

การเตรียมตัวรับของ
ไดโคคลีฟแนคโซเดียม-โคโคแซนไมโครสเฟียร์ และยาเม็ดเมทริกซ์
ด้วยเทคนิคการพ่นแห้ง และ เทคนิคการเตรียมเพลเลท

นายทวีศักดิ์ กมลศิริพิชัยพร

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาเภสัชศาสตรมหาบัณฑิต
สาขาวิชาเภสัชอุตสาหกรรม ภาควิชาเภสัชอุตสาหกรรม
บัณฑิตวิทยาลัย จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2541
ISBN 974-639-901-2
ลิขสิทธิ์ของบัณฑิตวิทยาลัย จุฬาลงกรณ์มหาวิทยาลัย

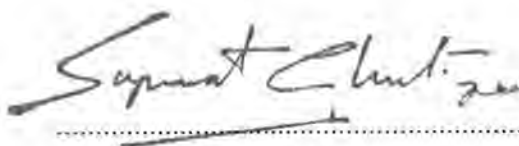
PREPARATION OF DICLOFENAC SODIUM-CHITOSAN MICROSPHERES
AND THEIR MATRIX TABLETS BY SPRAY DRYING AND PELLETIZATION
TECHNIQUES

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A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Sciences in Pharmacy
Department of Manufacturing Pharmacy
Graduate School
Chulalongkorn University
Academic Year 1998
ISBN 974-639-901-2

Thesis Titles Preparation of Diclofenac Sodium-Chitosan Microspheres and
 Their Matrix Tablets by Spray Drying and Pelletization Techniques
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Accepted by the Graduate School, Chulalongkorn University in Partial
Fulfillment of the Requirements for the Master's Degree.



.....Dean of Graduate School

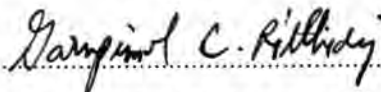
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ทวิศักดิ์ กมลศิริพิชัยพร : การเตรียมตัวรับของไดโคลฟีแนคโซเดียม-โคโตแซนไมโครสเฟียร์ และยาเม็ดเมทริกซ์ ด้วยเทคนิคการพ่นแห้ง และเทคนิคการเตรียมเพลเลต (PREPARATION OF DICLOFENAC SODIUM-CHITOSAN MICROSPHERES AND THEIR MATRIX TABLETS BY SPRAY DRYING AND PELLETIZATION TECHNIQUES) อ.ที่ปรึกษา : รศ.ดร. กาญจนพิมพ์ล ฤทธิเดช, 227 หน้า. ISBN 974-639-901-2.

ไดโคลฟีแนคโซเดียมไมโครสเฟียร์ ชนิดควบคุมการปลดปล่อยตัวยา เตรียมขึ้นด้วยเทคนิคการพ่นแห้ง ที่ใช้โคโตแซนที่มีความหนืดแตกต่างกัน 2 ชนิด มีการเลือกใช้โพรพีลีนไกลคอล และกลีเซอริน เพื่อปรับปรุงคุณสมบัติของไมโครแคปซูลที่ได้จากเทคนิคการพ่นแห้ง นอกจากนี้ยังมีการนำเทคนิคเอกทูรชันสเฟียร์โรโนซ์เซชัน มาใช้ในการเตรียมเพลเลตของไดโคลฟีแนคโซเดียมอีกด้วย

อินฟราเรดสเปกตรัมแสดงให้เห็นว่า ไม่เกิดปฏิกิริยาระหว่างตัวยา, โพลีเมอร์ และพลาสติกไซเซอร์ ความเข้มของพีคที่ลดลง ร่วมกับเส้นฐานที่สูงขึ้นของเอ็กซ์เรย์ดิฟแฟรคชัน และการเปลี่ยนตำแหน่งของเอกโซเทอร์มิก และเอนโดเทอร์มิกพีคของดีเอสซีเทอร์โมแกรม ของไมโครสเฟียร์ที่เตรียมได้ แสดงผลให้ทราบว่า มีตัวยาในรูปแบบอสัณฐาน หรือพหุสัณฐานอื่นๆเกิดขึ้น

