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**ENHANCING DISSOLUTION OF INDOMETHACIN USING BETA-CYCLODEXTRIN
AND SODIUM LAURYL SULFATE BY SPRAY DRYING TECHNIQUE**

Miss Alisara Thanmiksakul

A Thesis Submitted in Partial Fulfillment of the Requirements

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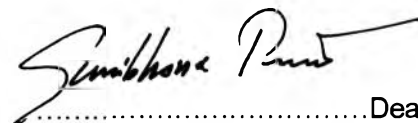
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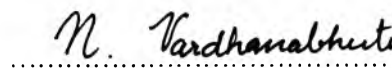
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อลิศรา ชรรณิกสกุล : การเพิ่มการละลายของอินโดเมทาซินโดยใช้เบต้าไซโคลเด็กซ์ทรินและโซเดียมลอริลซัลเฟตด้วยเทคนิคการพ่นแห้ง (ENHANCING DISSOLUTION OF INDOMETHACIN USING BETA-CYCLODEXTRIN AND SODIUM LAURYL SULFATE BY SPRAY DRYING TECHNIQUE) อ.ที่ปรึกษา : อ.ดร. นฤพร สุตินทวิบูลย์, 296 หน้า. ISBN 974-332-900-5

ในการวิจัยนี้ได้ทำการศึกษาถึง ผลขององค์ประกอบและสภาวะในกระบวนการพ่นแห้งเพื่อเพิ่มการละลายของตัวยาที่ละลายน้ำได้น้อย (อินโดเมทาซิน) โซลิดดิสเพอร์ชันระหว่างอินโดเมทาซินกับเบต้าไซโคลเด็กซ์ทรินที่อัตราส่วน 2:1, 1:1 และ 1:2 ในสารละลายฟอสเฟตบัฟเฟอร์พีเอช 7.4 และอินโดเมทาซินกับโซเดียมลอริลซัลเฟตที่ความเข้มข้น 13%, 20%, 27% และ 33% โดยน้ำหนัก ในสารละลายบัฟเฟอร์พีเอช 7.4 ได้เตรียมขึ้นโดยใช้สภาวะการพ่นแห้งที่แตกต่างกัน นำผลิตภัณฑ์ที่ได้มาประเมินด้วยอิเล็กตรอนสแกนนิ่งไมโครสโคปี เพาเคอร์เอ็กซ์เรย์ดิฟแฟรคโตมิทรี ดิฟเฟอเรนเชียลสแกนนิ่งแคลอริมิทรี และฟูเรียร์-ทรานฟอร์มอินฟราเรดสเปกโทรสโกปี พบว่ามีการเกิดปฏิกิริยาทางเคมีระหว่างอินโดเมทาซินและเบต้าไซโคลเด็กซ์ทรินในระหว่างกระบวนการพ่นแห้ง การศึกษาค่าการละลายและอัตราการละลายของอินโดเมทาซินกับเบต้าไซโคลเด็กซ์ทริน พบว่าความสามารถในการละลายและอัตราการละลายสูงขึ้นอย่างมีนัยสำคัญภายหลังจากกระบวนการพ่นแห้งเมื่อเทียบกับอินโดเมทาซินเดี่ยวๆ อินโดเมทาซินที่ผ่านกระบวนการพ่นแห้งและสารผสมแห้งระหว่างอินโดเมทาซินและเบต้าไซโคลเด็กซ์ทริน อย่างไรก็ตามอัตราส่วนโดยโมล สภาวะการพ่นแห้ง ได้แก่ อุณหภูมิในการพ่นแห้ง (130, 140 และ 150 องศาเซลเซียส) และอัตราเร็วในการป้อนน้ำยา (10, 15 และ 20 มิลลิลิตรต่อนาที) ไม่มีผลอย่างมีนัยสำคัญต่อความสามารถในการเพิ่มขึ้นของการละลายและอัตราการละลายเริ่มต้นของผลิตภัณฑ์ นอกจากนี้ วิธีไฮเพอร์ฟอร์แมนซ์ลิกวิดโครมาโตกราฟี พบว่าการเติมเบต้าไซโคลเด็กซ์ทรินในกระบวนการพ่นแห้งอินโดเมทาซินกับเบต้าไซโคลเด็กซ์ทรินจะทำให้การละลายตัวของตัวยาช้าลงอย่างมีนัยสำคัญในระหว่างกระบวนการพ่นแห้ง

