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APPENDICES

Appendix A Determination of Molecular Weight of Gelatin Hydrogels

The intrinsic viscosity, $[\eta]$, are determined by the measurements of solution viscosity. The measurements are described by comparing the elution times (t = elution time of polymer solution, t_0 = elution time of solvent) in the viscometer. The times are proportional to the viscosity of the polymer solution, η, and solvent, η_o, respectively (Abrusci *et al.*, 2004). The specific viscosity and relative viscosity are calculated by the following equations (A1) and (A2) (Abrusci *et al.*, 2004):

$$\eta_{rel} = \frac{\eta}{\eta_o} \tag{A2}$$

and

$$\eta_{sp} = \frac{\eta - \eta_o}{\eta_o} = \frac{t - t_o}{t_o} = \eta_{rel} - 1 \tag{A2}$$

The intrinsic viscosity, $[\eta]$, is calculated by extrapolation to infinite dilution of the equation of Huggins (A3) and Kramer (A4) (Derosa 2008).

$$\frac{\eta_{sp}}{c} = [\eta] + k'[\eta]^2 c \tag{A3}$$

and

$$\frac{\ln \eta_{rel}}{c} = [\eta] + k''[\eta]^2 c \tag{A4}$$

where η_{sp} is the specific viscosity, η_{rel} is the relative viscosity, c is concentration of polymer in grams per deciliter (g/dL) , η_{sp}/c is defined as reduced viscosity ,η_{red}, $\ln\eta_{rel}/c$ is defined as inherent viscosity, η_{inh}, and k' and k'' are the constants of Huggins and Kramer, respectively.

Molecular weight, M_w, of the porcine and fish gelatin were determined by the capillary viscometer. The relation between $[\eta]$ and M_w can be described in terms of the Mark–Houwink–Kuhn–Sakurada (MHKS) equation (A5) (Enrione *et al.*, 2011).

$$[\eta] = KM_w{}^a \tag{A5}$$

where K and a are the constant values of gelatins.

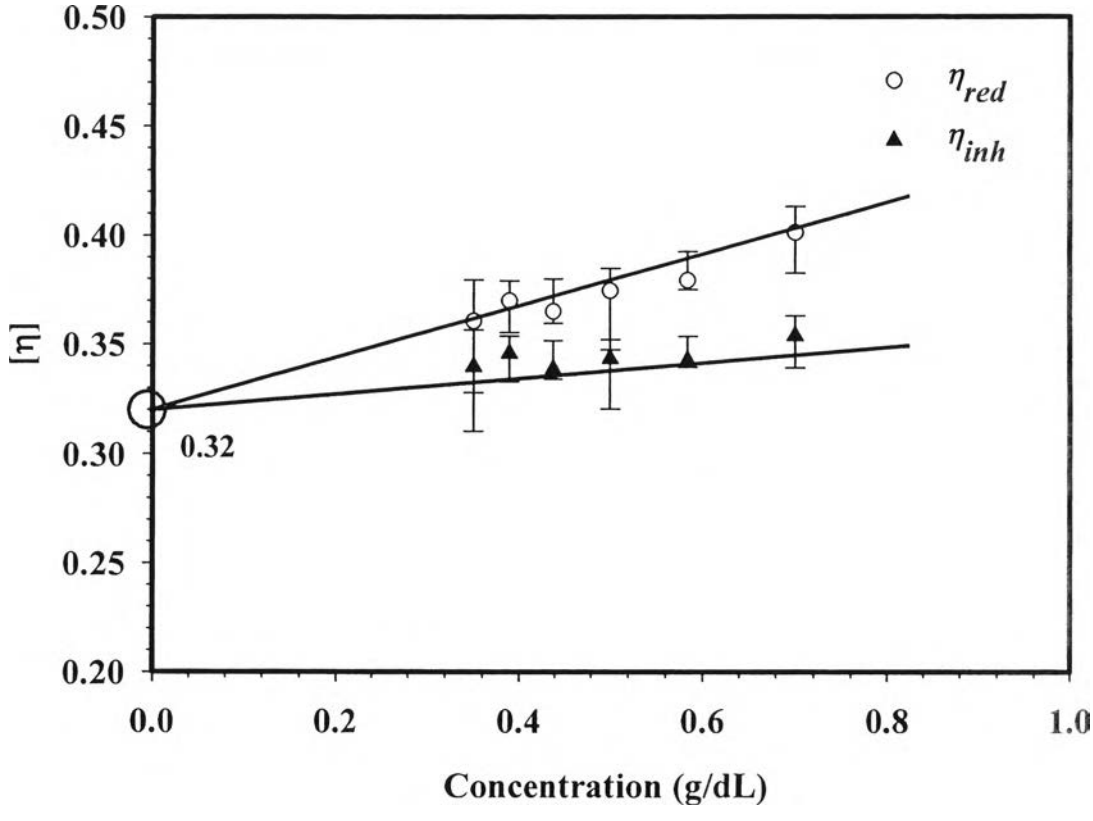


Figure A1 Double extrapolation of η_{red} and η_{inh} approach to zero concentration as the intrinsic viscosity [η] of PorGel at 37 °C

In figure A2, the intrinsic viscosity [η] is interception of the reduced, η_{red} and inherent, η_{inh}, viscosities. The reduced η_{red} and inherent η_{inh} viscosities, obtained from capillary viscometer, are presented as function of the fish gelatin concentration when the concentration of the solution varied from 0.35 to 0.7 g/dL at 37 °C. According from equation (A5), the value of the constants K and a were 1.66×10^{-5} and 0.885, respectively (Abrusci *et al.*, 2004).

$$0.32 = 1.66\times10^{-5}M_w^{0.885}$$

$$M_w = 69{,}480 \text{ Da}$$

Table A1 Raw data for determination of the reduced viscosity (η_{red}) and the inherent viscosity (η_{inh}) of PorGel

Sample	Concentration (g/dL)	t_0 (s)	t (s)	η_{rel}	η_{sp}	$\ln\eta_{rel}$	η_{red}	η_{inh}
1	0.7000	44.22	56.95	1.2879	0.2879	0.2530	0.4113	0.3614
	0.7000	44.22	56.64	1.2809	0.2809	0.2475	0.4012	0.3536
	0.7000	44.22	56.02	1.2668	0.2668	0.2365	0.3812	0.3379
Avg							**0.3979**	**0.3510**
SD							**0.0153**	**0.0120**
2	0.5833	44.22	54.38	1.2298	0.2298	0.2068	0.3939	0.3545
	0.5833	44.22	54.00	1.2212	0.2212	0.1998	0.3791	0.3425
	0.5833	44.22	53.98	1.2207	0.2207	0.1994	0.3784	0.3419
Avg							**0.3838**	**0.3463**
SD							**0.0087**	**0.0071**
3	0.5000	44.22	51.84	1.1723	0.1723	0.1590	0.3446	0.3180
	0.5000	44.22	52.50	1.1872	0.1872	0.1716	0.3745	0.3433
	0.5000	44.22	52.60	1.1895	0.1895	0.1735	0.3790	0.3471
Avg							**0.3660**	**0.3361**
SD							**0.0187**	**0.0158**
4	0.4375	44.22	51.60	1.1669	0.1669	0.1543	0.3815	0.3528
	0.4375	44.22	51.28	1.1597	0.1597	0.1481	0.3649	0.3386
	0.4375	44.22	51.24	1.1588	0.1588	0.1473	0.3629	0.3368
Avg							**0.3698**	**0.3427**
SD							**0.0102**	**0.0088**
5	0.3889	44.22	50.31	1.1377	0.1377	0.1290	0.3541	0.3318
	0.3889	44.22	50.71	1.1468	0.1468	0.1369	0.3774	0.3521
	0.3889	44.22	50.58	1.1438	0.1438	0.1344	0.3698	0.3455
Avg							**0.3671**	**0.3432**
SD							**0.0119**	**0.0104**
6	0.3500	44.22	50.03	1.1314	0.1314	0.1234	0.3754	0.3527
	0.3500	44.22	49.80	1.1262	0.1262	0.1188	0.3605	0.3395
	0.3500	44.22	49.25	1.1137	0.1137	0.1077	0.3250	0.3078
Avg							**0.3536**	**0.3333**
SD							**0.0259**	**0.0231**

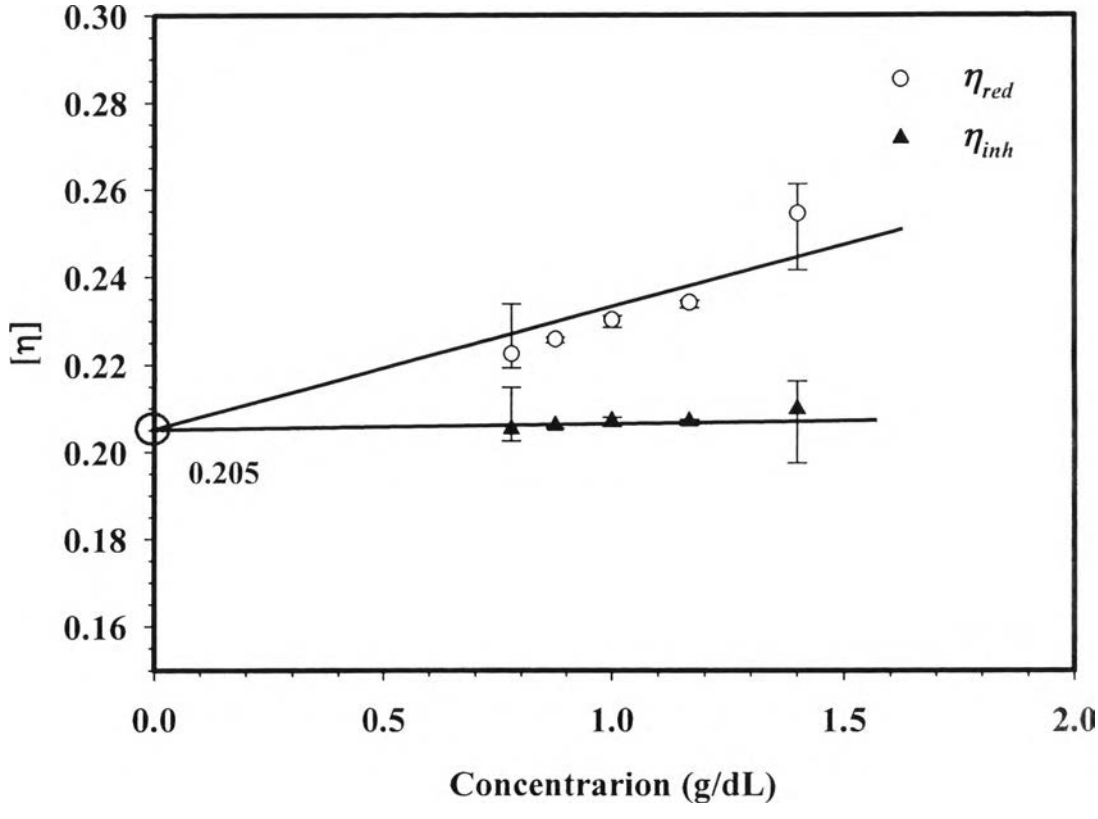


Figure A2 Double extrapolation of η_{red} and η_{inh} approach to zero concentration as the intrinsic viscosity [η] of FishGel.

In figure A2, the intrinsic viscosity [η] is interception of the reduced (η_{red}) and inherent (η_{inh}) viscosities. The reduced (η_{red}) and inherent (η_{inh}) viscosities, obtained from capillary viscometer are presented as function of the FishGel concentration when the concentration of the solution varied from 0.78 to 1.4 g/dL at 50 °C. According from equation (A5), the value of the constants K and a were 8.57×10^{-5} and 0.74, respectively (Enrione *et al.*, 2011).

$$0.205 = 8.57\times10^{-5}M_w^{0.74}$$

$$M_w = 36{,}800 \text{ Da}$$

Table A2 Raw data for determination of reduced viscosity (η_{red}) and inherent viscosity (η_{inh}) of FishGel

Sample	Concentration (g/dL)	t_0 (s)	t (s)	η_{rel}	η_{sp}	$\ln\eta_{rel}$	η_{red}	η_{inh}
1	1.400	38.36	51.79	1.3501	0.3501	0.3002	0.2593	0.2144
	1.400	38.36	50.50	1.3165	0.3165	0.2750	0.2404	0.1964
	1.400	38.36	51.46	1.3415	0.3415	0.2938	0.2546	0.2098
Avg							**0.2514**	**0.2069**
SD							**0.0098**	**0.0094**
2	1.1667	38.36	48.84	1.2732	0.2732	0.2415	0.2342	0.2070
	1.1667	38.36	48.85	1.2735	0.2735	0.2417	0.2344	0.2072
	1.1667	38.36	48.78	1.2716	0.2716	0.2403	0.2328	0.2060
Avg							**0.2338**	**0.2067**
SD							**0.0008**	**0.0007**
3	1.0000	38.36	47.12	1.2284	0.2284	0.2057	0.2284	0.2057
	1.0000	38.36	47.22	1.2310	0.2310	0.2078	0.2310	0.2078
	1.0000	38.36	47.19	1.2302	0.2302	0.2072	0.2302	0.2072
Avg							**0.2298**	**0.2069**
SD							**0.0013**	**0.0011**
4	0.8750	38.36	45.95	1.1979	0.1979	0.1805	0.2261	0.206
	0.8750	38.36	45.94	1.1976	0.1976	0.1803	0.2258	0.2061
	0.8750	38.36	45.91	1.1968	0.1968	0.1797	0.2249	0.2053
Avg							**0.2256**	**0.2059**
SD							**0.0006**	**0.0005**
5	0.7778	38.36	45.37	1.1827	0.1827	0.1678	0.2350	0.2158
	0.7778	38.36	44.99	1.1728	0.1728	0.1594	0.2222	0.2050
	0.7778	38.36	45.00	1.1731	0.1731	0.1596	0.2226	0.2053
Avg							**0.2266**	**0.2087**
SD							**0.0073**	**0.0062**

Appendix B Determination of Degree of Swelling and Weight Loss of Gelatin Hydrogels

The degree of swelling and the weight loss of the gelatin hydrogels were measured in an acetate buffer solution at 37°C for 48 h (Taepaiboon *et al.*, 2006) using the following equations (B1-B2):

$$\text{Degree of swelling (\%)} = \frac{M_s - M_d}{M_d} \times 100 \qquad \text{(B1)}$$

and

$$\text{Weight loss (\%)} = \frac{M_i - M_d}{M_i} \times 100 \qquad \text{(B2)}$$

where M_s is the weight of the sample after submersed in the buffer solution, M_d is the weight of sample after submersed in the buffer solution as dry state, M_i is the initial weight of the sample without submersed in the buffer solution as dry state.

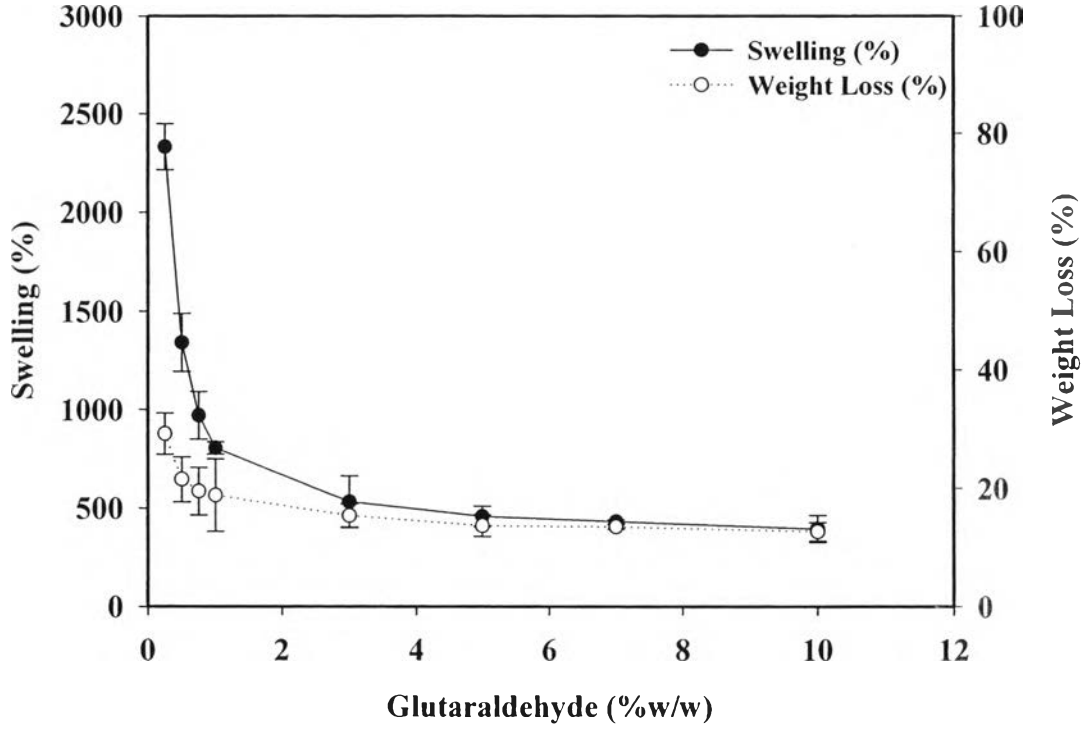


Figure B1 The degree of swelling (%) and the weight loss (%) of PorGel hydrogels at various crosslinking ratio between 0.25 and 10 %w/w (Number of samples = 3 and thickness of films = 0.5 mm).

Table B1 Raw data for determination for the degree of swelling (%) and the weight loss (%) of PorGel hydrogels at various crosslinking ratios (CR)

Sample	M_i (mg)	M_s (mg)	M_d (mg)	Swelling (%)	Weight loss (%)
CR0.25#1	44.7	801.2	33.4	2298.80	25.28
2	52.3	929.6	36.3	2460.88	30.59
3	54.9	873.0	37.4	2234.22	31.88
Avg				**2331.30**	**29.25**
SD				**116.77**	**3.50**
CR0.50#1	57.3	562.7	44.0	1178.86	23.21
2	40.2	523.0	33.3	1470.57	17.16
3	44.3	495.0	33.6	1373.21	24.15
Avg				**1340.88**	**21.51**
SD				**148.52**	**3.79**
CR0.75#1	59.9	514.0	50.8	911.81	15.19
2	46.6	432.9	35.8	1109.22	23.18
3	42.2	333.5	33.7	889.61	20.14
Avg				**970.21**	**19.50**
SD				**120.89**	**4.03**
CR1#1	47.5	341.9	37.4	814.17	21.26
2	44.9	320.1	34.4	830.52	23.39
3	55.6	426.5	49.0	770.41	11.87
Avg				**805.03**	**18.84**
SD				**31.08**	**6.13**
CR3#1	59.1	250.1	51.2	388.48	13.37
2	36.5	204	30.8	562.34	15.62
3	38.9	240.1	32.2	645.65	17.22
Avg				**532.16**	**15.40**
SD				**131.22**	**1.94**
CR5#1	49.8	220.6	44.0	401.36	11.65
2	44.6	218.7	38.3	471.02	14.13
3	47.1	240.4	39.9	502.51	15.29
Avg				**458.30**	**13.69**
SD				**51.76**	**1.86**
CR7#1	48.7	219.4	42.3	418.68	13.14
2	55.4	258.4	47.9	439.46	13.54
3	51.2	236.1	44.1	435.37	13.87
Avg				**431.17**	**13.52**
SD				**11.01**	**0.36**
CR10#1	51.2	189.7	44.9	322.49	12.30
2	42.4	188.0	37.6	400.00	11.32
3	38.3	183.4	32.8	459.15	14.36
Avg				**393.88**	**12.66**
SD				**68.53**	**1.55**

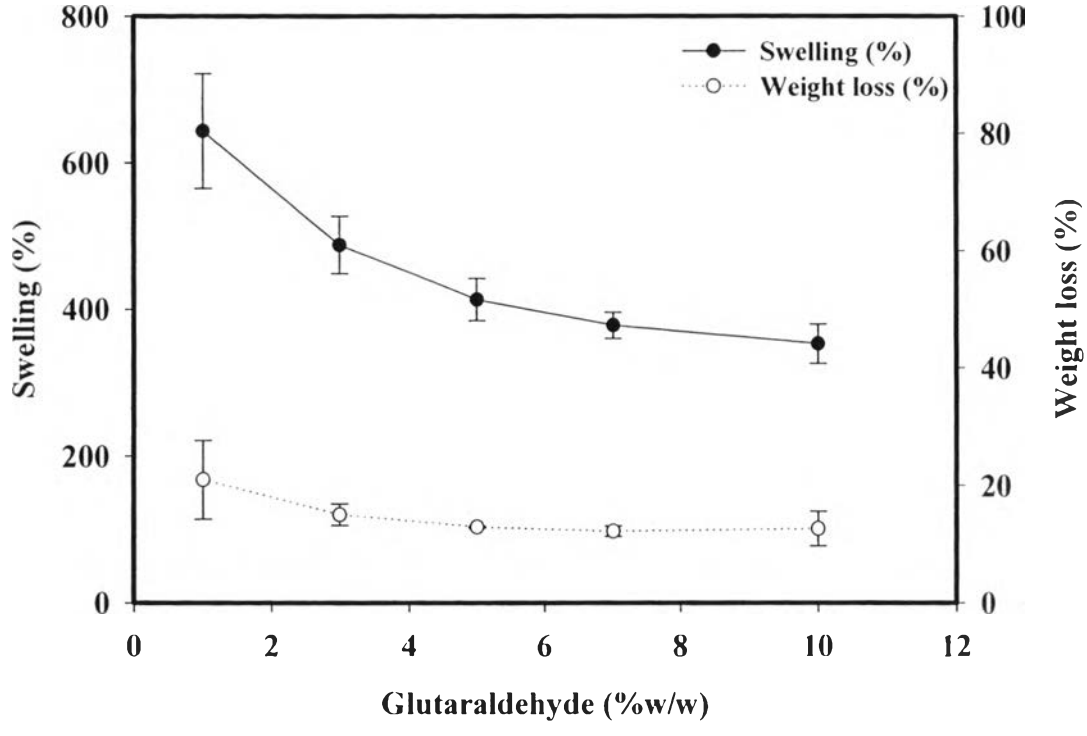


Figure B2 The degree of swelling (%) and the weight loss (%) of FishGel hydrogels at various crosslinking ratio between 1 and 10 %w/w (Number of samples = 3 and thickness of films = 0.5 mm).

Table B2 Raw data for determination of the degree of swelling (%) and weight loss (%) of FishGel hydrogels at various crosslinking ratios

Sample	M_i (mg)	M_s (mg)	M_d (mg)	Swelling (%)	Weight loss (%)
CR1#1	57.8	305.7	46.5	557.42	19.55
2	36.4	250.1	30.9	709.39	15.11
3	81	443.4	58.1	663.17	28.27
Avg				**643.32**	**20.98**
SD				**77.90**	**6.70**
CR3#1	40.6	200.1	34.0	488.53	16.26
2	40.0	210.7	33.6	527.08	16.00
3	50.9	242.9	44.3	448.31	12.97
Avg				**487.97**	**15.07**
SD				**39.39**	**1.83**
CR5#1	41.3	172.8	36.0	380.00	12.83
2	40.5	187.2	35.2	431.82	13.09
3	37.1	170.4	32.3	427.55	12.94
Avg				**413.12**	**12.95**
SD				**28.77**	**0.13**
CR7#1	42.8	187	38.0	392.11	11.21
2	45.4	192.1	39.7	383.88	12.56
3	48.8	194.5	42.5	357.65	12.91
Avg				**377.88**	**12.23**
SD				**18.00**	**0.89**
CR10#1	51.6	191.8	44.1	334.92	14.53
2	45.7	189.6	39.2	383.67	14.22
3	42.0	167.3	38.1	339.11	9.29
Avg				**352.57**	**12.68**
SD				**27.02**	**2.94**

Appendix C UV-Visible Spectrum of Salicylic Acid and 5-Sulfosalicylic Acid

A UV-Visible spectrophotometer (TECAN, Infinite M200) was used to determine the maximum spectra of model drugs. The model drugs in an acetate buffer solution were 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 5 mg in buffer solution 1000 ml and the correspond the model drug concentrations were calculated from the calibration curve with model drug concentration. Figures C shows the characteristic peak of salicylic acid and 5-sulfosalicylic acid at the wavelength 298 nm.

