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DEVELOPMENT OF CONTROLLED RELEASE
DICLOFENAC SODIUM BY SPRAY DRYING
WITH ACRYLATE AQUEOUS DISPERSION

Miss Anothai Tangsumranjit

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

Department of Manufacturing Pharmacy

Graduate School

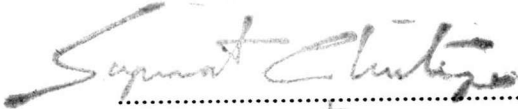
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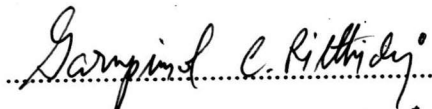
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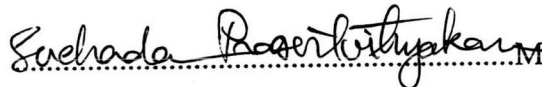
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อโนทัย ตั้งสำราญจิต : การพัฒนาตัวรับควบคุมการปลดปล่อยไดโคลฟีแนคโซเดียม โดยใช้เทคนิคการพ่นแห้งร่วมกับอะครีเลตชนิดกระจายตัวในน้ำ (DEVELOPMENT OF CONTROLLED RELEASE DICLOFENAC SODIUM BY SPRAY DRYING WITH ACRYLATE AQUEOUS DISPERSION) อ. ที่ปรึกษา : รศ. ดร. กาญจน์พิมล ฤทธิเดช, 148 หน้า. ISBN 974-637-114-2

การเตรียมไดโคลฟีแนคโซเดียมไมโครสเฟียร์โดยเทคนิคการพ่นแห้ง โดยใช้อะครีเลตชนิดกระจายตัวในน้ำ (ยูคราจิต เอ็น อี 30ดี, ยูคราจิต อาร์ แอล 30ดี และ ยูคราจิต อาร์ เอส 30ดี) เพื่อควบคุมการปลดปล่อยด้วยจากไมโครสเฟียร์ คอลลอยด์คอลล ซิลิกา (แอโรซิล) เป็นสารลดการยึดเกาะเดิมลงไปประมาณ 30% ของน้ำหนักโพลีเมอร์ ทำการศึกษาถึงผลของตัวแปรในกระบวนการ คืออุณหภูมิของลมเข้า โดยปรับเปลี่ยนในช่วง 150 ถึง 210 องศาเซลเซียส และปริมาณของ โพลีเมอร์ที่ใช้ตั้งแต่ 5 ถึง 20% ต่อคุณสมบัติทางเคมีฟิสิกส์ของผงพ่นแห้งที่ได้ รวมทั้งศึกษาลักษณะการปลดปล่อยด้วยจากไมโครสเฟียร์ในระบบที่มีการเปลี่ยนแปลงพีเอช และในระบบฟอสเฟตบัฟเฟอร์ที่มีพีเอช 6.8 ภายถ่ายจากกล้องจุลทรรศน์อิเล็กตรอนแสดงให้เห็นว่าขนาดของผงพ่นแห้งขึ้นอยู่กับทั้งอุณหภูมิของลมเข้าและปริมาณของโพลีเมอร์ แต่รูปร่างของผงพ่นแห้งจะขึ้นอยู่กับอุณหภูมิของลมเข้าเท่านั้น พบว่าขนาดของผงพ่นแห้งมีแนวโน้มที่จะใหญ่ขึ้นและรูปร่างจะกลมขึ้นเมื่ออุณหภูมิของลมเข้าเพิ่มขึ้น ขณะที่อุณหภูมิของลมเข้าต่ำๆ ดูเหมือนว่าขนาดของผงพ่นแห้งจะใหญ่ขึ้นถ้าลดปริมาณของ โพลีเมอร์ แต่ที่อุณหภูมิของลมเข้าสูงๆผลที่ได้จะกลับกัน ซึ่งสอดคล้องกับผลจากการวิเคราะห์หาพื้นที่ผิวเฉพาะและปริมาตรของช่องว่าง เอ็กซ์เรย์ดิฟแฟรคโตแกรมจะมีความเข้มของพีคลดลงและฐานของพีคสูงขึ้น เอนโดเทอร์มิกพีค และเอ็กซ์โซเทอร์มิกพีคในดีเอสซีเทอร์โมแกรมก็เกิดขึ้นในตำแหน่งที่อุณหภูมิต่ำลง แสดงให้เห็นว่าการเปลี่ยนแปลงรูปแบบของผลึกยาเพิ่มขึ้นเมื่อเพิ่มอุณหภูมิของลมเข้า อินฟราเรดสเปกตรัมแสดงให้เห็นว่าไม่เกิดการทำปฏิกิริยาระหว่างยาและโพลีเมอร์ การปลดปล่อยด้วยจากไมโครสเฟียร์ขึ้นกับตัวกลางในการทดสอบ ในระบบฟอสเฟตบัฟเฟอร์พีเอช 6.8 ยาถูกปลดปล่อยออกมาเร็วกว่าในระบบที่มีการเปลี่ยนแปลงพีเอช การปลดปล่อยด้วยจากจะลดลงเมื่อปริมาณของโพลีเมอร์เพิ่มขึ้น และอุณหภูมิของลมเข้าลดลง ไมโครสเฟียร์ที่เตรียมโดยใช้ ยูคราจิต เอ็น อี 30ดี จะให้เส้นกราฟที่ตรงกว่าการใช้ยูคราจิตชนิดอื่นๆ ในระบบที่มีการเปลี่ยนแปลงพีเอชยาจะค่อยๆ ละลายออกมาจนถึง 24 ชั่วโมง คล้ายกับผลิตภัณฑ์ที่มีจำหน่ายในท้องตลาด

