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จุฬาลงกรณ์มหาวิทยาลัย

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**PREPARATION AND EVALUATION OF SODIUM CARBOXYMETHYL
STARCH AS SUSPENDING AGENT IN DRY SYRUP**



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The preparation and evaluation of sodium carboxymethyl starch which prepared as suspending agent from three native starches (glutinous rice starch, rice starch and tapioca starch) were studied. Modified glutinous rice starch (MGS), modified rice starch (MRS) and modified tapioca starch (MTS) were prepared by Filbert's method to have degrees of substitution (DS) of 0.16, 0.26 and 0.38, respectively. The results indicated that Filbert's method gave MGS and MRS at DS of 0.16 and 0.26, respectively. However, the decreasing of reaction time from 2 hours to 90 minutes would be performed in order to synthesize MTS with DS of 0.38. In order to select optimum concentration of each prepared modified starches and Ultrasperse[®]2000 (UT, commercial modified starch) as suspending agent, 10 % w/v calcium carbonate suspension was prepared. The reconstitution time, redispersibility, sedimentation volume and viscosity of 10 % w/v calcium carbonate suspension when using different type and concentrations of suspending were compared. It was found the optimum concentrations of MGS, MRS, MTS and UT were 1.0, 2.0, 3.0 and 4.0 %, respectively. Then, the use of prepared modified starches and UT as suspending agent in dry syrups formulation of amoxicillin trihydrate and cephalexin monohydrate at the concentration of 125 mg/ 5 ml was studied. Citrate buffer was used to control the pH of amoxicillin trihydrate and cephalexin monohydrate dry syrup at 6.0 and 4.5, respectively. The citrate buffer at the concentration of 0.05 M had slight effect on the stability and viscosity of formulation which stored at room temperature and in refrigerator (8.0 ± 1 °C) for 14 days. The preliminary result indicated that MTS was not appropriate as suspending agent in dry syrups, since the bubble was occurred after shaking. The stability study of amoxicillin trihydrate dry syrup using MGS, MRS, UT at 2.5 %, 3.0 % and 4.0 % w/v, respectively, and cephalexin dry syrup using MGS, MRS, UT at 2.5 %, 2.5 % and 4.0 % w/v, respectively, were performed by storage at room temperature and 45 °C, 75 % RH for 4 months. The evaluation of drug content and physicochemical properties was performed every month. The drug content and physicochemical properties of dry powder and reconstituted suspension remained unchanged. In addition, the short reconstitution time and good redispersibility of formulation were observed. The viscosity and drug content of formulation were slightly decreased when storage at room temperature and 45 °C, 75% RH for 4 months.

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จิตรดี ลูประสงค์ : การเตรียมและประเมินคุณสมบัติของแป้งคาร์บอกซีเมทิลในการเป็นสารช่วยแขวนตะกอนในยาน้ำเชื่อมแห้ง (PREPARATION AND EVALUATION OF SODIUM CARBOXYMETHYL STARCH AS SUSPENDING AGENT IN DRY SYRUP) อ.ที่ปรึกษา : รศ.ดร.พจน์ กุลวานิช, 275 หน้า. ISBN 974-17-5708-5.

