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APPENDICES

Appendix A Determination of Functional Groups by Fourier Transform Infrared Spectroscopy

The PTh Precursor, PTh, and doped PTh were characterized by FTIR spectroscopy in order to identify functional groups. Optical grade KBr (Carlo Erba Reagent) was used as the background material. 10 mg sample was mixed with 50 mg KBr. An FTIR spectrum was observed by using an FTIR spectrometer (Thermo Nicolet, Nexus 670) in the absorption mode with 64 scans at a resolution of 4 cm^{-1}.

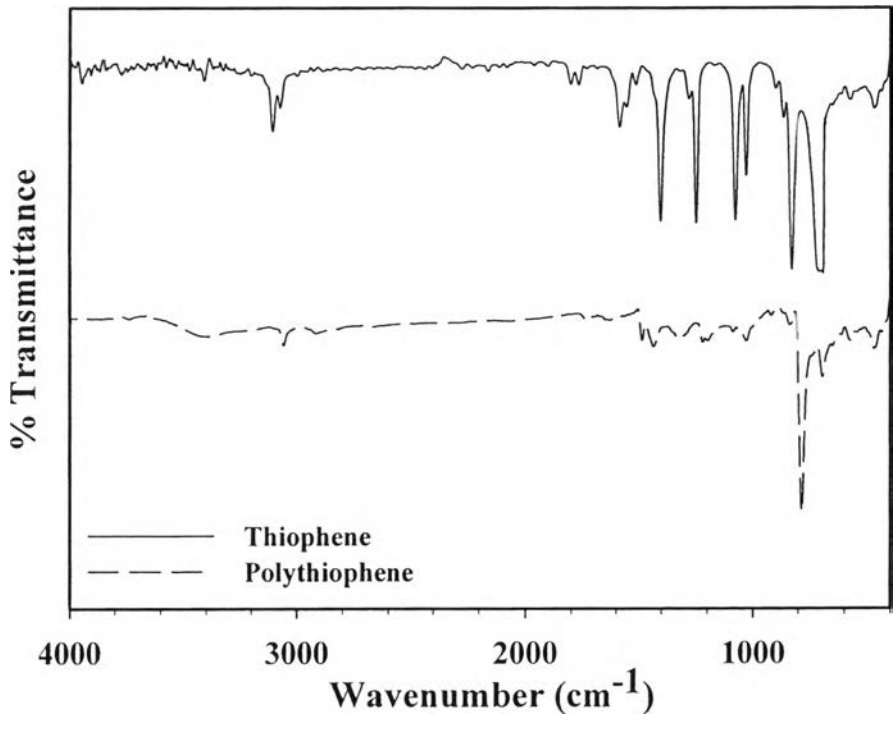


Figure A1 FTIR spectra of PTh Precursor and PTh.

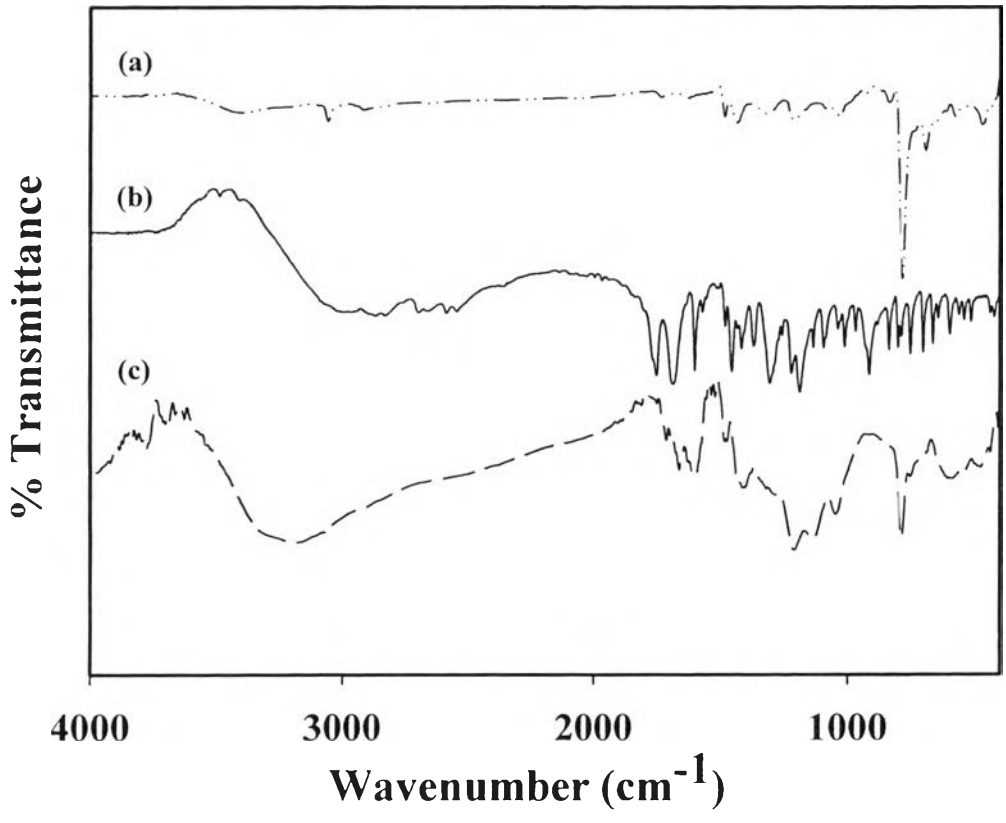


Figure A2 FTIR spectra of: (a) PTh powder; (b) ASA powder; and (c) ASA-doped PTh.

The transmittance spectra of PTh Precursor and PTh are shown in comparison in figure A1. The band at 3070 cm^{-1} is due to the C-H stretching. The presence of the band around 1410-1588 cm^{-1} can be identified as the asymmetric and the symmetric C=C / C-C strentching vibrations in the thiophene ring (Sari *et al.*, 2003, Yang *et at.*, 2005, and Cirpan *et al.*, 2002). The bands around 1034-1080 cm^{-1} represents the C–H in-plane bending and the band at 839 cm^{-1} shows the C–H out of plane bending, respectively (Sari *et al.*, 2003). The band at 714 cm^{-1} is assigned to the bending vibration of C-S bond (Sari *et al.*, 2003). After the polymerization, The C=C band shifts to 1440 cm^{-1}, the C-H in-plane bending shifts to around 1196-1221 cm^{-1} and the C-S bending band shifts to 697 cm^{-1} (Yang *et at.*, 2005).

Figure A2 shows the infared spectra of pure PTh, pure ASA, and ASA-doped PTh. The transmittance spectra of PTh exhibit the following characteristic peaks:

aromatic or olefinic C–H stretching at around 3070 cm^{-1}; the symmetric C=C stretching mode around 1440 cm^{-1}; the C–C stretching of the thiophene rings around 1508 cm^{-1}; the C–H in-plane bending around 1196-1221 cm^{-1}, the C–H out of plane bending at 789 cm^{-1} and the C–S stretching around 697 cm^{-1} (Yang *et at.*, 2005). For pure ASA, the FTIR spectra shows a strong and broad peak of the carboxylic acid group at 2500-3600 cm^{-1} and the peak at 1600 cm^{-1} represents the benzene ring. For ASA-doped PTh, the broad peak of carboxyl group in ASA at 2500-3600 cm^{-1} shifts to around 3000-3500 cm^{-1} and the peak of ester group occurs at 1100-1300 cm^{-1}. Moreover, the C–H out of plane bending of PTh occurs at 790 cm^{-1} (Sari *et al.*, 2003, Yang *et al.*, 2005, and Dolita *et al.*, 2012). Overall, all these peaks combined indicate that the product is ASA-doped PTh.

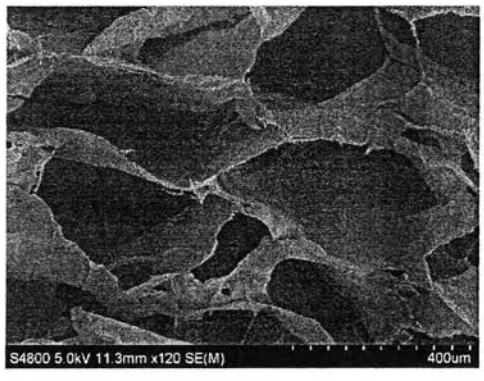
Table A1 Peak positions from FTIR spectra of PTh precursor and PTh

Functional groups	Wavenumber (cm^{-1})		References
	PTh Precursor	PTh	
C-H stretching	3089 (3070)	3089 (3070)	Sari *et al.* (2003)
C=C stretching	1411-1580 (1410-1588)	1450* (1440)	Sari *et al.* (2003) *Yang *et al.*(2005)
C-C ring stretching	1517 (1508)	1517 (1508)	Cirpan *et al.* (2002)
C–H in-plane bending	1036-1080 (1034-1080)	1156,1215* (1196,1221)	Sari *et al.* (2003) *Yang *et al.*(2005)
C–H out of plane bending	839 (836)	788* (789)	Sari *et al.* (2003) *Yang *et al.*(2005)
C–S bending	714 (714)	695* (697)	Sari *et al.* (2003) *Yang *et al.*(2005)

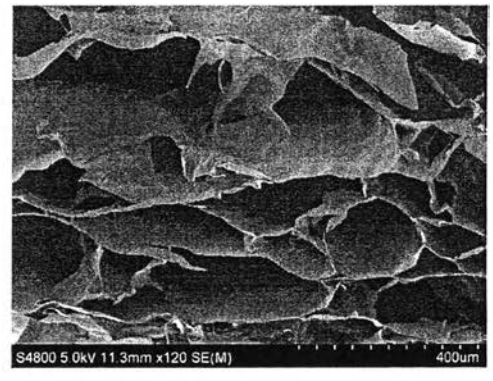
Table A2 The FTIR spectrum of pure PTh, pure ASA and ASA-doped PTh

Functional groups	Wavenumber (cm^{-1})			References
	pure PTh	pure ASA	Doped PTh	
O-H stretching	-	2500-3600 (2700-3300)	2500-3300 (2600-3500)	Dolita *et al.* (2012)
C-H stretching	3089 (3070)	-	-	Sari *et al.* (2003)
Vinyl ester C=O	-	1754 (1754)	-	Dolita *et al.* (2012)
Aromatic acid C=O	-	1690 (1692)	1690 (1704-)	Dolita *et al.* (2012)
Aromatic C=C stretching	-	1605, 1575, 1484 (1603, 1575, 1485)	1605, 1575, 1484 (1603,1485)	Dolita *et al.* (2012)
C=C stretching	1450 (1440)	-	-	Yang *et al.* (2005)
C-O stretching (ester/carboxylic acid)	-	1220, 1189 (1222, 1188)	1220, 1189 (1222,1149)	Dolita *et al.* (2012)
C–H in-plane bending	1156,1215 (1196,1221)	-	1156,1215 (1138,1210)	Yang *et al.* (2005)
C–H out of plane bending	788 (789)	-	788 (790)	Yang *et al.* (2005)
C–S bending	695 (697)	-	-	Yang *et al.* (2005)

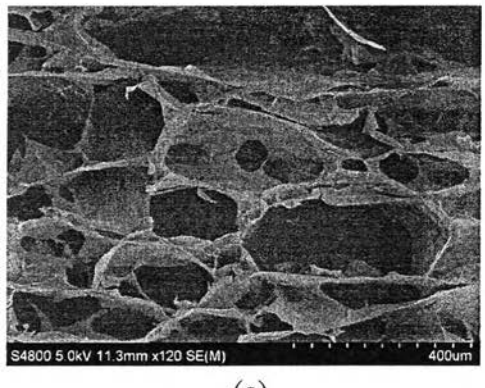
Appendix B Scanning Electron Micrographs of Various Crosslinked Carrageenan Hydrogels



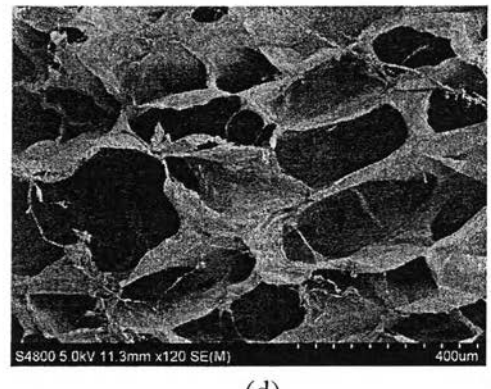
(a)



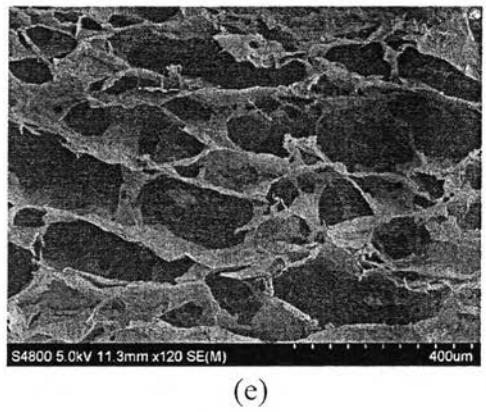
(b)



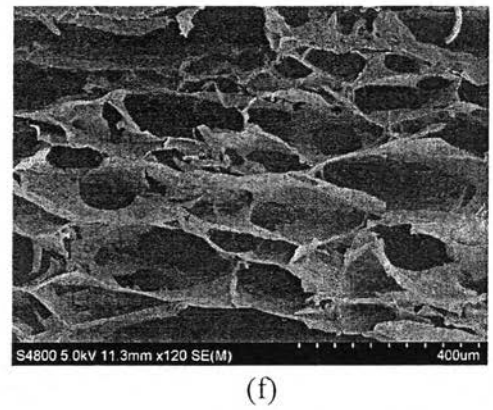
(c)



(d)



(e)



(f)

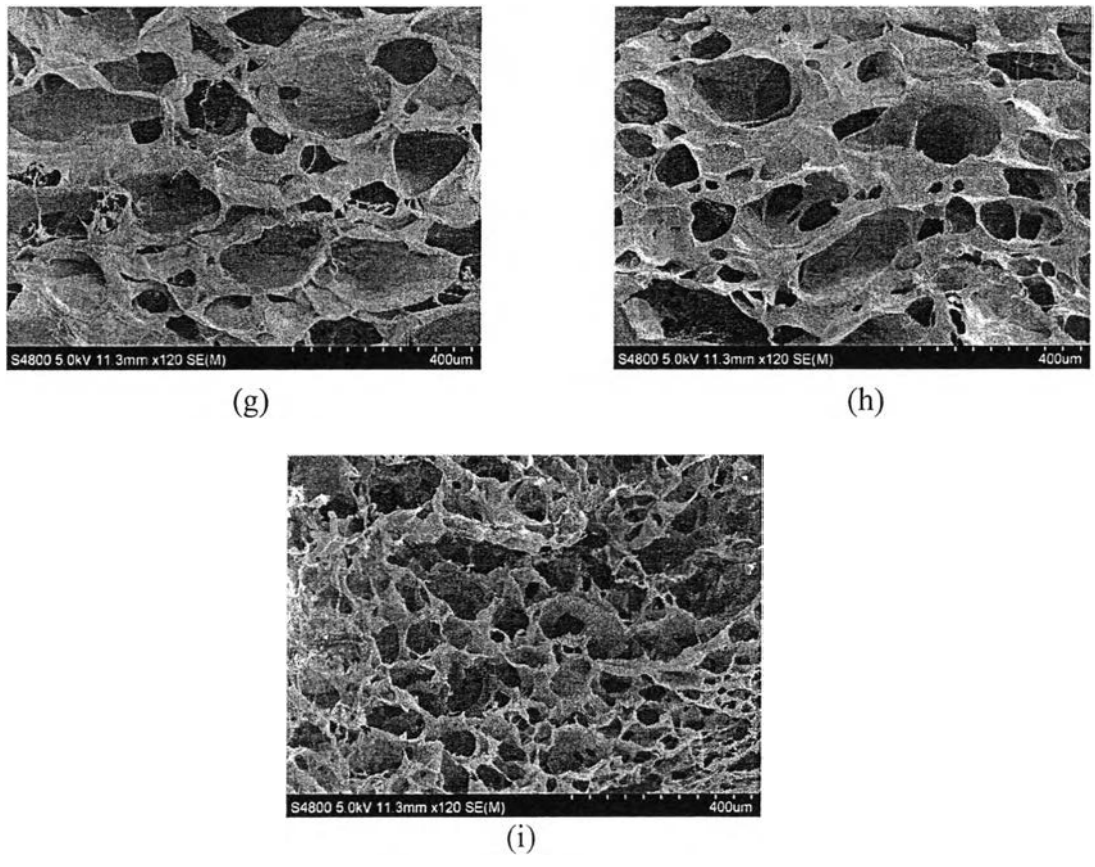


Figure B1 The morphology of carrageenan hydrogel after swelling: (a) Ba-CAR_0.4 ; (b) Ba-CAR_0.6; (c) Ba-CAR_1.0; (d) Ba-CAR_1.4; (e) Ba-CAR_2.0; (f) Ca-CAR_1.0; (g) Mg-CAR_1.0; (h) Ca-CAR_2.0; and (i) Mg-CAR_3.0 at magnification of 120x.

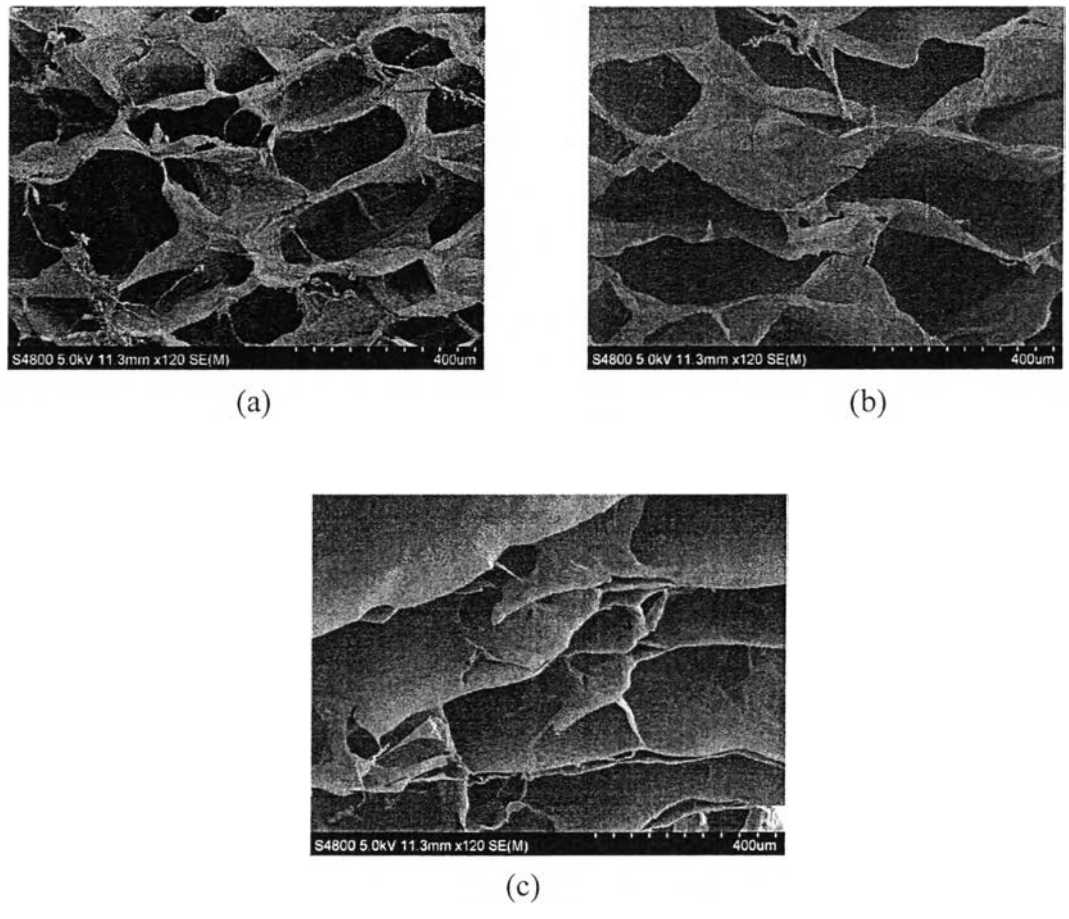


Figure B2 The morphology of carrageenan hydrogel (CAR_1.4) after swelling under electric field strengths of: (a) 0 V; (b) 2.0 V; and (c) 5.0 V at magnification of 120x.

Appendix C Conductivity Measurement

The electrical conductivity, which is the inversion of specific resistivity (ρ) of undoped PTh and doped PTh pellets was measured by using the two-point probe meter connected with a voltage supplier (Keithley, Model 6517A) whose constant voltage can be varied and the current is measured. The thickness of pellets was measured by a thickness gauge. The regime where responsive current is linearly proportional to the applied voltage is called the linear ohmic regime, which can be identified by plotting the applied voltage against the current. The voltage and the current in the regime were converted to the electrical conductivity of the polymer by using equation (C1) as follows:

$$\sigma = 1/\rho = 1/(R_s \times t) = I/(K \times V \times t) \qquad \text{(C1)}$$

where

	σ	=	specific conductivity (S/cm.)
	ρ	=	specific resistivity (Ω.cm.)
	R_s	=	sheet resistivity (Ω)
	I	=	measured current (A)
	K	=	geometric correction factor = 4.29×10^{-4}
	V	=	applied voltage (voltage drop) (V)
	t	=	pellet thickness (cm.)

From figure C1, the specific electrical conductivity of PTh increases with increasing the doping level because the number of charge carriers and the charge mobility increase. The highest specific electrical conductivity is 2.57×10^{-5} S/cm at doping level of 5:1. When doping level higher than 5:1, the specific electrical conductivity decreases due to over-oxidation.

For doped PTh, the specific electrical conductivity increases as the doping level is increased as present in Table C2.

Table C1 Determination the electrical conductivity (S/cm) of PTh

Sample	Electrical conductivity (S/cm)	Standard deviation
$FeCl_3$: Th = 3:1	2.12×10^{-6}	3.91×10^{-7}
$FeCl_3$: Th = 4:1	2.60×10^{-6}	1.60×10^{-7}
$FeCl_3$: Th = 5:1	2.57×10^{-5}	5.88×10^{-6}
$FeCl_3$: Th = 6:1	1.57×10^{-5}	5.20×10^{-6}
$FeCl_3$: Th = 8:1	7.85×10^{-6}	1.20×10^{-6}
$FeCl_3$: Th = 10:1	3.95×10^{-6}	9.24×10^{-7}

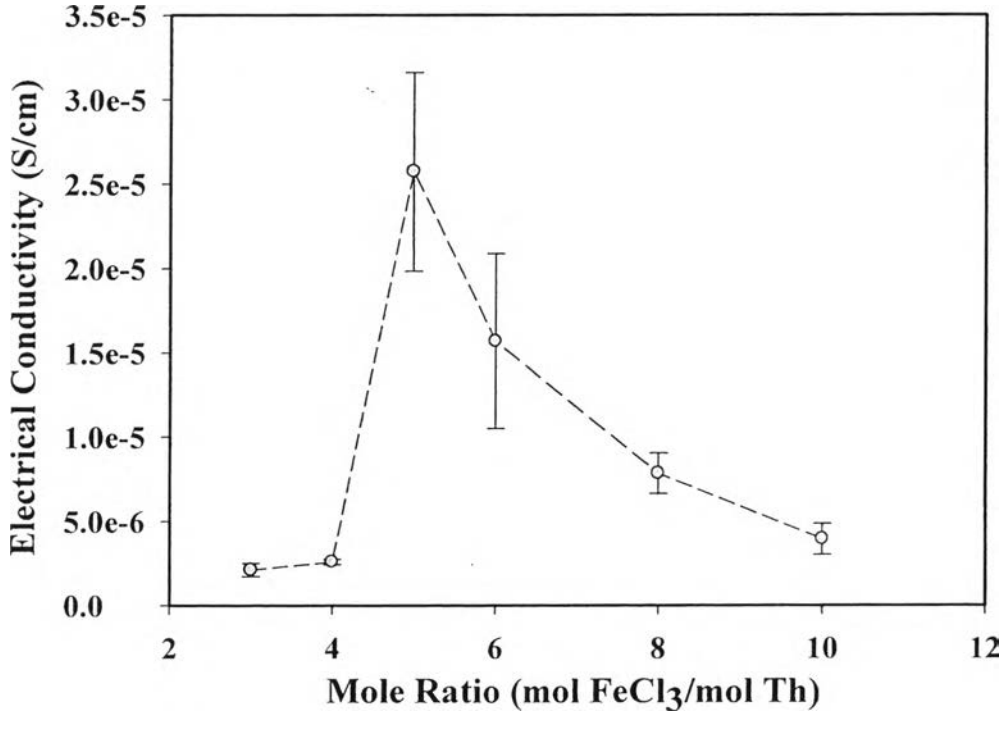


Figure C1 The electrical conductivity of PTh at various mole ratios.

Table C2 Determination the electrical conductivity (S/cm) of ASA doped PTh at various doping level

Sample	Electrical conductivity (S/cm)	Standard deviation
PTh	2.57×10^{-5}	5.88×10^{-6}
ASA : PTh = 0.01:1	2.22×10^{-4}	1.88×10^{-5}
ASA : PTh = 0.1:1	6.91×10^{-2}	0.035
ASA : PTh = 0.5:1	6.10×10^{-2}	0.045

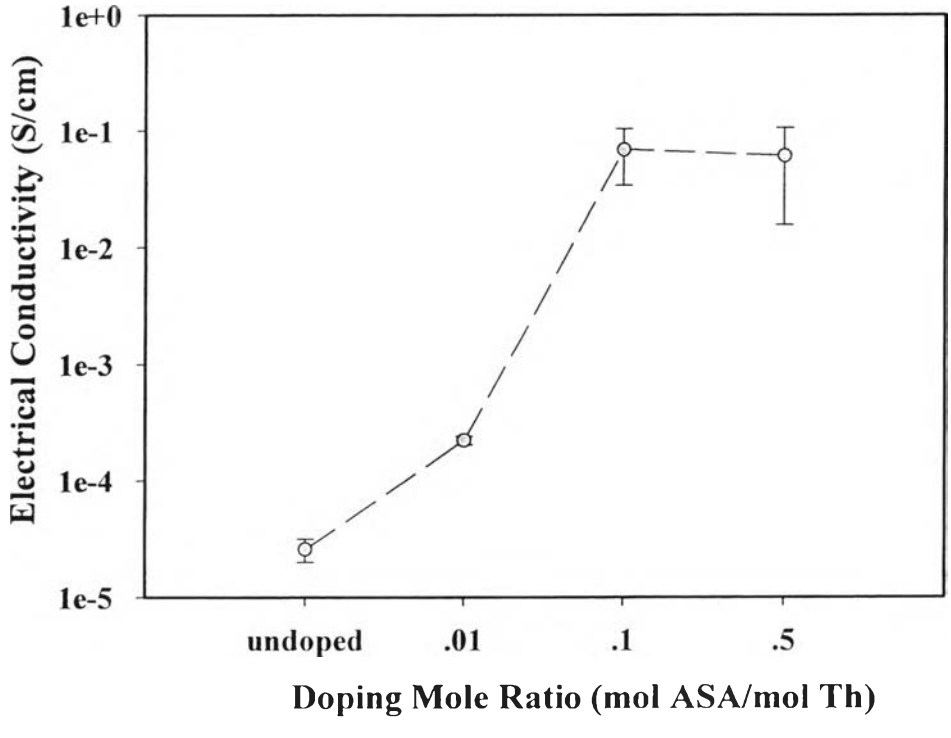


Figure C2 The electrical conductivity of ASA doped PTh at various doping level.

Appendix D UV-Visible Spectrum of Acetylsalicylic Acid (ASA)

A UV-Visible spectrophotometer (TECAN, Infinite M200) was used to determine the maximum spectra of model drug. The model drug in a MES buffer solution was prepared for scanning the maximum absorption wavelength. The characteristic peak was observed. The absorbance value at the maximum wavelength of model drug was read with model drug 10 mg in buffer solution 1000 ml and the correspond the model drug concentrations were calculated from the calibration curve with model drug concentration. Figure D shows the characteristic peak of acetylsalicylic acid at the wavelength 230 nm.

