Drug Development and Industrial Pharmacy, 24(7), 667–669 (1998)

COMMUNICATION

The Effect of Structural Changes on Swelling Kinetics of Polybasic/Hydrophobic pH-Sensitive Hydrogels

M. Falamarzian and J. Varshosaz

Faculty of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

ABSTRACT

The effect of pendent side-chain length and crosslinking agent concentration in methyl methacrylate/dimethylaminoethyl methacrylate as a polybasic/hydrophobic pH-sensitive hydrogel was studied. Increasing both side-chain length and crosslinking agent concentration decreased the sharpness of response to pH and water-uptake capacity of the polymer. A case-II water transport mechanism and a nonlinear swelling kinetic was observed for the homologues of this hydrogel.

INTRODUCTION

Drug release from hydrogel drug delivery systems depends on two simultaneous rate processes; water migration into the device and drug diffusion outward through the swollen hydrogel, i.e., drug release from hydrogels is diffusion and/or swelling controlled. The effect of environmental stimuli such as pH, ionic strength, and the buffer type on swelling of polybasic pH-sensitive hydrogels has been studied (1,2). The purpose of this work was to study the effects of structural changes of these copolymers on the rate at which the swelling equilibrium is reached.

MATERIALS

Methyl methacrylate (MMA), ethyl methacrylate (EMA), butyl methacrylate (BMA), *N*,*N*-dimethylaminoethyl methacrylate (DMA), 2,2-azo-bis-isobutyronitril (AIBN), and divinylbenzene (DVB) were from Merck Co. (Germany).

METHODS

Different types of hydrogels were prepared by a combination of monomers as MMA/DMA, EMA/DMA, and BMA/DMA, and the ratio of each *n*-alkyl methacrylate ester to DMA was kept constant at 70:30 mole %. Polymerization reaction was conducted according to the method reported by Siegel et al. (1). The resulting gel sheets were punched into disks approximately 13 mm in diameter. The thickness of the films varied between 0.33 and 0.4 mm.

Swelling studies were carried out in either citrate buffer (0.01 M) in pH 3, 5, 5.5, 6, or 6.5, or phosphate buffer (0.01 M) in neutral pH 7. The total ionic strength of each buffer was adjusted to 0.1 M by adding appropriate amounts of sodium chloride. Each hydrogel disk was soaked in a buffer solution with a specific pH at 37°C and water sorption was measured periodically with 0.01 mg precision. The swelling was assessed by the following equations:

$$\text{Swelling ratio (hydration)} = \frac{\text{weight uptake at time } t}{\text{weight of the dry polymer}} \tag{1}$$

$$\text{Equilibrium swelling} = \frac{\text{weight uptake at steady time}}{\text{weight of swollen polymer}} \tag{2}$$

RESULTS AND DISCUSSION

All studied polybasic hydrogels showed pH sensitivity and were collapsed by increasing the pH toward neutral (Fig. 1). By increasing the pendent side-chain length, the equilibrium hydration level and also the sharpness of the transitional pH between collapsed and swollen forms of these copolymers are decreased. The transitional pH is much sharper for copolymers with 0.1% DVB as the crosslinker compared to those with 1% DVB. As shown by Fig. 2, in heavier alkyl side chains and also in higher contents of crosslinking agent, the sharpness of response to pH is decreased.

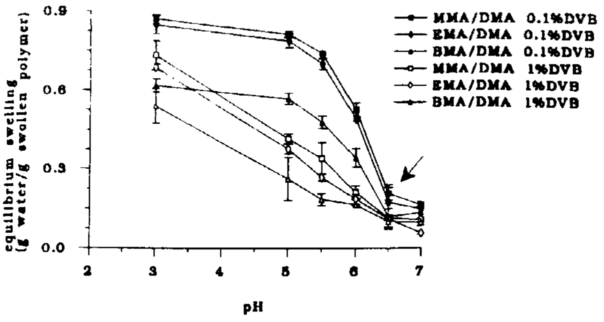

Figure 1. Equilibrium water fraction swelling of methyl methacrylate/dimethylaminoethyl methacrylate homologue series according to pH changes.

