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Matrix swelling: A simple model describing extent of swelling of HPMC matrices

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Abstract

The swelling of HPMC matrices was measured by determining the vertical displacement with time using a dial indicator. Curve fitting of the data of swelling was carried out by using the coupled Case I-Case II model. The thickness of the swollen layer formed around the matrix core was greater in HPMC compacts of higher viscosity grade. The rates of Case I (α_s coefficient) and Case II (β_s coefficient) swelling mechanisms increased with concentration and/or viscosity grade of HPMC.

Keywords: Hydroxypropylmethylcellulose; Swelling; Case I diffusion; Case II relaxation; Coupled Case I; Case II model; Viscosity

1. Introduction

Swelling measurements of cellulose and the relation between the rheological and swelling properties of cellulose were extensively discussed by Westman and Lindstrom (1981a,b,c,d). The swelling of cellulose was found to be influenced by cross-linking, heat treatment and pH of the liquid used. The swelling of core tablets during aqueous coating and a model describing the extent of swelling and water penetration for insoluble tablets containing a super-disintegrant was demonstrated by Faroongsarng and Peck (1991, 1992). Mitchell et al. (1991) showed that the swelling behaviour of cellulose ether matrices containing HPMC depends on the temperature, drug and polymer substitution type.

The swelling of HPMC-ibuprofen matrices could be described by a first-order kinetics (Wan et al., 1993a). Matrix swelling was affected by the concentration and viscosity grade of the polymer. On further examination, it was found that matrix swelling of HPMC-propranolol matrices deviates significantly from this $\sqrt{}$time relationship. In this study, the kinetics of matrix swelling was examined using the coupled Case I-Case II equation as was used for liquid uptake into these matrices (Wan et al., 1993b,c).

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2. Materials and methods

2.1. Materials

Propranolol hydrochloride (USP XXII) and ibuprofen (pharmaceutical grade, Italy) were chosen as model drugs to represent water-soluble and poorly water-soluble drugs, respectively.

Hydroxypropylmethylcelluloses, HPMC (Shin-Etsu Chemical Co., Japan) of different viscosity grades: 4000 (K4), 15000 (K15), 30000 (K30), 50000 (K50) and 100000 (K100) cps were used as matrix polymers. The apparent viscosities of 2% (w/v) aqueous solutions of the HPMC were 4380, 18200, 35800, 44400 and 100000 cps, respectively. The viscosity was determined by the USP XXII method.

2.2. Methods

2.2.1. Preparation of matrices

The drug and HPMC were thoroughly mixed in a mixing bag for 10 min. A weighed amount of the mixture was fed manually into the die of a single-punch tabletting machine (Manesty F3, UK) to produce a matrix tablet of 600 mg and porosity of 0.10 ± 0.01 using flat punches of diameter 14 mm for HPMC-ibuprofen matrices, and 300 mg and porosity of 0.15 ± 0.01 using flat punches of diameter 9.5 mm for HPMC-propranolol matrices. Matrices were prepared using the various viscosity grades of HPMC and with different concentrations of the drug.

2.2.2. Swelling studies

In a circular dish measuring 6.5 cm in diameter and 3.4 cm deep, the matrix was mounted between two filter papers (Whatman 54) and a glass cover slip was placed between the tip of the dial and the upper filter paper (Wan et al., 1993a). The whole assembly was placed in a water-bath thermostatically maintained at 37 ± 0.5°C. A fixed volume (50 ml) of the liquid, pre-equilibrated at 37 ± 0.5°C, was poured into the dish. The vertical increase in the matrix thickness was recorded with a dial indicator (Mitutoyo, 2118-50, Japan). For each formulation, the mean and standard deviation of the increase in thickness of three matrices were determined.

2.2.3. Treatment of data

All calculation was performed using SAS™ software on a personal computer.

3. Results and discussion

Taking a as the original thickness of the dry matrix, s as the thickness of the swollen matrix, the normalised increase in the matrix thickness, expressed as a percentage, δ, can be used as a swelling index where:

$$\delta = \frac{s - a}{a} \times 100\% \quad (1)$$

3.1. Kinetic models of the swelling mechanisms

The dynamic swelling of the matrix, represented by δ, as a function of time, t, was analyzed according to:

$$\log \delta = ns \log t + c_2 \quad (2)$$

where δ is the swelling index defined in Eq. 1, n_s is the exponent describing Fickian or anomalous swelling mechanism and c_2 is a constant. The values of c_2 and exponents n_s for the various formulations analyzed are given in Tables 1 and 2.