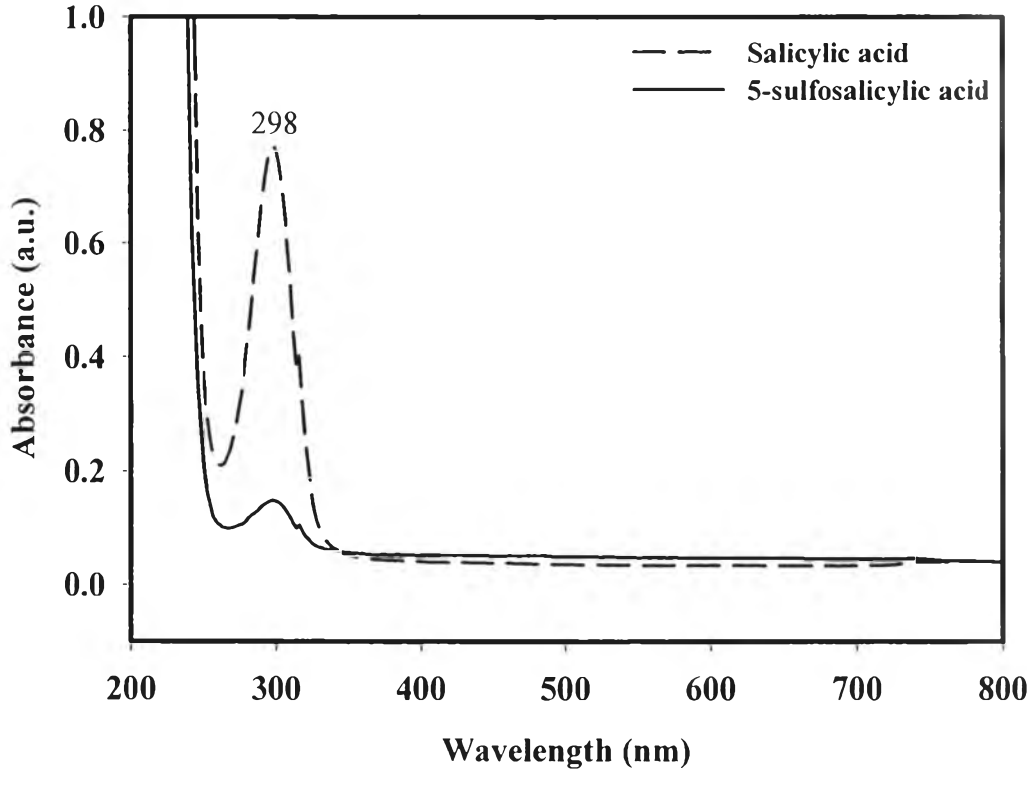


Figure C UV-Visible spectrum of salicylic acid and 5-sulfosalicylic acid.

Appendix D Calibration curve of Salicylic Acid and 5-sulfosalicylic Acid

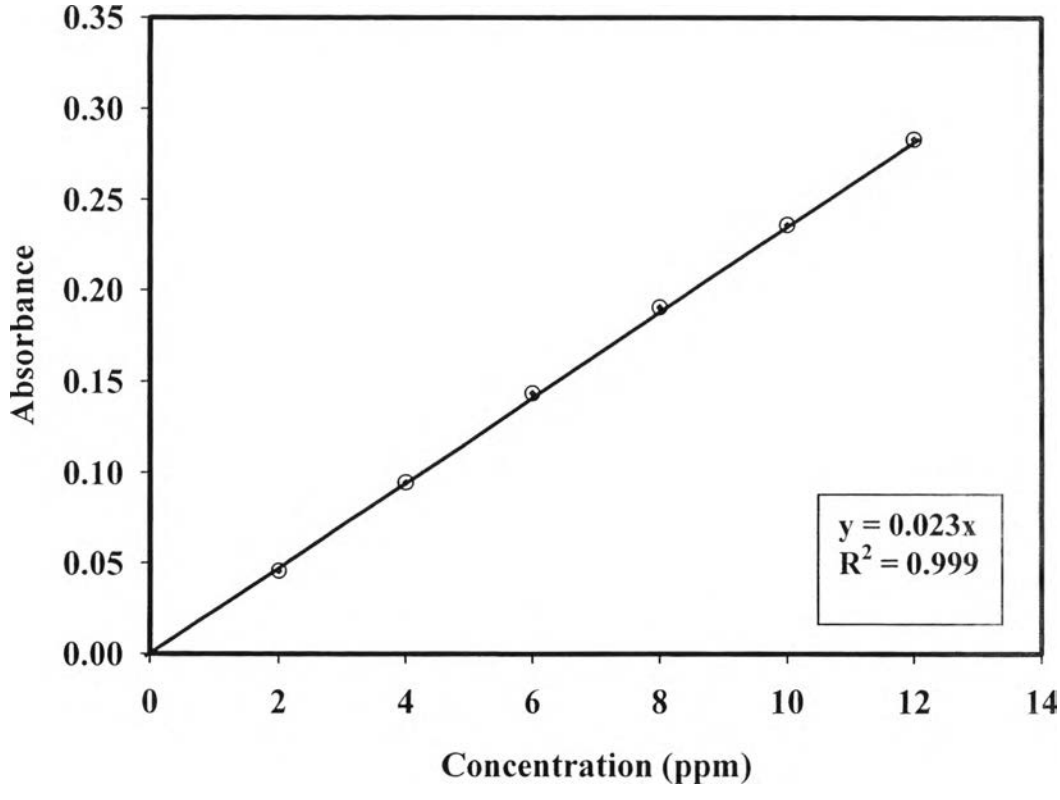


Figure D1 Calibration curve of salicylic acid in an acetate buffer solution at 298 nm.

Table D1 Raw data for determination of calibration curve of Salicylic acid at 298 nm

Concentration	Absorbance at 298 nm	Average	SD
2	0.0908	**0.0455**	**0.000663**
	0.0890		
	0.0906		
	0.0897		
	0.0904		
4	0.1397	**0.0945**	**0.000948**
	0.1401		
	0.1396		
	0.1378		
	0.1380		
6	0.1861	**0.1433**	**0.001526**
	0.1872		
	0.1877		
	0.1907		
	0.1877		
8	0.2341	**0.1904**	**0.000540**
	0.2350		
	0.2358		
	0.2350		
	0.2351		
10	0.2798	**0.2357**	**0.000984**
	0.2796		
	0.2811		
	0.2818		
	0.2792		
12	0.3272	**0.2831**	**0.001065**
	0.3271		
	0.3286		
	0.3264		
	0.3293		

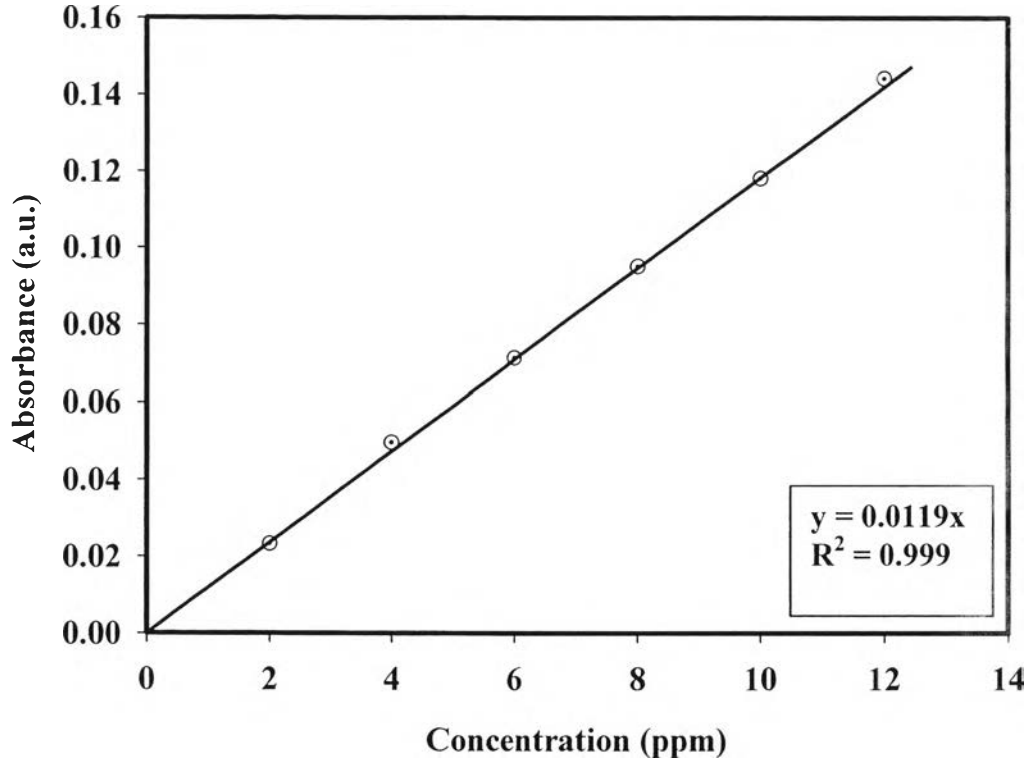


Figure D2 Calibration curve of 5-sulfosalicylic acid in an acetate buffer solution at 298 nm.

Table D2 Raw data for determination of calibration curve of 5-sulfosalicylic acid at 298 nm

Concentration	Absorbance at 298 nm	Average	SD
2	0.0231	**0.0232**	**0.000114**
	0.0232		
	0.0233		
	0.0232		
	0.0234		
4	0.0496	**0.0496**	**0.000158**
	0.0495		
	0.0494		
	0.0497		
	0.0498		
6	0.0716	**0.0713**	**0.000239**
	0.0715		
	0.0712		
	0.0713		
	0.0710		
8	0.0951	**0.0951**	**0.000152**
	0.0950		
	0.0949		
	0.0953		
	0.0950		
10	0.1179	**0.1181**	**0.000329**
	0.1179		
	0.1181		
	0.1181		
	0.1187		
12	0.1428	**0.1442**	**0.001235**
	0.1429		
	0.1451		
	0.1452		
	0.1450		

Appendix E Determinaion of the Molecular Weight between Crosslink, Mesh Size and Crosslinking Density of Gelatin Hydrogels

To determine the molecular weight between crosslinks, $\bar{M}_c$, the mesh size, ξ, and the crosslinking density, ρ_x, the sample of gelatin film was cut immediately after crosslinking (1 cm^2). 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. The volumes of the polymer sample in the dry, relaxed, and swollen states are calculated by using equations (E1) - (E3), respectively.

$$V_d = \frac{W_{a,d} - W_{h,d}}{\rho_h} \quad \text{(E1)}$$

$$V_r = \frac{W_{a,r} - W_{h,r}}{\rho_h} \quad \text{(E2)}$$

$$V_s = \frac{W_{a,s} - W_{h,s}}{\rho_h} \quad \text{(E3)}$$

where, $W_{a,d}$ is the weight of the dry polymer in air, $W_{h,d}$ is the weight of the dry polymer in heptane, $W_{a,r}$ is the weight of the relaxed polymer in air, $W_{h,r}$ is the weight of the relaxed polymer in heptane, $W_{a,s}$ is the weights of the swollen polymer in air and $W_{h,s}$ heptane, ρ_h is the density of heptanes, V_d is the volume of the polymer sample in the dry states, V_r is the volume of the polymer sample in the relaxed states and V_s is the volume of the polymer sample in the swollen states.

The calculattion of the polymer volume fraction in the relaxed, $\upsilon_{2,r}$, and swollen states, $\upsilon_{2,s}$, and by using equations (E4) and (E5), respectively (Peppas *et al.*, 1998).

$$\upsilon_{2,r} = \frac{V_d}{V_r} \tag{E4}$$

and

$$\upsilon_{2,s} = \frac{V_d}{V_s} \tag{E5}$$

The molecular weight between crosslinks, $\bar{M}_c$, was calculated from the swelling data by using equation (E6) (Peppas *et al.*, 1998).

$$\frac{1}{\bar{M}_c} = \frac{2}{\bar{M}_n} - \frac{\frac{\bar{\upsilon}}{\bar{V}_1}\left[\ln\left(1-\upsilon_{2,s}\right) + \upsilon_{2,s} + \chi{\upsilon_{2,s}}^2\right]}{\upsilon_2\left[\left(\frac{\upsilon_{2,s}}{\upsilon_{2,r}}\right)^{1/3} - \frac{1}{2}\left(\frac{\upsilon_{2,s}}{\upsilon_{2,r}}\right)\right]} \tag{E6}$$

where $\bar{M}_n$ is the number averaged molecular weight of the polymer before cross linking, $\bar{\upsilon}$ is the specific volume of gelatin ($\bar{\upsilon}$ = 0.69 cm^3/g of gelatin) (Sutter *et al.*, 2007), $\bar{V}_1$ is the molar volume of water ($\bar{V}_1$ = 18.1 mol/cm^3), χ is the Flory interaction parameter of gelatin (χ = 0.49) (Bohidar 1998) and the dissociation constant p*K*a is 4.7.

Generally, the presence of gelatin led to a more open network structure and resulted in a higher the molecular weight between cross-link, $\bar{M}_c$. The hydrogel mesh size, ξ was calculated by using equation (E7) (Peppas *et al.*, 1996).

$$\xi = {\upsilon_{2,s}}^{-1/3}\left[C_n\left(\frac{2\bar{M}_c}{\bar{M}_r}\right)\right]^{1/2} \cdot l \tag{E7}$$

where C_n is the Flory characteristic ratio for gelatin (C_n = 8.8) (Deiber *et al.*, 2009), $\bar{M}_r$ is the molecular weight of repeating unit of gelatin ($\bar{M}_r$ = 100 g/mol) (Sutter *et al.*, 2007), and l is the carbon–carbon bond length (l = 1.54 Å).

The crosslinking density of the hydrogel, ρ_x, was calculated by using equation (E8) (Peppas *et al.*, 1996).

$$\rho_x = \frac{1}{\bar{v}\bar{M}_c} \qquad \text{(E8)}$$

Table E1 and E2 shows the molecular weight between crosslink, $\bar{M}_c$, the mesh size, ξ, the crosslinking density, ρ_x, and drug size/mesh size, a/ξ, of porcine and fish gelatin hydrogels at various crosslinking ratios. The molecular weight between crosslink, $\bar{M}_c$ and mesh sizes, ξ, of porcine and fish gelatin hydrogels decreased with increasing crosslinking ratio. The mesh sizes, ξ, of porcine gelatin hydrogels vary from 148 to9 Å with crosslinking ratio 0.25 to 10% (based on porcine gelatin powder). For the mesh sizes, ξ, of fish gelatin hydrogels vary from 27 to 9 with crosslinking ratio 1 to 10% (based on fish gelatin powder) at 37°C.

Table E3 and E4 show the determination of the molecular weight between crosslink, $\bar{M}_c$, mesh size, ξ, and crosslinking density, ρ_x, of porcine and fish gelatin hydrogels at various crosslinking ratios.

Table E1 Summary of the molecular weight between crosslink, $\bar{M}_c$, mesh size, ξ, crosslinking density, ρ_x, and drug size/ mesh size, a/ξ, of porcince gelatin hydrogel at various crosslinking ratios

Sample	Crosslinking ratio, X	Number-average molecular weight between crosslinks, $\bar{M}_c$ (g/mol)	Mesh size, ξ (Å)	Crosslinking density, ρ_x (mol/cm^3 × 10^3)	Drugs size / Mesh size, a/ξ	
					Salicylic Acid (3.28 Å)	5-Sulfosalicylic Acid (9.25 Å)
PorGel_0.25	0.25%	16673 ± 2070	148 ± 15	0.09 ± 0.01	0.02 ± 0.00	0.06 ± 0.01
PorGel_0.50	0.50%	8851 ± 2371	101 ± 16	0.17 ± 0.04	0.03 ± 0.01	0.09 ± 0.02
PorGel_0.75	0.75%	2950 ± 739	49 ± 8	0.51 ± 0.11	0.07 ± 0.01	0.19 ± 0.03
PorGel_1.00	1%	1610 ± 143	35 ± 2	0.90 ± 0.08	0.09 ± 0.01	0.27 ± 0.02
PorGel_3.00	3%	529 ± 66	17 ± 1	2.77 ± 0.34	0.20 ± 0.01	0.56 ± 0.04
PorGel_5.00	5%	407 ± 92	14 ± 2	3.70 ± 0.94	0.23 ± 0.03	0.66 ± 0.08
PorGel_7.00	7%	254 ± 41	11 ± 1	5.82 ± 1.02	0.31 ± 0.04	0.88 ± 0.11
PorGel_10.00	10%	198 ± 24	9 ± 1	7.40 ± 0.94	0.37 ± 0.02	1.05 ± 0.07

Table E2 Summary of molecular weight between crosslink, $\bar{M}_c$, mesh size, ξ, crosslinking density, ρ_x, and drug size/ mesh size, a/ξ, of fish gelatin hydrogel at various crosslinking ratios

Sample	Crosslinking ratio, X	Number-average molecular weight between crosslinks, $\bar{M}_c$ (g/mol)	Mesh size, ξ (Å)	Crosslinking density, ρ_x (mol/cm^3 × 10^3)	Drugs size / Mesh size, a/ξ	
					Salicylic Acid (3.28 Å)	5-Sulfosalicylic Acid (9.25 Å)
FishGel_1.00	1%	1103 ± 113	27 ± 1	1.32 ± 0.13	0.12 ± 0.01	0.35 ± 0.02
FishGel_3.00	3%	467 ± 136	15 ± 2	3.19 ± 0.91	0.22 ± 0.03	0.62 ± 0.09
FishGel_5.00	5%	259 ± 32	11 ± 1	5.66 ± 0.70	0.29 ± 0.02	0.81 ± 0.06
FishGel_7.00	7%	220 ± 17	9 ± 0	6.62 ± 0.52	0.35 ± 0.02	0.99 ± 0.05
FishGel_10.00	10%	181 ± 16	9 ± 1	8.06 ± 0.67	0.36 ± 0.03	1.02 ±0.09

Table E3 Raw data for determination of the determination of the molecular weight between crosslink, $\bar{M}_c$, mesh size, ξ, and crosslinking density, ρ_x, of porcine gelatin hydrogels at various crosslinking ratios

Sample	$W_{a,r}$ (mg)	$W_{h,r}$ (mg)	$W_{a,s}$ (mg)	$W_{h,s}$ (mg)	$W_{a,d}$ (mg)	$W_{h,d}$ (mg)	$\bar{M}_c$ (g/mol)	ξ (Å)	ρ_x (mol/cm3)	a/ ξ (Salicylic acid)	a/ ξ 5-sulfosalicylic acid
CR0.25#1	684.7	679.9	932.6	885.5	36.3	32.8	18547	162	0.000078	0.02	0.06
2	644.1	641.0	873.0	840.0	37.4	34.6	17020	149	0.000085	0.02	0.06
3	640.2	636.2	801.2	764.9	33.4	30.0	14451	133	0.000100	0.02	0.07
Avg							**16673**	**148**	**0.000088**	**0.02**	**0.06**
SD							**2070**	**15**	**0.000011**	**0.00**	**0.01**
CR0.50#1	284.9	278.7	562.7	545.6	44.0	42.5	8133	102	0.000178	0.03	0.09
2	263.2	260.2	375.0	362.4	31.5	30.0	6923	85	0.000209	0.04	0.11
3	326.6	324.1	649.0	634.3	43.8	42.4	11498	118	0.000126	0.03	0.08
Avg							**8851**	**101**	**0.000171**	**0.03**	**0.09**
SD							**2371**	**16**	**0.000042**	**0.01**	**0.02**
CR0.75#1	503.5	499.1	716.0	700.0	70.8	67.5	2412	42	0.000601	0.08	0.22
2	319.1	316.1	434.5	428.5	35.8	34.9	2646	49	0.000548	0.07	0.19
3	251.5	248.3	378.2	366.9	34.0	32.2	3792	57	0.000382	0.06	0.16
Avg							**2950**	**49**	**0.000510**	**0.07**	**0.19**
SD							**739**	**8**	**0.000114**	**0.01**	**0.03**
CR1#1	287.2	281.5	500.7	489.6	56.5	54.5	1754	37	0.000826	0.09	0.25
2	295.0	289.4	522.1	510.0	56.5	54.1	1610	34	0.000900	0.10	0.27
3	246.4	240.7	443.9	431.8	49.5	47.0	1468	32	0.000987	0.10	0.28
Avg							1610	**35**	**0.000905**	**0.09**	**0.27**
SD							143	**2**	**0.000081**	**0.01**	**0.02**

Table E3 (continue) Raw data for determination of the determination of the molecular weight between crosslink, $\bar{M}_c$, mesh size, ξ, and crosslinking density, ρ_x, of porcine gelatin hydrogels at various crosslinking ratios

Sample	$W_{a,r}$ (mg)	$W_{h,r}$ (mg)	$W_{a,s}$ (mg)	$W_{h,s}$ (mg)	$W_{a,d}$ (mg)	$W_{h,d}$ (mg)	$\bar{M}_c$ (g/mol)	ξ (Å)	ρ_x (mol/cm3)	a/ ξ (Salicylic acid)	a/ ξ (5-sulfosalicylic acid)
CR3#1	118.4	116.6	209.1	204.7	34.0	32.5	597	18	0.002426	0.19	0.53
2	141.7	140.0	213.7	207.5	33.6	31.0	524	15	0.002763	0.21	0.60
3	138.7	134.6	264.0	259.2	41.6	40.3	466	17	0.003111	0.20	0.55
Avg							**529**	**17**	**0.002766**	**0.20**	**0.56**
SD							**66**	**1**	**0.000342**	**0.01**	**0.04**
CR5#1	109.4	104	256.6	249.5	64	61.5	303	12	0.004787	0.27	0.75
2	150.7	149.1	218.7	214.2	38.3	36.5	476	15	0.003043	0.22	0.62
3	100.3	98.3	195	191.9	58.9	57.9	441	15	0.003285	0.21	0.60
Avg							**407**	**14**	**0.003705**	**0.23**	**0.66**
SD							**92**	**2**	**0.000945**	**0.03**	**0.08**
CR7#1	156.5	153.5	219.4	215.0	42.3	40.5	269	11	0.005384	0.30	0.83
2	178.1	175.6	258.4	253.8	47.9	45.7	207	9	0.006991	0.36	1.00
3	169.0	166.6	236.1	232.3	44.1	42.6	284	12	0.005097	0.28	0.80
Avg							**254**	**11**	**0.005824**	**0.31**	**0.88**
SD							**41**	**1**	**0.001021**	**0.04**	**0.11**
CR10#1	118.6	116.3	186.7	182.8	44.9	43.1	209	9	0.006939	0.35	0.99
2	75.2	74.1	133.9	130.4	32.8	30.8	214	9	0.006777	0.37	1.05
3	148.1	146.1	237.4	234	68	66.3	171	8	0.008486	0.40	1.12
Avg							**198**	**9**	**0.007401**	**0.37**	**1.05**
SD							**24**	**1**	**0.000944**	**0.02**	**0.07**

Table E4 Raw data for determination of the determination of the molecular weight between crosslink, $\bar{M}_c$, mesh size, ξ, and crosslinking density, ρ_x, of fish gelatin hydrogels at various crosslinking ratios

Sample	$W_{a,r}$ (mg)	$W_{h,r}$ (mg)	$W_{a,s}$ (mg)	$W_{h,s}$ (mg)	$W_{a,d}$ (mg)	$W_{h,d}$ (mg)	$\bar{M}_c$ (g/mol)	ξ (Å)	ρ_x (mol/cm3)	a/ ξ (Salicylic acid)	a/ ξ (5-sulfosalicylic acid
CR1#1	201.1	198.6	331.9	325.5	46.4	44.7	1084	26	0.001337	0.13	0.36
2	220.9	218.6	383.1	378.0	55.4	54.2	1224	28	0.001184	0.12	0.33
3	306.2	303.0	427.5	422.2	55.0	53.8	1001	26	0.001448	0.13	0.36
Avg							**1103**	**27**	**0.001323**	**0.12**	**0.35**
SD							**113**	**1**	**0.000132**	**0.01**	**0.02**
CR3#1	139.0	137.8	214.0	210.4	40.8	39.4	538	16	0.002693	0.21	0.58
2	142.6	140.6	245.4	240.4	41.6	39.8	547	16	0.002647	0.20	0.56
3	110.2	108.2	176.3	172.5	34.0	32.5	342	13	0.004238	0.26	0.73
Avg							**476**	**15**	**0.003193**	**0.22**	**0.62**
SD							**116**	**2**	**0.000906**	**0.03**	**0.09**
CR5#1	86.2	75.0	154.8	148.2	36.0	34.5	228	12	0.006365	0.26	0.75
2	97.0	95.1	168.7	164.3	35.2	33.2	291	11	0.004973	0.29	0.83
3	86.2	84.0	153.9	150.3	32.3	30.8	257	11	0.005639	0.30	0.86
Avg							**259**	**11**	**0.005659**	**0.29**	**0.81**
SD							**32**	**1**	**0.000696**	**0.02**	**0.06**
CR7#1	100.8	99.8	197.0	194.6	38.0	36.8	237	10	0.006118	0.34	0.95
2	100.6	98.8	199.2	195.8	40.3	38.7	220	10	0.006575	0.34	0.97
3	118.3	116.9	210.5	207.4	42.5	40.9	202	9	0.007157	0.37	1.04
Avg							**220**	**9**	**0.006617**	**0.35**	**0.99**
SD							**17**	**0**	**0.000521**	**0.02**	**0.05**

Table E4 (continue) Raw data for determination of the determination of the molecular weight between crosslink, $\bar{M}_c$, mesh size, ξ, and crosslinking density, ρ_x, of fish gelatin hydrogels at various crosslinking ratios

Sample	$W_{a,r}$ (mg)	$W_{h,r}$ (mg)	$W_{a,s}$ (mg)	$W_{h,s}$ (mg)	$W_{a,d}$ (mg)	$W_{h,d}$ (mg)	$\bar{M}_c$ (g/mol)	ξ (Å)	ρ_x (mol/cm3)	a/ ξ (Salicylic acid)	a/ ξ (5-sulfosalicylic acid
CR10#1	87.1	84.5	161.7	156.8	41.0	38.6	199	9	0.007292	0.37	1.03
2	85.6	83.3	158.6	155.9	39.2	37.9	170	8	0.008535	0.39	1.10
3	159.6	154.6	261.2	258.0	78.1	77.2	173	10	0.008362	0.33	0.92
Avg							**181**	**9**	**0.008063**	**0.36**	**1.02**
SD							**16**	**1**	**0.000673**	**0.03**	**0.09**

Appendix F TGA Thermograms of Uncrosslinked and Crosslinked Gelatin Hydrogel

The thermal gravimetric analyzer (DT-TGA 1790) was used to determine the thermal behavior of polymers. Measurements were taken with the temperature scans from 25 to 800°C and a heating rate of 10°C/min. The samples were weighed in the range of 1-5 mg and loaded into a platinum pan, and then were heated under N_2 flow (Rujitanaroj *et al.*, 2008).

