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APPENDICES

Appendix A FT-IR Spectrum of Sulfosalicylic Acid-Loaded Poly(vinyl alcohol) Hydrogel and Poly(vinyl alcohol) Hydrogel

The PVA film and drug-loaded PVA films were characterized by ATR-FTIR spectroscopy to study the polymer/drug interaction. The sample was 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 $4cm^{-1}$.

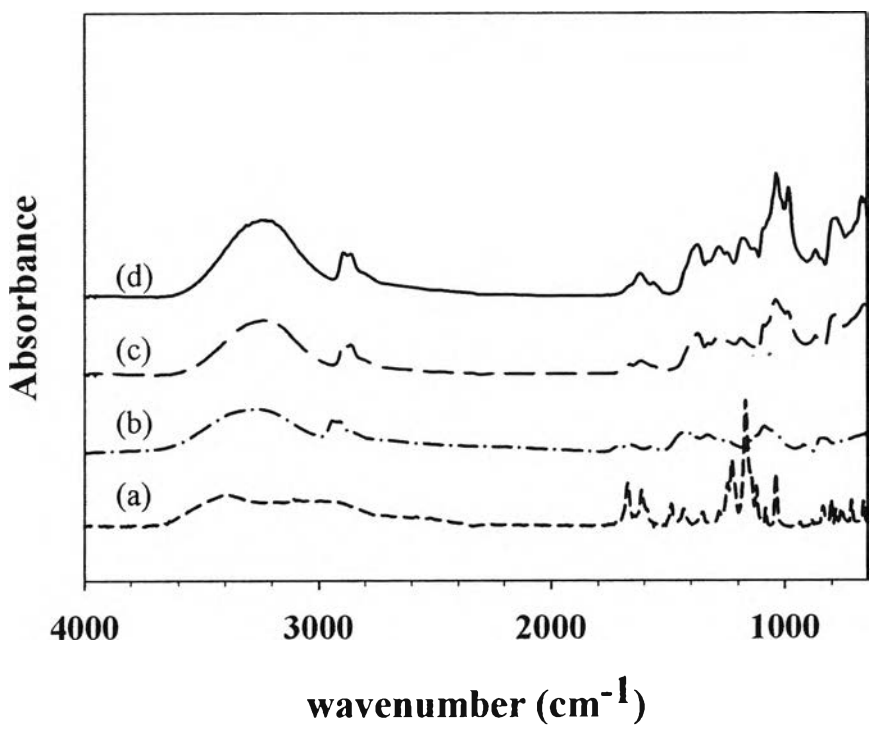

Figure A1 Absorption infrared spectra of poly(vinyl alcohol) hydrogel loaded with sulfosalicylic acid: (a) SSA powder; (b) pure PVA hydrogel; (c) 10%SSA-loaded PVA hydrogel; and (d) 25%SSA-loaded PVA hydrogel.

The absorption infrared spectra of poly(vinyl alcohol) hydrogel loaded with 10 and 25% sulfosalicylic acid is shown in comparison with poly(vinyl alcohol) free hydrogel and sulfosalicylic acid power in Figure A1. In pure PVA, we observed peak at 1330, 2941 cm^{-1} and a broad region around 3000 to 3600 cm^{-1}. They are characteristic of PVA and have been assigned to the CO stretching, CH_2 stretching and OH stretching, respectively. In pure SSA, two peaks at 1036 and around 716 cm^{-1} have been assigned to sulfonate groups (SO^{3-}) stretching. For drug-loaded PVA hydrogel the sulfonate groups (SO^{3-}) stretching grows and has a gradual shift of OH stretching. These results indicate the H-bonding between the sulfonate groups of sulfosalicylic acid with hydroxyl group of PVA hydrogel (Wu *et al.*, 2006).

Table A1 The FT-IR absorption spectrum of sulfosalicylic acid-loaded poly(vinyl alcohol) hydrogel and poly(vinyl alcohol) hydrogel

Wavenumber (cm^{-1})	**Assignments**	**References**
3000-3600 [3000-3500]	O-H stretching	Wu *et al.* (2006)
2941 [2940]	CH_2 stretching	Bhat *et al.* (2005)
1421 [1430]	CH_2 bending	Bhat *et al.* (2005)
1330 [1300]	C-O stretching	Wu *et al.* (2006)
1089 [1096]	C=O stretching vibration	Bhat *et al.* (2005)
847 [850]	C-C stretching	Bhat *et al.* (2005)
1036 [1030]	S=O symmetric stretching	Wu *et al.* (2006)
716 [700]	S-O symmetric stretching	Wu *et al.* (2006)

Appendix B TGA Thermograms of Sulfosalicylic Acid-Loaded Poly(vinyl alcohol) Hydrogel and Poly(vinyl alcohol) 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 30 to 600°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.

The summary of percent weight loss in the TGA thermogram are shown in TableB1. Figure B1 shows the TGA thermograms for pure PVA and drug-loaded PVA hydrogels. There are three transitions for pure PVA hydrogel and the drug-loaded PVA hydrogel. The first occurs in the temperature range of about 50-100 °C corresponding to the loss of moisture, while the second and the third transitions cover the temperature range of 255 to 320 °C and 400-500 °C, corresponding to the thermal degradation of PVA. The TGA thermogram of drug-loaded PVA hydrogel also exhibits four steps of weight loss. The results show that the presence of SSA (drug) seems to expedite the thermal degradation of the pure PVA matrix. It is known that PVA is a semicrystalline polymer which exhibits a strong intermolecular interaction .through hydrogen bonding between hydroxyl group and ionic drug (Hidalgo *et al.*, 1999; Wu *et al.*, 2006).

Table B1 Summary of pure PVA film and drug-loaded PVA film degradation step

sample	Transition temperature (°C)				% Weight loss				%Residue
	1st	2nd	3rd	4th	1st	2nd	3rd	4th	
pure PVA	50-100	255-320	400-500	-	9.0	71.6	11.0	-	8.4
drug - loaded PVA	50-100	120-190	200-300	400-500	8.3	30.6	10.0	31.5	19.6

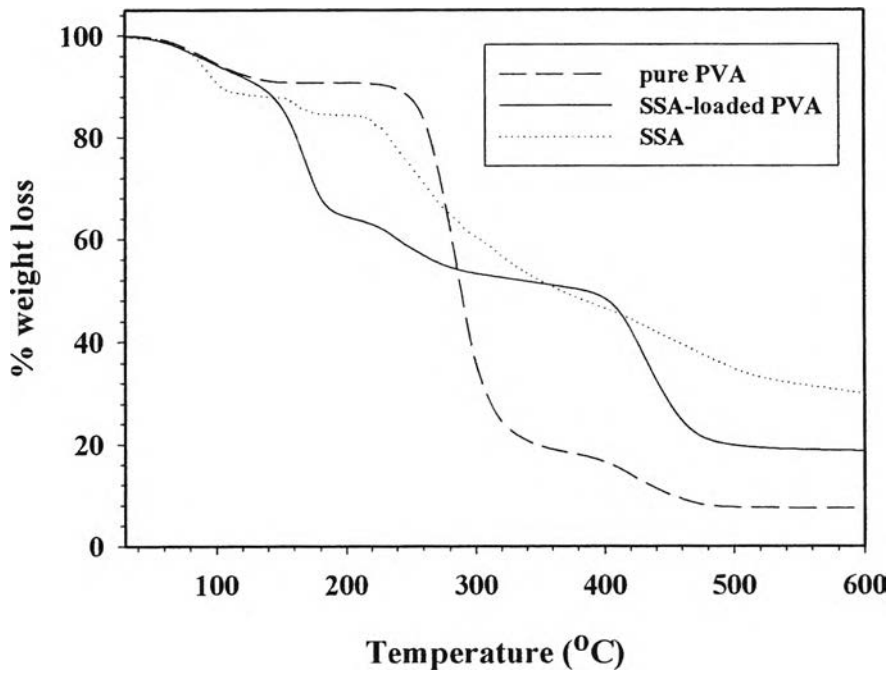

Figure B1 The TGA thermograms of pure PVA hydrogel, drug-loaded PVA hydrogel and pure model drug.

Appendix C DSC Thermograms of Sulfosalicylic Acid-Loaded Poly(vinyl alcohol) Hydrogel and Poly(vinyl alcohol) Hydrogel

The thermal behavior of the PVA hydrogel, the drug, and the drug-loaded PVA hydrogel were determined by a differential scanning calorimeter (DSC; Mettler Toledo 822e/400). The DSC thermogram (equilibrated with an indium standard; each sample weighed 3–5 mg) was obtained during heating from 25 to 350 °C at a heatingrate of 10 °C min−1 under nitrogen purge (60 ml min−1).

Figure C1 shows DSC thermograms for pure PVA and drug-loaded PVA hydrogel. The DSC thermogram for pure PVA hydrogel exhibits a loss of moisture coupled with a glass transition over a temperature range between 40-120 °C, a melting range at 200-225 °C and a thermal degradation range between 250-350 °C. The drug-loaded PVA hydrogel exhibits a loss of moisture coupled with a glass transition at the same temperature range of the pure PVA hydrogel, while the melting temperatures (T_m) of both drug and PVA in drug-loaded samples shift to about 140 °C and 170 °C, respectively. The possible reason for the peak shift is the interaction between polymer and drug molecule since SSA had a potential to form H-bonding with the hydroxyl group of PVA (Taepaiboon et al., 2006).

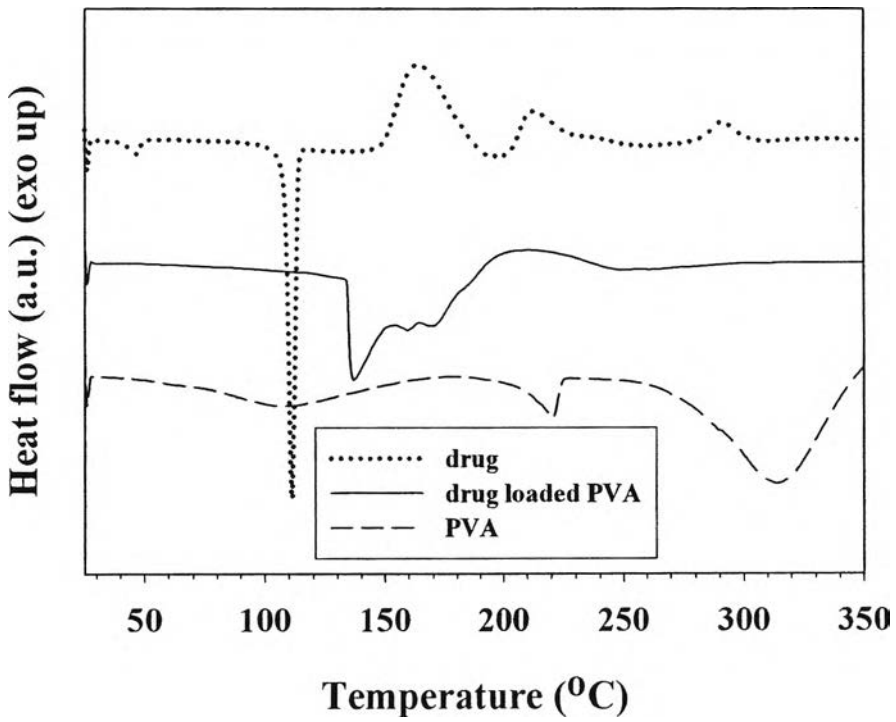

Figure C1 The DSC thermograms of pure PVA hydrogel, drug-loaded PVA hydrogel and pure model drug.

Appendix D Scanning Electron Micrograph of Various Crosslinked PVA Hydrogels: PVA_0 and PVA_2.5 under Electric Field of 0, 1 and 5 V

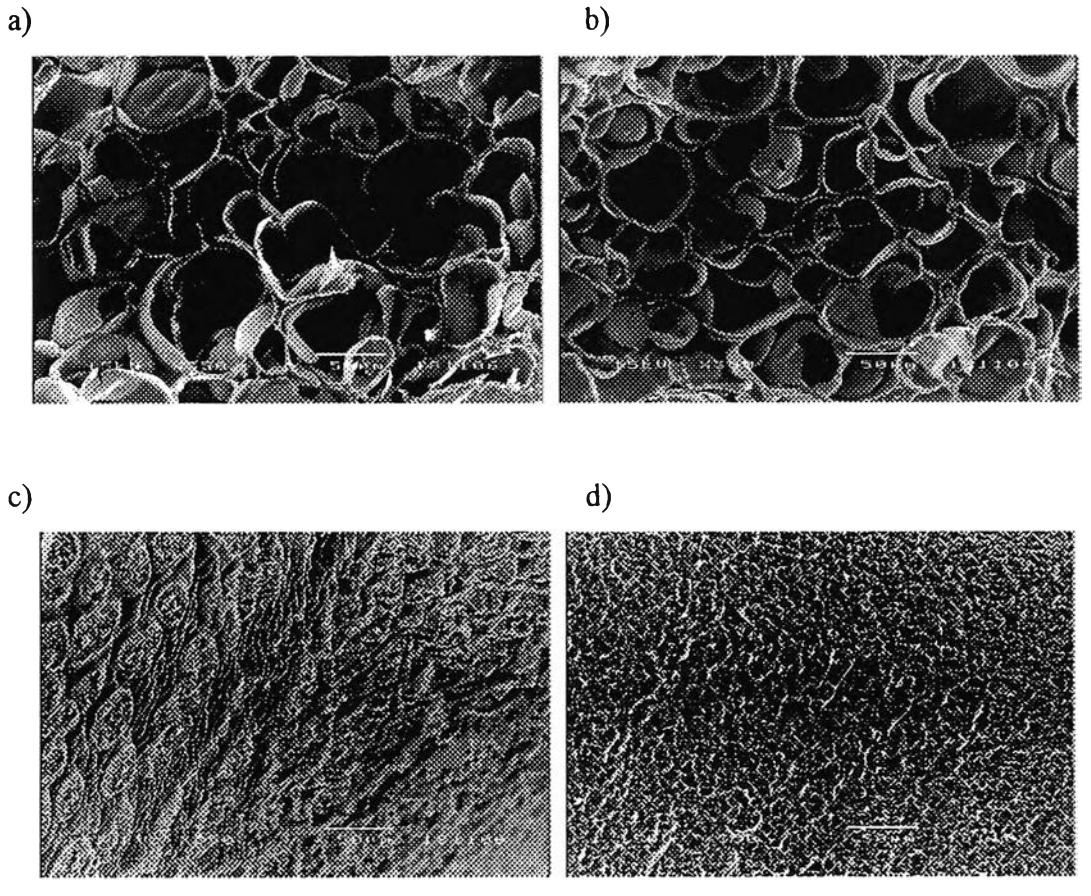

Figure D1 The morphology of poly(vinyl alcohol) after swelling: a) PVA_0; b) PVA_0.5; c) PVA_2.5; and d) PVA_ 5.0 at magnification of 350.