The swelling mechanism of HPMC-ibuprofen matrices in pH 7.2 buffer solution was approximately Case I (Fickian) with n_s clustering around 0.5 (Table 1). At very low HPMC concentration (5–10%), the estimation of n_s was less accurate, probably due to the limited number of data points collected for these matrices, in comparison with others. This was also true for n_s values observed in HPMC-propranolol matrices containing similar amount of HPMC (Table 2). This was because the amount of increase in matrix swelling in these matrices were very low and in some instances, the matrices collapsed after a maximum increase in thickness was attained. For HPMC-propranolol matrices, the swelling mechanism in water became non-Fickian with increasing amounts of

Table 1
Values of kinetic exponent (n_s), c_2 and correlation coefficient (r^2) following linear regression analysis of data from swelling studies of HPMC-ibuprofen matrices at pH 7.2

Viscosity grade	Percent HPMC	Log $\delta = n_s \log t + c_2$		
		n_s	c_2	r^2
K4	5	0.12±0.01	−2.45	0.8511
	10	0.30±0.00	−1.54	0.9853
	20	0.40±0.01	−0.88	0.9725
	30	0.41±0.01	−0.76	0.9867
	40	0.48±0.00	−0.99	0.9968
	50	0.50±0.00	−0.89	0.9968
	100	0.56±0.01	−1.44	0.9952
K15	5	0.16±0.01	−4.36	0.8473
	10	0.32±0.01	−1.86	0.9664
	20	0.42±0.01	−0.89	0.9834
	30	0.43±0.01	−0.82	0.9876
	40	0.47±0.00	−0.82	0.9970
	50	0.50±0.00	−1.05	0.9985
	100	0.58±0.00	−1.60	0.9977
K30	5	0.22±0.01	−2.25	0.9675
	10	0.37±0.01	−2.20	0.9535
	20	0.47±0.00	−1.28	0.9940
	30	0.45±0.00	−0.88	0.9944
	40	0.47±0.00	−0.70	0.9984
	50	0.48±0.00	−0.79	0.9992
	100	0.58±0.00	−1.45	0.9980
K50	5	0.52±0.02	−3.82	0.9435
	10	0.44±0.01	−2.47	0.9884
	20	0.42±0.00	−0.88	0.9942
	30	0.43±0.00	−0.69	0.9933
	40	0.47±0.00	−0.82	0.9970
	50	0.48±0.00	−0.72	0.9958
	100	0.60±0.01	−1.46	0.9956

HPMC (Table 2). This indicated the increasing importance of Case II relaxational mechanism to overall matrix swelling.

In order to ascertain the importance of the two swelling mechanisms to overall matrix swelling, the kinetics of swelling was re-evaluated by considering that the swelling of matrices depends on two processes: liquid diffusion into the matrix and polymer swelling due to the penetrant. Calculation of the approximate contributions of the two mechanisms to overall swelling process was carried out by fitting the data to the second order equation analogous to that proposed by Peppas and Sahlin (1989) for release from swellable matrices. The equation of the model is:

$$\delta = \alpha_s t^{1/2} + \beta_s t + c_3 \quad (3)$$

where the first term on the right-hand side represents Case I (Fickian) contribution and the second term is the Case II (relaxational) contribution, δ is the swelling index of matrix, α_s and β_s correspond to swelling rates of the Case I and Case II mechanisms respectively, c_3 is a constant and t is time. The goodness-of-fit of the swelling data was also tested according to two other models representing Case II alone (Eq. 4) and Case I alone (Eq. 5):

$$\delta = \beta'_s t + c_4 \quad (4)$$

$$\delta = \alpha'_s t^{1/2} + c_5 \quad (5)$$

Table 2
Values of kinetic exponent (n_s), c_2 and correlation coefficient (r^2) following linear regression analysis of data from swelling studies of HPMC-propranolol matrices in water

Viscosity grade	Percent HPMC	Log $\delta = n_s \log t + c_2$		
		n_s	c_2	r^2
K4	5	0.25±0.03	0.43	0.7739
	10	0.06±0.01	1.28	0.6502
	25	0.79±0.03	−3.78	0.9344
	50	0.64±0.02	−1.96	0.9±49
	75	1.58±0.08	−8.74	0.9036
K15	5	0.69±0.18	−3.19	0.4999
	10	0.50±0.02	−2.16	0.9327
	25	0.39±0.00	−0.55	0.9948
	50	0.89±0.03	−3.77	0.9502
	75	0.89±0.02	−3.37	0.9787
K30	5	0.11±0.04	0.57	0.2716
	10	0.16±0.00	0.74	0.9518
	25	0.36±0.00	−0.17	0.9898
	50	0.52±0.00	−0.81	0.9955
	75	0.63±0.00	−1.45	0.9993
K50	5	0.63±0.00	−1.45	0.9993
	10	0.40±0.05	−0.58	0.6735
	25	0.32±0.00	−0.22	0.9977
	50	0.52±0.00	−0.73	0.9981
	75	1.80±0.07	−10.21	0.9258
K100	5	1.16±0.12	−3.80	0.8807
	10	0.44±0.05	−1.05	0.6291
	25	0.29±0.00	0.51	0.9969
	50	1.17±0.03	−5.53	0.9528
	75	1.10±0.03	−4.73	0.9647

where β'_s and α'_s are the rate constants of Case II and Case I transport, respectively, and c_4 and c_5 are constants.