The summary of percent weight loss from the TGA thermogram is shown in Table F1. Figures F1-F2 show the TGA thermograms of uncrosslinked and crosslinked of porcine and fish gelatin hydrogels. The transitions of both uncrosslinked gelatins appear as two transitions. The first occurring in the temperature range between 25 and 90°C can be referred to as the loss of moisture. The moisture content of the gelatin samples ranges between 13.25 and 15.00%. For the second transition, it is the onset thermal decomposition ($T_{d,onset}$) of porcine and fish gelatins (Rujitanaroj *et al.*, 2008), occurring at the temperature of 267 to272°C and 266 to 270°C, respectively.

Figures F3-F4 show the TGA thermograms of pure salicylic acid (SA) and SA-loaded porcine and fish gelatin hydrogels. For pure SA, the thermogram shows the T_d in the range of 130-180°C, due to the loss of SA (Niamlang *et al.* 2009). For the SA-loaded gelatins, the transitions of the both gelatins appear in three transitions. The first occurs in the temperature range between 25 and 90°C, which can be referred to the loss of moisture. For the second transition, it is the gelatin onset thermal decomposition ($T_{d,onset}$) of the porcine gelatin hydrogel (PorGel) and the fish gelatin hydrogel (FishGel), where $T_{d,onset}$ shifts from 272 and 270 to 236 and 230°C, respectively. For the shift of $T_{d,onset}$, this can be used to confirm the presence of SA in the gelatin hydrogels.

Figures F5-F6 show the TGA thermograms of pure 5-sulfosalicylic acid (SSA) and the SSA-loaded porcine and fish gelatin hydrogels. For pure SSA, the thermogram has three transitions. The first transition refers to the loss of moisture in the range of 60-100°C, The second one refers to the melting point at 160°C, and the last one identifies the T_d of SSA at 220°C (Juntanon *et al.*, 2008). For the SSA-

loaded gelatins the transitions of the both gelatins appear in three transitions. The first occurs in the temperature range of 25 to 90°C which can be referred to as the loss of moisture. For the second transition, is the $T_{d,onset}$ of the SSA-loaded PorGel and FishGel, in which $T_{d,onset}$ shifts from 272 and 270 to 249 and 245°C, respectively. For the shift of $T_{d,onset}$, this can be used to confirm the presence of SA in the gelatin hydrogels.

Table F1 Summary of porcine and fish gelatin hydrogels degradation step

Type of gelatin	% CR ratio	Transition temperature (°C)		Weight loss (%)		Residue (%)
		1	2	1	2	
Porcine	0	25-90	267	15.30	68.95	15.75
	0.25	25-90	269	14.80	67.87	17.33
	0.50	25-90	271	14.40	65.20	20.40
	1	25-90	272	14.44	64.86	20.70
	3	25-90	272	14.56	59.77	25.67
Fish	0	25-90	266	15.00	63.11	21.89
	1	25-90	270	13.20	61.14	25.66
	3	25-90	270	13.25	60.52	26.23

Table F2 Summary of drugs-loaded PorGel and FishGel hydrogels degradation step

Sample		Transition temperature (°C)		Weight loss (%)		Residue (%)
Type	Drug-loaed	1	2	1	2	
PorGel_ 1.00	Unloaded	25-90	272	14.44	64.86	20.27
	1% SA-loaded	25-90	236	12.60	68.30	19.10
	1%SSA-loaded	25-90	249	9.90	63.82	26.28
FishGel _1.00	Unloaded	25-90	270	13.20	61.14	25.66
	1% SA-loaded	25-90	230	10.00	66.00	24.00
	1%SSA-loaded	25-90	245	9.50	62.00	28.50

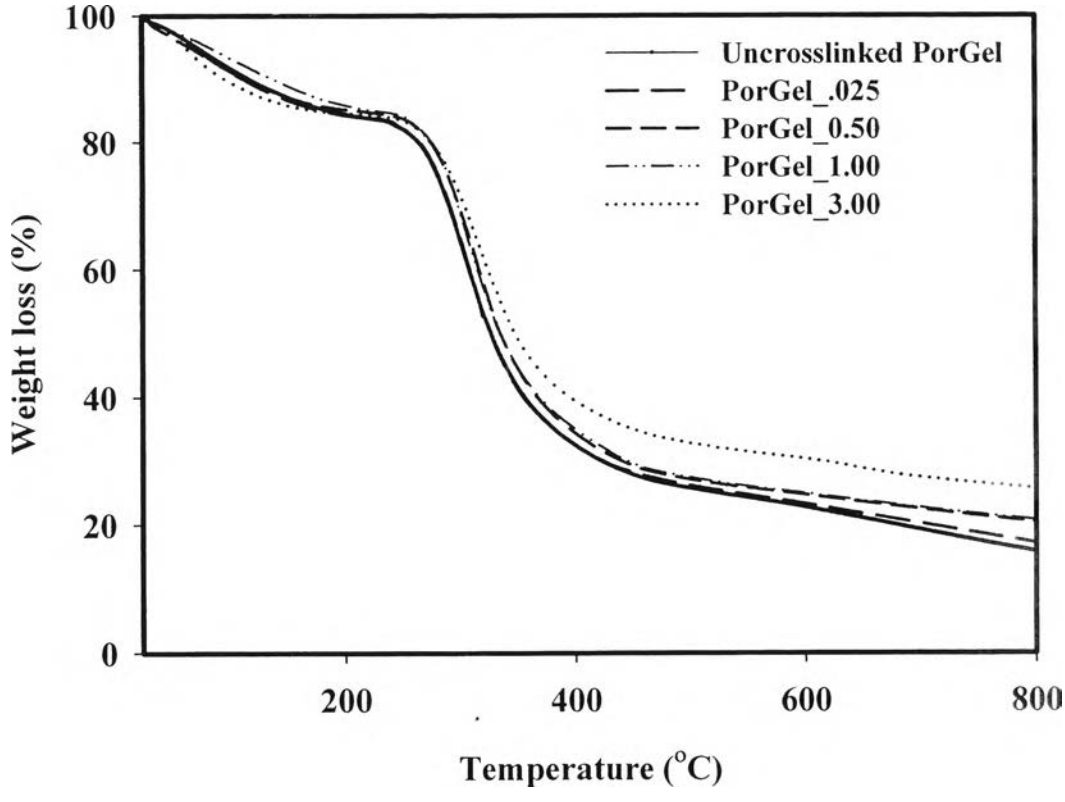


Figure F1 The TGA thermograms of uncrosslinked PorGel and PorGel hydrogels at various crosslinking ratios.

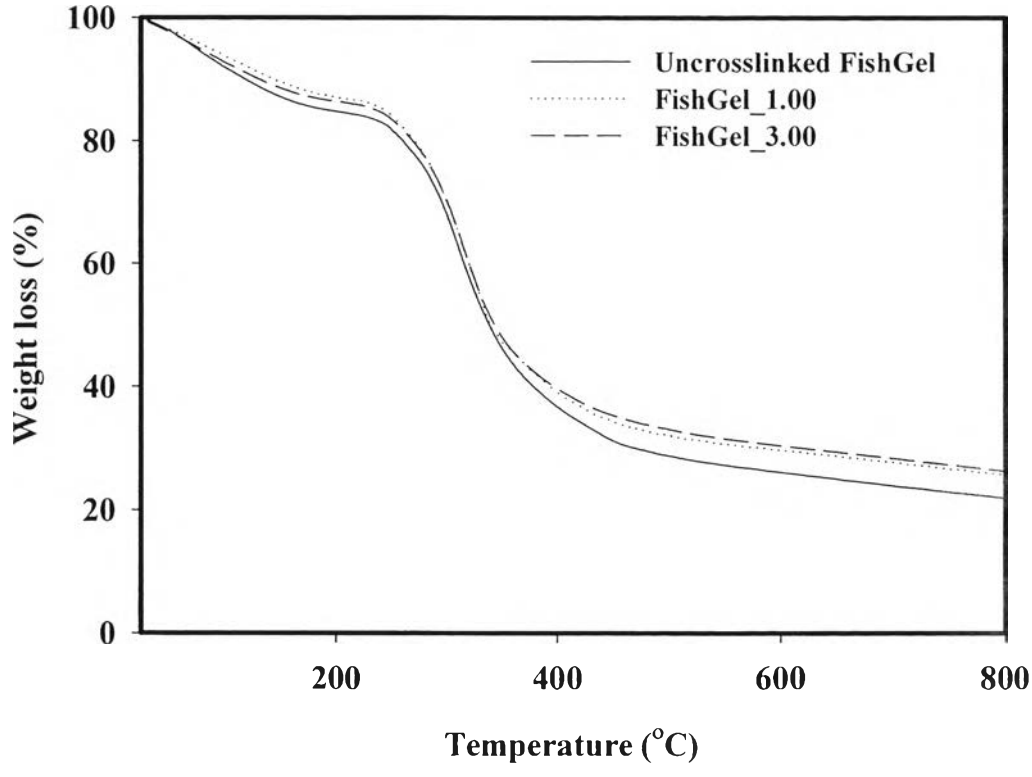


Figure F2 The TGA thermograms of uncrosslinked FishGel and FishGel hydrogels at various crosslinking ratios.

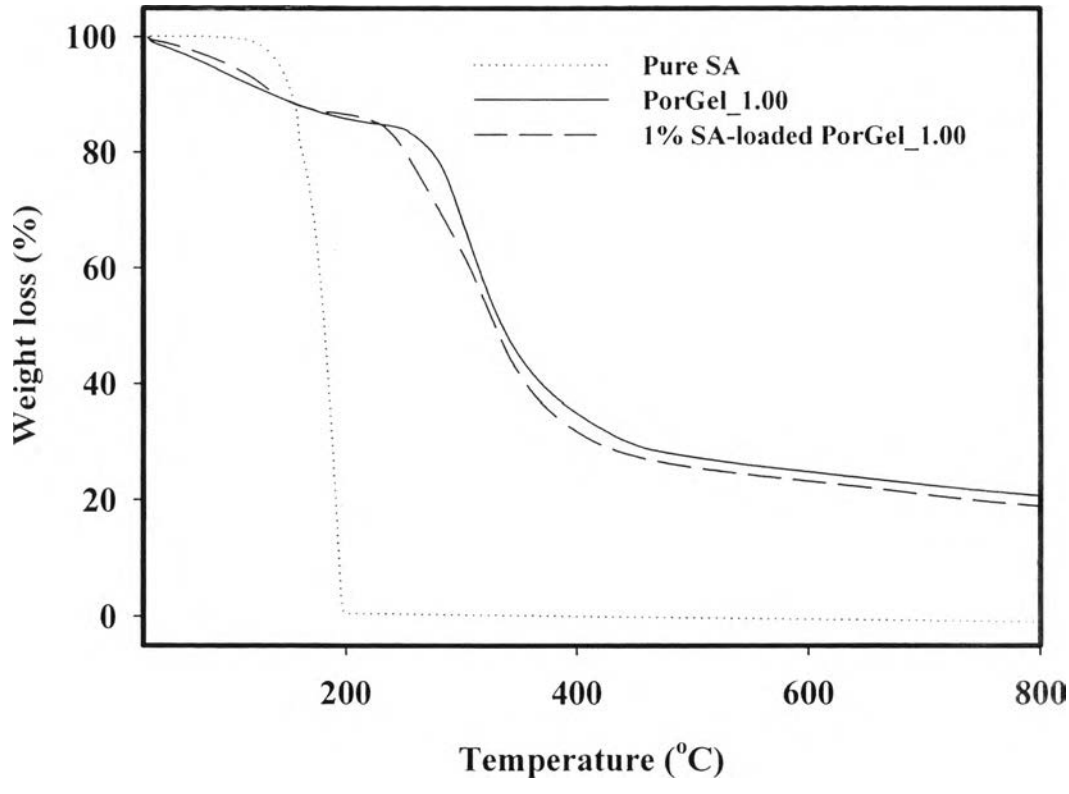


Figure F3 The TGA thermograms of pure SA, PorGel_1.00, SA-loaded PorGel_1.00 hydrogels.

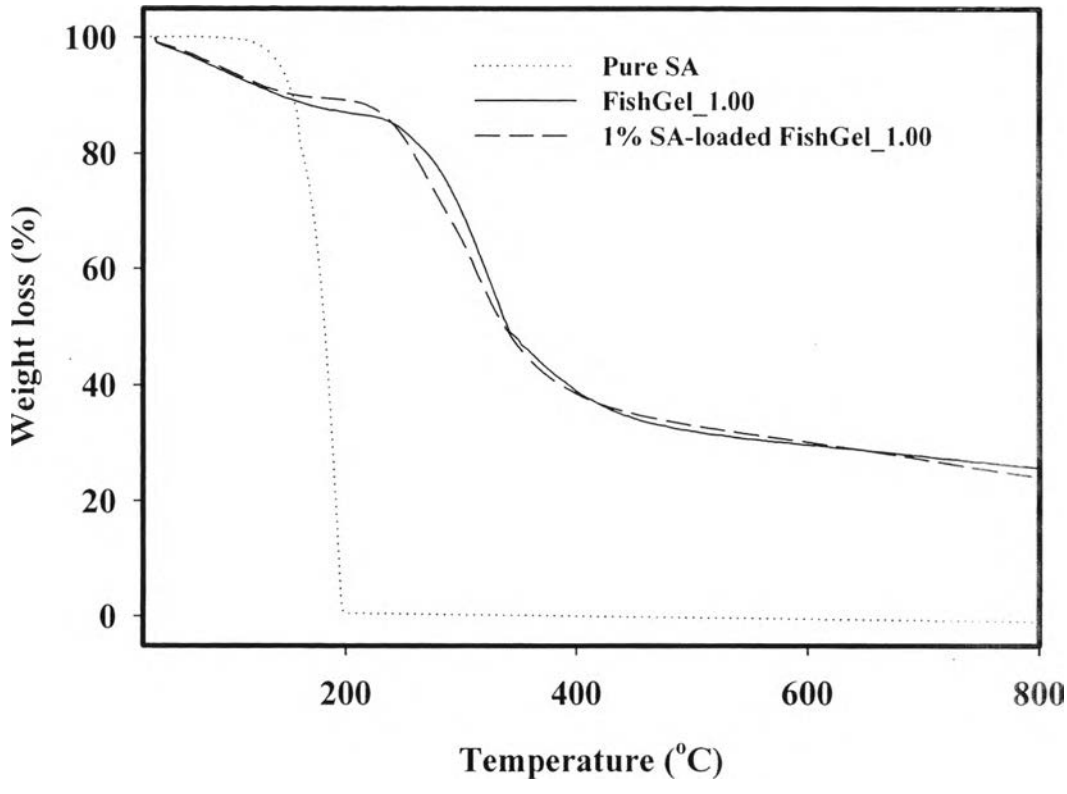


Figure F4 The TGA thermograms of pure SA, FishGel_1.00, and SA-loaded FishGel_1.00 hydrogels.

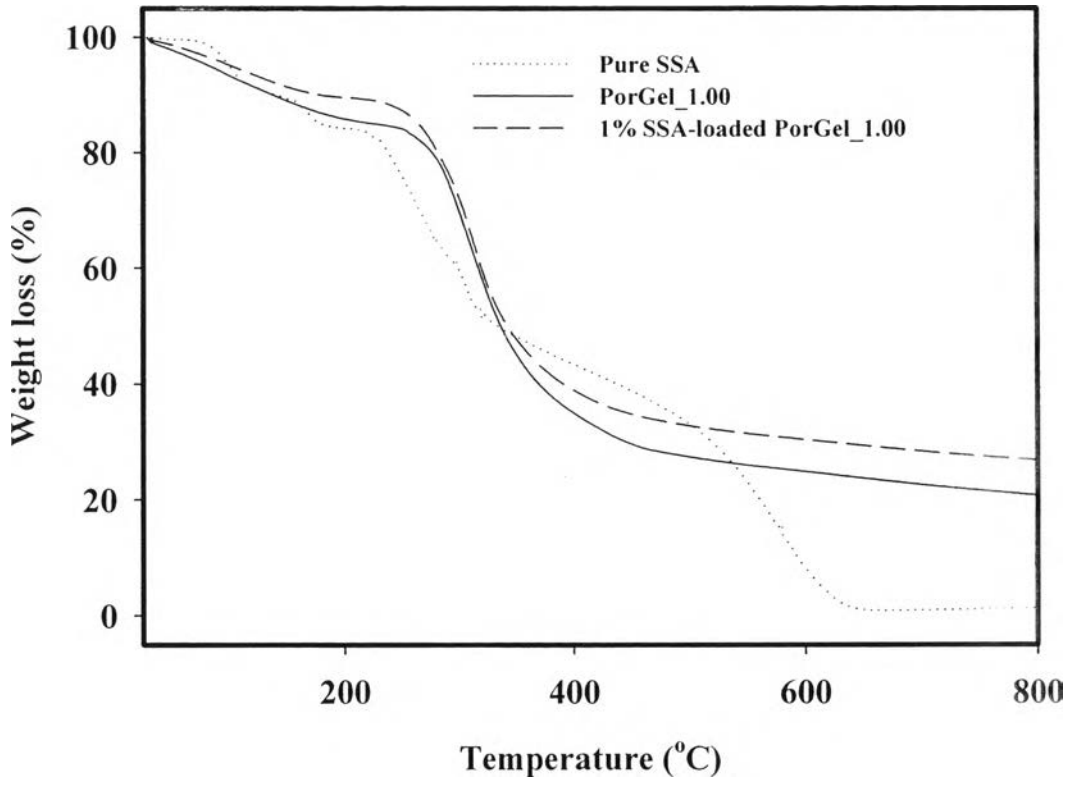


Figure F5 The TGA thermograms of pure SSA, PorGel_1.00, SSA-loaded PorGel_1.00 hydrogels.

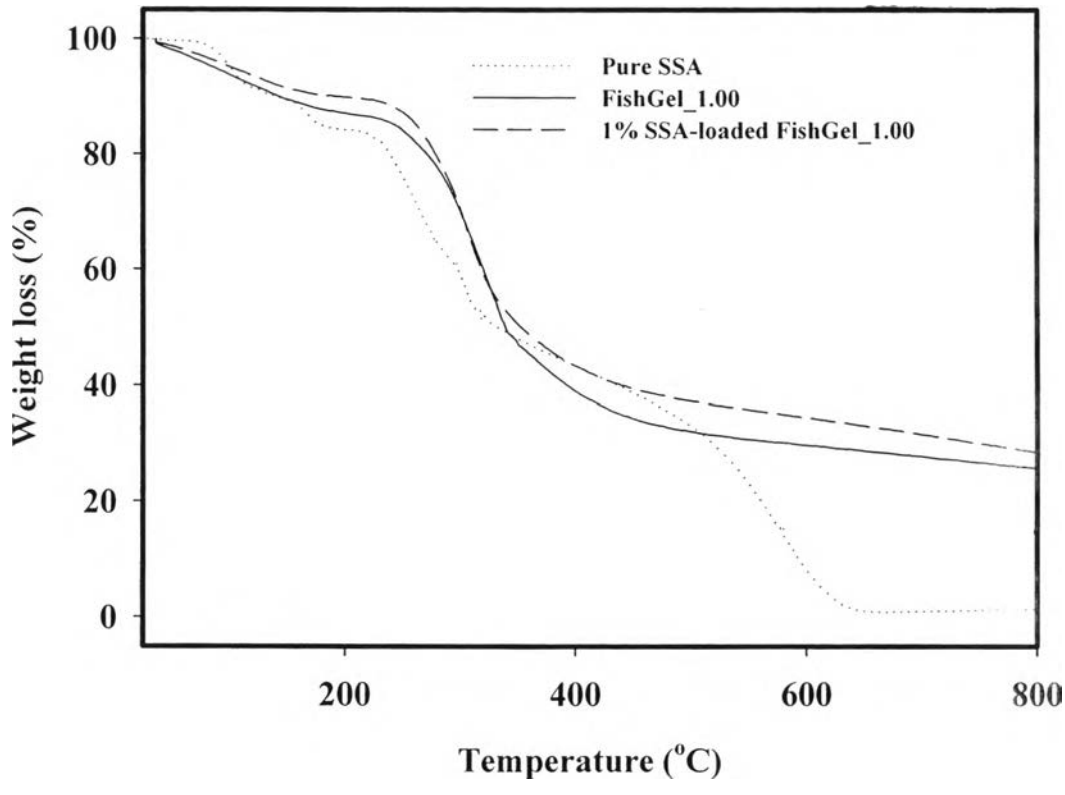


Figure F6 The TGA thermograms of pure SSA, FishGel_1.00, SSA-loaded FishGel_1.00 hydrogels.

Appendix G FT-IR Spectrum of Drug-Loaded Gelatins Hydrogel

Salicylic Acid

The spectra of salicylic acid (SA) as a model drug was obtained from discs containing the salicylic acid (SA) and potassium bromide (KBr), using a Bruker infrared spectrophotometer (Bruker Instruments) with the absorption mode 32 scans at the resolution of 4 cm^{-1} at 4000 to 400 cm^{-1}.

To study the cross-linked polymer/drug interaction the gelatin films and drug-loaded gelatin films were characterized by ATR-FTIR spectroscopy. The samples were placed on the crystal and spectra were taken to determine any interactions between the drug and polymer. The FT-IR spectrum was observed by using an FT-IR spectrometer (Thermo Nicolet) with the absorption mode 32 scans at the resolution of 4 cm^{-1} at 4000 to 650 cm^{-1}.

5-sulfosalicylic Acid

The spectrum of 5-sulfosalicylic acid (SSA) as a model drug was obtained from discs containing the 5-sulfosalicylic acid (SSA) and potassium bromide (KBr), using a Bruker infrared spectrophotometer (Bruker Instruments) with the absorption mode 32 scans at the resolution of 4 cm^{-1} at 4000 to 400 cm^{-1}.

The gelatin film and drug-loaded gelatin films were characterized by ATR-FTIR spectroscopy to study the cross-linked polymer/drug interaction. The sample was placed on the crystal and spectra were taken to determine any interactions between the drug and the polymers. The FT-IR spectrum was observed by using an FT-IR spectrometer (Thermo Nicolet) with the absorption mode 32 scans at the resolution of 4 cm^{-1} at 4000 to 650 cm^{-1}.

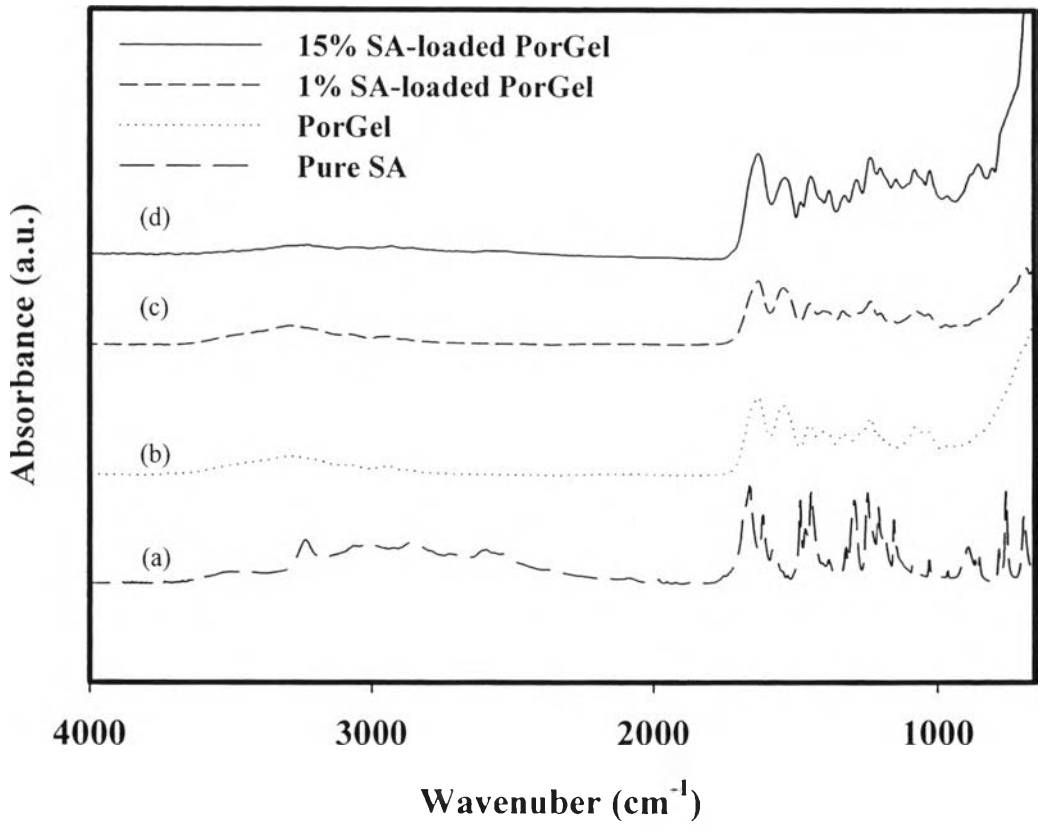


Figure G1 Absorption infrared spectra of salicylic acid (SA) and salicylic acid loaded porcine gelatin hydrogel: (a) Pure salicylic acid; (b) Porcine gelatin hydrogel ; (c) 1% SA-loaded porcine gelatin hydrogel; and (d) 15% SA-loaded porcine gelatin hydrogel.