ภาควิชาเภสัชอุตสาหกรรม
สาขาวิชาเภสัชอุตสาหกรรม
ปีการศึกษา 2540

ลายมือชื่อนิติ อโนทัย ตั้งสำราญจิต
ลายมือชื่ออาจารย์ที่ปรึกษา
ลายมือชื่ออาจารย์ที่ปรึกษาร่วม

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KEY WORD: DICLOFENAC SODIUM / ACRYLATE AQUEOUS DISPERSION / SPRAY DRYING
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ANOTHAI TANGSUMRANJIT : DEVELOPMENT OF CONTROLLED RELEASE
DICLOFENAC SODIUM BY SPRAY DRYING WITH ACRYLATE AQUEOUS
DISPERSION. THESIS ADVISOR : ASSO. PROF. GARNPIMOL C. RITTHIDEJ, Ph.D.
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Diclofenac sodium microspheres were prepared by spray drying technique. Acrylate aqueous dispersions (Eudragit[®] NE 30D, Eudragit[®] RL 30D and Eudragit[®] RS 30D) were used to control the release of drug from microspheres. Colloidal silica (Aerosil[®]) of 30% w/w of polymer was added as an antiadherent agent. The influence of processing variables, inlet air temperature of 150 to 210°C and the amount of polymer varied from 5 to 20% on the physicochemical properties of spray dried powders were studied. The release characteristics of drug from the obtained microspheres were performed in both pH-change and phosphate buffer pH 6.8 systems. The scanning electron photomicrographs showed that the size of spray dried powders was affected by both the inlet temperature and the amount of polymer but the shape was only by the former. The powders tended to be larger and more spherical when increasing the inlet temperature. At lower inlet temperatures, the size seemed to be larger when decreasing the amount of polymer. The results were reversed at higher inlet temperature. These were corresponding to their specific surface area and total pore volume. The X-ray diffractograms and DSC thermograms of the obtained microspheres showed lower intensity with higher baseline and lower endothermic and exothermic peaks, respectively, indicating of an increment of amorphous form when increasing the inlet temperature. The IR spectra revealed no interaction between drug and polymer. The release of drug from microspheres was strongly medium dependent. It was much faster in phosphate buffer pH 6.8 than in pH-change system. Increasing the amount of polymer or decreasing the inlet temperature decreased the release of drug. The release profile of drug from Eudragit[®] NE 30D microspheres was more linear than from other grades of the polymer. Moreover, the drug could be sustained release throughout 24 hours in the pH-change medium, comparable to commercial products.

ภาควิชา.....เภสัชอุตสาหกรรม
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ABBREVIATIONS

bar	kg/cm ²
°C	degree celsius
cm	centimeter
DS	diclofenac sodium
DSC	differential scanning calorimetry
g	gram
hr	hour
IR	infrared
kg	kilogram
L	liter
min	minute
mg	milligram
ml	milliliter
N	normal
nm	nanometer
q.s.	make to volume
r ²	coefficient of determination
rpm	revolution per minute
RT	room temperature
SD	standard deviation
SEM	scanning electron microscopy
UV	ultraviolet
w/w	weight by weight
µm	micrometer