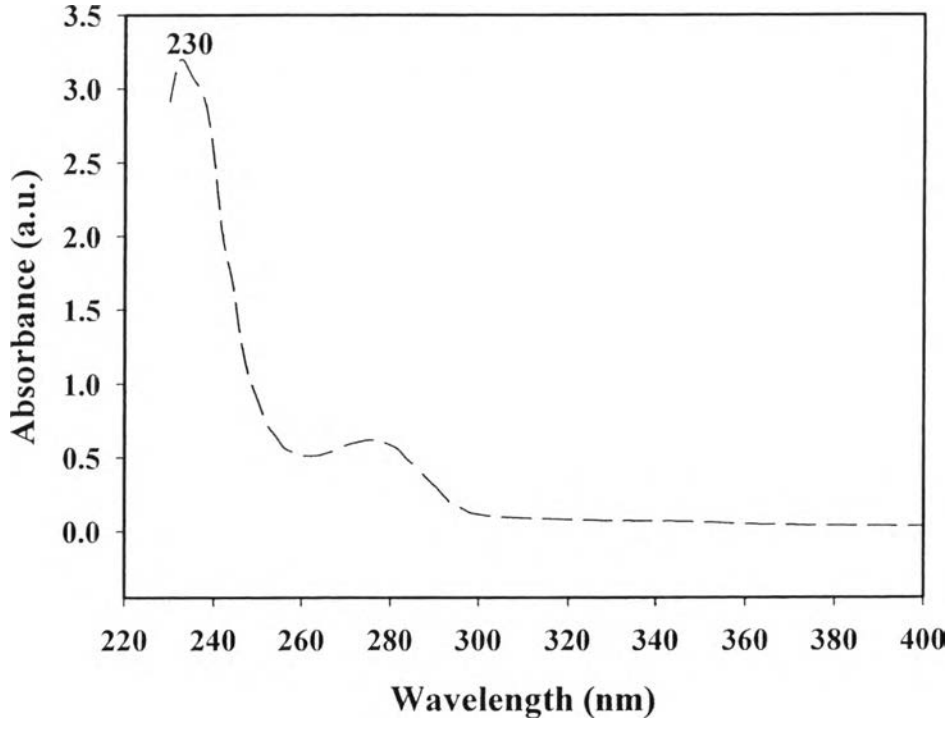


Figure D UV-Visible spectrum of acetylsalicylic acid.

Appendix E Calibration curve of Acetylsalicylic Acid (ASA)

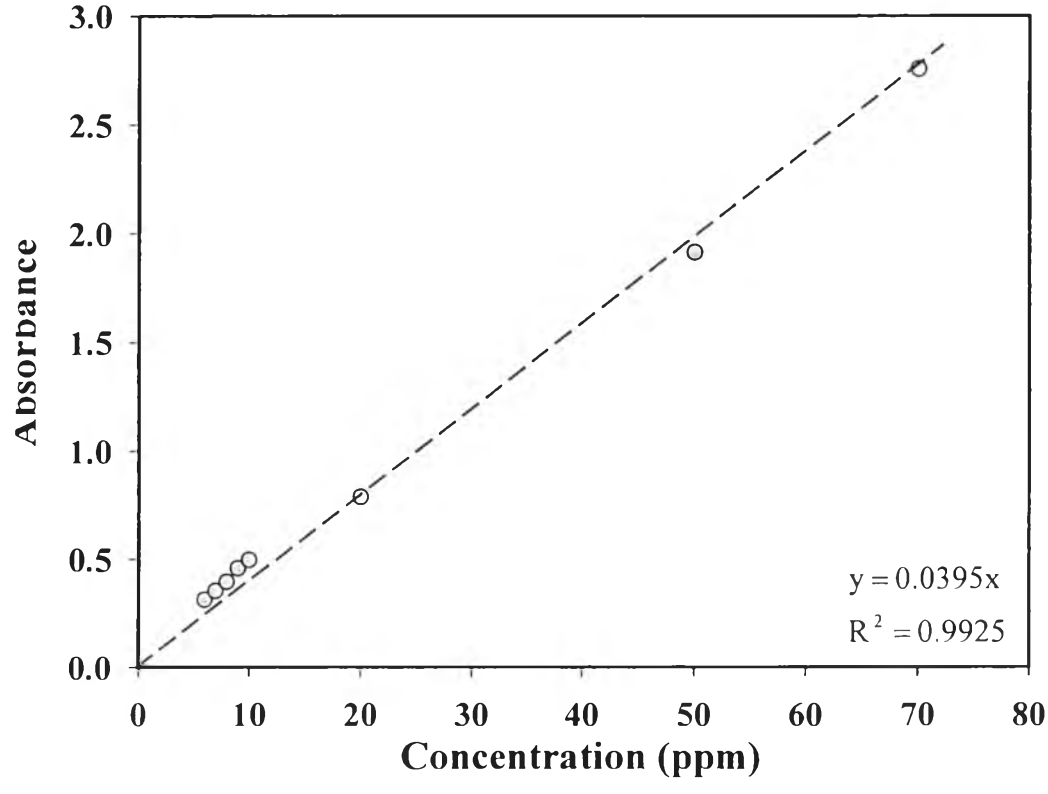


Figure E Calibration curve of acetylsalicylic acid in MES buffer (pH 5.5) at 230 nm.

Table E Raw data for determination of calibration curve of Acetylsalicylic acid at 230 nm

Concentration (ppm)	Absorbance at 230 nm (a.u.)	Average	SD
6	0.3201	0.3132	0.00166
	0.3234		
	0.3220		
7	0.3575	0.3532	0.00425
	0.3532		
	0.349		
8	0.3915	0.3949	0.00398
	0.3993		
	0.3940		
9	0.4490	0.4575	0.00845
	0.4659		
	0.4575		
10	0.5017	0.4974	0.00378
	0.4945		
	0.4961		
20	0.7967	0.7874	0.00915
	0.7874		
	0.7784		
50	1.9188	1.9124	0.00558
	1.9101		
	1.9084		
70	2.7559	2.7562	0.00035
	2.7562		
	2.7566		

Appendix F Determination of Degree of Swelling and Weight Loss of Carrageenan Hydrogels

The degree of swelling and the weight loss of the carrageenan hydrogels were measured in an MES buffer solution at 37°C for 48 h according to the following equations (F1-F2) (Taepaiboon *et al.*, 2006):

$$\text{Degree of swelling (\%)} = \frac{M_s - M_d}{M_d} \times 100 \qquad \text{(F1)}$$

and

$$\text{Weight loss (\%)} = \frac{M_i - M_d}{M_i} \times 100 \qquad \text{(F2)}$$

where M_s = the weight of the sample after submersed in the buffer solution.

M_d = the weight of sample after submersed in the buffer solution as dry state.

M_i = the initial weight of the sample without submersed in the buffer solution as dry state.

The degree of swelling (%) and the weight loss (%) of carrageenan hydrogels with $BaCl_2$ at various crosslinking ratios between 0.4 and 2.0 is illustrated in figure F1. The degree of swelling of Ba-carrageenan hydrogels decrease with increasing crosslinking ratio because crosslinking agent resulting in denser and more rigid hydrogel leading to reduction in the degree of swelling. But the weight loss of crosslinked carrageenan hydrogels increase with increasing crosslinking ratios. As a result, excess salts, which remain in the system, coat on hydrogel surface and dissolve when we study swelling test.

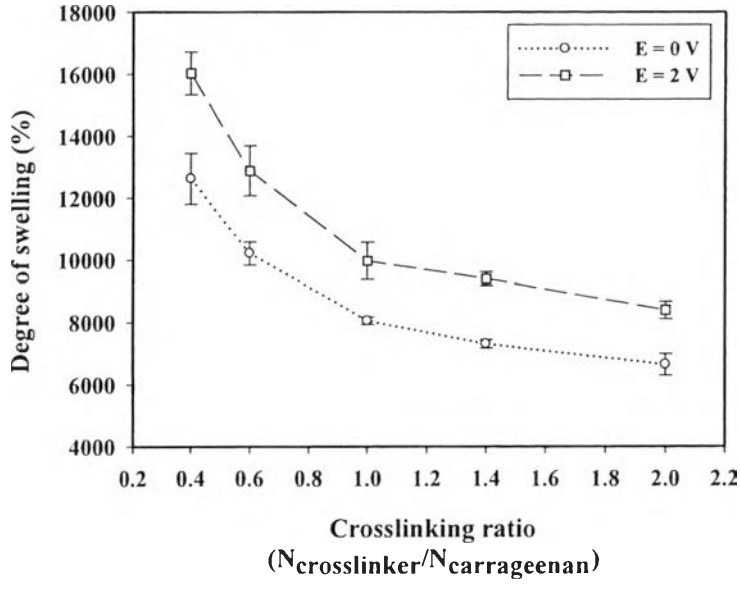


Figure F1 The degree of swelling (%)of carrageenan hydrogels with $BaCl_2$ at various crosslinking ratios between 0.4 and 2.0 (Number of samples = 3) of E = 0 and 2 V.

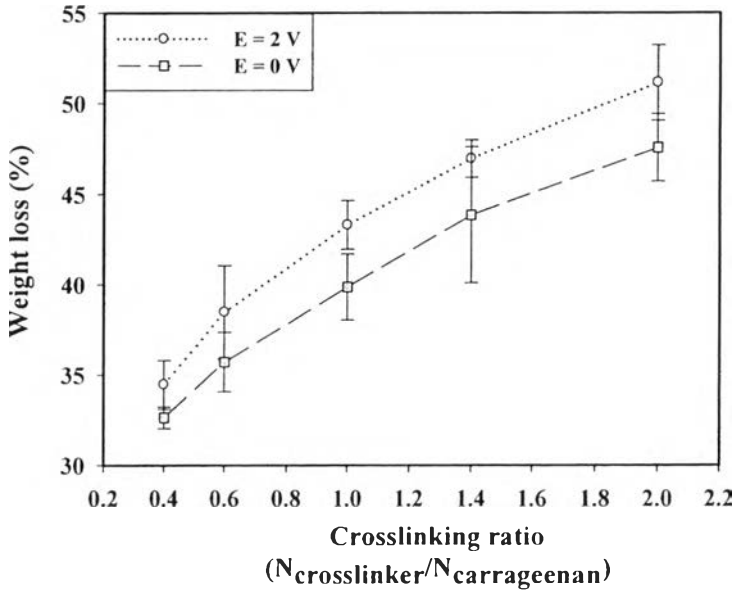


Figure F2 The weight loss (%)of carrageenan hydrogels with $BaCl_2$ at various crosslinking ratios between 0.4 and 2.0 (Number of samples = 3) of E = 0 and 2 V.

Table F1 Value of the degree of swelling (%) and weight loss (%) of carrageenan hydrogels with $BaCl_2$ at various crosslinking ratios (CR) of E = 0 V

Sample	M_i	M_s	M_d	Degree of swelling (%)	Weight loss (%)
CR0.4#1	0.0215	1.7375	0.0146	11,801	32.0
2	0.0192	1.7473	0.0129	13,445	32.8
3	0.0269	2.2960	0.0180	12,656	33.1
Avg				12,634	32.6
SD				822	0.6
CR0.6#1	0.0300	1.9800	0.0196	10,002	34.6
2	0.0231	1.4545	0.0144	10,001	37.7
3	0.0228	1.5904	0.0148	10,646	35.1
Avg				10,216	35.8
SD				372	1.7
CR1.0#1	0.0277	1.4005	0.017	8,138	38.6
2	0.0299	1.4582	0.0182	7,912	39.1
3	0.0298	1.4188	0.0173	8,101	41.9
Avg				8,050	39.9
SD				121	1.8
CR1.4#1	0.0323	1.4353	0.0190	7,454	41.2
2	0.0300	1.1351	0.0156	7,176	48.0
3	0.0291	1.244	0.0168	7,305	42.3
Avg				7,312	43.8
SD				139	3.7

Sample	M_i	M_s	M_d	Degree of swelling (%)	Weight loss (%)
CR2.0#1	0.0318	1.1773	0.0168	6,908	47.2
2	0.0390	1.2525	0.0197	6,258	49.5
3	0.0331	1.2319	0.0179	6,782	45.9
Avg				6,649	47.5
SD				345	1.8

Table F2 Value of the degree of swelling (%) and weight loss (%) of carrageenan hydrogels with $BaCl_2$ at various crosslinking ratios (CR) of E = 2 V

Sample	M_i	M_s	M_d	Degree of swelling (%)	Weight loss (%)
CR0.4#1	0.0365	3.9918	0.0239	16,602	34.5
2	0.0284	2.9206	0.0190	15,272	33.1
3	0.0458	4.8658	0.0298	16,228	34.9
Avg				16,034	34.2
SD				686	1.0
CR0.6#1	0.0321	2.9200	0.0210	13,805	34.6
2	0.0308	2.4035	0.0194	12,289	37.0
3	0.0241	1.8375	0.0145	12,572	39.8
Avg				12,889	37.1
SD				806	2.6
CR1.0#1	0.0271	1.5477	0.0157	9,758	42.1
2	0.0255	1.5904	0.0148	10,646	42.0
3	0.0299	1.6233	0.0169	9,505	43.5
Avg				9,970	42.5
SD				599	0.8
CR1.4#1	0.0324	1.5524	0.0168	9,140	48.1
2	0.0241	1.2534	0.0130	9,542	46.1
3	0.0392	2.0066	0.0209	9,501	46.7
Avg				9,394	47.0
SD				221	1.1

Sample	M_i	M_s	M_d	Degree of swelling (%)	Weight loss (%)
CR2.0#1	0.0583	2.4624	0.0294	8,276	49.6
2	0.0357	1.4622	0.0166	8,708	53.5
3	0.0342	1.4100	0.0170	8,194	50.3
Avg				8,393	51.1
SD				276	2.1

Table F3 Value of the degree of swelling (%) and weight loss (%) of carrageenan hydrogels with $CaCl_2$ at various crosslinking ratios (CR) of E = 0 V

Sample	M_i	M_s	M_d	Degree of swelling (%)	Weight loss (%)
CR1.0#1	0.1872	6.7212	0.1165	5,669	37.8
2	0.1829	6.3523	0.1163	5,362	36.4
3	0.1981	6.6237	0.1186	5,485	40.1
Avg				5,505	38.1
SD				155	1.9
CR2.0#1	0.3509	9.834	0.1904	5,065	45.7
2	0.3555	9.3128	0.1893	4,820	46.8
3	0.3574	9.2707	0.1889	4,808	47.1
Avg				4,897	46.5
SD				145	0.7

Table F4 Value of the degree of swelling (%) and weight loss (%) of carrageenan hydrogels with $MgCl_2$ at various crosslinking ratios (CR) of E = 0 V

Sample	M_i	M_s	M_d	Degree of swelling (%)	Weight loss (%)
CR1.0#1	0.1978	9.5366	0.1282	7,339	35.2
2	0.2100	9.5851	0.1380	6,846	34.3
3	0.1810	9.3231	0.1060	8,695	41.4
Avg				7,627	37.0
SD				958	3.9
CR3.0#1	0.3358	4.8032	0.153	3,039	54.4
2	0.3219	4.3201	0.184	2,248	42.8
3	0.3132	4.0275	0.146	2,659	53.4
Avg				2,649	50.0
SD				396	6

Appendix G Determinaion of the Molecular Weight between Crosslinks, Mesh Size and Crosslinking Density of Carrageenan Hydrogels

To determine the molecular weight between crosslinks, $\bar{M}_c$, the mesh size, ξ, and the crosslinking density, ρ_x, the sample of carrageenan film was cut immediately after crosslinking (1 cm^2 square).This sample was weighted in air and heptane. The sample was then placed in distilled water at 37 °C for 5 days that allow it swelling to equilibrium, then weighted in air and heptane again. Finally, the sample was dried at 25 °C in vacuum oven for 5 days. Once again, it was weighted in air and heptane. These weights were used to calculattion the polymer volume fraction in the relaxed, $\upsilon_{2,r}$, and swollen states, $\upsilon_{2,s}$, respectively(Peppas *et al.*, 1998):

$$\upsilon_{2,r} = \frac{V_d}{V_r} \tag{G1}$$

and

$$\upsilon_{2,s} = \frac{V_d}{V_s} \tag{G2}$$

where V_d = the volumes of the polymer sample in the dry states

V_r = the volumes of the polymer sample in the relaxed states

V_s = the volumes of the polymer sample in the swollen states

The volumes of the polymer sample in the dry, relaxed, and swollen states are calculated by using equations (G3) - (G5),respectively.

$$V_d = \frac{W_{a,d} - W_{h,d}}{\rho_h} \tag{G3}$$

$$V_r = \frac{W_{a,r} - W_{h,r}}{\rho_h} \tag{G4}$$

$$V_s = \frac{W_{a,s} - W_{h,s}}{\rho_h} \qquad \text{(G5)}$$

where W_d = the weights of the dry polymer in air and heptane

W_r = the weights of the relaxed polymer in air and heptane

W_s = the weights of the swollen polymer in air and heptane

and ρ_h = the density of heptane

The molecular weight between crosslinks, $\bar{M}_c$, was calculated from the swelling data by using equation (G6) (Peppas *et al.*, 1998):

$$\frac{1}{\bar{M}_c} = \frac{2}{\bar{M}_n} - \frac{\frac{\bar{v}}{V_1}[\ln(1-v_{2,s}) + v_{2,s} + \chi v_{2,s}^2]}{v_2[\left(\frac{v_{2,s}}{v_{2,r}}\right)^{1/3} - \frac{1}{2}\left(\frac{v_{2,s}}{v_{2,r}}\right)]} \qquad \text{(G6)}$$

where $\bar{M}_n$ = the number-average molecular weight of the polymer before crosslinking (400000)

$\bar{v}$ = the specific volume of carrageenan (0.49 ml/g)

V_1 = the molar volume of water (18.1 cm^3/mol)

x = the Flory interaction parameter of carrageenan (0.44) and the dissociation constant is pKa = 4.7.

Generally, the presence of carrageenan led to a more open network structure and resulted ina higherthe molecular weight between crosslink, $\bar{M}_c$. The hydrogel mesh size, ξ was calculated by using equation (G7) (Peppas *et al.*, 1996).

$$\xi = v_{2,s}^{-1/3}\left[C_n\left(\frac{2\bar{M}_c}{\bar{M}_r}\right)\right]^{1/2} \cdot l \qquad \text{(G7)}$$

where C_n = the Flory characteristic ratio for carrageenan (33)

l = the carbon-carbon bond length of the monomer unit (5.5 Å)

The crosslinking density of the hydrogel, ρ_x, was calculated by using equation (G8) (Peppas *et al.*, 1996).

$$\rho_x = \frac{1}{\bar{v}\bar{M}_c} \qquad \text{(G8)}$$

Table G1 shows the molecular weight between crosslinks, mesh size and crosslinking density of each carrageenan hydrogel with $BaCl_2$ at various crosslinking ratios. The molecular weight between crosslinks increase with decreasing crosslinking ratios or concentration of $BaCl_2$leading to a larger network mesh size. In addition, the lower crosslinked hydrogel has a longer carrageenan strand between crosslinks or a looser network, it can more appreciably swell, and increasing the pore size. In this work, acetylsalicylic acid, ASA is used as the model drug and the mesh of drug is 6.60 Å. The increase in the mesh sizes of hydrogels, drug size/mesh size decrease.

Table G1 Summary of the molecular weight between crosslinks, $\bar{M}_c$, mesh size, ξ, crosslinking density, ρ_x, and drug size/ mesh size, a/ξ, of carrageenan hydrogel with $BaCl_2$ at various crosslinking ratios with and without electric field

Sample	Crosslinking ratio	Number-average molecular weight between crosslinks, $\bar{M}_c$ (g/mol)		Mesh size, ξ (Å)		Crosslinking density, ρ_x (mol/cm^3 × 10^4)	
		E = 0 V	E = 2 V	E = 0 V	E = 2 V	E = 0 V	E = 2 V
Ba-CAR_0.4	0.4	(1.99 ± 0.65) x 10^4	(3.64 ± 0.21) x 10^4	1229 ± 289	1710 ± 112	1.03 ± 0.01	0.96 ± 0.15
Ba-CAR_0.6	0.6	(1.52 ± 0.68) x 10^4	(2.41 ± 0.16) x 10^4	713 ± 162	972 ± 164	1.34 ± 0.20	1.21 ± 0.13
Ba-CAR_1.0	1.0	(0.93 ± 0.10) x 10^4	(1.86 ± 0.09) x 10^4	656 ± 49	794 ± 104	2.19 ± 0.05	2.05 ± 0.05
Ba-CAR_1.4	1.4	(0.84 ± 0.02) x 10^4	(1.72 ± 0.15) x 10^4	451 ± 121	634 ± 79	2.43 ± 0.12	2.31 ± 0.21
Ba-CAR_2.0	2.0	(0.33 ± 0.05) x 10^4	(0.96 ± 0.07) x 10^4	265 ± 10	356 ± 34	6.18 ± 0.09	6.04 ± 0.11
Ca-CAR_1.0	1.0	(7.89 ± 0.12) x 10^3	(8.96 ± 0.04) x 10^3	99 ± 7	154 ± 16	9.42 ± 0.03	9.15 ± 0.31
Mg-CAR_1.0	1.0	(6.39 ± 0.09) x 10^3	(7.59 ± 0.11) x 10^3	90 ± 4	113 ± 21	15.01 ± 0.31	14.81 ± 0.08
Ca-CAR_2.0	2.0	(3.32 ± 0.13) x 10^3	(4.73 ± 0.15) x 10^3	57 ± 11	78 ± 17	23.15 ± 0.21	21.03 ± 1.21
Mg-CAR_3.0	3.0	(1.33 ± 0.04) x 10^3	(2.12 ± 0.05) x 10^3	25 ± 4	42 ± 11	44.21 ± 8.76	29.26 ± 5.12

Appendix H Determination of Actual Drug Content

The actual amount of drug in the acetylsalicylic acid-loaded carrageenan hydrogel, circular disc about 2.5 cm in diameter, was measured by dissolving the sample in 5 ml of dimethylsulfoxide (DMSO) and then 0.1 ml of the solution was added into 0.4 ml of DMSO. The amounts of drugs in the solution were quantified by using the UV-Visible spectrophotometer at a wavelength of 230 nm.

The actual amount of drugs present in the sample was reported as the percentage of the initial content of drug loaded in carrageenan solution. The actual amount of acetylsalicylic acid presented in the sample is about 95.16 ± 4.57 %.

Table H1 The raw data of the determination of actual amount of acetylsalicylic acid in the samples

Sample	Absorbance intensity	Concentration (mg/l)	Actual amount of drug (%)
1	0.2275	9.6325	96.32
2	0.2088	8.8407	88.41
3	0.2325	9.8442	98.44
4	0.2195	9.2938	92.94
5	0.2355	9.9712	99.71
Avg			95.16
SD			4.57

Appendix I Determination of Amounts and Diffusion Coefficient of Acetylsalicylic Acid Released from Acetylsalicylic Acid-Loaded Carrageenan Hydrogel at Various Crosslinking Ratios in an Absence of Electric field

The diffusion coefficients were studied by using the modified Franz-Diffusion cells which consists of two half-cells. The first is the donor half cell that is exposed to ambient condition. The second part is the receptor half cell that is exposed to 2-(N-morpholino)ethanesulfonic acid buffer (MES buffer) solution pH 5.5 at 37°C by a circulating water bath. The drug-loaded carrageenan hydrogels with various crosslinking ratios were placed over the nylon net on the top of the receptor chamber. The drug diffuses through the polymer matrix and the net towards the buffer solution. The 0.1 ml of solution was withdrawn and simultaneously replaced with equal volume of fresh buffer solution at various time intervals. The drug concentrations in these samples were determined by the UV-Visible spectrophotometer at the wavelength of 230 nm.

The amounts of acetylsalicylic acid (ASA) released from acetylsalicylic acid-loaded carrageenan hydrogels versus time at various crosslinking ratios in an absence of electric field during 48 h are shown in Figure I1. The amounts of drug released gradually increase with time and then reach constant values. But the amounts of drug released decrease with increasing crosslinking ratios.

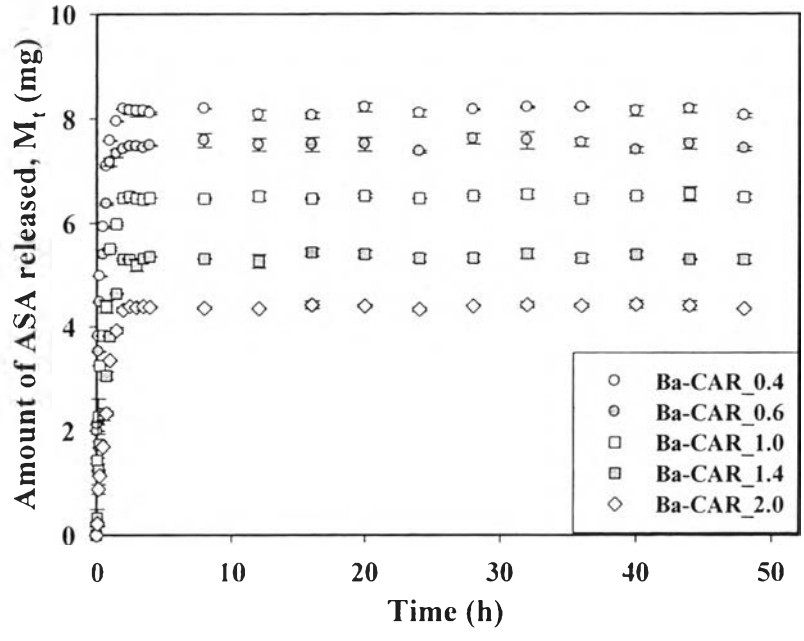


Figure I1 Amounts of acetylsalicylic acid released from acetylsalicylic acid-loaded carrageenan hydrogels versus time at various crosslinking ratios, E = 0 V, pH 5.5, and at 37 °C, n = number of samples = 3.