Tables 3 and 4 give the goodness-of-fit of the three models based on Eq. 3–5. As can be seen from the square of the correlation coefficients, the Case I model (Eq. 5) generally fits the swelling data better than the Case II model (Eq. 4). However, on further examination using the polynomial model (Eq. 3), the second-order polynomial equation gave the best data fit. As an example of the data obtained, plotting the swelling data as a function of time (Fig. 1) a good fit of the polynomial model to the actual data collected. Typically, the Case I model tends to overestimate the swelling index in the early stage and to underestimate the swelling index at a much later stage of the study. The converse is true for the Case II model. Based on these results, Eq. 3 is used subsequently for the analysis of all data on matrix swelling.

3.2. Swelling of HPMC

HPMC is a hydrophilic polymer. It swells on contact with water. The swelling of HPMC compacts of different viscosity grade were determined in pH 7.2. The thickness of swollen layer formed around the matrix core was greater in matrices containing HPMC of higher viscosity grade. The hydrodynamic volume occupied by the hydrated polymer chains is larger in high viscosity grade polymer. Consequently, greater swollen mass of the matrices was formed (Table 5).

Table 3
Values of correlation coefficient (r^2) following linear regression analysis of data from swelling studies of HPMC-ibuprofen matrices at pH 7.2 using Eq. 3–5

Viscosity grade	Percent HPMC	$\delta = \beta'_s t + c_4$	$\delta = \alpha'_s t^{1/2} + c_5$	$\delta = \alpha_s t^{1/2} + \beta_s t + c_3$
K4	5	0.3344	0.5535	0.8202
	10	0.9079	0.9875	0.9879
	20	0.9491	0.9940	0.9967
	30	0.9505	0.9963	0.9988
	40	0.9439	0.9987	0.9998
	50	0.9442	0.9985	0.9996
	100	0.9794	0.9831	0.9996
K15	5	0.4434	0.6712	0.8828
	10	0.9509	0.9863	0.9910
	20	0.9431	0.9974	0.9985
	30	0.9420	0.9985	0.9993
	40	0.9400	0.9992	0.9998
	50	0.9472	0.9983	0.9999
	100	0.9785	0.9841	0.9997
K30	5	0.8582	0.9683	0.9747
	10	0.9747	0.9776	0.9944
	20	0.9453	0.9983	0.9996
	30	0.9878	0.9976	0.9993
	40	0.9312	0.9998	0.9999
	50	0.9367	0.9996	0.9999
	100	0.9727	0.9887	0.9999
K50	5	0.7435	0.9242	0.9809
	10	0.9375	0.9977	0.9982
	20	0.9377	0.9989	0.9993
	30	0.9295	0.9987	0.9988
	40	0.9414	0.9989	0.9997
	50	0.9606	0.9936	0.9991
	100	0.9863	0.9749	0.9993

Table 4
Values of correlation coefficient (r^2) following linear regression analysis of data from swelling studies of HPMC-propranolol matrices in distilled water using Eq. 3–5

Viscosity grade	Percent HPMC	$\delta = \beta'_s t + c_4$	$\delta = \alpha'_s t^{1/2} + c_5$	$\delta = \alpha_s t^{1/2} + \beta_s t + c_3$
K4	5	0.4416	0.6870	0.9822
	10	0.1377	0.2897	0.5921
	25	0.8523	0.9815	0.9981
	50	0.8812	0.9912	0.9867
	75	0.9782	0.9555	0.9867
K15	5	0.3759	0.5869	0.7921
	10	0.7984	0.9444	0.9894
	25	0.8146	0.9696	0.9991
	50	0.8923	0.9821	0.9835
	75	0.9536	0.9917	0.9958
K30	5	0.1165	0.3253	0.9004
	10	0.5382	0.7253	0.9135
	25	0.7623	0.9433	0.9978
	50	0.8768	0.9919	0.9993
	75	0.9535	0.9944	0.9979
K50	5	0.8171	0.8819	0.8820
	10	0.4719	0.6928	0.9372
	25	0.8091	0.9659	0.9970
	50	0.9059	0.9959	0.9981
	75	0.9866	0.9967	0.9903
K100	5	0.7809	0.8696	0.8711
	10	0.5550	0.7640	0.9451
	25	0.7923	0.9559	0.9933
	50	0.9314	0.9891	0.9898
	75	0.9654	0.9870	0.9960

