

CONTROLLED DRUGS RELEASE FROM GELATIN HYDROGELS

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A Thesis Submitted in Partial Fulfilment of the Requirements
for the Degree of Master of Science
The Petroleum and Petrochemical College, Chulalongkorn University
in Academic Partnership with
The University of Michigan, The University of Oklahoma,
and Case Western Reserve University

2012


I26374587

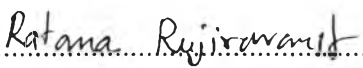
Thesis Title: Controlled Drugs Release from Gelatin Hydrogels
By: Marutpong Rattana
Program: Polymer Science
Thesis Advisor: Prof. Dr. Anuvat Sirivat

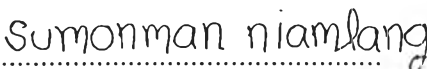
Accepted by The Petroleum and Petrochemical College, Chulalongkorn University, in partial fulfilment of the requirements for the Degree of Master of Science.


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ABSTRACT

5372009063: Polymer Science Program
Marutpong Rattana: Controlled Drugs Released from Gelatin
Hydrogels.
Thesis Advisor: Professor Anuvat Sirivat 157 pp.
Keyword: Gelatin hydrogels/ Crosslink/ Diffusion coefficient/ Controlled drug
release

This study evaluates and characterizes the use of porcine and fish gelatin hydrogels as the matrix in a controlled drug delivery system. The drug-loaded gelatin hydrogels were prepared by solution-casting using salicylic acid and 5-sulfosalicylic acid as the model drugs and glutaraldehyde as the crosslinking agent. The average molecular weight between crosslink, the crosslinking density, and the mesh size of the gelatin hydrogels were determined using the equilibrium swelling theory, as well as by scanning electron microscopy. The release mechanisms and the diffusion coefficients of the hydrogels were determined by using a modified Franz-Diffusion cell in an acetate buffer (at pH 5.5 and at a temperature of 37 °C for 48 hours) in order to investigate the effect of the crosslinking ratio. The diffusion coefficient of the drug was determined through the Higuchi equation at various crosslink ratios and different drug size. The diffusion coefficients of drug in the gelatin hydrogels decrease with increasing crosslink ratio due to the smaller mesh sizes of gelatin hydrogels. The diffusion coefficient of a smaller drug size is higher than that of a larger drug size. The diffusion coefficients obey the power law of the drug size over the mesh size ratio with the scaling exponent m equal to 0.45.

บทคัดย่อ

มารุตพงศ์ รัตนะ : การควบคุมการปลดปล่อยของยาจากไฮโดรเจลเจลาติน (Controlled Drugs Released from Gelatin Hydrogels) อ. ที่ปรึกษา: ศ.ดร. อนุวัฒน์ ศิริวัฒน์ 157 หน้า

ในงานวิจัยฉบับนี้ได้จัดทำเพื่อการเปรียบเทียบและพิสูจน์เอกลักษณ์ของเจลาตินไฮโดรเจลที่ได้จากหมูและเจลาตินที่ได้จากปลาซึ่งใช้เป็นตัวส่งผ่านยา เจลาตินไฮโดรเจลผสมด้วยยาได้เตรียมโดยวิธีการเตรียมเป็นแผ่นด้วยสารละลายระหว่างซาลิกไซคลิกเอซิดและซัลโฟซาลิกไซคลิกเอซิดแทน โมเดลยาและ กลูตารัลดีไฮด์เป็นสารเชื่อมโยงนำหนักโมเลกุลระหว่างตัวเชื่อมโยง ความหนาแน่นของตัวเชื่อมโยง และขนาดช่องว่างภายในเจลาตินไฮโดรเจล ได้คำนวณจากทฤษฎีการดูดซับน้ำของเปปไทด์และเมอร์ลและตรวจสอบด้วยเครื่องจุลทรรศน์อิเล็กตรอนแบบส่องกราด กลไกการปลดปล่อยและค่าการแพร่ของยาผ่านไฮโดรเจลนี้ได้ศึกษาโดยใช้ modified Franz-Diffusion cell ในสารละลายอะซิเตตบัฟเฟอร์ที่พีเอช 5.5 อุณหภูมิ 37 องศาเซลเซียสเป็นเวลา 48 ชั่วโมง โดยทำการศึกษาผลของปริมาณสารเชื่อมโยง ค่าการแพร่ของยาได้ศึกษาโดยใช้สมการของฮิโกชิ (Higuchi equation) ที่ปริมาณอัตราส่วนของสารเชื่อมโยงที่แตกต่างกัน และขนาดของยาที่แตกต่างกัน ซึ่งพบว่าค่าการแพร่ของยาผ่านเจลาตินไฮโดรเจลลดลงเพราะขนาดช่องว่างภายในเจลาตินไฮโดรเจลลดเมื่อเพิ่มปริมาณอัตราส่วนของสารเชื่อมโยง และ ค่าการแพร่ของยาของยาที่มีขนาดเล็กมีค่ามากกว่ายาที่มีขนาดใหญ่ และค่าสัมประสิทธิ์การแพร่กระจายที่ไปตามกฎหมายอำนาจของขนาดยาที่อัตราส่วนด้วยขนาดช่องว่างภายในเจลาตินไฮโดรเจลมีค่าเท่ากับ 0.45

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to all those who gave the possibility to complete this thesis work

This thesis work is funded by the Petroleum and Petrochemical College; and the National Center of Excellence for Petroleum, Petrochemicals, and Advanced Materials, Thailand.

I am deeply indebted to my thesis advisors, Professor Anuvat Sirivat whose giving admirable guidance, encourage, stimulating suggestions and helped me in all time of my research.

My sincere thank are due to the official committees, Assoc. Prof. Ratana and Dr. Sumonman Niamlang, for their detailed review, constructive criticism and excellent advices.

I would like to thank all special senior students in the AS group and room 515; especially, to Ms. Nophawan Paradee for encouraging and helpful suggestions.

Lastly, this special thesis would not have been possible without the knowledge received from all the lecturers and staffs at the Petroleum and Petrochemical College, plus love and constant support from my family and lovely friends.

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ABBREVIATIONS

DDS	Drug Delivery System
TDDS	Transdermal Drug Delivery System
PorGel	Porcine gelatin
FishGel	Fish gelatin
GTA	Glutaraldehyde
SA	Salicylic acid
SSA	5-Sulfosalicylic acid
FT-IR	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

$[\eta]$	intrinsic viscosity
η	viscosity of the polymer solution
η_o	viscosity of the polymer solvent
η_{sp}	specific viscosity
η_{rel}	relative viscosity
c	concentration of polymer in grams per deciliter (g/dL)
η_{red}	reduced viscosity
η_{inh}	inherent viscosity
k'	Huggins constant
k''	Kramer constant
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)
$W_{a,s}$	weights of the swollen polymer in air (g)
$W_{h,s}$	weights 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
$v_{2,r}$	polymer volume fraction in the relaxed state
$v_{2,s}$	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 (\AA)
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 (\AA)
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_1	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