

ลักษณะการปลดปล่อยตัวยาที่มีค่าการละลายต่างกันจากเมทริกซ์เพลเลทที่ประกอบด้วยกลีเซอโริโนร์

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RELEASE CHARACTERISTICS OF DRUG HAVING DIFFERENT
SOLUBILITIES FROM MATRIX PELLETS CONTAINING GLYCERIDES

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ศูนย์วิทยบริการ
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ศึกษาคุณสมบัติการปลดปล่อยของยาที่มีค่าการละลายต่างกัน 2 ชนิด (โพรพราโนอล ไฮโดรคลอไรด์ และไดโคลฟิแนค โซเดียม) จากกลีเซอไรด์เมทริกซ์เพลเลทที่เตรียมขึ้นด้วยเทคนิคเอกซ์ทรูชันสเฟียโรไนเซชัน โดยใช้กลีเซอริลโมโนสเตียเรต ไฮดร็อเจนตเหตคอดตอนซีดอย (ลูบิเทป) และกลีเซอริลบีอีเนต (คอมไพรอตอล) เป็นสารก่อเมทริกซ์ แคนติส และ ไมโครคริสตัลลีนเซลลูโลส (อะวิเซลพีเอช 101) เป็นสารช่วยในกระบวนการการทำเพลเลท รวมทั้งศึกษาปัจจัยที่มีอิทธิพลต่อการปลดปล่อยยา คือ ปริมาณของกลีเซอไรด์ บริมาณของตัวยาสำคัญในเพลเลท ขนาดของเพลเลท และกระบวนการรอบเพลเลทที่ได้ เพลเลಥของโพรพราโนอลไฮโดรคลอไรด์ไม่สามารถยึดเวลาการปลดปล่อยของตัวยาได้ ยกเว้นในสูตรตัวบับที่ประกอบด้วย คอมไพรอตอล สามารถยึดเวลาการปลดปล่อยออกไซป์ได้ถึง 8 ชั่วโมง ไดโคลฟิแนค โซเดียมเพลเลทมีการปลดปล่อยตัวยาต่ำกว่า 3 เพรอร์เซ็นต์ตัวกลางที่เป็นกรดเนื่องจากมีค่าการละลายที่ต่ำมาก แต่ในสูตรที่เป็นต่งเพลเลทที่เตรียมด้วยกลีเซอไรด์ทั้ง 3 ชนิดสามารถยึดระยะเวลาการปลดปล่อยตัวยาได้ถึง 12 ชั่วโมง เพลเลทที่มีขนาดเล็กจะมีการปลดปล่อยตัวยาเร็วกว่าขนาดใหญ่ การเติมโพลิเอทิลิน ไกลคอล 1450 (พีอีจี 1450) และโพลิชอร์เบต 80 (ทวีน 80) ลงในไดโคลฟิแนค โซเดียมเพลเลท ไม่มีผลต่อการเพิ่มการปลดปล่อยตัวยาในตัวกลางที่เป็นกรด เมื่อนำโพรพราโนอล ไฮโดรคลอไรด์เพลเลทมาอบในเครื่องอบแห้งแบบฟลูอิดไดซ์บด พบร่างสามารถลดอัตราการปลดปล่อยตัวยาจากเพลเลทที่ประกอบด้วยลูบิเทปได้เมื่อเปรียบเทียบกับเพลเลทที่ไม่ได้อบ สามารถสรุปได้ว่ากลีเซอไรด์เมทริกซ์เพลเลทเหมาะสมสำหรับระบบที่ประกอบด้วยตัวยาที่มีค่าการละลายต่ำ การนำเพลเลทเมทริกซ์ไปตอกอัดเป็นเม็ดจะช่วยยึดระยะเวลาการปลดปล่อยตัวยาออกไซป์ได้ทั้งในโพรพราโนอลไฮโดรคลอไรด์และไดโคลฟิแนค โซเดียม

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The release properties of drug having different solubilities (propranolol hydrochloride and diclofenac sodium) from the glycerides matrix pellets were investigated. The pellets were prepared using extrusion and spheroidization technique. Glycerol monostearate, hydrogenated cottonseed oil (Lubritab[®]) and glyceryl behenate (Compritol[®]ATO 888) were used as matrix forming agents. Lactose and microcrystalline cellulose (Avicel[®]PH 101) were chosen as pelletization aids. The following factors that might influence the drug release were examined: amounts of glycerides, drug loadings, sizes of pellet, and pellets curing process. The glycerides pellets of propranolol hydrochloride could not provide the prolonged drug release except the formulation containing Compritol[®]ATO 888 that could maintain the release for eight hours. Due to its very low solubility in acidic medium, diclofenac sodium pellets exhibits lower than 3 percent release in 0.1 N HCl throughout the duration of twelve hours, while could give sustained action for twelve hours in phosphate buffer pH 6.8 with all glycerides employed. Smaller sizes of the pellets were found to give the faster release of the drugs. The addition of polyethylene glycol 1450 (PEG 1450) and polysorbate 80 (Tween[®] 80) into diclofenac sodium pellets did not exerted an increasing effect on drug release in acidic medium. Following the curing of propranolol hydrochloride matrix pellets in fluidized bed dryer, only Lubritab[®] containing pellets showed reduction of drug release compared with uncured pellets. It could be concluded that the glyceride pellets matrix might be suitable for low solubility drug substance. If more prolonged release action is required, the pellets should be compressed into the tablet matrices. As it was shown, the matrix tablets prepared by compression of the pellets provided the better-sustained release actions of both propranolol hydrochloride and diclofenac sodium.

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ศูนย์วิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

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LIST OF ABBREVIATIONS

°C	degree Celsius
DI	deionized
DS	diclofenac sodium
DSC	differential scanning calorimetry
e.g.	exampli gratia (for example)
et al.	Et alli, and others
g	gram(s)
GMS	glyceryl monostearate
HCl	hydrochloric acid or hydrochloride
hr	hours
IR	infrared
k	rate constant
No.	number
MCC	microcrystalline cellulose (Avicel®PH 101)
mg	milligram(s)
min	minute(s)
ml	milliliter(s)
mm	millimeter(s)
%	percentage
PEG	Polyethylene glycol
pH	the negative logarithm of the hydrogen ion concentration
pK _a	the negative logarithm of the dissociation constant
PL	propranolol hydrochloride
q.s.	make to volume
®	Registered
r ²	coefficient of determination
rpm	revolution per minute
RT	room temperature
SEM	Scanning Electron Microscope
μg	microgram
UV-VIS	ultraviolet-visible

LIST OF ABBREVIATIONS (cont.)

w/v	weight by volume
w/w	weight by weight
λ	wavelength
λ_{max}	wavelength of maximum absorbance
>	more than
<	less than