The swelling profiles of HPMC compacts could be accurately described by the polynomial model (Eq. 3), as shown by the results of linear regression analysis of HPMC compacts in Table 4. The coefficients of the Case I and Case II mechanisms on the HPMC compacts of various viscosity grades showed that the coefficients of the Case I mechanism were rather similar while that of the Case II mechanism was slightly larger for the HPMC K50 compact.

3.3. Swelling studies of matrices containing HPMC and ibuprofen as a poorly water-soluble drug

The plots of percent increase in matrix swelling against t for matrices containing ibuprofen and

Table 5
The swelling behaviour of HPMC compacts at pH 7.2

Viscosity grade	α_s ($\times 10^{-1}$) (%/$\sqrt{s}$)	β_s ($\times 10^{-3}$) (%/s)	y-intercept c_3	$\delta_{30\,min}$
K4	2.34 ± 0.04	3.68 + 0.08	0.32	16.67 ± 0.48
K15	2.30 ± 0.30	3.42 ± 0.06	0.21	15.97 ± 1.25
K30	3.00 ± 0.02	3.35 ± 0.04	0.03	18.77 ± 0.72
K50	2.30 ± 0.07	5.49 ± 0.16	0.48	20.06 ± 0.19

different amount of HPMC of various viscosity grades are presented in Fig. 2. The swelling of matrices increases with the concentration of polymer. Matrices containing 5% HPMC did not have sufficient polymer for significant measurable swelling of matrices to occur, the amount of swollen layer formed at 30 min ($\delta_{30\,min}$) being less than 1% of the original thickness (Table 6). A minimum amount of 20% HPMC was required for the matrices to swell to 10% of their initial thickness.

The swelling rates attributed to the Case I mechanism increased sharply when the HPMC concentration was varied from 5 to 50% of the total weight content (Fig. 3). The effect of HPMC concentration on swelling rates was less marked at higher polymer content (> 50% HPMC of high viscosity grade). A saturation state was attained beyond 40% HPMC content of these matrices. This is because as the HPMC becomes hydrated and forms a swollen gel, dissolution and surface erosion of this waterlogged gel occur simultaneously. The water uptake rate also slows down in very high polymer concentration as the swollen polymer can in turn affect the water uptake rate.

The contribution of the Case II mechanism to matrix swelling was relatively less than that of the Case I mechanism (Table 6). As observed in the case of Case I swelling rates, the rates of swelling of the Case II mechanism generally increased with HPMC concentration. It is interesting to note that negative rates were obtained for matrices containing 5% HPMC and 10% HPMC K4. This could be due to the partial collapse of matrices during swelling measurement which will be discussed shortly.

3.4. Swelling behaviour of matrices containing HPMC and propranolol as a water-soluble drug

The swelling behaviour of matrices containing HPMC of various viscosity grade and propranolol

Table 6
Effect of varying the amount of HPMC of various viscosity grade on the swelling of HPMC-ibuprofen matrices at pH 7.2

