# การใช้แป้งโซเดียมคาร์บอกซีเมทิล เป็นสารช่วยเอ๊กซ์ทรูชันในการผลิตเพลเลต โดย กระบวนการเอ๊กซ์ทรูชันและสเฟียโรไนเซชัน

นางสาว สุพัตรา นิยมธรรมกิจ



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# USE OF SODIUM CARBOXYMETHYL STARCH AS EXTRUSION AID IN THE PRODUCTION OF PELLET BY EXTRUSION AND SPHERONIZATION PROCESS

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Thesis Title Use of Sodium Carboxymethyl Starch as Extrusion Aid in the Production of Pellet by Extrusion and Spheronization **Process** By Miss Supattra Niyomthamakit Department Manufacturing Pharmacy Thesis Advisor Associate Professor Poj Kulvanich, Ph.D. Thesis Co-advisor Assistant Professor Wichein Thanindratarn Accepted by the Graduate School, Chulalongkorn University in Partial Fulfillment of the Requirements for the Master's Degree. .....Dean of Graduate School (Professor Supawat Chutivongse, M.D.) Thesis Commitee Gampinol C Killing Chairman (Associate Professor Garnpimol C. Ritthidej, Ph.D.) P. Kolvanil Thesis Advisor (Associate Professor Poj Kulvanich , Ph.D.) W. Thanindraharn Thesis Co-advisor (Assistant Professor Wichein Thanindratarn, M.Sc.) Breeya Atriyanan Member (Associate Professor Preeya Atmiyanan , Docteur en Pharmacie)

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#### พิมพ์ตับฉบับบทคัดย่อวิทยานิพนธ์ภายในกรอบสีเขียวนี้เพียงแผ่นเดียว

สุพัตรา นิยมธรรมกิจ : การใช้แป้งโชเดียมคาร์บอกซีเมทิล เป็นสารช่วยเอ๊กซ์ทรูซันในการผลิตเพลเลต โดยกระบวนการเอ๊กซ์ทรูซันและสเพียโรในเซซัน (USE OF SODIUM CARBOXYMETHYL STARCH AS EXTRUSION AID IN THE PRODUCTION OF PELLET BY EXTRUSION AND SPHERONIZATION PROCESS.) อ.ที่ปรึกษา : รศ.ดร. พจน์ กุลวานิช, อ.ที่ปรึกษาร่วม : ผศ. วิเซียร ธานินทร์ธราธาร, 291 หน้า, ISBN 974-638-858-4

การวิจัยนี้ได้ทำการดัดแปรแป้งข้าวเหนียวที่ได้จากธรรมชาติด้วยปฏิกริยาแทนที่ทางเคมี เพื่อให้ได้แป้ง โซเดียมคาร์บอกซีเมทิลที่มีระดับการแทนที่อยู่ในช่วงที่เหมาะสมแตกต่างกัน 3 ระดับ เพื่อนำมาประเมินคุณสมบัติในการ ใช้เป็นสารช่วยในการผลิตเพลเลตด้วยเทคนิดเอ๊กซ์ทรูชัน/สเฟียโรในเซชัน ได้ศึกษาคุณสมบัติทางกายภาพของเพลเลต ที่เตรียมขึ้นโดยใช้สารตั้งดันหลักแตกต่างกัน 3 ชนิดคือ ซูโครส แลคโตส และไดแคลเซียมฟอสเฟต ได้ไฮเดรต ร่วมกับ แป้งโซเดียมคาร์บอกซีเมทิล เปรียบเทียบกับเพลเลตที่ไม่มีแป้งดัดแปรนี้เป็นส่วนประกอบ จากผลการทดลองพบว่า ใน สูตรตำรับเพลเลตที่ใช้ซูโครสมีลักษณะเป็นแท่งไม่เป็นอนุภาคทรงกลม ในสูตรตำรับเพลเลตของแลคโตสและไดแคลเซียม ฟอสเฟตที่ใช้แป้งดัดแปรเป็นส่วนประกอบมีคุณสมบัติของเพลเลตดีขึ้นกว่าสูตรตำรับเพลเลตที่ไม่ใช้แป้งดัดแปร และ พบว่าการใช้แป้งดัดแปรในสูตรตำรับทำให้การใช้ไมโครดริสตัลไลน์ เซลลูโลส ซึ่งมักใช้เป็นสารช่วยในการทำเพลเลตมี ปริมาณที่ใช้ต่ำลง เพลเลตซึ่งเตรียมโดยใช้แป้งดัดแปรร่วมด้วยนี้จะมีขนาดอนุภาคเฉลี่ยใหญ่ขึ้น ความแข็งและความกลม มากขึ้น มีการเกาะกลุ่มกันระหว่างอนุภาคลดลงและมีพื้นผิวที่เรียบกว่าเพลเลตที่ไม่มีแป้งดัดแปร