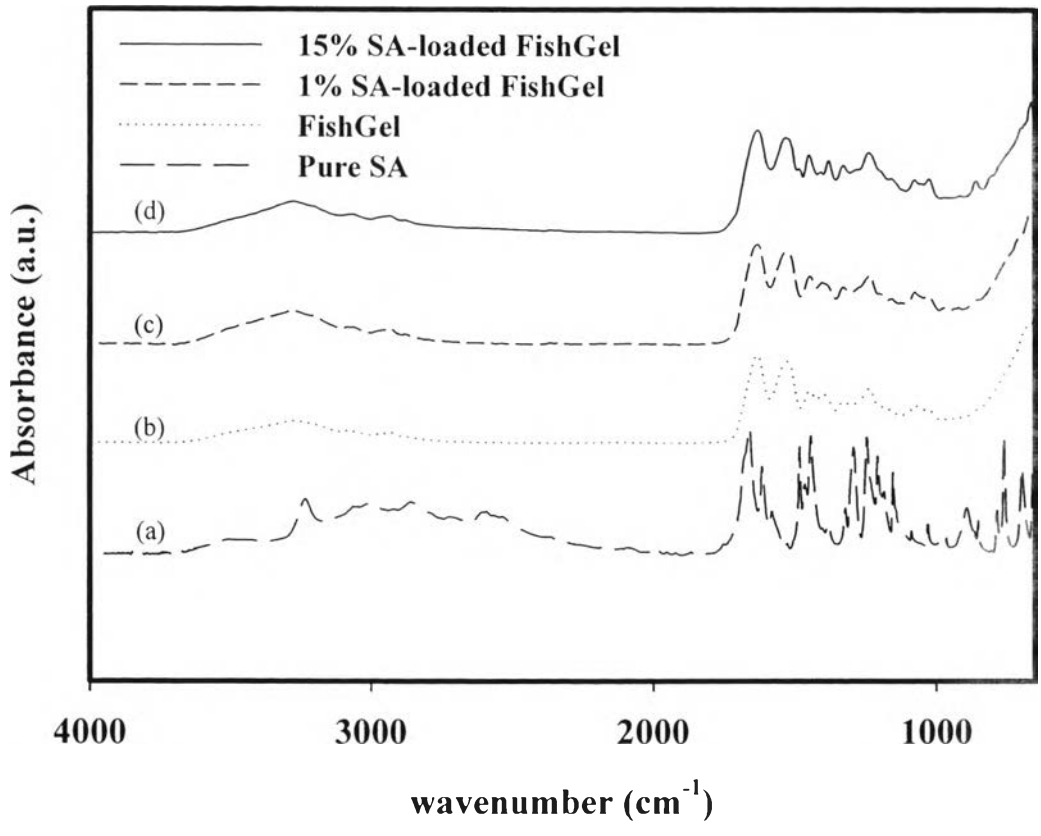


Figure G2 Absorption infrared spectra of salicylic acid (SA) and salicylic loaded fish gelatin hydrogel: (a) Pure salicylic acid; (b) Fish gelatin hydrogel; (c) 1% SA-loaded fish gelatin hydrogel; and (d) 15% SA-loaded fish gelatin hydrogel.

Figures G1-G2 show the absorption infrared spectrums of cross-linked gelatin hydrogels in comparison with SA-loaded gelatin hydrogels. For pure SA, peaks at 867 and 1483 cm^{-1} can be observed. These characteristic peaks can be referred to the C-H out of plane bending and C-C ring stretching, respectively (Mohan, J. 2004). For the porcine and fish gelatins, observed peaks are at 1400, 1540, and 3290 cm^{-1}. These characteristic peaks can be assigned to the O-H bending (Stancu *et al.*, 2010), the N–H bending of amide II (Muyouga *et al.*, 2004), and the N-H stretching from primary amine (Stancu *et al.*, 2010), respectively. For the drug-loaded gelatin hydrogels, the spectrum shows the characteristic peaks at 861 cm^{-1} and 1479 cm^{-1} for FishGel, at 856 cm^{-1} and 1476 cm^{-1} for PorGel. The peak at 1400 cm^{-1}

slightly shifts to 1402 and 1405 cm^{-1} for PorGel and FishGel, respectively. These results suggest that the hydrogen bond is created between the COOH group of salicylic acid and the O-H group of gelatins.

Table G1 The FT-IR absorption spectrum of salicylic acid-loaded gelatin hydrogels and the gelatin hydrogels

Wavenumber	**assignment**	**reference**
3290	N-H stretching from preimary amine	Stancu *et al.*, 2010
1540	N-H bending coupled with CN stretching (amide II)	Muyonga *et al.*, 2004
1476-1479	C-C stretching ring	Mohan, J. 2004
1400	O-H bending from primary amine	Stancu *et al.*, 2010
856-861 [900-860]	C-H out of plane bending	Mohan, J. 2004
~1483	C-C stretching ring	Mohan, J. 2004
~ 867 [900-860]	C-H out of plane bending	Mohan, J. 2004

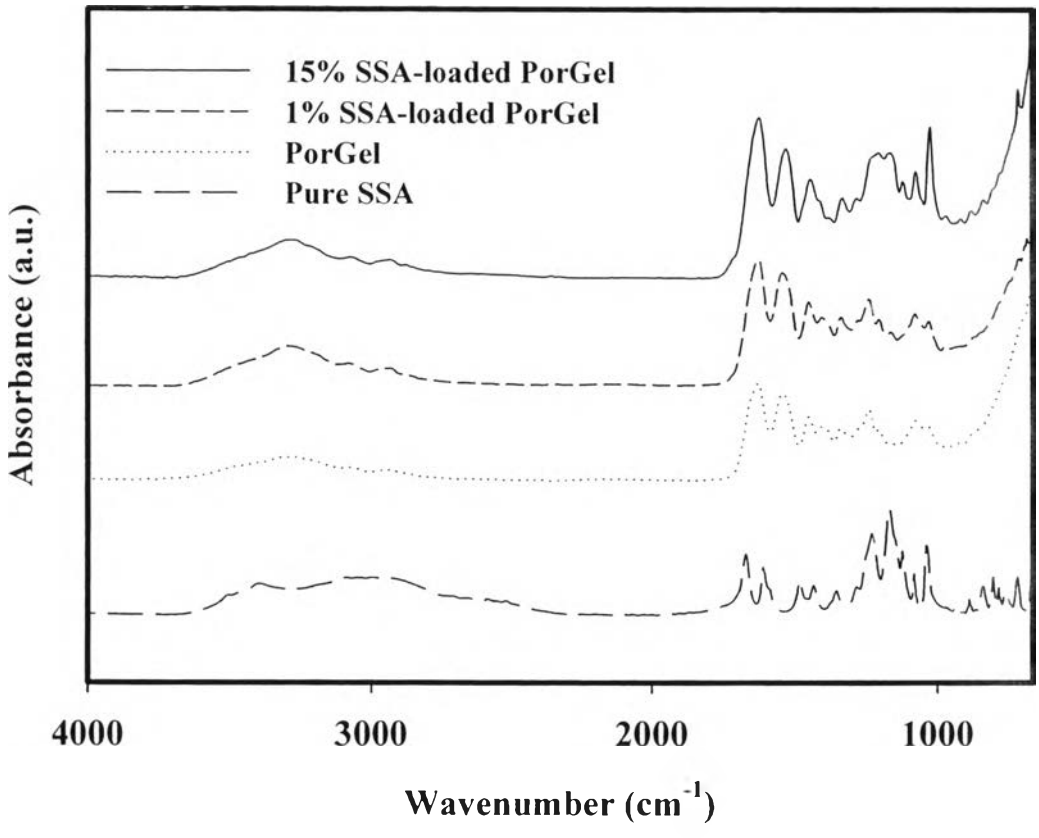


Figure G3 Absorption infrared spectra of 5-sulfosalicylic acid (SSA) and salicylic acid (SA) loaded porcine gelatin hydrogel: (a) Pure SSA powder; (b) Pure porcine gelatin hydrogel; (c) 1% SSA-loadedporcine gelatin hydrogel; and (d) 15% SSA-loaded porcine gelatin hydrogel.

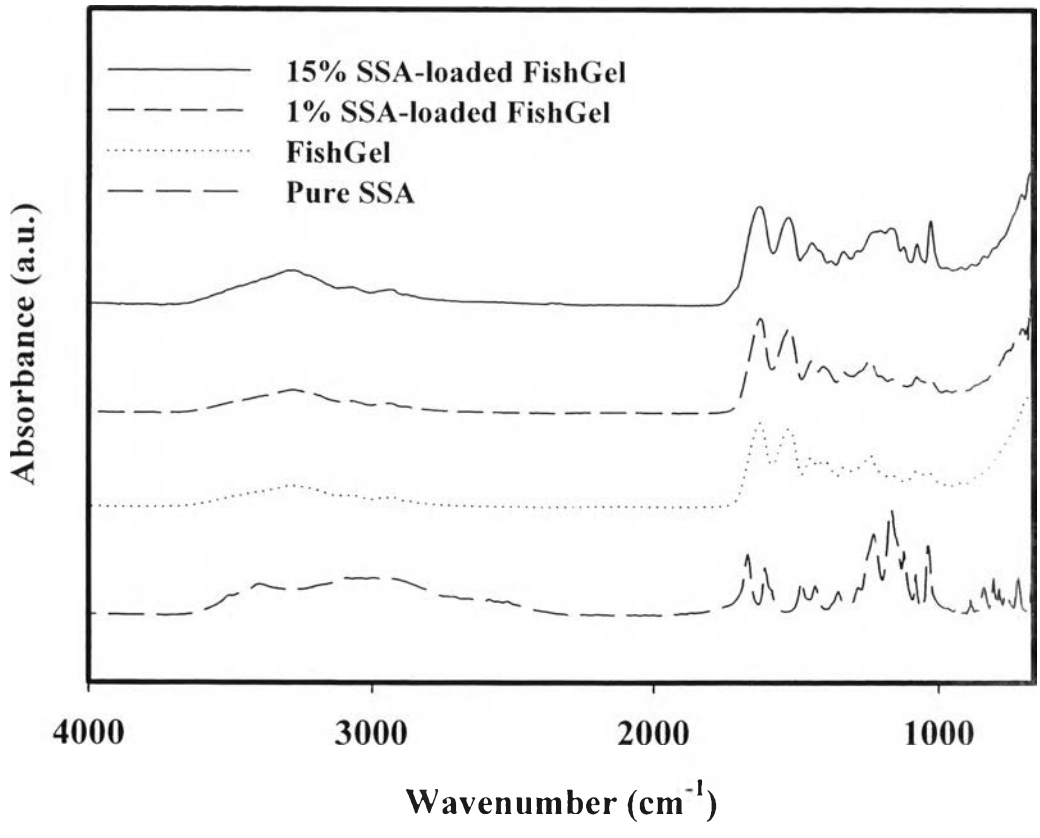


Figure G4 Absorption infrared spectra of 5-sulfosalicylic acid (SSA) and salicylic acid (SA) loaded fish gelatin hydrogel: (a) Pure SSA powder; (b) Pure fish gelatin hydrogel; (c) 1% SSAloaded fish gelatin hydrogel; and (d) 15% SSA-loaded fish gelatin hydrogel.

Figures G3-G4 show the absorption infrared spectra of the cross-linked gelatin hydrogels, in comparison with the SSA-loaded gelatin hydrogels. For pure SSA, peaks at 1038 and 1167 cm^{-1}can be observed. These characteristic peaks can be referred to the SO^{3-} symmetric stretching and the asymmetric SO^{3-} stretching, respectively (Mohan, J. 2004). For the porcine and fish gelatins, peaks are observed at 1400, 1540, and 3290 cm^{-1}. These characteristic peaks can be assigned to the O-H bending (Stancu *et al.*, 2010), the N–H bending of amide II (Muyouga *et al.*, 2004), and the N-stretching from primary amine Stancu *et al.*, 2010), respectively. For the drug-loaded gelatin hydrogels, the spectra show the characteristic peaks at 1074 and

1160 cm^{-1} for both gelatins. The peak at 1400 cm^{-1} slightly shifts to 1402 for both gelatins. These results suggest that the hydrogen bond is creasted between the COOH group of sulfosalicylic acid and the O-H group of gelatins.

Table G2 The FT-IR absorption spectrum of 5-sulfosalicylic acid-loaded gelatin hydrogels and the gelatin hydrogels

Wavenumber	**assignment**	**reference**
3290	N-H stretching from primary amine	Stancu *et al.*, 2010
1543	N-H bending coupled with CN stretching (amide II)	Muyonga *et al* .,2004
1400	O-H bending from primary amine	Stancu *et al* .,2010
1160 [1260-1150]	SO^{-3} strecthing asymmertic	Mohan, J. 2004
1077 [1080-1010]	SO^{-3} strecthing symmertric	Mohan, J. 2004
~1167 [1260-1150]	SO^{-3} strecthing asymmertic	Mohan, J. 2004
~1038 [1080-1010]	SO^{-3} strecthing symmertric	Mohan, J. 2004

Appendix H Scanning Electron Micrographs of Various Crosslinked Gelatin Hydrogels

Porcine Gelatin (PorGel) Hydrigels

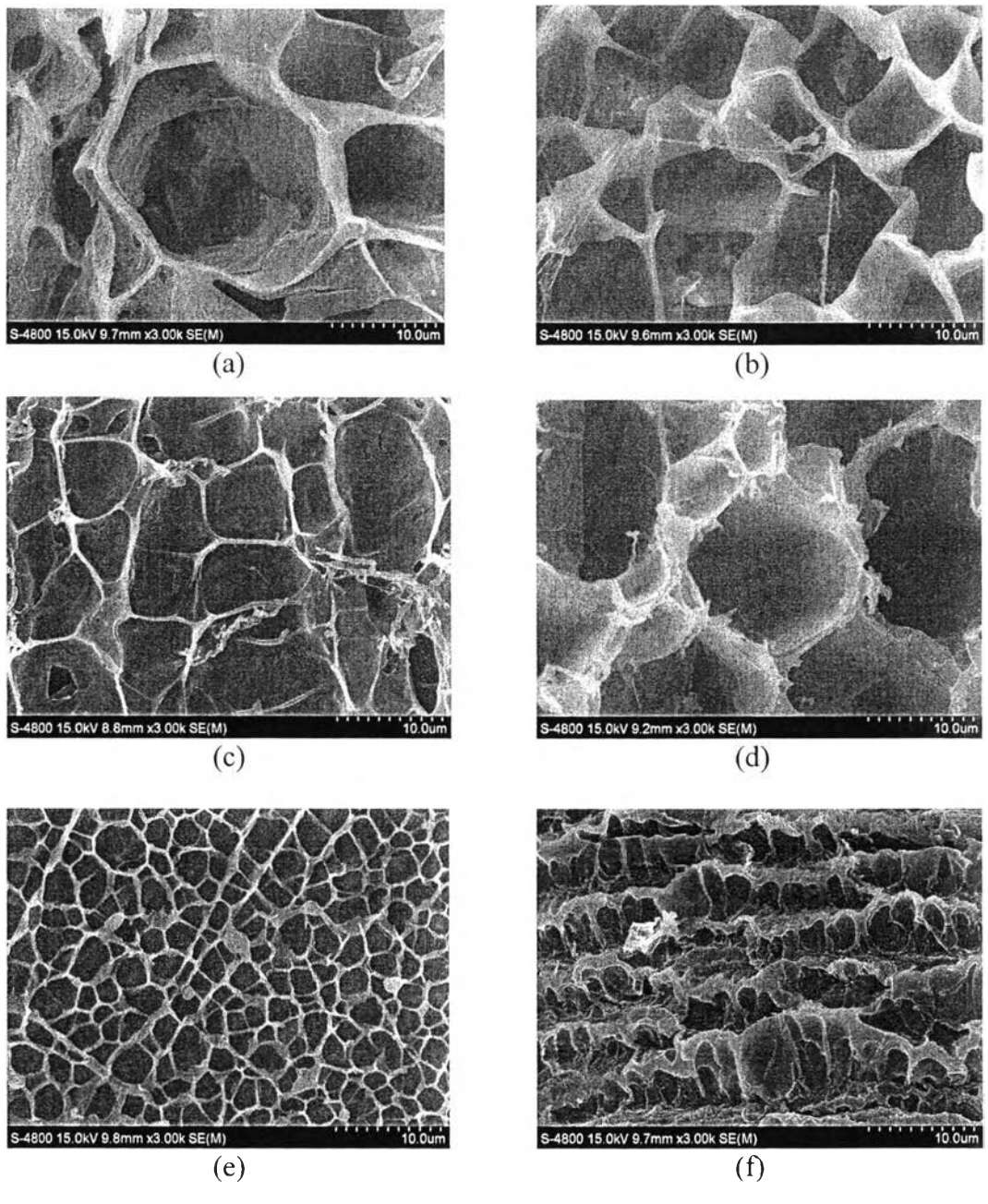
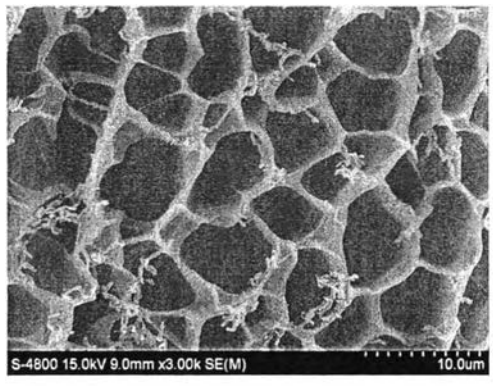
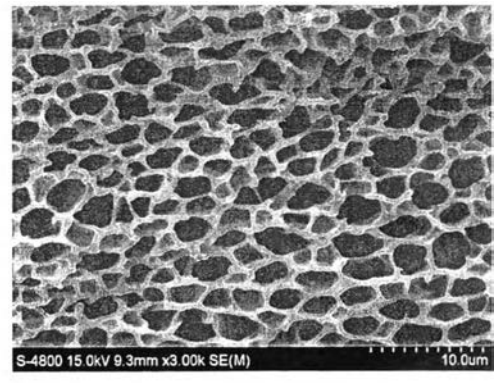


Figure H1 The morphology of PorGel samples after swelling: (a) PorGel_0.25; (b) PorGel_0.5; (c) PorGel_0.75; (d) PorGel_1; (e) PorGel_3; and (f) PorGel_7 at magnification of 3000X.

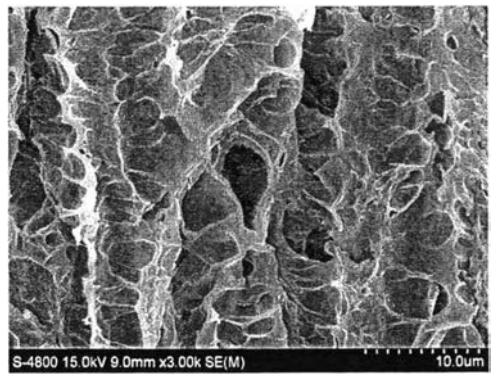
Fish Gelatin (FishGel) Hydrogels



(a)



(b)



(c)

Figure H2 The morphology of FishGel samples after swelling: (a) FishGel_1; (b) FishGel_3; and (c) FishGel_7 at magnification of 3000X.

Appendix I Determination of Actual Drug Content

Initially, The actual amount of drug in the drug-loaded gelatin hydrogel, circular disc about 2.5 cm in diameter, was quantified by dissolving the sample in 4 ml of dimethylsulfoxide (DMSO) and then 0.5 ml of the solution was added into 8 ml of the an acetate buffer solution. The amounts of drugs in the solution were measured by using the UV-Visible spectrophotometer at a wavelength of 298 nm.

The actual amount of drugs present in the sample is reported as the percentage of the initial content of drugs loaded in gelatin solution. The actual amount of salicylic acid and 5-sulfosalicylic acid presented in the sample are about 91.75 ± 5.51 % and 92.83 ± 3.96 %, respectively.

Table I1 Raw data for determination of actual amount of salicylic acid in the sample

Sample	absorbance	Concentration (mg/l)	Diluted 8.5ml	Dissolved in 4 ml DMSO	Actual amount of drug (%)
1	0.2162	8.8648	0.0735	0.5881	94.09
2	0.2060	8.2400	0.0700	0.5603	89.65
3	0.2252	9.0080	0.0766	0.6125	98.01
4	0.1959	7.8360	0.0667	0.5328	85.26
Avg					**91.75**
SD					**5.51**

Table I2 Raw data for determination of actual amount of 5-sulfosalicylic acid in the sample

Sample	absorbance	Concentration (mg/l)	Diluted 8.5ml	Dissolved in 4 ml DMSO	Actual amount of drug (%)
1	0.1056	8.8739	0.0754	0.6034	96.55
2	0.1036	8.7059	0.0740	0.5920	94.72
3	0.0956	8.0336	0.0683	0.5463	87.41
4	0.1009	8.4790	0.0721	0.5766	92.25
Avg					**92.73**
SD					**3.96**

Appendix J Determination of Amounts and Diffusion Coefficient of Salicylic Acid Released from Salicylic Acid-Loaded Porcine Gelatin Hydrogel at Various Crosslinking Ratios

The diffusion of drug was observed by custom built modified Franz-Diffusion cells. A diffusion cell consists of two compartments. First one is a water jacket compartment that is used to exposed to an ambient condition. Other is a receptor chamber containing an acetate buffer solution pH 5.5 and maintained at 37°C by a circulating water bath. To study the effect of crosslinking ratios (0.25, 0.50, 0.75, 1.00, 3.00, and 7.00) on the porcine gelatin hydrogel (PorGel), a sample of drug-loaded PorGel hydrogel was 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 298 nm.

The amounts of salicylic acid (SA) released from SA-loaded PorGel hydrogel versus time at various crosslinking ratios (PorGel_0.25, PorGel _0.50, PorGel _0.75, PorGel _1.00, PorGel _3.00, and PorGel _7.00) during 48 h are shown in Figure J1. The amounts of released drug gradually increase with time and then reach constant values.

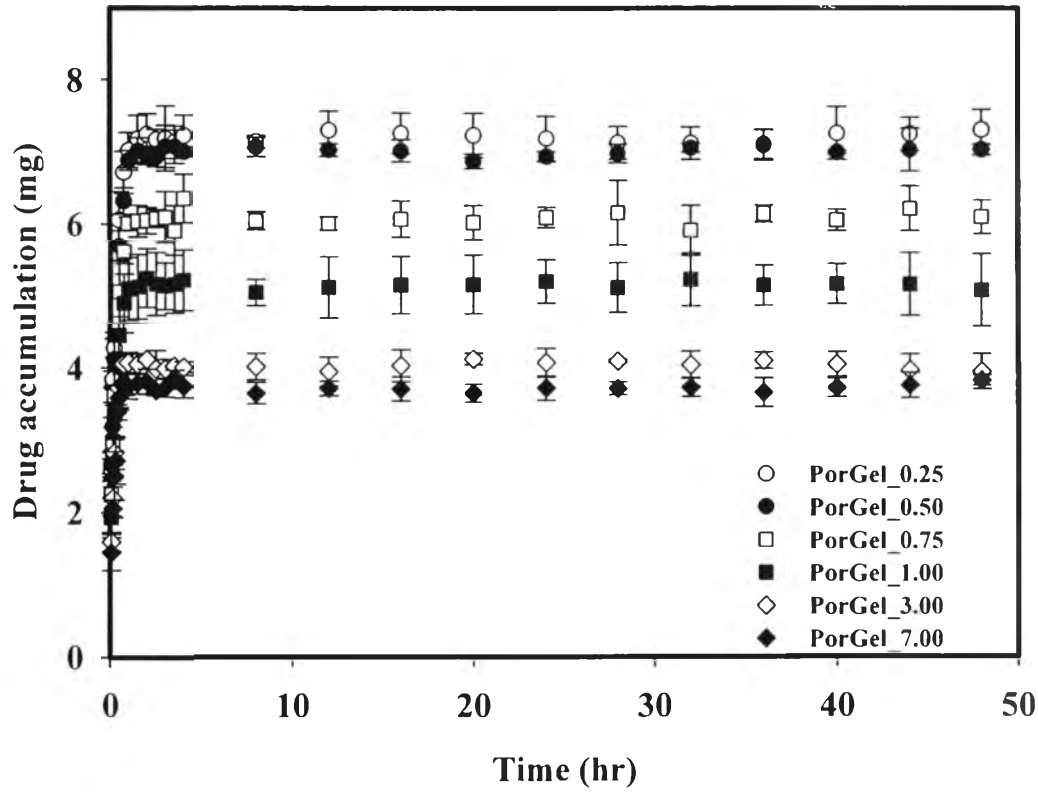


Figure J1 Amounts of salicylic acid release from SA-loaded PorGel hydrogel versus time at various crosslink ratios, pH 5.5, and at 37°C, number of samples = 3.