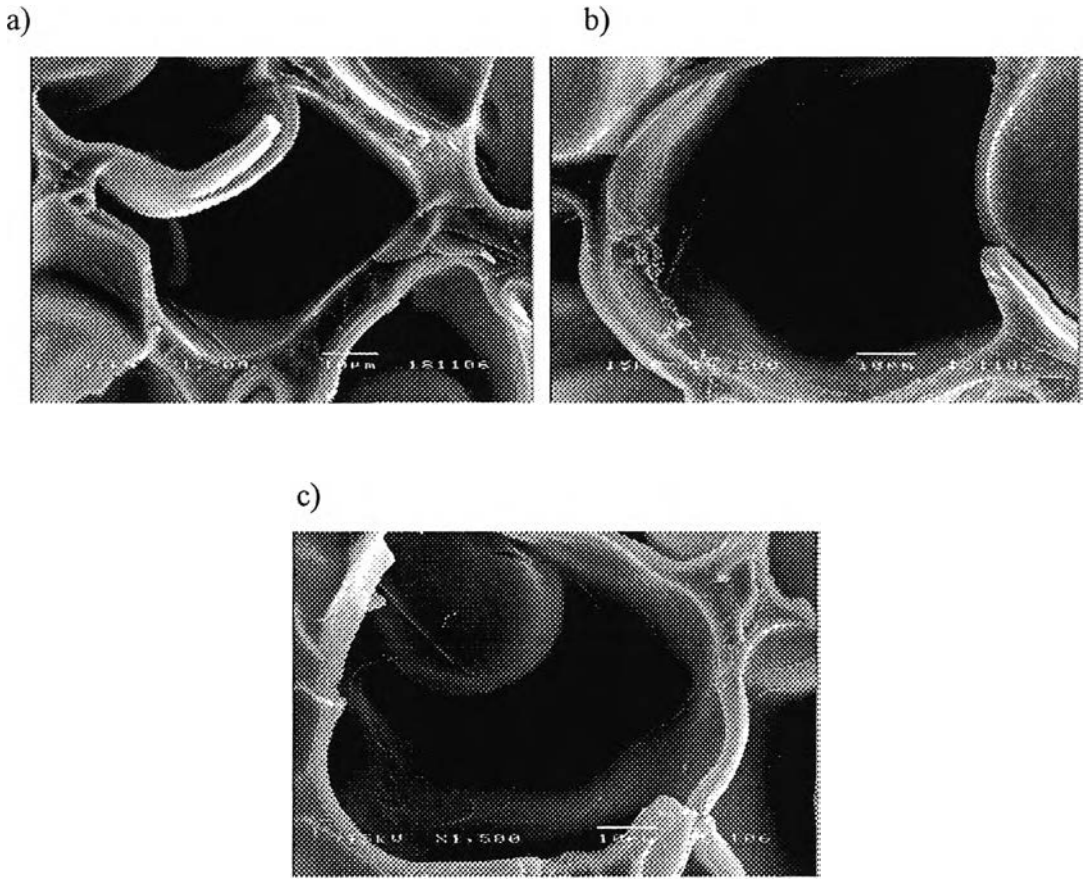

Figure D2 The morphology of poly(vinyl alcohol) (PVA_0) after swelling under electric field strength of: a) 0 V ; b) 0.1 V; and d) 5 V at magnification of 1500.

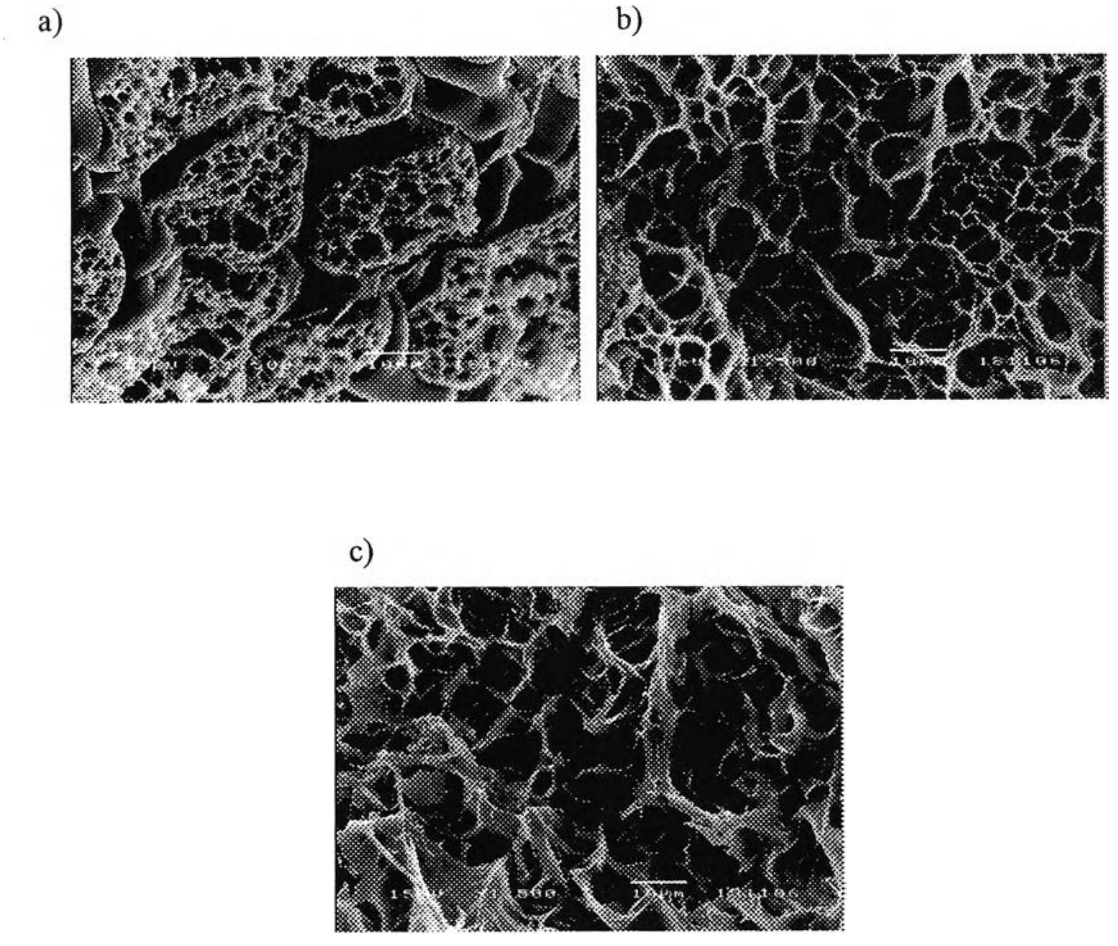

Figure D3 The morphology of poly(vinyl alcohol) (PVA_2.5) after swelling under electric field strength of: a) 0 V ; b) 0.1 V; and d) 5 V at magnification of 1500.

Appendix E Determination of Degree of Swelling and Weight Loss of PVA Hydrogels

The degree of swelling and weight loss of PVA hydrogels were measured in an acetate buffer solution at 37 °C for 24 h according to the following equations (Taepaiboon et al., 2006):

$$\text{Degree of swelling (\%)} = \frac{M - M_d}{M_d} \times 100 \qquad (1)$$

and

$$\text{Weight loss (\%)} = \frac{M_i - M_d}{M_i} \times 100 \qquad (2)$$

where M is the weight of each sample after submersion in the buffer solution, M_d is the weight of sample after submersion in the buffer solution in its dry state, M_i is the initial weight of the sample in its dry state.

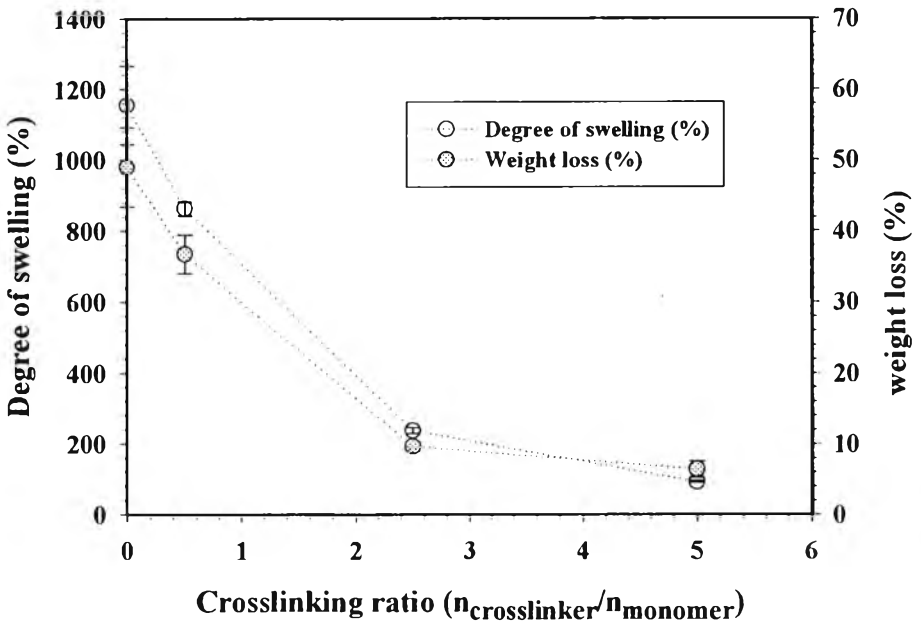

Figure E1 Degree of swelling (%) and weight loss (%) of poly(vinyl alcohol) hydrogels at various crosslinking ratios (PVA_0, PVA_0.5, PVA_2.5 and PVA_5.0) at 37^0C after 5 day, each data point was obtained from 5 samples.

Table E1 Values of the degree of swelling (%) and weight loss (%) of poly(vinyl alcohol) hydrogels at various crosslinking ratios

Sample	Wa,r (mg)	Wa,s (mg)	Wa,d (mg)	swelling ratio (s,d)	%weight loss
CR0/1	0.03092	0.18836	0.01428	1219.05	53.82
2	0.03161	0.2079	0.01472	1312.36	53.43
3	0.03051	0.18715	0.01526	1126.41	49.98
4	0.04215	0.2913	0.02524	1054.12	40.12
5	0.03229	0.19624	0.01694	1058.44	47.54
Avg				1154.08	48.98
SD				110.88	5.59
CR0.5/1	0.03869	0.20845	0.02601	701.42	32.77
2	0.03483	0.16554	0.02091	691.68	39.97
3	0.04648	0.27701	0.02856	869.92	38.55
4	0.02951	0.146	0.01884	674.95	36.16
5	0.03079	0.14624	0.0196	646.12	36.34
Avg				716.82	36.76
SD				88.12	2.74
CR2.5/1	0.06736	0.20919	0.06126	241.48	9.06
2	0.06015	0.19145	0.05452	251.16	9.36
3	0.08545	0.26705	0.07648	249.18	10.50
4	0.06362	0.19496	0.05785	237.01	9.07
5	0.08156	0.2616	0.07341	256.35	9.99
Avg				247.03	9.60
SD				7.74	0.63
CR5.0/1	0.09007	0.15885	0.08366	89.88	7.12
2	0.08401	0.14705	0.07779	89.03	7.40
3	0.07883	0.14012	0.07329	91.19	7.03
4	0.06789	0.12568	0.06445	95.00	5.07
5	0.06868	0.12588	0.06514	93.25	5.15
Avg				91.67	6.35
SD				2.45	1.14

Appendix F Determinaion of The Molecular Weight between Crosslinks, Mesh Size and Crosslinking Density

To determine the molecular weight between crosslinks, Mc the mesh size, ξ, and the crosslinking density, a sample of PVA film was cut immediately after crosslinking. This sample was weighted in air and heptane. The sample was then placed in distilled water at 37 ^{0}C for 5 days to allow it to swell to equilibrium, and weighted in air and heptane. Finally, the sample was dried at 25 ^{0}C in vacuum oven for 5 days. Once again, it was weighted in air and heptane. These weights were used to calculate the polymer volume fraction in the relaxed and swellen states, $\upsilon_{2,r}$ and $\upsilon_{2,s}$, respectively (Peppas *et al.*, 1998).

$$\upsilon_{2,r} = \frac{V_d}{V_r} \tag{1}$$

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

where V_d, V_r, and V_s are the volumes of the polymer sample in dry, relaxed, and swollen stated, respectively. The volumes were calculated using following equation which utilize the weights of the dry polymer, W_d, the relaxed polymer, W_r, and the swollen polymer, W_s, in air and heptane and ρ_h is the density of heptane.

$$V_d = \frac{W_{a,d} - W_{h,d}}{\rho_h} \tag{3}$$

$$V_r = \frac{W_{a,r} - W_{h,r}}{\rho_h} \tag{4}$$

$$V_s = \frac{W_{a,s} - W_{h,s}}{\rho_h} \tag{5}$$

The molecular weight between crosslinks, $\bar{M}_c$, was calculated from the swelling data using Eq (6) (Peppas *et al.*, 1998).

$$\frac{1}{\bar{M}_c} = \frac{2}{\bar{M}_n} - \frac{\frac{\bar{\upsilon}}{\bar{V}_1}[\ln(1-\upsilon_{2,S}) + \upsilon_{2,S} + \chi\upsilon_{2,S}^{\ 2}]}{\upsilon_{2,r}[(\frac{\upsilon_{2,S}}{\upsilon_{2,r}})^{1/3} - \frac{1}{2}(\frac{\upsilon_{2,S}}{\upsilon_{2,r}})]} \qquad (6)$$

where Mn is the number-average molecular weight of the polymer before crosslinking, $\bar{\upsilon}$ is the specific volume of polymer, $\bar{V}_1$ is the molar volume of the solvent, $\upsilon_{2,r}$ is the volume fraction of the polymer in the relaxed state, $\upsilon_{2,S}$ is the volume fraction of the polymer in the swollen state, and χ is the interaction parameter of the polymer-solvent system in water.

The hydrogel mesh size, ξ, defines the linear distance between consecutive crosslinks. It indicates the diffusional space available for solute transport and can be calculated using Eq (7) (Hickey *et al.*, 1995).

$$\xi = \upsilon_{2,s}^{-1/3} [C_n(2\bar{M}_c/M_r)]^{1/2} l \qquad (7)$$

where C_n is the Flory characteristic ratio, l is the carbon-carbon bond length, $\bar{M}_r$ is the molecular weight of the repeating unit of polymer, and $\bar{M}_c$ is the molecular weight between crosslinks.

