

ผลของสูตรตำรับ แสง และความชื้นสัมพัทธ์ ต่อความคงตัวในสถานะของแข็ง
ของไมโครสเฟียร์โดยการพ่นแห้งของไนเฟดิพีน

เรื่อตรีหญิง ปณยา บาลโพธิ์



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EFFECTS OF FORMULATION, LIGHT AND RELATIVE HUMIDITY ON SOLID-STATE STABILITY
OF NIFEDIPINE SPRAY DRIED MICROSPHERES

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การศึกษาความคงตัวในสถานะของแข็งของไมโครสเฟียร์ของไนเฟดีพีนโดยการพ่นแห้ง ได้ศึกษาถึงอิทธิพลของอัตราส่วนระหว่างพอลิเมอร์รวม (ยูตราจิต อาร์เอส100 และพีวีพี เค30) อุณหภูมิของลมเข้า ขนาดของไมโครสเฟียร์ อัตราส่วนระหว่างยาต่อพอลิเมอร์ ความเข้มของแสง และการเติมสารดูดกลืนรังสียูวี (เคอร์คิวมิน สารสกัดเคอร์คิวมิน ทาร์ทราซีน และซันเซตเยลโลว์) และสารต้านออกซิเดชัน (โซเดียมไบซัลไฟต์) ต่อความคงตัวต่อแสงของไมโครสเฟียร์ของไนเฟดีพีน และอิทธิพลของความชื้นสัมพัทธ์ต่อความคงตัวทางเคมีและกายภาพของไมโครสเฟียร์ของไนเฟดีพีน การวิเคราะห์ปริมาณไนเฟดีพีนใช้วิธีลิควิดโครมาโทกราฟีชนิดความดันสูง พบว่าการเสื่อมสลายเป็นไปตามจลนศาสตร์อันดับหนึ่ง การเพิ่มปริมาณพีวีพี เค30 ในสูตรตำรับ อุณหภูมิของลมเข้า และอัตราส่วนระหว่างยาต่อพอลิเมอร์ ทำให้ค่าคงที่อัตราการเสื่อมสลายโดยแสงของไมโครสเฟียร์ของไนเฟดีพีนเพิ่มขึ้น ($p < 0.05$) การลดขนาดอนุภาคซึ่งวัดขนาดโดยอิมเมจอนาไลเซอร์พบว่าเพิ่มค่าคงที่อัตราการเสื่อมสลาย ($p < 0.05$) การเพิ่มปริมาณความเข้มของแสงทำให้ค่าคงที่อัตราการเสื่อมสลายโดยแสงของไมโครสเฟียร์ของไนเฟดีพีนเพิ่มขึ้นเช่นเดียวกัน ($p < 0.05$) การเติมเคอร์คิวมินสามารถป้องกันการเสื่อมสลายโดยแสงของไนเฟดีพีนได้ดีที่สุดในกลุ่มของสารดูดกลืนรังสียูวีและสารต้านออกซิเดชันที่ศึกษา ทั้งในรูปสารละลาย และของแข็งของไนเฟดีพีน ความชื้นสัมพัทธ์ไม่มีผลต่อความคงตัวทางเคมีของไมโครสเฟียร์ของไนเฟดีพีน การดูดความชื้นของไมโครสเฟียร์ของไนเฟดีพีนเพิ่มขึ้นตามค่าความชื้นสัมพัทธ์และปริมาณพีวีพี เค30 ค่าความชื้นสัมพัทธ์วิกฤตของไมโครสเฟียร์สามารถหาได้จากความชื้นสัมพัทธ์ซึ่งอัตราการดูดความชื้นเป็นศูนย์ การสัมผัสต่อแสง ความชื้น และอุณหภูมิในบรรยากาศ ไม่ทำให้ไมโครสเฟียร์ของไนเฟดีพีนซึ่งมีเคอร์คิวมินเกิดการเสื่อมสลาย ไม่มีความแตกต่างระหว่างค่าคงที่อัตราการละลายตามสมการของฮิกซ์ของไมโครสเฟียร์ของไนเฟดีพีน และไมโครสเฟียร์ของไนเฟดีพีนซึ่งมีเคอร์คิวมิน

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 สาขาวิชาเภสัชกรรม..... ลายมือชื่ออาจารย์ที่ปรึกษา
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The solid-state of nifedipine spray dried microspheres was investigated to determine the effect of the ratio between combined polymers (Eudragit RS100 and PVP K30), the inlet air temperature, the microsphere size, the drug-polymer ratio, the light intensity and the addition of UV absorbers (curcumin, curcumin crude extract, tartrazine and sunset yellow) and antioxidant (sodium bisulfite) on the photostability of nifedipine microspheres and the effect of relative humidity on the chemical and physical stabilities of nifedipine microspheres. The high pressure liquid chromatographic method was used for nifedipine analysis. The degradation was shown to follow the first-order kinetics. The increase of PVP K30 in formula, inlet air temperature and drug-polymer ratio increased the photodegradation rate constant (p<0.05). The small particle size as measured by the image analyzer was found to significantly increase the degradation rate constant (p<0.05). The light intensity increment also increased the degradation rate constant of nifedipine microspheres (p<0.05). The addition of curcumin gave the highest protection power among other UV absorbers and antioxidant studied, both in solution and solid-state of nifedipine. The relative humidity did not influence the chemical stability of nifedipine microspheres. The moisture uptake of nifedipine microspheres increased with the relative humidity and the PVP K30 content. The critical relative humidities were determined from the relative humidity at which the water uptake rate was zero. On exposure to light, relative humidity and temperature in the ambient atmosphere, no degradation was found in the stabilized nifedipine microspheres by curcumin. There was no difference between the Higuchi dissolution rate constants of nifedipine microspheres with and without curcumin.

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Field of Study.....Pharmacy.....	Advisor' s signature.....
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LIST OF ABBREVIATIONS

μm	=	micrometer
ANOVA	=	analysis of variance
CRH	=	critical relative humidity
CV	=	coefficient of variation
h	=	hour
HPLC	=	high pressure liquid chromatography
k	=	degradation rate constant
K	=	release rate constant
klux	=	kilolux
mg	=	milligram
min	=	minute
ml	=	milliliter
mm	=	millimeter
ng	=	nanogram
nm	=	nanometer
$^{\circ}\text{C}$	=	degree Celcius
PVP K30	=	Povidone K30
R	=	correlation coefficient
R^2	=	coefficient of determination
RH	=	relative humidity
rpm	=	revolution per minute
SD	=	standard deviation
UV	=	ultraviolet
w/v	=	weight by volume