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MECHANISMS OF INCREASING DISSOLUTION OF INDOMETHACIN
SOLID DISPERSION AND CORRESPONDING CAPSULES
PREPARED BY VARIOUS AMOUNT AND TYPES OF CARRIERS

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สมลักษณ์ คงเมือง : กลไกการเพิ่มการละลายของอินโดเมทาซิน โขลิต ดิสเพอร์ชัน และยาบรรจุแคปซูล ซึ่งเตรียมโดยเปลี่ยนอัตราส่วนและชนิดของตัวพา (MECHANISMS OF INCREASING DISSOLUTION OF INDOMETHACIN SOLID DISPERSION AND CORRESPONDING CAPSULES PREPARED BY VARIOUS AMOUNT AND TYPES OF CARRIERS) อ.ที่ปรึกษา : รศ.ดร. กาญจน์พิมพ์ ฤทธิเดช, อ.ที่ปรึกษาร่วม : รศ.ดร. สุนิพนธ์ ภูมิมางกูร, 241 หน้า ISBN 974-579-648-4

การศึกษานี้จะศึกษาถึงความสามารถและกลไกการเพิ่มการละลายของอินโดเมทาซิน (IDM) ซึ่งเตรียมโดยวิธีใช้ตัวพาละลาย โขลิตดิสเพอร์ชัน เทคนิค โดยปรับอัตราและเปลี่ยนชนิดของตัวพาซึ่งมี 4 ชนิด ได้แก่ mannitol, PEG 4000, PVP K 30 และ sodium lauryl sulfate (SLS) โดยจะเปรียบเทียบกับระบบของการผสมทางกายภาพ นอกจากนี้ยังรวมถึงการศึกษาการละลายของยาบรรจุแคปซูล

ระบบของโซลิตดิสเพอร์ชันจะแสดงการละลายสูงสุด ตามด้วยระบบผสมทางกายภาพ, ตัวพาที่ถูกกระทำโดยตัวพาละลาย และตัวพาเดี่ยว ตามลำดับ ระบบของ PEG 4000, PVP K 30 และ SLS จะแสดงการละลายของยาค่อยๆลดลงและจะให้มากกว่าระบบของ mannitol เมื่อเพิ่มปริมาณของตัวพาจะพบว่ามีการเพิ่มการละลายทุกรูปแบบ ยกเว้นระบบของ IDM-SLS ที่ผสมทางกายภาพจะให้ผลตรงข้าม การละลายของแคปซูลของระบบโซลิตดิสเพอร์ชันจะให้ดีกว่าระบบอื่นและระบบของ IDM-SLS โขลิตดิสเพอร์ชัน จะใช้เวลาอันน้อยที่สุดในการละลายยาครบ 80%

รูปถ่ายจาก Scanning Electron Microscope แสดงให้เห็นถึงการลดขนาดของอนุภาค การแยกกลุ่มก้อนของทุกระบบโซลิตดิสเพอร์ชัน รวมถึงระบบ IDM-PVP K 30, IDM-PEG 4000 ที่ผสมทางกายภาพ ซึ่งจะเปรียบเทียบกับยาเดี่ยว การเปลี่ยนแปลงของจุลสภาวะของยาจะพบในระบบของ IDM-PVP K 30, IDM-PEG 4000 โขลิตดิสเพอร์ชัน Thermograms, Infrared spectra และ X-ray diffractogram แสดงถึงการเปลี่ยนแปลงรูปผลึกของยา โดยเปลี่ยนจากแบบที่ I เป็นแบบที่ II ในระบบโซลิตดิสเพอร์ชัน ซึ่งคล้ายกับยาที่ถูกกระทำโดยตัวพาละลาย ยกเว้นระบบของ IDM-PVP K 30 จะมีการเปลี่ยนแปลงเป็นรูปแบบออสัญฐาน การเกิดสารประกอบเชิงซ้อนจะพบในระบบของ IDM-PVP K 30 และอัตราส่วนที่มากขึ้นของ IDM-SLS โขลิตดิสเพอร์ชัน จากวิธีการใช้ของเหลวซึมผ่าน พบว่า ความเปียกของผงยาจะดีขึ้นทั้งระบบโซลิตดิสเพอร์ชันและการผสมทางกายภาพ

ในการเพิ่มปริมาณของตัวพา จะมีผลต่อการเปลี่ยนแปลงของกลไกที่เด่นชัดได้แก่ การลดขนาดของอนุภาค, การลดการรวมกลุ่มก้อน และการเพิ่มความเปียกของผงยา



ภาควิชาเภสัชอุตสาหกรรม
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ลายมือชื่อนิติ
ลายมือชื่ออาจารย์ที่ปรึกษา
ลายมือชื่ออาจารย์ที่ปรึกษาร่วม

SOMLAK KONGMUANG : MECHANISMS OF INCREASING DISSOLUTION OF
INDOMETHACIN SOLID DISPERSION AND CORRESPONDING CAPSULES PREPARED
BY VARIOUS AMOUNT AND TYPES OF CARRIERS. THESIS ADVISOR : ASSOC.
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This study is to elucidate the ability and mechanisms of enhancing dissolution of indomethacin (IDM). The systems, prepared by solvent solid dispersion technique with various amount and four types of carriers, mannitol, PEG 4000, PVP K 30 and sodium lauryl sulfate (SLS), compared with physical mixture systems. The dissolution of capsule containing the prepared systems was also studied.

Of four systems, solid dispersion systems showed the greatest dissolution, followed by physical mixture systems, treated IDM and untreated IDM respectively. Amount four types of carriers, PEG 4000, PVP K 30 and SLS seemed to produce the same dissolution of IDM but still more than mannitol. Increasing the amount of carriers increased the dissolution in all systems of all carriers except IDM-SLS physical mixture that exhibited the reversed effect. The dissolution of drug from capsule was better than the corresponding powder. IDM-SLS coprecipitate in capsule showed the fastest time for dissolving 80% of drug.

Scanning Electron photomicrograph showed that size reduction, deaggregation with deagglomeration appeared in all IDM-carrier solid dispersions and both IDM-PVP K 30, IDM PEG 4000 physical mixture when compared to untreated drug. Moreover, microenvironmental changing seemed to be occurred in IDM-PVP K 30, IDM-PEG 4000 solid dispersion. Differential thermal analysis thermograms; Infrared spectra and X-ray diffractograms revealed that IDM polymorph was changed from Form I to Form II in all solid dispersion as in treated drug, except IDM-PVP K 30 solid dispersion which showed an amorphous form. Complex formation was also appeared in IDM-PVP K 30 and higher ratio of IDM-SLS solid dispersion. Liquid penetration studies demonstrated that wettability increased in both solid dispersion and physical mixture.

Increasing the amount of carriers affected some degree of mechanisms especially particle size reduction, deaggregation and deagglomeration and wettability.

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FIGURE

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ABBREVIATIONS

AVG	average
°C	celcius degree
cm	centimeter
CO ₂	carbon dioxide
Cu	Copper
% CV	percent of variation coefficient
DTA	differential thermal analysis
gm	gram
IDM	Indomethacin
IR	Infrared
kv	kilo volt
mA	milliampere
Man	Mannitol
mcg	microgram
min	minute
ml	milliliter
mm	millimeter
NMR	Nuclear Magnetic Resonance
no or #	number
PEG	polyethylene glycol
PHY	physical mixture
PVP	polyvinylpyrrolidone
SLS	Sodium lauryl sulfate
SOL	Solid dispersion or coprecipitate
UV	ultraviolet