ระดับการแทนที่ของแป้งดัดแปรที่แตกต่างกันไม่มีอิทธิพลที่มีนัยสำคัญต่อคุณสมบัติทางกายภาพโดยทั่วไป ของเพลเลต แต่มีผลที่สำคัญต่อความแข็งและลักษณะพื้นผิว พบว่าเพลเลตของแลคโตสซึ่งประกอบด้วยแป้งดัดแปรที่มี ระดับการแทนที่ 0.26 จะมีความแข็งสูงสุด ขณะที่เพลเลตของไดแคลเซียมฟอสเฟตจะมีความแข็งมากที่สุดเมื่อใช้แป้ง ดัดแปรที่มีระดับการแทนที่ 0.16 และ 0.32 นอกจากนี้การใช้แป้งดัดแปรที่มีระดับการแทนที่ 0.16 ในสูตรตำรับของ โดแคลเซียมฟอสเฟต จะทำให้เกิดเพลเลตที่มีลักษณะพื้นผิวเรียบกว่าการใช้แป้งดัดแปรซึ่งมีระดับการแทนที่อื่น ๆ พบว่าปริมาณน้ำมีอิทธิพลที่สำคัญในกระบวนการเอ๊กซ์ทรูซันและสเฟียโรไนเซชัน ปริมาณน้ำที่เพิ่มขึ้นจะทำให้เกิด เพลเลตที่มีขนาดใหญ่ขึ้น ความแข็งและความกลมเพิ่มขึ้น แต่ให้ลักษณะพื้นผิวที่ขรุขระมากขึ้น เมื่อปริมาณแป้งดัดแปรที่ ใช้ในสูตรตำรับเพิ่มขึ้นจาก 0.3% ถึง 0.8% โดยน้ำหนัก จะทำให้คุณสมบัติบางประการของเพลเลตดีขึ้นกล่าวคือ ความแข็งและความเรียบของพื้นผิวมากขึ้น ผลจากการศึกษาความพรุนของเพลเลตแสดงให้เห็นว่าการใช้แป้งดัดแปร ในสูตรตำรับแลคโตสไม่มีผลต่อความพรุน แต่ทำให้ความพรุนของเพลเลตไดแคลเซียมฟอสเฟตเพิ่มขึ้นเมื่อเปรียบเทียบ กับสูตรตำรับที่ไม่ได้ใช้แป้งดัดแปร และพบว่าความพรุนของเพลเลตแลดโดสสูงกว่าของเพลเลตไดแคลเซียมฟอสเฟต

ภาควิชา	สัชอศสาหกรรม	ลายมือชื่อนิสิต	ล์นี้ผม	น์งม <i>ต</i> เม	do
	เภสัชอุ์ฅสาหกรรม	ลายมือชื่ออาจารย์ที่ปริ	/ กษา	~	
ปีการศึกษา	2541	ลายมือชื่ออาจารย์ที่ปรึ	กษาร่วม	DEV.	Bon !

