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Carbohydrate Polymers 71 (2008) 682–689

Carbohydrate Polymers

www.elsevier.com/locate/carbpol

Study of the swelling dynamics with overshooting effect of hydrogels based on sodium alginate-*g*-acrylic acid

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Received 11 June 2007; received in revised form 5 July 2007; accepted 16 July 2007
Available online 24 July 2007

Abstract

A series of hydrogels were synthesized by graft cross-link copolymerization of sodium alginate (SA) and acrylic acid (AA) using N, *N*-methylene-bis-(acrylamide) as a cross-linker. By study of the swelling kinetics of the hydrogels in different buffer solutions, the overshooting effect was observed in acidic medium, namely the gels firstly *swelled* to a maximum value *following* by a gradual deswelling until the equilibrium. The phenomenon is interpreted *as* a cooperative physical cross-linking caused by the hydrogen bond formation between the carboxyl groups of the hydrogels in a hydrophobic environment. The hydrogen bond formation was further confirmed by FT-IR spectra. The dependence of overshooting effect on the pH of buffer solution *was* more noticeable in comparison with the composition of hydrogels, demonstrating that the cooperative physical cross-linking caused by the hydrogen bond formation is dominant. Whether or not the overshooting effect appears is not only *relative* to the pH of *buffer* solution, but also depends on the pK_a of carboxyl groups on the network. The overshoot processes of the hydrogels under acidic medium at pH below the pK_a follow a quantitative model proposed by Díez-Peña et al., and the theoretical curves are in very good agreement with the experimental data. While in pH > pK_a buffer solutions, the overshoot phenomenon does not appear arising from the repulsive interaction between the ionized carboxyl groups, the swelling processes follow Schott second-order rate equation.

Keywords: Hydrogel; Hydrogen bond; Cooperative physical cross-link; Overshoot effect; Swelling kinetics

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1. Introduction

Stimuli-responsive hydrogels, which change their structure and physical properties in response to external stimuli, are very attractive materials for application in biomaterial science and technology. Especially, the utilization of a stimuli-responsive hydrogel system would be important to drug delivery systems. An important parameter to consider in the design of these systems is the degree of swelling. Not only is the delivery of drugs accomplished by the swelling characteristics of hydrogels (i.e., pH-sensitive hydrogels) (Yin, Yang, & Xu, 2001), but the release of *drugs is also relative* to the swelling behavior of hydrogels (Yin, Yang, & Xu, 2002). So much attention has been paid to studies on the swelling behavior of hydrogels.

It is well known that PAA has carboxylic acid groups which could develop different intermolecular interaction like electrostatic interaction, hydrogen bonds, and dipole-ion with other polymers. Many investigations have shown that these interactions exert strong influence on the swelling behavior of hydrogels and there is a great potential for their application in pharmaceutical preparations, particularly in drug delivery systems. For example, the structure and swelling behavior of hydrogels based on MAA and *N*-iPAAm have been recently studied by Díez-Peña, Quijada-Garrido, and Barrales-Rienda (2002, 2003). The obtained results have revealed that the hydrogen bonds between carboxyl and amide lead to some anomalous features. A swelling–deswelling process under acidic pH, which is actually known as overshooting effect, may be

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doi:10.1016/j.carbpol.2007.07.012

attributed to the dynamic hydrogen bond formation (Díez-Peña et al., 2003).

The utilization of natural polysaccharides in drug delivery continues to be a subject of intense investigation because of their biodegradability and biocompatibility. Many polymeric networks based on polysaccharides (e.g: Chitosan, Dextran, Guar gum and Konjac glucomannan et al.) and acrylic acid (de la Torre, Enobakhare, Torrado, & Torrado, 2003; Kim & Oh, 2005; Huang, Yu, & Xiao, 2007; Liu, Hu, & Zhuo, 2004) have been prepared. Their swelling properties have also been studied. However, these studies are mostly concerned with the equilibrium swelling values and their changes with composition, temperature and pH, fewer investigations were dedicated to the study on the influence of the weak interaction such as hydrogen-bonding degree and electrostatic interaction on *swelling kinetics of gels*. In this paper, a series of hydrogels were synthesized by graft cross-link copolymerization of sodium alginate (SA) and acrylic acid (AA) using *N*,*N*′-methylene-bis-(acrylamide) as a cross-linker. The swelling kinetics of the hydrogels in different buffer solutions has been studied, a remarkable overshooting effect was observed in acidic medium. The effect was given *an* interpretation on the network structure and a cooperative physical cross-linking caused by the hydrogen bond formation between the carboxyl groups of the hydrogels in a hydrophobic environment. The influence of composition and pH of *buffer* solution was also investigated. The swelling data are analyzed by means of rigorous quantitative kinetics models.