Viscosity grade	Percent HPMC	α_s [a] ($\times 10^{-2}$) (%/$\sqrt{s}$)	β_s [b] ($\times 10^{-4}$) (%/s)	y-intercept c_3	$\delta_{30\,min}$
K4	5	0.66 ± 0.05	−0.84 ± 0.09	0.09	0.20 ± 0.08
	10	4.36 ± 0.22	0.46 ± 0.38	0.37	2.17 ± 0.23
	20	16.38 ± 0.56	6.68 ± 0.98	0.67	8.96 ± 0.52
	30	20.07 ± 0.42	7.93 ± 0.72	0.77	10.82 ± 1.34
	40	29.48 ± 0.24	7.12 ± 0.41	0.25	14.13 ± 1.36
	50	36.49 ± 0.39	9.10 ± 0.68	0.19	17.36 ± 1.32
K15	5	0.14 ± 0.01	−0.17 ± 0.02	0.01	0.04 ± 0.02
	10	2.82 ± 0.17	1.68 ± 0.30	0.31	1.76 ± 0.15
	20	19.97 ± 0.42	4.96 ± 0.74	0.54	10.04 ± 1.07
	30	24.74 ± 0.34	5.31 ± 0.60	0.52	12.01 ± 0.66
	40	32.03 ± 0.26	5.59 ± 0.45	0.37	15.03 ± 1.49
	50	32.02 ± 0.15	9.65 ± 0.26	0.15	15.58 ± 0.88
K30	5	1.26 ± 0.08	−0.52 ± 0.13	0.16	0.59 ± 0.14
	10	2.41 ± 0.16	3.87 ± 0.29	0.27	2.00 ± 0.43
	20	19.94 ± 0.42	5.38 ± 0.37	0.23	9.72 ± 0.53
	30	24.19 ± 0.35	7.85 ± 0.61	0.59	12.35 ± 2.58
	40	39.44 ± 0.21	1.67 ± 0.37	0.28	17.33 ± 0.42
	50	38.08 ± 0.18	4.60 ± 0.32	0.26	17.10 ± 1.68
K50	5	4.47 ± 0.16	−3.80 ± 0.28	−0.14	1.06 ± 0.33
	10	4.99 ± 0.11	0.79 ± 0.20	0.11	2.35 ± 0.25
	20	21.21 ± 0.30	3.07 ± 0.51	0.57	10.19 ± 0.53
	30	27.87 ± 0.48	0.93 ± 0.84	0.71	12.71 ± 0.42
	40	34.53 ± 0.32	6.86 ± 0.56	0.68	16.49 ± 0.71
	50	31.65 ± 0.64	20.73 ± 1.11	0.79	17.92 ± 0.57

[a] $p < 0.0001$.
[b] Not significant.

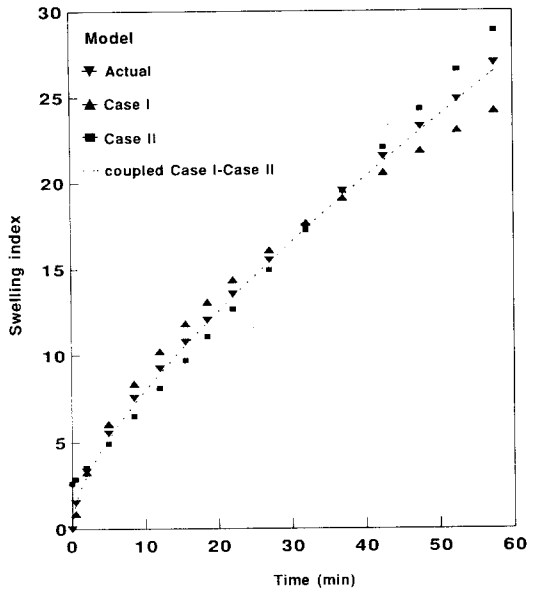

Fig. 1. A typical graph showing the goodness-of-fit of various models compared to the actual swelling data of HPMC K4 compact at pH 7.2.

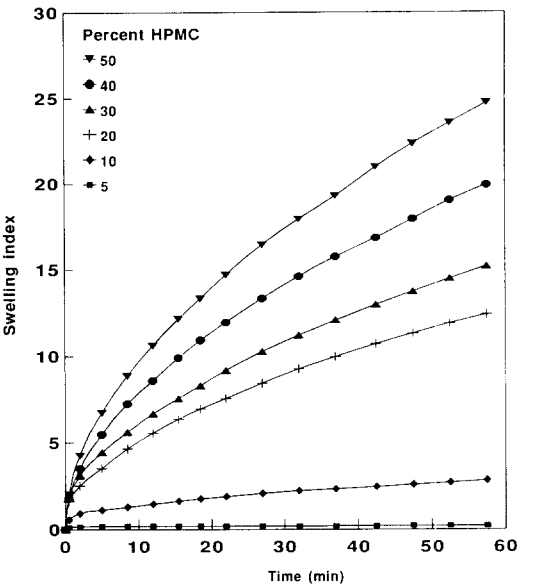

Fig. 2. Effect of variation of amounts of HPMC K4 on the swelling of HPMC-ibuprofen matrices at pH 7.2.

Table 7
Swelling profiles of HPMC-propranolol matrices containing varying amounts of HPMC in distilled water

