



Swelling and water transport in temperature-sensitive hydrogels based on 2-methoxyethylacrylate

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Abstract

A series of thermoresponsive hydrogels based on copolymers of 2-methoxyethylacrylate with acrylamide or *N,N*-dimethylacrylamide were prepared by radiation-induced polymerization in dimethylformamide solution in the presence of a crosslinking agent. The swelling behaviour of the hydrogels was studied by immersing the polymer samples in water at 5°C, 10°C and 37°C. The data were found to satisfactorily fit Fick's law with a constant diffusion coefficient. The results indicate that the swelling ratio increases with increasing the content of the hydrophilic monomers in the hydrogels and at the same time the equilibrium swelling time decreases. The effect of temperature on water transport mechanism was observed. © 2001 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Some crosslinked polymers and copolymers swell in water to form environmentally responsive hydrogels which can undergo a reversible discontinuous volume change in response to a continuous change in the external conditions, such as temperature. Owing to this behaviour, many different applications have been suggested for this thermoreversible hydrogels such as drug delivery systems and different biomedical uses (Palasis and Gehrke, 1992; Hoffman, 1995; Sousa et al., 1998).

Recently, copolymers of hydrophilic dimethylacrylamide (DMAA) with hydrophobic 2-methoxyethylacrylate (MOEA) were found to exhibit a lower critical solution temperature (LCST) with values in the range between 7°C and 78°C (Mueller, 1991, 1992; El-Ejmi

et al. (1997). In this work, a series of thermoresponsive copolymer hydrogels were prepared by radiation-induced copolymerization of MOEA with both acrylamide (Am) and DMAA in the presence of small amounts of a crosslinker.

The advantage of the radiation-induced methods for the preparation of polymeric materials compared with traditional methods lies in the purity of the materials, since the addition of ingredients during the synthesis is not required, the possibility of carrying out the processes at low temperatures and the easy regulation of the kinetic rate of the reaction by varying the radiation parameters (Carenza, 1992; Rosiak et al., 1995; Kaetsu, 1996; Kabanov, 1998).

The use of swellable materials for drug delivery applications has followed experimental and theoretical investigations of solvent and solute transport in polymeric systems (Lee, 1985; Masaro and Zhu, 1999; Grassi et al., 1999). In the recent years, the measurement of diffusion in hydrogels is a topic which has received considerable attention since the nature of water transport is of paramount importance for a proper

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Nomenclature			
B	slope of the linear correlation	M_0	mass of the dry sample
C	water concentration	M^*	non-dimensional water uptake
C^*	non-dimensional water concentration	M_0^*	non-dimensional mass of the dry sample
C_∞	water concentration at the sample surface	M_∞	asymptotic water uptake
d	sample diameter	t	time
D	diffusion coefficient	Sw	kinetic swelling
H	sample thickness	Sw_∞	asymptotic swelling
Fo	Fourier number	Sw_∞ (%)	percent asymptotic swelling
j_c	concentration flux	W_∞	weight of the dry sample
M	water uptake	W_0	asymptotic weight of the swollen sample
		x	position
		x^*	non-dimensional position

understanding of transport phenomena of solutes through the hydrogels.

Here, we report on the determination of degree of swelling as a function of temperature of different hydrogels and the diffusion coefficients at 5°C, 10°C and 37°C.

2. Experimental

2.1. Materials

MOEA from Polysciences Ltd., DMAA, Am and trimethylolpropane trimethylacrylate (TMPTMA) from Aldrich Chemical Co. were used as received.

2.2. Copolymerization of thermoresponsive hydrogels

The hydrogels based on MOEA were obtained by γ -rays polymerization at room temperature at a dose rate of 0.14 Gy/s and total dose of 10 kGy of the mixtures MOEA/DMAA and MOEA/Am in 50% dimethylformamide (DMF) solutions in the presence of 1% TMPTMA as a crosslinking agent after flushing nitrogen.

The hydrogels were obtained in a cylindrical form and cut into 6 mm diameter and 2 mm height discs that were repeatedly washed with cool water to remove the unreacted monomer.

2.3. Swelling and water transport measurements

Hydrogel samples were equilibrium swollen at different temperatures and, after wiping the excess surface water, weighted. Subsequently, they were lyophilized until their weight reached a constant value. The swelling ratio, Sw , was calculated according to the equation:

$$Sw(\%) = \frac{W_\infty - W_0}{W_\infty} \times 100, \quad (1)$$

where W_∞ and W_0 are the weights of the swollen and dried samples, respectively.

The water transport was derived by dynamic swelling that was followed by measuring gravimetrically the water uptake as a function of time (time intervals of 30 min) at the temperatures of 5°C, 10°C and 37°C. Measurements were taken in triplicate and standard deviations were calculated.