Table I1 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_0.4 at time t, pH 5.5 at 37 °C, in an absence of electric field

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0470	0.0469	0.0499	1.99	1.99	2.11	**2.03**	**0.07**
0.16667	0.0904	0.0900	0.1020	3.83	3.81	4.32	**3.99**	**0.29**
0.25	0.1177	0.1174	0.1180	4.98	4.97	5.00	**4.98**	**0.01**
0.5	0.1404	0.1396	0.1414	5.94	5.91	5.99	**5.95**	**0.04**
0.75	0.1672	0.1680	0.1725	7.08	7.11	7.30	**7.17**	**0.12**
1	0.1792	0.1790	0.1815	7.59	7.58	7.68	**7.62**	**0.06**
1.5	0.1877	0.1880	0.1912	7.95	7.96	8.10	**8.00**	**0.08**
2	0.1937	0.1933	0.1943	8.20	8.18	8.23	**8.20**	**0.02**
2.5	0.1916	0.1941	0.1929	8.11	8.22	8.17	**8.17**	**0.05**
3	0.1906	0.1943	0.1932	8.07	8.23	8.18	**8.16**	**0.08**
3.5	0.1909	0.1942	0.1919	8.08	8.22	8.13	**8.14**	**0.07**
4	0.1912	0.1919	0.1925	8.09	8.13	8.15	**8.12**	**0.03**
8	0.1934	0.1936	0.1949	8.19	8.20	8.25	**8.21**	**0.03**
12	0.1890	0.1923	0.1917	8.00	8.14	8.12	**8.09**	**0.07**
16	0.1915	0.1895	0.1920	8.11	8.02	8.13	**8.09**	**0.06**
20	0.1927	0.1955	0.1918	8.16	8.28	8.12	**8.19**	**0.08**
24	0.1903	0.1926	0.1921	8.06	8.15	8.13	**8.12**	**0.05**
28	0.1934	0.1928	0.1899	8.19	8.16	8.04	**8.13**	**0.08**
32	0.1946	0.1939	0.1923	8.24	8.21	8.14	**8.20**	**0.05**
36	0.1940	0.1944	0.1913	8.22	8.23	8.10	**8.18**	**0.07**
40	0.1909	0.1941	0.1936	8.08	8.22	8.20	**8.17**	**0.07**
44	0.1947	0.1922	0.1922	8.25	8.14	8.14	**8.17**	**0.06**
48	0.1897	0.1911	0.1909	8.03	8.09	8.08	**8.07**	**0.03**

Table I2 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_0.6 at time t, pH 5.5 at 37 °C, in an absence of electric field

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0500	0.0502	0.0510	2.12	2.13	2.16	**2.13**	**0.02**
0.16667	0.0834	0.0831	0.0811	3.53	3.52	3.43	**3.52**	**0.01**
0.25	0.1060	0.1055	0.1049	4.49	4.47	4.44	**4.48**	**0.02**
0.5	0.1273	0.1274	0.1299	5.39	5.39	5.50	**5.39**	**0.00**
0.75	0.1502	0.1509	0.1499	6.36	6.39	6.35	**6.37**	**0.02**
1	0.1682	0.1707	0.1695	7.12	7.23	7.18	**7.17**	**0.07**
1.5	0.1720	0.1745	0.1755	7.28	7.39	7.43	**7.34**	**0.07**
2	0.1752	0.1754	0.1769	7.42	7.43	7.49	**7.42**	**0.00**
2.5	0.1764	0.1767	0.1801	7.47	7.48	7.63	**7.48**	**0.01**
3	0.1760	0.1770	0.1798	7.45	7.49	7.61	**7.47**	**0.03**
3.5	0.1763	0.1753	0.1740	7.46	7.42	7.37	**7.44**	**0.03**
4	0.1768	0.1772	0.1794	7.49	7.50	7.60	**7.49**	**0.01**
8	0.1770	0.1814	0.1784	7.49	7.68	7.55	**7.59**	**0.13**
12	0.1753	0.1793	0.1756	7.42	7.59	7.44	**7.51**	**0.12**
16	0.1751	0.1797	0.1754	7.41	7.61	7.43	**7.51**	**0.14**
20	0.1754	0.1797	0.1783	7.43	7.61	7.55	**7.52**	**0.13**
24	0.1738	0.1746	0.1758	7.36	7.39	7.44	**7.38**	**0.03**
28	0.1783	0.1816	0.1734	7.55	7.69	7.34	**7.62**	**0.10**
32	0.1765	0.1820	0.1746	7.47	7.71	7.39	**7.59**	**0.16**
36	0.1769	0.1796	0.1784	7.49	7.60	7.55	**7.55**	**0.08**
40	0.1760	0.1739	0.1756	7.45	7.37	7.44	**7.41**	**0.06**
44	0.1760	0.1793	0.1788	7.45	7.59	7.57	**7.52**	**0.10**
48	0.1762	0.1750	0.1728	7.46	7.41	7.32	**7.43**	**0.04**

Table I3 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_1.0 at time t, pH 5.5 at 37 °C, in an absence of electric field

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0345	0.0327	0.0333	1.46	1.38	1.41	**1.42**	**0.04**
0.16667	0.0592	0.0479	0.0548	2.51	2.03	2.32	**2.29**	**0.24**
0.25	0.0769	0.0768	0.0749	3.26	3.25	3.17	**3.23**	**0.05**
0.5	0.0902	0.0908	0.0990	3.82	3.84	4.19	**3.95**	**0.21**
0.75	0.1058	0.1016	0.1049	4.48	4.30	4.44	**4.41**	**0.09**
1	0.1295	0.1305	0.1342	5.48	5.53	5.68	**5.56**	**0.10**
1.5	0.1419	0.1410	0.1451	6.01	5.97	6.14	**6.04**	**0.09**
2	0.1531	0.1532	0.1520	6.48	6.49	6.44	**6.47**	**0.03**
2.5	0.1537	0.1542	0.1549	6.51	6.53	6.56	**6.53**	**0.03**
3	0.1530	0.1532	0.1547	6.48	6.49	6.55	**6.50**	**0.04**
3.5	0.1526	0.1526	0.1567	6.46	6.46	6.63	**6.52**	**0.10**
4	0.1533	0.1533	0.1542	6.49	6.49	6.53	**6.50**	**0.02**
8	0.1525	0.1533	0.1568	6.46	6.49	6.64	**6.53**	**0.10**
12	0.1527	0.1554	0.1537	6.47	6.58	6.51	**6.52**	**0.06**
16	0.1532	0.1526	0.1545	6.49	6.46	6.54	**6.50**	**0.04**
20	0.1535	0.1549	0.1584	6.50	6.56	6.71	**6.59**	**0.11**
24	0.1531	0.1529	0.1575	6.48	6.47	6.67	**6.54**	**0.11**
28	0.1538	0.1548	0.1564	6.51	6.55	6.62	**6.56**	**0.06**
32	0.1535	0.1564	0.1557	6.50	6.62	6.59	**6.57**	**0.06**
36	0.1535	0.1524	0.1550	6.50	6.45	6.56	**6.50**	**0.06**
40	0.1535	0.1549	0.1531	6.50	6.56	6.48	**6.51**	**0.04**
44	0.1527	0.1574	0.1584	6.47	6.66	6.71	**6.61**	**0.13**
48	0.1527	0.1546	0.1546	6.46	6.55	6.55	**6.52**	**0.05**

Table I4 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_1.4 at time t, pH 5.5 at 37 °C, in an absence of electric field

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0105	0.0048	0.0099	0.44	0.20	0.42	**0.36**	**0.13**
0.16667	0.0295	0.0288	0.0254	1.25	1.22	1.08	**1.18**	**0.09**
0.25	0.0399	0.0419	0.0444	1.69	1.77	1.88	**1.78**	**0.1**
0.5	0.0527	0.0567	0.0546	2.23	2.40	2.31	**2.31**	**0.08**
0.75	0.0709	0.0734	0.0749	3.00	3.11	3.17	**3.09**	**0.09**
1	0.0900	0.0905	0.0946	3.81	3.83	4.01	**3.88**	**0.11**
1.5	0.1098	0.1093	0.1106	4.65	4.63	4.68	**4.65**	**0.03**
2	0.1249	0.1257	0.1277	5.29	5.32	5.41	**5.34**	**0.06**
2.5	0.1250	0.1255	0.1264	5.29	5.31	5.35	**5.32**	**0.03**
3	0.1244	0.1205	0.1249	5.27	5.10	5.29	**5.22**	**0.1**
3.5	0.1255	0.1258	0.1212	5.31	5.33	5.13	**5.26**	**0.11**
4	0.1265	0.1265	0.1241	5.36	5.36	5.25	**5.32**	**0.06**
8	0.1257	0.1254	0.1279	5.32	5.31	5.42	**5.35**	**0.06**
12	0.1265	0.1222	0.1287	5.36	5.17	5.45	**5.33**	**0.14**
16	0.1272	0.1296	0.1245	5.38	5.49	5.27	**5.38**	**0.11**
20	0.1265	0.1288	0.1257	5.36	5.45	5.32	**5.38**	**0.07**
24	0.1269	0.1245	0.1248	5.37	5.27	5.28	**5.31**	**0.06**
28	0.1270	0.1247	0.1266	5.38	5.28	5.36	**5.34**	**0.05**
32	0.1262	0.1294	0.1278	5.34	5.48	5.41	**5.41**	**0.07**
36	0.1270	0.1246	0.1284	5.38	5.28	5.44	**5.37**	**0.08**
40	0.1264	0.1286	0.1294	5.35	5.45	5.48	**5.43**	**0.07**
44	0.1255	0.1251	0.1238	5.31	5.30	5.24	**5.28**	**0.04**
48	0.1266	0.1239	0.1259	5.36	5.25	5.33	**5.31**	**0.06**

Table I5 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_2.0 at time t, pH 5.5 at 37 °C, in an absence of electric field

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0045	0.0057	0.0049	0.19	0.24	0.21	**0.21**	**0.03**
0.16667	0.0192	0.0223	0.0214	0.81	0.94	0.91	**0.89**	**0.07**
0.25	0.0269	0.0268	0.0251	1.14	1.13	1.06	**1.11**	**0.04**
0.5	0.0402	0.0397	0.0384	1.70	1.68	1.63	**1.67**	**0.04**
0.75	0.0558	0.0544	0.0512	2.36	2.30	2.17	**2.28**	**0.10**
1	0.0795	0.0789	0.0745	3.37	3.34	3.15	**3.29**	**0.12**
1.5	0.0919	0.0939	0.0943	3.89	3.98	3.99	**3.95**	**0.05**
2	0.1031	0.1014	0.1029	4.37	4.29	4.36	**4.34**	**0.04**
2.5	0.1037	0.1041	0.1055	4.39	4.41	4.47	**4.42**	**0.04**
3	0.1030	0.1039	0.1064	4.36	4.40	4.51	**4.42**	**0.08**
3.5	0.1026	0.1051	0.1028	4.34	4.45	4.35	**4.38**	**0.06**
4	0.1033	0.1038	0.1046	4.37	4.39	4.43	**4.40**	**0.03**
8	0.1025	0.1035	0.1037	4.34	4.38	4.39	**4.37**	**0.03**
12	0.1027	0.1029	0.1034	4.35	4.36	4.38	**4.36**	**0.02**
16	0.1032	0.1057	0.1069	4.37	4.48	4.53	**4.46**	**0.08**
20	0.1035	0.1045	0.1001	4.38	4.42	4.24	**4.35**	**0.10**
24	0.1031	0.1017	0.1051	4.37	4.31	4.45	**4.37**	**0.07**
28	0.1038	0.1043	0.1027	4.40	4.42	4.35	**4.39**	**0.03**
32	0.1035	0.1056	0.1022	4.38	4.47	4.33	**4.39**	**0.07**
36	0.1035	0.1048	0.1056	4.38	4.44	4.47	**4.43**	**0.04**
40	0.1035	0.1060	0.1048	4.38	4.49	4.44	**4.44**	**0.05**
44	0.1027	0.1057	0.1067	4.35	4.48	4.52	**4.45**	**0.09**
48	0.1027	0.1029	0.1062	4.35	4.36	4.50	**4.40**	**0.08**

Table I6 The raw data of the determination of amounts of acetylsalicylic acid released from Ca-CAR_1.0 at time t, pH 5.5 at 37 °C, in an absence of electric field

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0069	0.0055	0.0049	0.29	0.23	0.21	**0.24**	**0.04**
0.16667	0.0148	0.0152	0.0102	0.63	0.64	0.43	**0.57**	**0.12**
0.25	0.0222	0.0256	0.0249	0.94	1.08	1.05	**1.03**	**0.08**
0.5	0.0387	0.0395	0.0354	1.64	1.67	1.50	**1.60**	**0.09**
0.75	0.0554	0.0524	0.0498	2.35	2.22	2.11	**2.23**	**0.12**
1	0.0609	0.0652	0.0664	2.58	2.76	2.81	**2.72**	**0.12**
1.5	0.0784	0.0796	0.0754	3.32	3.37	3.19	**3.29**	**0.09**
2	0.0859	0.0860	0.0894	3.64	3.64	3.79	**3.69**	**0.08**
2.5	0.0889	0.0843	0.0878	3.76	3.57	3.72	**3.68**	**0.10**
3	0.0864	0.0893	0.0845	3.66	3.78	3.58	**3.67**	**0.10**
3.5	0.0851	0.0874	0.0847	3.60	3.70	3.59	**3.63**	**0.06**
4	0.0897	0.0836	0.0894	3.80	3.54	3.79	**3.71**	**0.15**
8	0.0827	0.0890	0.0867	3.50	3.77	3.67	**3.65**	**0.14**
12	0.0849	0.0854	0.0887	3.59	3.62	3.76	**3.66**	**0.09**
16	0.0867	0.0861	0.0869	3.67	3.65	3.68	**3.67**	**0.02**
20	0.0882	0.0886	0.0857	3.73	3.75	3.63	**3.70**	**0.07**
24	0.0885	0.0829	0.0898	3.75	3.51	3.80	**3.69**	**0.16**
28	0.0847	0.0862	0.0865	3.59	3.65	3.66	**3.63**	**0.04**
32	0.0856	0.0909	0.0879	3.62	3.85	3.72	**3.73**	**0.11**
36	0.0847	0.0916	0.0887	3.59	3.88	3.76	**3.74**	**0.15**
40	0.0854	0.0855	0.0868	3.62	3.62	3.68	**3.64**	**0.03**
44	0 0865	0.0898	0.0839	3.66	3.80	3.55	**3.67**	**0.12**
48	0 0874	0.0846	0.0879	3.70	3.58	3.72	**3.67**	**0.08**

Table I7 The raw data of the determination of amounts of acetylsalicylic acid released from Mg-CAR_1.0 at time t, pH 5.5 at 37 °C, in an absence of electric field

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0049	0.0054	0.0064	0.21	0.23	0.27	**0.24**	**0.03**
0.16667	0.0128	0.0119	0.0154	0.54	0.50	0.65	**0.57**	**0.08**
0.25	0.0225	0.0249	0.0217	0.95	1.05	0.92	**0.97**	**0.07**
0.5	0.0338	0.0347	0.0354	1.43	1.47	1.50	**1.47**	**0.03**
0.75	0.0469	0.0458	0.0487	1.98	1.94	2.06	**2.00**	**0.06**
1	0.0561	0.0554	0.0598	2.37	2.35	2.53	**2.42**	**0.10**
1.5	0.0671	0.0697	0.0687	2.84	2.95	2.91	**2.90**	**0.06**
2	0.0725	0.0716	0.0701	3.07	3.03	2.97	**3.02**	**0.05**
2.5	0.0751	0.0768	0.0749	3.18	3.25	3.17	**3.20**	**0.04**
3	0.0762	0.0777	0.0784	3.23	3.29	3.32	**3.28**	**0.05**
3.5	0.0818	0.0800	0.0789	3.46	3.39	3.34	**3.40**	**0.06**
4	0.0805	0.0812	0.0800	3.41	3.44	3.39	**3.41**	**0.03**
8	0.0775	0.0794	0.0784	3.28	3.36	3.32	**3.32**	**0.04**
12	0.0809	0.0784	0.0745	3.43	3.32	3.15	**3.30**	**0.14**
16	0.0769	0.0758	0.0796	3.26	3.21	3.37	**3.28**	**0.08**
20	0.0774	0.0786	0.0785	3.28	3.33	3.32	**3.31**	**0.03**
24	0.0804	0.0795	0.0773	3.40	3.37	3.27	**3.35**	**0.07**
28	0.0790	0.0782	0.0792	3.34	3.31	3.35	**3.34**	**0.02**
32	0.0780	0.0732	0.0783	3.30	3.10	3.32	**3.24**	**0.12**
36	0.0789	0.0795	0.0771	3.34	3.37	3.26	**3.32**	**0.05**
40	0.0755	0.0793	0.0763	3.20	3.36	3.23	**3.26**	**0.09**
44	0.0780	0.0803	0.0794	3.30	3.40	3.36	**3.35**	**0.05**
48	0.0802	0.0789	0.0787	3.39	3.34	3.33	**3.36**	**0.03**

Table I8 The raw data of the determination of amounts of acetylsalicylic acid released from Ca-CAR_2.0 at time t, pH 5.5 at 37 °C, in an absence of electric field

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0067	0.0059	0.0070	0.28	0.25	0.30	**0.28**	**0.02**
0.16667	0.0105	0.0125	0.0119	0.44	0.53	0.50	**0.49**	**0.04**
0.25	0.0187	0.0178	0.0164	0.79	0.75	0.69	**0.75**	**0.05**
0.5	0.0255	0.0224	0.0211	1.08	0.95	0.89	**0.97**	**0.10**
0.75	0.0355	0.0345	0.0334	1.50	1.46	1.41	**1.46**	**0.04**
1	0.0416	0.0409	0.0445	1.76	1.73	1.88	**1.79**	**0.08**
1.5	0.0495	0.0478	0.0489	2.10	2.02	2.07	**2.06**	**0.04**
2	0.0605	0.0621	0.0598	2.56	2.63	2.53	**2.57**	**0.05**
2.5	0.0654	0.0648	0.0664	2.77	2.74	2.81	**2.77**	**0.03**
3	0.0669	0.0678	0.0694	2.83	2.87	2.94	**2.88**	**0.05**
3.5	0.0680	0.0697	0.0645	2.88	2.95	2.73	**2.85**	**0.11**
4	0.0684	0.0668	0.0687	2.90	2.83	2.91	**2.88**	**0.04**
8	0.0696	0.0649	0.0648	2.95	2.75	2.74	**2.81**	**0.12**
12	0.0637	0.0685	0.0689	2.70	2.90	2.92	**2.84**	**0.12**
16	0.0688	0.0654	0.0678	2.91	2.77	2.87	**2.85**	**0.07**
20	0.0705	0.0675	0.0665	2.99	2.86	2.82	**2.89**	**0.09**
24	0.0636	0.0698	0.0683	2.69	2.96	2.89	**2.85**	**0.14**
28	0.0612	0.0648	0.0661	2.59	2.74	2.80	**2.71**	**0.11**
32	0.0628	0.0665	0.0691	2.66	2.82	2.93	**2.80**	**0.13**
36	0.0688	0.0689	0.0667	2.91	2.92	2.82	**2.88**	**0.05**
40	0.0658	0.0644	0.0682	2.79	2.73	2.89	**2.80**	**0.08**
44	0.0699	0.0651	0.0693	2.96	2.76	2.93	**2.88**	**0.11**
48	0.0649	0.0653	0.0678	2.75	2.76	2.87	**2.79**	**0.07**

Table I9 The Raw data of the determination of amounts of acetylsalicylic acid released from Mg-CAR_3.0 at time t, pH 5.5 at 37 °C, in an absence of electric field

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0029	0.0033	0.0044	0.12	0.14	0.19	**0.15**	**0.03**
0.16667	0.0079	0.0087	0.0069	0.33	0.37	0.29	**0.33**	**0.04**
0.25	0.0125	0.0134	0.0145	0.53	0.57	0.61	**0.57**	**0.04**
0.5	0.0175	0.0187	0.0182	0.74	0.79	0.77	**0.77**	**0.03**
0.75	0.0229	0.0212	0.0234	0.97	0.90	0.99	**0.95**	**0.05**
1	0.0275	0.0298	0.0289	1.16	1.26	1.22	**1.22**	**0.05**
1.5	0.0313	0.0323	0.0331	1.33	1.37	1.40	**1.36**	**0.04**
2	0.0336	0.0348	0.0354	1.42	1.47	1.50	**1.47**	**0.04**
2.5	0.0364	0.0379	0.0384	1.54	1.60	1.63	**1.59**	**0.04**
3	0.0381	0.0389	0.0397	1.61	1.65	1.68	**1.65**	**0.03**
3.5	0.0385	0.0401	0.0381	1.63	1.70	1.61	**1.65**	**0.04**
4	0.0397	0.0399	0.0413	1.68	1.69	1.75	**1.71**	**0.04**
8	0.0404	0.0403	0.0415	1.71	1.71	1.76	**1.72**	**0.03**
12	0.0431	0.0412	0.0423	1.82	1.74	1.79	**1.79**	**0.04**
16	0.0395	0.0389	0.0389	1.67	1.65	1.65	**1.66**	**0.01**
20	0.0398	0.0378	0.0379	1.69	1.60	1.60	**1.63**	**0.05**
24	0.0420	0.0403	0.0401	1.78	1.71	1.70	**1.73**	**0.04**
28	0.0382	0.0415	0.0406	1.62	1.76	1.72	**1.70**	**0.07**
32	0.0364	0.0397	0.0398	1.54	1.68	1.69	**1.64**	**0.08**
36	0.0373	0.0406	0.0387	1.58	1.72	1.64	**1.65**	**0.07**
40	0.0401	0.0418	0.0388	1.70	1.77	1.64	**1.70**	**0.06**
44	0.0425	0.0412	0.0412	1.80	1.74	1.74	**1.76**	**0.03**
48	0.0397	0.0394	0.0427	1.68	1.67	1.81	**1.72**	**0.08**

Release Kinetics of Model Drug from Drug-Loaded Carrageenan Hydrogel

The study of acetylsalicylic acid transport mechanism from the carrageenan hydrogels, Fickian diffusion models are considered to fit the experimental data.

The power law model is described by the Ritger-Peppas equation (Venkatesh *et al.*, 1992):

$$\frac{M_t}{M_\infty} = k_1 t^n \qquad \text{(I1)}$$

where M_t/M_∞ = the fractional drug release

k_1 = a kinetic constant (with the unit of T^{-n})

t = the release time

and n = the scaling exponent that can be related to the drug transport mechanism.

For a thin hydrogel film, when n = 0.5, the drug release mechanism is observed by the Fickian diffusion:

$$\frac{M_t}{M_\infty} = k_H t^{1/2} \qquad \text{(I2)}$$

where M_t/M_∞ = the fractional drug release

k_H = a kinetic constant (with the unit of T^{-n})

and t = the release time.

The diffusion coefficients of acetylsalicylic acid from the carrageenan hydrogels are determined from the slopes of plots of drug accumulation versus square root of time according to Higuchi's equation (Higuchi, 1961):

$$Q = \frac{M_t}{A} = 2C_0(Dt/\pi)^{1/2} \qquad \text{(I3)}$$

where Q = the amount of material flowing through a unit cross section of barrier (g/cm^2) in unit time, t (s)

C_0 = the initial drug concentration in the hydrogel (g/cm^3)

and D = the diffusion coefficient of a drug (cm^2/s)

The diffusion coefficients of each system were calculated from the slopes of the plot of the amounts of acetylsalicylic acid released from acetylsalicylic acid-loaded carrageenan hydrogels at time t versus time$^{1/2}$ at various crosslinking ratios in an absence of electric field during 48 h using the Higuchi's equation (see figure I2).

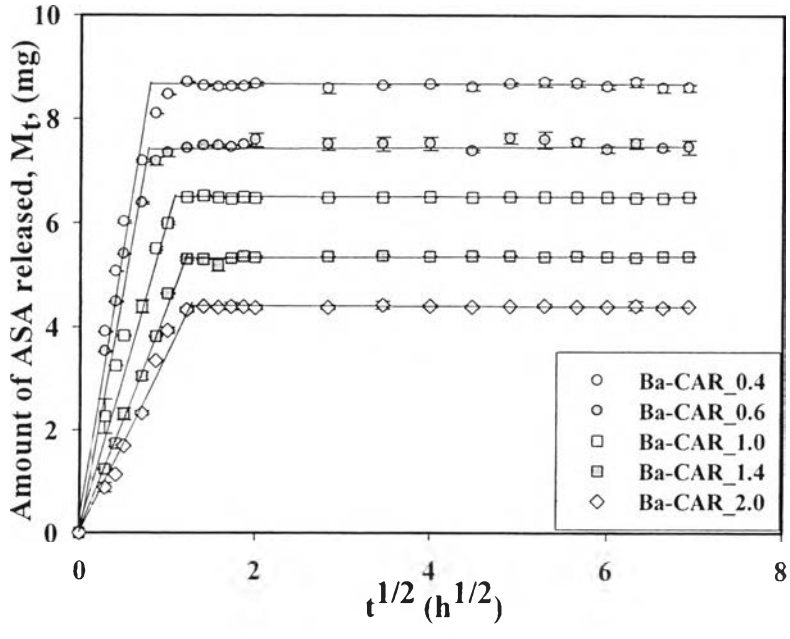


Figure I2 Amounts of acetylsalicylic acid release from acetylsalicylic acid-loaded carrageenan hydrogels versus time$^{1/2}$ at various crosslink ratios, E = 0 V, pH 5.5, and at 37°C, number of samples = 3.

Figure I3 shows the diffusion coefficients of acetylsalicylic acid from carrageenan hydrogels versus crosslinking ratio without electric field at 37 °C.

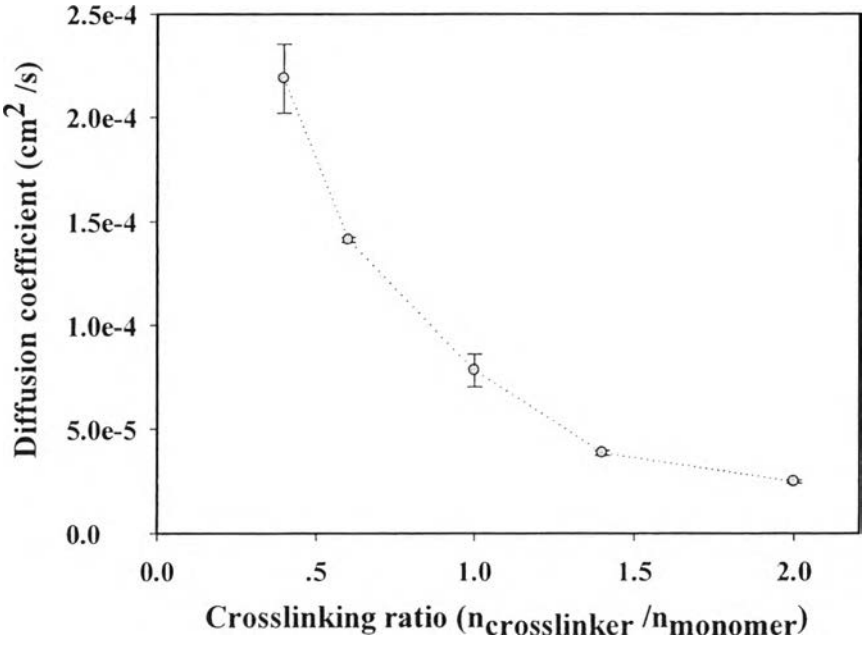


Figure I3 Diffusion coefficients of acetylsalicylic acid from carrageenan hydrogels versus crosslinking ratio, E = 0 V, pH 5.5, 37°C, number of samples = 3.

Figure I4 shows the diffusion coefficients of acetylsalicylic acid from carrageenan hydrogels versus mesh size without electric field at 37 °C.

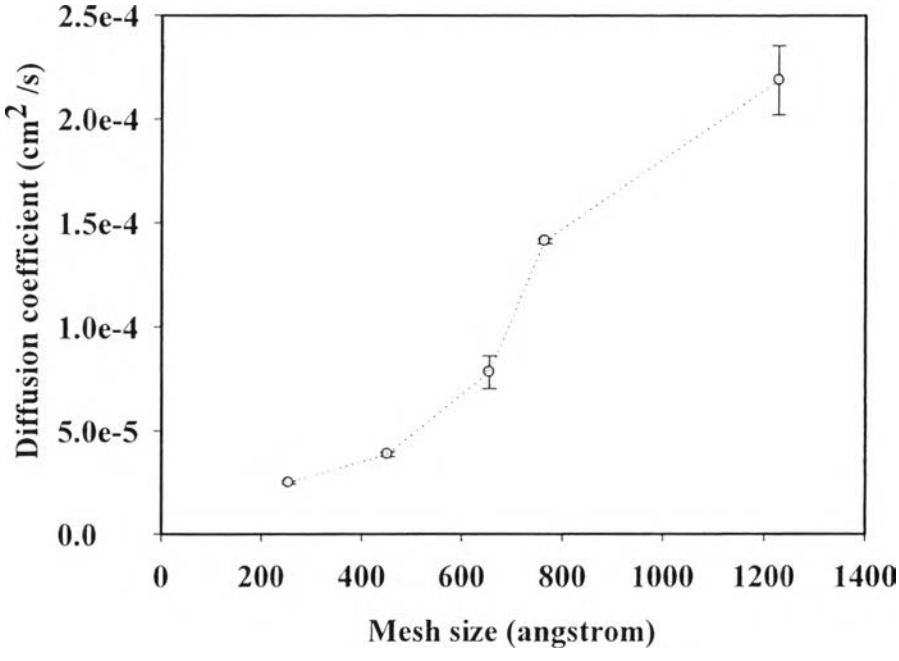


Figure I4 Diffusion coefficients of acetylsalicylic acid from carrageenan hydrogels versus mesh size, E = 0 V, pH 5.5, 37°C, number of samples = 3.