The crosslinking density of the hydrogel was calculated using Eq (8) (Peppas *et al.*, 1996).

$$\rho_x = \frac{1}{v\bar{M}_c} \qquad (8)$$

Table 1 shows the molecular weight between crosslinks, mesh size and crosslinking density of each PVA hydrogel at various crosslinking ratios with and without electric field. The molecular weight between crosslinks and mesh size values

of PVA hydrogels are larger at lower crosslinking ratio. The mesh sizes of hydrogels vary between 36 and 230 A° for no current and between 33 and 250 A° under applied current. Thus the comparison of mesh size values between the system with electric field and without electric field suggests that the electric field has no effect on their structure change.

Table F1 The molecular weight between crosslinks, mesh size and crosslinking density of PVA hydrogels at various crosslinking ratios with and without the electric field

Sample	Crosslinking ratio, X	Number-average molecular weight between crosslinks, M_c (g/mol)		Mesh size ξ (A^0)		Crosslinking density ($mol/cm^3 \times 10^4$)	
		E = 0 V	E = 1 V	E = 0 V	E = 1 V	E = 0 V	E = 1 V
PVA_0	0	13464 ± 1733	15400 ± 2100	232 ± 23	250 ± 28	0.95 ± 0.13	0.83 ± 0.11
PVA_0.5	0.5	6484 ± 2069	6800 ± 940	143 ± 31	150 ± 13	1.99 ± 0.57	1.88 ± 0.28
PVA_2.5	2.5	2063 ± 734	2600 ± 750	71 ± 15	85 ± 15	6.26 ± 1.57	4.99 ± 1.34
PVA_5.0	5.0	691 ± 176	570 ± 270	36 ± 6	33 ± 10	18.36 ± 4.29	23.60 ± 8.30

Table F2 The raw data of the determination of the M_c, mesh size and crosslinking density of PVA hydrogels at various crosslinking ratios without the electric field

Sample	Wa,r (mg)	Wh,r (mg)	Wa,s (mg)	Wh,s (mg)	Wa,d (mg)	Wh,d (mg)	Mc(g/mol)	ξ(A0)	ρ(mol/cm3)
CR0/1	0.03092	0.03021	0.18836	0.18010	0.01428	0.01322	10855.99	195.39	0.0001169
2	0.03161	0.03084	0.20790	0.19957	0.01472	0.01389	14455.44	245.31	0.0000878
3	0.03051	0.02968	0.18415	0.17397	0.01526	0.01425	15337.49	253.05	0.0000827
4	0.04215	0.04115	0.29130	0.28116	0.02524	0.02423	14046.25	241.84	0.0000903
5	0.03229	0.03134	0.19624	0.18690	0.01694	0.01595	12839.70	226.48	0.0000988
Avg							13464.26	231.96	0.0000953
SD							1733.07	22.84	0.0000134
CR0.5/1	0.03869	0.03781	0.21145	0.20444	0.02601	0.02496	6932.77	148.30	0.0001830
2	0.03483	0.03404	0.16554	0.15952	0.02091	0.01980	4714.32	114.11	0.0002692
3	0.04648	0.04562	0.27891	0.27331	0.02856	0.02764	5211.41	124.68	0.0002435
4	0.02912	0.02843	0.14600	0.14050	0.01884	0.01819	9962.05	192.39	0.0001274
5	0.03049	0.02961	0.14864	0.14302	0.01960	0.01885	7282.42	157.96	0.0001743
Avg							6483.93	143.17	0.0001995
SD							2068.84	30.66	0.0000568
CR2.5/1	0.06736	0.06640	0.20949	0.20593	0.06126	0.06048	2004.87	70.25	0.0006330
2	0.06015	0.05916	0.19145	0.18845	0.05452	0.05392	2041.56	73.08	0.0006216
3	0.08545	0.08450	0.26705	0.26228	0.07648	0.07559	3451.37	97.25	0.0003677
4	0.06362	0.06253	0.19795	0.19289	0.05785	0.05653	1673.62	60.56	0.0007583
5	0.08156	0.08045	0.26290	0.25860	0.07341	0.07237	1698.16	62.56	0.0007473
Avg							2062.66	70.76	0.0006256
SD							733.93	14.65	0.0001573
CR5.0/1	0.09007	0.08915	0.15950	0.15677	0.08366	0.08265	536.94	30.53	0.0023635
2	0.08391	0.08276	0.14800	0.14468	0.07779	0.07665	622.43	33.70	0.0020389
3	0.07863	0.07785	0.14012	0.13778	0.07329	0.07261	932.45	43.61	0.0013610
4	0.06789	0.06701	0.12568	0.12279	0.06445	0.06342	638.45	33.71	0.0019877
5	0.06868	0.06775	0.12708	0.12436	0.06514	0.06434	888.74	42.40	0.0014279
Avg							691.28	35.89	0.0018358
SD							175.51	5.83	0.0004285

Table F3 The raw data of the determination of the M_c, mesh size and crosslinking density of PVA hydrogels at various crosslinking ratios with the electric field

Sample	Wa,r (mg)	Wh,r (mg)	Wa,s (mg)	Wh,s (mg)	Wa,d (mg)	Wh,d (mg)	Mc(g/mol)	ξ(A0)	ρ(mol/cm3)
CR0/1	0.0653	0.0647	0.4381	0.4284	0.0311	0.0300	14829.64	237.98	0.00008557
2	0.0621	0.0614	0.4228	0.4126	0.0265	0.0256	18471.44	288.77	0.00006870
3	0.0674	0.0666	0.4511	0.4406	0.0325	0.0314	14852.23	244.54	0.00008544
4	0.0642	0.0633	0.4458	0.4327	0.0299	0.0283	12939.31	216.86	0.00009808
5	0.0695	0.0686	0.4610	0.4477	0.0358	0.0345	16804.73	266.20	0.00007552
Avg							15377.31	248.13	0.00008266
SD							2116.98	27.54	0.00001118
CR0.5/1	0.0755	0.0738	0.3812	0.3728	0.0463	0.0451	5506.65	134.27	0.00023045
2	0.0833	0.0817	0.3984	0.3903	0.0542	0.0532	7113.55	160.22	0.00017840
3	0.0630	0.0619	0.3743	0.3662	0.0351	0.0340	7730.11	161.80	0.00016417
4	0.0759	0.0744	0.3828	0.3747	0.0474	0.0463	6360.33	146.76	0.00019952
5	0.0877	0.0864	0.4041	0.3962	0.0587	0.0577	7674.18	165.03	0.00016536
Avg							6767.44	152.44	0.00018758
SD							943.93	12.86	0.00002787
CR2.5/1	0.0701	0.0686	0.2211	0.2158	0.0641	0.0632	3164.33	96.09	0.00040104
2	0.0668	0.0658	0.2157	0.2115	0.0613	0.0606	3733.87	105.03	0.00033987
3	0.0644	0.0627	0.2105	0.2063	0.0570	0.0562	1891.09	71.49	0.00067106
4	0.0553	0.0538	0.1918	0.1877	0.0500	0.0493	2548.80	86.08	0.00049790
5	0.0676	0.0666	0.2194	0.2153	0.0627	0.0618	2161.58	72.90	0.00058709
Avg							2591.75	84.87	0.00049939
SD							750.26	14.54	0.00013443
CR5.0/1	0.0738	0.0728	0.1295	0.1274	0.0668	0.0663	1037.76	49.16	0.00122286
2	0.0776	0.0766	0.1363	0.1341	0.0703	0.0695	427.09	27.39	0.00297137
3	0.0664	0.0657	0.1195	0.1179	0.0600	0.0594	411.90	26.62	0.00308096
4	0.0887	0.0875	0.1497	0.1472	0.0800	0.0793	729.23	39.04	0.00174023
5	0.0632	0.0621	0.1155	0.1134	0.0571	0.0564	455.49	29.12	0.00278611
Avg							569.78	33.21	0.00236031
SD							270.99	9.71	0.00082951

Appendix G UV-Visible Spectrum of Sulfosalicylic Acid Model Drug

A UV/Visible spectrophotometer (Shimadzu, UV-2550) was used to determine the maximum spectra of model drug. Model drug in aqueous solution was prepared for scanning the maximum absorption wavelength. The characteristic peak was observed. The absorbance value at the maximum wavelength of model drug was read and the correspondent model drug concentrations were calculated from the calibration curve with various model drug concentration. Figure G1 shows the characteristic peak at the wavelength of 298 nm.

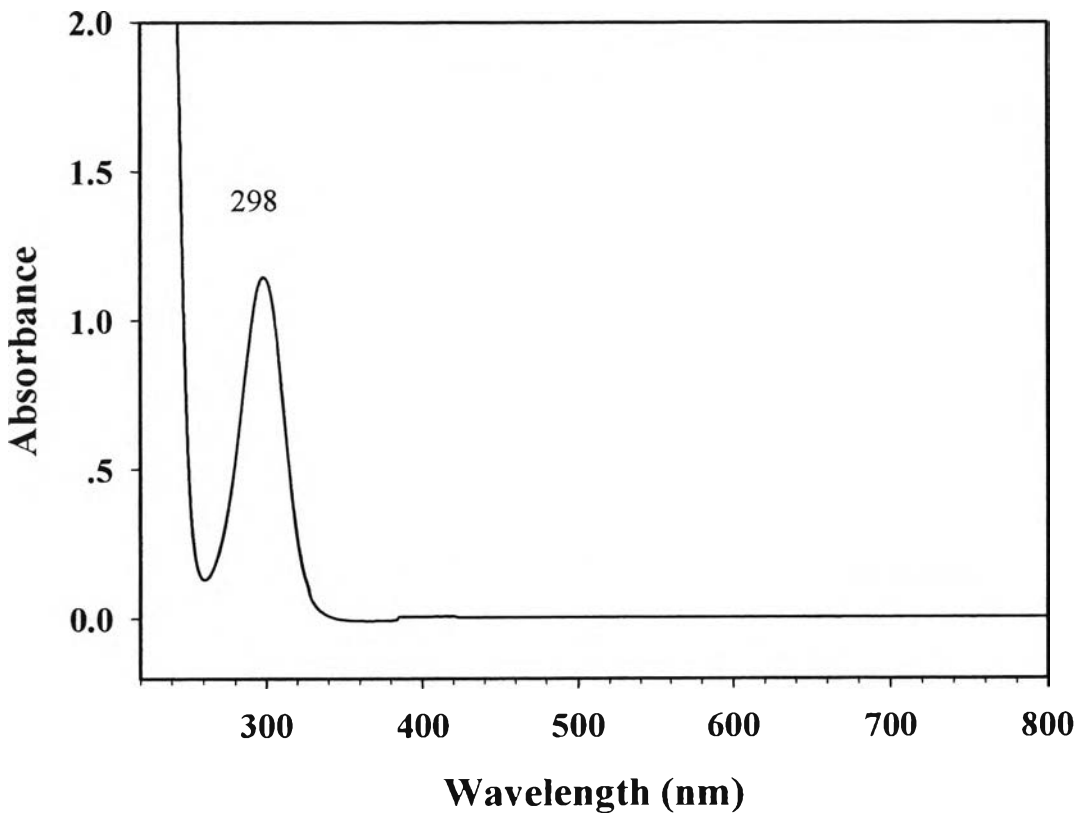

Figure G1 UV-Visible spectrum of 5-sulfosalicylic acid.

Appendix H Calibration curve of Sulfosalicylic Acid Model Drug

Table H1 Raw data of calibration curve of 5-sulfosalicylic acid at 298 nm

Concentration (ppm)	Absorbance (298 nm)
20	0.231
	0.232
	0.233
	0.232
	0.233
Average	0.2322
SD	0.00083666
40	0.496
	0.495
	0.494
	0.497
	0.498
Average	0.496
SD	0.001581139
60	0.716
	0.715
	0.712
	0.713
	0.71
Average	0.7132
SD	0.002387467
80	0.951
	0.95
	0.949
	0.951
	0.95
Average	0.9502
SD	0.00083666
100	1.179
	1.179
	1.181
	1.181
	1.187
Average	1.1814
SD	0.003286335

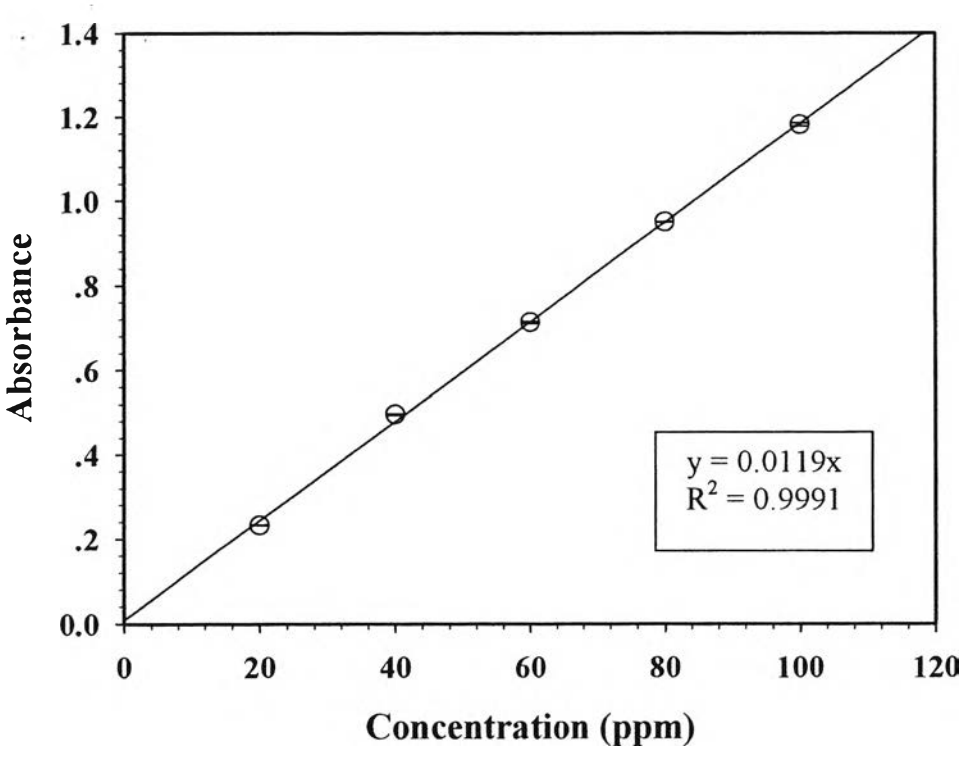

Figure H1 Calibration curve of 5-sulfosalicylic acid at 298 nm.

