# การควบคุมการปลดปล่อยของนิเฟดิพีนจากตัวพาร่วมระหว่างยูดราจิตและ

# โพวิโดน เค30 เตรียมโดยเทคนิคการพ่นแห้ง

นางสาว ชุติมา สินสืบผล



วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาเภสัชศาสตรมหาบัณฑิต สาขาวิชาเภสัชกรรม ภาควิชาเภสัชกรรม คณะเภสัชศาสตร์ จูพาลงกรณ์มหาวิทยาลัย ปีการศึกษา 2542 ISBN 974-334-628-7 ถิขสิทธิ์ของ จูพาลงกรณ์มหาวิทยาลัย

# CONTROLLED RELEASE OF NIFEDIPINE FROM COMBINED CARRIERS BETWEEN EUDRAGIT AND POVIDONE K30 PREPARED BY SPRAY DRYING TECHNIQUE

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A Thesis Submitted in Partial Fulfillment of the Requirements

for the Degree of Master of Science in Pharmacy

Department of Pharmacy

Faculty of Pharmaceutical Sciences
Chulalongkorn University
Academic Year 1999

ISBN 974-334-628-7

Thesis Title Controlled release of nifedipine from combined carriers between

Eudragit and povidone K30 prepared by spray drying technique

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ชุติมา สินสิบผล: การควบคุมการปลดปล่อยของนิเฟติพีนจากตัวพาร่วมระหว่างชุดราจิตและ ไพวิโคนเค30 เตรียมโดยเทคนิคการพ่นแห้ง (CONTROLLED RELEASE OF NIFEDIPINE FROM COMBINED CARRIERS BETWEEN EUDRAGIT AND POVIDONE K30 PREPARED BY SPRAY DRYING TECHNIQUE)

อ.ที่ปรึกษา : รศ. สุชาคา ชุติมาวรพันธ์ อ.ที่ปรึกษาร่วม : รศ. คร. กาญจน์พิมถ ฤทธิเคช, 237 หน้า, ISBN 974-334-628-7

การควบคุมการปลดปล่อยของนิเฟดิพีนจากตัวพาร่วม ได้แก่ ยูคราจิตอาร์เอส 100, ยูคราจิต อาร์แอล 100 และโพวิโคนเค30 (พีวีพีเค30) สามารถเครียนได้โดยเทคนิกการพ่นแห้ง เมื่อใช้อัคราส่วน ของยาต่อตัวพาร่วมเป็น1:10 ได้เปลี่ยนแปลงปริมาณพีวีพีเค30 เพื่อให้มีอัตราส่วนผสมนิเฟดิพีน-ยูคราจิต อาร์เอส 100หรือยูคราจิต อาร์แอล 100-พีวีพีเค30เป็น1:10:0, 1:8:2, 1:5:5, 1:2:8, และ 1:0:10 ได้ศึกษา อิทธิพลของอุณหภูมิของลมเข้า, ความเข้มข้นของสารละลายที่พ่น, ชนิคและอัตราส่วนของตัวพาร่วมที่ มีต่อคุณสมบัติของผงพ่นแห้งและลักษณะการปลดปล่อยของตัวยาจากไมโครสเพียร์ที่เครียมได้ จากรูป แบบของเอกซ์เรย์ดิฟแฟรกซัน เทอร์ไมแกรมจากดิฟเฟอเรนเซียลสแกนนิงแกลอริเมครีพบผลสอดกล้อง กันว่านิเฟดิพีนในแมทริกซ์ของพอลิเมอร์เปลี่ยนแปลงจากรูปผลึกเป็นรูปอสัณฐาน จากโฟเรีย ทรานฟอร์มอินฟาเรคสเปกทราได้แสดงว่ามีปฏิกิริยาระหว่างไมเลกุลของนิเฟดิพีนและพอลิเมอร์ใน ไมโครสเพียร์ จลนศาสคร์ของการปลดปล่อยนิเฟดิพีนจากไมโครสเพียร์แสดงชัดเจนว่าเป็นกลโกการ ปลดปล่อยถูกควบคุมโดยการแพร่ตามสมการของฮิกุชิ การประเมินลักษณะการละลายของนิเฟดิพีน ไมโครสเพียร์ซึ่งใช้ค่าประสิทธิภาพการละลายและค่าคงที่อัตราการละลายของชิกุชิ พบว่าปริมาณ พีวีพีเค30 ควบคุมการปลดปล่อยตัวยาจากยูคราจิดแมทริกซ์ซึ่งไม่ละลายน้ำ การใช้อุณหภูมิของถมเจ้าต่ำ ความเข็มขึ้นของสารละลายที่พ่นสูงและยูคราจิดอาร์แอล 100ซึ่งมีความขอบน้ำมากกว่าเป็นปิจจัยเสริม ให้ประสิทธิภาพการละลายและค่าคงที่อัตราการละลายสูงขึ้น