Table I10 The raw data of the determination of the diffusion coefficients of acetylsalicylic acid released from various crosslinked carrageenan hydrogels, pH 5.5 at 37°C, E = 0 V

Sample	Slope			Diffusion Coefficient (cm^2/s)				
	1	2	3	1	2	3	Avg	SD
Ba-CAR_0.4	10.45	10.45	11.15	2.09E-04	2.09E-04	2.38E-04	**2.19E-04**	**1.67E-05**
Ba-CAR_0.6	8.54	8.62	8.61	1.40E-04	1.42E-04	1.42E-04	**1.41E-04**	**1.15E-06**
Ba-CAR_1.0	6.50	6.02	6.64	8.10E-05	6.94E-05	8.45E-05	**7.83E-05**	**7.90E-06**
Ba-CAR_1.4	4.40	4.52	4.53	3.71E-05	3.91E-05	3.93E-05	**3.85E-05**	**1.22E-06**
Ba-CAR_2.0	3.65	3.61	3.55	2.55E-05	2.49E-05	2.41E-05	**2.48E-05**	**7.02E-07**
Ca-CAR_1.0	3.12	3.07	3.07	1.86E-05	1.81E-05	1.81E-05	**1.82E-05**	**3.15E-07**
Mg-CAR_1.0	2.75	2.79	2.86	1.45E-05	1.49E-05	1.57E-05	**1.50E-05**	**6.04E-07**
Ca-CAR_2.0	2.07	2.05	2.04	8.23E-06	8.05E-06	7.97E-06	**8.09E-06**	**1.34E-07**
Mg-CAR_3.0	1.35	1.39	1.41	3.47E-06	3.70E-06	3.81E-06	**3.66E-06**	**1.74E-07**

Appendix J Determination of Amounts and Diffusion Coefficient of Acetylsalicylic Acid Released from Acetylsalicylic Acid-Loaded Carrageenan Hydrogel at Various Crosslinking Agents in an Absence of Electric field

The amounts of acetylsalicylic acid (ASA) released from acetylsalicylic acid-loaded carrageenan hydrogels versus time at various crosslinking agents in an absence of electric field during 48 h are shown in Figure J1. The amounts of drug released gradually increase with time and then reach constant values. But the amounts of drug released decrease with decreasing the ion size of crosslinking agent (the ion size of barium is the biggest follow by calcium and magnesium, respectively) (Al-Musa *et al*, 1999).

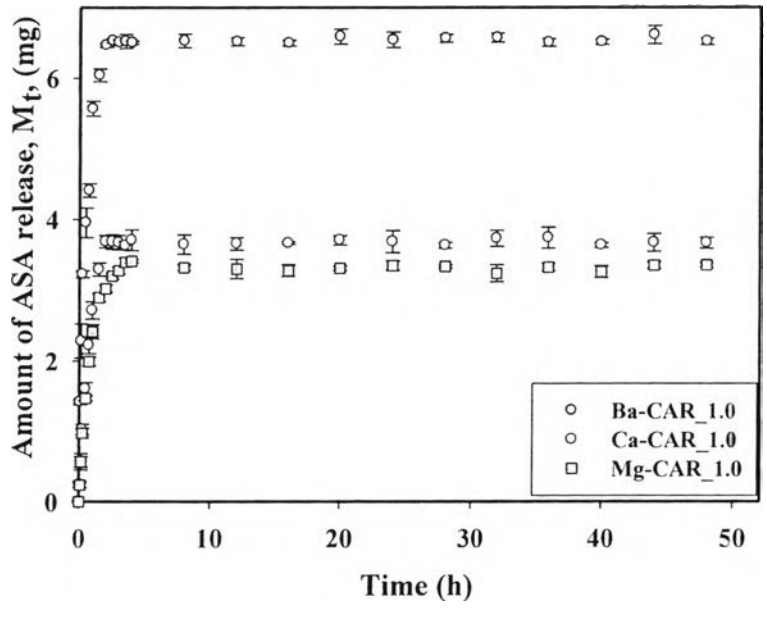


Figure J1 Amounts of acetylsalicylic acid released from acetylsalicylic acid-loaded carrageenan hydrogels versus time at various crosslinking ratios, E = 0 V, pH 5.5, and at 37 °C, n = number of samples = 3.

Table J1 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_1.0 at time t, pH 5.5 at 37 °C , in an absence of electric field

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0 0345	0.0327	0.0333	1.46	1.38	1.41	**1.42**	**0.04**
0.16667	0 0592	0.0479	0.0548	2.51	2.03	2.32	**2.29**	**0.24**
0.25	0 0769	0.0768	0.0749	3.26	3.25	3.17	**3.23**	**0.05**
0.5	0.0902	0.0908	0.0990	3.82	3.84	4.19	**3.95**	**0.21**
0.75	0.1058	0.1016	0.1049	4.48	4.30	4.44	**4.41**	**0.09**
1	0.1295	0.1305	0.1342	5.48	5.53	5.68	**5.56**	**0.10**
1.5	0.1419	0.1410	0.1451	6.01	5.97	6.14	**6.04**	**0.09**
2	0.1531	0.1532	0.1520	6.48	6.49	6.44	**6.47**	**0.03**
2.5	0.1537	0.1542	0.1549	6.51	6.53	6.56	**6.53**	**0.03**
3	0.1530	0.1532	0.1547	6.48	6.49	6.55	**6.50**	**0.04**
3.5	0.1526	0.1526	0.1567	6.46	6.46	6.63	**6.52**	**0.10**
4	0.1533	0.1533	0.1542	6.49	6.49	6.53	**6.50**	**0.02**
8	0.1525	0.1533	0.1568	6.46	6.49	6.64	**6.53**	**0.10**
12	0.1527	0.1554	0.1537	6.47	6.58	6.51	**6.52**	**0.06**
16	0.1532	0.1526	0.1545	6.49	6.46	6.54	**6.50**	**0.04**
20	0.1535	0.1549	0.1584	6.50	6.56	6.71	**6.59**	**0.11**
24	0.1531	0.1529	0.1575	6.48	6.47	6.67	**6.54**	**0.11**
28	0.1538	0.1548	0.1564	6.51	6.55	6.62	**6.56**	**0.06**
32	0.1535	0.1564	0.1557	6.50	6.62	6.59	**6.57**	**0.06**
36	0.1535	0.1524	0.1550	6.50	6.45	6.56	**6.50**	**0.06**
40	0.1535	0.1549	0.1531	6.50	6.56	6.48	**6.51**	**0.04**
44	0.1527	0.1574	0.1584	6.47	6.66	6.71	**6.61**	**0.13**
48	0.1527	0.1546	0.1546	6.46	6.55	6.55	**6.52**	**0.05**

Table J2 The raw data of the determination of amounts of acetylsalicylic acid released from Ca-CAR_1.0 at time t, pH 5.5 at 37 °C , in an absence of electric field

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0069	0.0055	0.0049	0.29	0.23	0.21	**0.24**	**0.04**
0.16667	0.0148	0.0152	0.0102	0.63	0.64	0.43	**0.57**	**0.12**
0.25	0.0222	0.0256	0.0249	0.94	1.08	1.05	**1.03**	**0.08**
0.5	0.0387	0.0395	0.0354	1.64	1.67	1.50	**1.60**	**0.09**
0.75	0.0554	0.0524	0.0498	2.35	2.22	2.11	**2.23**	**0.12**
1	0.0609	0.0652	0.0664	2.58	2.76	2.81	**2.72**	**0.12**
1.5	0.0784	0.0796	0.0754	3.32	3.37	3.19	**3.29**	**0.09**
2	0.0859	0.0860	0.0894	3.64	3.64	3.79	**3.69**	**0.08**
2.5	0.0889	0.0843	0.0878	3.76	3.57	3.72	**3.68**	**0.10**
3	0.0864	0.0893	0.0845	3.66	3.78	3.58	**3.67**	**0.10**
3.5	0.0851	0.0874	0.0847	3.60	3.70	3.59	**3.63**	**0.06**
4	0.0897	0.0836	0.0894	3.80	3.54	3.79	**3.71**	**0.15**
8	0.0827	0.0890	0.0867	3.50	3.77	3.67	**3.65**	**0.14**
12	0.0849	0.0854	0.0887	3.59	3.62	3.76	**3.66**	**0.09**
16	0.0867	0.0861	0.0869	3.67	3.65	3.68	**3.67**	**0.02**
20	0.0882	0.0886	0.0857	3.73	3.75	3.63	**3.70**	**0.07**
24	0.0885	0.0829	0.0898	3.75	3.51	3.80	**3.69**	**0.16**
28	0.0847	0.0862	0.0865	3.59	3.65	3.66	**3.63**	**0.04**
32	0.0856	0.0909	0.0879	3.62	3.85	3.72	**3.73**	**0.11**
36	0.0847	0.0916	0.0887	3.59	3.88	3.76	**3.74**	**0.15**
40	0.0854	0.0855	0.0868	3.62	3.62	3.68	**3.64**	**0.03**
44	0.0865	0.0898	0.0839	3.66	3.80	3.55	**3.67**	**0.12**
48	0.0874	0.0846	0.0879	3.70	3.58	3.72	**3.67**	**0.08**

Table J3 The raw data of the determination of amounts of acetylsalicylic acid released from Mg-CAR_1.0 at time t, pH 5.5 at 37 °C , in an absence of electric field

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0049	0.0054	0.0064	0.21	0.23	0.27	**0.24**	**0.03**
0.16667	0.0128	0.0119	0.0154	0.54	0.50	0.65	**0.57**	**0.08**
0.25	0.0225	0.0249	0.0217	0.95	1.05	0.92	**0.97**	**0.07**
0.5	0.0338	0.0347	0.0354	1.43	1.47	1.50	**1.47**	**0.03**
0.75	0.0469	0.0458	0.0487	1.98	1.94	2.06	**2.00**	**0.06**
1	0.0561	0.0554	0.0598	2.37	2.35	2.53	**2.42**	**0.10**
1.5	0.0671	0.0697	0.0687	2.84	2.95	2.91	**2.90**	**0.06**
2	0.0725	0.0716	0.0701	3.07	3.03	2.97	**3.02**	**0.05**
2.5	0.0751	0.0768	0.0749	3.18	3.25	3.17	**3.20**	**0.04**
3	0.0762	0.0777	0.0784	3.23	3.29	3.32	**3.28**	**0.05**
3.5	0.0818	0.0800	0.0789	3.46	3.39	3.34	**3.40**	**0.06**
4	0.0805	0.0812	0.0800	3.41	3.44	3.39	**3.41**	**0.03**
8	0.0775	0.0794	0.0784	3.28	3.36	3.32	**3.32**	**0.04**
12	0.0809	0.0784	0.0745	3.43	3.32	3.15	**3.30**	**0.14**
16	0.0769	0.0758	0.0796	3.26	3.21	3.37	**3.28**	**0.08**
20	0.0774	0.0786	0.0785	3.28	3.33	3.32	**3.31**	**0.03**
24	0.0804	0.0795	0.0773	3.40	3.37	3.27	**3.35**	**0.07**
28	0.0790	0.0782	0.0792	3.34	3.31	3.35	**3.34**	**0.02**
32	0.0780	0.0732	0.0783	3.30	3.10	3.32	**3.24**	**0.12**
36	0.0789	0.0795	0.0771	3.34	3.37	3.26	**3.32**	**0.05**
40	0.0755	0.0793	0.0763	3.20	3.36	3.23	**3.26**	**0.09**
44	0.0780	0.0803	0.0794	3.30	3.40	3.36	**3.35**	**0.05**
48	0.0802	0.0789	0.0787	3.39	3.34	3.33	**3.36**	**0.03**

Release Kinetics of Model Drug from Drug-Loaded Carrageenan Hydrogel

The study of acetylsalicylic acid transport mechanism from the carrageenan hydrogels, Fickian diffusion models are considered to fit the experimental data.

The power law model is described by the Ritger-Peppas equation (Venkatesh *et al.*, 1992):

$$\frac{M_t}{M_\infty} = k_1 t^n \quad \text{(J1)}$$

where M_t/M_∞ = the fractional drug release

k_1 = a kinetic constant (with the unit of T^{-n})

t = the release time

and n = the scaling exponent that can be related to the drug transport mechanism.

For a thin hydrogel film, when n = 0.5, the drug release mechanism is observed by the Fickian diffusion:

$$\frac{M_t}{M_\infty} = k_H t^{1/2} \quad \text{(J2)}$$

where M_t/M_∞ = the fractional drug release

k_H = a kinetic constant (with the unit of T^{-n})

and t = the release time.

The diffusion coefficients of acetylsalicylic acid from the carrageenan hydrogels are determined from the slopes of plots of drug accumulation versus square root of time according to Higuchi's equation (Higuchi, 1961):

$$Q = \frac{M_t}{A} = 2C_0(Dt/\pi)^{1/2} \quad \text{(J3)}$$

where Q = the amount of material flowing through a unit cross section of barrier (g/cm^2) in unit time, t (s)

C_0 = the initial drug concentration in the hydrogel (g/cm^3)

and D = the diffusion coefficient of a drug (cm^2/s)

The diffusion coefficients of each system were calculated from the slopes of the plot of the amounts of acetylsalicylic acid released from acetylsalicylic acid-loaded carrageenan hydrogels at time t versus time$^{1/2}$ at various crosslinking agents in an absence of electric field during 48 h using the Higuchi's equation (see figure J2).

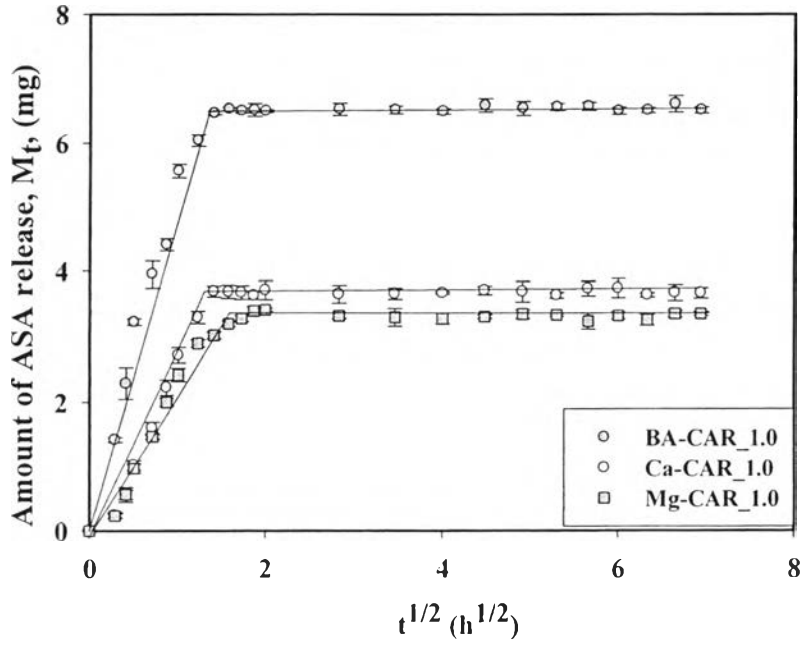


Figure J2 Amounts of acetylsalicylic acid release from acetylsalicylic acid-loaded carrageenan hydrogels versus time$^{1/2}$ at various crosslink ratios, E = 0 V, pH 5.5, and at 37 °C, number of samples = 3.

Figure J3 shows the diffusion coefficients of acetylsalicylic acid from carrageenan hydrogels versus mesh size without electric field at 37 °C.

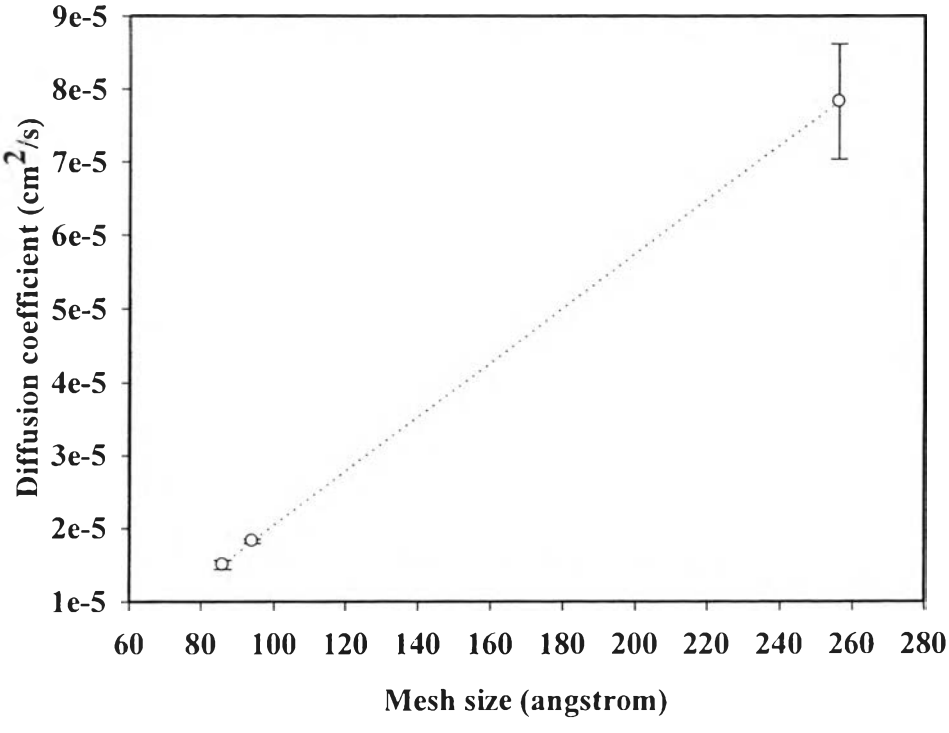


Figure J3 Diffusion coefficients of acetylsalicylic acid from carrageenan hydrogels versus mesh size, E = 0 V, pH 5.5, 37 °C, number of samples = 3.

Table J4 The raw data of the determination of the diffusion coefficients of acetyl-salicylic acid released from various crosslinked carrageenan hydrogels, pH 5.5 at 37 °C, E = 0 V

Sample	Slope			Diffusion Coefficient (cm^2/s)				
	1	2	3	1	2	3	Avg	SD
Ba-CAR_1.0	6.50	6.02	6.64	8.10E-05	6.94E-05	8.45E-05	**7.83E-05**	**7.90E-06**
Ca-CAR_1.0	3.12	3.07	3.07	1.86E-05	1.81E-05	1.81E-05	**1.82E-05**	**3.15E-07**
Mg-CAR_1.0	2.75	2.79	2.86	1.45E-05	1.49E-05	1.57E-05	**1.50E-05**	**6.04E-07**

Appendix K Determination of Amounts and Diffusion Coefficient of Acetylsalicylic Acid Released from Acetylsalicylic Acid-Loaded Carrageenan Hydrogel at Crosslinking Ratio = 1.4 and Various Electric Field Strengths under Cathode

The amounts of acetylsalicylic acid (ASA) released from acetylsalicylic acid-loaded carrageenan hydrogels versus time atcrosslinking ratio = 1.4 and various electric field strengths under the negatively charged electrode during 48 h are shown in Figure K1. The amounts of drug released gradually increase with time and then reach constant values. Moreover, the amounts of drug released increase with increasing the electric field strength and then reach equilibrium values.

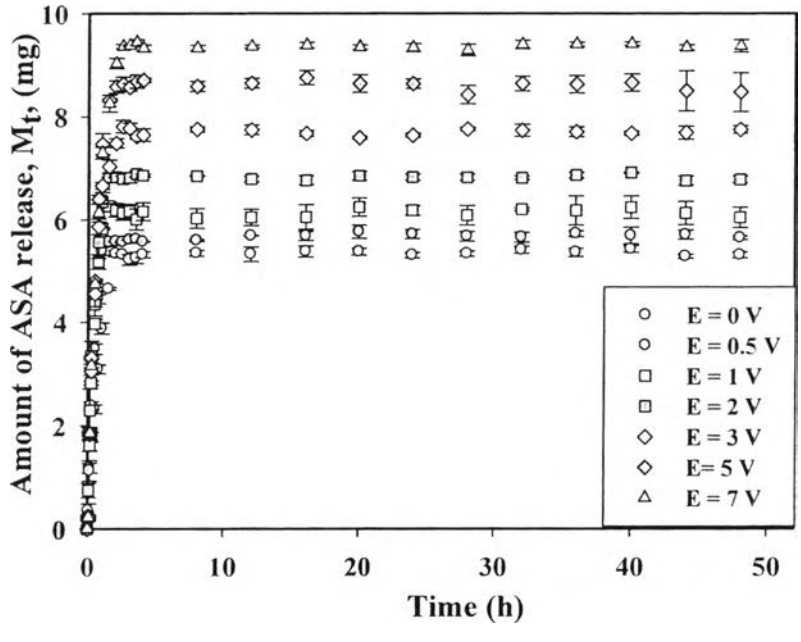


Figure K1 Amounts of acetylsalicylic acid released from acetylsalicylic acid-loaded carrageenan hydrogels versus time at the crosslinking ratio = 1.4 and various electric field strengths, pH 5.5, and at 37 °C, n = number of samples = 3.

Table K1 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_1.4 at time t, E= 0 V, pH 5.5 at 37 °C

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0105	0.0048	0.0099	0.44	0.20	0.42	**0.36**	**0.13**
0.16667	0.0295	0.0288	0.0254	1.25	1.22	1.08	**1.18**	**0.09**
0.25	0.0399	0.0419	0.0444	1.69	1.77	1.88	**1.78**	**0.1**
0.5	0.0527	0.0567	0.0546	2.23	2.40	2.31	**2.31**	**0.08**
0.75	0.0709	0.0734	0.0749	3.00	3.11	3.17	**3.09**	**0.09**
1	0.0900	0.0905	0.0946	3.81	3.83	4.01	**3.88**	**0.11**
1.5	0.1098	0.1093	0.1106	4.65	4.63	4.68	**4.65**	**0.03**
2	0.1249	0.1257	0.1277	5.29	5.32	5.41	**5.34**	**0.06**
2.5	0.1250	0.1255	0.1264	5.29	5.31	5.35	**5.32**	**0.03**
3	0.1244	0.1205	0.1249	5.27	5.10	5.29	**5.22**	**0.1**
3.5	0.1255	0.1258	0.1212	5.31	5.33	5.13	**5.26**	**0.11**
4	0.1265	0.1265	0.1241	5.36	5.36	5.25	**5.32**	**0.06**
8	0.1257	0.1254	0.1279	5.32	5.31	5.42	**5.35**	**0.06**
12	0.1265	0.1222	0.1287	5.36	5.17	5.45	**5.33**	**0.14**
16	0.1272	0.1296	0.1245	5.38	5.49	5.27	**5.38**	**0.11**
20	0.1265	0.1288	0.1257	5.36	5.45	5.32	**5.38**	**0.07**
24	0.1269	0.1245	0.1248	5.37	5.27	5.28	**5.31**	**0.06**
28	0.1270	0.1247	0.1266	5.38	5.28	5.36	**5.34**	**0.05**
32	0.1262	0.1294	0.1278	5.34	5.48	5.41	**5.41**	**0.07**
36	0.1270	0.1246	0.1284	5.38	5.28	5.44	**5.37**	**0.08**
40	0.1264	0.1286	0.1294	5.35	5.45	5.48	**5.43**	**0.07**
44	0.1255	0.1251	0.1238	5.31	5.30	5.24	**5.28**	**0.04**
48	0.1266	0.1239	0.1259	5.36	5.25	5.33	**5.31**	**0.06**

Table K2 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_1.4 at time t, E= 0.5 V, pH 5.5 at 37 °C

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0046	0.0035	0.0053	0.19	0.15	0.22	**0.19**	**0.04**
0.16667	0.0299	0.0289	0.0213	1.26	1.22	0.90	**1.13**	**0.20**
0.25	0.0560	0.0549	0.0584	2.37	2.32	2.47	**2.39**	**0.08**
0.5	0.0807	0.0814	0.0851	3.42	3.45	3.60	**3.49**	**0.10**
0.75	0.1028	0.1062	0.1066	4.35	4.50	4.51	**4.45**	**0.09**
1	0.1252	0.1285	0.1283	5.30	5.44	5.43	**5.39**	**0.08**
1.5	0.1310	0.1336	0.1298	5.55	5.66	5.50	**5.57**	**0.08**
2	0.1315	0.1319	0.1318	5.57	5.59	5.58	**5.58**	**0.01**
2.5	0.1310	0.1320	0.1315	5.55	5.59	5.57	**5.57**	**0.02**
3	0.1324	0.1327	0.1326	5.60	5.62	5.61	**5.61**	**0.01**
3.5	0.1333	0.134	0.1309	5.64	5.67	5.54	**5.62**	**0.07**
4	0.1318	0.1315	0.1316	5.58	5.57	5.57	**5.57**	**0.01**
8	0.1318	0.1320	0.1328	5.58	5.59	5.62	**5.60**	**0.02**
12	0.1342	0.1342	0.1345	5.68	5.68	5.69	**5.69**	**0.01**
16	0.1366	0.1337	0.1325	5.78	5.66	5.61	**5.68**	**0.09**
20	0.1355	0.1335	0.1395	5.74	5.65	5.91	**5.77**	**0.13**
24	0.1334	0.1343	0.1374	5.65	5.69	5.82	**5.72**	**0.09**
28	0.1316	0.1352	0.1356	5.57	5.72	5.74	**5.68**	**0.09**
32	0.1310	0.1351	0.1348	5.55	5.72	5.71	**5.66**	**0.10**
36	0.1354	0.1339	0.1365	5.73	5.67	5.78	**5.73**	**0.06**
40	0.1385	0.1335	0.1311	5.86	5.65	5.55	**5.69**	**0.16**
44	0.1368	0.1348	0.1327	5.79	5.71	5.62	**5.71**	**0.09**
48	0.1326	0.1343	0.1334	5.61	5.68	5.65	**5.65**	**0.04**

Table K3 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_1.4 at time t, E= 1 V, pH 5.5 at 37 °C

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0059	0.0049	0.0061	0.25	0.21	0.26	**0.24**	**0.03**
0.16667	0.0406	0.0356	0.0384	1.72	1.51	1.63	**1.62**	**0.11**
0.25	0.0679	0.0659	0.0666	2.87	2.79	2.82	**2.83**	**0.04**
0.5	0.0914	0.0954	0.0948	3.87	4.04	4.01	**3.97**	**0.09**
0.75	0.1193	0.1259	0.1219	5.05	5.33	5.16	**5.18**	**0.14**
1	0.1378	0.1380	0.1371	5.83	5.84	5.80	**5.83**	**0.02**
1.5	0.1459	0.1493	0.1485	6.18	6.32	6.29	**6.26**	**0.07**
2	0.1493	0.1431	0.1459	6.32	6.06	6.18	**6.19**	**0.13**
2.5	0.1476	0.1458	0.1412	6.25	6.17	5.98	**6.13**	**0.14**
3	0.1493	0.1439	0.1435	6.32	6.09	6.08	**6.16**	**0.14**
3.5	0.1474	0.1387	0.1395	6.24	5.87	5.91	**6.01**	**0.20**
4	0.1467	0.1488	0.1408	6.21	6.30	5.96	**6.16**	**0.18**
8	0.1474	0.1390	0.1406	6.24	5.88	5.95	**6.03**	**0.19**
12	0.1470	0.1397	0.1415	6.22	5.92	5.99	**6.04**	**0.16**
16	0.1491	0.1379	0.1419	6.31	5.84	6.01	**6.05**	**0.24**
20	0.1507	0.1491	0.1427	6.38	6.31	6.04	**6.24**	**0.18**
24	0.1477	0.1468	0.1435	6.25	6.21	6.08	**6.18**	**0.09**
28	0.1486	0.1399	0.1428	6.29	5.92	6.05	**6.09**	**0.19**
32	0.1470	0.1457	0.1465	6.22	6.17	6.20	**6.20**	**0.03**
36	0.1527	0.1393	0.1459	6.47	5.90	6.18	**6.18**	**0.28**
40	0.1533	0.1433	0.1457	6.49	6.07	6.17	**6.24**	**0.22**
44	0.1509	0.1411	0.1422	6.39	5.97	6.02	**6.13**	**0.23**
48	0.1480	0.1389	0.1414	6.27	5.88	5.99	**6.04**	**0.20**