Appendix I Determination of Actual Drug Content

Initially, the actual amount of drug within the sample was measured. The actual amount of drug in the drug-loaded PVA 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 pipetted and added into 8 ml of the acetate buffer solution. The drug solution was measured for the amount of drug using the UV/Visible spectrophotometer at a wavelength of 298 nm.

The actual amount of drug present in the sample is reported as the percentage of the initial content of drug loaded in PVA solution. The actual amount of drug presented in the sample is about 93.1 ± 5.8 %.

Table I1 The raw data of the determination of actual amount of sulfosalicylic acid in the sample

Sample	Absorbance	Concentration (mg/l)	Diluted 8.5ml (mg)	dissolved in 4ml DMSO (mg)	Actual amount of drug (%)
D1	1.169	98.269	0.835	6.682	86.60
D2	1.221	102.605	0.872	6.977	90.42
D3	1.288	108.269	0.920	7.362	95.42 .
D4	1.349	113.345	0.963	7.707	99.89
Avg	1.257	105.622	0.898	7.182	93.08
SD	0.078	6.578	0.056	0.447	5.80

Appendix J Determination of Amounts and Diffusion Coefficient of Sulfosalicylic Acid Released from Sulfosalicylic Acid-Loaded Poly(vinyl alcohol) Hydrogel at Various Crosslinking Ratios

The custom built modified Franz-Diffusion cells were used for the diffusion studies. A diffusion cell consisted of two compartments; a donor compartment, which was exposed to an ambient condition, and a receptor compartment which was filled with the acetate buffer solution pH 5.5 and maintained at 37 °C by a circulating water bath. In the study of effect of crosslinking ratio, a unit of drug-loaded PVA hydrogel with various crosslinking ratios (0, 0.5, 2.5 and 5.0) was placed over the pig skin mounted on the receptor compartment. The drug diffused through the polymer matrix and the pig skin towards the solution. Sample of 0.3 ml was withdrawn at various time intervals simultaneously replaced with equal volume of fresh buffer solution. The drug concentrations in these samples were determined by the UV/Visible spectrophotometer at wavelength of 298 nm.

The amounts of sulfosalicylic acid released from sulfosalicylic acid- loaded poly(vinyl alcohol) hydrogel at time t vs. t at various crosslinking ratios (PVA_0, PVA_0.5, PVA_2.5, PVA_5.0) in an absence of electric field during 48 h is illustrated in Figure J1. The amount of released drug gradually increases with time and then reaches an equilibrium value.

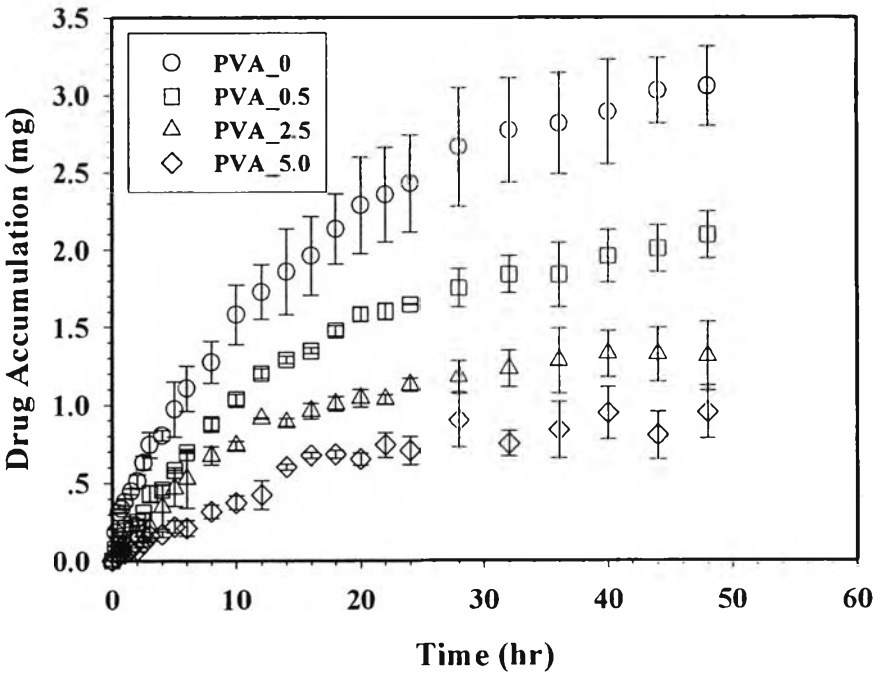

Figure J1 Amounts of sulfosalicylic acid release from sulfosalicylic acid-loaded poly(vinyl alcohol) hydrogel vs. time at various crosslink ratios, E = 0 V, pH 5.5, 37^0C, n = # samples =2.

Table J1 The raw data of the determination of amounts of sulfosalicylic acid released from PVA_0at time t, pH 5.5 at 37^0C, in an absence of electric field

Time	Absorbance		Drug Accumulation (mg)			
Hour	1	2	1	2	Average	SD
0	0.000	0.000	0.000	0.000	0.000	0.000
0.25	0.092	0.076	0.201	0.166	0.184	0.025
0.5	0.139	0.141	0.308	0.312	0.310	0.003
0.75	0.147	0.150	0.333	0.339	0.336	0.004
1	0.173	0.158	0.397	0.364	0.380	0.024
1.5	0.198	0.186	0.460	0.433	0.447	0.019
2	0.231	0.205	0.542	0.484	0.513	0.042
2.5	0.281	0.253	0.663	0.599	0.631	0.046
3	0.338	0.288	0.802	0.688	0.745	0.081
4	0.342	0.324	0.828	0.781	0.805	0.033
5	0.458	0.347	1.099	0.848	0.973	0.177
6	0.498	0.411	1.209	1.005	1.107	0.144
8	0.560	0.481	1.370	1.179	1.274	0.135
10	0.707	0.592	1.719	1.446	1.582	0.193
12	0.752	0.650	1.853	1.602	1.728	0.177
14	0.827	0.663	2.055	1.663	1.859	0.277
16	0.847	0.702	2.140	1.782	1.961	0.253
18	0.898	0.774	2.294	1.975	2.135	0.226
20	0.975	0.798	2.508	2.066	2.287	0.312
22	0.982	0.814	2.572	2.141	2.357	0.305
24	0.996	0.825	2.652	2.207	2.429	0.315
28	1.104	0.892	2.939	2.395	2.667	0.385
32	1.113	0.936	3.014	2.536	2.775	0.338
36	1.103	0.938	3.048	2.587	2.818	0.326
40	1.115	0.947	3.130	2.654	2.892	0.336
44	1.112	1.029	3.180	2.881	3.030	0.211
48	1.113	1.003	3.238	2.876	3.057	0.256

Table J2 The raw data of the determination of amounts of sulfosalicylic acid released from PVA_0.5 at time t, pH 5.5 at 37^0C, in an absence of electric field

Time	Absorbance		Drug Accumulation (mg)			
Hour	1	2	1	2	Average	SD
0	0.000	0.000	0.000	0.000	0.000	0.000
0.25	0.032	0.040	0.070	0.087	0.079	0.012
0.5	0.041	0.049	0.091	0.109	0.100	0.013
0.75	0.054	0.066	0.122	0.149	0.135	0.019
1	0.088	0.104	0.199	0.235	0.217	0.026
1.5	0.097	0.109	0.223	0.251	0.237	0.020
2	0.101	0.113	0.236	0.265	0.251	0.021
2.5	0.131	0.133	0.307	0.315	0.311	0.006
3	0.168	0.201	0.394	0.470	0.432	0.053
4	0.182	0.201	0.434	0.480	0.457	0.033
5	0.240	0.249	0.569	0.595	0.582	0.018
6	0.291	0.292	0.693	0.702	0.697	0.006
8	0.380	0.353	0.902	0.850	0.876	0.037
10	0.421	0.441	1.011	1.060	1.035	0.035
12	0.509	0.486	1.224	1.180	1.202	0.031
14	0.535	0.518	1.307	1.275	1.291	0.023
16	0.547	0.533	1.360	1.334	1.347	0.019
18	0.599	0.576	1.501	1.455	1.478	0.033
20	0.637	0.608	1.614	1.553	1.584	0.043
22	0.599	0.634	1.564	1.641	1.602	0.055
24	0.622	0.624	1.644	1.651	1.648	0.005
28	0.699	0.617	1.844	1.667	1.755	0.125
32	0.721	0.644	1.927	1.757	1.842	0.120
36	0.732	0.600	1.987	1.694	1.840	0.208
40	0.758	0.653	2.081	1.840	1.960	0.171
44	0.757	0.667	2.117	1.903	2.010	0.151
48	0.779	0.691	2.203	1.989	2.096	0.151

Table J3 The raw data of the determination of amounts of sulfosalicylic acid released from PVA_2.5 at time t, pH 5.5 at 37^0C, in an absence of electric field

Time	Absorbance		Drug Accumulation (mg)			
Hour	1	2	1	2	Average	SD
0	0.000	0.000	0.000	0.000	0.000	0.000
0.25	0.016	0.017	0.035	0.037	0.036	0.002
0.5	0.031	0.032	0.069	0.071	0.070	0.002
0.75	0.040	0.047	0.090	0.105	0.097	0.011
1	0.056	0.062	0.127	0.140	0.134	0.010
1.5	0.058	0.081	0.134	0.185	0.159	0.036
2	0.057	0.079	0.135	0.185	0.160	0.035
2.5	0.057	0.104	0.138	0.243	0.190	0.075
3	0.062	0.121	0.151	0.286	0.218	0.095
4	0.104	0.192	0.246	0.447	0.347	0.142
5	0.166	0.234	0.387	0.548	0.468	0.114
6	0.166	0.280	0.395	0.661	0.528	0.188
8	0.271	0.299	0.633	0.716	0.675	0.059
10	0.305	0.312	0.721	0.760	0.740	0.027
12	0.385	0.377	0.911	0.917	0.914	0.004
14	0.358	0.363	0.872	0.906	0.889	0.024
16	0.406	0.364	0.995	0.926	0.960	0.048
18	0.417	0.377	1.039	0.973	1.006	0.047
20	0.427	0.382	1.082	1.003	1.043	0.056
22	0.406	0.379	1.058	1.016	1.037	0.030
24	0.443	0.408	1.159	1.098	1.129	0.043
28	0.476	0.404	1.253	1.110	1.182	0.101
32	0.493	0.413	1.314	1.150	1.232	0.116
36	0.535	0.397	1.431	1.136	1.284	0.209
40	0.524	0.428	1.434	1.224	1.329	0.149
44	0.518	0.408	1.447	1.202	1.324	0.174
48	0.516	0.378	1.469	1.157	1.313	0.221

Table J4 The raw data of the determination of amounts of sulfosalicylic acid released from PVA_5.0 at time t, pH 5.5 at 37^0C, in an absence of electric field

Time	Absorbance		Drug Accumulation (mg)			
Hour	1	2	1	2	Average	SD
0	0.000	0.000	0.000	0.000	0.000	0.000
0.25	0.013	0.011	0.028	0.023	0.026	0.003
0.5	0.015	0.018	0.033	0.039	0.036	0.004
0.75	0.019	0.023	0.042	0.050	0.046	0.006
1	0.018	0.024	0.041	0.054	0.047	0.009
1.5	0.037	0.028	0.082	0.063	0.073	0.013
2	0.026	0.035	0.060	0.080	0.070	0.014
2.5	0.055	0.042	0.124	0.096	0.110	0.019
3	0.079	0.065	0.177	0.147	0.162	0.021
4	0.080	0.068	0.183	0.157	0.170	0.019
5	0.108	0.083	0.247	0.192	0.220	0.039
6	0.105	0.072	0.246	0.173	0.209	0.052
8	0.151	0.123	0.349	0.285	0.317	0.045
10	0.174	0.148	0.406	0.345	0.375	0.043
12	0.209	0.151	0.489	0.358	0.423	0.092
14	0.251	0.268	0.588	0.615	0.602	0.019
16	0.293	0.285	0.690	0.664	0.677	0.018
18	0.275	0.296	0.666	0.702	0.684	0.025
20	0.249	0.279	0.624	0.680	0.652	0.039
22	0.273	0.329	0.688	0.800	0.744	0.080
24	0.246	0.307	0.644	0.770	0.707	0.089
28	0.304	0.419	0.779	1.024	0.902	0.173
32	0.257	0.309	0.694	0.810	0.752	0.082
36	0.259	0.376	0.711	0.968	0.839	0.181
40	0.308	0.413	0.828	1.065	0.947	0.167
44	0.239	0.332	0.696	0.913	0.805	0.153
48	0.298	0.400	0.834	1.074	0.954	0.170

Release Kinetics of Model Drug from Drug-Loaded PVA Hydrogel

In order to study sulfosalicylic acid transport mechanism from the PVA hydrogels, two diffusion models are considered to fit the experimental data.

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

$$\frac{M_t}{M_\infty} = k_1 t^n \tag{1}$$

where M_t/M_∞ is the fractional drug release, k_1 is a kinetic constant and 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 the value of n is between 0.5 and 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:

$$\frac{M_t}{M_\infty} = k_H t^{1/2} \tag{2}$$

where M_t/M_∞ is the fractional drug release, k_H is a kinetic constant and t is the release time.

The diffusion coefficients of sulfosalicylic acid from the PVA hydrogels are calculated from the slopes of plots of drug accumulation *vs.* square root of time according to Higuchi's equation (A-sasutjarit *et al.*, 2005):

$$Q = 2C_0 (Dt/\pi)^{1/2} \tag{3}$$

where Q is the amount of material flowing through a unit cross-section of barrier in unit time, t; C_0 is the initial drug concentration in the hydrogel; and D is the diffusion coefficient of a drug.

The diffusion coefficients of each system were calculated from the slopes of the plot of the amounts of sulfosalicylic acid released from sulfosalicylic acid-loaded poly(vinyl alcohol) hydrogel at time t vs. $t^{1/2}$ at various crosslinking ratios (PVA_0, PVA_0.5, PVA_2.5, PVA_5.0) in an absence of electric field during 48 h using the Higuchi's equation (see figure J2).