Table J1 Raw data of the determination of amounts of salicylic acid released from PorGel 0.25% crosslinked (PorGel_0.25) at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0722	0.0716	0.0795	2.5113	2.4904	2.7652	**2.5890**	**0.1530**
0.166667	0.1122	0.1075	0.1068	3.9026	3.9130	3.7148	**3.8435**	**0.1116**
0.25	0.1265	0.1191	0.1232	4.4000	4.1426	4.2852	**4.2759**	**0.1289**
0.5	0.1709	0.1652	0.1868	5.9443	5.7461	6.4974	**6.0626**	**0.3894**
0.75	0.1850	0.1927	0.2018	6.4348	6.7026	7.0191	**6.7188**	**0.2925**
1	0.1951	0.2019	0.2091	6.7861	7.0226	7.2730	**7.0272**	**0.2435**
1.5	0.1965	0.2149	0.2082	6.8348	7.4748	7.2417	**7.1838**	**0.3239**
2	0.1990	0.2140	0.2120	6.9217	7.4435	7.3753	**7.2468**	**0.2836**
2.5	0.2018	0.2075	0.2096	7.0191	7.2174	7.2904	**7.1757**	**0.1404**
3	0.1921	0.2112	0.2167	6.6817	7.3461	7.5374	**7.1884**	**0.4491**
3.5	0.1984	0.2058	0.2113	6.9009	7.1583	7.3496	**7.1362**	**0.2252**
4	0.1984	0.2128	0.2123	6.9009	7.4017	7.3843	**7.2290**	**0.2843**
8	0.2029	0.2051	0.2079	7.0574	7.1339	7.2313	**7.1409**	**0.0872**
12	0.2014	0.2118	0.2163	7.0052	7.3670	7.5235	**7.2986**	**0.2658**
16	0.2029	0.2051	0.2179	7.0574	7.1339	7.5791	**7.2568**	**0.2817**
20	0.1976	0.2117	0.2140	6.8730	7.3635	7.4435	**7.2267**	**0.3088**
24	0.1963	0.2132	0.2100	6.8278	7.4157	7.3043	**7.1826**	**0.3123**
28	0.1974	0.2073	0.2097	6.8661	7.2104	7.2939	**7.1235**	**0.2268**
32	0.1982	0.2112	0.2047	6.8939	7.3461	7.1200	**7.1200**	**0.2261**
36	0.1973	0.2047	0.2095	6.8626	7.1200	7.2870	**7.0899**	**0.2138**
40	0.1977	0.2097	0.2187	6.8765	7.2939	7.6070	**7.2591**	**0.3665**
44	0.2007	0.2107	0.2134	6.9809	7.3287	7.4226	**7.2441**	**0.2327**
48	0.2017	0.2107	0.2176	7.0157	7.3287	7.5687	**7.3043**	**0.2773**

Table J2 Raw data of the determination of amounts of salicylic acid released from PorGel 0.50% crosslinked (PorGel_0.50) at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0724	0.0819	0.0755	2.5183	2.8487	2.6261	**2.6643**	**0.1685**
0.166667	0.0841	0.1025	0.0886	2.9252	3.5652	3.0817	**3.1907**	**0.3336**
0.25	0.1071	0.1281	0.1205	3.7252	4.4557	4.1913	**4.1241**	**0.3698**
0.5	0.1566	0.1669	0.1678	5.4470	5.8052	5.8365	**5.6962**	**0.2164**
0.75	0.1764	0.1824	0.1866	6.1357	6.3443	6.4904	**6.3235**	**0.1783**
1	0.1844	0.1998	0.2007	6.7270	6.9496	6.9809	**6.8858**	**0.1384**
1.5	0.1957	0.2037	0.2058	6.8070	7.0852	7.1583	**7.0168**	**0.1854**
2	0.1960	0.2032	0.2005	6.8174	7.0678	6.9739	**6.9530**	**0.1265**
2.5	0.2008	0.1949	0.2017	6.9843	6.7791	7.0157	**6.9264**	**0.1285**
3	0.1988	0.1983	0.2132	6.9148	6.8974	7.4157	**7.0759**	**0.2943**
3.5	0.1998	0.1994	0.2111	6.9496	6.9357	7.3426	**7.0759**	**0.2310**
4	0.2037	0.2002	0.2002	7.0852	6.9635	6.9635	**7.0041**	**0.0703**
8	0.2032	0.1993	0.2070	7.0678	6.9322	7.2000	**7.0667**	**0.1339**
12	0.2049	0.1997	0.2016	7.1270	6.9461	7.0122	**7.0284**	**0.0915**
16	0.2020	0.1970	0.2058	7.0261	6.8522	7.1583	**7.0122**	**0.1535**
20	0.1947	0.1971	0.2005	6.7722	6.8557	6.9739	**6.8672**	**0.1014**
24	0.1978	0.1985	0.2017	6.8800	6.9043	7.0157	**6.9333**	**0.0723**
28	0.1966	0.2010	0.2041	6.8383	6.9913	7.0991	**6.9762**	**0.1311**
32	0.2007	0.2038	0.2037	6.9809	7.0887	7.0852	**7.0516**	**0.0613**
36	0.2008	0.2011	0.2111	6.9843	6.9948	7.3426	**7.1072**	**0.2039**
40	0.2012	0.2004	0.2016	6.9983	6.9704	7.0122	**6.9936**	**0.0213**
44	0.2008	0.1941	0.2111	6.9843	6.7513	7.3426	**7.0261**	**0.2979**
48	0.2012	0.2004	0.2046	6.9983	6.9704	7.1165	**7.0284**	**0.0776**

Table J3 Raw data of the determination of amounts of salicylic acid released from PorGel 0.75% crosslinked (PorGel_0.75)at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0551	0.0692	0.0697	1.9165	2.4070	2.4243	**2.2493**	**0.2883**
0.166667	0.0762	0.0857	0.0953	2.6504	2.9809	3.3148	**2.9820**	**0.3322**
0.25	0.1085	0.1004	0.1036	3.7739	3.4922	3.6035	**3.6232**	**0.1419**
0.5	0.1308	0.1526	0.1525	4.5496	5.3078	5.3043	**5.0539**	**0.4368**
0.75	0.1661	0.1569	0.1608	5.7774	5.4574	5.5930	**5.6093**	**0.1606**
1	0.1738	0.1698	0.1748	6.0452	5.9061	6.0800	**6.0104**	**0.0920**
1.5	0.1672	0.1746	0.1796	5.8157	6.0730	6.2470	**6.0452**	**0.2170**
2	0.1699	0.1723	0.1800	5.9096	5.9930	6.2609	**6.0545**	**0.1835**
2.5	0.1742	0.1716	0.1786	6.0591	5.9687	6.2122	**6.0800**	**0.1231**
3	0.1650	0.1754	0.1855	5.7391	6.1009	6.4522	**6.0974**	**0.3565**
3.5	0.1590	0.1723	0.1786	5.5304	5.9930	6.2122	**5.9119**	**0.3480**
4	0.1720	0.1861	0.1903	5.9826	6.4730	6.6191	**6.3583**	**0.3334**
8	0.1698	0.1748	0.1768	5.9061	6.0800	6.1496	**6.0452**	**0.1254**
12	0.1738	0.1698	0.1747	6.0452	5.9061	6.0765	**6.0093**	**0.0907**
16	0.1672	0.1746	0.1816	5.8157	6.0730	6.3165	**6.0684**	**0.2505**
20	0.1661	0.1733	0.1797	5.7774	6.0278	6.2504	**6.0186**	**0.2367**
24	0.1742	0.1716	0.1796	6.0591	5.9687	6.2470	**6.0916**	**0.1419**
28	0.1650	0.1754	0.1905	5.7391	6.1009	6.6261	**6.1554**	**0.4460**
32	0.1590	0.1723	0.1786	5.5304	5.9930	6.2122	**5.9119**	**0.3480**
36	0.1733	0.1765	0.1800	6.0278	6.1391	6.2609	**6.1426**	**0.1166**
40	0.1733	0.1701	0.1786	6.0278	5.9165	6.2122	**6.0522**	**0.1493**
44	0.1686	0.1816	0.1855	5.8643	6.3165	6.4522	**6.2110**	**0.3078**
48	0.1676	0.1797	0.1786	5.8296	6.2504	6.2122	**6.0974**	**0.2327**

Table J4 Raw data of the determination of amounts of salicylic acid released from PorGel 1.00% crosslinked (PorGel_1.00) at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0565	0.0630	0.0473	1.9652	2.1913	1.6452	**1.9339**	**0.2744**
0.166667	0.0763	0.0927	0.0698	2.6539	3.2243	2.4278	**2.7687**	**0.4105**
0.25	0.0977	0.1058	0.0860	3.3983	3.6800	2.9913	**3.3565**	**0.3462**
0.5	0.1357	0.1272	0.1212	4.7200	4.4243	4.2157	**4.4533**	**0.2534**
0.75	0.1538	0.1371	0.1313	5.3496	4.7687	4.5670	**4.8951**	**0.4063**
1	0.1606	0.1415	0.1371	5.5861	4.9217	4.7687	**5.0922**	**0.4345**
1.5	0.1583	0.1506	0.1330	5.5061	5.2383	4.6261	**5.1235**	**0.4511**
2	0.1621	0.1516	0.1387	5.6383	5.2730	4.8243	**5.2452**	**0.4077**
2.5	0.1610	0.1483	0.1359	5.6000	5.1583	4.7270	**5.1617**	**0.4365**
3	0.1538	0.1521	0.1368	5.3496	5.2904	4.7583	**5.1328**	**0.3257**
3.5	0.1584	0.1510	0.1356	5.5096	5.2522	4.7165	**5.1594**	**0.4046**
4	0.1597	0.1538	0.1363	5.5548	5.3496	4.7409	**5.2151**	**0.4233**
8	0.1479	0.1484	0.1391	5.1443	5.1617	4.8383	**5.0481**	**0.1819**
12	0.1607	0.1440	0.1369	5.5896	5.0087	4.7617	**5.1200**	**0.4250**
16	0.1598	0.1479	0.1368	5.5583	5.1443	4.7583	**5.1536**	**0.4001**
20	0.1587	0.1507	0.1356	5.5200	5.2417	4.7165	**5.1594**	**0.4080**
24	0.1568	0.1521	0.1399	5.4539	5.2904	4.8661	**5.2035**	**0.3034**
28	0.1576	0.1460	0.1377	5.4817	5.0783	4.7896	**5.1165**	**0.3477**
32	0.1616	0.1488	0.1405	5.6209	5.1757	4.8870	**5.2278**	**0.3697**
36	0.1559	0.1484	0.1398	5.4226	5.1617	4.8626	**5.1490**	**0.2802**
40	0.1559	0.1497	0.1400	5.4226	5.2070	4.8696	**5.1664**	**0.2787**
44	0.1612	0.1479	0.1361	5.6070	5.1443	4.7339	**5.1617**	**0.4368**
48	0.1602	0.1467	0.1313	5.5722	5.1026	4.5670	**5.0806**	**0.5030**

Table J5 Raw data of the determination of amounts of salicylic acid released from PorGel 3.00% crosslinked (PorGel_3.00) at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0416	0.0478	0.0485	1.4470	1.6626	1.6870	**1.5988**	**0.1321**
0.166667	0.0573	0.0603	0.0720	1.9930	2.0974	2.5043	**2.1983**	**0.2702**
0.25	0.0741	0.0825	0.0871	2.5774	2.8696	3.0296	**2.8255**	**0.2293**
0.5	0.0989	0.1077	0.1142	3.4400	3.7461	3.9722	**3.7194**	**0.2671**
0.75	0.1130	0.1168	0.1201	3.9304	4.0626	4.1774	**4.0568**	**0.1236**
1	0.1128	0.1176	0.1210	3.9235	4.0904	4.2087	**4.0742**	**0.1433**
1.5	0.1119	0.1195	0.1182	3.8922	4.1565	4.1113	**4.0533**	**0.1414**
2	0.1175	0.1192	0.1186	4.0870	4.1461	4.1252	**4.1194**	**0.0300**
2.5	0.1071	0.1164	0.1209	3.7252	4.0487	4.2052	**3.9930**	**0.2448**
3	0.1104	0.1163	0.1173	3.8400	4.0452	4.0800	**3.9884**	**0.1297**
3.5	0.1154	0.1161	0.1156	4.0139	4.0383	4.0209	**4.0243**	**0.0125**
4	0.1129	0.1168	0.1164	3.9270	4.0626	4.0487	**4.0128**	**0.0746**
8	0.1096	0.1196	0.1173	3.8122	4.1600	4.0800	**4.0174**	**0.1822**
12	0.1070	0.1174	0.1163	3.7217	4.0835	4.0452	**3.9501**	**0.1987**
16	0.1089	0.1173	0.1214	3.7878	4.0800	4.2226	**4.0301**	**0.2216**
20	0.1208	0.1161	0.1188	4.2017	4.0383	4.1322	**4.1241**	**0.0820**
24	0.1104	0.1204	0.1205	3.8400	4.1878	4.1913	**4.0730**	**0.2018**
28	0.1181	0.1182	0.1170	4.1078	4.1113	4.0696	**4.0962**	**0.0232**
32	0.1104	0.1210	0.1173	3.8400	4.2087	4.0800	**4.0429**	**0.1871**
36	0.1142	0.1203	0.1194	3.9722	4.1843	4.1530	**4.1032**	**0.1145**
40	0.1110	0.1205	0.1180	3.8609	4.1913	4.1043	**4.0522**	**0.1713**
44	0.1067	0.1166	0.1189	3.7113	4.0557	4.1357	**3.9675**	**0.2255**
48	0.1075	0.1118	0.1213	3.7391	3.8887	4.2191	**3.9490**	**0.2456**

Table J6 Raw data of the determination of amounts of salicylic acid released from PorGel 7.00% crosslinked (PorGel_7.00)at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0478	0.0435	0.0338	1.6626	1.5130	1.1757	**1.4504**	**0.2494**
0.166667	0.0632	0.0572	0.0572	2.1983	1.9896	1.9896	**2.0591**	**0.1205**
0.25	0.0831	0.0665	0.0665	2.8904	2.3130	2.3130	**2.5055**	**0.3334**
0.333333	0.0888	0.0727	0.0727	3.0887	2.5287	2.5287	**2.7154**	**0.3233**
0.416667	0.1009	0.0956	0.0956	3.5096	3.3252	3.3252	**3.3867**	**0.1064**
0.5	0.1031	0.1081	0.0983	3.5861	3.7600	3.4191	**3.5884**	**0.1704**
0.666667	0.1081	0.1128	0.1048	3.7600	3.9235	3.6452	**3.7762**	**0.1398**
0.833333	0.1090	0.1130	0.1039	3.7913	3.9304	3.6139	**3.7786**	**0.1586**
1	0.1084	0.1124	0.1023	3.7704	3.9096	3.5583	**3.7461**	**0.1769**
1.5	0.1075	0.1135	0.1055	3.7391	3.9478	3.6696	**3.7855**	**0.1448**
2	0.1120	0.1127	0.1037	3.8957	3.9200	3.6070	**3.8075**	**0.1741**
2.5	0.1060	0.1080	0.1039	3.6870	3.7565	3.6139	**3.6858**	**0.0713**
3	0.1080	0.1099	0.1030	3.7565	3.8226	3.5826	**3.7206**	**0.1240**
3.5	0.1077	0.1147	0.1086	3.7461	3.9896	3.7774	**3.8377**	**0.1325**
4	0.1085	0.1115	0.1028	3.7739	3.8783	3.5757	**3.7426**	**0.1537**
8	0.1076	0.1072	0.0999	3.7426	3.7287	3.4748	**3.6487**	**0.1508**
12	0.1090	0.1080	0.1035	3.7913	3.7565	3.6000	**3.7159**	**0.1019**
16	0.1083	0.1103	0.1012	3.7670	3.8365	3.5200	**3.7078**	**0.1663**
20	0.1065	0.1075	0.1008	3.7043	3.7391	3.5061	**3.6499**	**0.1257**
24	0.1087	0.1107	0.1014	3.7809	3.8504	3.5270	**3.7194**	**0.1703**
28	0.1079	0.1089	0.1039	3.7530	3.7878	3.6139	**3.7183**	**0.0920**
32	0.1090	0.1100	0.1030	3.7913	3.8261	3.5826	**3.7333**	**0.1317**
36	0.1086	0.1086	0.0986	3.7774	3.7774	3.4296	**3.6614**	**0.2008**
40	0.1088	0.1098	0.1028	3.7843	3.8191	3.5757	**3.7264**	**0.1317**
44	0.1087	0.1127	0.1027	3.7809	3.9200	3.5722	**3.7577**	**0.1751**
48	0.1083	0.1123	0.1096	3.7670	3.9061	3.8122	**3.8284**	**0.0710**

Release Kinetics of Model Drug from Drug-Loaded PorGel Hydrogel

In order to study SA transport mechanism from the PorGel hydrogels, two diffusion models are considered to fit the experimental data.

Model 1 is described by the Ritger-Peppas equation (Venkatesh *et al.*, 1992):

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

where M_t/M_∞ is the fractional drug release, k_1 is a kinetic constant (with the unit of T^{-n}) t is the release time, and n is 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 the Fickian diffusion. When n = 1, Case II transport occurs, corresponding to the zero-order release. When $0.5 < n < 1$, the anomalous transport is observed.

Model 2 is based on the Higuchi's equation (Serra *et al.*, 2006) and described the Fickian diffusion of the drug:

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

where M_t/M_∞ is the fractional drug release, k_H is a kinetic constant (with the unit of T^{-n}) and t is the release time.

The diffusion coefficients of SA from the PorGel hydrogels are determined from the slopes of plots of drug accumulation versus square root of time according to Higuchi's equation (A-sasutjarit *et al.*, 2005):

$$Q = 2C_0(Dt/\pi)^{1/2} \qquad \text{(J3)}$$

where Q is the amount of material flowing through a unit cross-section of barrier (g/cm^2) in unit time, t (s); C_0 is the initial drug concentration in the hydrogel (g/cm^3); and D is 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 SA released from SA-loaded PorGel hydrogels at time t versus $time^{1/2}$ at various crosslinking ratios (PorGel_0.25, PorGel _0.50, PorGel _0.75, PorGel _1.00, PorGel _3.00, and PorGel _7.00) during 48 h as shown in Figure J2 using the Higuchi's equation.

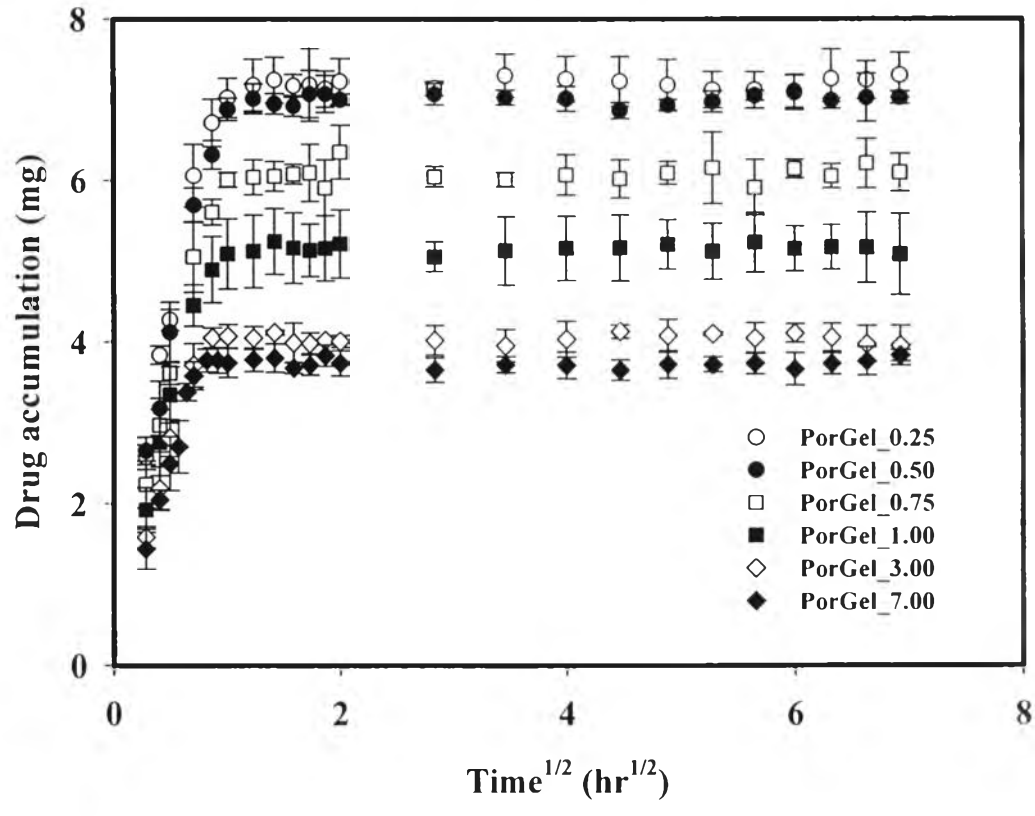


Figure J2 Amounts of salicylic acid release from SA-loaded PorGel hydrogel versus time$^{1/2}$ at various crosslink ratios, pH 5.5, and at 37°C, number of samples = 3.

Figure J3 shows the diffusion coefficients of SA from PorGel hydrogels versus crosslinking ratios and mesh size at 37°C. The results show the diffusion coefficients of salicylic acid are ranked in the following order: PorGel_0.25 > PorGel _0.50 > PorGel _0.75 > PorGel _1.00 > PorGel _3.00 >PorGel _7.00.

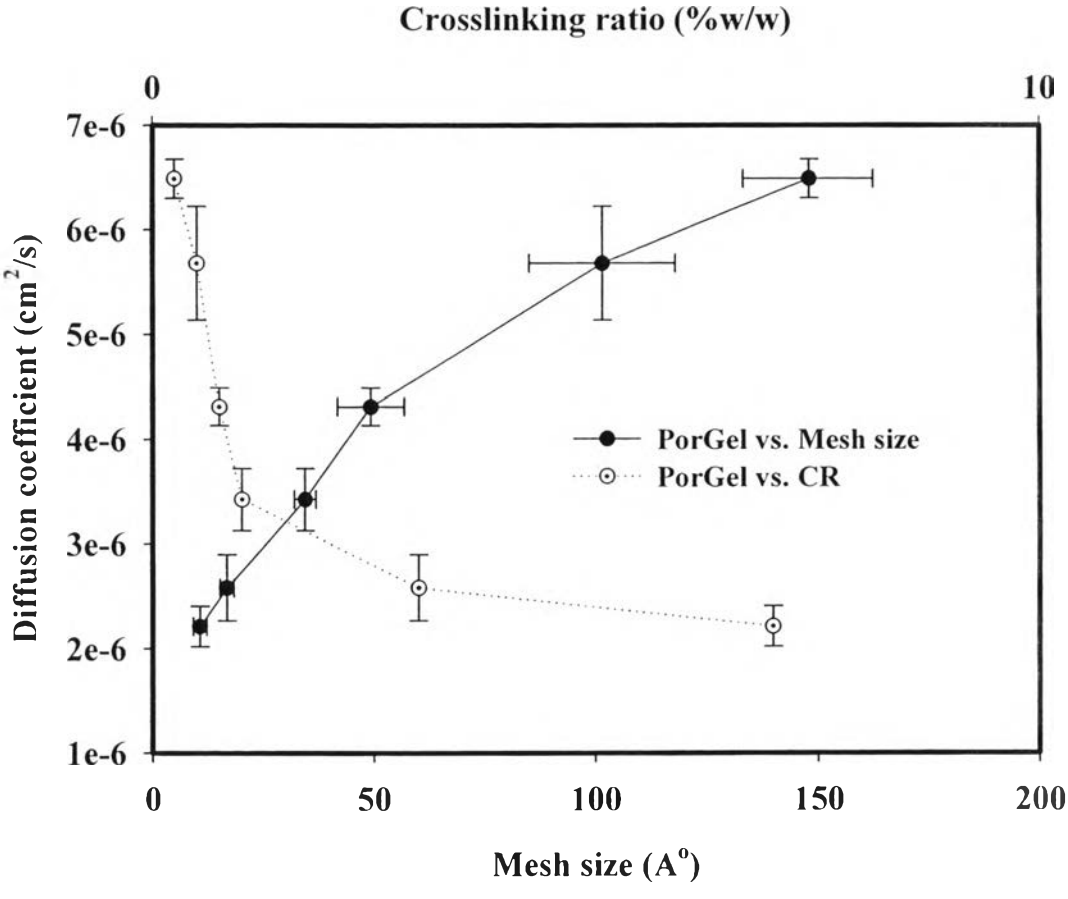


Figure J3 Diffusion coefficient of salicylic acid from PorGel hydrogels versus crosslinking ratios and mesh size, pH 5.5, and at 37°C, number of samples = 3.

Table J7 Raw data of the determination of the diffusion coefficient of salicylic acid released from various crosslinked PorGel hydrogel, pH 5.5 at 37°C

Sample	Slope			Diffusion Coefficient (cm^2/s)				
	1	2	3	1	2	3	Avg	SD
PorGel_0.25	7.979	8.064	8.208	6.32E-06	6.45E-06	6.69E-06	**6.49E-06**	**1.86E-07**
PorGel_0.50	7.154	7.656	7.866	5.08E-06	5.82E-06	6.14E-06	**5.68E-06**	**5.44E-07**
PorGel_0.75	6.468	6.561	6.737	4.15E-06	4.27E-06	4.50E-06	**4.31E-06**	**1.79E-07**
PorGel_1.00	6.147	5.806	5.655	3.75E-06	3.35E-06	3.17E-06	**3.42E-06**	**2.96E-07**
PorGel_3.00	4.775	5.107	5.400	2.26E-06	2.59E-06	2.89E-06	**2.58E-06**	**3.16E-07**
PorGel_7.00	4.904	4.757	4.494	2.39E-06	2.25E-06	2.00E-06	**2.21E-06**	**1.93E-07**

Appendix K Determination of Amounts and Diffusion Coefficient of Salicylic Acid Released from Salicylic Acid-Loaded Fish Gelatin Hydrogel at Various Crosslinking Ratios

The diffusion of drug was observed by custom built modified Franz-Diffusion cells. A diffusion cell consisted of two compartments. First one is a water jacket compartment that is used to exposed to an ambient condition. Other is a receptor chamber containing an acetate buffer solution pH 5.5 and maintained at 37°C by a circulating water bath. To study the effect of crosslinking ratios (1.00, 3.00, and 7.00) on the fish gelatin hydrogel (FishGel), a sample of drug-loaded FishGel hydrogel was 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 298 nm.