Table K4 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_1.4 at time t, E= 2 V, pH 5.5 at 37 °C

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0139	0.019	0.0201	0.59	0.81	0.85	**0.75**	**0.14**
0.16667	0.0527	0.0453	0.0648	2.23	1.92	2.74	**2.30**	**0.42**
0.25	0.0814	0.0714	0.0845	3.45	3.02	3.58	**3.35**	**0.29**
0.5	0.1089	0.0989	0.1006	4.61	4.19	4.26	**4.35**	**0.23**
0.75	0.1333	0.1233	0.1379	5.64	5.22	5.84	**5.57**	**0.32**
1	0.1492	0.1459	0.1546	6.32	6.18	6.55	**6.35**	**0.19**
1.5	0.1613	0.1615	0.1607	6.83	6.84	6.80	**6.82**	**0.02**
2	0.1610	0.1615	0.1616	6.82	6.84	6.84	**6.83**	**0.01**
2.5	0.1595	0.1619	0.1598	6.75	6.86	6.77	**6.79**	**0.06**
3	0.1615	0.1631	0.1584	6.84	6.91	6.71	**6.82**	**0.10**
3.5	0.1618	0.1622	0.1645	6.85	6.87	6.97	**6.89**	**0.06**
4	0.1625	0.1612	0.1623	6.88	6.83	6.87	**6.86**	**0.03**
8	0.1617	0.1622	0.1617	6.84	6.87	6.85	**6.85**	**0.01**
12	0.1594	0.1619	0.1599	6.75	6.86	6.77	**6.79**	**0.06**
16	0.1599	0.162	0.1578	6.77	6.86	6.68	**6.77**	**0.09**
20	0.1641	0.1614	0.1601	6.95	6.83	6.78	**6.85**	**0.09**
24	0.1596	0.1620	0.1624	6.76	6.86	6.88	**6.83**	**0.06**
28	0.1595	0.1620	0.1622	6.75	6.86	6.87	**6.83**	**0.06**
32	0.1617	0.1612	0.1600	6.85	6.82	6.77	**6.82**	**0.04**
36	0.1638	0.1614	0.1614	6.94	6.83	6.83	**6.87**	**0.06**
40	0.1637	0.1634	0.1630	6.93	6.92	6.90	**6.92**	**0.02**
44	0.1594	0.1619	0.1578	6.75	6.86	6.68	**6.76**	**0.09**
48	0.1599	0.1620	0.1589	6.77	6.86	6.73	**6.79**	**0.07**

Table K5 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_1.4 at time t, E= 3 V, pH 5.5 at 37 °C

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0059	0.0055	0.0049	0.25	0.23	0.21	**0.23**	**0.02**
0.16667	0.0453	0.0401	0.0445	1.92	1.70	1.88	**1.83**	**0.12**
0.25	0.0739	0.0705	0.0721	3.13	2.98	3.05	**3.06**	**0.07**
0.5	0.1127	0.1012	0.1089	4.77	4.28	4.61	**4.56**	**0.25**
0.75	0.1414	0.1345	0.1397	5.99	5.70	5.92	**5.87**	**0.15**
1	0.1589	0.1558	0.1574	6.73	6.59	6.66	**6.66**	**0.07**
1.5	0.1633	0.1693	0.1659	6.91	7.17	7.02	**7.03**	**0.13**
2	0.1749	0.1791	0.1765	7.41	7.58	7.47	**7.49**	**0.09**
2.5	0.1813	0.1858	0.1865	7.67	7.87	7.90	**7.81**	**0.12**
3	0.1810	0.1856	0.1845	7.66	7.86	7.81	**7.78**	**0.10**
3.5	0.1795	0.1790	0.1812	7.60	7.58	7.67	**7.62**	**0.05**
4	0.1815	0.1775	0.1832	7.68	7.52	7.76	**7.65**	**0.12**
8	0.1818	0.1838	0.1840	7.70	7.78	7.79	**7.76**	**0.05**
12	0.1825	0.1854	0.1810	7.73	7.85	7.66	**7.75**	**0.10**
16	0.1817	0.1825	0.1798	7.69	7.73	7.61	**7.68**	**0.06**
20	0.1794	0.1801	0.1786	7.59	7.63	7.56	**7.59**	**0.03**
24	0.1799	0.1816	0.1801	7.62	7.69	7.63	**7.64**	**0.04**
28	0.1841	0.1836	0.1824	7.79	7.77	7.72	**7.76**	**0.04**
32	0.1796	0.1842	0.1845	7.60	7.80	7.81	**7.74**	**0.12**
36	0.1795	0.1832	0.1836	7.60	7.76	7.77	**7.71**	**0.10**
40	0.1817	0.1822	0.1803	7.69	7.71	7.63	**7.68**	**0.04**
44	0.1838	0.1783	0.1829	7.78	7.55	7.74	**7.69**	**0.12**
48	0.1837	0.1812	0.1845	7.78	7.67	7.81	**7.75**	**0.07**

Table K6 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_1.4 at time t, E= 5 V, pH 5.5 at 37 °C

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0064	0.006	0.0054	0.27	0.26	0.23	**0.25**	**0.02**
0.16667	0.0427	0.0453	0.0434	1.81	1.92	1.84	**1.85**	**0.06**
0.25	0.0793	0.0773	0.0784	3.36	3.27	3.32	**3.32**	**0.04**
0.5	0.1136	0.1124	0.1145	4.81	4.76	4.85	**4.81**	**0.05**
0.75	0.1519	0.1490	0.1526	6.43	6.31	6.46	**6.40**	**0.08**
1	0.1800	0.1710	0.1784	7.62	7.24	7.55	**7.47**	**0.20**
1.5	0.1973	0.1957	0.1965	8.35	8.29	8.32	**8.32**	**0.03**
2	0.2015	0.2005	0.2059	8.53	8.49	8.72	**8.58**	**0.12**
2.5	0.2030	0.2013	0.2074	8.60	8.52	8.78	**8.63**	**0.13**
3	0.2045	0.2015	0.2013	8.66	8.53	8.52	**8.57**	**0.08**
3.5	0.208	0.2018	0.2054	8.81	8.54	8.70	**8.68**	**0.13**
4	0.2050	0.2050	0.2068	8.68	8.68	8.76	**8.71**	**0.04**
8	0.2055	0.2012	0.2019	8.70	8.52	8.55	**8.59**	**0.10**
12	0.2040	0.2022	0.2065	8.64	8.56	8.74	**8.65**	**0.09**
16	0.2097	0.2031	0.2074	8.88	8.60	8.78	**8.75**	**0.14**
20	0.2036	0.2003	0.2084	8.62	8.48	8.82	**8.64**	**0.17**
24	0.2051	0.2054	0.2015	8.68	8.70	8.53	**8.64**	**0.09**
28	0.1992	0.2031	0.1948	8.43	8.60	8.25	**8.43**	**0.18**
32	0.2068	0.2048	0.2003	8.76	8.67	8.48	**8.64**	**0.14**
36	0.2070	0.2049	0.1994	8.77	8.68	8.44	**8.63**	**0.17**
40	0.1999	0.2064	0.2069	8.46	8.74	8.76	**8.65**	**0.17**
44	0.1910	0.2019	0.2091	8.09	8.55	8.85	**8.50**	**0.39**
48	0.1900	0.2037	0.2067	8.04	8.63	8.75	**8.47**	**0.38**

Table K7 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_1.4 at time t, E= 7 V, pH 5.5 at 37 °C

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0063	0.0056	0.0041	0.27	0.24	0.17	**0.23**	**0.05**
0.16667	0.0468	0.0417	0.0432	1.98	1.76	1.83	**1.86**	**0.11**
0.25	0.0755	0.0746	0.0739	3.20	3.16	3.13	**3.16**	**0.03**
0.5	0.1132	0.1103	0.1125	4.79	4.67	4.76	**4.74**	**0.06**
0.75	0.1488	0.1406	0.1451	6.30	5.95	6.14	**6.13**	**0.17**
1	0.1705	0.1711	0.1754	7.22	7.24	7.43	**7.30**	**0.11**
1.5	0.1984	0.1908	0.1958	8.40	8.08	8.29	**8.26**	**0.16**
2	0.2106	0.2151	0.2142	8.92	9.11	9.07	**9.03**	**0.10**
2.5	0.221	0.2221	0.2201	9.36	9.40	9.32	**9.36**	**0.04**
3	0.2219	0.2212	0.2213	9.40	9.37	9.37	**9.38**	**0.02**
3.5	0.2218	0.2232	0.2241	9.39	9.45	9.49	**9.44**	**0.05**
4	0.2219	0.2195	0.2194	9.40	9.29	9.29	**9.33**	**0.06**
8	0.2218	0.2198	0.2195	9.39	9.31	9.29	**9.33**	**0.05**
12	0.2216	0.2212	0.2203	9.38	9.36	9.33	**9.36**	**0.03**
16	0.2214	0.2231	0.2205	9.38	9.45	9.34	**9.39**	**0.06**
20	0.2217	0.2197	0.2209	9.39	9.30	9.35	**9.35**	**0.04**
24	0.2216	0.2216	0.2184	9.38	9.38	9.25	**9.34**	**0.08**
28	0.2217	0.2199	0.2165	9.39	9.31	9.17	**9.29**	**0.11**
32	0.2213	0.2241	0.2204	9.37	9.49	9.33	**9.40**	**0.08**
36	0.2215	0.2232	0.2216	9.38	9.45	9.38	**9.40**	**0.04**
40	0.2215	0.2222	0.2231	9.38	9.41	9.45	**9.41**	**0.03**
44	0.2219	0.2202	0.2197	9.40	9.32	9.30	**9.34**	**0.05**
48	0.2213	0.2241	0.2184	9.37	9.49	9.25	**9.37**	**0.12**

Release Kinetics of Model Drug from Drug-Loaded Carrageenan Hydrogel

The study of acetylsalicylic acid transport mechanism from the carrageenan hydrogels, Fickian diffusion models are considered to fit the experimental data.

The power law model is described by the Ritger-Peppas equation (Venkatesh *et al.*, 1992):

$$\frac{M_t}{M_\infty} = k_1 t^n \qquad \text{(K1)}$$

where M_t/M_∞ = the fractional drug release

k_1 = a kinetic constant (with the unit of T^{-n})

t = the release time

and n = the scaling exponent that can be related to the drug transport mechanism.

For a thin hydrogel film, when n = 0.5, the drug release mechanism is observed by the Fickian diffusion:

$$\frac{M_t}{M_\infty} = k_H t^{1/2} \qquad \text{(K2)}$$

where M_t/M_∞ = the fractional drug release

k_H = a kinetic constant (with the unit of T^{-n})

and t = the release time.

The diffusion coefficients of acetylsalicylic acid from the carrageenan hydrogels are determined from the slopes of plots of drug accumulation versus square root of time according to Higuchi's equation (Higuchi, 1961):

$$Q = \frac{M_t}{A} = 2C_0(Dt/\pi)^{1/2} \qquad \text{(K3)}$$

where Q = the amount of material flowing through a unit cross section of barrier (g/cm^2) in unit time, t (s)

C_0 = the initial drug concentration in the hydrogel (g/cm^3)

and D = the diffusion coefficient of a drug (cm^2/s)

The diffusion coefficients of each system were calculated from the slopes of the plot of the amounts of acetylsalicylic acid released from acetylsalicylic acid-loaded carrageenan hydrogels at time t versus time$^{1/2}$ at the crosslinking ratio = 1.4 and at various electric field strengths during 48 h using the Higuchi's equation (see figure K2).

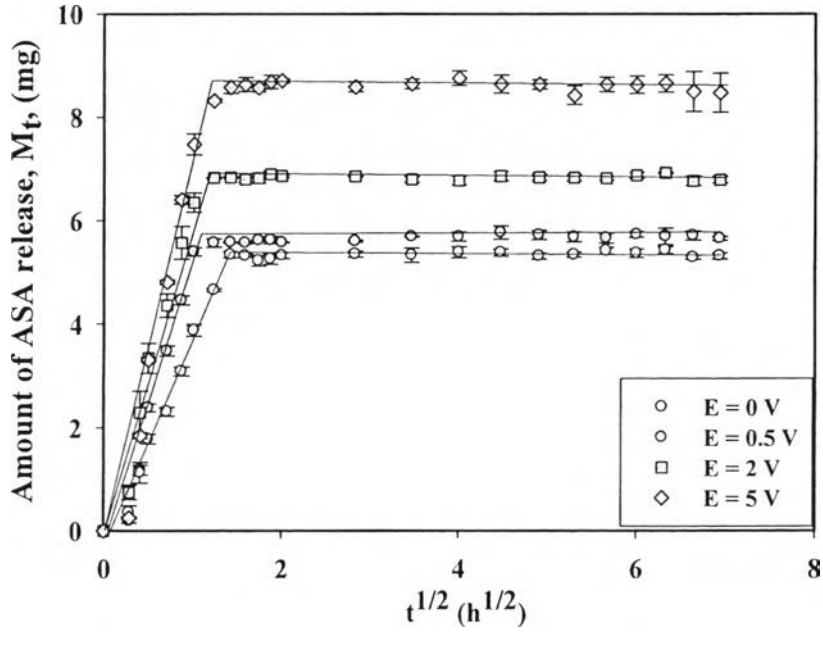


Figure K2 Amounts of acetylsalicylic acid release from acetylsalicylic acid-loaded carrageenan hydrogels versus time$^{1/2}$ at crosslinking ratio = 1.4 and at various electric field strengths, pH 5.5, and at 37 °C, n = number of samples = 3.

Figure K3 shows the diffusion coefficients of acetylsalicylic acid from carrageenan hydrogels versus electric field strength at 37°C.

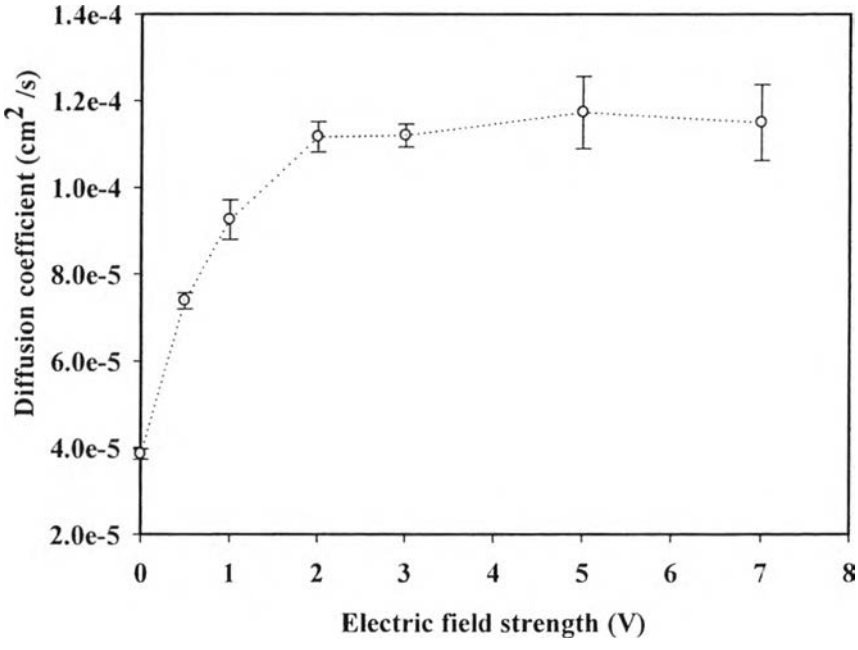


Figure K3 Diffusion coefficients of acetylsalicylic acid from carrageenan hydrogels versus electric field strength at the crosslinking ratio = 1.4, pH 5.5, and at 37 °C, n = number of samples = 3.

Table K8 The raw data of the determination of the diffusion coefficients of acetylsalicylic acid released from various crosslinked carrageenan hydrogels, pH 5.5 at 37 °C, E = 0 V

Electric field strength (V)	Slope			Diffusion Coefficient (cm^2/s)				
	1	2	3	1	2	3	Avg	SD
0	4.40	4.52	4.53	3.71E-05	3.91E-05	3.93E-05	**3.85E-05**	**1.22E-06**
0.5	6.24	6.27	6.12	7.45E-05	7.52E-05	7.17E-05	**7.38E-05**	**1.85E-06**
1	6.99	7.10	6.76	9.36E-05	9.66E-05	8.76E-05	**9.26E-05**	**4.58E-06**
2	7.51	7.76	7.63	1.08E-04	1.15E-04	1.12E-04	**1.12E-04**	**3.66E-06**
3	7.71	7.55	7.66	1.14E-04	1.09E-04	1.13E-04	**1.12E-04**	**2.38E-06**
5	7.93	8.06	7.49	1.20E-04	1.24E-04	1.08E-04	**1.17E-04**	**8.78E-06**
7	8.07	7.54	7.61	1.25E-04	1.09E-04	1.11E-04	**1.15E-04**	**8.64E-06**

Appendix L Determination of Amounts and Diffusion Coefficient of Acetylsalicylic Acid Released from Acetylsalicylic acid-Loaded Carrageenan Hydrogel at Various Crosslinking Ratios with Electric Field Strength of 2 V (E = 2 V)

The amounts of acetylsalicylic acid (ASA) released from acetylsalicylic acid-loaded carrageenan hydrogels versus time at various crosslinking ratios at electric field strength of 2 V during 48 h are shown in Figure L1. The amounts of drug released gradually increase with time and then reach constant values. But the amounts of drug released decrease with increasing crosslinking ratio.

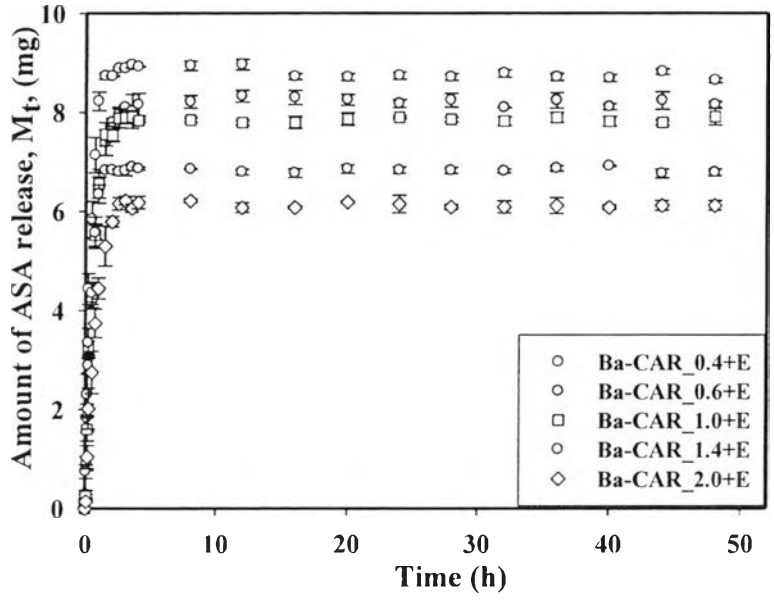


Figure L1 Amounts of acetylsalicylic acid released from acetylsalicylic acid-loaded carrageenan hydrogels versus time at various crosslinking ratios, E = 2 V, pH 5.5, and at 37 °C, n = number of samples = 3.

Table L1 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_0.4+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0046	0.0089	0.00648	0.20	0.38	0.27	**0.28**	**0.09**
0.16667	0.0449	0.0360	0.0489	1.90	1.52	2.07	**1.83**	**0.28**
0.25	0.0982	0.1126	0.1035	4.16	4.77	4.38	**4.44**	**0.31**
0.5	0.1299	0.1369	0.1469	5.50	5.80	6.22	**5.84**	**0.36**
0.75	0.1600	0.1686	0.1769	6.77	7.14	7.49	**7.14**	**0.36**
1	0.1914	0.1919	0.1993	8.10	8.12	8.44	**8.22**	**0.19**
1.5	0.2062	0.2077	0.2047	8.73	8.80	8.67	**8.73**	**0.06**
2	0.2060	0.2065	0.2059	8.72	8.74	8.72	**8.73**	**0.01**
2.5	0.2089	0.2106	0.2097	8.85	8.92	8.88	**8.88**	**0.04**
3	0.2094	0.2104	0.2099	8.87	8.91	8.89	**8.89**	**0.02**
3.5	0.2100	0.2118	0.2129	8.89	8.97	9.01	**8.96**	**0.06**
4	0.2108	0.2106	0.2106	8.93	8.92	8.92	**8.92**	**0.01**
8	0.2099	0.2138	0.2098	8.89	9.05	8.88	**8.94**	**0.10**
12	0.2095	0.2111	0.2144	8.87	8.94	9.08	**8.96**	**0.11**
16	0.2061	0.2045	0.2074	8.73	8.66	8.78	**8.72**	**0.06**
20	0.2073	0.2039	0.2058	8.78	8.63	8.71	**8.71**	**0.07**
24	0.2081	0.2066	0.2046	8.81	8.75	8.66	**8.74**	**0.07**
28	0.2076	0.2048	0.2048	8.79	8.67	8.67	**8.71**	**0.07**
32	0.2059	0.2071	0.2094	8.72	8.77	8.87	**8.78**	**0.08**
36	0.2067	0.2038	0.2068	8.75	8.63	8.76	**8.71**	**0.07**
40	0.2039	0.2047	0.2071	8.63	8.67	8.77	**8.69**	**0.07**
44	0.2087	0.2094	0.2068	8.84	8.87	8.76	**8.82**	**0.06**
48	0.2054	0.2032	0.2038	8.70	8.60	8.63	**8.64**	**0.05**

Table L2 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_0.6+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0031	0.0033	0.0043	0.13	0.14	0.18	**0.15**	**0.03**
0.16667	0.0192	0.0201	0.0255	0.81	0.85	1.08	**0.91**	**0.14**
0.25	0.0712	0.0646	0.0688	3.01	2.73	2.91	**2.89**	**0.14**
0.5	0.0995	0.0955	0.1001	4.21	4.04	4.24	**4.16**	**0.11**
0.75	0.1310	0.1289	0.1354	5.55	5.46	5.73	**5.58**	**0.14**
1	0.1590	0.1488	0.1478	6.73	6.30	6.26	**6.43**	**0.26**
1.5	0.1756	0.1679	0.1801	7.44	7.11	7.63	**7.39**	**0.26**
2	0.1820	0.1847	0.1859	7.71	7.82	7.87	**7.80**	**0.08**
2.5	0.1836	0.1898	0.1900	7.77	8.04	8.04	**7.95**	**0.15**
3	0.1924	0.1905	0.1909	8.15	8.07	8.08	**8.10**	**0.04**
3.5	0.1845	0.1849	0.1987	7.81	7.83	8.41	**8.02**	**0.34**
4	0.1864	0.1959	0.1956	7.89	8.29	8.28	**8.16**	**0.23**
8	0.1906	0.1948	0.1964	8.07	8.25	8.32	**8.21**	**0.13**
12	0.1985	0.1979	0.1934	8.40	8.38	8.19	**8.32**	**0.12**
16	0.1989	0.1967	0.1922	8.42	8.33	8.14	**8.30**	**0.14**
20	0.1978	0.1937	0.1931	8.37	8.20	8.18	**8.25**	**0.11**
24	0.1939	0.1944	0.1909	8.21	8.23	8.08	**8.17**	**0.08**
28	0.1909	0.1962	0.1970	8.08	8.31	8.34	**8.24**	**0.14**
32	0.1913	0.1911	0.1912	8.10	8.09	8.10	**8.10**	**0.00**
36	0.1988	0.1919	0.1931	8.42	8.13	8.18	**8.24**	**0.16**
40	0.1932	0.1909	0.1905	8.18	8.08	8.07	**8.11**	**0.06**
44	0.1985	0.1949	0.1902	8.40	8.25	8.05	**8.24**	**0.18**
48	0.1942	0.1914	0.1921	8.22	8.10	8.13	**8.15**	**0.06**

Table L3 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_1.0+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0053	0.0055	0.0069	0.22	0.23	0.29	**0.25**	**0.04**
0.16667	0.0420	0.0315	0.0397	1.78	1.34	1.68	**1.60**	**0.23**
0.25	0.0805	0.0649	0.0746	3.41	2.75	3.16	**3.10**	**0.33**
0.5	0.1081	0.0875	0.0978	4.58	3.70	4.14	**4.14**	**0.44**
0.75	0.1310	0.1055	0.1249	5.54	4.47	5.29	**5.10**	**0.56**
1	0.1523	0.1326	0.1497	6.45	5.61	6.34	**6.13**	**0.45**
1.5	0.1758	0.1548	0.1649	7.44	6.55	6.98	**6.99**	**0.44**
2	0.1751	0.1778	0.1809	7.41	7.53	7.66	**7.53**	**0.12**
2.5	0.1810	0.1875	0.1897	7.66	7.94	8.03	**7.88**	**0.19**
3	0.1842	0.1896	0.1854	7.80	8.03	7.85	**7.89**	**0.12**
3.5	0.1832	0.1874	0.1894	7.76	7.93	8.02	**7.90**	**0.13**
4	0.1852	0.1857	0.1842	7.84	7.86	7.80	**7.83**	**0.03**
8	0.1845	0.1849	0.1865	7.81	7.83	7.90	**7.85**	**0.04**
12	0.1830	0.1854	0.1837	7.75	7.85	7.78	**7.79**	**0.05**
16	0.1824	0.1875	0.1824	7.72	7.94	7.72	**7.79**	**0.12**
20	0.1829	0.1888	0.1854	7.74	7.99	7.85	**7.86**	**0.13**
24	0.1859	0.1872	0.1865	7.87	7.93	7.90	**7.90**	**0.03**
28	0.1847	0.1869	0.1852	7.82	7.91	7.84	**7.86**	**0.05**
32	0.1824	0.1855	0.1863	7.72	7.85	7.89	**7.82**	**0.09**
36	0.1863	0.1889	0.1842	7.89	8.00	7.80	**7.90**	**0.10**
40	0.1872	0.1841	0.1826	7.93	7.79	7.73	**7.82**	**0.10**
44	0.1833	0.1834	0.1855	7.76	7.77	7.85	**7.79**	**0.05**
48	0.1874	0.1905	0.1826	7.93	8.07	7.73	**7.91**	**0.17**

Table L4 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_1.4+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0139	0.019	0.0201	0.59	0.81	0.85	**0.75**	**0.14**
0.16667	0.0527	0.0453	0.0648	2.23	1.92	2.74	**2.30**	**0.42**
0.25	0.0814	0.0714	0.0845	3.45	3.02	3.58	**3.35**	**0.29**
0.5	0.1089	0.0989	0.1006	4.61	4.19	4.26	**4.35**	**0.23**
0.75	0.1333	0.1233	0.1379	5.64	5.22	5.84	**5.57**	**0.32**
1	0.1492	0.1459	0.1546	6.32	6.18	6.55	**6.35**	**0.19**
1.5	0.1613	0.1615	0.1607	6.83	6.84	6.80	**6.82**	**0.02**
2	0.1610	0.1615	0.1616	6.82	6.84	6.84	**6.83**	**0.01**
2.5	0.1595	0.1619	0.1598	6.75	6.86	6.77	**6.79**	**0.06**
3	0.1615	0.1631	0.1584	6.84	6.91	6.71	**6.82**	**0.10**
3.5	0.1618	0.1622	0.1645	6.85	6.87	6.97	**6.89**	**0.06**
4	0.1625	0.1612	0.1623	6.88	6.83	6.87	**6.86**	**0.03**
8	0.1617	0.1622	0.1617	6.84	6.87	6.85	**6.85**	**0.01**
12	0.1594	0.1619	0.1599	6.75	6.86	6.77	**6.79**	**0.06**
16	0.1599	0.1620	0.1578	6.77	6.86	6.68	**6.77**	**0.09**
20	0.1641	0.1614	0.1601	6.95	6.83	6.78	**6.85**	**0.09**
24	0.1596	0.1620	0.1624	6.76	6.86	6.88	**6.83**	**0.06**
28	0.1595	0.1620	0.1622	6.75	6.86	6.87	**6.83**	**0.06**
32	0.1617	0.1612	0.160	6.85	6.82	6.77	**6.82**	**0.04**
36	0.1638	0.1614	0.1614	6.94	6.83	6.83	**6.87**	**0.06**
40	0.1637	0.1634	0.1630	6.93	6.92	6.90	**6.92**	**0.02**
44	0.1594	0.1619	0.1578	6.75	6.86	6.68	**6.76**	**0.09**
48	0.1599	0.1620	0.1589	6.77	6.86	6.73	**6.79**	**0.07**