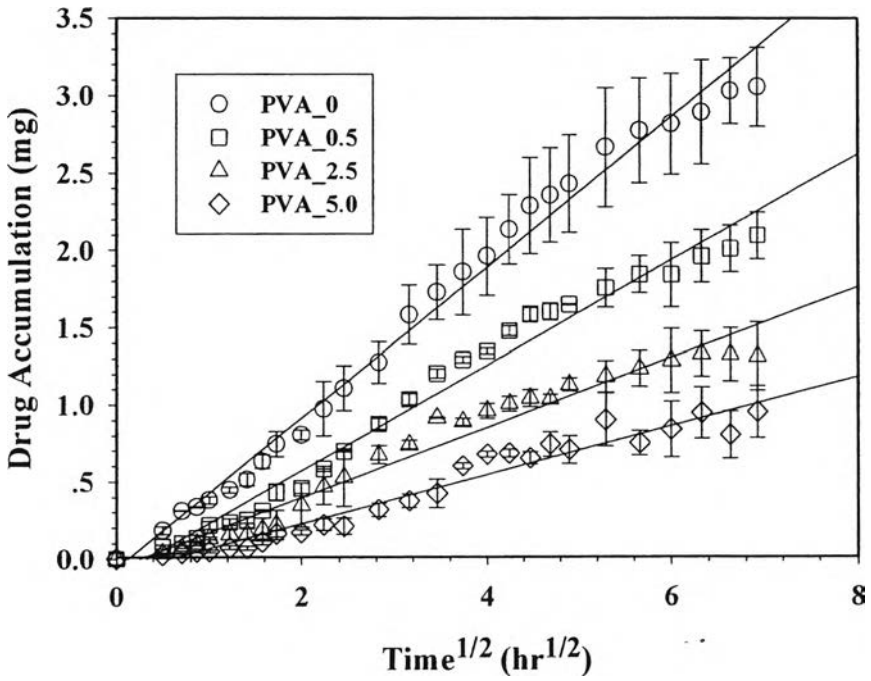

Figure J2 Amounts of sulfosalicylic acid release from sulfosalicylic acid-loaded poly(vinyl alcohol) hydrogel vs. $t^{1/2}$ at various crosslink ratios, E = 0 V, pH 5.5, 37^{0}C, n = # samples =2.

Figure J3 shows the diffusion coefficients of sulfosalicylic acid from poly(vinyl alcohol) hydrogels vs. crosslinking ratios and mesh size without electric field at 37 ^{0}C. From results, sulfosalicylic acid diffusion coefficients in each system are ranked in the following order: PVA_0 > PVA_0.5 > PVA_2.5 > PVA_5.0.

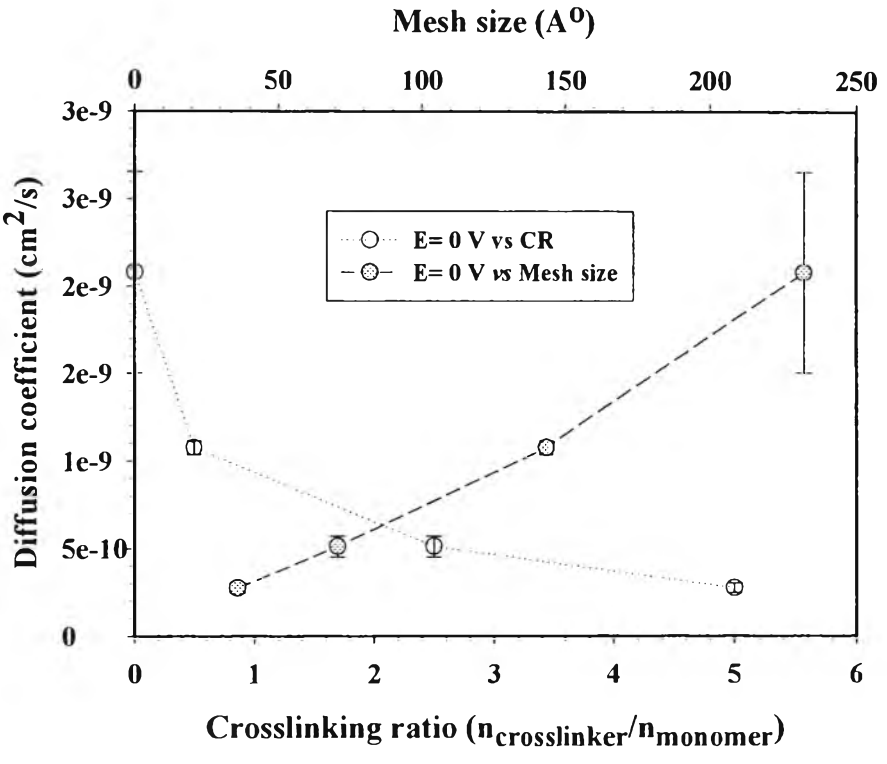

Figure J3 Diffusion coefficient of sulfosalicylic acid from poly(vinyl alcohol) hydrogels vs. crosslinking ratios and Mesh size without electric field , pH 5.5, 37 ^{0}C, n = # samples = 2.

Table J5 The raw data of the determination of the diffusion coefficient of sulfosalicylic acid released from various crosslinked PVA hydrogel, pH 5.5 at 37^{0}C, in an absence of electric field

Sample	Slope		Diffusion Coefficient (cm2/s)			
	1	2	1	2	Average	SD
PVA_0	0.5790	0.4751	2.49E-09	1.67E-09	2.08E-09	5.75E-10
PVA_0.5	0.3858	0.3762	1.10E-09	1.05E-09	1.08E-09	3.84E-11
PVA_2.5	0.2736	0.2520	5.55E-10	4.71E-10	5.13E-10	5.96E-11
PVA_5.0	0.1672	0.1796	2.56E-10	2.95E-10	2.76E-10	2.79E-11

Appendix K Determination of Amounts and Diffusion Coefficient of Sulfosalicylic Acid Released from Sulfosalicylic Acid-Loaded Poly(vinyl alcohol) Hydrogel at Various Crosslinking Ratios with Electric Field (E = 1 V)

The amounts of sulfosalicylic acid released from sulfosalicylic acid- loaded poly(vinyl alcohol) hydrogel at time t vs. t at various crosslinking ratios (PVA_0, PVA_0.5, PVA_2.5, PVA_5.0) at electric field strength 1 V during 48 h is illustrated in Figure K1. The amount of released drug gradually increases with time and then reaches an equilibrium value.

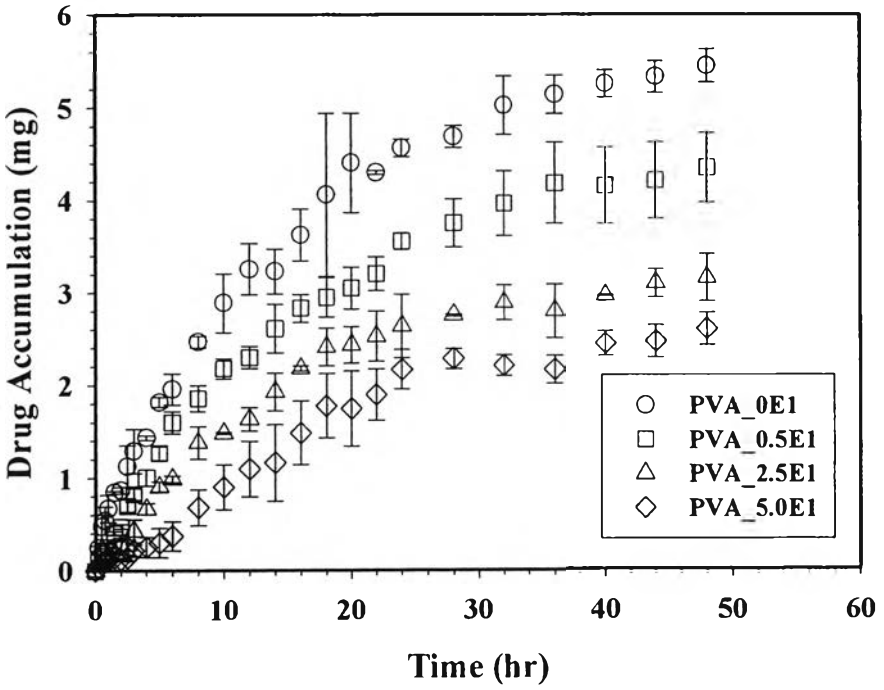

Figure K1 Amounts of sulfosalicylic acid release from sulfosalicylic acid-loaded poly(vinyl alcohol) hydrogel vs. time at various crosslink ratios, E = 1 V, pH 5.5, 37^0C, n = # samples =2.

Table K1 The raw data of the determination of amounts of sulfosalicylic acid released from PVA_0at time t, pH 5.5 at 37^0C, with the electric field (E = 1 V)

Time	Absorbance		Drug Accumulation (mg)			
Hour	1	2	1	2	Average	SD
0	0.000	0.000	0.000	0.000	0.000	0.000
0.25	0.080	0.068	0.262	0.223	0.243	0.028
0.5	0.115	0.173	0.383	0.572	0.478	0.134
0.75	0.128	0.192	0.434	0.647	0.541	0.151
1	0.165	0.226	0.565	0.773	0.669	0.147
1.5	0.243	0.246	0.833	0.856	0.845	0.016
2	0.240	0.252	0.842	0.894	0.868	0.037
2.5	0.272	0.365	0.965	1.284	1.124	0.225
3	0.313	0.409	1.120	1.456	1.288	0.237
4	0.406	0.387	1.448	1.414	1.431	0.024
5	0.497	0.512	1.777	1.853	1.815	0.054
6	0.576	0.495	2.074	1.836	1.955	0.168
8	0.697	0.663	2.514	2.424	2.469	0.063
10	0.726	0.858	2.662	3.114	2.888	0.320
12	0.830	0.941	3.057	3.450	3.254	0.278
14	0.812	0.905	3.061	3.404	3.232	0.242
16	0.904	1.012	3.424	3.823	3.623	0.282
18	0.887	1.251	3.437	4.683	4.060	0.881
20	1.046	1.253	4.025	4.784	4.404	0.537
22	1.110	1.072	4.314	4.285	4.300	0.020
24	1.140	1.153	4.496	4.632	4.564	0.096
28	1.146	1.169	4.602	4.771	4.687	0.120
32	1.179	1.286	4.797	5.243	5.020	0.316
36	1.212	1.269	4.994	5.285	5.139	0.206
40	1.232	1.262	5.151	5.358	5.255	0.146
44	1.221	1.261	5.208	5.450	5.329	0.171
48	1.226	1.270	5.317	5.575	5.446	0.182

Table K2 The raw data of the determination of amounts of sulfosalicylic acid released from PVA_0.5 at time t, pH 5.5 at 37^0C, with the electric field (E = 1 V)

Time	Absorbance		Drug Accumulation (mg)			
Hour	1	2	1	2	Average	SD
0	0.000	0.000	0.000	0.000	0.000	0.000
0.25	0.024	0.034	0.079	0.111	0.095	0.023
0.5	0.040	0.054	0.133	0.180	0.156	0.033
0.75	0.040	0.082	0.136	0.275	0.206	0.099
1	0.064	0.084	0.218	0.288	0.253	0.050
1.5	0.114	0.121	0.386	0.416	0.401	0.021
2	0.133	0.142	0.457	0.494	0.475	0.026
2.5	0.219	0.187	0.749	0.652	0.701	0.069
3	0.224	0.249	0.782	0.869	0.826	0.062
4	0.305	0.266	1.064	0.944	1.004	0.085
5	0.375	0.341	1.317	1.210	1.263	0.076
6	0.426	0.477	1.512	1.681	1.597	0.119
8	0.490	0.550	1.754	1.957	1.856	0.143
10	0.584	0.628	2.100	2.254	2.177	0.109
12	0.606	0.653	2.216	2.383	2.300	0.118
14	0.656	0.764	2.426	2.796	2.611	0.262
16	0.732	0.789	2.724	2.936	2.830	0.150
18	0.737	0.821	2.796	3.101	2.948	0.215
20	0.748	0.835	2.888	3.209	3.048	0.227
22	0.788	0.853	3.075	3.331	3.203	0.181
24	0.897	0.921	3.492	3.618	3.555	0.089
28	0.900	0.997	3.570	3.937	3.753	0.259
32	0.923	1.057	3.713	4.209	3.961	0.350
36	0.950	1.119	3.872	4.492	4.182	0.439
40	0.925	1.079	3.862	4.446	4.154	0.413
44	0.920	1.070	3.915	4.498	4.206	0.412
48	0.949	1.079	4.080	4.608	4.344	0.374

Table K3 The raw data of the determination of amounts of sulfosalicylic acid released from PVA_2.5 at time t, pH 5.5 at 37^0C, with the electric field (E = 1 V)

Time	Absorbance		Drug Accumulation (mg)			
Hour	1	2	1	2	Average	SD
0	0.000	0.000	0.000	0.000	0.000	0.000
0.25	0.014	0.017	0.046	0.056	0.051	0.007
0.5	0.024	0.026	0.080	0.086	0.083	0.005
0.75	0.031	0.036	0.104	0.121	0.113	0.012
1	0.056	0.049	0.189	0.167	0.178	0.016
1.5	0.057	0.055	0.196	0.190	0.193	0.004
2	0.096	0.062	0.328	0.217	0.273	0.079
2.5	0.090	0.067	0.316	0.238	0.277	0.055
3	0.149	0.097	0.516	0.341	0.429	0.124
4	0.178	0.207	0.622	0.709	0.666	0.061
5	0.272	0.250	0.944	0.866	0.905	0.055
6	0.287	0.274	1.014	0.963	0.989	0.036
8	0.354	0.433	1.255	1.505	1.380	0.177
10	0.417	0.413	1.488	1.472	1.480	0.011
12	0.479	0.425	1.723	1.543	1.633	0.127
14	0.574	0.488	2.071	1.782	1.926	0.204
16	0.600	0.592	2.199	2.159	2.179	0.028
18	0.694	0.611	2.553	2.266	2.410	0.202
20	0.684	0.605	2.572	2.293	2.433	0.198
22	0.712	0.603	2.716	2.332	2.524	0.271
24	0.746	0.608	2.881	2.394	2.638	0.344
28	0.688	0.706	2.747	2.761	2.754	0.010
32	0.755	0.687	3.019	2.752	2.886	0.188
36	0.732	0.621	3.001	2.588	2.794	0.292
40	0.703	0.718	2.961	2.953	2.957	0.006
44	0.760	0.711	3.201	2.984	3.093	0.153
48	0.782	0.690	3.331	2.969	3.150	0.256

Table K4 The raw data of the determination of amounts of sulfosalicylic acid released from PVA_5.0at time t, pH 5.5 at 37^0C, with the electric field (E = 1 V)

Time	Absorbance		Drug Accumulation (mg)			
Hour	1	2	1	2	Average	SD
0	0.000	0.000	0.000	0.000	0.000	0.000
0.25	0.008	0.012	0.026	0.038	0.032	0.009
0.5	0.019	0.024	0.061	0.078	0.069	0.012
0.75	0.028	0.032	0.092	0.105	0.098	0.010
1	0.030	0.039	0.100	0.130	0.115	0.021
1.5	0.034	0.050	0.115	0.168	0.141	0.037
2	0.034	0.036	0.117	0.127	0.122	0.007
2.5	0.032	0.047	0.114	0.164	0.139	0.036
3	0.048	0.076	0.167	0.261	0.214	0.066
4	0.050	0.096	0.177	0.330	0.254	0.108
5	0.052	0.119	0.187	0.411	0.299	0.158
6	0.074	0.140	0.261	0.487	0.374	0.159
8	0.161	0.241	0.545	0.820	0.682	0.195
10	0.215	0.314	0.729	1.071	0.900	0.242
12	0.258	0.380	0.883	1.305	1.094	0.299
14	0.248	0.417	0.870	1.452	1.161	0.411
16	0.358	0.493	1.240	1.725	1.482	0.343
18	0.440	0.574	1.528	2.021	1.774	0.348
20	0.408	0.564	1.458	2.031	1.745	0.405
22	0.473	0.569	1.696	2.088	1.892	0.277
24	0.562	0.628	2.016	2.319	2.167	0.215
28	0.609	0.626	2.207	2.359	2.283	0.107
32	0.570	0.589	2.128	2.287	2.207	0.113
36	0.534	0.570	2.055	2.270	2.162	0.152
40	0.612	0.639	2.343	2.532	2.438	0.134
44	0.596	0.640	2.337	2.583	2.460	0.173
48	0.623	0.668	2.468	2.719	2.593	0.178

Release Kinetics of Model Drug from Drug-Loaded PVA Hydrogel

In order to study sulfosalicylic acid transport mechanism from the PVA hydrogels, two diffusion models are considered to fit the experimental data.