3. Results and discussion

The swelling ratio of copolymer hydrogels as a function of both temperature and composition are shown in Fig. 1. It can be seen that Sw decreases with increasing temperature while increases with increasing of the amount of the hydrophilic monomers, DMAA or Am, thus indicating a higher affinity of the gel for water. Moreover, for percentages of DMAA less than 20% a phase transition takes place while for values higher than 25% a continuous decrease of swelling with increasing temperature is apparent. The swelling of hydrogels based on Am shows a similar behaviour, i.e. a relatively clear transition for contents of 10% and 15%. It should be also noted that the phase transition in the case of Am hydrogels is less pronounced than that in the case of DMAA ones.

Designing matrix-based controlled release dosage forms and predicting the rate of release of ingredients require an understanding of the swelling kinetics of the polymer matrices.

We studied the swelling kinetics of different hydrogels by measuring the water sorption of thin discs immersed in water at 5°C, 10°C and 37°C. The swelling kinetics was investigated by the dynamic swelling as a function of time for hydrogels at the different temperatures (see Figs. 2–4).

Data correlation was performed by assuming that the water uptake can be described by a one-dimensional diffusion process, this is, radial diffusion can be

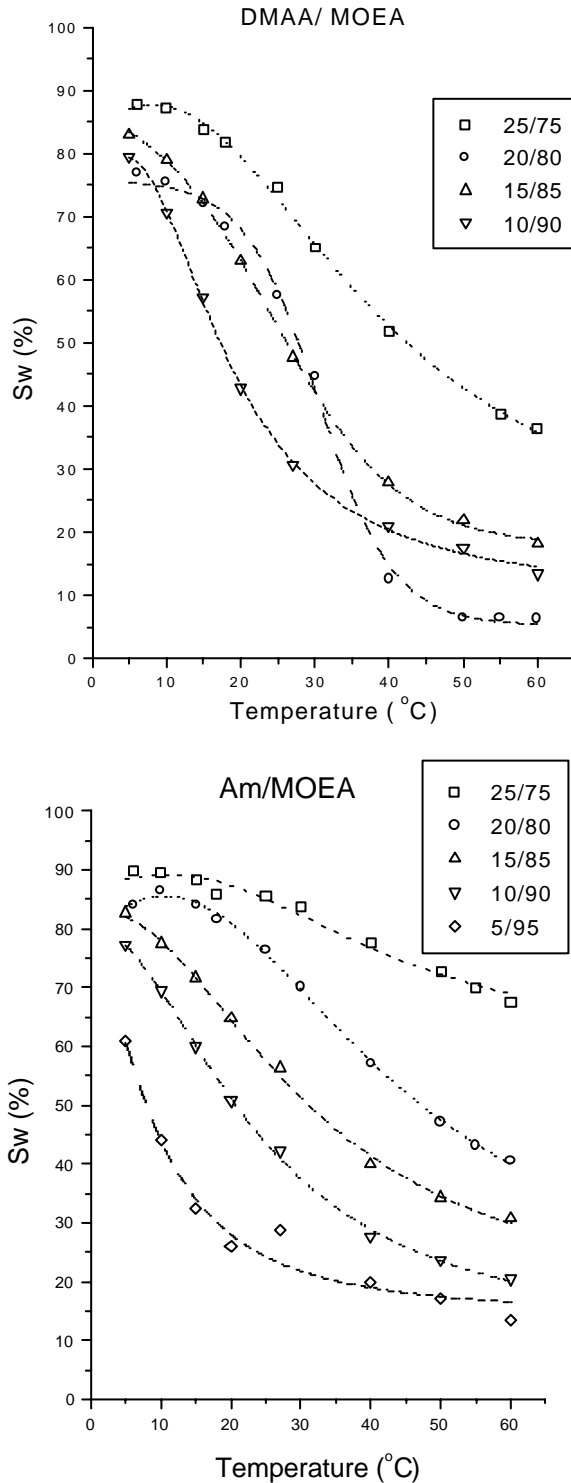


Fig. 1. Swelling ratio as a function of temperature of the hydrogels obtained by radiation-induced polymerization of mixtures DMAA/MOEA and Am/MOEA in the ratio (w/w) indicated in the inset.