ค่าการละลายและอัตราการละลายเริ่มต้นของอินโดเมทาซินและโซเดียมลอริลซัลเฟตที่ได้จากการพ่นแห้งจะสูงกว่าอินโดเมทาซินเดี่ยวๆ อินโดเมทาซินที่ผ่านกระบวนการพ่นแห้ง และสารผสมแห้งระหว่างอินโดเมทาซินและโซเดียมลอริลซัลเฟต การศึกษาด้วยวิธีไฮเพอร์ฟอร์แมนซ์ลิกวิดโครมาโตกราฟี พบว่ามีการละลายตัวอย่างรวดเร็วของอินโดเมทาซิน เมื่อนำมาผ่านกระบวนการพ่นแห้งร่วมกับโซเดียมลอริลซัลเฟต

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INDOMETHACIN USING BETA-CYCLIDEXTRIN AND SODIUM
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The effects of compositions and spray drying conditions on dissolution rate enhancement of poorly soluble drug indomethacin (IMC) were investigated in this study. Solid dispersion between IMC and beta cyclodextrin (BCD) at molar ratios of 2:1, 1:1 and 1:2 in phosphate buffer pH 7.4 and IMC and sodium lauryl sulfate (SLS) at concentrations of 13%, 20%, 27% and 33% w/w in phosphate buffer pH 7.4 were prepared by various spray drying conditions. The products were characterized by scanning electron microscopy (SEM), powder X-ray diffractometry (PXRD), differential scanning calorimetry (DSC) and fourier transform infrared (FTIR) spectrometry. Chemical interactions between IMC and BCD were found during the spray drying process. Solubility study and dissolution rate study of spray dried IMC/BCD suggested that there were significant solubility and dissolution rate increase with spray drying process compared to pure IMC, spray dried IMC and its physical mixtures. The spray drying conditions, such as inlet air temperatures (130 , 140 and 150 °C) and feed rates (10, 15 and 20 ml/min), however, were not shown to have significant effect on the solubility and initial dissolution rates. Moreover, High Performance Liquid Chromatography (HPLC) study showed that the addition of BCD in the spray dried powder of IMC/BCD retarded the degradation process of IMC during spray drying.

The solubility and initial dissolution rate of spray dried IMC/ SLS were higher than pure IMC, spray dried IMC and its physical mixtures. HPLC study showed that the degradation of IMC was accelerated by the spray drying process with SLS.

ภาควิชาเภสัชอุตสาหกรรม.....ลายมือชื่อहित **อลิสรา** **ธนะมิศกุล**
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LIST OF ABBREVIATIONS

BCD	=	beta cyclodextrin
Bar	=	kg/cm ²
B	=	bulk density
°C	=	degree celcius
%CV	=	percent coefficient of variation
conc.	=	concentration
DSC	=	differential scanning calorimetry
FTIR	=	fourier-transform infrared spectroscopy
g	=	gram (s)
hr	=	hour
HPLC	=	high-performance liquid chlomatography
K _c	=	apparent stability constant
IMC	=	indomethacin
M	=	molarity
mcg	=	microgram
mg	=	milligram
min	=	minute
ml	=	millilitre
nm	=	nanometer
no.	=	number
pH	=	the negative logarithm of the hydrogen ion
PM	=	physical mixture
pKa	=	the negative logarithm of the dissociation constant
q.s.	=	make to volume
PXRD	=	powder X-ray diffractometry
r	=	correlation coefficient
SD	=	standard deviation
SEM	=	scanning electron microscopy
SLS	=	sodium lauryl sulfate
T	=	tapped density
TGA	=	thermogravimetry analysis

USP	=	The United States Pharmacopoeia
UV	=	ultraviolet
w/w	=	weight by weight
%	=	percent