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

$$\frac{M_t}{M_\infty} = k_1 t^n \tag{1}$$

where M_t/M_∞ is the fractional drug release, k_1 is a kinetic constant and 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, leading to zero-order release. When the value of n is between 0.5 and 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:

$$\frac{M_t}{M_\infty} = k_H t^{1/2} \tag{2}$$

where M_t/M_∞ is the fractional drug release, k_H is a kinetic constant and t is the release time.

The diffusion coefficients of sulfosalicylic acid from the PVA hydrogels are calculated from the slopes of plots of drug accumulation *vs.* square root of time according to Higuchi's equation (A-sasutjarit *et al.*, 2005):

$$Q = 2C_0(Dt/\pi)^{1/2} \tag{3}$$

where Q is the amount of material flowing through a unit cross-section of barrier in unit time, t; C_0 is the initial drug concentration in the hydrogel; and D is the diffusion coefficient of a drug.

The diffusion coefficients of each system are calculated from the slopes of the plot of the amounts of sulfosalicylic acid released from sulfosalicylic acid-loaded poly(vinyl alcohol) hydrogel at time t vs. $t^{1/2}$ at various crosslinking ratios (PVA_0, PVA_0.5, PVA_2.5, PVA_5.0) with the electric field 1 V during 48 h using the Higuchi's equation (see figure K2).

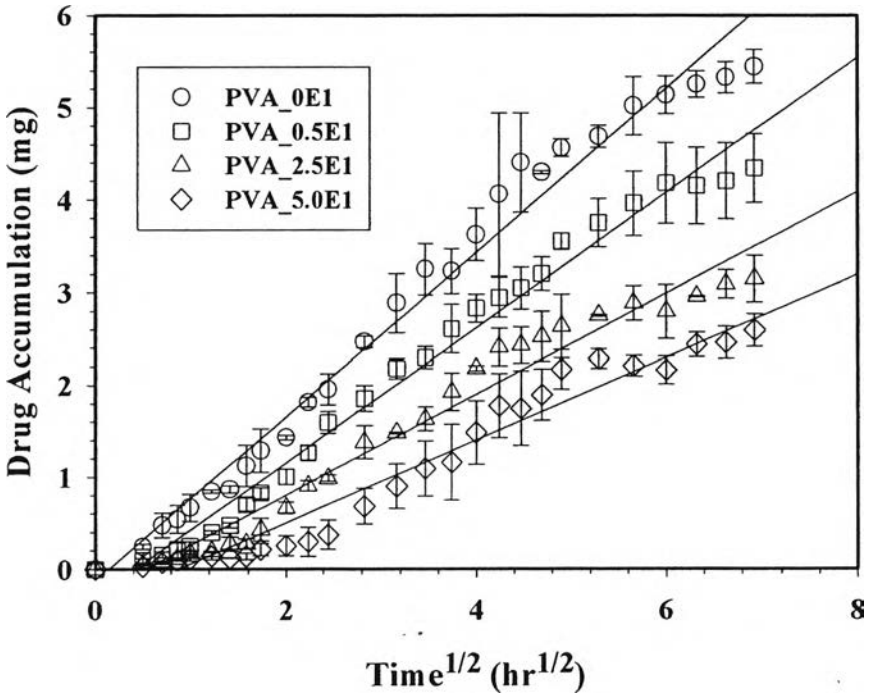

Figure K2 Amounts of sulfosalicylic acid release from sulfosalicylic acid-loaded poly(vinyl alcohol) hydrogel vs. $t^{1/2}$ at various crosslink ratios, E = 1 V, pH 5.5, 37^0C, n = # samples =2.

The diffusion coefficients of each system were calculated from the slopes of these plots using the Higuchi's equation (see figure K2). Figure K3 shows the diffusion coefficients of sulfosalicylic acid from poly(vinyl alcohol) hydrogels vs. crosslinking ratios and mesh size at electric field strength of 0 and 1 V at 37 ^{0}C. From results, sulfosalicylic acid diffusion coefficients of our systems are ranked in the following order: PVA_0 > PVA_0.5 > PVA_2.5 > PVA_5.0.

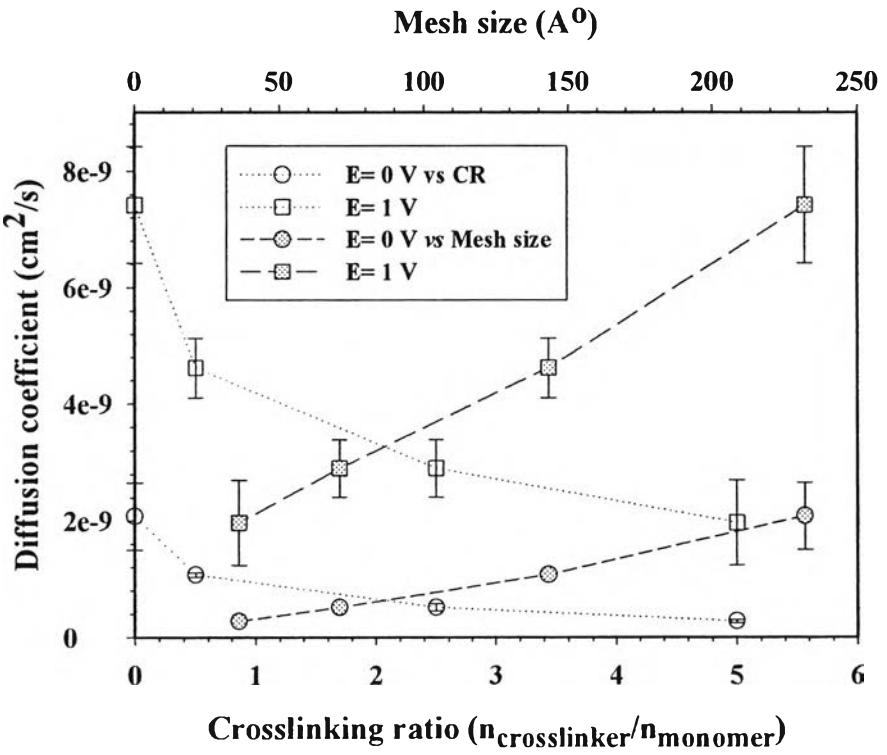

Figure K3 Diffusion coefficient of sulfosalicylic acid from poly(vinyl alcohol) hydrogels vs. crosslinking ratios and Mesh size at electric field strength of 0 and 1 V, pH 5.5, 37 ^{0}C, n = # samples = 2.

Table K5 The raw data of the determination of the diffusion coefficient of sulfosalicylic acid released from various crosslinked PVA hydrogel, pH 5.5, at 37^{0}C, E = 1 V.

Sample	Slope		Diffusion Coefficient (cm2/s)			
	1	2	1	2	Average	SD
PVA_0	0.9515	1.0468	6.72E-09	8.13E-09	7.42E-09	9.98E-10
PVA_0.5	0.7577	0.8196	4.26E-09	4.98E-09	4.62E-09	5.12E-10
PVA_2.5	0.6616	0.5866	3.25E-09	2.55E-09	2.9E-09	4.91E-10
PVA_5.0	0.3986	0.5209	1.46E-09	2.48E-09	1.97E-09	7.28E-10

Figure K4 shows the log-log plot of diffusion coefficients of sulfosalicylic acid from poly(vinyl alcohol) hydrogels vs. drug size/mesh size of hydrogel at electric field strength of 0 and 1 V at 37 ^{0}C. From these results, the scaling exponents m were determined from the following equation:

$$D = D_0 (a/\xi)^{-m} \tag{4}$$

where D is the diffusion coefficient of a drug, D_0 is the initial diffusion coefficient; a is the size of drug, ξ is the mesh size of hydrogel, and m is the scaling exponent. The scaling exponent m value of the system for the sulfosalicylic acid to diffuse through the poly(vinyl alcohol) matrix and the pig skin under electric field strength of 0 and 1 V are 1.07 and 0.71, respectively.

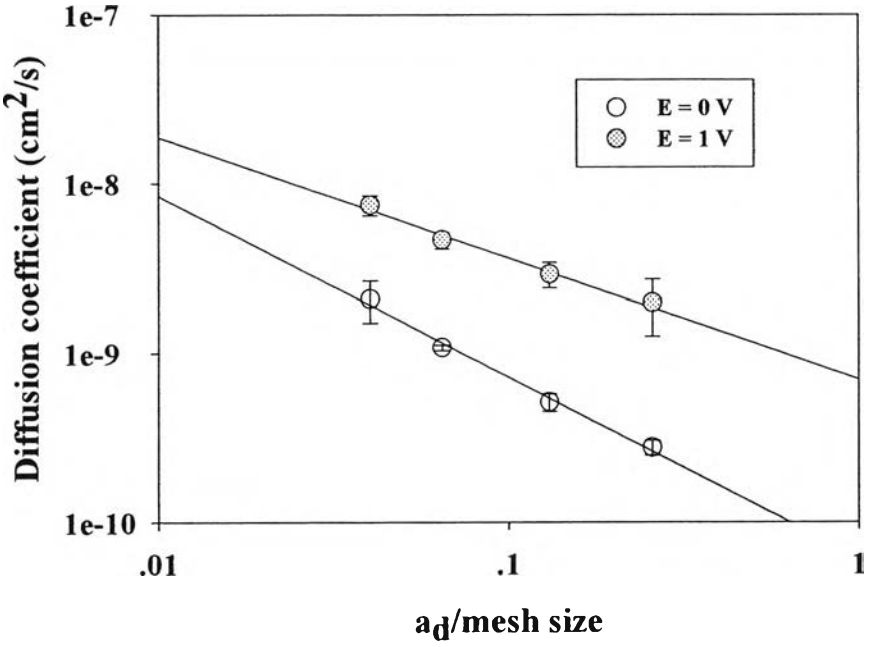

Figure K4 Diffusion coefficient of sulfosalicylic acid from poly(vinyl alcohol) hydrogels vs. drug size/mesh size of hydrogel at electric field strength of 0 and 1 V, pH 5.5, 37 ^{0}C, n = # samples = 2.

From a plot of ln M_t/M_∞ versus lnt, the scaling exponents n were determined from equation 1 as shown in table K6. The n value of uncrosslinked PVA hydrogel without electric field is near the Fickian exponent value of n = 0.5. Thus, sulfosalicylic acid release is controlled by Fickian diffusion mechanism and the change in their structure had effect on the mechanism of release.

Table K6 Release kinetic parameters and linear regression values obtained from fitting drug release experimental data to the Ritger-Peppas model

Sample	Crosslinking ratio	Diffusional exponent(n)		Kinetic constant (K)(hr^{-n})		r^2	
		E= 0 V	E= 1 V	E= 0 V	E= 1 V	E= 0 V	E= 1 V
PVA_0	0	0.58	0.63	0.1313	0.1197	0.9903	0.9842
PVA_0.5	0.5	0.72	0.83	0.0954	0.0708	0.9854	0.9831
PVA_2.5	2.5	0.77	0.93	0.1117	0.0549	0.8448	0.9720
PVA_5.0	5	0.82	0.93	0.0672	0.0429	0.8956	0.9466

Appendix L Determination of Amounts and Diffusion Coefficient of Sulfosalicylic Acid Released from Sulfosalicylic Acid-Loaded Poly(vinyl alcohol) Hydrogel at Various Electric Field Strength

Figure L1 shows the amounts of sulfosalicylic acid released from sulfosalicylic acid-loaded poly(vinyl alcohol) hydrogel with crosslinking ratio 0 at time t vs. $t^{1/2}$ at various electric field strengths under the negatively charge electrode (cathode). The data from figure L2 and L3 show that the amount of released drug and the diffusion coefficients increase with increasing electric field strength because a higher electrical current, higher force for driving the charged drug through the polymer matrix (Kantaria *et al.*, 1999).