คุณสมบัติทางกายภาพ และทางเคมีของผงที่ได้จากการพ่นแห้งขึ้นอยู่กับชนิด และปริมาณของโพลีเมอร์ และพลาสติกไซเซอร์ ไมโครแคปซูลที่สมบูรณ์สามารถเตรียมขึ้นได้ โดยการใช้ปริมาณของโพลีเมอร์ที่เหมาะสม ร่วมกับพลาสติกไซเซอร์ แต่ไม่มีสูตรตัวรับใดที่สามารถแสดงการปลดปล่อยตัวยาได้ตามต้องการ การดองอัดผงที่ได้จากการพ่นแห้งให้เป็นยาเม็ดเมทริกซ์ เป็นวิธีที่มีประสิทธิภาพสูงในการยืดระยะเวลาในการปลดปล่อยตัวยาให้ช้าลง สูตรตัวรับที่ดีที่สุดสามารถปลดปล่อยตัวยาได้เพียง 60 เปอร์เซ็นต์ เมื่อสิ้นสุดชั่วโมงที่ 24 การปลดปล่อยตัวยาจะเพิ่มขึ้น เมื่อปริมาณของโพลีเมอร์ลดลง และปริมาณของพลาสติกไซเซอร์เพิ่มขึ้น ในขณะที่โพลีเมอร์แสดงอิทธิพลในการปลดปล่อยตัวยาได้มากกว่าพลาสติกไซเซอร์ โพรพีลีนไกลคอลมีแนวโน้มที่จะเร่งการปลดปล่อยตัวยา ในขณะที่กลีเซอรินกลับแสดงผลในทางตรงข้าม จากการศึกษาเกี่ยวกับการเตรียมเพลเลต พบว่าสามารถเตรียมเพลเลตที่ประกอบด้วยไมโครคริสตัลลินเซลลูโลส และไมโครคริสตัลลินเซลลูโลสกับแลกโตสขึ้นได้ ปัจจัยที่มีผลต่อคุณสมบัติทางกายภาพและทางเคมี และลักษณะการละลายของตัวยา ได้แก่ ชนิด และปริมาณของสารช่วยในการเตรียมเพลเลต และโพลีเมอร์ ในขณะที่สภาวะในการเตรียมเพลเลต มีอิทธิพลต่อเรื่องดังกล่าวอย่างน้อยมาก การปลดปล่อยตัวยาไดโคลฟีแนคโซเดียมจากทุกสูตรตัวรับที่เตรียมได้ ขึ้นอยู่กับสภาพแวดล้อมที่เป็นกรดและด่าง ประสิทธิภาพในการยืดระยะเวลาในการปลดปล่อยตัวยาจากผงที่ได้จากการพ่นแห้ง, ยาเม็ดเมทริกซ์ และเมทริกซ์เพลเลตนั้นแตกต่างกัน และไม่สามารถเทียบเคียงกันได้

ภาควิชาเภสัชอุตสาหกรรม.....
สาขาวิชาเภสัชอุตสาหกรรม.....
ปีการศึกษา2541.....

ลายมือชื่อนิติกร ทวิศักดิ์ กมลศิริพิชัยพร
ลายมือชื่ออาจารย์ที่ปรึกษา
ลายมือชื่ออาจารย์ที่ปรึกษาพร้อม


#3970617433 : MAJOR MANUFACTURING PHARMACY

KEY WORD: DICLOFENAC SODIUM / CHITOSAN / MICROSPHERES / MATRIX TABLET /
SPRAY DRYING / PELLETIZATION

TAVEESAK KAMOLSIRIPICHAIPORN : PREPARATION OF DICLOFENAC SODIUM-
CHITOSAN MICROSPHERES AND THEIR MATRIX TABLETS BY SPRAY
DRYING AND PELLETIZATION TECHNIQUES. THESIS ADVISOR : ASSO. PROF.
GARNPIMOL C. RITTHIDEJ, Ph.D., 227 pp. ISBN 974-639-901-2.

Diclofenac sodium (DS) controlled release microspheres were prepared by spray drying technique using two different viscosity grades of chitosan. Propylene glycol (PG) and glycerin were chosen for improving the properties of the microcapsules. Extrusion-spheronization technique was also used to prepare matrix pellets of DS.