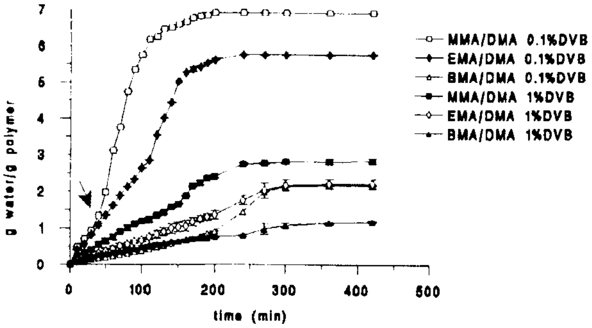

Figure 2. Swelling isotherms of hydrogels of methyl methacrylate/dimethylaminoethyl methacrylate homologue series at pH 3.

The rate of swelling was studied by Robinson's second-order equation (3,4):

$$t/w = A + Bt \tag{3}$$

where t and w are the time and weight of the solution absorbed, respectively. A and B are intercept and slope of the plot of t/w versus t. Fig. 3 shows the isothermal swelling kinetic of hydrogels with 0.1% DVB at pH 3. Unlike gelatin strips which show a linear relationship between t/w versus t (5), a nonlinear regression was seen in swelling isotherms of all members of these hydrogels (Fig. 3). It is proposed that this deviation from linearity may be related to the multilayer adsorption of water molecules to the hydrophilic segments of the polymer,

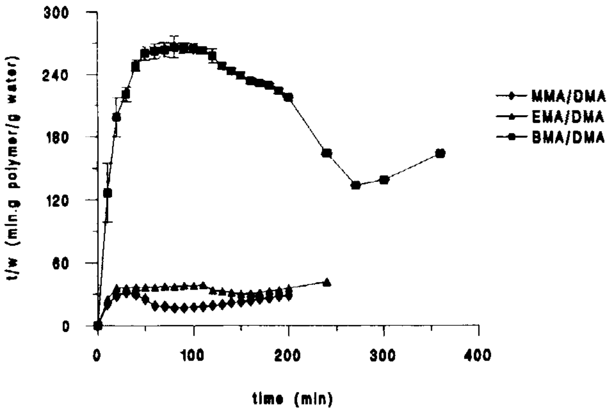

Figure 3. Nonlinear regression isothermal swelling kinetic of methyl methacrylate/dimethylaminoethyl methacrylate homologue series crosslinked with 0.1% divinylbenzene at pH 3.

similar to the adsorption of gases to the surface of the solids proposed by Langmuir (6).

Analysis of water sorption data according to equation $M_t/M_\infty = Kt^n$ (7) showed a case-II water transport mechanism for all homologues (0.1% DVB, pH 3 and 5). This means that a simple diffusion of water produced by gradient of Fick's first law cannot explain the swelling properties of the polybasic hydrogels, but the speed of macromolecular relaxation is the rate-limiting step in the swelling process, as stated by Robert et al. (8).

CONCLUSION

Increasing the pendent side-chain length or increasing the crosslinking agent concentration in polybasic hydrogels provides less flexibility of the polymer segments, which in turn decreases the polymer swelling ability or pH sensitivity. A case-II transport or swelling–stress–relaxation mechanism is observed throughout the water sorption process of these polymers.

REFERENCES

1. R. A. Siegel, M. Falamarzian, B. A. Firestone, and B. C. Moxley, J. Controlled Release, 8, 179 (1988).
2. R. A. Siegel, I. Johannes, C. A. Hunt, and B. A. Firestone, Pharm. Res., 9(1), 76 (1992).
3. I. D. Robinson, Phot. Sci. Eng., 8, 220 (1964).
4. C. M. Offner III and H. Schott, J. Pharm. Sci., 75(8), 790 (1986).
5. H. Schott, J. Pharm. Sci., 81(5), 467 (1992).
6. I. Langmuir, J. Am. Chem. Soc., 40, 1361 (1918).
7. G. W. Sinclair and N. A. Peppas, J. Membr. Sci., 17, 329 (1984).
8. C. C. R. Robert, P. A. Buri, and N. A. Peppas, J. Controlled Release, 5, 151 (1987).