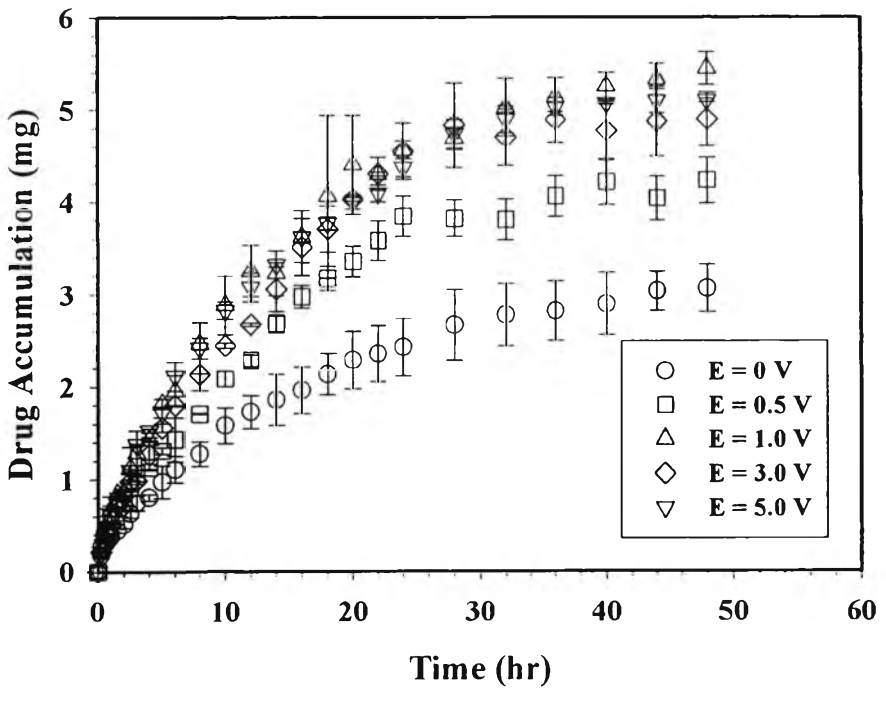

Figure L1 Amounts of sulfosalicylic acid release from sulfosalicylic acid-loaded poly(vinyl alcohol) hydrogel vs. time at various electric field strength, crosslinking ratio = 0, pH 5.5, 37^0C, n = # samples =2.

Table L1 The raw data of the determination of amounts of sulfosalicylic acid released from PVA_0at time t, pH 5.5 at 37^0C, with the electric field (E = 0 V)

Time	Absorbance		Drug Accumulation (mg)			
Hour	1	2	1	2	Average	SD
0	0.000	0.000	0.000	0.000	0.000	0.000
0.25	0.092	0.076	0.201	0.166	0.184	0.025
0.5	0.139	0.141	0.308	0.312	0.310	0.003
0.75	0.147	0.150	0.333	0.339	0.336	0.004
1	0.173	0.158	0.397	0.364	0.380	0.024
1.5	0.198	0.186	0.460	0.433	0.447	0.019
2	0.231	0.205	0.542	0.484	0.513	0.042
2.5	0.281	0.253	0.663	0.599	0.631	0.046
3	0.338	0.288	0.802	0.688	0.745	0.081
4	0.342	0.324	0.828	0.781	0.805	0.033
5	0.458	0.347	1.099	0.848	0.973	0.177
6	0.498	0.411	1.209	1.005	1.107	0.144
8	0.560	0.481	1.370	1.179	1.274	0.135
10	0.707	0.592	1.719	1.446	1.582	0.193
12	0.752	0.650	1.853	1.602	1.728	0.177
14	0.827	0.663	2.055	1.663	1.859	0.277
16	0.847	0.702	2.140	1.782	1.961	0.253
18	0.898	0.774	2.294	1.975	2.135	0.226
20	0.975	0.798	2.508	2.066	2.287	0.312
22	0.982	0.814	2.572	2.141	2.357	0.305
24	0.996	0.825	2.652	2.207	2.429	0.315
28	1.104	0.892	2.939	2.395	2.667	0.385
32	1.113	0.936	3.014	2.536	2.775	0.338
36	1.103	0.938	3.048	2.587	2.818	0.326
40	1.115	0.947	3.130	2.654	2.892	0.336
44	1.112	1.029	3.180	2.881	3.030	0.211
48	1.113	1.003	3.238	2.876	3.057	0.256

Table L2 The raw data of the determination of amounts of sulfosalicylic acid released from PVA_0at time t, pH 5.5 at 37^0C, with the electric field (E = 0.5 V)

Time	Absorbance		Drug Accumulation (mg)			
Hour	1	2	1	2	Average	SD
0	0.000	0.000	0.000	0.000	0.000	0.000
0.25	0.066	0.075	0.216	0.246	0.231	0.021
0.5	0.084	0.119	0.280	0.396	0.338	0.082
0.75	0.120	0.142	0.405	0.480	0.442	0.053
1	0.164	0.173	0.558	0.592	0.575	0.024
1.5	0.202	0.202	0.695	0.701	0.698	0.004
2	0.238	0.220	0.828	0.775	0.801	0.038
2.5	0.267	0.249	0.941	0.886	0.914	0.039
3	0.308	0.290	1.096	1.040	1.068	0.040
4	0.320	0.304	1.158	1.107	1.133	0.036
5	0.367	0.351	1.337	1.285	1.311	0.037
6	0.336	0.439	1.263	1.599	1.431	0.238
8	0.462	0.463	1.701	1.711	1.706	0.007
10	0.551	0.585	2.028	2.146	2.087	0.084
12	0.631	0.601	2.332	2.243	2.287	0.063
14	0.746	0.700	2.756	2.613	2.684	0.101
16	0.822	0.768	3.062	2.889	2.975	0.122
18	0.865	0.809	3.265	3.081	3.173	0.130
20	0.909	0.838	3.474	3.237	3.356	0.168
22	0.967	0.877	3.733	3.428	3.581	0.216
24	1.026	0.936	4.000	3.688	3.844	0.220
28	0.990	0.912	3.959	3.680	3.820	0.197
32	0.967	0.881	3.959	3.648	3.803	0.220
36	1.023	0.938	4.215	3.901	4.058	0.222
40	1.052	0.957	4.388	4.034	4.211	0.250
44	0.970	0.883	4.199	3.864	4.031	0.237
48	1.010	0.920	4.403	4.052	4.228	0.248

Table L3 The raw data of the determination of amounts of sulfosalicylic acid released from PVA_0at time t, pH 5.5 at 37^0C, with the electric field (E = 1.0 V)

Time	Absorbance		Drug Accumulation (mg)			
Hour	1	2	1	2	Average	SD
0	0.000	0.000	0.000	0.000	0.000	0.000
0.25	0.080	0.068	0.262	0.223	0.243	0.028
0.5	0.115	0.173	0.383	0.572	0.478	0.134
0.75	0.128	0.192	0.434	0.647	0.541	0.151
1	0.165	0.226	0.565	0.773	0.669	0.147
1.5	0.243	0.246	0.833	0.856	0.845	0.016
2	0.240	0.252	0.842	0.894	0.868	0.037
2.5	0.272	0.365	0.965	1.284	1.124	0.225
3	0.313	0.409	1.120	1.456	1.288	0.237
4	0.406	0.387	1.448	1.414	1.431	0.024
5	0.497	0.512	1.777	1.853	1.815	0.054
6	0.576	0.495	2.074	1.836	1.955	0.168
8	0.697	0.663	2.514	2.424	2.469	0.063
10	0.726	0.858	2.662	3.114	2.888	0.320
12	0.830	0.941	3.057	3.450	3.254	0.278
14	0.812	0.905	3.061	3.404	3.232	0.242
16	0.904	1.012	3.424	3.823	3.623	0.282
18	0.887	1.251	3.437	4.683	4.060	0.881
20	1.046	1.253	4.025	4.784	4.404	0.537
22	1.110	1.072	4.314	4.285	4.300	0.020
24	1.140	1.153	4.496	4.632	4.564	0.096
28	1.146	1.169	4.602	4.771	4.687	0.120
32	1.179	1.286	4.797	5.243	5.020	0.316
36	1.212	1.269	4.994	5.285	5.139	0.206
40	1.232	1.262	5.151	5.358	5.255	0.146
44	1.221	1.261	5.208	5.450	5.329	0.171
48	1.226	1.270	5.317	5.575	5.446	0.182

Table L4 The raw data of the determination of amounts of sulfosalicylic acid released from PVA_0at time t, pH 5.5 at 37^0C, with the electric field (E = 3.0 V)

Time	Absorbance		Drug Accumulation (mg)			
Hour	1	2	1	2	Average	SD
0	0.000	0.000	0.000	0.000	0.000	0.000
0.25	0.065	0.069	0.213	0.226	0.220	0.009
0.5	0.110	0.098	0.365	0.326	0.346	0.028
0.75	0.131	0.098	0.443	0.334	0.388	0.077
1	0.143	0.153	0.492	0.521	0.507	0.021
1.5	0.222	0.203	0.762	0.697	0.729	0.046
2	0.218	0.192	0.765	0.676	0.721	0.063
2.5	0.295	0.263	1.034	0.923	0.979	0.078
3	0.282	0.268	1.014	0.960	0.987	0.038
4	0.386	0.323	1.376	1.160	1.268	0.153
5	0.442	0.427	1.589	1.525	1.557	0.045
6	0.496	0.501	1.799	1.800	1.800	0.001
8	0.624	0.554	2.256	2.012	2.134	0.173
10	0.673	0.668	2.464	2.427	2.446	0.026
12	0.726	0.725	2.688	2.665	2.677	0.017
14	0.770	0.880	2.888	3.228	3.058	0.240
16	0.876	1.013	3.293	3.730	3.512	0.309
18	0.928	1.035	3.530	3.879	3.704	0.247
20	1.053	1.060	4.010	4.039	4.024	0.021
22	1.156	1.078	4.427	4.178	4.302	0.176
24	1.232	1.100	4.763	4.332	4.548	0.305
28	1.323	1.128	5.155	4.507	4.831	0.458
32	1.218	1.094	4.911	4.481	4.696	0.304
36	1.235	1.139	5.059	4.711	4.885	0.246
40	1.187	1.061	4.995	4.541	4.768	0.321
44	1.202	1.054	5.134	4.599	4.866	0.378
48	1.163	1.057	5.097	4.688	4.892	0.289

Table L5 The raw data of the determination of amounts of sulfosalicylic acid released from PVA_0at time t, pH 5.5 at 37^0C, with the electric field (E = 5.0 V)

Time	Absorbance		Drug Accumulation (mg)			
Hour	1	2	1	2	Average	SD
0	0.000	0.000	0.000	0.000	0.000	0.000
0.25	0.078	0.057	0.256	0.187	0.221	0.049
0.5	0.128	0.076	0.425	0.253	0.339	0.122
0.75	0.155	0.114	0.524	0.384	0.454	0.099
1	0.203	0.166	0.693	0.563	0.628	0.092
1.5	0.238	0.200	0.823	0.687	0.755	0.096
2	0.242	0.224	0.854	0.780	0.817	0.052
2.5	0.315	0.313	1.111	1.089	1.100	0.016
3	0.391	0.391	1.384	1.368	1.376	0.011
4	0.430	0.425	1.542	1.509	1.526	0.023
5	0.464	0.494	1.686	1.768	1.727	0.058
6	0.618	0.553	2.225	1.998	2.112	0.160
8	0.723	0.610	2.616	2.227	2.422	0.275
10	0.791	0.759	2.894	2.761	2.828	0.094
12	0.861	0.804	3.183	2.966	3.075	0.153
14	0.878	0.898	3.304	3.335	3.320	0.022
16	0.940	0.977	3.573	3.662	3.618	0.063
18	0.962	1.002	3.717	3.818	3.767	0.072
20	1.009	1.051	3.943	4.054	3.999	0.078
22	1.049	1.018	4.151	4.026	4.088	0.089
24	1.112	1.078	4.437	4.299	4.368	0.097
28	1.210	1.152	4.842	4.623	4.733	0.155
32	1.165	1.239	4.786	4.996	4.891	0.148
36	1.199	1.229	4.985	5.056	5.021	0.050
40	1.194	1.204	5.060	5.067	5.064	0.005
44	1.204	1.154	5.183	4.995	5.089	0.133
48	1.154	1.154	5.110	5.082	5.096	0.020

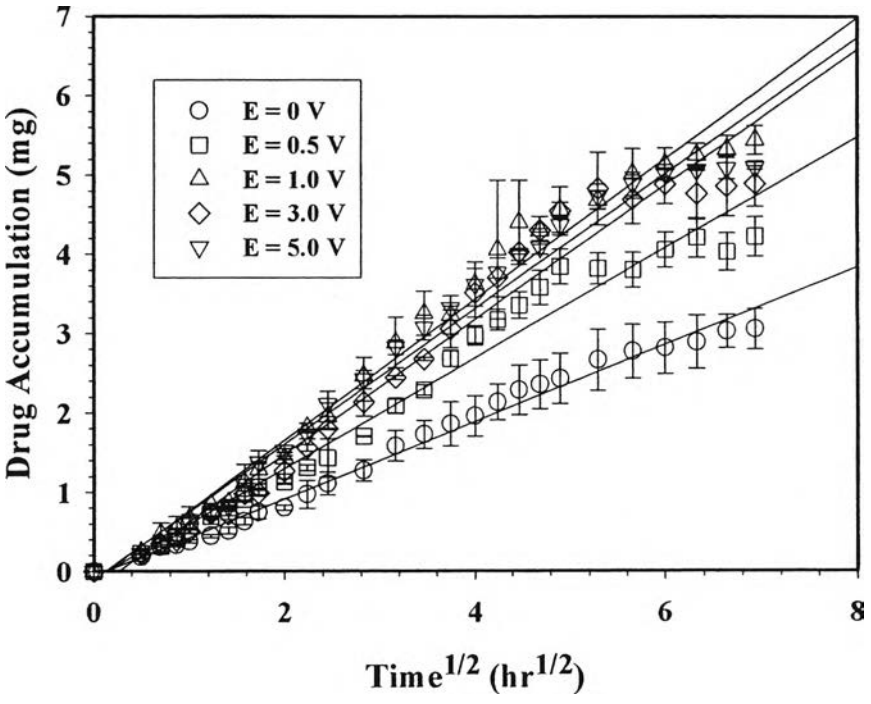

Figure L2 Amounts of sulfosalicylic acid release from sulfosalicylic acid-loaded poly(vinyl alcohol) hydrogel at time t vs. $t^{1/2}$ at various electric field strength, crosslinking ratio = 0 , pH 5.5, 37^{0}C, n = # samples = 2.