ภาควิชาเกสัชกรรม	ลายมือชื่อนิสิครู้
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##4176562133: MAJOR PHARMACY

KEY WORD: NIFEDIPINE / SPRAY DRYING / PVP K30 / EUDRAGIT RS /

**EUDRAGIT RL/MICROSPHERES** 

CHUTIMA SINSUEBPOL: CONTROLLED RELEASE OF NIFEDIPINE FROM COMBINED CARRIERS BETWEEN EUDRAGIT AND POVIDONE K30 PREPARED

BY SPRAY DRYING TECHNIQUE.

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237 pp. ISBN 974-334-628-7

Controlled release of nifedipine from combined carriers namely, Eudragit RS 100, Eudragit RL 100 and povidone K30 were attained by spray drying technique. The drug-combined carriers ratio of 1:10 with the mixing ratios of nifedipine:Eudragit RS 100 or Eudragit RL 100:PVP K30 as 1:10:0, 1:8:2, 1:5:5, 1:2:8 and 1:0:10 were investigated. The effects of inlet air temperature, the spray concentration, types and the ratios of combined carriers on physicochemical properties of the spray dried powders and on the release characteristics of the resultant microspheres were investigated. As shown by the powder X-ray diffraction patterns, differential scanning calorimetric thermograms, nifedipine was consistently transformed from crystalline from to amorphous form in the polymer matrices. The Fourier transform infrared spectra demonstrated intermolecular interaction between nifedipine and the polymers in the microspheres. The kinetics of nifedipine release from microspheres were evidenced to follow the Higuchi diffusion-controlled mechanism. The dissolution characteristics of nifedipine microspheres were evaluated in the terms of dissolution efficiency and Higuchi rate constant. It was found that PVP K30 content controlled the drug release from Eudragit insoluble matrix. Low inlet temperature, high spray concentration and more hydrophilic Eudragit RL100 were promoting factors for higher dissolution efficiency and release rate constant.

ภาควิชาเกสัชกรรม	ถายมือชื่อนิสิครู้
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ปีการศึกษา <u>2542</u>	ลายมือชื่ออาจารย์ที่ปรึกษาร่วม

#### **ACKNOWLEDGEMENT**



The first most grateful person I would like to mention is my advisor,
Associate Professor Suchada Chutimaworapan, thanks for her advice, patience,
and understanding throughout this study.

I wish to express my gratitude to thesis co-advisor, Associate Professor Dr. Gampimol C. Ritthidej and all the members of my thesis committee for their valuable scrutinized comments and discussions. The investigation was supported in part by the Graduate School, Department of Pharmacy and the Research Fund from the Faculty of Pharmaceutical Sciences, Chulalongkorn University. Assistance and encouragement from all Faculty members in the Department of Pharmacy are also acknowledged.

I would like to give thanks to Department of Food Chemistry for the allowance to use the spray dryer and to Associate Professor Uthai Suvanakoot for the dissolution apparatus. Thanks are made to Asia Drug & Chemical Ltd., Partn., VIV Interchem Co., Ltd. Union Carbide Thailand Ltd., BASF (THAI) Ltd. and Rohm Pharma, Ltd. for their kind advice and support of chemical substances.

My deep appreciation goes to my mother, my friends and the other special person whose name has not been mentioned for helping me in anyway during the time of my study.

Above all, I would like to express my sincere thanks to my parents, without whose love this degree would not have been completed.

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สถาบันวิทยบริการ

จุฬาลงกรณ์มหาวิทยาลัย

#### LIST OF ABBREVIATIONS

ANOVA = analysis of variance

°C = Degree Celsius

cps = count per seconds

DE = dissolution efficiency

DSC = differential scanning calorimetry

GI = gastrointestinal

h = hour

IR = infrared

k = release rate constant

LSD = least significant different

mcg = microgram

mg = milligram

min = minute

ml = milliliter

μm micrometer

nm = nanometer

psi = pound per square inch

PVP K30 = Povidone K30

R<sup>2</sup> = coefficient of determination

SEM = scanning electron microscopy

UV = ultraviolet

XRD = X-ray diffraction