#### พิมพ์ตันฉบับบทกัดย่อวิทยานิพบธ์ภายในกรอบสีเขียวนี้เพียงแผ่นเดียว

# # C875248 : MAJOR : MANUFACTURING PHARMACY
KEY WORD: SODIUM CARBOXYMETHYL STARCH / DEGREE OF SUBSTITUTION / PELLET / EXTRUSION AID /
EXTRUSION-SPHERONIZATION

SUPATTRA NIYOMTHAMAKIT: USE OF SODIUM CARBOXYMETHYL STARCH AS EXTRUSION AID IN THE PRODUCTION OF PELLET BY EXTRUSION AND SPHERONIZATION PROCESS. THESIS ADVISOR: ASSOCIATE PROFESSOR POJ KULVANICH, Ph.D. THESIS CO-ADVISOR: ASSISTANT PROFESSOR WICHEIN THANINDRATARN 291 pp. ISBN 974-638-858-4

Native glutinous rice starch was chemically modified by etherification reaction to obtain sodium carboxymethyl starch with three different degrees of substitution and evaluated for their properties as the aid in pellet formulations produced by extrusion/spheronization technique. The physical properties of pellets prepared using three different pellet bases (sucrose, hydrous lactose and dicalcium phosphate dihydrate) in combination with this modified starch were characterized in comparison with blank pellets without adding modified starch. It was found that only rod shaped particles were generated in sucrose formulations prepared with modified starch. The improvable physical properties of lactose and dicalcium phosphate pellets employing modified starch could be obtained and the amount of microcrystalline cellulose which commonly used as the extrusion aid in pellet formulation could be decreased. Lactose and dicalcium phosphate pellets prepared with modified starches were larger in size, harder, more spherical, with less agglomeration and smoother surface than blank pellets.

The degrees of substitution of modified starch had a negligibly effect on the physical properties of pellets except hardness and surface characteristic. Among various degrees of substitution, the highest hardness of lactose pellets was yielded by using 0.26 degree of substitution whereas the hardest dicalcium phosphate pellets was obtained when using 0.16 and 0.32 degree of substitution. Moreover, modified starch at 0.16 degree of substitution produced dicalcium phosphate pellets with smoother surface than the others. The amount of added water played a critical role in extrusion/spheronization process. Increasing the amount of water imparted the greater size, hardness, sphericity and surface roughness. Using the higher amount of modified starch (increased from 0.3% to 0.8% w/w) could improve some pellet properties, i.e. more hardness and surface smoothness. For porosity of pellets, the result showed that modified starch did not affect the porosity of lactose pellets while the porosity of dicalcium phosphate pellets using modified starch was higher than that of blank pellets. It was found that the porosity of lactose pellets was higher than that of dicalcium phosphate pellets.

ภาควิชา	เกสัชอุตสาหกรรม	ลายมือชื่อนิสิต	ษัฐนม หุลทางมาจุง	
สาขาวิชา	เภสัชอุตสาหกรรม	ลายมือชื่ออาจารย์ที่ปรึกษา	ar a	
ปีการศึกษา	2541	ลายมือชื่ออาจารย์ที่ปรึกษาร่	A Sell Mar	,

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#### **Abbreviations**

°C degree Celsius

BU Brabender unit

DS degree of substitution

GI gastro-intestinal

gm gram

M milliequivalent of base required for neutralization of 1 gm of MGS

m²/gm squaremeter per gram

MGS modified glutinous rice starch

min minute ml milliliter

μm micrometermm millimeterN Normality

rpm rounds per minute

TS. Test solution

VS. Volumetric solution

w/w weight by weight

6S<sub>()</sub> 65 % sucrose pellet formulations

7S<sub>()</sub> 70 % sucrose pellet formulations

8S<sub>()</sub> 80 % sucrose pellet formulations

9S<sub>()</sub> 90 % sucrose pellet formulations

6L<sub>()</sub> 65 % lactose pellet formulations

8L<sub>()</sub> 80 % lactose pellet formulations

6D<sub>()</sub> 65 % dicalcium phosphate pellet formulations

8D<sub>()</sub> 80 % dicalcium phosphate pellet formulations

()<sub>3()</sub> pellet formulations using MGS produced by method A (DS = 0.32)

()<sub>2()</sub> pellet formulations using MGS produced by method B (DS = 0.26)

()<sub>1()</sub> pellet formulations using MGS produced by method C (DS = 0.16)