิลเซลลูโลส อี 15 และไฮดรอกซีโพรพิลเซลลูโลสผ่านเยื่อไคอะไลซิสภายใน 60 นาที ขณะที่การปลดปล่อยยาออกจากฟิล์มที่เตรียมจากไคโตซานจะใช้เวลานานกว่านี้ จลนศาสตร์ของการปลดปล่อยยาออกจากฟิล์มที่เตรียมได้ผ่านเยื่อไคอะไลซิสเป็นไปตามแบบจำลองของวิลบูล โดยการปลดปล่อยยาผ่านเยื่อดังกล่าว ถูกควบคุมโดยกลไกการแพร่และการคลายตัวของสายพอลิเมอร์

ภาควิชา เกษัตริศาสตร์ ลายมือชื่อนิสิต 15 ก. ทวีคุณธรรม
 สาขาวิชา เกษัตริศาสตร์ ลายมือชื่ออาจารย์ที่ปรึกษา
 ปีการศึกษา 2544 ลายมือชื่ออาจารย์ที่ปรึกษาร่วม

437 66070 33 : MAJOR INDUSTRIAL PHARMACY

KEY WORD: LIDOCAINE/ MUCOADHESIVE/ FILM

REANU TAWEEKUNTHUM : PREPARATION AND IN-VITRO
EVALUATION OF LIDOCAINE HYDROCHLORIDE ORAL
MUCOADHESIVE FILMS. THESIS ADVISOR : ASSOC. PROF.
GARNPIMOL C. RITTHIDEJ, Ph.D., 220 pp. ISBN 974-03-1381-7.

The purpose of this present study was to prepare mucoadhesive film for oral mucosal administration of lidocaine HCl as a viable alternative dosage form to lidocaine HCl injection in dentistry. The mucoadhesive film was prepared using various mucoadhesive polymers, hydroxypropyl methylcellulose (HPMC) of different grades, Methocel[®] E4M and E15, hydroxypropyl cellulose (HPC), sodium carboxymethylcellulose (CMC) and chitosan. Citric acid and menthol were added in formulation to improve the taste of the obtained films. The adhesive properties, tensile properties, morphology, physicochemical properties, and in vitro release and penetration were evaluation. The results showed that the drug loading films of CMC were precipitated. Chitosan provided yellowish films while HPMCs and HPC provided clear films. The obtained films were thin and so flexible to be used along the curvature of the oral cavity. The formulations containing HPMC E15 as mucoadhesive polymer produced films with the highest mucoadhesive strength. The physicochemical characterization revealed the compatibility of ingredients in films and lidocaine HCl existed in the films as molecular dispersed or amorphous form. Increasing the drug to polymer ratios trended to obtain unhomogeneous films. Combination of HPMC E15 and HPC provided rough and porous films. HPMC E4M films were harder and stronger than HPMC E15 films. Chitosan provided hard and brittle films, while HPC provided soft and tough films. Incorporation of HPC into HPMC E15 film was to reduce the rigidity of HPMC E15 film. Eighty percent of drug penetrated from films of HPMCs, HPC and combination of HPMC E15 and HPC through dialysis membrane within 60 minutes while the release of drug from chitosan films was more sustained. The penetrations kinetic of the drug from the obtained films were the best fitted with Weibull model. The drug penetrate from obtained films through dialysis membrane was controlled by the combination of diffusion and polymer chain relaxation mechanisms.

DepartmentManufacturing Pharmacy..... Student's signature *Reanu Taweekunthum*.....
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ACKNOWLEDGEMENTS

Many people have contributed to accomplish this study of which I sincerely appreciate their advice and kind cooperation. First, I would like to express my sincere gratitude to my thesis advisor, Associate Professor Garnpimol C. Ritthidej, Ph.D., for her invaluable advice, guidance and encouragement. Her patience and kindness are also deeply appreciated.

I also wish express deep appreciation to all members of the thesis committee for their suggestions and comments.

My grateful appreciation is expressed to the Government Pharmaceutical Organization for supplying lidocaine hydrochloride.

Thanks are also due to Chulalongkorn University and the Ministry of University Affairs for granting partial financial support to fulfill this study.

I wish to thank my friends, colleagues, staffs of Department of Manufacturing Pharmacy and other person whose names have not been mentioned here for their assistance and encouragement.

Finally, I would like to express my infinite thanks and deepest gratitude to my family especially, my parents, my sisters and my brother for their care, help, understanding and encouragement.

จุฬาลงกรณ์มหาวิทยาลัย

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LIST OF ABBREVIATIONS

θ	=	theta
$^{\circ}\text{C}$	=	degree celsius
ANOVA	=	analysis of variance
CS	=	chitosan
cm	=	centimetre (s)
cm^{-1}	=	per centimetre
cm^2	=	squared centimetre (s)
CMC	=	sodium carboxymethylcellulose
CV	=	coefficient of variation
DSC	=	differential scanning calorimetry
FT-IR	=	fourier transform infrared spectrophotometry
g	=	gram (s)
h	=	hour (s)
HCl	=	hydrochloride
HPC	=	hydroxypropyl cellulose
HPLC	=	high performance liquid chromatography
HPMC	=	hydroxypropyl methylcellulose
KBr	=	potassium bromide
mcg	=	microgram (s)
mg	=	milligram (s)
mim	=	minute (s)
ml	=	millilitre (s)
mm	=	millimetre (s)
Mpa	=	megapascal (s)
N	=	Newton (s)
ng	=	nanogram (s)
R^2	=	coefficient of determination
RH	=	relative humidity
rpm	=	revolutions per minute
SD	=	standard deviation

μl	=	microlitre (s)
μv	=	microvolt
w/w	=	weight by weight



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