Viscosity grade	Percent HPMC	α_s ($\times 10^{-1}$) (%/$\sqrt{s}$)	β_s ($\times 10^{-2}$) (%/s)	y-intercept c_{27}	$\delta_{30\,min}$
K4	5	9.68 ± 0.38	−4.79 ± 0.26	−0.01	0.00 ± 0.00
	10	1.40 ± 0.17	−0.20 ± 0.03	3.52	5.56 ± 0.89
	25	2.47 ± 0.04	−0.14 ± 0.01	−1.06	10.14 ± 2.28
	50	4.59 ± 0.10	−0.17 ± 0.02	−1.25	15.37 ± 2.35
	75	1.97 ± 0.31	0.66 ± 0.06	−2.06	19.25 ± 0.89
K15	5	2.38 ± 0.42	−1.36 ± 0.34	−0.28	0.00 ± 0.00
	10	1.84 ± 0.07	−0.32 ± 0.02	−0.22	0.91 ± 1.57
	25	3.35 ± 0.03	−0.23 ± 0.00	−0.27	10.14 ± 2.28
	50	5.05 ± 0.28	−0.11 ± 0.05	−2.91	17.27 ± 1.12
	75	4.83 ± 0.17	0.26 ± 0.03	−2.29	23.68 ± 1.00
K30	5	8.13 ± 0.72	−5.64 ± 0.59	0.10	1.87 ± 1.96
	10	3.10 ± 0.22	−0.60 ± 0.06	1.81	2.31 ± 3.83
	25	4.28 ± 0.53	−0.36 ± 0.09	0.52	11.95 ± 1.78
	50	6.56 ± 0.06	−0.28 ± 0.01	−0.99	21.94 ± 0.33
	75	4.53 ± 0.15	0.26 ± 0.03	−1.25	27.07 ± 2.29
K50	5	2.53 ± 0.95	0.10 ± 0.90	−0.34	0.00 ± 0.00
	10	5.83 ± 0.37	−1.66 ± 0.14	−0.09	2.31 ± 2.73
	25	4.22 ± 0.07	−0.30 ± 0.01	1.38	13.67 ± 0.12
	50	6.21 ± 0.11	−0.13 ± 0.02	−0.63	23.51 ± 0.46
	75	1.44 ± 0.30	0.85 ± 0.05	−1.76	20.99 ± 2.62
K100	5	4.03 ± 1.33	−0.49 ± 1.27	−0.49	0.00 ± 0.00
	10	4.18 ± 0.23	−0.80 ± 0.07	−0.16	3.84 ± 2.34
	25	4.50 ± 0.11	−0.34 ± 0.02	2.04	14.57 ± 0.12
	50	4.80 ± 0.26	0.09 ± 0.04	−2.97	19.77 ± 0.20
	75	4.97 ± 0.23	0.47 ± 0.04	−2.88	27.60 ± 0.66

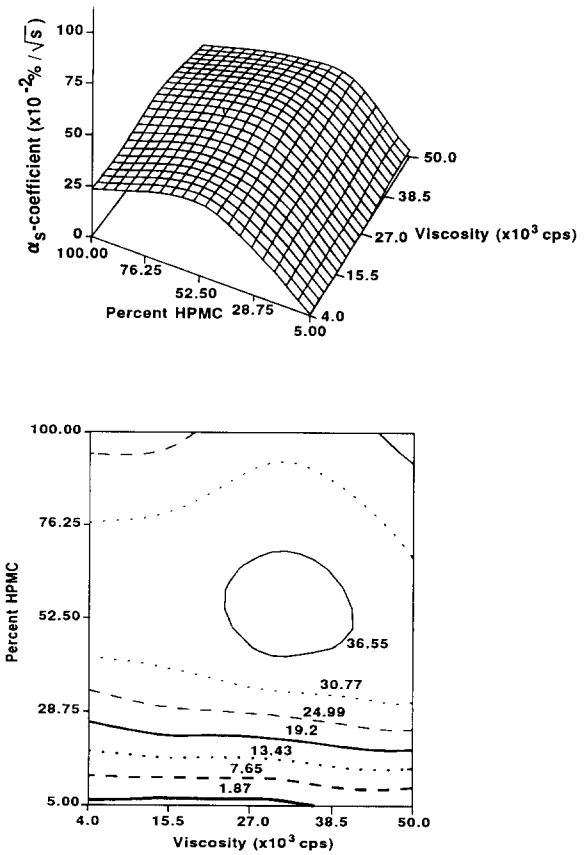

Fig. 3. Surface and contour plots depicting the effect of concentration and viscosity of HPMC on the α_s coefficient of HPMC ibuprofen matrices at pH 7.2.

in distilled water was studied. Swelling of matrices was faster during the first few minutes for matrices containing a low polymer content (5–10%). This was due to a faster hydration of these matrices with abundant soluble drug. When the swelling measurement was allowed to extend over a longer period, matrices containing a low HPMC level swelled to a maximum thickness. This was followed by a period of constant swelling rate before a reduction in the δ values was achieved. The swollen mass diminished in thickness and slowly collapsed. This observation was often seen in matrices with polymer content $\leq 10\%$ and can be attributed to dissolution of the water-soluble drug. The thickness of the swollen layer around the matrix core varied with the polymer content of the matrix systems. The percent swelling at 30 min, $\delta_{30\ \mathrm{min}}$ was used to compare the influence of HPMC concentration and viscosity grade on the swelling behaviour of HPMC-propranolol matrices (Table 7). Generally, $\delta_{30\ \mathrm{min}}$ increased with the concentration of polymer in the formulations. The amount of gelatinous layer formed also varied with the viscosity grade of HPMC used, generally a thicker layer of swollen mass was obtained with matrices containing similar HPMC content of higher viscosity grade.