The amounts of salicylic acid (SA) released from SA-loaded FishGel hydrogel versus time at various crosslinking ratios (FishGel_1.00, FishGel_3.00, and FishGel_7.00) during 48 h are shown in Figure K1. The amounts of released drug gradually increase with time and then reach constant values.

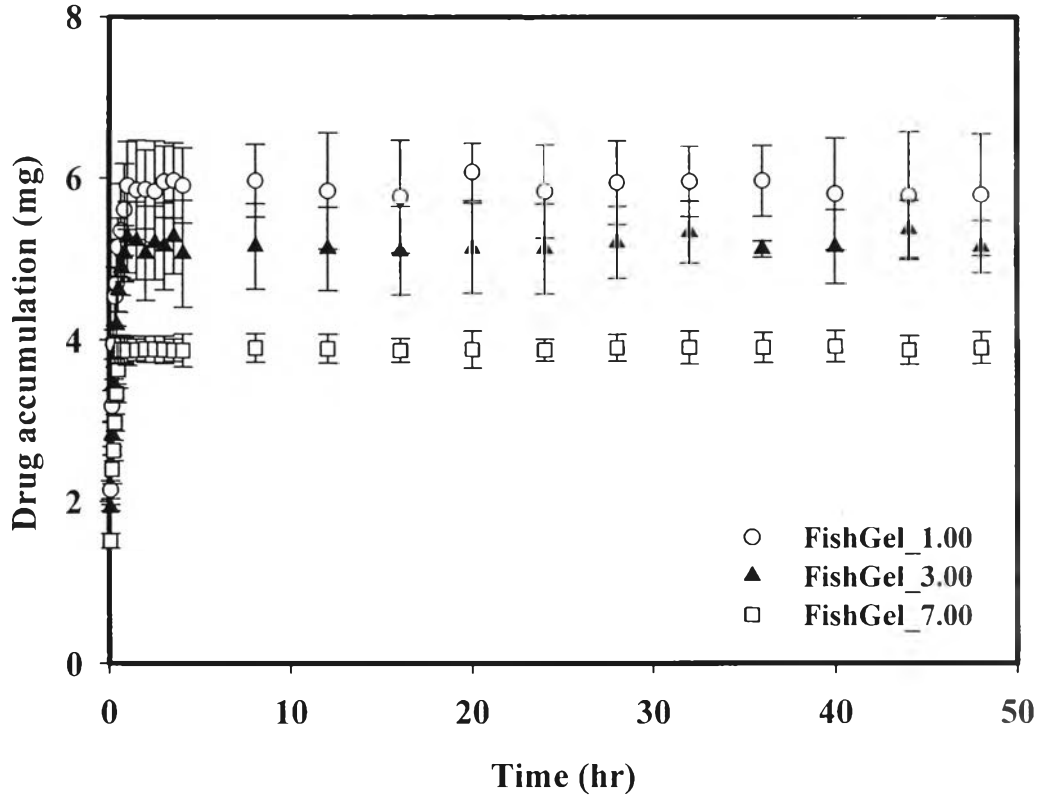


Figure K1 Amounts of salicylic acid release from SA-loaded FishGel hydrogel versus time at various crosslink ratios, pH 5.5, and at 37°C, number of samples = 3.

Table K1 Raw data of the determination of amounts of salicylic acid released from FishGel 1% crosslinked (FishGel_1) at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0579	0.0639	0.0630	2.0139	2.2226	2.1929	**2.1431**	**0.1129**
0.166667	0.0855	0.0960	0.0932	2.9736	3.3391	3.2412	**3.1846**	**0.1892**
0.25	0.1084	0.1187	0.1132	3.7696	4.1287	3.9360	**3.9447**	**0.1797**
0.333333	0.1186	0.1386	0.1339	4.1256	4.8209	4.6561	**4.5342**	**0.3633**
0.416667	0.1196	0.1498	0.1352	4.1616	5.2104	4.7037	**4.6919**	**0.5245**
0.5	0.1362	0.1554	0.1520	4.7376	5.4052	5.2878	**5.1435**	**0.3564**
0.666667	0.1354	0.1678	0.1580	4.7096	5.8365	5.4965	**5.3475**	**0.5781**
0.833333	0.1439	0.1763	0.1633	5.0045	6.1322	5.6806	**5.6058**	**0.5675**
1	0.1531	0.1842	0.1718	5.3264	6.4070	5.9757	**5.9030**	**0.5439**
1.5	0.1488	0.1835	0.1721	5.1762	6.3826	5.9861	**5.8483**	**0.6149**
2	0.1545	0.1825	0.1681	5.3734	6.3478	5.8470	**5.8561**	**0.4873**
2.5	0.1476	0.1822	0.1732	5.1339	6.3374	6.0243	**5.8319**	**0.6244**
3	0.1571	0.1819	0.1742	5.4643	6.3270	6.0591	**5.9501**	**0.4415**
3.5	0.1569	0.1833	0.1743	5.4574	6.3757	6.0626	**5.9652**	**0.4668**
4	0.1554	0.1817	0.1722	5.4052	6.3200	5.9896	**5.9049**	**0.4632**
8	0.1584	0.1842	0.1719	5.5096	6.4070	5.9791	**5.9652**	**0.4489**
12	0.1451	0.1854	0.1733	5.0470	6.4487	6.0278	**5.8412**	**0.7193**
16	0.1436	0.1824	0.1717	4.9948	6.3443	5.9722	**5.7704**	**0.6970**
20	0.1647	0.1851	0.1742	5.7287	6.4383	6.0591	**6.0754**	**0.3551**
24	0.1506	0.1836	0.1691	5.2383	6.3861	5.8817	**5.8354**	**0.5753**
28	0.1551	0.1847	0.1728	5.3948	6.4243	6.0104	**5.9432**	**0.5181**
32	0.1588	0.1840	0.1711	5.5235	6.4000	5.9513	**5.9583**	**0.4383**
36	0.1583	0.1830	0.1732	5.5061	6.3652	6.0243	**5.9652**	**0.4326**
40	0.1442	0.1810	0.1752	5.0157	6.2957	6.0939	**5.8017**	**0.6882**
44	0.1405	0.1838	0.1743	4.8870	6.3930	6.0626	**5.7809**	**0.7916**
48	0.1425	0.1847	0.1722	4.9565	6.4243	5.9896	**5.7901**	**0.7540**

Table K2 Raw data of the determination of amounts of salicylic acid released from FishGel 3% crosslinked (FishGel_3) at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0541	0.0634	0.0562	1.8817	1.9270	1.9565	**1.9217**	**0.0377**
0.166667	0.0771	0.0857	0.0814	2.6817	2.9809	2.8313	**2.8313**	**0.1496**
0.25	0.0974	0.1011	0.0992	3.3878	3.5165	3.4522	**3.4522**	**0.0643**
0.333333	0.1111	0.1154	0.1053	3.8643	4.0139	3.6609	**3.8464**	**0.1772**
0.416667	0.1201	0.1251	0.1156	4.1774	4.3513	4.0209	**4.1832**	**0.1653**
0.5	0.1307	0.1412	0.1260	4.5461	4.9113	4.3809	**4.6128**	**0.2714**
0.666667	0.1412	0.1503	0.1305	4.9113	5.2278	4.5391	**4.8928**	**0.3447**
0.833333	0.1455	0.1555	0.1355	5.0609	5.4087	4.7130	**5.0609**	**0.3478**
1	0.1457	0.1658	0.1425	5.0678	5.7670	4.9565	**5.2638**	**0.4393**
1.5	0.1409	0.1660	0.1434	4.9009	5.7739	4.9896	**5.2214**	**0.4805**
2	0.1363	0.1649	0.1356	4.7409	5.7357	4.7165	**5.0643**	**0.5815**
2.5	0.1410	0.1644	0.1427	4.9043	5.7183	4.9635	**5.1954**	**0.4538**
3	0.1448	0.1650	0.1347	5.0365	5.7391	4.6852	**5.1536**	**0.5366**
3.5	0.1497	0.1653	0.1393	5.2070	5.7496	4.8452	**5.2672**	**0.4552**
4	0.1453	0.1646	0.1266	5.0539	5.7252	4.4035	**5.0609**	**0.6609**
8	0.1424	0.1653	0.1367	4.9530	5.7496	4.7548	**5.1525**	**0.5265**
12	0.1403	0.1644	0.1374	4.8800	5.7183	4.7791	**5.1258**	**0.5156**
16	0.1392	0.1647	0.1361	4.8417	5.7287	4.7339	**5.1014**	**0.5459**
20	0.1408	0.1658	0.1360	4.8974	5.7670	4.7304	**5.1316**	**0.5565**
24	0.1420	0.1653	0.1348	4.9391	5.7496	4.6887	**5.1258**	**0.5545**
28	0.1479	0.1632	0.1379	5.1443	5.6765	4.7965	**5.2058**	**0.4432**
32	0.1493	0.1657	0.1448	5.1930	5.7635	5.0365	**5.3310**	**0.3826**
36	0.1446	0.1473	0.1503	5.0296	5.1235	5.2278	**5.1270**	**0.0992**
40	0.1372	0.1625	0.1447	4.7733	5.6522	5.0330	**5.1528**	**0.4515**
44	0.1540	0.1646	0.1444	5.3573	5.7252	5.0226	**5.3684**	**0.3514**
48	0.1448	0.1585	0.1410	5.0365	5.5130	4.9043	**5.1513**	**0.3202**

Table K3 Raw data of the determination of amounts of salicylic acid released from FishGel 7% crosslinked (FishGel_7) at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0444	0.0455	0.0405	1.5443	1.5826	1.4087	**1.5119**	**0.0914**
0.166667	0.0632	0.0730	0.0708	2.1983	2.5391	2.4626	**2.4000**	**0.1789**
0.25	0.0718	0.0763	0.0789	2.4974	2.6539	2.7443	**2.6319**	**0.1249**
0.333333	0.0822	0.0869	0.0879	2.8591	3.0226	3.0574	**2.9797**	**0.1059**
0.416667	0.0959	0.0994	0.0929	3.3357	3.4574	3.2313	**3.3414**	**0.1132**
0.5	0.1035	0.1114	0.0985	3.6000	3.8748	3.4261	**3.6336**	**0.2262**
0.666667	0.1120	0.1164	0.1063	3.8957	4.0487	3.6974	**3.8806**	**0.1761**
0.833333	0.1121	0.1157	0.1066	3.8991	4.0243	3.7078	**3.8771**	**0.1594**
1	0.1109	0.1165	0.1063	3.8574	4.0522	3.6974	**3.8690**	**0.1777**
1.5	0.1131	0.1141	0.1071	3.9339	3.9687	3.7252	**3.8759**	**0.1317**
2	0.1127	0.1157	0.1067	3.9200	4.0243	3.7113	**3.8852**	**0.1594**
2.5	0.1135	0.1151	0.1065	3.9478	4.0035	3.7043	**3.8852**	**0.1591**
3	0.1111	0.1165	0.1071	3.8643	4.0522	3.7252	**3.8806**	**0.1641**
3.5	0.1107	0.1154	0.1077	3.8504	4.0139	3.7461	**3.8701**	**0.1350**
4	0.1121	0.1166	0.1051	3.8991	4.0557	3.6557	**3.8701**	**0.2016**
8	0.1145	0.1156	0.1065	3.9826	4.0209	3.7043	**3.9026**	**0.1728**
12	0.1134	0.1161	0.1064	3.9443	4.0383	3.7009	**3.8945**	**0.1741**
16	0.1126	0.1147	0.1066	3.9165	3.9896	3.7078	**3.8713**	**0.1462**
20	0.1106	0.1186	0.1056	3.8470	4.1252	3.6730	**3.8817**	**0.2281**
24	0.1121	0.1149	0.1071	3.8991	3.9965	3.7252	**3.8736**	**0.1374**
28	0.1147	0.1151	0.1067	3.9896	4.0035	3.7113	**3.9014**	**0.1648**
32	0.1136	0.1173	0.1059	3.9513	4.0800	3.6835	**3.9049**	**0.2023**
36	0.1149	0.1159	0.1061	3.9965	4.0313	3.6904	**3.9061**	**0.1876**
40	0.1151	0.1166	0.1063	4.0035	4.0557	3.6974	**3.9188**	**0.1935**
44	0.1123	0.1160	0.1059	3.9061	4.0348	3.6835	**3.8748**	**0.1777**
48	0.1119	0.1179	0.1066	3.8922	4.1009	3.7078	**3.9003**	**0.1966**

Release Kinetics of Model Drug from Drug-Loaded FishGel Hydrogel

In order to study SA transport mechanism from the FishGel hydrogels, two diffusion models are considered to fit the experimental data.

Model 1 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_∞ is the fractional drug release, k_1 is a kinetic constant (with the unit of T^{-n}) t is the release time, and n is 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 the Fickian diffusion. When n = 1, Case II transport occurs, corresponding to the zero-order release. When $0.5 < n < 1$, the anomalous transport is observed.

Model 2 is based on the Higuchi's equation (Serra *et al.*, 2006) and described the Fickian diffusion of the drug:

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

where M_t/M_∞ is the fractional drug release, k_H is a kinetic constant (with the unit of T^{-n}) and t is the release time.

The diffusion coefficients of SA from the FishGel hydrogels are determined from the slopes of plots of drug accumulation versus square root of time according to Higuchi's equation (A-sasutjarit *et al.*, 2005):

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

where Q is the amount of material flowing through a unit cross-section of barrier (g/cm^2) in unit time, t (s) ; C_0 is the initial drug concentration in the hydrogel (g/cm^3); and D is 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 SA released SA- loaded FishGel hydrogels at time t versus $time^{1/2}$ at various crosslinking ratios (FishGel_1.00, FishGel_3.00, and FishGel_7.00) during 48 h as shown in Figure K2 using the Higuchi's equation.

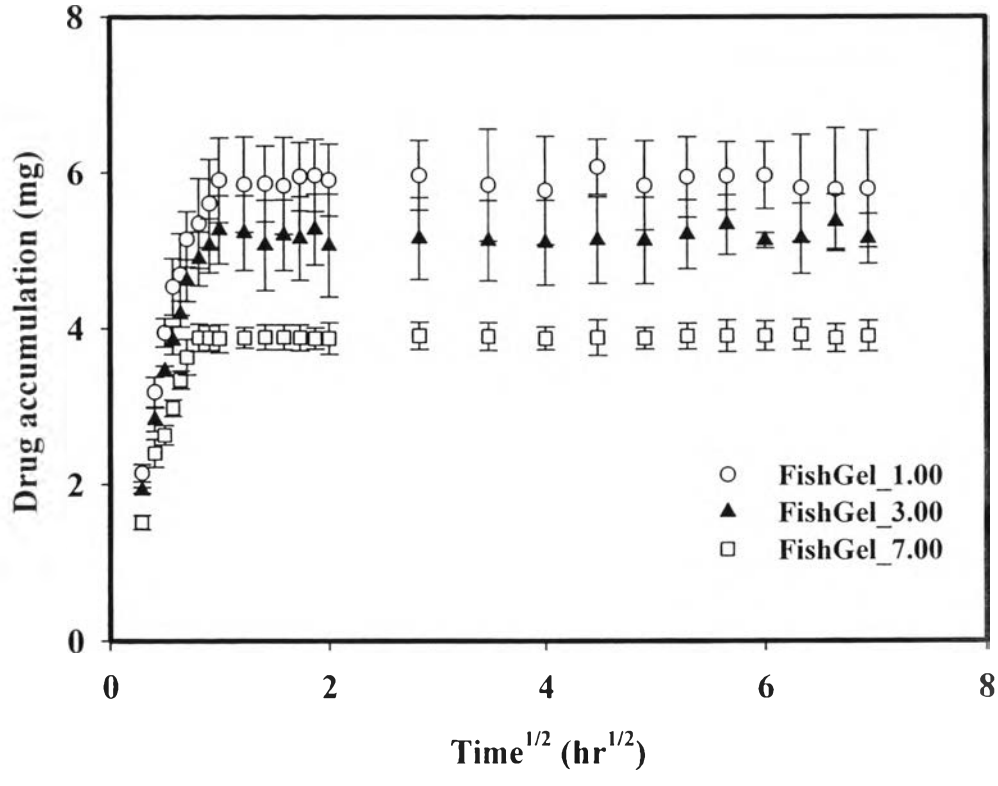


Figure K2 Amounts of salicylic acid release from salicylic acid-loaded FishGel hydrogel versus time$^{1/2}$ at various crosslink ratios, pH 5.5, and at 37 °C, number of samples = 3.

Figure K3 shows the diffusion coefficients of SA from fish gelatin hydrogels versus crosslinking ratios and mesh size at 37°C. The results show the diffusion coefficients of SA are ranked in the following order: FishGel_1.00 > FishGel_3.00 > FishGel_7.00.

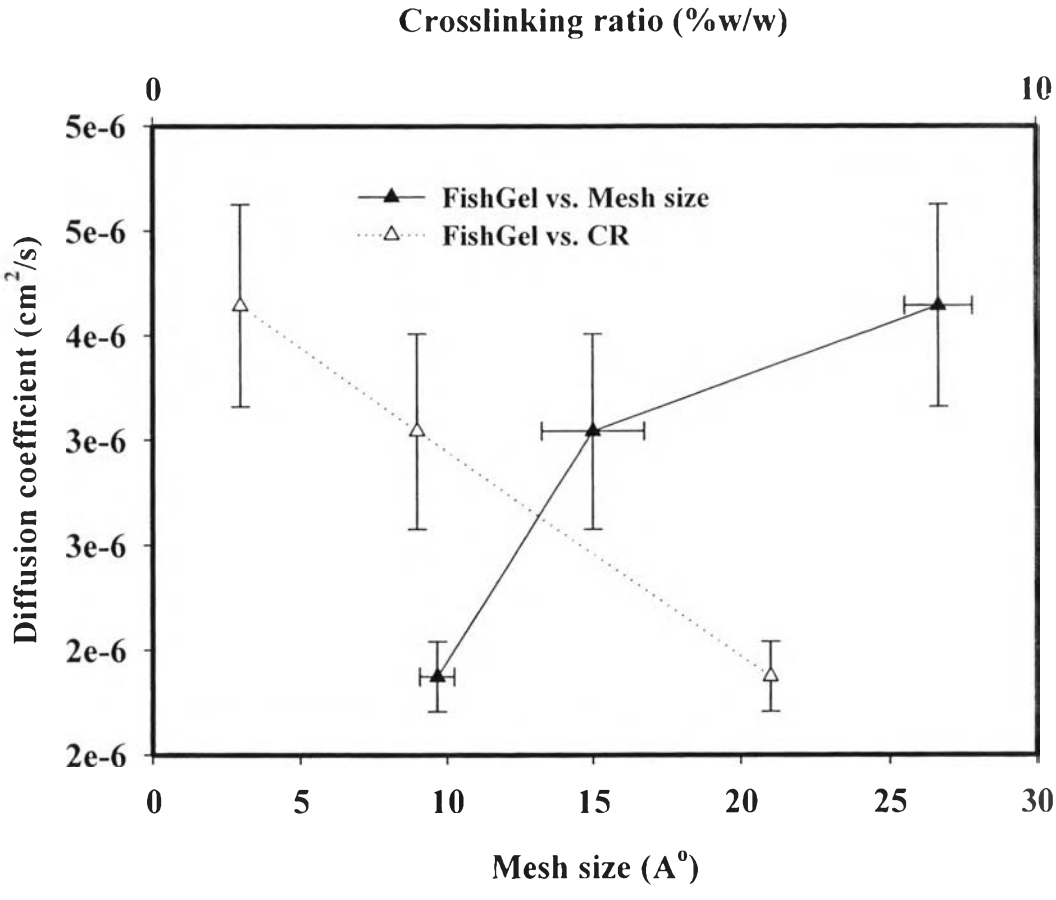


Figure K3 Diffusion coefficient of salicylic acid from FishGel hydrogels versus crosslinking ratios and mesh size, pH 5.5, and at 37°C, number of samples = 3.

Table K4 Raw data of the determination of the diffusion coefficient of salicylic acid released from various crosslinked FishGel hydrogel, pH 5.5 at 37°C

Sample	Slope			Diffusion Coefficient (cm^2/s)				
	1	2	3	1	2	3	Avg	SD
FishGel_1.00	6.079	6.449	6.832	3.67E-06	4.13E-06	4.63E-06	**4.14E-06**	**4.83E-07**
FishGel_3.00	5.922	6.377	5.598	3.48E-06	4.04E-06	3.11E-06	**3.54E-06**	**4.66E-07**
FishGel_7.00	4.825	5.082	4.757	2.31E-06	2.56E-06	2.25E-06	**2.37E-06**	**1.68E-07**

Appendix L Determination of Amounts and Diffusion Coefficient of 5-Sulfoalicylic Acid Released from 5-Sulfoalicylic Acid-Loaded Porcine Gelatin Hydrogel at Various Crosslinking Ratios

The diffusion of drug was observed by custom built modified Franz-Diffusion cells. A diffusion cell consisted of two compartments. First one is a water jacket compartment that is used to exposed to an ambient condition. Other is a receptor chamber containing an acetate buffer solution pH 5.5 and maintained at 37°C by a circulating water bath. To study the effect of crosslinking ratios (0.25, 0.50, 0.75, 1.00, 3.00, and 7.00) on the porcine gelatin hydrogel (PorGel), a sample of drug-loaded PorGel hydrogel was placed over the nylon net on the top of the receptor chamber. The drug diffuses through the polymer matrix and the net towards in 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 298 nm.

The amounts of 5-sulfosalicylic acid (SSA) released from SSA- loaded PorGel hydrogel versus time at various crosslinking ratios (PorGel_0.25, PorGel _0.50, PorGel _0.75, PorGel _1.00, PorGel _3.00, and PorGel _7.00) during 48 h are shown in Figure L1. The amounts of released drug gradually increase with time and then reach constant values.

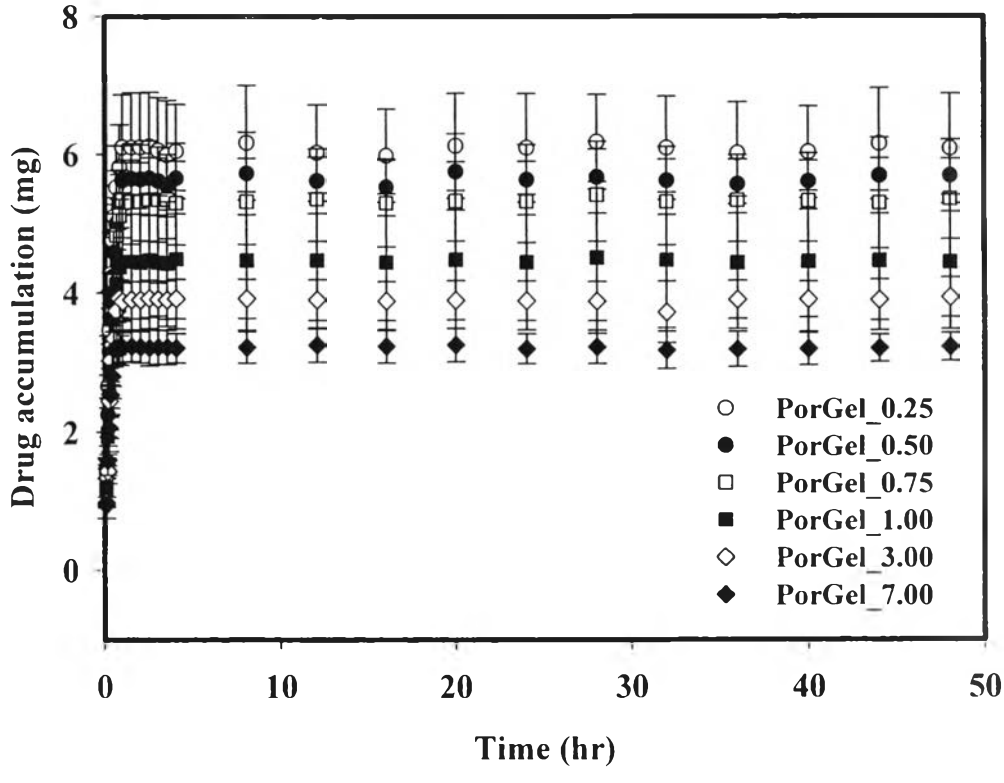


Figure L1 Amounts of 5-sulfosalicylic acid release from SSA-loaded PorGel hydrogel versus time at various crosslink ratios, pH 5.5, and at 37°C, number of samples = 3.