Table L5 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_2.0+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	0.00	0.00
0.08333	0.0035	0.0032	0.0033	0.15	0.13	0.14	0.14	0.01
0.16667	0.0296	0.0187	0.0255	1.25	0.79	1.08	1.04	0.23
0.25	0.0569	0.0375	0.0488	2.41	1.59	2.07	2.02	0.41
0.5	0.0751	0.0549	0.0649	3.18	2.32	2.75	2.75	0.43
0.75	0.0946	0.0812	0.0895	4.01	3.44	3.79	3.74	0.29
1	0.1098	0.0999	0.1055	4.65	4.23	4.47	4.45	0.21
1.5	0.1255	0.1156	0.1345	5.31	4.90	5.69	5.30	0.40
2	0.1346	0.1365	0.1395	5.70	5.78	5.91	5.79	0.10
2.5	0.1422	0.1479	0.1460	6.02	6.26	6.18	6.15	0.12
3	0.1456	0.1492	0.1457	6.16	6.32	6.17	6.22	0.09
3.5	0.1415	0.1427	0.1453	5.99	6.04	6.15	6.06	0.08
4	0.1462	0.1487	0.1428	6.19	6.30	6.05	6.18	0.13
8	0.1478	0.1462	0.1462	6.26	6.19	6.19	6.21	0.04
12	0.1411	0.1435	0.1457	5.97	6.08	6.17	6.07	0.10
16	0.1429	0.1444	0.1434	6.05	6.11	6.07	6.08	0.03
20	0.1457	0.1461	0.1465	6.17	6.19	6.20	6.19	0.02
24	0.1445	0.1413	0.1497	6.12	5.98	6.34	6.15	0.18
28	0.1434	0.1429	0.1451	6.07	6.05	6.14	6.09	0.05
32	0.1449	0.1459	0.1406	6.14	6.18	5.95	6.09	0.12
36	0.1434	0.1486	0.1413	6.07	6.29	5.98	6.12	0.16
40	0.1447	0.1437	0.1425	6.13	6.08	6.03	6.08	0.05
44	0.1455	0.1418	0.1462	6.16	6.00	6.19	6.12	0.10
48	0.1432	0.1471	0.1432	6.06	6.23	6.06	6.12	0.10

Table L6 The raw data of the determination of amounts of acetylsalicylic acid released from Ca-CAR_1.0+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0026	0.0031	0.0035	0.11	0.13	0.15	**0.13**	**0.02**
0.16667	0.0176	0.0169	0.0184	0.75	0.72	0.78	**0.75**	**0.03**
0.25	0.0370	0.0379	0.0389	1.57	1.60	1.65	**1.61**	**0.04**
0.5	0.0549	0.0554	0.0564	2.32	2.35	2.39	**2.35**	**0.03**
0.75	0.0648	0.0639	0.0654	2.74	2.71	2.77	**2.74**	**0.03**
1	0.0858	0.0884	0.0864	3.63	3.74	3.66	**3.68**	**0.06**
1.5	0.0958	0.0987	0.0979	4.06	4.18	4.15	**4.13**	**0.06**
2	0.1098	0.1100	0.1106	4.65	4.66	4.68	**4.66**	**0.02**
2.5	0.1157	0.1126	0.1154	4.90	4.77	4.89	**4.85**	**0.07**
3	0.1123	0.1124	0.1165	4.75	4.76	4.93	**4.82**	**0.10**
3.5	0.1167	0.1154	0.1142	4.94	4.89	4.84	**4.89**	**0.05**
4	0.1139	0.1135	0.1165	4.82	4.81	4.93	**4.85**	**0.07**
8	0.1200	0.1126	0.1142	5.08	4.77	4.84	**4.89**	**0.16**
12	0.1160	0.1154	0.1165	4.91	4.89	4.93	**4.91**	**0.02**
16	0.1180	0.1165	0.1126	5.00	4.93	4.77	**4.90**	**0.12**
20	0.1130	0.1174	0.1152	4.78	4.97	4.88	**4.88**	**0.09**
24	0.1130	0.1152	0.1134	4.78	4.88	4.80	**4.82**	**0.05**
28	0.1148	0.1165	0.1112	4.86	4.93	4.71	**4.83**	**0.11**
32	0.1160	0.1110	0.1174	4.91	4.70	4.97	**4.86**	**0.14**
36	0.1102	0.1165	0.1184	4.67	4.93	5.01	**4.87**	**0.18**
40	0.1101	0.1132	0.1165	4.66	4.79	4.93	**4.80**	**0.14**
44	0.1110	0.1125	0.1124	4.70	4.76	4.76	**4.74**	**0.04**
48	0.1156	0.1143	0.1153	4.89	4.84	4.88	**4.87**	**0.03**

Table L7 The raw data of the determination of amounts of acetylsalicylic acid released from Mg-CAR_1.0+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0024	0.0029	0.0031	0.10	0.12	0.13	**0.12**	**0.02**
0.16667	0.0145	0.0155	0.0159	0.61	0.66	0.67	**0.65**	**0.03**
0.25	0.0285	0.0278	0.0291	1.21	1.18	1.23	**1.21**	**0.03**
0.5	0.0430	0.0421	0.0441	1.82	1.78	1.87	**1.82**	**0.04**
0.75	0.0549	0.0553	0.0543	2.32	2.34	2.30	**2.32**	**0.02**
1	0.0655	0.0678	0.0665	2.77	2.87	2.82	**2.82**	**0.05**
1.5	0.0785	0.0794	0.0775	3.32	3.36	3.28	**3.32**	**0.04**
2	0.0885	0.0881	0.0845	3.75	3.73	3.58	**3.68**	**0.09**
2.5	0.0988	0.0976	0.0956	4.18	4.13	4.05	**4.12**	**0.07**
3	0.1011	0.0946	0.0995	4.28	4.01	4.21	**4.17**	**0.14**
3.5	0.0950	0.0999	0.0987	4.02	4.23	4.18	**4.14**	**0.11**
4	0.0925	0.1023	0.0968	3.92	4.33	4.10	**4.12**	**0.21**
8	0.1015	0.0984	0.0991	4.30	4.17	4.20	**4.22**	**0.07**
12	0.0930	0.0978	0.1034	3.94	4.14	4.38	**4.15**	**0.22**
16	0.0997	0.1021	0.0985	4.22	4.32	4.17	**4.24**	**0.08**
20	0.0967	0.0957	0.1034	4.09	4.05	4.38	**4.17**	**0.18**
24	0.0930	0.1038	0.0956	3.94	4.40	4.05	**4.13**	**0.24**
28	0.0939	0.0978	0.0946	3.98	4.14	4.01	**4.04**	**0.09**
32	0.0966	0.0968	0.0958	4.09	4.10	4.06	**4.08**	**0.02**
36	0.0941	0.0948	0.0966	3.98	4.01	4.09	**4.03**	**0.05**
40	0.0905	0.1061	0.0961	3.83	4.49	4.07	**4.13**	**0.33**
44	0.0972	0.0954	0.0951	4.12	4.04	4.03	**4.06**	**0.05**
48	0.1031	0.0987	0.0932	4.37	4.18	3.95	**4.16**	**0.21**

Table L8 The raw data of the determination of amounts of acetylsalicylic acid released from Ca-CAR_2.0+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0020	0.0025	0.0019	0.08	0.11	0.08	**0.09**	**0.01**
0.16667	0.0123	0.0131	0.0114	0.52	0.55	0.48	**0.52**	**0.04**
0.25	0.0205	0.0213	0.0221	0.87	0.90	0.94	**0.90**	**0.03**
0.5	0.0316	0.0329	0.0331	1.34	1.39	1.40	**1.38**	**0.04**
0.75	0.0407	0.0411	0.0425	1.72	1.74	1.80	**1.75**	**0.04**
1	0.0485	0.0479	0.0497	2.05	2.03	2.10	**2.06**	**0.04**
1.5	0.0548	0.0555	0.0531	2.32	2.35	2.25	**2.31**	**0.05**
2	0.0655	0.0674	0.0667	2.77	2.85	2.82	**2.82**	**0.04**
2.5	0.0741	0.0745	0.0754	3.14	3.15	3.19	**3.16**	**0.03**
3	0.0729	0.0725	0.0739	3.09	3.07	3.13	**3.10**	**0.03**
3.5	0.0758	0.0743	0.0724	3.21	3.15	3.07	**3.14**	**0.07**
4	0.0780	0.0762	0.0754	3.30	3.23	3.19	**3.24**	**0.06**
8	0.0789	0.0739	0.0764	3.34	3.13	3.23	**3.23**	**0.11**
12	0.0792	0.0729	0.0784	3.35	3.09	3.32	**3.25**	**0.15**
16	0.0763	0.0731	0.0789	3.23	3.10	3.34	**3.22**	**0.12**
20	0.0783	0.0738	0.0755	3.31	3.12	3.20	**3.21**	**0.10**
24	0.0789	0.0742	0.0761	3.34	3.14	3.22	**3.23**	**0.10**
28	0.0740	0.0746	0.0774	3.13	3.16	3.28	**3.19**	**0.08**
32	0.0724	0.0751	0.0795	3.07	3.18	3.37	**3.20**	**0.15**
36	0.0725	0.0761	0.0756	3.07	3.22	3.20	**3.16**	**0.08**
40	0.0765	0.0752	0.0754	3.24	3.18	3.19	**3.21**	**0.03**
44	0.0746	0.0746	0.0773	3.16	3.16	3.27	**3.20**	**0.07**
48	0.0748	0.0755	0.0789	3.17	3.20	3.34	**3.23**	**0.09**

Table L9 The raw data of the determination of amounts of acetylsalicylic acid released from Mg-CAR_3.0+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0010	0.0015	0.0021	0.04	0.06	0.09	**0.06**	**0.02**
0.16667	0.0062	0.0069	0.0072	0.26	0.29	0.30	**0.29**	**0.02**
0.25	0.0104	0.0112	0.0121	0.44	0.47	0.51	**0.48**	**0.04**
0.5	0.0181	0.0198	0.0185	0.77	0.84	0.78	**0.80**	**0.04**
0.75	0.0249	0.0265	0.0256	1.05	1.12	1.08	**1.09**	**0.03**
1	0.0341	0.0353	0.0349	1.44	1.49	1.48	**1.47**	**0.03**
1.5	0.0430	0.0445	0.0446	1.82	1.88	1.89	**1.86**	**0.04**
2	0.0514	0.0521	0.0531	2.18	2.21	2.25	**2.21**	**0.04**
2.5	0.0554	0.0532	0.0521	2.35	2.25	2.21	**2.27**	**0.07**
3	0.0524	0.0512	0.0542	2.22	2.17	2.29	**2.23**	**0.06**
3.5	0.0484	0.0546	0.0551	2.05	2.31	2.33	**2.23**	**0.16**
4	0.0549	0.0584	0.0569	2.32	2.47	2.41	**2.40**	**0.07**
8	0.0506	0.0532	0.0574	2.14	2.25	2.43	**2.28**	**0.15**
12	0.0507	0.0556	0.0532	2.15	2.35	2.25	**2.25**	**0.10**
16	0.0557	0.0542	0.0541	2.36	2.29	2.29	**2.31**	**0.04**
20	0.0485	0.0562	0.0558	2.05	2.38	2.36	**2.27**	**0.18**
24	0.0555	0.0529	0.0501	2.35	2.24	2.12	**2.24**	**0.11**
28	0.0462	0.0527	0.0509	1.96	2.23	2.16	**2.11**	**0.14**
32	0.0462	0.0538	0.0514	1.96	2.28	2.18	**2.14**	**0.16**
36	0.0579	0.0521	0.0527	2.45	2.21	2.23	**2.30**	**0.14**
40	0.0579	0.0548	0.0518	2.45	2.32	2.19	**2.32**	**0.13**
44	0.0555	0.0553	0.0512	2.35	2.34	2.17	**2.29**	**0.10**
48	0.0465	0.0542	0.0542	1.97	2.29	2.29	**2.19**	**0.19**

Release Kinetics of Model Drug from Drug-Loaded Carrageenan Hydrogel

The study of acetylsalicylic acid transport mechanism from the carrageenan hydrogels, Fickian diffusion models are considered to fit the experimental data.

The power law model is described by the Ritger-Peppas equation (Venkatesh *et al.*, 1992):

$$\frac{M_t}{M_\infty} = k_1 t^n \qquad \text{(L1)}$$

where M_t/M_∞ = the fractional drug release

k_1 = a kinetic constant (with the unit of T^{-n})

t = the release time

and n = the scaling exponent that can be related to the drug transport mechanism.

For a thin hydrogel film, when n = 0.5, the drug release mechanism is observed by the Fickian diffusion:

$$\frac{M_t}{M_\infty} = k_H t^{1/2} \qquad \text{(L2)}$$

where M_t/M_∞ = the fractional drug release

k_H = a kinetic constant (with the unit of T^{-n})

and t = the release time.

The diffusion coefficients of acetylsalicylic acid from the carrageenan hydrogels are determined from the slopes of plots of drug accumulation versus square root of time according to Higuchi's equation (Higuchi, 1961):

$$Q = \frac{M_t}{A} = 2C_0(Dt/\pi)^{1/2} \qquad \text{(L3)}$$

where Q = the amount of material flowing through a unit cross section of barrier (g/cm^2) in unit time, t (s)

C_0 = the initial drug concentration in the hydrogel (g/cm^3)

and D = the diffusion coefficient of a drug (cm^2/s)

The diffusion coefficients of each system were calculated from the slopes of the plot of the amounts of acetylsalicylic acid released from acetylsalicylic acid-loaded carrageenan hydrogels at time t versus time$^{1/2}$ at various crosslinking ratios with the electric field strength 2 V during 48 h using the Higuchi's equation (see figure L2).

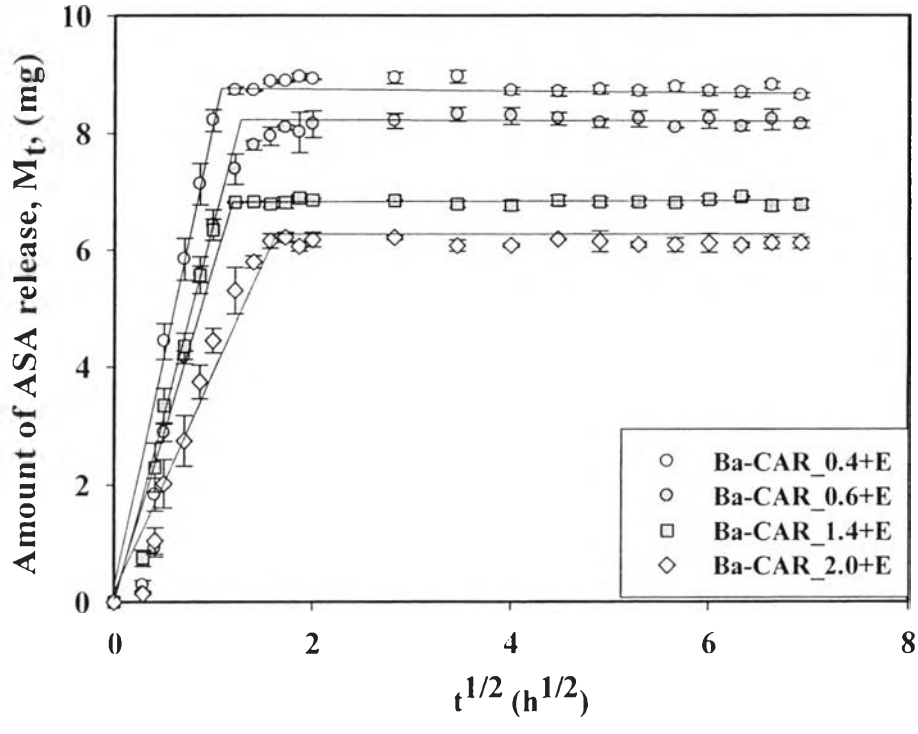


Figure L2 Amounts of acetylsalicylic acid release from acetylsalicylic acid-loaded carrageenan hydrogels versus time$^{1/2}$ at various crosslink ratios, E = 2 V, pH 5.5, and at 37°C, number of samples = 3.

Figure L3 shows the diffusion coefficients of acetylsalicylic acid from carrageenan hydrogels versus crosslinking ratio and mesh size at electric field strength 2 V at 37 °C. Figure L4 presents the diffusion coefficients of acetylsalicylic acid from carrageenan hydrogels versus crosslinking ratio and mesh size at the electric field strength of 0 and 2 V at 37 °C.

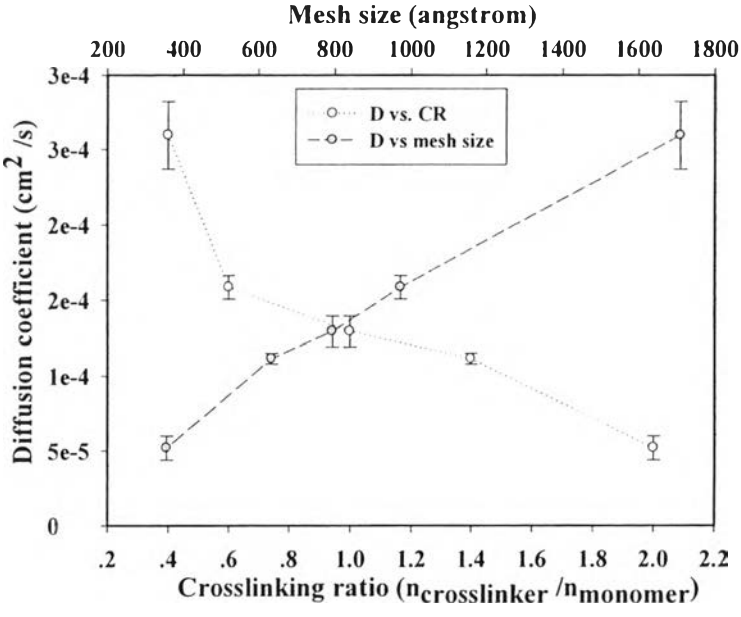


Figure L3 Diffusion coefficients of acetylsalicylic acid from carrageenan hydrogels versus crosslinking ratio and mesh size, E = 2 V, pH 5.5, 37°C, number of samples = 3.

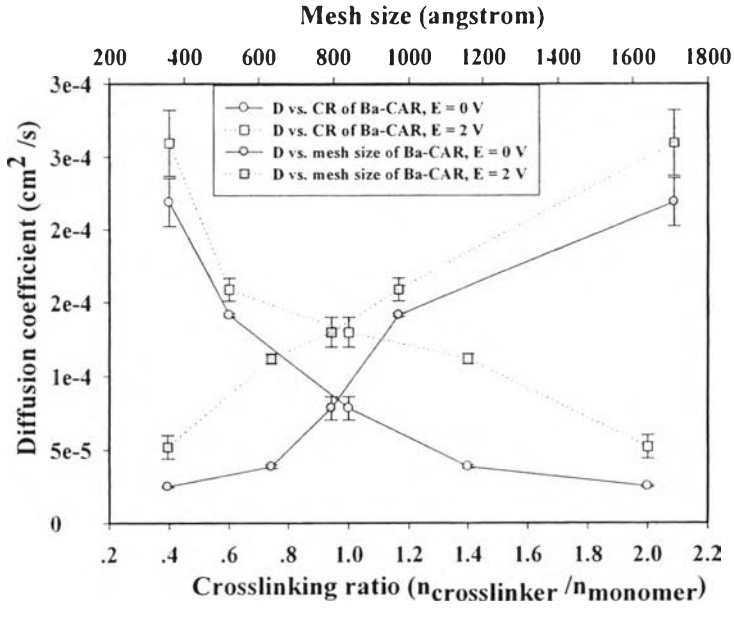


Figure L4 Diffusion coefficients of acetylsalicylic acid from carrageenan hydrogels versus crosslinking ratio and mesh size, E = 0 and 2 V, pH 5.5, 37°C, number of samples = 3.

Table L10 The raw data of the determination of the diffusion coefficients of acetylsalicylic acid released from various crosslinked carrageenan hydrogels, pH 5.5 at 37 °C, E = 2 V

Sample	Slope			Diffusion Coefficient (cm^2/s)				
	1	2	3	1	2	3	Avg	SD
Ba-CAR_0.4	11.11	11.68	12.11	2.36E-04	2.62E-04	2.81E-04	**2.60E-04**	**2.23E-05**
Ba-CAR_0.6	9.17	9.27	8.85	1.61E-04	1.65E-04	1.50E-04	**1.59E-04**	**7.50E-06**
Ba-CAR_1.0	8.39	7.86	8.42	1.35E-04	1.18E-04	1.36E-04	**1.29E-04**	**9.77E-05**
Ba-CAR_1.4	7.51	7.76	7.63	1.08E-04	1.15E-04	1.12E-04	**1.12E-04**	**3.66E-06**
Ba-CAR_2.0	5.49	5.37	4.74	5.78E-05	5.53E-05	4.30E-05	**5.20E-05**	**7.93E-06**
Ca-CAR_1.0	4.07	4.13	4.13	3.17E-05	3.27E-05	3.27E-05	**3.24E-05**	**5.44E-07**
Mg-CAR_1.0	3.25	3.30	3.26	2.02E-05	2.09E-05	2.04E-05	**2.50E-05**	**3.32E-07**
Ca-CAR_2.0	2.36	2.39	2.39	1.07E-05	1.09E-05	1.09E-05	**1.08E-05**	**1.39E-07**
Mg-CAR_3.0	1.62	1.70	1.68	5.03E-06	5.54E-06	5.41E-06	**5.32E-06**	**2.64E-07**

Figure L5 shows the log-log plot of diffusion coefficients of acetylsalicylic acid from carrageenan hydrogels versus drug size/mesh size of hydrogel at electric field strength of 0 and 2 V at 37 °C. From these results, the scaling exponents m were determined from the following equation:

$$D = D_0(a/\xi)^{-m} \qquad \text{(L4)}$$

Where D = the diffusion coefficient of drug

D_0 = the initial diffusion coefficient of drug

a = the size of drug

ξ = the mesh size of hydrogel

and m = the scaling exponent

The scaling exponent m values for the acetylsalicylic acid diffusion through the carrageenan matrix without and with an electric field are 0.96 and 0.97, respectively. Corresponding D_0 values are 1.05×10^{-6} and 1.64×10^{-6} cm^2/s, respectively.

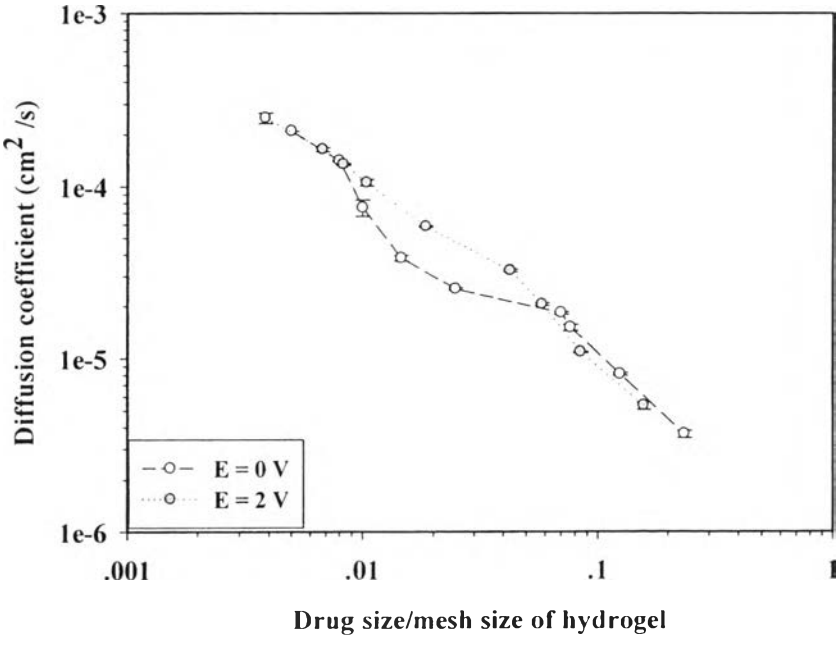


Figure L5 The log-log plot between the diffusion coefficients of acetylsalicylic acid from carrageenan hydrogels versus drug size/mesh size, E = 0 and 2 V, pH 5.5, 37°C, number of samples = 3.

Appendix M Determination of Amounts and Diffusion Coefficient of Acetylsalicylic Acid Released from Acetylsalicylic acid-Loaded Polythiophene/ Carrageenan Blend Film at Various Crosslinking Ratios with Electric Field Strength of 2 V (E = 2 V) under Cathode

The amounts of acetylsalicylic acid (ASA) released from acetylsalicylic acid-loaded polythiophene/carrageenan blend films versus time at various crosslinking ratios with electric field strength of 2 V during 48 h are shown in Figure M1. The amounts of drug released gradually increase with time and then reach constant values. But the amounts of drug released decrease with increasing crosslinking ratio.

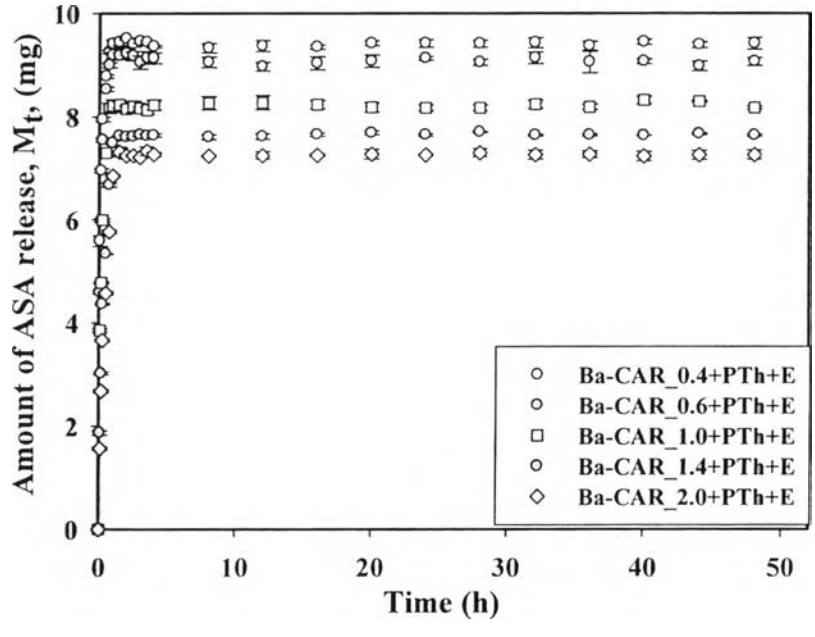


Figure M1 Amounts of acetylsalicylic acid released from acetylsalicylic acid-loaded polythiophene/carrageenan blend films versus timeat various crosslinking ratios, E = 2 V, pH 5.5, and at 37 °C, n = number of samples = 3.