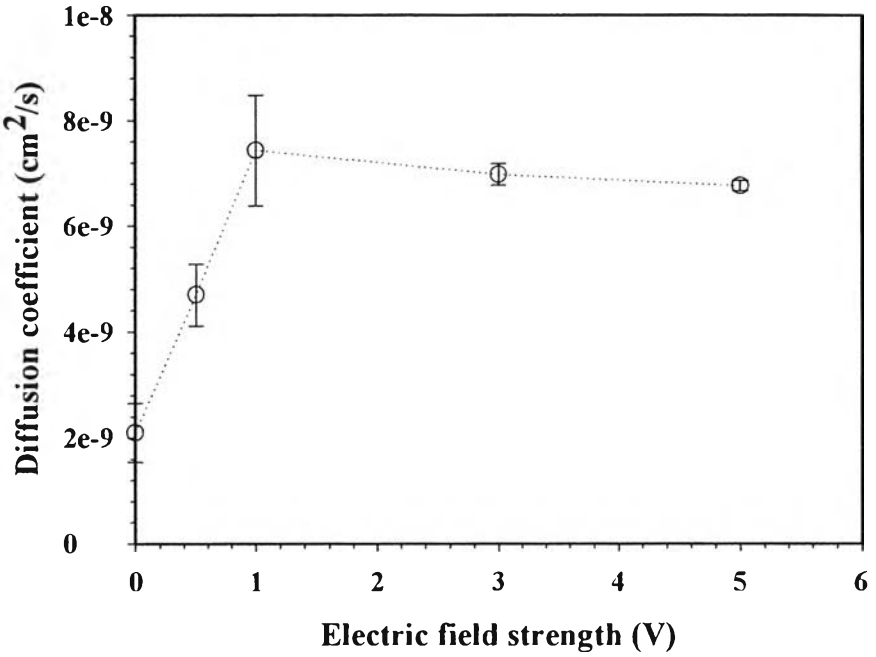

Figure L3 Diffusion coefficient of sulfosalicylic acid from poly(vinyl alcohol) hydrogels vs. electric field strength at crosslinking ratio of 0 , pH 5.5, 37 ^{0}C, n = # samples = 2.

Table L6 The raw data of the determination of the diffusion coefficient of sulfosalicylic acid released from various electric field strength, crosslinking ratio =0, pH 5.5, at 37^{0}C.

Sample	Slope		Diffusion Coefficient (cm2/s)			
E (V)	1	2	1	2	Average	SD
0	0.58	0.48	2.49E-09	1.71E-09	2.1E-09	5.56E-10
0.5	0.83	0.76	5.11E-09	4.28E-09	4.7E-09	5.84E-10
1	0.95	1.05	6.69E-09	8.18E-09	7.44E-09	1.05E-09
3	0.96	0.98	6.84E-09	7.12E-09	6.98E-09	2.03E-10
5	0.95	0.96	6.69E-09	6.84E-09	6.76E-09	1E-10

Appendix M Determination of Amounts and Diffusion Coefficient of Sulfosalicylic Acid Released from Sulfosalicylic Acid-Loaded Poly(vinyl alcohol) Hydrogel under The Positive Charge Electrode (Anode in Donor) and Negative Charge Electrode (Cathode in Donor)

Figures M1, M2 show the amounts of sulfosalicylic acid released from sulfosalicylic acid-loaded poly(vinyl alcohol) hydrogel with crosslinking ratio 0 at time t vs.t and $t^{1/2}$ under the positive charge electrode (anode in donor), negative charge electrode (cathode in donor) and no current system delivery over 48 h.

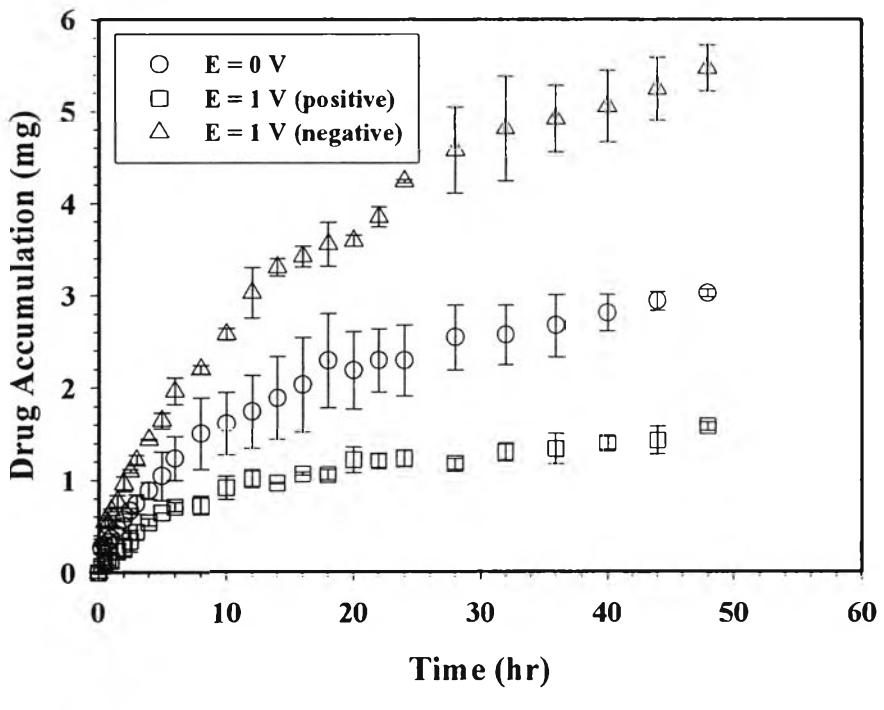

Figure M1 Amounts of sulfosalicylic acid release from sulfosalicylic acid-loaded poly(vinyl alcohol) hydrogel vs. time under the positive charge electrode (anode in donor), negative charge electrode (cathode in donor) and no current system crosslinking ratio = 0, pH 5.5, 37^0C, n = # samples =2.

Table M1 The raw data of the determination of amounts of sulfosalicylic acid released from PVA_0at time t, pH 5.5 at 37^0C, with the electric field (E = 0 V)

Time	Absorbance		Drug Accumulation (mg)			
Hour	1	2	1	2	Average	SD
0	0.000	0.000	0.000	0.000	0.000	0.000
0.25	0.106	0.134	0.232	0.293	0.262	0.043
0.5	0.108	0.151	0.241	0.337	0.289	0.067
0.75	0.123	0.163	0.280	0.371	0.325	0.064
1	0.140	0.175	0.323	0.405	0.364	0.058
1.5	0.206	0.206	0.474	0.481	0.478	0.005
2	0.241	0.248	0.561	0.584	0.572	0.016
2.5	0.292	0.270	0.685	0.644	0.664	0.029
3	0.345	0.273	0.815	0.664	0.740	0.107
4	0.399	0.339	0.950	0.822	0.886	0.091
5	0.519	0.347	1.233	0.857	1.045	0.266
6	0.585	0.434	1.403	1.065	1.234	0.239
8	0.743	0.500	1.778	1.231	1.504	0.387
10	0.759	0.553	1.850	1.372	1.611	0.338
12	0.820	0.581	2.022	1.461	1.741	0.397
14	0.885	0.617	2.205	1.569	1.887	0.450
16	0.950	0.649	2.392	1.670	2.031	0.511
18	1.048	0.755	2.654	1.934	2.294	0.509
20	0.945	0.718	2.482	1.891	2.186	0.418
22	0.948	0.776	2.536	2.054	2.295	0.341
24	0.940	0.743	2.566	2.021	2.294	0.385
28	1.021	0.851	2.791	2.295	2.543	0.351
32	1.001	0.853	2.798	2.342	2.570	0.323
36	1.029	0.876	2.910	2.435	2.673	0.336
40	1.022	0.961	2.947	2.665	2.806	0.199
44	1.027	1.029	3.009	2.862	2.935	0.104
48	1.022	1.064	3.050	2.990	3.020	0.042

Table M2 The raw data of the determination of amounts of sulfosalicylic acid released from PVA_0at time t, pH 5.5 at 37^0C, under anode, E = 1 V

Time	Absorbance		Drug Accumulation (mg)			
Hour	1	2	1	2	Average	SD
0	0.000	0.000	0.000	0.000	0.000	0.000
0.25	0.013	0.051	0.028	0.111	0.070	0.059
0.5	0.020	0.060	0.044	0.134	0.089	0.063
0.75	0.044	0.077	0.098	0.174	0.136	0.054
1	0.034	0.075	0.078	0.173	0.126	0.067
1.5	0.073	0.127	0.165	0.291	0.228	0.089
2	0.087	0.146	0.199	0.339	0.269	0.098
2.5	0.111	0.181	0.256	0.422	0.339	0.118
3	0.166	0.210	0.382	0.495	0.438	0.080
4	0.223	0.239	0.515	0.569	0.542	0.038
5	0.276	0.267	0.642	0.642	0.642	0.000
6	0.285	0.308	0.675	0.745	0.710	0.049
8	0.268	0.325	0.653	0.798	0.725	0.103
10	0.340	0.410	0.824	1.000	0.912	0.125
12	0.385	0.437	0.939	1.080	1.009	0.099
14	0.389	0.371	0.967	0.957	0.962	0.007
16	0.418	0.417	1.050	1.077	1.063	0.019
18	0.392	0.414	1.014	1.091	1.053	0.054
20	0.429	0.506	1.115	1.313	1.214	0.140
22	0.436	0.468	1.152	1.256	1.204	0.073
24	0.432	0.476	1.165	1.297	1.231	0.093
28	0.405	0.427	1.128	1.214	1.171	0.061
32	0.441	0.487	1.227	1.366	1.297	0.098
36	0.427	0.516	1.219	1.454	1.336	0.166
40	0.475	0.500	1.345	1.445	1.395	0.071
44	0.453	0.530	1.321	1.536	1.428	0.152
48	0.575	0.522	1.610	1.545	1.578	0.046

Table M3 The raw data of the determination of amounts of sulfosalicylic acid released from PVA_0at time t, pH 5.5 at 37^0C, under cathode, E = 1 V

Time	Absorbance		Drug Accumulation (mg)			
Hour	1	2	1	2	Average	SD
0	0.000	0.000	0.000	0.000	0.000	0.000
0.25	0.071	0.079	0.233	0.259	0.246	0.019
0.5	0.154	0.116	0.510	0.386	0.448	0.088
0.75	0.165	0.150	0.558	0.506	0.532	0.036
1	0.198	0.193	0.678	0.659	0.669	0.014
1.5	0.206	0.235	0.720	0.811	0.765	0.065
2	0.256	0.291	0.899	1.012	0.956	0.080
2.5	0.313	0.305	1.105	1.080	1.093	0.018
3	0.350	0.328	1.250	1.178	1.214	0.051
4	0.400	0.397	1.440	1.429	1.435	0.008
5	0.470	0.433	1.700	1.577	1.639	0.087
6	0.569	0.509	2.060	1.859	1.960	0.142
8	0.607	0.589	2.228	2.160	2.194	0.048
10	0.685	0.715	2.529	2.617	2.573	0.062
12	0.762	0.882	2.833	3.219	3.026	0.273
14	0.867	0.907	3.235	3.367	3.301	0.094
16	0.879	0.926	3.340	3.498	3.419	0.112
18	0.872	0.972	3.384	3.719	3.551	0.237
20	0.902	0.923	3.548	3.632	3.590	0.060
22	0.997	0.944	3.927	3.771	3.849	0.111
24	1.065	1.068	4.226	4.248	4.237	0.016
28	1.046	1.244	4.244	4.906	4.575	0.468
32	1.072	1.308	4.408	5.210	4.809	0.567
36	1.125	1.266	4.663	5.171	4.917	0.359
40	1.134	1.284	4.778	5.326	5.052	0.388
44	1.176	1.303	5.001	5.485	5.243	0.342
48	1.237	1.322	5.290	5.646	5.468	0.252

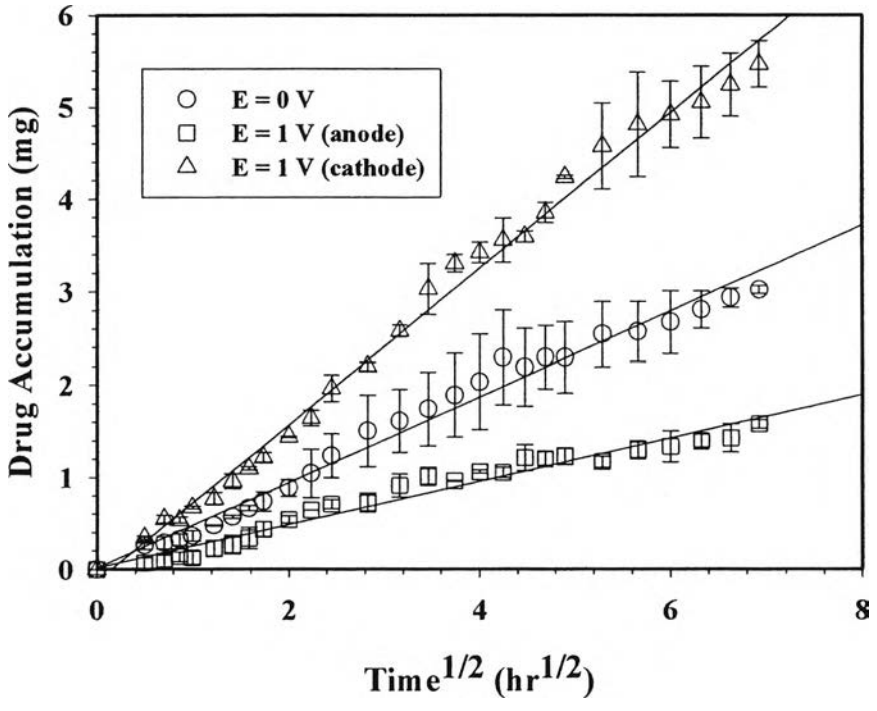

Figure M2 Amounts of sulfosalicylic acid release from sulfosalicylic acid-loaded poly(vinyl alcohol) hydrogel vs. $t^{1/2}$ under the positive charge electrode (anode in donor), negative charge electrode (cathode in donor) and no current system crosslinking ratio = 0, pH 5.5, 37^{0}C, n = # samples =2.

The diffusion coefficient under cathode is much higher than that under anode and no current (table M4) due to the electrorepulsion between charge drug and charge electrode driving the charged drug through the polymer matrix and the pig skin into the solution (Green *et al.*, 1996). Passive delivery (no current) result in low permeation similar to anodic delivery. Sulfosalicylic acid model drug has negative charge at pH 5.5 and this study establishes that it should be delivered under cathode.

Table M4 Diffusion coefficients of sulfosalicylic acid from poly(vinyl alcohol) hydrogels under anode and cathode

Electric field strength (V)	Slope		Diffusion Coefficient (cm2/s)			
	1	2	1	2	Average	SD
0	0.6102	0.4277	2.76E-09	1.36E-09	2.06E-09	9.93E-10
1(Anode)	0.2769	0.2844	5.69E-10	6.00E-10	5.84E-10	2.21E-11
1(Cathode)	0.8669	0.8970	5.57E-09	5.97E-09	5.77E-09	2.79E-10

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