Table L1 Raw data of the determination of amounts of 5-sulfosalicylic acid released from PorGel 0.25% crosslinked (PorGel_0.25) at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0197	0.0239	0.0229	1.3244	1.6067	1.5395	**1.4902**	**0.1475**
0.166667	0.0329	0.0339	0.0522	2.2118	2.2790	3.5092	**2.6667**	**0.7305**
0.25	0.0448	0.0494	0.0607	3.0118	3.3210	4.0807	**3.4711**	**0.5500**
0.333333	0.0541	0.0643	0.0720	3.6370	4.3227	4.8403	**4.2667**	**0.6036**
0.416667	0.0626	0.0722	0.0778	4.2084	4.8538	5.2303	**4.7641**	**0.5168**
0.5	0.0685	0.0771	0.0820	4.6050	5.1832	5.5126	**5.1003**	**0.4594**
0.666667	0.0722	0.0848	0.0896	4.8538	5.7008	6.0235	**5.5261**	**0.6041**
0.833333	0.0760	0.0928	0.0908	5.1092	6.2387	6.1042	**5.8174**	**0.6169**
1	0.0779	0.0958	0.0988	5.2370	6.4403	6.6420	**6.1064**	**0.7597**
1.5	0.0774	0.0955	0.0995	5.2034	6.4202	6.6891	**6.1042**	**0.7917**
2	0.0774	0.0957	0.0994	5.2034	6.4336	6.6824	**6.1064**	**0.7919**
2.5	0.0777	0.0959	0.0995	5.2235	6.4471	6.6891	**6.1199**	**0.7856**
3	0.0770	0.0955	0.0979	5.1765	6.4202	6.5815	**6.0594**	**0.7689**
3.5	0.0755	0.0961	0.0958	5.0756	6.4605	6.4403	**5.9922**	**0.7938**
4	0.0782	0.0959	0.0957	5.2571	6.4471	6.4336	**6.0459**	**0.6832**
8	0.0780	0.0956	0.1019	5.2437	6.4269	6.8504	**6.1737**	**0.8328**
12	0.0776	0.0958	0.0955	5.2168	6.4403	6.4202	**6.0258**	**0.7007**
16	0.0774	0.0954	0.0941	5.2034	6.4134	6.3261	**5.9810**	**0.6748**
20	0.0782	0.0956	0.0995	5.2571	6.4269	6.6891	**6.1244**	**0.7624**
24	0.0773	0.0954	0.0993	5.1966	6.4134	6.6756	**6.0952**	**0.7892**
28	0.0803	0.0960	0.0995	5.3983	6.4538	6.6891	**6.1804**	**0.6874**
32	0.0778	0.0961	0.0979	5.2303	6.4605	6.5815	**6.0908**	**0.7477**
36	0.0768	0.0959	0.0958	5.1630	6.4471	6.4403	**6.0168**	**0.7394**
40	0.0783	0.0952	0.0957	5.2639	6.4000	6.4336	**6.0325**	**0.6659**
44	0.0780	0.0956	0.1009	5.2437	6.4269	6.7832	**6.1513**	**0.8059**
48	0.0771	0.0949	0.0995	5.1832	6.3798	6.6891	**6.0840**	**0.7953**

Table L2 Raw data of the determination of amounts of 5-sulfosalicylic acid released from PorGel 0.50% crosslinked (PorGel_0.50) at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0219	0.0197	0.0224	1.4723	1.3244	1.5059	**1.4342**	**0.0966**
0.166667	0.0432	0.0272	0.0302	2.9042	1.8286	2.0303	**2.2543**	**0.5718**
0.25	0.0517	0.0530	0.0366	3.4756	3.5630	2.4605	**3.1664**	**0.6129**
0.333333	0.0630	0.0598	0.0523	4.2353	4.0202	3.5160	**3.9238**	**0.3692**
0.416667	0.0688	0.0633	0.0566	4.6252	4.2555	3.8050	**4.2286**	**0.4107**
0.5	0.0730	0.0682	0.0633	4.9076	4.5849	4.2555	**4.5826**	**0.3261**
0.666667	0.0806	0.0697	0.0729	5.4185	4.6857	4.9008	**5.0017**	**0.3767**
0.833333	0.0818	0.0727	0.0832	5.4992	4.8874	5.5933	**5.3266**	**0.3833**
1	0.0898	0.0754	0.0859	6.0370	5.0689	5.7748	**5.6269**	**0.5007**
1.5	0.0905	0.0756	0.0860	6.0840	5.0853	5.7815	**5.6503**	**0.5122**
2	0.0904	0.0757	0.0856	6.0773	5.0905	5.7546	**5.6408**	**0.5031**
2.5	0.0905	0.0751	0.0869	6.0840	5.0502	5.8420	**5.6587**	**0.5407**
3	0.0889	0.0752	0.0866	5.9765	5.0572	5.8218	**5.6185**	**0.4922**
3.5	0.0868	0.0749	0.0861	5.8353	5.0359	5.7882	**5.5531**	**0.4486**
4	0.0867	0.0756	0.0901	5.8286	5.0806	6.0571	**5.6554**	**0.5108**
8	0.0929	0.0755	0.0873	6.2454	5.0736	5.8689	**5.7293**	**0.5982**
12	0.0865	0.0756	0.0886	5.8151	5.0794	5.9563	**5.6170**	**0.4708**
16	0.0851	0.0751	0.0863	5.7210	5.0490	5.8017	**5.5239**	**0.4132**
20	0.0905	0.0760	0.0900	6.0840	5.1081	6.0504	**5.7475**	**0.5540**
24	0.0903	0.0755	0.0856	6.0706	5.0742	5.7546	**5.6331**	**0.5092**
28	0.0905	0.0756	0.0869	6.0840	5.0847	5.8420	**5.6702**	**0.5213**
32	0.0889	0.0752	0.0866	5.9765	5.0537	5.8218	**5.6173**	**0.4942**
36	0.0868	0.0755	0.0861	5.8353	5.0777	5.7882	**5.5671**	**0.4245**
40	0.0867	0.0764	0.0871	5.8286	5.1361	5.8555	**5.6067**	**0.4078**
44	0.0919	0.0757	0.0863	6.1782	5.0891	5.8017	**5.6896**	**0.5531**
48	0.0905	0.0758	0.0876	6.0840	5.0958	5.8891	**5.6896**	**0.5234**

Table L3 Raw data of the determination of amounts of 5-sulfosalicylic acid released from PorGel 0.75% crosslinked (PorGel_0.75) at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0211	0.0197	0.0218	1.4185	1.3244	1.4655	**1.4028**	**0.0719**
0.166667	0.0351	0.0227	0.0286	2.3597	1.5261	1.9227	**1.9361**	**0.4170**
0.25	0.0436	0.0294	0.0400	2.9311	1.9765	2.6891	**2.5322**	**0.4963**
0.333333	0.0536	0.0386	0.0537	3.6034	2.5950	3.6101	**3.2695**	**0.5842**
0.416667	0.0598	0.0467	0.0580	4.0202	3.1395	3.8992	**3.6863**	**0.4774**
0.5	0.0678	0.0513	0.0671	4.5580	3.4487	4.5109	**4.1725**	**0.6273**
0.666667	0.0745	0.0568	0.0843	5.0084	3.8185	5.6672	**4.8314**	**0.9370**
0.833333	0.0784	0.0654	0.0846	5.2706	4.3966	5.6874	**5.1182**	**0.6587**
1	0.0799	0.0711	0.0873	5.3714	4.7798	5.8689	**5.3401**	**0.5452**
1.5	0.0803	0.0694	0.0874	5.3983	4.6655	5.8756	**5.3132**	**0.6095**
2	0.0800	0.0703	0.0870	5.3782	4.7261	5.8487	**5.3176**	**0.5638**
2.5	0.0801	0.0703	0.0883	5.3849	4.7261	5.9361	**5.3490**	**0.6058**
3	0.0805	0.0700	0.0880	5.4118	4.7059	5.9160	**5.3445**	**0.6078**
3.5	0.0804	0.0708	0.0875	5.4050	4.7597	5.8824	**5.3490**	**0.5634**
4	0.0795	0.0695	0.0875	5.3445	4.6723	5.8824	**5.2997**	**0.6063**
8	0.0809	0.0691	0.0874	5.4387	4.6454	5.8756	**5.3199**	**0.6237**
12	0.0810	0.0700	0.0880	5.4454	4.7059	5.9160	**5.3557**	**0.6100**
16	0.0793	0.0692	0.0877	5.3311	4.6521	5.8958	**5.2930**	**0.6227**
20	0.0797	0.0705	0.0874	5.3580	4.7395	5.8756	**5.3244**	**0.5688**
24	0.0805	0.0698	0.0870	5.4118	4.6924	5.8487	**5.3176**	**0.5839**
28	0.0838	0.0694	0.0883	5.6336	4.6655	5.9361	**5.4118**	**0.6637**
32	0.0794	0.0696	0.0880	5.3378	4.6790	5.9160	**5.3109**	**0.6189**
36	0.0806	0.0699	0.0875	5.4185	4.6992	5.8824	**5.3333**	**0.5962**
40	0.0799	0.0702	0.0875	5.3714	4.7193	5.8824	**5.3244**	**0.5829**
44	0.0800	0.0685	0.0877	5.3782	4.6050	5.8958	**5.2930**	**0.6496**
48	0.0802	0.0708	0.0880	5.3916	4.7597	5.9160	**5.3557**	**0.5790**

Table L4 Raw data of the determination of amounts of 5-sulfosalicylic acid released from PorGel 1.00% crosslinked (PorGel_1.00)at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0160	0.0247	0.0123	1.0756	1.6605	0.8270	**1.1877**	**0.4279**
0.166667	0.0272	0.0379	0.0224	1.8286	2.5479	1.5037	**1.9600**	**0.5344**
0.25	0.0344	0.0498	0.0272	2.3126	3.3479	1.8319	**2.4975**	**0.7747**
0.333333	0.0488	0.0591	0.0326	3.2807	3.9731	2.1949	**3.1496**	**0.8963**
0.416667	0.0554	0.0676	0.0390	3.7244	4.5445	2.6187	**3.6292**	**0.9664**
0.5	0.0578	0.0735	0.0469	3.8857	4.9412	3.1559	**3.9943**	**0.8976**
0.666667	0.0600	0.0772	0.0472	4.0336	5.1899	3.1703	**4.1313**	**1.0134**
0.833333	0.0618	0.0810	0.0524	4.1546	5.4454	3.5219	**4.3740**	**0.9803**
1	0.0612	0.0829	0.0545	4.1143	5.5731	3.6613	**4.4496**	**0.9990**
1.5	0.0617	0.0824	0.0545	4.1479	5.5395	3.6665	**4.4513**	**0.9727**
2	0.0614	0.0824	0.0542	4.1277	5.5395	3.6458	**4.4377**	**0.9841**
2.5	0.0621	0.0827	0.0548	4.1748	5.5597	3.6820	**4.4721**	**0.9735**
3	0.0619	0.0820	0.0541	4.1613	5.5126	3.6370	**4.4370**	**0.9677**
3.5	0.0623	0.0805	0.0546	4.1882	5.4118	3.6717	**4.4239**	**0.8937**
4	0.0624	0.0832	0.0546	4.1950	5.5933	3.6717	**4.4866**	**0.9935**
8	0.0618	0.0830	0.0545	4.1546	5.5798	3.6665	**4.4670**	**0.9942**
12	0.0622	0.0826	0.0545	4.1815	5.5529	3.6665	**4.4670**	**0.9751**
16	0.0619	0.0824	0.0541	4.1613	5.5395	3.6363	**4.4457**	**0.9829**
20	0.0621	0.0832	0.0548	4.1748	5.5933	3.6820	**4.4834**	**0.9923**
24	0.0620	0.0823	0.0542	4.1681	5.5328	3.6437	**4.4482**	**0.9752**
28	0.0619	0.0853	0.0541	4.1613	5.7345	3.6390	**4.5116**	**1.0907**
32	0.0621	0.0828	0.0549	4.1748	5.5664	3.6910	**4.4774**	**0.9736**
36	0.0616	0.0818	0.0546	4.1412	5.4992	3.6717	**4.4373**	**0.9491**
40	0.0610	0.0833	0.0546	4.1008	5.6000	3.6717	**4.4575**	**1.0124**
44	0.0620	0.0830	0.0542	4.1681	5.5798	3.6458	**4.4646**	**1.0005**
48	0.0619	0.0821	0.0544	4.1613	5.5193	3.6592	**4.4466**	**0.9623**

Table L5 Raw data of the determination of amounts of 5-sulfosalicylic acid released from PorGel 3.00% crosslinked (PorGel_3.00) at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0135	0.0156	0.0152	0.9076	1.0487	1.0218	**0.9927**	**0.0750**
0.166667	0.0197	0.0200	0.0245	1.3244	1.3445	1.6471	**1.4387**	**0.1808**
0.25	0.0379	0.0328	0.0386	2.5479	2.2050	2.5950	**2.4493**	**0.2128**
0.333333	0.0483	0.0399	0.0475	3.2471	2.6824	3.1933	**3.0409**	**0.3117**
0.416667	0.0479	0.0490	0.0488	3.2202	3.2941	3.2807	**3.2650**	**0.0394**
0.5	0.0493	0.0498	0.0505	3.3143	3.3479	3.3950	**3.3524**	**0.0405**
0.666667	0.0568	0.0530	0.0575	3.8185	3.5630	3.8655	**3.7490**	**0.1628**
0.833333	0.0623	0.0543	0.0585	4.1882	3.6504	3.9328	**3.9238**	**0.2690**
1	0.0617	0.0537	0.0576	4.1479	3.6101	3.8723	**3.8768**	**0.2689**
1.5	0.0622	0.0544	0.0575	4.1815	3.6571	3.8655	**3.9014**	**0.2640**
2	0.0619	0.0541	0.0581	4.1613	3.6370	3.9059	**3.9014**	**0.2622**
2.5	0.0621	0.0543	0.0585	4.1748	3.6504	3.9328	**3.9193**	**0.2624**
3	0.0615	0.0545	0.0584	4.1345	3.6639	3.9261	**3.9081**	**0.2358**
3.5	0.0623	0.0543	0.0576	4.1882	3.6504	3.8723	**3.9036**	**0.2703**
4	0.0627	0.0545	0.0576	4.2151	3.6639	3.8723	**3.9171**	**0.2783**
8	0.0624	0.0542	0.0584	4.1950	3.6437	3.9261	**3.9216**	**0.2757**
12	0.0626	0.0541	0.0574	4.2084	3.6370	3.8588	**3.9014**	**0.2881**
16	0.0625	0.0544	0.0567	4.2017	3.6571	3.8118	**3.8902**	**0.2806**
20	0.0624	0.0541	0.0575	4.1950	3.6370	3.8655	**3.8992**	**0.2805**
24	0.0625	0.0542	0.0570	4.2017	3.6437	3.8319	**3.8924**	**0.2839**
28	0.0624	0.0542	0.0569	4.1950	3.6437	3.8252	**3.8880**	**0.2809**
32	0.0626	0.0542	0.0496	4.2084	3.6437	3.3345	**3.7289**	**0.4432**
36	0.0626	0.0546	0.0572	4.2084	3.6706	3.8454	**3.9081**	**0.2743**
40	0.0624	0.0549	0.0572	4.1950	3.6908	3.8454	**3.9104**	**0.2583**
44	0.0628	0.0542	0.0572	4.2218	3.6437	3.8454	**3.9036**	**0.2934**
48	0.0629	0.0545	0.0585	4.2286	3.6639	3.9328	**3.9417**	**0.2825**

Table L6 Raw data of the determination of amounts of 5-sulfosalicylic acid released from PorGel 7.00% crosslinked (PorGel_7.00) at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0146	0.0161	0.0136	0.9815	0.9479	0.9143	**0.9479**	**0.0336**
0.166667	0.0268	0.0205	0.0238	1.8017	1.3782	1.6000	**1.5933**	**0.2118**
0.25	0.0290	0.0333	0.0299	1.9496	2.2387	2.0101	**2.0661**	**0.1525**
0.333333	0.0381	0.0404	0.0348	2.5613	2.7160	2.3395	**2.5389**	**0.1892**
0.416667	0.0431	0.0455	0.0365	2.8975	3.0588	2.4538	**2.8034**	**0.3133**
0.5	0.0476	0.0513	0.0438	3.2000	3.4487	2.9445	**3.1978**	**0.2521**
0.666667	0.0475	0.0515	0.0445	3.1933	3.4622	2.9916	**3.2157**	**0.2361**
0.833333	0.0477	0.0518	0.0443	3.2067	3.4824	2.9782	**3.2224**	**0.2525**
1	0.0478	0.0512	0.0448	3.2134	3.4420	3.0118	**3.2224**	**0.2153**
1.5	0.0490	0.0509	0.0446	3.2941	3.4218	2.9983	**3.2381**	**0.2173**
2	0.0479	0.0516	0.0447	3.2202	3.4689	3.0050	**3.2314**	**0.2321**
2.5	0.0475	0.0518	0.0442	3.1933	3.4824	2.9714	**3.2157**	**0.2562**
3	0.0479	0.0517	0.0444	3.2202	3.4756	2.9849	**3.2269**	**0.2454**
3.5	0.0476	0.0518	0.0445	3.2000	3.4824	2.9916	**3.2246**	**0.2463**
4	0.0477	0.0510	0.0447	3.2067	3.4286	3.0050	**3.2134**	**0.2118**
8	0.0471	0.0517	0.0451	3.1664	3.4756	3.0319	**3.2246**	**0.2275**
12	0.0494	0.0516	0.0444	3.3210	3.4689	2.9849	**3.2583**	**0.2480**
16	0.0478	0.0519	0.0448	3.2134	3.4891	3.0118	**3.2381**	**0.2396**
20	0.0492	0.0516	0.0445	3.3076	3.4689	2.9916	**3.2560**	**0.2428**
24	0.0478	0.0507	0.0443	3.2134	3.4084	2.9782	**3.2000**	**0.2154**
28	0.0479	0.0517	0.0445	3.2202	3.4756	2.9916	**3.2291**	**0.2421**
32	0.0473	0.0513	0.0433	3.1798	3.4487	2.9109	**3.1798**	**0.2689**
36	0.0478	0.0511	0.0436	3.2134	3.4353	2.9311	**3.1933**	**0.2527**
40	0.0466	0.0514	0.0446	3.1328	3.4555	2.9983	**3.1955**	**0.2349**
44	0.0477	0.0507	0.0448	3.2067	3.4084	3.0118	**3.2090**	**0.1983**
48	0.0482	0.0509	0.0449	3.2403	3.4218	3.0185	**3.2269**	**0.2020**

Release Kinetics of Model Drug from Drug-Loaded PorGel Hydrogel

In order to study SSA transport mechanism from the PorGel hydrogels, two diffusion models are considered to fit the experimental data.

Model 1 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_∞ is the fractional drug release, k_1 is a kinetic constant (with the unit of T^{-n}) t is the release time and n is 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 the Fickian diffusion. When n = 1, Case II transport occurs, corresponding to the zero-order release. When $0.5 < n < 1$, the anomalous transport is observed.

Model 2 is based on the Higuchi's equation (Serra *et al.*, 2006) and described the Fickian diffusion of the drug:

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

where M_t/M_∞ is the fractional drug release, k_H is a kinetic constant (with the unit of T^{-n}) and t is the release time.

The diffusion coefficients of SSA from the PorGel hydrogels are determined from the slopes of plots of drug accumulation versus square root of time according to Higuchi's equation (A-sasutjarit *et al.*, 2005):

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

where Q is the amount of material flowing through a unit cross-section of barrier (g/cm^2)in unit time, t (s); C_0 is the initial drug concentration in the hydrogel (g/cm^3); and D is 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 SSA released from SSA-loaded PorGel hydrogels at time t versus $time^{1/2}$ at various crosslinking ratios (PorGel_0.25, PorGel _0.50, PorGel _0.75, PorGel _1.00, PorGel _3.00, and PorGel _7.00) during 48 h as shown in Figure L2 using the Higuchi's equation.

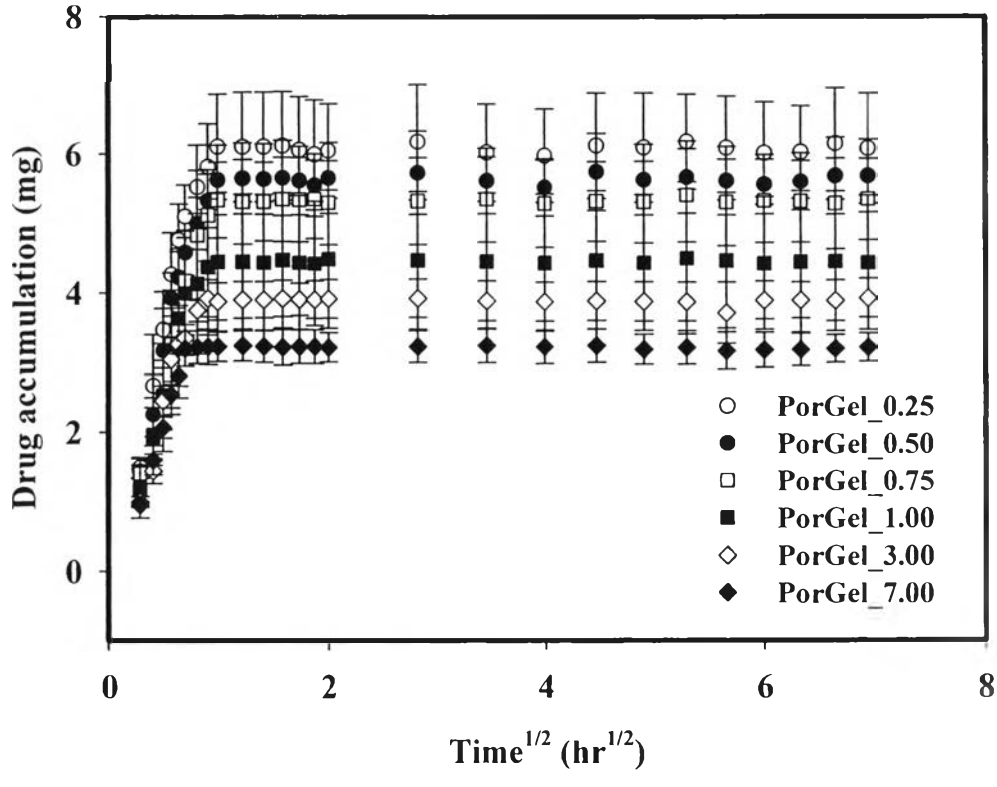


Figure L2 Amounts of sulfosalicylic acid release from SSA-loaded PorGel hydrogel versus time$^{1/2}$ at various crosslink ratios, pH 5.5, and at 37°C, number of samples = 3.

Figure L3 shows the diffusion coefficients of SSA from PorGel hydrogels versus crosslinking ratios and mesh size at 37°C. The results show the diffusion coefficients of SSA are ranked in the following order: PorGel_0.25 > PorGel _0.50 > PorGel _0.75 > PorGel _1.00 > PorGel _3.00 >PorGel _7.00.

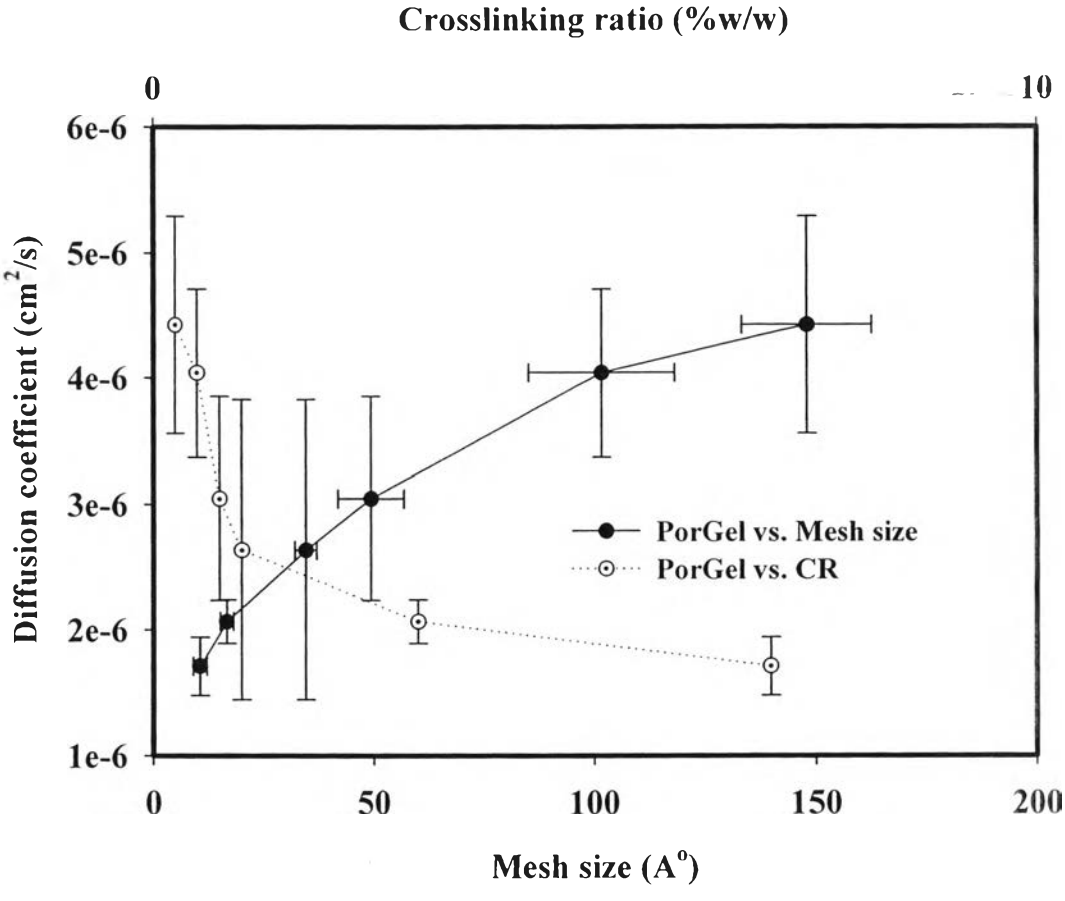


Figure L3 Diffusion coefficient of 5-sulfosalicylic acid from PorGel hydrogels versus crosslinking ratios and mesh size, pH 5.5, and at 37°C, number of samples = 3.