ศึกษาการเตรียมและประเมินแป้งโซเดียมคาร์บอกซีเมทิล เป็นสารช่วยแขวนตะกอนจากแป้งธรรมชาติ 3 ชนิด คือ แป้งข้าวเหนียว แป้งข้าวเจ้า และแป้งมันสำปะหลัง เตรียมแป้งข้าวเหนียวตัดแปร (MGS) แป้งข้าวเจ้าตัดแปร (MRS) และแป้งมันสำปะหลังตัดแปร (MTS) เป็นสารช่วยแขวนตะกอนด้วยวิธีของ Filbert ณ ระดับการแทนที่ 0.16, 0.26 และ 0.38 ตามลำดับ พบว่าวิธีการดังกล่าวสามารถเตรียม MGS และ MRS ได้ ณ ระดับการแทนที่ 0.16 และ 0.26 ตามลำดับ แต่อย่างไรก็ตามก็การสังเคราะห์ MTS ณ ระดับการแทนที่ 0.38 ต้องลดเวลาในการทำปฏิกิริยาจาก 2 ชั่วโมงเป็น 90 นาที เตรียมตำรับยาน้ำแขวนตะกอนของแคลเซียมคาร์บอเนตความเข้มข้น 10 % w/v เพื่อที่จะคัดเลือกความเข้มข้นที่เหมาะสมของแป้งตัดแปรที่เตรียมได้ และ Ultrasperse[®] 2000 (UT, แป้งตัดแปรที่มีขายในท้องตลาด) โดยเปรียบเทียบจากคุณสมบัติการกระจายตัวหลังจากที่เติมน้ำลงไป ความง่ายของสารแขวนลอยในการกระจายตัวกลับ ปริมาตรการตกตะกอน และความหนืดของตำรับยาน้ำแขวนตะกอนของแคลเซียมคาร์บอเนตความเข้มข้น 10 % w/v เมื่อใช้ชนิดและความเข้มข้นของสารแขวนตะกอนแตกต่างกัน พบว่าความเข้มข้นที่เหมาะสมของ MGS, MRS, MTS และ UT คือ 1.0 %, 2.0 %, 3.0 % และ 4.0 % w/v ตามลำดับ จากนั้นศึกษาการใช้แป้งตัดแปรที่เตรียมได้และ UT เป็นสารช่วยแขวนตะกอนในตำรับยาน้ำเชื่อมแห้งของอะมอกซิซิลลินไตรไฮเดรต และเซฟฟาแลกซินโมโนไฮเดรตที่ความเข้มข้น 125 mg/5ml ควบคุม pH ของยาน้ำเชื่อมแห้งอะมอกซิซิลลินไตรไฮเดรตและเซฟฟาแลกซินโมโนไฮเดรตเท่ากับ 6.0 และ 4.5 ตามลำดับโดยใช้ซิงโครทรีตพีเพอร์ ซิงโครทรีตพีเพอร์ความเข้มข้น 0.05 โมลาร์ ส่งผลกระทบต่อความคงตัวและความหนืดของสูตรตำรับที่เก็บไว้ที่อุณหภูมิห้องและในตู้เย็น (8.0 ± 1 °C) เป็นเวลา 14 วัน ผลการทดลองตำรับเบื้องต้นพบว่า MTS ไม่เหมาะสมในการเป็นสารช่วยแขวนตะกอนในตำรับยาน้ำเชื่อมแห้งเนื่องจากพบฟองหลังการเขย่า ศึกษาความคงตัวของยาน้ำเชื่อมแห้งโดยทำการเก็บยาน้ำเชื่อมแห้งที่อุณหภูมิ 45 °C ความชื้นสัมพัทธ์ 75 % และที่อุณหภูมิห้องเป็นเวลา 4 เดือน โดยความเข้มข้นของ MGS, MRS และ UT ที่ใช้ในยาน้ำเชื่อมแห้งอะมอกซิซิลลินไตรไฮเดรตเท่ากับ 2.5 %, 3.0 % และ 4.0 % w/v ตามลำดับ และความเข้มข้นของ MGS, MRS และ UT ที่ใช้ในยาน้ำเชื่อมแห้งเซฟฟาแลกซินโมโนไฮเดรตเท่ากับ 2.5 %, 2.5 % และ 4.0 % w/v ตามลำดับ ทำการประเมินปริมาณยาและคุณสมบัติทางเคมีกายภาพทุกเดือน ปริมาณยาและคุณสมบัติทางเคมีกายภาพของยาน้ำเชื่อมแห้งและยาน้ำเชื่อมเมื่อกระจายตัวในน้ำไม่เปลี่ยนแปลง นอกจากนี้พบว่าสูตรตำรับมีค่าการกระจายตัวหลังจากที่เติมน้ำลงไปและค่าความง่ายของสารแขวนลอยในการกระจายตัวกลับต่ำเมื่อเก็บยาน้ำเชื่อมแห้งที่อุณหภูมิ 45 °C ความชื้นสัมพัทธ์ 75 % และที่อุณหภูมิห้องเป็นเวลา 4 เดือน

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สาขาวิชา.....เภสัชอุตสาหกรรม.....ลายมือชื่ออาจารย์ที่ปรึกษา.....
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List of Abbreviations

$^{\circ}\text{C}$	degree Celsius
cm	centimeter(s)
cm^2	square centimeter(s)
cm^3	cubic centimeter(s)
cP	centipoises (s)
e.g.	exempli gratia, “for example”
et al	et alii, “and others”
l	liter(s)
M	molar
g	gram(s)
mg	milligram(s)
min	minute(s)
ml	milliliter(s)
mol	mole(s)
μg	microgram(s)
mm	micrometer(s)
MGS	modified glutinous rice starch
MRS	modified rice starch
MTS	modified tapioca starch
UT	ULTRASPERSE [®] 2000
pH	the negative logarithm of hydrogen ion concentration.
pKa	the negative logarithm of the dissociation constant.
ppm	parts per million.
RH	relative humidity
rpm	revolutions per minute
s	second(s)
USP	The United States Pharmacopeia
UV	ultraviolet spectrometry
w/v	weight in volume
w/w	weight in weight