

ผลของตัวแปรในกระบวนการผลิตและสูตรตำรับต่อการเกิด
เพลเลตไดโคลฟีแนคโซเดียมที่เตรียมโดยเทคนิคการหลอม



นางสาวสุนทรียา รงรองเมือง

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต

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EFFECT OF PROCESS AND FORMULATION VARIABLES
ON FORMATION OF DICLOFENAC SODIUM PELLETS
PREPARED BY MELT TECHNIQUE

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สุนทรียา รวงรวงเมือง : ผลของตัวแปรในกระบวนการผลิตและสูตรตำรับต่อการเกิดเพลเล็ตไดโคลฟีแนคโซเดียมที่เตรียมโดยเทคนิคการหลอม (EFFECT OF PROCESS AND FORMULATION VARIABLES ON FORMATION OF DICLOFENAC SODIUM PELLETS PREPARED BY MELT TECHNIQUE.) อ.ที่ปรึกษา : อ.ดร.จิตติมา ชัชวาลย์สายสินธ์, อ.ที่ปรึกษาร่วม : ผศ.วิเชียร ธานินทร์ธรราร, 186 หน้า. ISBN 974-17-5006-4.

การวิจัยนี้เป็นการศึกษาการผลิตเพลเล็ตโดยเทคนิคการหลอม โดยใช้เครื่องผสมแบบแพลเนทารีซึ่งมีอุปกรณ์หุ้มให้ความร้อนและควบคุมอุณหภูมิ การศึกษาผลของตัวแปรในกระบวนการผลิตและสูตรตำรับต่อการเกิดเพลเล็ตไดโคลฟีแนคโซเดียม ทำโดยใช้กลีเซอรอลโมโนสเตียเรตเป็นสารยึดเกาะ และออกแบบการทดลองแบบแฟคทอเรียล โดยเปลี่ยนแปลงความเร็วของใบพัด (100 รอบ และ 200 รอบ) อุณหภูมิที่ใช้ในการผสม (58 องศาเซลเซียส และ 78 องศาเซลเซียส) เวลาที่ใช้ในการผสม (5 นาที และ 15 นาที) และสารเพิ่มปริมาณ (แลกโทส และ ไดเบสิดแคลเซียมฟอสเฟต) นอกจากนี้การศึกษามลของจุดหลอมเหลวและความหนืดของสารยึดเกาะ ทำโดยการเตรียมเพลเล็ตไดโคลฟีแนคโซเดียมที่มีแลกโทสเป็นสารเพิ่มปริมาณ และกลีเซอรอลโมโนสเตียเรต Precirol® AT05 Compritol 888 ATO® Gelucire 50/02 หรือ Tristearin® เป็นสารยึดเกาะ

ผลการวิจัยพบว่า ปริมาณของสารยึดเกาะที่ใช้ในการเตรียมเพลเล็ตขึ้นกับชนิดของสารยึดเกาะและชนิดของสารเพิ่มปริมาณที่ใช้ ความเร็วของใบพัดและชนิดของสารเพิ่มปริมาณเป็นตัวแปรสำคัญที่มีผลต่อการเปลี่ยนแปลงคุณสมบัติทางกายภาพของเพลเล็ต เมื่อความเร็วที่ใช้ในการผสมเพิ่มขึ้นทำให้เพลเล็ตมีขนาดโตขึ้นและการกระจายของขนาดแคบ เพลเล็ตที่เตรียมโดยใช้ไดเบสิดแคลเซียมฟอสเฟตมีผิวเรียบและกลมกว่าเพลเล็ตที่เตรียมจากแลกโทส ความหนาแน่นจริงของเพลเล็ตขึ้นกับความหนาแน่นจริงของสารเพิ่มปริมาณที่นำมาใช้เตรียม สารยึดเกาะที่มีจุดหลอมเหลวต่ำทำให้เพลเล็ตที่กลมกว่า สารยึดเกาะที่มีความหนืดต่ำทำให้เพลเล็ตที่มีการกระจายของขนาดแคบ เพลเล็ตที่เตรียมได้จากการวิจัยนี้พบว่าการไหลที่ดี ปริมาณตัวยาสสำคัญของเพลเล็ตที่เตรียมจากแลกโทสผ่านมาตรฐานตำรายาประเทศสหรัฐอเมริกา 27 และพบว่ามี ความคงสภาพภายหลังการเก็บในสภาวะเร่งที่ 45 องศาเซลเซียส ความชื้นสัมพัทธ์ 75 เปอร์เซ็นต์เป็นเวลา 4 เดือน เพลเล็ตที่เตรียมจากไดเบสิดแคลเซียมฟอสเฟตอาจเกิดการเสื่อมสลายของตัวยาสสำคัญ แต่ตรวจวิเคราะห์ไม่พบ diclofenac related compound A เพลเล็ตส่วนใหญ่มีการปลดปล่อยยานอกร่างกายมากกว่า 80 เปอร์เซ็นต์ ผลการวิจัยนี้พิสูจน์ว่าตัวแปรของกระบวนการและสูตรตำรับมีผลต่อคุณภาพของเพลเล็ตที่เตรียมโดยเครื่องผสมแบบแพลเนทารี