Table M1 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_0.4+PTh+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.1310	0.1299	0.1346	5.55	5.50	5.70	**5.58**	**0.10**
0.16667	0.1641	0.1651	0.1632	6.95	6.99	6.91	**6.95**	**0.04**
0.25	0.1865	0.1885	0.1879	7.90	7.98	7.96	**7.94**	**0.04**
0.5	0.2080	0.2064	0.2077	8.81	8.74	8.79	**8.78**	**0.04**
0.75	0.2185	0.2195	0.2179	9.25	9.29	9.23	**9.26**	**0.03**
1	0.2245	0.2210	0.2213	9.51	9.36	9.37	**9.41**	**0.08**
1.5	0.2244	0.2231	0.2215	9.50	9.45	9.38	**9.44**	**0.06**
2	0.2232	0.2245	0.2241	9.45	9.51	9.49	**9.48**	**0.02**
2.5	0.2222	0.2209	0.2231	9.41	9.35	9.45	**9.40**	**0.05**
3	0.2232	0.2243	0.2226	9.45	9.50	9.43	**9.46**	**0.04**
3.5	0.2222	0.2232	0.2234	9.41	9.45	9.46	**9.44**	**0.03**
4	0.2205	0.2216	0.2209	9.34	9.38	9.35	**9.36**	**0.02**
8	0.2226	0.2199	0.2184	9.43	9.31	9.25	**9.33**	**0.09**
12	0.2236	0.2186	0.2215	9.47	9.26	9.38	**9.37**	**0.11**
16	0.2203	0.2201	0.2219	9.33	9.32	9.40	**9.35**	**0.04**
20	0.2213	0.2236	0.2224	9.37	9.47	9.42	**9.42**	**0.05**
24	0.2216	0.2212	0.2243	9.38	9.37	9.50	**9.42**	**0.07**
28	0.2236	0.2205	0.2228	9.47	9.34	9.43	**9.41**	**0.07**
32	0.2199	0.2241	0.2239	9.31	9.49	9.48	**9.43**	**0.10**
36	0.2200	0.2200	0.2236	9.32	9.31	9.47	**9.37**	**0.09**
40	0.2234	0.2240	0.2217	9.46	9.48	9.39	**9.44**	**0.05**
44	0.2216	0.2231	0.2205	9.38	9.45	9.34	**9.39**	**0.06**
48	0.2194	0.2229	0.2245	9.29	9.44	9.51	**9.41**	**0.11**

Table M2 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_0.6+PTh+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.1083	0.1091	0.1075	4.59	4.62	4.55	**4.59**	**0.03**
0.16667	0.1403	0.1420	0.1414	5.94	6.01	5.99	**5.98**	**0.04**
0.25	0.1774	0.1784	0.1791	7.51	7.55	7.58	**7.55**	**0.04**
0.5	0.2010	0.2009	0.2026	8.51	8.51	8.58	**8.53**	**0.04**
0.75	0.2134	0.2129	0.2112	9.04	9.01	8.94	**9.00**	**0.05**
1	0.2182	0.2171	0.2156	9.24	9.19	9.13	**9.19**	**0.06**
1.5	0.2178	0.2150	0.2174	9.22	9.10	9.20	**9.18**	**0.06**
2	0.2192	0.2146	0.2194	9.28	9.09	9.29	**9.22**	**0.12**
2.5	0.2190	0.2154	0.2154	9.27	9.12	9.12	**9.17**	**0.09**
3	0.2143	0.2104	0.2164	9.07	8.91	9.16	**9.05**	**0.13**
3.5	0.2164	0.2126	0.2184	9.16	9.00	9.25	**9.14**	**0.12**
4	0.2183	0.2135	0.2153	9.24	9.04	9.12	**9.13**	**0.10**
8	0.2125	0.2124	0.2165	9.00	8.99	9.17	**9.05**	**0.10**
12	0.2104	0.2109	0.2142	8.91	8.93	9.07	**8.97**	**0.09**
16	0.2107	0.2127	0.2165	8.92	9.01	9.17	**9.03**	**0.13**
20	0.2120	0.2134	0.2175	8.98	9.04	9.21	**9.07**	**0.12**
24	0.2158	0.2147	0.2163	9.14	9.09	9.16	**9.13**	**0.03**
28	0.2128	0.2131	0.2154	9.01	9.02	9.12	**9.05**	**0.06**
32	0.2132	0.2156	0.2184	9.03	9.13	9.25	**9.13**	**0.11**
36	0.2107	0.2114	0.2195	8.92	8.95	9.29	**9.06**	**0.21**
40	0.2151	0.2129	0.2145	9.11	9.01	9.08	**9.07**	**0.05**
44	0.2104	0.2145	0.2112	8.91	9.08	8.94	**8.98**	**0.09**
48	0.2161	0.2132	0.2128	9.15	9.03	9.01	**9.06**	**0.08**

Table M3 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_1.0+PTh+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0903	0.0919	0.0911	3.82	3.89	3.86	**3.86**	**0.03**
0.16667	0.1121	0.1129	0.1131	4.74	4.78	4.79	**4.77**	**0.02**
0.25	0.1409	0.1414	0.1421	5.96	5.99	6.02	**5.99**	**0.03**
0.5	0.1711	0.1726	0.1731	7.24	7.31	7.33	**7.29**	**0.04**
0.75	0.1910	0.1954	0.1921	8.09	8.27	8.13	**8.16**	**0.10**
1	0.1910	0.1964	0.1945	8.09	8.32	8.24	**8.21**	**0.12**
1.5	0.1937	0.1935	0.1962	8.20	8.19	8.31	**8.23**	**0.06**
2	0.1910	0.1942	0.1923	8.09	8.22	8.14	**8.15**	**0.07**
2.5	0.1905	0.1956	0.1945	8.07	8.28	8.24	**8.19**	**0.11**
3	0.1936	0.1923	0.1926	8.20	8.14	8.15	**8.17**	**0.03**
3.5	0.1902	0.1926	0.1932	8.05	8.15	8.18	**8.13**	**0.07**
4	0.1919	0.1945	0.1965	8.13	8.24	8.32	**8.23**	**0.10**
8	0.1945	0.1985	0.1925	8.24	8.40	8.15	**8.26**	**0.13**
12	0.1990	0.1926	0.1945	8.43	8.15	8.24	**8.27**	**0.14**
16	0.1944	0.1926	0.1965	8.23	8.15	8.32	**8.23**	**0.08**
20	0.1957	0.1917	0.1923	8.29	8.12	8.14	**8.18**	**0.09**
24	0.1919	0.1926	0.1945	8.13	8.15	8.24	**8.17**	**0.06**
28	0.1920	0.1945	0.1925	8.13	8.24	8.15	**8.17**	**0.06**
32	0.1944	0.1965	0.1929	8.23	8.32	8.17	**8.24**	**0.08**
36	0.1928	0.1925	0.1948	8.16	8.15	8.25	**8.19**	**0.05**
40	0.1976	0.1945	0.1974	8.37	8.24	8.36	**8.32**	**0.07**
44	0.1961	0.1962	0.1954	8.30	8.31	8.27	**8.29**	**0.02**
48	0.1939	0.1926	0.1926	8.21	8.15	8.15	**8.17**	**0.03**

Table M4 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_1.4+PTh+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0440	0.0431	0.0451	1.86	1.82	1.91	**1.87**	**0.04**
0.16667	0.0709	0.0710	0.0720	3.00	3.01	3.05	**3.02**	**0.03**
0.25	0.1031	0.1022	0.1029	4.36	4.33	4.36	**4.35**	**0.02**
0.5	0.1256	0.1259	0.1261	5.32	5.33	5.34	**5.33**	**0.01**
0.75	0.1571	0.1586	0.1569	6.65	6.72	6.64	**6.67**	**0.04**
1	0.1760	0.1779	0.1769	7.45	7.53	7.49	**7.49**	**0.04**
1.5	0.1804	0.1802	0.1801	7.64	7.63	7.63	**7.63**	**0.01**
2	0.1805	0.1785	0.1799	7.64	7.56	7.62	**7.61**	**0.04**
2.5	0.1807	0.1789	0.1803	7.65	7.57	7.63	**7.62**	**0.04**
3	0.1810	0.1799	0.1812	7.66	7.62	7.67	**7.65**	**0.03**
3.5	0.1801	0.1792	0.1811	7.63	7.59	7.67	**7.63**	**0.04**
4	0.1812	0.1803	0.1798	7.67	7.63	7.61	**7.64**	**0.03**
8	0.1799	0.1805	0.1784	7.62	7.64	7.55	**7.60**	**0.05**
12	0.1795	0.1813	0.1789	7.60	7.68	7.57	**7.62**	**0.05**
16	0.1804	0.1816	0.1802	7.64	7.69	7.63	**7.65**	**0.03**
20	0.1820	0.1819	0.1806	7.71	7.70	7.65	**7.69**	**0.03**
24	0.1811	0.1800	0.1807	7.67	7.62	7.65	**7.65**	**0.02**
28	0.1819	0.1821	0.1816	7.70	7.71	7.69	**7.70**	**0.01**
32	0.1808	0.1805	0.1800	7.66	7.64	7.62	**7.64**	**0.02**
36	0.1802	0.1811	0.1803	7.63	7.67	7.63	**7.64**	**0.02**
40	0.1803	0.1802	0.1804	7.63	7.63	7.64	**7.63**	**0.00**
44	0.1815	0.1809	0.1806	7.69	7.66	7.65	**7.66**	**0.02**
48	0.1798	0.1808	0.1805	7.61	7.66	7.64	**7.64**	**0.02**

Table M5 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_2.0+PTh+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0370	0.0364	0.0379	1.57	1.54	1.60	**1.57**	**0.03**
0.16667	0.0631	0.0626	0.0641	2.67	2.65	2.71	**2.68**	**0.03**
0.25	0.0873	0.0859	0.0864	3.70	3.64	3.66	**3.66**	**0.03**
0.5	0.1086	0.1079	0.1071	4.60	4.57	4.53	**4.57**	**0.03**
0.75	0.1370	0.1354	0.1361	5.80	5.73	5.76	**5.77**	**0.03**
1	0.1611	0.1619	0.1623	6.82	6.85	6.87	**6.85**	**0.02**
1.5	0.1717	0.1754	0.1714	7.27	7.43	7.26	**7.32**	**0.09**
2	0.1711	0.1703	0.1721	7.24	7.21	7.29	**7.25**	**0.04**
2.5	0.1713	0.1718	0.1706	7.25	7.27	7.22	**7.25**	**0.03**
3	0.1704	0.1699	0.1709	7.21	7.19	7.24	**7.21**	**0.02**
3.5	0.1729	0.1754	0.1715	7.32	7.43	7.26	**7.34**	**0.08**
4	0.1724	0.1721	0.1706	7.30	7.29	7.22	**7.27**	**0.04**
8	0.1712	0.1712	0.1704	7.25	7.25	7.21	**7.24**	**0.02**
12	0.1703	0.1732	0.1702	7.21	7.33	7.21	**7.25**	**0.07**
16	0.1709	0.1721	0.1711	7.24	7.29	7.24	**7.26**	**0.03**
20	0.1699	0.1742	0.1713	7.19	7.38	7.25	**7.27**	**0.09**
24	0.1711	0.1719	0.1715	7.25	7.28	7.26	**7.26**	**0.02**
28	0.1719	0.1745	0.1709	7.28	7.39	7.24	**7.30**	**0.08**
32	0.1727	0.1726	0.1691	7.31	7.31	7.16	**7.26**	**0.09**
36	0.1724	0.1728	0.1700	7.30	7.32	7.20	**7.27**	**0.06**
40	0.1721	0.1684	0.1721	7.29	7.13	7.29	**7.24**	**0.09**
44	0.1722	0.1169	0.1729	7.29	7.16	7.32	**7.22**	**0.09**
48	0.1723	0.1691	0.1731	7.30	7.16	7.33	**7.26**	**0.09**

Table M6 The raw data of the determination of amounts of acetylsalicylic acid released from Ca-CAR_1.0+PTh+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0300	0.0296	0.0310	1.27	1.25	1.31	**1.28**	**0.03**
0.16667	0.0514	0.0521	0.0531	2.18	2.21	2.25	**2.21**	**0.04**
0.25	0.0646	0.0651	0.0662	2.73	2.76	2.80	**2.76**	**0.04**
0.5	0.0855	0.0849	0.0861	3.62	3.59	3.65	**3.62**	**0.03**
0.75	0.1046	0.1040	0.1039	4.43	4.40	4.40	**4.41**	**0.01**
1	0.1246	0.1239	0.1255	5.27	5.25	5.31	**5.28**	**0.03**
1.5	0.1400	0.1412	0.1409	5.93	5.98	5.97	**5.96**	**0.03**
2	0.1520	0.1542	0.1532	6.43	6.53	6.49	**6.48**	**0.05**
2.5	0.1577	0.1526	0.1542	6.68	6.46	6.53	**6.56**	**0.11**
3	0.1490	0.1500	0.1532	6.31	6.35	6.49	**6.38**	**0.09**
3.5	0.1548	0.1532	0.1502	6.55	6.49	6.36	**6.47**	**0.10**
4	0.1600	0.1542	0.1532	6.77	6.53	6.49	**6.60**	**0.16**
8	0.1551	0.1526	0.1549	6.57	6.46	6.56	**6.53**	**0.06**
12	0.1523	0.1532	0.1562	6.45	6.49	6.61	**6.52**	**0.09**
16	0.1527	0.1542	0.1532	6.47	6.53	6.49	**6.49**	**0.03**
20	0.1529	0.1574	0.1524	6.47	6.66	6.45	**6.53**	**0.12**
24	0.1503	0.1562	0.1523	6.36	6.61	6.45	**6.48**	**0.13**
28	0.1522	0.1523	0.1509	6.44	6.45	6.39	**6.43**	**0.03**
32	0.1531	0.1515	0.1511	6.48	6.41	6.40	**6.43**	**0.04**
36	0.1551	0.1548	0.1532	6.57	6.55	6.49	**6.54**	**0.04**
40	0.1526	0.1515	0.1521	6.46	6.41	6.44	**6.44**	**0.02**
44	0.1547	0.1564	0.1534	6.55	6.62	6.50	**6.56**	**0.06**
48	0.1549	0.1598	0.1574	6.56	6.77	6.66	**6.66**	**0.10**

Table M7 The raw data of the determination of amounts of acetylsalicylic acid released from Mg-CAR_1.0+PTh+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0290	0.0278	0.0284	1.23	1.18	1.20	**1.20**	**0.03**
0.16667	0.0417	0.0424	0.0431	1.76	1.80	1.82	**1.79**	**0.03**
0.25	0.0560	0.0546	0.0555	2.37	2.31	2.35	**2.34**	**0.03**
0.5	0.0715	0.0721	0.0732	3.03	3.05	3.10	**3.06**	**0.04**
0.75	0.0846	0.0851	0.0861	3.58	3.60	3.65	**3.61**	**0.03**
1	0.1023	0.1016	0.1032	4.33	4.30	4.37	**4.33**	**0.03**
1.5	0.1125	0.1112	0.1132	4.76	4.71	4.79	**4.75**	**0.04**
2	0.1266	0.1254	0.1295	5.36	5.31	5.48	**5.38**	**0.09**
2.5	0.1255	0.1238	0.1284	5.31	5.24	5.44	**5.33**	**0.10**
3	0.1290	0.1295	0.1257	5.46	5.48	5.32	**5.42**	**0.09**
3.5	0.1351	0.1274	0.1265	5.72	5.39	5.36	**5.49**	**0.20**
4	0.1271	0.1285	0.1284	5.38	5.44	5.44	**5.42**	**0.03**
8	0.1297	0.1245	0.1283	5.49	5.27	5.43	**5.40**	**0.11**
12	0.1262	0.1256	0.1254	5.34	5.32	5.31	**5.32**	**0.02**
16	0.1249	0.1287	0.1296	5.29	5.45	5.49	**5.41**	**0.11**
20	0.1279	0.1289	0.1275	5.42	5.46	5.40	**5.42**	**0.03**
24	0.1300	0.1275	0.1262	5.50	5.40	5.34	**5.42**	**0.08**
28	0.1281	0.1285	0.1272	5.42	5.44	5.39	**5.42**	**0.03**
32	0.1287	0.1295	0.1274	5.45	5.48	5.39	**5.44**	**0.04**
36	0.1212	0.1256	0.1278	5.13	5.32	5.41	**5.29**	**0.14**
40	0.1299	0.1248	0.1274	5.50	5.28	5.39	**5.39**	**0.11**
44	0.1254	0.1236	0.1259	5.31	5.23	5.33	**5.29**	**0.05**
48	0.1287	0.1284	0.1247	5.45	5.44	5.28	**5.39**	**0.09**

Table M8 The raw data of the determination of amounts of acetylsalicylic acid released from Ca-CAR_2.0+PTh+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0201	0.0211	0.0222	0.85	0.89	0.94	**0.89**	**0.04**
0.16667	0.0306	0.0312	0.0321	1.30	1.32	1.36	**1.33**	**0.03**
0.25	0.0401	0.0403	0.0416	1.70	1.71	1.76	**1.72**	**0.03**
0.5	0.0515	0.0521	0.0539	2.18	2.21	2.28	**2.22**	**0.05**
0.75	0.0615	0.0620	0.0631	2.60	2.63	2.67	**2.63**	**0.04**
1	0.0746	0.0751	0.0739	3.16	3.18	3.13	**3.16**	**0.03**
1.5	0.0846	0.0857	0.0849	3.58	3.63	3.59	**3.60**	**0.02**
2	0.0903	0.0912	0.0926	3.82	3.86	3.92	**3.87**	**0.05**
2.5	0.0953	0.0932	0.0945	4.04	3.95	4.00	**3.99**	**0.04**
3	0.0958	0.0916	0.0939	4.06	3.88	3.98	**3.97**	**0.09**
3.5	0.0901	0.0923	0.0945	3.81	3.91	4.00	**3.91**	**0.09**
4	0.0912	0.0945	0.0915	3.86	4.00	3.87	**3.91**	**0.08**
8	0.0918	0.0928	0.0964	3.89	3.93	4.08	**3.97**	**0.10**
12	0.0914	0.0965	0.0951	3.87	4.09	4.03	**3.99**	**0.11**
16	0.0983	0.0942	0.0961	4.16	3.99	4.07	**4.07**	**0.09**
20	0.0883	0.0912	0.0908	3.74	3.86	3.84	**3.82**	**0.07**
24	0.0943	0.0945	0.0965	3.99	4.00	4.09	**4.03**	**0.05**
28	0.0932	0.0962	0.0934	3.95	4.07	3.95	**3.99**	**0.07**
32	0.0874	0.0912	0.0926	3.70	3.86	3.92	**3.83**	**0.11**
36	0.0901	0.0921	0.0935	3.81	3.90	3.96	**3.89**	**0.07**
40	0.0912	0.0945	0.0915	3.86	4.00	3.87	**3.91**	**0.08**
44	0.0932	0.0962	0.0945	3.95	4.07	4.00	**4.01**	**0.06**
48	0.0941	0.0948	0.0926	3.98	4.01	3.92	**3.97**	**0.05**

Table M9 The raw data of the determination of amounts of acetylsalicylic acid released from Mg-CAR_3.0+PTh+E at time t, pH 5.5 at 37 °C, with the electric field 2 V

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0103	0.0113	0.0121	0.44	0.48	0.51	**0.48**	**0.04**
0.16667	0.0204	0.0212	0.0222	0.86	0.90	0.94	**0.90**	**0.04**
0.25	0.0301	0.0312	0.0321	1.28	1.32	1.36	**1.32**	**0.04**
0.5	0.0405	0.0410	0.0421	1.71	1.74	1.78	**1.74**	**0.03**
0.75	0.0451	0.0461	0.0471	1.91	1.95	1.99	**1.95**	**0.04**
1	0.0495	0.0499	0.0501	2.10	2.11	2.12	**2.11**	**0.01**
1.5	0.0592	0.0585	0.0574	2.51	2.48	2.43	**2.47**	**0.04**
2	0.0699	0.0689	0.0615	2.96	2.92	2.60	**2.83**	**0.19**
2.5	0.0651	0.0623	0.0654	2.76	2.64	2.77	**2.72**	**0.07**
3	0.0640	0.0652	0.0628	2.71	2.76	2.66	**2.71**	**0.05**
3.5	0.0693	0.0614	0.0658	2.93	2.60	2.79	**2.77**	**0.17**
4	0.0631	0.0653	0.0674	2.67	2.76	2.85	**2.76**	**0.09**
8	0.0631	0.0690	0.0658	2.67	2.92	2.79	**2.79**	**0.13**
12	0.0643	0.0684	0.0695	2.72	2.90	2.94	**2.85**	**0.12**
16	0.0720	0.0654	0.0648	3.05	2.77	2.74	**2.85**	**0.17**
20	0.0635	0.0674	0.0689	2.69	2.85	2.92	**2.82**	**0.12**
24	0.0715	0.0652	0.0625	3.03	2.76	2.65	**2.81**	**0.20**
28	0.0697	0.0635	0.0648	2.95	2.69	2.74	**2.79**	**0.14**
32	0.0700	0.0645	0.0649	2.96	2.73	2.75	**2.81**	**0.13**
36	0.0712	0.0685	0.0689	3.01	2.90	2.92	**2.94**	**0.06**
40	0.0715	0.0649	0.0678	3.03	2.75	2.87	**2.88**	**0.14**
44	0.0669	0.0699	0.0698	2.83	2.96	2.96	**2.92**	**0.07**
48	0.0699	0.0678	0.0655	2.96	2.87	2.77	**2.87**	**0.09**

Release Kinetics of Model Drug from Drug-Loaded Carrageenan Hydrogel

The study of acetylsalicylic acid transport mechanism from the carrageenan hydrogels, Fickian diffusion models are considered to fit the experimental data.

The power law model is described by the Ritger-Peppas equation (Venkatesh *et al.*, 1992):

$$\frac{M_t}{M_\infty} = k_1 t^n \qquad \text{(M1)}$$

where M_t/M_∞ = the fractional drug release

k_1 = a kinetic constant (with the unit of T^{-n})

t = the release time

and n = the scaling exponent that can be related to the drug transport mechanism.

For a thin hydrogel film, when n = 0.5, the drug release mechanism is observed by the Fickian diffusion:

$$\frac{M_t}{M_\infty} = k_H t^{1/2} \qquad \text{(M2)}$$

where M_t/M_∞ = the fractional drug release

k_H = a kinetic constant (with the unit of T^{-n})

and t = the release time.

The diffusion coefficients of acetylsalicylic acid from the carrageenan hydrogels are determined from the slopes of plots of drug accumulation versus square root of time according to Higuchi's equation (Higuchi, 1961):

$$Q = \frac{M_t}{A} = 2C_0(Dt/\pi)^{1/2} \qquad \text{(M3)}$$

where Q = the amount of material flowing through a unit cross section of barrier (g/cm^2) in unit time, t (s)

C_0 = the initial drug concentration in the hydrogel (g/cm^3)

and D = the diffusion coefficient of a drug (cm^2/s)

The diffusion coefficients of each system were calculated from the slopes of the plot of the amounts of acetylsalicylic acid released from acetylsalicylic acid-loaded polythiophene/carrageenan blend films at time t versus time$^{1/2}$ at various crosslinking ratios with the electric field strength 2 V during 48 h using the Higuchi's equation (see figure M2).

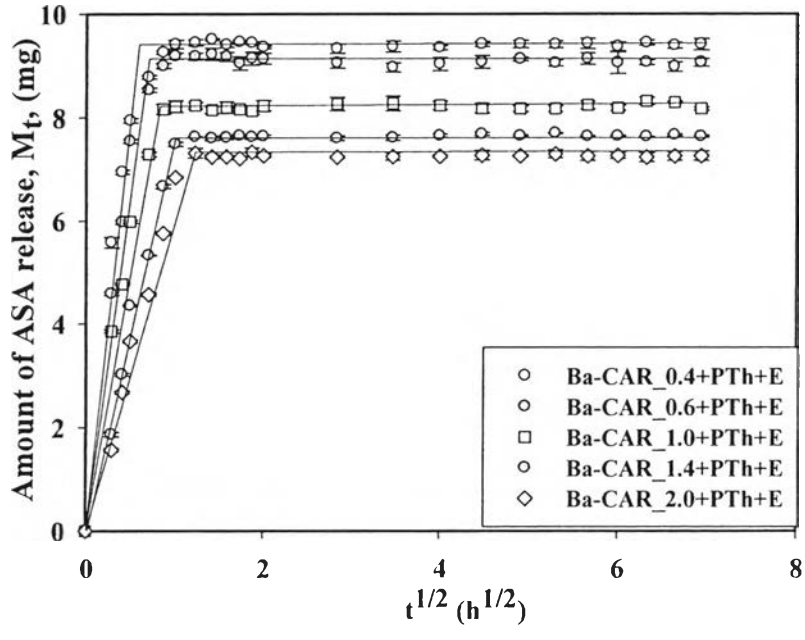


Figure M2 Amounts of acetylsalicylic acid release from acetylsalicylic acid-loaded polythiophene/carrageenan blend films versus time$^{1/2}$ at various crosslink ratios, E = 2 V, pH 5.5, and at 37°C, number of samples = 3.

Figure M3 shows the amounts of acetylsalicylic acid released from acetylsalicylic acid-loaded carrageenan hydrogels and polythiophene/carrageenan blend films at time versus $t^{1/2}$ at the crosslinking ratios = 1 with the electric field 2 V during 48 h.

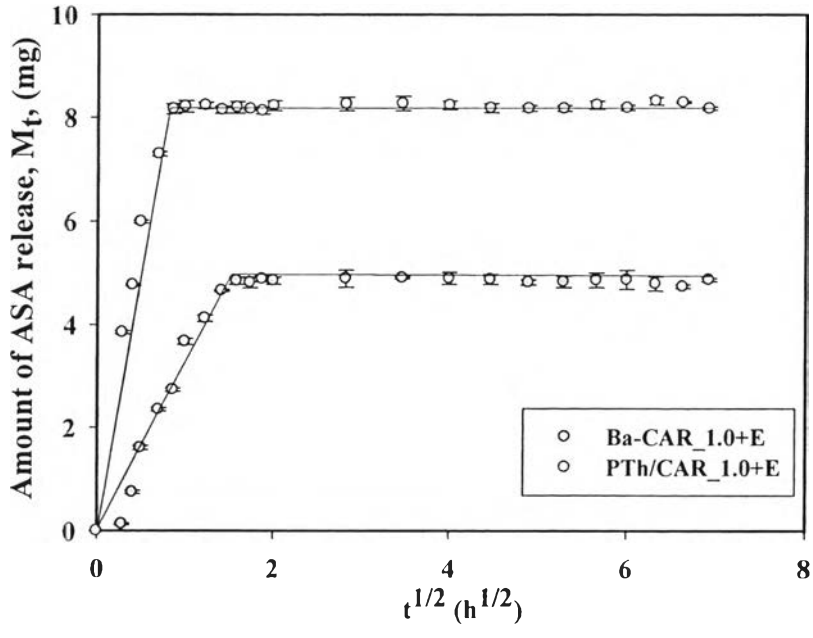


Figure M3 Amounts of acetylsalicylic acid release from acetylsalicylic acid-loaded carrageenan hydrogels and polythiophene/carrageenan blend films at time versus time$^{1/2}$ at crosslink ratio= 1, E = 2 V, pH 5.5, and at 37 °C, number of samples = 3.

Figure M4 shows the diffusion coefficients of acetylsalicylic acid from polythiophene/carrageenan blend films versus crosslinking ratio and mesh size at the electric field strength of 2 V at 37 °C.