neglected compared to axial. This condition is satisfied if $d \ll H$, where d and H are correspondingly the sample diameter and thickness. The concentration balance equation in the region $-H/2 \leq x \leq H/2$ can be written as (Incropera and De Witt, 1990)

$$\frac{\partial C}{\partial t} = -\frac{\partial j_C}{\partial x}, \quad (2)$$

where x is the position, t is the time, C is the water concentration and j_C is the concentration flux. According to Fick's law of diffusion:

$$j_C = -D \frac{\partial C}{\partial x}, \quad (3)$$

where D is the diffusion coefficient. Substituting Eq. (3) in Eq. (2) and considering a constant diffusion coefficient, we have:

$$\frac{\partial C}{\partial t} = D \frac{\partial^2 C}{\partial x^2}. \quad (4)$$

For Eq. (4), we consider as boundary conditions a constant water concentration C_∞ at the sample surface, while a zero concentration is considered as initial condition:

$$C\left(-\frac{H}{2}, t\right) = C\left(\frac{H}{2}, t\right) = C_\infty, \quad (5)$$

$$C(x, 0) = 0. \quad (6)$$

Eqs. (4) to (6) can be rewritten in a non-dimensional form as

$$\frac{\partial C^*}{\partial Fo} = \frac{\partial^2 C^*}{\partial x^{*2}}, \quad (7)$$

$$C^*\left(-\frac{1}{2}, Fo\right) = C^*\left(\frac{1}{2}, Fo\right) = 1, \quad (8)$$

$$C^*(x^*, 0) = 0, \quad (9)$$

where the non-dimensional concentration C^* and the Fourier number Fo are defined as

$$C^* = \frac{C}{C_\infty}, \quad (10)$$

$$Fo = \frac{Dt}{H^2}. \quad (11)$$

It can be shown that the non-dimensional instantaneous water uptake M^* can be obtained by integrating the solution of this problem as (Crank and Park, 1968)

$$M^* = \int_{-1/2}^{1/2} C^* dx^* = \frac{4}{\sqrt{\pi}} \sqrt{Fo} \left\{ 1 + 2\sqrt{\pi} \left[\sum_{n=1}^{\infty} (-1)^n \text{ierfc} \left(\frac{n}{2\sqrt{Fo}} \right) \right] \right\}, \quad (12)$$

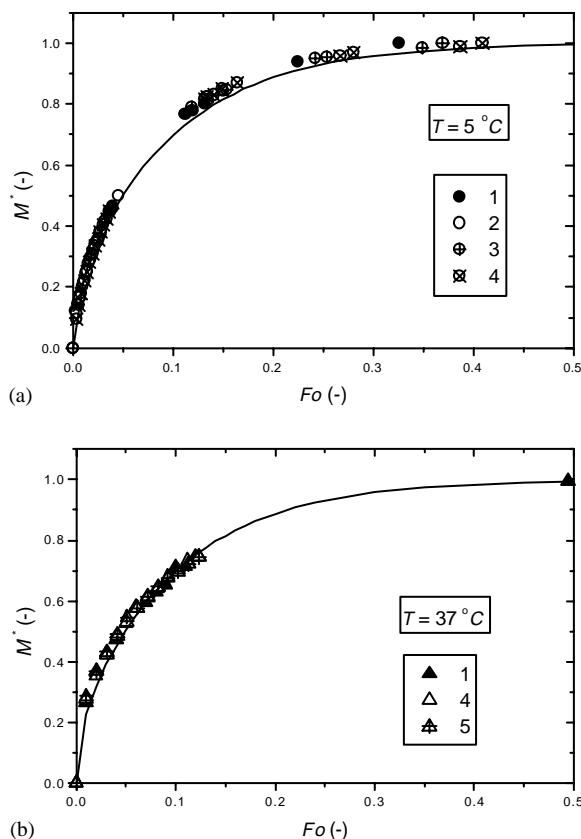


Fig. 2. Non-dimensional water uptake as a function of the Fourier number for poly(DMAA-co-MOEA) in the ratio 20/80 (w/w) at temperatures of 5°C (a) and 37°C (b).

where

$$M^* = \frac{M}{M_\infty}. \quad (13)$$

In Eq. (13) $M_\infty = C_\infty H$ is the asymptotic water uptake (attained at infinite time).

From Eq. (12), the kinetic swelling can be calculated as

$$Sw = \frac{M^*}{M^* + M_0^*}, \quad (14)$$

where $M_0^* = M_0/M_\infty$ is the non-dimensional mass corresponding to the dry sample. From Eq. (14), the asymptotic swelling results:

$$Sw_\infty = \frac{1}{1 + M_0^*}. \quad (15)$$

For $M^* \leq 0.8$, Eq. (12) can be reasonably approximated by

$$M^* \cong \frac{4}{\sqrt{\pi}} \sqrt{Fo}. \quad (16)$$

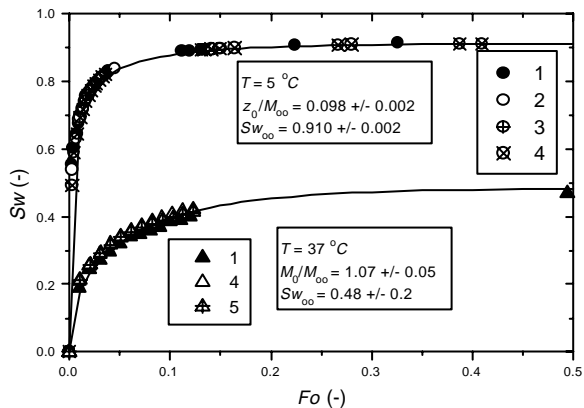


Fig. 3. Non-dimensional kinetic swelling as a function of the Fourier number for a poly(DMAA-co-MOEA) in the ratio 20/80 (w/w) at the temperatures of 5°C and 37°C .

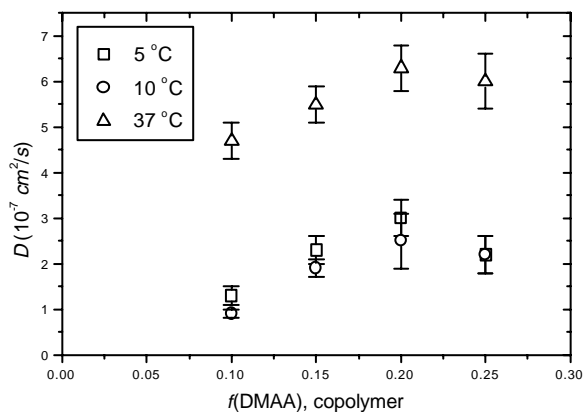


Fig. 4. Values of the diffusion coefficient, D , as a function of DMAA weight fraction at various temperatures.

Based on Eq. (16), the data can be fitted with a linear correlation of the form:

$$M^* = B\sqrt{t}, \quad (17)$$

where

$$B = \frac{4}{H} \sqrt{\frac{D}{\pi}}. \quad (18)$$

The experimental data was correlated by using Eq. (17). For each experiment a mean value (D/H^2) was calculated from Eq. (18). Since the film thickness did not remain constant in the experiments, the mean value \bar{H} was taken for the selected data. A mean diffusion coefficient can be calculated from these values.

In analyzing the uncertainties in the calculation of the diffusion coefficient, it was observed that the main source of errors was due to the sample thickness, due to both the accuracy in the individual measurements and

Table 1
Diffusion coefficients for poly(DMAA-co-MOEA) and poly(-Am-co-MOEA) hydrogels

Composition		D (10^{-7} cm ² /s)		
		5°C	10°C	37°C
DMAA/MOEA	25/75	2.2±0.4	2.2±0.4	6.0±0.6
	20/80	6.0±0.6	2.5±0.6	6.3±0.5
	15/85	2.3±0.3	1.9±0.2	5.5±0.4
	10/90	1.3±0.2	0.9±0.1	4.7±0.4
Am/MOEA	15/85	1.7±0.2	1.3±0.3	4.8±0.4
	10/90	1.1±0.1	1.0±0.2	4.0±0.3

the thickness changes in the swelling process. Several repetitions of the experiments were performed in order to improve data reliability.

Examples of experimental non-dimensional water uptakes are shown in Fig. 2, for a hydrogel poly (DMAA-co-MOEA) with the weight ratio 20/80 at the temperatures of 5°C and 37°C, as a function of the Fourier number F_0 . This Fourier number was calculated as a product of (D/H^2) times the time t . It can be observed a good repeatability of the data and a Fickian behaviour, by comparing the experimental points with the theoretical non-dimensional solution, Eq. (12), shown in continuous lines.

An example of the experimental kinetic swelling, corresponding to the same sample, is shown in Fig. 3. The agreement with the theoretical curves (shown in continuous lines), given by Eq. (15), is excellent.

MOEA is a hydrophobic monomer and, hence, its homopolymer is completely insoluble in water. However, if hydrophilic monomers, such as DMAA or Am, are added to the polymerizing MOEA, the swelling behaviour and the rate of water uptake increase (Fig. 1). This information is important for the identification of polymers that could expand slowly to allow a prolonged solute release.

As it can be seen from the data of the Table 1 for DMAA/MOEA and Am/MOEA hydrogels, the mean diffusion coefficient increases with temperature.

A significant variation can be observed in the diffusion coefficient for different temperatures, while the range of variation as a function of their chemical composition is smaller.

Changes in the diffusion coefficient for temperatures below LCST (corresponding to data for 5°C and 10°C) for the different hydrogels are not significant and lie within the experimental errors.

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