Table L7 Raw data of the determination of the diffusion coefficient of 5-sulfosalicylic acid released from various crosslinked PorGel hydrogel, pH 5.5 at 37°C

Sample	Slope			Diffusion Coefficient (cm^2/s)				
	1	2	3	1	2	3	Avg	SD
PorGel_0.25	5.997	6.856	7.322	3.49E-06	4.57E-06	5.21E-06	**4.42E-06**	**8.66E-07**
PorGel_0.50	6.524	6.002	5.852	4.14E-06	4.66E-06	3.33E-06	**4.04E-06**	**6.70E-07**
PorGel_0.75	5.884	4.674	6.125	3.36E-06	2.12E-06	3.65E-06	**3.04E-06**	**8.10E-07**
PorGel_1.00	5.194	6.281	3.864	2.62E-06	3.83E-06	1.45E-06	**2.64E-06**	**1.19E-06**
PorGel_3.00	4.712	4.380	4.730	2.16E-06	1.86E-06	2.17E-06	**2.07E-06**	**1.74E-07**
PorGel_7.00	4.226	4.453	3.882	1.74E-06	1.93E-06	1.46E-06	**1.71E-06**	**2.32E-07**

Appendix M Determination of Amounts and Diffusion Coefficient of Sulfoalicylic Acid Released from Sulfoalicylic Acid-Loaded FishGel Hydrogel at Various Crosslinking Ratios

The diffusion of drug was observed by custom built modified Franz-Diffusion cells. A diffusion cell consisted of two compartments. First one is a water jacket compartment that is used to exposed to an ambient condition. Other is a receptor chamber containing an acetate buffer solution pH 5.5 and maintained at 37°C by a circulating water bath. To study the effect of crosslinking ratios (1.00, 3.00, and 7.00) on the fish gelatin hydrogel (FishGel), a sample of drug-loaded FishGel hydrogel was 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 298 nm.

The amounts of 5-sulfosalicylic acid (SSA) released from SSA-loaded FishGel hydrogel versus time at various crosslinking ratios (FishGel_1.00, FishGel_3.00, and FishGel_7.00) during 48 h are shown in Figure M1. The amounts of released drug gradually increase with time and then reach constant values.

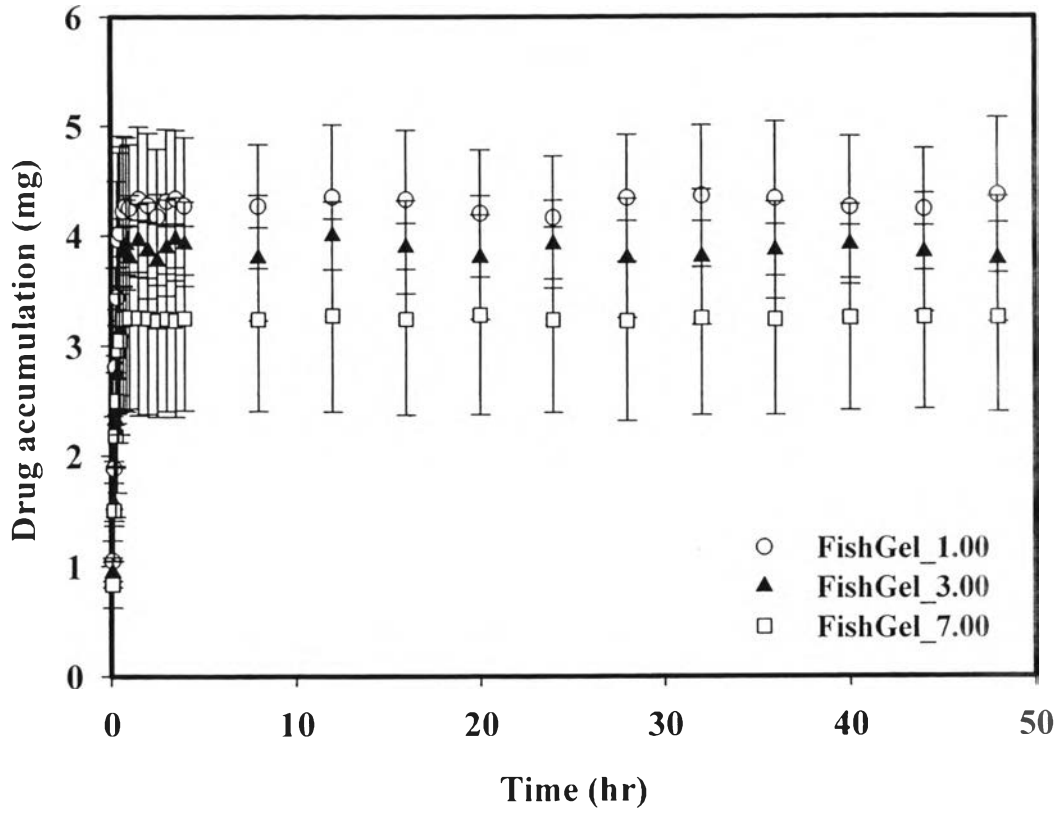


Figure M1 Amounts of 5-sulfosalicylic acid release from SSA-loaded FishGel hydrogel versus time at various crosslink ratios, pH 5.5, and at 37°C, number of samples = 3.

Table M1 Raw data of the determination of amounts of 5-sulfosalicylic acid released from FishGel 1% crosslinked (FishGel_1) at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0186	0.0147	0.0134	1.2520	0.9882	0.9008	**1.0470**	**0.1828**
0.166667	0.0307	0.0334	0.0200	2.0629	2.2454	1.3445	**1.8843**	**0.4762**
0.25	0.0455	0.0529	0.0269	3.0610	3.5563	1.8084	**2.8086**	**0.9009**
0.333333	0.0538	0.0654	0.0343	3.6146	4.3966	2.3059	**3.4390**	**1.0564**
0.416667	0.0643	0.0671	0.0455	4.3241	4.5109	3.0588	**3.9646**	**0.7900**
0.5	0.0652	0.0679	0.0464	4.3865	4.5647	3.1193	**4.0235**	**0.7881**
0.666667	0.0690	0.0684	0.0510	4.6360	4.5983	3.4286	**4.2210**	**0.6865**
0.833333	0.0705	0.0671	0.0530	4.7373	4.5109	3.5630	**4.2704**	**0.6230**
1	0.0700	0.0662	0.0535	4.7035	4.4504	3.5966	**4.2502**	**0.5800**
1.5	0.0706	0.0696	0.0531	4.7451	4.6790	3.5697	**4.3313**	**0.6603**
2	0.0706	0.0678	0.0524	4.7451	4.5580	3.5227	**4.2753**	**0.6584**
2.5	0.0702	0.0638	0.0521	4.7218	4.2891	3.5025	**4.1711**	**0.6181**
3	0.0704	0.0692	0.0529	4.7296	4.6521	3.5563	**4.3127**	**0.6562**
3.5	0.0704	0.0693	0.0538	4.7296	4.6588	3.6168	**4.3351**	**0.6230**
4	0.0705	0.0671	0.0530	4.7373	4.5109	3.5630	**4.2704**	**0.6230**
8	0.0707	0.0654	0.0543	4.7529	4.3966	3.6504	**4.2667**	**0.5626**
12	0.0704	0.0704	0.0534	4.7295	4.7328	3.5899	**4.3507**	**0.6589**
16	0.0712	0.0683	0.0536	4.7841	4.5916	3.6034	**4.3264**	**0.6335**
20	0.0704	0.0638	0.0533	4.7296	4.2891	3.5832	**4.2006**	**0.5783**
24	0.0698	0.0628	0.0532	4.6907	4.2218	3.5765	**4.1630**	**0.5595**
28	0.0702	0.0688	0.0547	4.7218	4.6252	3.6773	**4.3414**	**0.5772**
32	0.0705	0.0703	0.0537	4.7373	4.7261	3.6101	**4.3578**	**0.6476**
36	0.0707	0.0703	0.0524	4.7529	4.7261	3.5227	**4.3339**	**0.7027**
40	0.0702	0.0674	0.0523	4.7218	4.5311	3.5160	**4.2563**	**0.6482**
44	0.0697	0.0656	0.0538	4.6831	4.4101	3.6168	**4.2367**	**0.5539**
48	0.0707	0.0713	0.0528	4.7529	4.7933	3.5496	**4.3653**	**0.7067**

Table M2 Raw data of the determination of amounts of 5-sulfosalicylic acid released from FishGel CR_3% at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0149	0.0117	0.0154	1.0017	0.7866	1.0353	**0.9412**	**0.1350**
0.166667	0.0256	0.0240	0.0200	1.7210	1.6134	1.3445	**1.5597**	**0.1939**
0.25	0.0387	0.0271	0.0379	2.6017	1.8218	2.5479	**2.3238**	**0.4355**
0.333333	0.0450	0.0331	0.0443	3.0252	2.2252	2.9782	**2.7429**	**0.4489**
0.416667	0.0481	0.0344	0.0485	3.2336	2.3126	3.2605	**2.9356**	**0.5397**
0.5	0.0528	0.0367	0.0504	3.5496	2.4672	3.3882	**3.1350**	**0.5839**
0.666667	0.0581	0.0524	0.0614	3.9059	3.5227	4.1277	**3.8521**	**0.3061**
0.833333	0.0586	0.0521	0.0642	3.9395	3.5025	4.3160	**3.9193**	**0.4071**
1	0.0574	0.0477	0.0645	3.8588	3.2067	4.3361	**3.8006**	**0.5670**
1.5	0.0582	0.0543	0.0641	3.9126	3.6504	4.3092	**3.9574**	**0.3317**
2	0.0575	0.0510	0.0640	3.8655	3.4286	4.3025	**3.8655**	**0.4370**
2.5	0.0578	0.0463	0.0641	3.8857	3.1126	4.3092	**3.7692**	**0.6068**
3	0.0587	0.0510	0.0639	3.9462	3.4286	4.2958	**3.8902**	**0.4363**
3.5	0.0587	0.0536	0.0648	3.9462	3.6034	4.3563	**3.9686**	**0.3770**
4	0.0579	0.0530	0.0643	3.8924	3.5630	4.3227	**3.9261**	**0.3809**
8	0.0577	0.0475	0.0643	3.8790	3.1933	4.3227	**3.7983**	**0.5690**
12	0.0588	0.0553	0.0644	3.9529	3.7176	4.3294	**4.0000**	**0.3086**
16	0.0571	0.0521	0.0646	3.8387	3.5025	4.3429	**3.8947**	**0.4230**
20	0.0576	0.0477	0.0643	3.8723	3.2067	4.3227	**3.8006**	**0.5614**
24	0.0585	0.0523	0.0642	3.9328	3.5160	4.3160	**3.9216**	**0.4001**
28	0.0578	0.0478	0.0637	3.8857	3.2134	4.2824	**3.7938**	**0.5403**
32	0.0583	0.0467	0.0647	3.9193	3.1395	4.3496	**3.8028**	**0.6134**
36	0.0575	0.0509	0.0640	3.8655	3.4218	4.3025	**3.8633**	**0.4403**
40	0.0580	0.0530	0.0638	3.8992	3.5630	4.2891	**3.9171**	**0.3634**
44	0.0579	0.0488	0.0648	3.8924	3.2807	4.3563	**3.8431**	**0.5395**
48	0.0579	0.0471	0.0638	3.8924	3.1664	4.2891	**3.7826**	**0.5693**

Table M3 Raw data of the determination of amounts of 5-sulfosalicylic acid released from FishGel 7% crosslinked (FishGel_7) at time t, pH 5.5 at 37°C

Time (hr)	Absorbance (a.u.)			Drug Accumulation (mg)				
	1	2	3	1	2	3	Avg	SD
0.083333	0.0089	0.0134	0.0149	0.5975	0.9008	0.9995	**0.8326**	**0.2095**
0.166667	0.0146	0.0258	0.0266	0.9788	1.7345	1.7874	**1.5002**	**0.4523**
0.25	0.0205	0.0419	0.0349	1.3753	2.8168	2.3450	**2.1790**	**0.7349**
0.333333	0.0238	0.0483	0.0394	1.5997	3.2471	2.6467	**2.4978**	**0.8337**
0.416667	0.0305	0.0553	0.0466	2.0486	3.7176	3.1316	**2.9659**	**0.8468**
0.5	0.0313	0.0559	0.0488	2.1009	3.7580	3.2790	**3.0460**	**0.8527**
0.666667	0.0347	0.0589	0.0512	2.3328	3.9597	3.4400	**3.2442**	**0.8309**
0.833333	0.0345	0.0591	0.0514	2.3179	3.9731	3.4540	**3.2483**	**0.8466**
1	0.0349	0.0590	0.0515	2.3478	3.9664	3.4610	**3.2584**	**0.8281**
1.5	0.0336	0.0589	0.0527	2.2580	3.9597	3.5452	**3.2543**	**0.8873**
2	0.0340	0.0594	0.0516	2.2879	3.9933	3.4680	**3.2498**	**0.8734**
2.5	0.0337	0.0592	0.0512	2.2655	3.9798	3.4400	**3.2285**	**0.8765**
3	0.0345	0.0588	0.0516	2.3179	3.9529	3.4680	**3.2463**	**0.8398**
3.5	0.0337	0.0592	0.0513	2.2655	3.9798	3.4470	**3.2308**	**0.8774**
4	0.0346	0.0590	0.0514	2.3254	3.9664	3.4540	**3.2486**	**0.8396**
8	0.0347	0.0591	0.0508	2.3328	3.9731	3.4120	**3.2393**	**0.8337**
12	0.0340	0.0589	0.0532	2.2879	3.9597	3.5732	**3.2736**	**0.8752**
16	0.0339	0.0592	0.0515	2.2805	3.9798	3.4610	**3.2404**	**0.8709**
20	0.0337	0.0597	0.0529	2.2655	4.0134	3.5592	**3.2794**	**0.9069**
24	0.0343	0.0586	0.0515	2.3029	3.9395	3.4610	**3.2345**	**0.8415**
28	0.0330	0.0593	0.0516	2.2206	3.9866	3.4680	**3.2251**	**0.9077**
32	0.0341	0.0599	0.0510	2.2954	4.0269	3.4260	**3.2494**	**0.8791**
36	0.0339	0.0590	0.0515	2.2805	3.9664	3.4610	**3.2360**	**0.8652**
40	0.0350	0.0598	0.0502	2.3553	4.0202	3.3769	**3.2508**	**0.8396**
44	0.0348	0.0591	0.0514	2.3403	3.9731	3.4540	**3.2558**	**0.8342**
48	0.0343	0.0591	0.0519	2.3029	3.9731	3.4891	**3.2550**	**0.8593**

Release Kinetics of Model Drug from Drug-Loaded FishGel Hydrogel

In order to study SSA transport mechanism from the FishGel hydrogels, two diffusion models are considered to fit the experimental data.

Model 1 is described by the Ritger-Peppas equation (Venkatesh *et al.*, 1992):

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

where M_t/M_∞ is the fractional drug release, k_1 is a kinetic constant (with the unit of T^{-n}) t is the release time, and n is 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 the Fickian diffusion. When n = 1, Case II transport occurs, corresponding to the zero-order release. When $0.5 < n < 1$, the anomalous transport is observed.

Model 2 is based on the Higuchi's equation (Serra *et al.*, 2006) and described the Fickian diffusion of the drug:

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

where M_t/M_∞ is the fractional drug release, k_H is a kinetic constant (with unit of T^{-n}) and t is the release time.

The diffusion coefficients of SSA from the FishGel hydrogels are determined from the slopes of plots of drug accumulation versus square root of time according to Higuchi's equation (A-sasutjarit *et al.*, 2005):

$$Q = 2C_0(Dt/\pi)^{1/2} \quad \text{(K3)}$$

where Q is the amount of material flowing through a unit cross-section of barrier (g/cm^2) in unit time, t (s); C_0 is the initial drug concentration in the hydrogel (g/cm^3); and D is 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 SSA released from SSA-loaded FishGel hydrogels at time t versus $time^{1/2}$ at various crosslinking ratios (FishGel_1.00, FishGel_3.00, and FishGel_7.00) during 48 h as shown in Figure M2 using the Higuchi's equation.

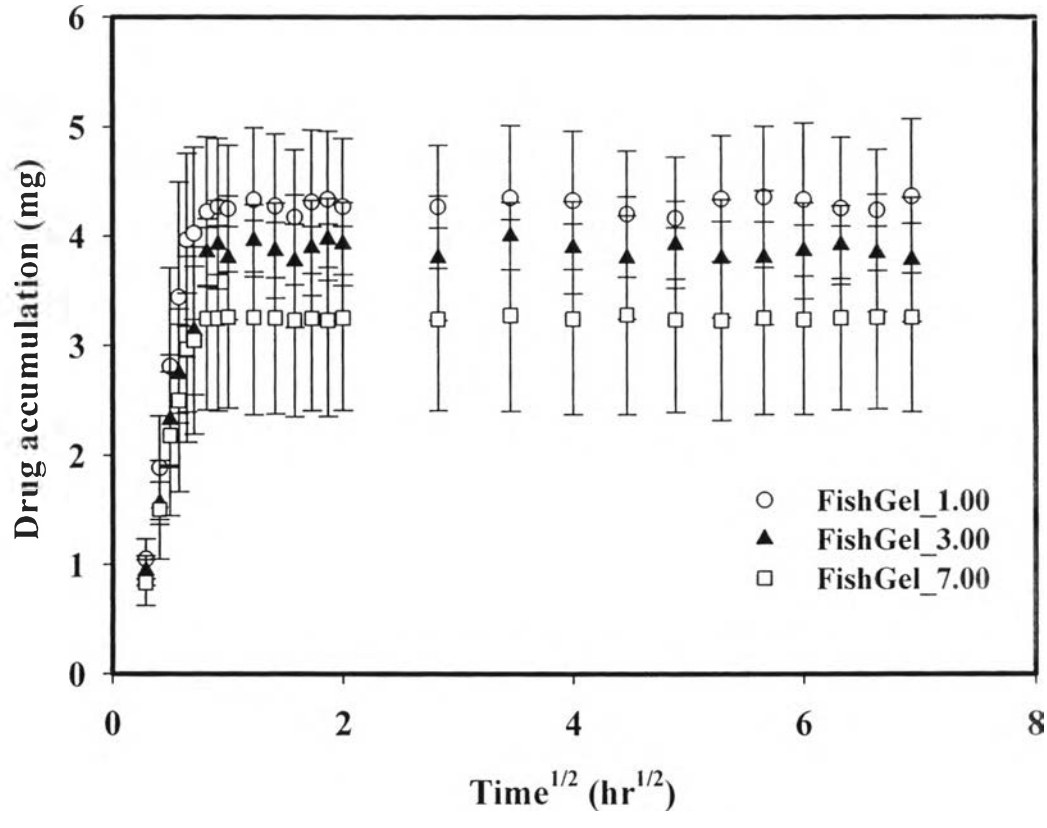


Figure M2 Amounts of 5-sulfosalicylic acid release from SSA-loaded FishGel hydrogel versus time$^{1/2}$ at various crosslink ratios, pH 5.5, and at 37°C, number of samples = 3.

Figure M3 shows the diffusion coefficients of SSA from FishGel hydrogels versus crosslinking ratios and mesh size at 37°C. The results show the diffusion coefficients of SSA are ranked in the following order: FishGel_1.00 > FishGel_3.00 > FishGel_7.00.

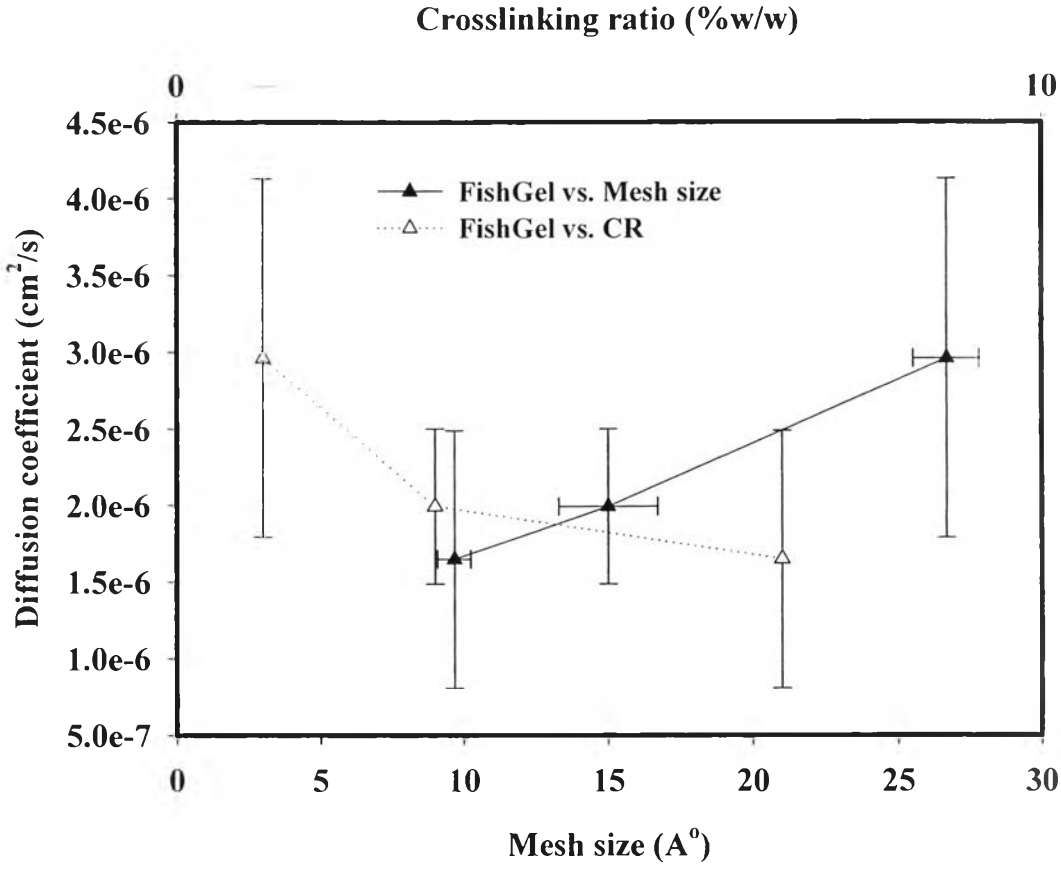


Figure M3 Diffusion coefficient of sulfosalicylic acid from FishGel hydrogels versus crosslinking ratios and mesh size, pH 5.5, and at 37°C, number of samples = 3.

Table M4 Raw data of the determination of the diffusion coefficient of 5-sulfosalicylic acid released from various crosslinked FishGel hydrogel, pH 5.5 at 37°C

Sample	Slope			Diffusion Coefficient (cm^2/s)				
	1	2	3	1	2	3	Avg	SD
FishGel_1.00	5.791	6.377	4.147	3.26E-06	3.95E-06	1.67E-06	**2.96E-06**	**1.17E-06**
FishGel_3.00	4.893	3.813	4.816	2.33E-06	1.41E-06	2.25E-06	**2.00E-06**	**5.08E-07**
FishGel_7.00	2.772	4.974	4.314	7.47E-07	2.40E-06	1.81E-06	**1.65E-06**	**8.40E-07**

Appendix N Determination of Mechanical Properties of Gelatins

Table N1 Summarize the gelatin mechanical properties

Types	Tensile stress at break, σ_b (MPa)	Elongation at break, ε_b(%)	Young's modulus, E (MPa)
FishGel_1	48.35 ± 3.23	4.04 ± 0.33	1,974.03 ± 143.87
FishGel_3	61.13 ± 3.41	3.65 ± 0.29	2,341.79 ± 76.03
PorGel_0.25	63.30 ± 2.77	6.26 ± 0.37	2,086.86 ± 79.56
PorGel_3	72.02 ± 4.04	4.88 ± 0.52	2952.09 ± 70.15

Tensile stress at break, σ_b, and elongation at break, ε_b were determined by using Universal Testing Machine (Lloyd). Initial grip separation and cross-head speed were set at 4 cm and 50 mm/min, respectively. The sample films were cut into 1×10 cm. The thickness of the sample films was observed via Digital thickness Gauge (Peacock).

Table N1 shows the parameters of gelatin mechanical property. The increasing of crosslinking ratio, resulting in an increase tensile strength and a decrease in the percentage elongation of gelatin films because the restriction of molecular mobility (Baj *et al.*, 2009). For the same crosslinking ratio (3%), porcine gelatin films show young's modulus higher than that of fish gelatin films (PorGel_3 ≈ 2,952 MPa and FishGel ≈ 2,341 MPa) since the molecular weight of porcine gelatin was higher. This result confirms that the porcine gelatin has higher molecular weight than that of fish gelatin.

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