

**POLYTHOPHENE/CARRAGEENAN HYDROGEL AS DRUG RELEASE
MATRIX UNDER ELECTRIC FIELD**

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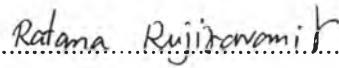
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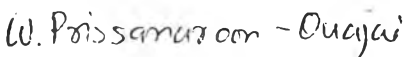
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ABSTRACT

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Development of the conductive polymer-hydrogel blend between polythiophene (PTh) doped with acetylsalicylic acid (ASA) and a carrageenan hydrogel for the transdermal drug delivery was investigated, in which the characteristic releases depend on the electric field applied. The carrageenan and their blend films were prepared by the solution casting using acetylsalicylic acid as the model drug and doping agent for PTh and $MgCl_2$, $CaCl_2$, and $BaCl_2$ as the crosslinking agents. The average molecular weight between crosslinks, the crosslinking density, and the mesh size of the carrageenan hydrogels were determined using the equilibrium swelling theory, as well as by scanning electron microscopy. The release mechanism and diffusion coefficients of blend PTh/carrageenan hydrogels and the non-blended ones were determined by using a modified Franz-Diffusion cell in an MES buffer solution, pH 5.5, at 37 °C, for a period of 48 h in order to investigate the effects of the crosslinking ratio, the type of crosslinking agent and the electric field strength. The amounts of drug released were analyzed by UV-Visible spectrophotometry. The diffusion coefficient of drug was calculated through the Higuchi equation. The diffusion coefficient decreases with increasing the crosslinking ratio and decreasing the crosslinking ion size with and without the conductive polymer. The diffusion coefficients are greater at the applied electric field of 2.0 V by an order of magnitude relative to those without electric field. Moreover, the diffusion coefficients with the conductive polymer are better than without the conductive polymer.

บทคัดย่อ

ศนิดา ไพรัชเวชภักดิ์ : การควบคุมการปลดปล่อยยาด้วยกระแสไฟฟ้าจากพอลิไทโอโอฟีน/คาราจีแนนไฮโดรเจล (Polythiophene/Carrageenan Hydrogel as Drug Release Matrix under Electric Field) อ. ที่ปรึกษา : ศ.ดร. อนุวัฒน์ ศิริวัฒน์ 184 หน้า

งานวิจัยนี้เป็นการพัฒนาแผ่นปลดปล่อยยาทางผิวหนังที่เตรียมขึ้นจากพอลิเมอร์ผสมระหว่างคาราจีแนน และพอลิไทโอโอฟีน โดยใช้กระแสไฟฟ้าเป็นตัวกระตุ้น ซึ่งมีการใช้เมกนีเซียมคลอไรด์, แคลเซียมคลอไรด์ และแบรียมคลอไรด์เป็นสารเชื่อมโยงสำหรับการเตรียมแผ่นผสม และใช้อะซิติกซาลิกไซคลิกเอซิดเป็นตัวแทนของยา ความหนาแน่นของตัวเชื่อมโยง และขนาดช่องว่างภายในคาราจีแนนไฮโดรเจล สามารถคำนวณจากทฤษฎีการดูดซับน้ำของ Peppas และตรวจสอบด้วยเครื่องจุลทรรศน์อิเล็กตรอนแบบส่องกราด กลไกการปลดปล่อยและอัตราการแพร่ของยาผ่านไฮโดรเจลนี้ถูกศึกษาโดยใช้ modified Franz-Diffusion cell ในสารละลาย MES บัฟเฟอร์พีเอช 5.5 อุณหภูมิ 37 องศาเซลเซียส เป็นเวลา 48 ชั่วโมง ภายใต้อิทธิพลของปริมาณสารเชื่อมโยง, ชนิดของสารเชื่อมโยง และกระแสไฟฟ้า ปริมาณยาที่ถูกปลดปล่อยได้ถูกวิเคราะห์ด้วยเครื่องวัดการดูดกลืนแสง และใช้สมการของฮิโกชิ (Higuchi equation) ในการคำนวณหาอัตราการแพร่ของยา จากการทดลองพบว่า อัตราการแพร่ของยาลดลงเมื่อปริมาณสารเชื่อมโยงเพิ่มขึ้น และขนาดอนุภาคของสารเชื่อมโยงลดลง ทั้งในกรณีที่มีและไม่มีพอลิเมอร์ที่นำกระแสไฟฟ้า นอกจากนี้ยังพบว่าในกรณีที่ใช้กระแสไฟฟ้า 2 โวลต์ และการใส่พอลิไทโอโอฟีนลงในแผ่นไฮโดรเจลช่วยให้อัตราการแพร่กระจายของยาเพิ่มขึ้น

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ABBREVIATIONS

DDS	Drug Delivery System
TDDS	Transdermal Drug Delivery System
ASA	Acetylsalicylic acid
FTIR	Fourier Transform Infrared Spectrometer
TG-DTA	Thermal Gravimetric/Differential Thermal Analyzer
SEM	Scanning Electron Microscope
UV-Vis	UV-VIS spectrophotometer
SD	Standard deviation

LIST OF SYMBOLS

M_s	weight of the sample after submersed in the buffer solution (g)
M_d	weight of sample after submersed in the buffer solution as dry state (g)
M_i	initial weight of the sample without submersed in the buffer solution as dry state (g)
$W_{a,d}$	weight of the dry polymer in air (g)
$W_{h,d}$	weight of the dry polymer in heptanes (g)
$W_{a,r}$	weight of the relaxed polymer in air (g)
$W_{h,r}$	weight of the relaxed polymer in heptanes (g)
$W_{a,s}$	weight of the swollen polymer in air (g)
$W_{h,s}$	weight of the swollen polymer in heptanes (g)
ρ_h	density of heptanes
V_d	volume of the polymer sample in the dry states
V_r	volume of the polymer sample in the relaxed states
V_s	volume of the polymer sample in the swollen states
$u_{2,r}$	polymer volume fraction in the relaxed state
$u_{2,s}$	polymer volume fraction in the swollen state
\bar{M}_n	number averaged molecular weight of the polymer before cross linking (g/mol)
\bar{v}	specific volume of polymer (cm ³ /g)
\bar{V}_1	molar volume of water (mol/cm ³)
χ	Flory interaction parameter of polymer
ξ	(Mesh size) linear distance between consecutive crosslinks (Å)
C_n	Flory characteristic ratio
\bar{M}_c	molecular weight between crosslinks (g/mol)
\bar{M}_r	average molecular weight of repeating unit (g/mol)
l	carbon-carbon bond length (Å)
ρ_x	crosslinking density of the hydrogel (mol/cm ³)
M_t	amounts of drug release at time (mg)

M_{∞}	amounts of drug release at time infinity (mg)
M_t/M_{∞}	fractional of drug release
k	kinetic constant (T^{-n})
k_H	Higuchi kinetic constant (h^{-n})
n	diffusional exponent
Q	amount of material flowing through a unit cross-section of barrier (g/cm^2)
C_0	initial drug concentration in the hydrogel (g/cm^3)
D	diffusion coefficient of a drug (cm^2/s)
D_0	diffusion coefficient of a very small drug size (cm^2/s)
m	scaling exponent