The measurement of matrix swelling involved the use of a gauge to record the vertical increase in the thickness of the swollen mass. In response to the swelling pressure of the matrix with time, the compression of the tip of the gauge would result in a constant back pressure (1.47 N) on the swelling matrix. If the upward swelling force of the matrix were low, the opposing back pressure would result in a lower reading. This produced negative values of Case II coefficients due to an underestimation of the extent of matrix swelling. In matrices with low HPMC content, leaching of drug weakened the swollen mass. As the matrix swelled, the drug-depleted swollen mass increased in volume and the swollen structure weakened. Hydration of the polymer caused a viscous gelatinous layer to be formed around the matrix. This could act as a shield that regulated liquid entry into the matrix. The matrix core was not wetted and remained dry. The swollen peripheral layer and the inner dry core were distinctly separate under light microscopic examination.

Two opposing forces occur in the matrix when polymer swells. The adhesive force of HPMC binds the matrix together. As the particle swells, the matrix experiences intramatrix swelling force promoting disintegration. The amount of gel-forming substance was small in matrices with a low polymer content ($< 10\%$). On the other hand, these matrices had a large amount of highly soluble drug ($> 90\%$). A continuous HPMC gel was not formed and pockets of polymer mass were found within the matrix. Dissolution of drug created void spaces within the swollen portion of the matrix. This further weakened the gel structure. In the meantime, water continued to enter the matrix. When the water-logged matrix could not

support the amount of fluid in the matrix, the swollen mass collapsed due to the small back pressure exerted by the gauge. This observation was often seen in matrices containing the soluble drug, propranolol or with low HPMC content (5–10% HPMC in HPMC-ibuprofen matrices).

In the initial stage (< 5 min), HPMC-propranolol matrices with ≥ 25% polymer swelled slower than those with a lower polymer content. A high amount of propranolol improved the surface wetting of the matrix. This difference in the swelling profiles can be contrasted by comparing with the swelling profiles of HPMC-ibuprofen matrices.

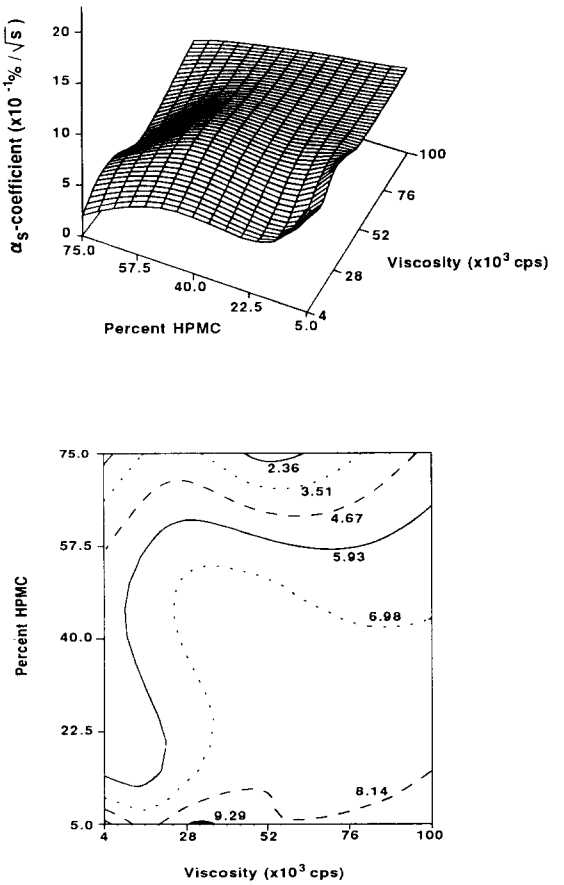

Fig. 4. Surface and contour plots depicting the effect of concentration and viscosity of HPMC on the α_s coefficient of HPMC-propranolol matrices.