ภาควิชา.....เภสัชอุตสาหกรรม.....ลายมือชื่อนิสิต.....สุนทรียา รวงรวงเมือง
สาขาวิชา.....เภสัชอุตสาหกรรม.....ลายมือชื่ออาจารย์ที่ปรึกษา.....จิตติมา ชัชวาลย์สายสินธ์
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KEY WORD : DICLOFENAC SODIUM / PELLETS / MELT TECHNIQUE / PELLETTIZATION / GLYCERYL MONOSTEARATE

SOONTHARIYA RONGRONGMUANG : EFFECT OF PROCESS AND FORMULATION VARIABLES ON FORMATION OF DICLOFENAC SODIUM PELLETS PREPARED BY MELT TECHNIQUE. THESIS ADVISOR : JITTIMA CHATCHAWALSAISIN, Ph.D., THESIS CO-ADVISOR : ASST. PROF. WICHEIN THANINDRATRAN, M.Sc.in Pharm., 186 pp. ISBN 974-17-5006-4.

A melt pelletization process was investigated in a planetary mixer with heat from heating jacket. The effect of process variables, i.e. mixing speed (100 rpm and 200 rpm), temperature (58°C and 78°C) and time (5 min and 15 min), and formulation variable, i.e. types of filler (lactose and dibasic calcium phosphate), on formation of diclofenac sodium pellets, were investigated by mean of factorially designed experiments using glyceryl monostearate as a binder. The effect of binder melting point and viscosity was also investigated through the formulation containing lactose and glyceryl monostearate, Precirol® ATO5, Compritol 888 ATO®, Gelucire 50/02 or Tristearin®.

The amounts of binder required to form pellets were dependent on types of binders and fillers. Mixing speed and types of filler were the most important variables affecting the physical properties of pellets. Increased mixing speed produced larger pellets with narrow size distribution. Pellets with dibasic calcium phosphate were smoother and rounder than pellets with lactose. True density of pellets depended on true density of filler. The binder of lower melting point gave rounder pellets. The binder of lower viscosity produced narrow size distribution of pellets. All the pellets possessed good flowability. Drug content of pellets prepared with lactose complied with USP 27 and the pellets were stable after storage at 45°C and 75% relative humidity for 4 months. Drug degradation could occur in pellets prepared with dibasic calcium phosphate. However, diclofenac related compound A was not presented. The 80 % drug release was obtained for most formulations. The results obtained from this study proved that the process and formulation variables affecting quality of pellets prepared by planetary mixer.

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LIST OF ABBREVIATIONS

%	percentage
#	number
µg	microgram (s)
µm	micrometer
°	degree
° C	degree celcius (centigrade)
CA	dibasic calcium phosphate formulation
CP	Compritol formulation
DS	diclofenac sodium
dbcp	dibasic calcium phosphate
d _g	geometric weight mean
g	gram (s)
GMS	glyceryl monostearate
GL	Gelucire50/02 formulation
HCl	hydrochloric acid
hr	hour (s)
IR	infrared
LA	lactose formulation
mg	milligram (s)
min	minute (s)
ml	milliliter (s)
MP	melting point
mPa.s	millipascal.second
PEGs	polyethylene glycols
pH	the negative logarithm of the hydrogen ion concentration
PR	Precirol formulation
q.s.	make to volume
rpm	round per minute

RSD	relative standard deviation
sec.	second
s_g	geometric standard deviation
SEM	scanning electron microscopy
TS	Tristearin formulation
UV	ultraviolet