2. Experimental

2.1. Materials and methods

Sodium alginate (SA) (Analar grade). Ceric ammonium nitrate (CAN), *N*, *N*′-methylene- bis-(acrylamide) (MBAA) was used without any further purification. Acrylic acid (AA) was vacuum distilled.

The chemical compositions of the dried gels were determined using a CHN EA1106- Elemental Analyzer (Carlo Erba Instruments, Italy).

2.2. Synthesis of graft copolymers

Sodium alginate-*graft*-poly(acrylic acid) (SA-*g*-PAA) hydrogels cross-linked with *N*,*N*′-methylene-bis-(acrylamide) (MBAA) were prepared by radical graft copolymerization with CAN as an initiator as previously described (Shah, Patel, & Trivedi, 1995). The compositions of the materials used for the synthesis of hydrogels *were* listed in Table 1. As a general procedure, SA and MBAA dissolved in moderate deionized water and AA neutralized with 6.0 mol/l NaOH solution were mixed with stirring and bubbling of a slow stream of nitrogen gas for about 30 min. A freshly prepared solution of 60 mg CAN dissolved in moderate deionized water was slowly added into the mixture to initiate the graft copolymerization. After polymerization at 50 °C for 5 h, the solid copolymer slab was taken out, and cut into 9.5-mm diameter circular disks *by punches*. These disks were divided into two parts. One part was directly used for the determination of grafting percentage; the other part was immersed in deionized water for 4 days to remove the unreacted chemicals, during this time the water was changed once every 8 h, then this part was dried under vacuum at 40 °C until constant weight was obtained and used for *swelling* kinetics.

2.3. FT-IR analysis

The FT-IR was performed by using Nicolet fourier transform infrared spectroscopy (made by Thermo Nicolet), over the *range* 500–2500 cm^{-1}. Sample B_2 was soaked in *buffer* solution of pH 2.2 till the swelling equilibrium, and then dried in vacuum at 60 °C for 24 h. Each sample B_2 before and after soaked was ground with 2 mg of KBr and then pressed to form transparent discs.

2.4. Determination of grafting percentage

The samples of the crude copolymers were weighed about 2.0 g, and extracted with *acetone* as solvent for 10 h. After complete removal of the homopolymers the residues were dried under vacuum at 60 °C for 12 h. The extractors were weighed. The grafting parameters were calculated as:

$$\text{Grafting percentage (G\%)} = [(W_2 - W_1)/W_1] \times 100\% \tag{1}$$

where W_1 and W_2 denote the weight of SA and the extractors, respectively.

Grafting percentage of each graft copolymer is given in Table 1.

2.5. Analysis of graft copolymer compositions

The samples purified in deionized water were weighed, the mass percentages of SA in the dried gels (W_{SA}) were calculated as:

$$\begin{aligned} W_{\text{SA}}\ (\%) &= \{[W_1 - (W_2 - W_3)]/W_3\} \times 100 \\ &= 100 - \text{G} \times W_1//W_3 \times 100 \end{aligned} \tag{2}$$

where W_3 denotes the weight of graft copolymers.

The mass percentages of nitrogen in the dried gels (W_{N}) were determined using a CHN EA1106- Elemental Analyzer (Carlo Erba Instruments, Italy). The mass percentages of AA and MBAA in the dried gels were calculated as, respectively

$$W_{\text{MBAA}}\ (\%) = (W_{\text{N}}/14) \times 154 \tag{3}$$

$$\begin{aligned} W_{\text{AA}}\ (\%) &= 100 - W_{\text{SA}} - W_{\text{MBAA}} \\ &= \text{G} \times W_1//W_3 - (W_{\text{N}}/14) \times 154 \end{aligned} \tag{4}$$