The swelling characteristics of HPMC-propranolol matrices could be described by a polynomial equation (Eq. 3). The coefficients of both Case I and Case II mechanisms generally increased when the concentration and/or viscosity grade of HPMC were increased (Table 7). Unlike HPMC-ibuprofen matrices, the coefficients of the Case I mechanism of HPMC-propranolol matrices did not increase proportionally to the HPMC content but exhibited a minimum-maximum relationship (Fig. 4). This was due to the difference in drug solubilities of the matrices. The structure of the swollen mass of HPMC-ibuprofen matrices was more rigid and firmer than that of HPMC-propranolol matrices. Being a highly soluble drug, more propranolol leached out of the swollen mass compared to the poorly water-soluble drug, ibuprofen. Leaching of drug left behind a highly porous and weak matrix structure. The back pressure exerted by the gauge on the swollen mass compressed the swollen mass. In the cases of matrices with 5% polymer, the amount of swollen mass formed was small. Swelling of HPMC in the matrices was not summative. Isolated HPMC gel pockets formed as HPMC swelled were responsible for the very high α_s coefficients obtained (Fig. 4). A rather linear portion of the graph between 10 and 25% indicates the effect of increasing polymer content on the Case I swelling coefficients. In matrices with high polymer concentration (> 25%), the highly porous swollen mass was severely compressed and the thickness of the swollen layer was reduced. The tortuosity of the matrix was increased. The rate of Case I diffusion of liquid into the matrix was therefore reduced.

4. Conclusions

The swelling characteristics of HPMC matrices were described by a polynomial equation. The coefficients of both Case I and Case II mechanisms generally increased when the concentration and/or viscosity grade of HPMC were increased. For HPMC-ibuprofen matrices, the swelling rates attributed to the Case I mechanism increased sharply when the HPMC concentration was varied from 5 to 50% of total weight content. The

effect of HPMC concentration on swelling rates was less marked at higher polymer content (> 50% HPMC of high viscosity grade). A saturation state was attained beyond 40% HPMC content of these matrices. Unlike HPMC-ibuprofen matrices, the coefficients of the Case I mechanism of HPMC-propranolol matrices did not increase in proportion to HPMC content but exhibited a minimum-maximum relationship. This was due the difference in drug solubilities in the matrices.

References

Faroongsarng, D. and Peck, G.E., The swelling of core tablets during aqueous coatings: I. A simple model describing extent of swelling and water penetration for insoluble tablets containing a superdisintegrant. *Drug Dev. Ind. Pharm.*, 17 (1991) 2439–2455.

Faroongsarng, D. and Peck, G.E., The swelling of core tablets during aqueous coating: II. An application of the model describing extent of swelling and water penetration for insoluble tablets. *Drug Dev. Ind. Pharm.*, 18 (1992) 1527.

Mitchell, K., Ford, J.L., Roston, C., Armstrong, D.J., Elliot, P.N.C. and Hogan, J.E., Swelling behaviour of cellulose ether matrix tablets. *J. Pharm. Pharmacol.*, 43 (1991) 76P.

Peppas, N.A. and Sahlin, J.J., A simple equation for the description of solution release: III. Coupling of diffusion and relaxation. *Int. J. Pharm.*, 57 (1989) 169–172.

Wan, L.S.C., Heng, P.W.S. and Wong, L.F., Effect of additives on liquid uptake into HPMC matrices. *Sci. Tech. Pharm. Pharm. Sci. (France)*, (1993c) in press.

Wan, L.S.C., Heng, P.W.S. and Wong, L.F., Liquid penetration into matrices. *Sci. Tech. Pharm. Pharm. Sci. (France)*, 3 (1993b) 477–487.

Wan, L.S.C., Heng, P.W.S. and Wong, L.F., Relationship between swelling and drug release in a hydrophilic matrix. *Drug Dev. Ind. Pharm.*, 19 (1993a) 1201–1210.

Westman, L. and Lindstrom, T., Swelling and mechanical properties of cellulose hydrogels: I. Preparation, characterisation and swelling behaviour. *J. Appl. Polym. Sci.*, 26 (1981a) 2519–2532.

Westman, L. and Lindstrom, T., Swelling and mechanical properties of cellulose hydrogels: II. The relation between the degree of swelling and creep compliance. *J. Appl. Polym. Sci.*, 26 (1981b) 2533–2544.

Westman, L. and Lindstrom, T., Swelling and mechanical properties of cellulose hydrogels: III. Temperature effects on the swelling and compliance levels studied by dilatometry and ^{1}H-NMR spectroscopy. *J. Appl. Polym. Sci.*, 26 (1981c) 2545–2560.

Westman, L. and Lindstrom, T., Swelling and mechanical properties of cellulose hydrogels: IV. Kinetics of swelling in liquid water. *J. Appl. Polym. Sci.*, 26 (1981d) 2561–2572.