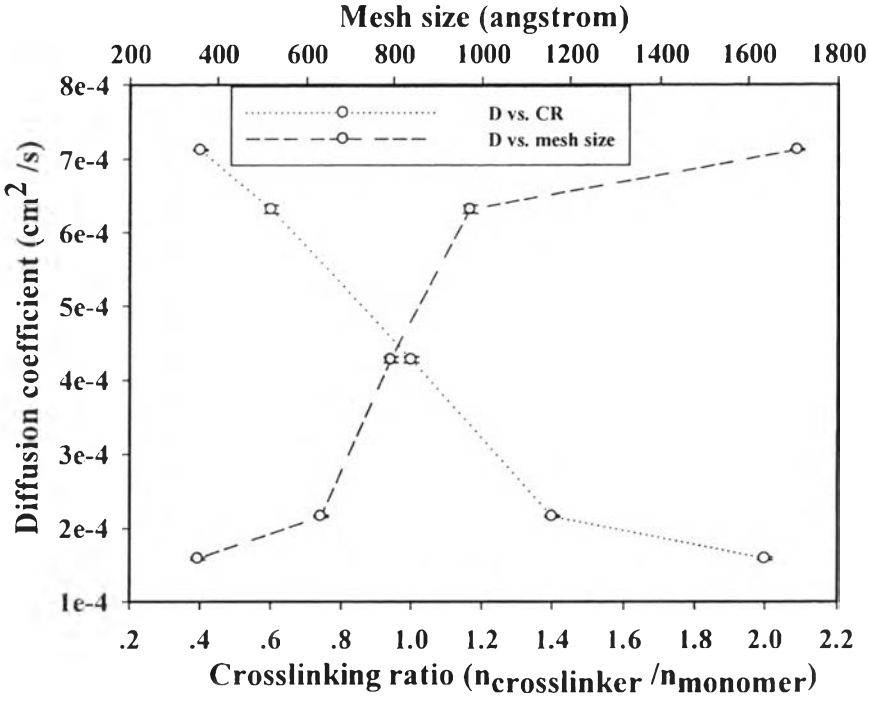
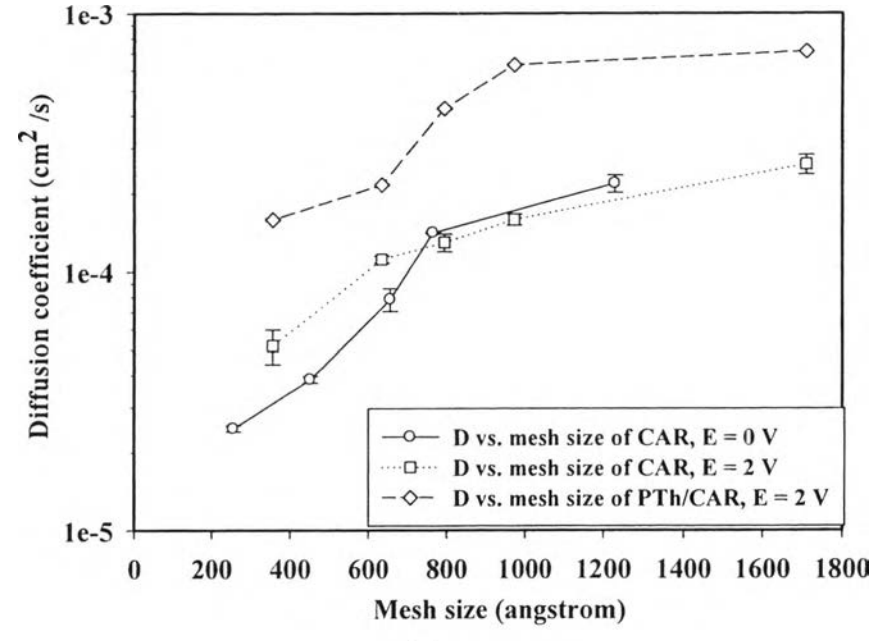
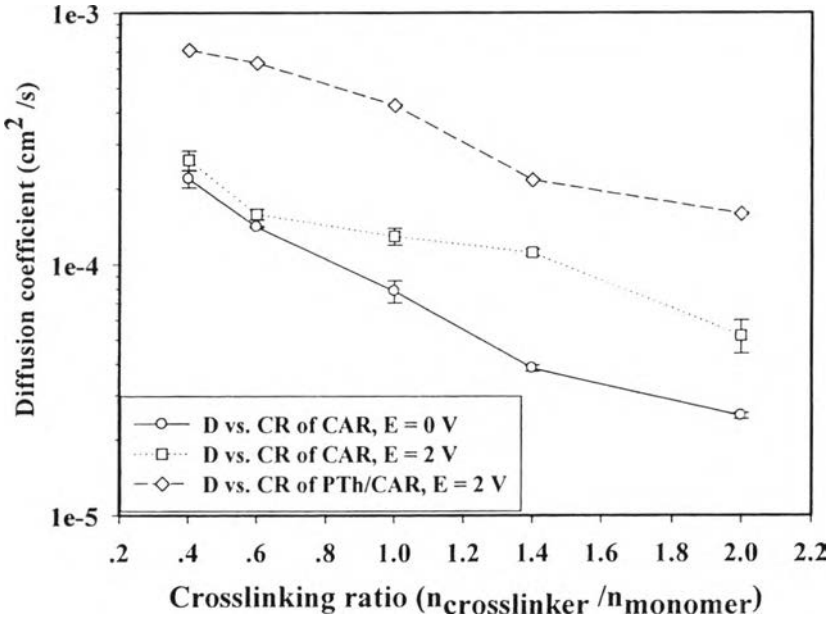


Figure M4 Diffusion coefficients of acetylsalicylic acid from polythiophene/ carrageenan blend films versus crosslinking ratio and mesh size, E = 2 V, pH 5.5, 37°C, number of samples = 3.

Figure M5 (a) and (b) show the diffusion coefficients of acetylsalicylic acid from carrageenan hydrogels and polythiophene/carrageenan blend films versus crosslinking ratio and mesh size at the electric field strengths of 0 and 2 V at 37 °C, respectively.



(a)



(b)

Figure M5 Diffusion coefficients of acetylsablicylic acid from carrageenan hydrogels and polythiophene/ carrageenan blend films versus (a) mesh size and (b) crosslinking ratio, E = 0 and 2 V, pH 5.5, 37°C, number of samples = 3.

Table M10 The raw data of the determination of the diffusion coefficients of acetylsalicylic acid released from various crosslinkedPTh/carrageenan blend films, pH 5.5 at 37 °C, E = 2 V

Sample	Slope			Diffusion Coefficient (cm^2/s)				
	1	2	3	1	2	3	Avg	SD
Ba-CAR_0.4+PTh	19.27	19.29	19.28	7.11E-04	7.13E-04	7.12E-04	**7.12E-04**	**9.29E-07**
Ba-CAR_0.6+PTh	18.07	18.15	18.23	6.26E-04	6.31E-04	6.37E-04	**6.31E-04**	**5.43E-06**
Ba-CAR_1.0+PTh	14.85	14.97	15.00	4.23E-04	4.29E-04	4.31E-04	**4.28E-04**	**4.44E-06**
Ba-CAR_1.4+PTh	10.62	10.60	10.66	2.16E-04	2.15E-04	2.18E-04	**2.16E-04**	**1.27E-06**
Ba-CAR_2.0+PTh	9.16	9.07	9.09	1.61E-04	1.58E-04	1.58E-04	**1.59E-04**	**1.61E-06**
Ca-CAR_1.0+PTh	7.11	7.12	7.23	9.68E-05	9.71E-05	1.00E-04	**9.80E-05**	**1.83E-06**
Mg-CAR_1.0+PTh	5.98	5.98	6.07	6.85E-05	6.84E-05	7.06E-05	**6.92E-05**	**1.21E-06**
Ca-CAR_2.0+PTh	4.32	4.36	4.51	3.57E-05	3.64E-05	3.89E-05	**3.70E-05**	**5.43E-06**
Mg-CAR_3.0+PTh	3.26	3.33	3.44	2.03E-05	2.13E-05	2.26E-05	**2.14E-05**	**1.16E-06**

Figure M6 shows the log-log plot between the diffusion coefficients of acetylsalicylic acid from carrageenan hydrogels and PTh/carrageenan blend films versus drug size/mesh size, E = 0 and 2 V, pH 5.5, 37°C, number of samples = 3, the scaling exponents m were determined from the following equation:

$$D = D_0(a/\xi)^{-m} \qquad \text{(M4)}$$

where D = the diffusion coefficient of drug

D_0 = the initial diffusion coefficient of drug

a = the size of drug

ξ = the mesh size of hydrogel

and m = the scaling exponent

The scaling exponent m values forthe acetylsalicylic acid to diffuse through the carrageenan hydrogelunder the electric field strengths of 0 and 2 V and the acetylsalicylic acid to diffuse through the PTh/carrageenan film under electric field strength of 2 V are 0.96, 0.97, and 5.20,respectively. Corresponding D_o values are 1.05×10^{-6}, 1.64×10^{-6}, and 6.32×10^{-6}cm^2/s, respectively.

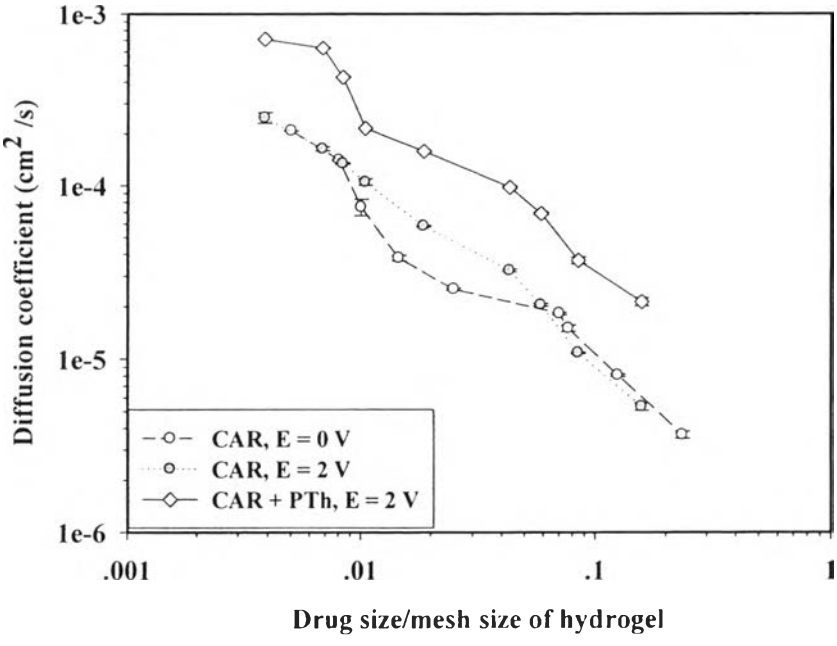


Figure M6 The log-log plot between the diffusion coefficients of acetylsalicylic acid from carrageenan hydrogels and PTh/carrageenan blend films versus drug size/mesh size, E = 0 and 2 V, pH 5.5, 37°C, number of samples = 3.

From a plot of $\ln(M_t/M_\infty)$ versus ln(t), the scaling exponents n were determined from Eq.1 as show in table M11. The n value of carrageenan hydrogel without electric field is near the Fickian exponent value of n = 0.5. Thus, acetylsalicylic acid realased is controlled by Fickian diffusion mechanism and the change in their structures has effect on the mechanism of release.

Table M11 Release kinetic parameters and linear regression values obtained from fitting drug release experimental data to the Ritger-Peppas model

Sample	E(V)	Diffusional exponent (n)	Kinetic constant (K)(h^{-n})	r^2
Ba-CAR_0.4	0	0.33	1.21	0.98
Ba-CAR_0.6	0	0.34	1.15	0.99
Ba-CAR_1.0	0	0.36	0.99	0.98
Ba-CAR_1.4	0	0.52	0.83	0.99
Ba-CAR_2.0	0	0.57	0.80	0.99
Ca-CAR_1.0	0	0.60	0.84	0.96
Mg-CAR_1.0	0	0.56	0.87	0.97
Ca-CAR_2.0	0	0.59	0.72	0.95
Mg-CAR_3.0	0	0.54	0.76	0.94
Ba-CAR_0.4+E	2	0.46	1.06	0.92
Ba-CAR_0.6+E	2	0.47	0.96	0.94
Ba-CAR_1.0+E	2	0.48	0.92	0.95
Ba-CAR_1.4+E	0.5	0.51	1.04	0.98
Ba-CAR_1.4+E	1	0.56	1.02	0.97
Ba-CAR_1.4+E	2	0.44	0.85	0.98
Ba-CAR_1.4+E	3	0.42	0.93	0.98
Ba-CAR_1.4+E	5	0.48	0.94	0.98
Ba-CAR_1.4+E	7	0.48	0.91	0.98
Ba-CAR_2.0+E	2	0.54	0.81	0.97
Ca-CAR_1.0+E	2	0.60	0.83	0.94
Mg-CAR_1.0+E	2	0.60	0.65	0.95
Ca-CAR_2.0+E	2	0.56	0.49	0.96
Mg-CAR_3.0+E	2	0.74	0.35	0.95

Sample	E(V)	Diffusional exponent (n)	Kinetic constant (K)(h^{-n})	r^2
Ba-CAR_0.4+PTh+E	2	0.14	1.48	0.93
Ba-CAR_0.6+PTh+E	2	0.23	1.31	0.92
Ba-CAR_1.0+PTh+E	2	0.43	1.23	0.94
Ba-CAR_1.4+PTh+E	2	0.45	1.03	0.98
Ba-CAR_2.0+PTh+E	2	0.49	0.94	0.99
Ca-CAR_1.0+PTh+E	2	0.39	1.47	0.98
Mg-CAR_1.0+PTh+E	2	0.40	1.06	0.98
Ca-CAR_2.0+PTh+E	2	0.40	0.79	0.98
Mg-CAR_3.0+PTh+E	2	0.39	0.67	0.96

Appendix N Determination of Amounts and Diffusion Coefficient of Acetylsalicylic Acid Released from Acetylsalicylic Acid-Loaded Carrageenan Hydrogel at Crosslinking Ratio = 1.4 under Cathode, Anode and Without an Applied Electric Field

The amounts of acetylsalicylic acid (ASA) released from acetylsalicylic acid-loaded carrageenan hydrogels versus time at crosslinking ratio = 1.4 under the negatively charged electrode (cathode in the donor part), the positively charged electrode (anode in the donor part), and without an applied electric field during 48 h are shown in Figure N1. The amount of drug release under cathode is higher than those under no electric field and under anode, respectively.

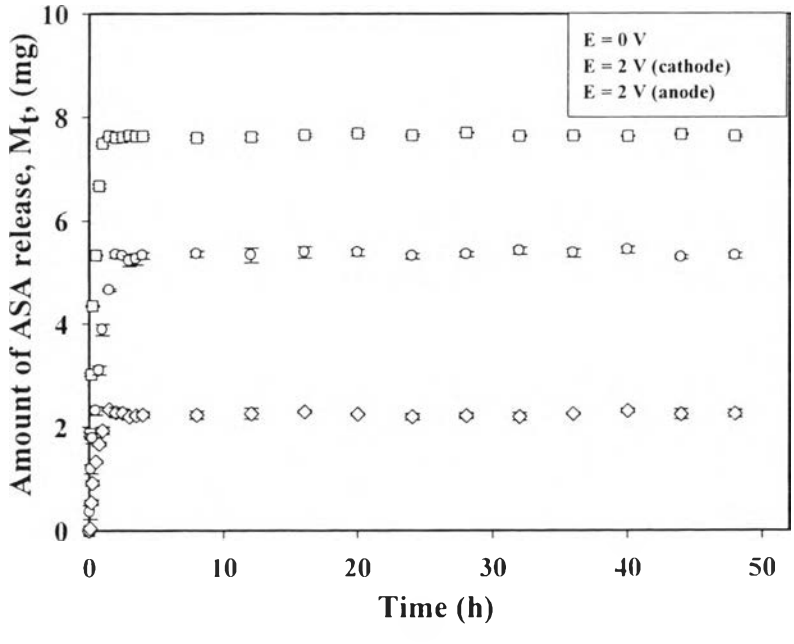


Figure N1 Amounts of acetylsalicylic acid released from Ba-carrageenan hydrogels versus time with the hydrogel samples attached to the anode or cathode, CAR_1.4 hydrogels

Table N1 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_1.4+PTh+E at time t, pH 5.5 at 37 °C, with the electric field 2 V under cathode

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0440	0.0431	0.0451	1.86	1.82	1.91	**1.87**	**0.04**
0.16667	0.0709	0.0710	0.0720	3.00	3.01	3.05	**3.02**	**0.03**
0.25	0.1031	0.1022	0.1029	4.36	4.33	4.36	**4.35**	**0.02**
0.5	0.1256	0.1259	0.1261	5.32	5.33	5.34	**5.33**	**0.01**
0.75	0.1571	0.1586	0.1569	6.65	6.72	6.64	**6.67**	**0.04**
1	0.1760	0.1779	0.1769	7.45	7.53	7.49	**7.49**	**0.04**
1.5	0.1804	0.1802	0.1801	7.64	7.63	7.63	**7.63**	**0.01**
2	0.1805	0.1785	0.1799	7.64	7.56	7.62	**7.61**	**0.04**
2.5	0.1807	0.1789	0.1803	7.65	7.57	7.63	**7.62**	**0.04**
3	0.1810	0.1799	0.1812	7.66	7.62	7.67	**7.65**	**0.03**
3.5	0.1801	0.1792	0.1811	7.63	7.59	7.67	**7.63**	**0.04**
4	0.1812	0.1803	0.1798	7.67	7.63	7.61	**7.64**	**0.03**
8	0.1799	0.1805	0.1784	7.62	7.64	7.55	**7.60**	**0.05**
12	0.1795	0.1813	0.1789	7.60	7.68	7.57	**7.62**	**0.05**
16	0.1804	0.1816	0.1802	7.64	7.69	7.63	**7.65**	**0.03**
20	0.1820	0.1819	0.1806	7.71	7.70	7.65	**7.69**	**0.03**
24	0.1811	0.1800	0.1807	7.67	7.62	7.65	**7.65**	**0.02**
28	0.1819	0.1821	0.1816	7.70	7.71	7.69	**7.70**	**0.01**
32	0.1808	0.1805	0.1800	7.66	7.64	7.62	**7.64**	**0.02**
36	0.1802	0.1811	0.1803	7.63	7.67	7.63	**7.64**	**0.02**
40	0.1803	0.1802	0.1804	7.63	7.63	7.64	**7.63**	**0.00**
44	0.1815	0.1809	0.1806	7.69	7.66	7.65	**7.66**	**0.02**
48	0.1798	0.1808	0.1805	7.61	7.66	7.64	**7.64**	**0.02**

Table N2 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_1.4 at time t, pH 5.5 at 37 °C, in an absence of electric field

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0105	0.0048	0.0099	0.44	0.20	0.42	**0.36**	**0.13**
0.16667	0.0295	0.0288	0.0254	1.25	1.22	1.08	**1.18**	**0.09**
0.25	0.0399	0.0419	0.0444	1.69	1.77	1.88	**1.78**	**0.1**
0.5	0.0527	0.0567	0.0546	2.23	2.40	2.31	**2.31**	**0.08**
0.75	0.0709	0.0734	0.0749	3.00	3.11	3.17	**3.09**	**0.09**
1	0.0900	0.0905	0.0946	3.81	3.83	4.01	**3.88**	**0.11**
1.5	0.1098	0.1093	0.1106	4.65	4.63	4.68	**4.65**	**0.03**
2	0.1249	0.1257	0.1277	5.29	5.32	5.41	**5.34**	**0.06**
2.5	0.1250	0.1255	0.1264	5.29	5.31	5.35	**5.32**	**0.03**
3	0.1244	0.1205	0.1249	5.27	5.10	5.29	**5.22**	**0.1**
3.5	0.1255	0.1258	0.1212	5.31	5.33	5.13	**5.26**	**0.11**
4	0.1265	0.1265	0.1241	5.36	5.36	5.25	**5.32**	**0.06**
8	0.1257	0.1254	0.1279	5.32	5.31	5.42	**5.35**	**0.06**
12	0.1265	0.1222	0.1287	5.36	5.17	5.45	**5.33**	**0.14**
16	0.1272	0.1296	0.1245	5.38	5.49	5.27	**5.38**	**0.11**
20	0.1265	0.1288	0.1257	5.36	5.45	5.32	**5.38**	**0.07**
24	0.1269	0.1245	0.1248	5.37	5.27	5.28	**5.31**	**0.06**
28	0.1270	0.1247	0.1266	5.38	5.28	5.36	**5.34**	**0.05**
32	0.1262	0.1294	0.1278	5.34	5.48	5.41	**5.41**	**0.07**
36	0.1270	0.1246	0.1284	5.38	5.28	5.44	**5.37**	**0.08**
40	0.1264	0.1286	0.1294	5.35	5.45	5.48	**5.43**	**0.07**
44	0.1255	0.1251	0.1238	5.31	5.30	5.24	**5.28**	**0.04**
48	0.1266	0.1239	0.1259	5.36	5.25	5.33	**5.31**	**0.06**

Table N3 The raw data of the determination of amounts of acetylsalicylic acid released from Ba-CAR_1.4+PTh+E at time t, pH 5.5 at 37 °C, with the electric field 2 V under anode

Time (h)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0	0.0000	0.0000	0.0000	0.00	0.00	0.00	**0.00**	**0.00**
0.08333	0.0012	0.0010	0.0010	0.05	0.04	0.04	**0.05**	**0.00**
0.16667	0.0129	0.0139	0.0115	0.55	0.59	0.49	**0.54**	**0.05**
0.25	0.2100	0.0231	0.0209	0.89	0.98	0.88	**0.92**	**0.05**
0.5	0.0311	0.0321	0.0306	1.32	1.36	1.30	**1.32**	**0.03**
0.75	0.0395	0.0405	0.0384	1.67	1.71	1.63	**1.67**	**0.04**
1	0.0454	0.0474	0.0441	1.92	2.01	1.87	**1.93**	**0.07**
1.5	0.0562	0.0551	0.0549	2.38	2.33	2.32	**2.35**	**0.03**
2	0.0541	0.0561	0.0516	2.29	2.38	2.18	**2.28**	**0.10**
2.5	0.0523	0.0559	0.0526	2.21	2.37	2.23	**2.27**	**0.08**
3	0.0521	0.0512	0.0524	2.21	2.17	2.22	**2.20**	**0.03**
3.5	0.0529	0.0532	0.0518	2.24	2.25	2.19	**2.23**	**0.03**
4	0.0512	0.0541	0.0534	2.17	2.29	2.26	**2.24**	**0.06**
8	0.0509	0.0524	0.0549	2.16	2.22	2.32	**2.23**	**0.09**
12	0.0526	0.0561	0.0512	2.23	2.38	2.17	**2.26**	**0.11**
16	0.0534	0.0547	0.0546	2.26	2.32	2.31	**2.30**	**0.03**
20	0.0538	0.0526	0.0528	2.28	2.23	2.24	**2.25**	**0.03**
24	0.0504	0.0529	0.0526	2.13	2.24	2.23	**2.20**	**0.06**
28	0.0529	0.0534	0.0509	2.24	2.26	2.16	**2.22**	**0.06**
32	0.0541	0.0511	0.0510	2.29	2.16	2.16	**2.20**	**0.07**
36	0.0526	0.0537	0.0539	2.23	2.27	2.28	**2.26**	**0.03**
40	0.0537	0.0558	0.0549	2.27	2.36	2.32	**2.32**	**0.04**
44	0.0521	0.0515	0.0557	2.21	2.18	2.36	**2.25**	**0.10**
48	0.0516	0.0536	0.0551	2.18	2.27	2.33	**2.26**	**0.07**

Release Kinetics of Model Drug from Drug-Loaded Carrageenan Hydrogel

The study of acetylsalicylic acid transport mechanism from the carrageenan hydrogels, Fickian diffusion models are considered to fit the experimental data.

The power law model is described by the Ritger-Peppas equation (Venkatesh *et al.*, 1992):

$$\frac{M_t}{M_\infty} = k_1 t^n \qquad \text{(M1)}$$

where M_t/M_∞ = the fractional drug release

k_1 = a kinetic constant (with the unit of T^{-n})

t = the release time

and n = the scaling exponent that can be related to the drug transport mechanism.

For a thin hydrogel film, when n = 0.5, the drug release mechanism is observed by the Fickian diffusion:

$$\frac{M_t}{M_\infty} = k_H t^{1/2} \qquad \text{(M2)}$$

where M_t/M_∞ = the fractional drug release

k_H = a kinetic constant (with the unit of T^{-n})

and t = the release time.

The diffusion coefficients of acetylsalicylic acid from the carrageenan hydrogels are determined from the slopes of plots of drug accumulation versus square root of time according to Higuchi's equation (Higuchi, 1961):

$$Q = \frac{M_t}{A} = 2C_0(Dt/\pi)^{1/2} \qquad \text{(M3)}$$

where Q = the amount of material flowing through a unit cross section of barrier (g/cm^2) in unit time, t (s)

C_0 = the initial drug concentration in the hydrogel (g/cm^3)

and D = the diffusion coefficient of a drug (cm^2/s)

The diffusion coefficients of each system were calculated from the slopes of the plot of the amounts of acetylsalicylic acid released from Ba-carrageenan hydrogels versus $t^{1/2}$ with the hydrogel samples attached to the anode or cathode, CAR_1.4 hydrogels during 48 h using the Higuchi's equation (see figure N2).

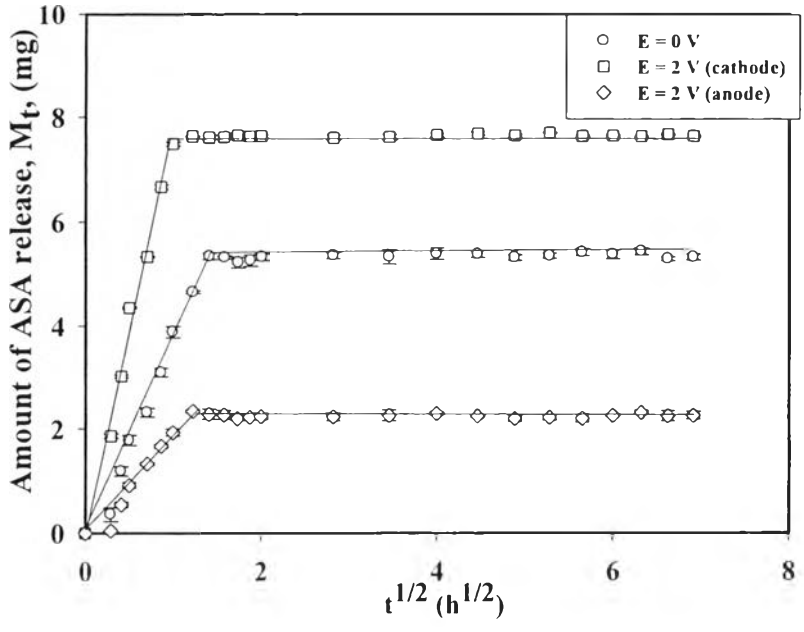


Figure N2 Amounts of acetylsalicylic acid released from Ba-carrageenan hydrogels versus $t^{1/2}$ with the hydrogel samples attached to the anode or cathode at crosskinking ratio of 1.4, E = 0 and 2 V, pH 5.5, and at 37°C, number of samples = 3.

Table N4 The diffusion coefficients of acetylsalicylic acid released from Ba-carrageenan hydrogels with the hydrogel samples attached to the anode or cathode at crosskinking ratio of 1.4 with and without electric field

Sample	Electric field (V)	Diffusion coefficient (cm^2/s)
CAR_1.4	0	3.85×10^{-5}
CAR_1.4	2 (cathode)	1.12×10^{-4}
CAR_1.4	2 (anode)	5.93×10^{-6}

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Proceedings:

1. Pairatwachapun, S.; and Sirivat, A. (2013, April 23) Electrically Controlled Release of Acetylsalicylic Acid from Carrageenan Hydrogel. Proceedings of the 4th Research Symposium on Petrochemical and Materials Technology and the 19th PPC Symposium on Petroleum, Petrochemicals, and Polymers, Bangkok, Thailand.

Presentations:

1. Pairatwachapun, S.; and Sirivat, A. (2013, April 22) Controlled Transdermal Delivery of Acetylsalicylic Acid from Carrageenan Hydrogel. Paper Presented at the 1st Annual Symposium Conductive and Electroactive Polymer, Bangkok, Thailand.
2. Pairatwachapun, S.; and Sirivat, A. (2013, April 23) Electrically Controlled Release of Acetylsalicylic Acid from Carrageenan Hydrogel. Paper Presented at the 4th Research Symposium on Petrochemical and Materials Technology and the 19th PPC Symposium on Petroleum, Petrochemicals, and Polymers, Bangkok, Thailand.
3. Pairatwachapun, S.; and Sirivat, A. (2013, May 21-23) Polythiophene/ carrageenan Hydrogel as Drug Release Matrix under Electric Field. Paper Presented at the 3rd International Symposium Frontiers in Polymer Science In association with the journal polymer, Sitges, Spain.