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INCREASED DISSOLUTION RATE OF HYDROCHLOROTHIAZIDE THROUGH SOLID DISPERSION

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ขวัญจิต อึ้งโพธิ์ : การเพิ่มอัตราการละลายของไฮโดรคลอโรไธเอไซด์โดยโซลิดดิสเพอร์สชัน (INCREASED DISSOLUTION RATE OF HYDROCHLOROTHIAZIDE THROUGH SOLID DISPERSION) อาจารย์ที่ปรึกษา : ผศ.สุชาดา ประเสริฐวิทยาการ อาจารย์ที่ปรึกษาร่วม : รศ.ดร.สุนิพนธ์ ภุมมางกูร, 146 หน้า.

เทคนิคโซลิดดิสเพอร์สชันโดยวิธีการใช้ตัวทำละลายและวิธีการหลอมละลาย ถูกนำมาใช้เพื่อเพิ่มอัตราการละลายของไฮโดรคลอโรไธเอไซด์ โซลิดดิสเพอร์สชันของไฮโดรคลอโรไธเอไซด์ที่ประกอบด้วยตัวยาและตัวพาในอัตราส่วนต่างๆ ได้ถูกเตรียมขึ้นโดยใช้ตัวพาชนิดต่างๆ คือ PVP (K-17, K-30, K-90), PEG (4000, 6000, 20000) และยูเรีย(urea) พบว่าอัตราการละลายของตัวยาจากโซลิดดิสเพอร์สชันสูงขึ้นมากเมื่อเปรียบเทียบกับตัวยาเดี่ยวๆและสารผสมทางกายภาพ วิธีเตรียมชนิดและอัตราส่วนของตัวพาที่ใช้ มีอิทธิพลต่ออัตราการละลายของตัวยาจากโซลิดดิสเพอร์สชัน โซลิดดิสเพอร์สชันของไฮโดรคลอโรไธเอไซด์และยูเรียในอัตราส่วน 1:3 โดยวิธีหลอมละลายมีอัตราการละลายสูงสุด จากการวิเคราะห์โดยวิธีเตรียม x-ray diffraction, infrared spectroscopy และ differential thermal analysis พบว่าไฮโดรคลอโรไธเอไซด์ในโซลิดดิสเพอร์สชัน อยู่ในรูปอสัณฐาน(amorphous form) จากการศึกษาความคงตัวของไฮโดรคลอโรไธเอไซด์ ในสารหลอมละลายของตัวยาและยูเรียในอัตราส่วน 1:3 พบว่าตัวยามีความคงตัวทางเคมีต่อความร้อนและความชื้น แต่การเก็บสารหลอมละลายภายใต้สภาวะที่มีความชื้นสูง มีผลทำให้อัตราการละลายของตัวยาลดลง จากผลของการวิเคราะห์โดยวิธีข้างต้นทั้งสามพบว่า ตัวยาบางส่วนได้เปลี่ยนไปอยู่ในรูปผลึกเมื่อเก็บไว้ที่ความชื้นสูง ดังนั้นการเก็บรักษาสารหลอมละลายนี้ จึงควรหลีกเลี่ยงความชื้นซึ่งทำให้อัตราการละลายของตัวยาลดลง

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KAWUNCHIT OUNGBHO : INCREASED DISSOLUTION RATE OF HYDROCHLOROTHIAZIDE THROUGH SOLID DISPERSION. THESIS ADVISOR : ASST. PROF. SUCHADA PRASERTVITHYAKARN. THESIS CO-ADVISOR ASSO. PROF. SUNIBHOND PUMMANGURA., Ph.D. 146 PP.

Solid dispersion techniques by solvent and melting methods were used to increase the dissolution rate of hydrochlorothiazide (HCTZ). Dispersed systems containing various ratios of drug to carrier were prepared using PVP (K-17, K-30, K-90), PEG (4000, 6000, 20000)and urea. The results of the dissolution rates obtained revealed a marked increase in the HCTZ released from the solid dispersions when compared with that of the plain drug and physical mixtures. Methods of preparation, types and fractions of carriers used influenced dissolution behavior of HCTZ from solid dispersions. The 1:3 HCTZ-urea melt was by far the best combination. X-ray diffraction, infrared spectroscopy and differential thermal analysis of solid dispersions suggested the presence of an amorphous form of HCTZ in dispersed systems. The chemical and physicochemical stability of HCTZ in 1:3 HCTZ-urea melt was studied. It was found that HCTZ in the melt was chemically stable to heat and humidity. The storage of the melt under humid condition was found to influence the dissolution behavior. X-ray diffraction, infrared spectroscopy and differential thermal analysis of the melt stored under humid condition suggested the partial crystallization of amorphous HCTZ in the system. It was concluded that the melt of HCTZ and urea should be stored in such a way that it is not exposed to humidity so as to avoid a decrease of HCTZ dissolution rate.

ภาควิชา เภสัชกรรม ..... ลายมือชื่อนิสิต .....

สาขาวิชา เภสัชกรรม .....

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ABBREVIATIONS

AR	Analytical Reagent
°C	degree celcius
cm	centimeter
CO_2	Carbon dioxide
conc	concentration
Cu	Copper
DTA	Differential thermal analysis
g	gram
HCTZ	Hydrochlorothiazide
IR	Infrared
K	Potassium
kV	kilovolt
mA	milliampere
mcg	microgram
mcV	microvolt
mg	milligram
min	minute
ml	milliliter
N_2	Nitrogen
NaOH	Sodium hydroxide
Ni	Nickel
nm	nanometer
No.	number
PEG	Polyethylene glycol

ABBREVIATIONS (cont.)

PVP	Polyvinylpyrrolidone
R.H.	relative humidity
r.p.m.	revolutions per minute
RS	Reference Standard
S.D.	Standard Deviation
UV	Ultraviolet