The IR spectra revealed no interaction between drug, polymers and plasticizers. The lower intensity with higher baseline of X-ray diffractograms and the shifts in exothermic and endothermic peaks of DSC thermograms of the obtained microspheres indicated an occurrence of amorphous form or other polymorphs.

The physicochemical properties of spray dried powders depended on the type and amount of polymers and plasticizers. The complete microcapsules were produced by proper amount of the polymer used with the aid of plasticizer, but no formulation had capability to present satisfactory drug release. Compression of spray dried powders into matrix tablets was very effective for delayed release system. The best formulation achieved about 60% drug released at the 24th hour. The release characteristic was increased with an decrease in the amount of polymers and an increase in amount of plasticizers, while the polymers exhibited stronger effect than plasticizers. PG tended to increase the drug release, whereas glycerin played the opposite role. Study on pelletization suggested that pellets containing microcrystalline cellulose and microcrystalline cellulose with lactose could be produced. Parameters affected the physicochemical properties and dissolution characteristics were type and amount of pelletization aids and polymer, whereas pelletization conditions showed very weak influence. The release characteristics of DS from all formulations were dependent on environmental pH. The efficiency in delay drug released from spray dried powders, matrix tablets and matrix pellets were different and incomparable.

ภาควิชา.....เภสัชอุตสาหกรรม

สาขาวิชา.....เภสัชอุตสาหกรรม

ปีการศึกษา.....2541

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ACKNOWLEDGMENTS

I would like to express my genuine thankfulness to my thesis advisor, Associate Professor Garmpimol C. Ritthidej, Ph.D. for her creative knowledge, encouragement and support throughout this work. Her kindness and helpfulness are really appreciated.

My special thanks send to Professor Kenji Yamamoto Ph.D. and Associate Professor Toshio Oguchi Ph.D., Pharmaceutical Technology Department, Faculty of Pharmaceutical Sciences, Chiba University for their helpfulness and support for special technology in this study. The other special thank go to Mr. Paisan Setsuwan Ph.D., National Metal and Material Technology Center (MTEC), Ministry of Science, Technology and Environment, Thailand for supporting in X-ray diffractometry evaluations and good advises.

I would like to express my thankfulness to Associate Professor Poj Kulvanich Ph.D., Ajarn Pienkit Dangprasirt Ph.D. and Ajarn Narueporn Sutantaviboon Ph.D. for spending their valuable time to be my thesis committee and for their good advises and suggestions.

A special appreciation is expressed to Chulalongkorn University for granting partial financial support to fulfill this investigation and being my special place for learning knowledge and life. A special thankfulness is also given to all staffs and members in the Department of Manufacturing Pharmacy and my friends those who help in the early days for their kind assistance and encouragement.

Extra special thanks to my family for their immeasurable love and encouragement. I am grateful for all your supports.

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LIST OF ABBREVIATIONS

bar	kg/cm ²
°C	degree celcius (centrigrade)
cGMP	current Good Manufacturing Practices
cm	centrimeter (s)
cm ³	centimeter cube (s)
cps	cycle per second
CS	chitosan
DS	diclofenac sodium
DSC	differential scanning calorimetry
DTA	differential thermal analysis
e.g.	exempli gratia, for example
et al.	et alli, and others
g	gram (s)
hr	hour (s)
HCl	hydrochloric acid or hydrochloride salt
IR	infrared
JP	The Japanese Pharmacopoeia
kg	kilogram (s)
kp	kilopound (s)
M	molarity
MFT	minimum film-forming temperature
mg	milligram (s)
min	minute (s)
ml	milliliter (s)
mm	milimeter (s)
mPa s	millipascal (s)

N	normality
NaOH	sodium hydroxide
nm	nanometer (s)
No.	number
P	pascal (s)
PDR	Physician's Desk Reference
PEG	polyethylene glycol
PG	propylene glycol
pH	the negative logarithm of the hydrogen ion concentration
pKa	the negative logarithm of the dissociation constant
q.s.	make to volume
RT	room temperature
rpm	revolution per minute
SD	standard deviation
SEM	scanning electron microscopy
sp.gr.	specific gravity
T _g	glass transition temperature
TG	thermal gravimetry
USP	The United States Pharmacopoeia
UV	ultraviolet
w/v	weight by volume
w/w	weight by weight
μg	microgram (s)
%	percentage
°	degree