Synthesis and characterization of temperature/pH-sensitive hydroxypropylcellulose/ sodium alginate hydrogel

Hui Li, Guo-li Gong

1College of Resource and Environment, Shaanxi University of Science and Technology, Xi'an 710021, China; e-mail: lihui0209@gmail.com
2College of Life Science and Engineering, Shaanxi University of Science and Technology, Xi'an 710021, China; e-mail: gongguoli@sust.edu.cn

(Received: 05 January, 2010; published: 12 November, 2010)

Abstract: A series of temperature and pH responsive hydrogels were synthesized by using hydroxypropylcellulose (HPC) as temperature natural sensitive material, sodium alginate (SA) as pH sensitive material. The effect of SA to LCST has been studied and the mechanism of the influence has been presented. In addition, the swelling ratio and controlling factor of swelling process were all researched in this paper. The main results obtained are as follows: the LCST decreased gradually as SA was added into HPC; the HPC/SA hydrogel responded to both temperature and pH value of the medium; the swelling ratio reached maximum value at pH value of 6.

Introduction

In recent years, considerable research attention has been given to the environment-sensitive materials. Hydrogel as a kind of intelligent soft material has been regarded extensively by many researchers. Because it has great potential applications in many fields, such as robotics, chemical industries, drug delivery system, enzyme immobilization and biomaterials separation and purification, etc. However, major hurdles in their development are slow response to velocity, low efficiency swelling/deswelling ratios, and poor mechanical properties due to difficulty in processing them into mechanically strong and fine structures [1, 2]. In the past decade, several researchers have paid attention to develop quickly responsive intelligent hydrogel materials. Hansen, Smith and Reneker [3] studied the electrospun nanofibers structured hydrogel; excellent strength and elasticity of these structured hydrogels were displayed in many uses, including wound care, drug delivery and sanitary goods. Zhang [4] developed the macroporous structure hydrogel with fast response rate and temperature-sensitivity. And found that these macroporous hydrogels had higher swelling ratios at temperatures lower than the LCST and exhibited faster response rate when the phase transitions occur. Among those smart polymers that can respond to external stimuli, HPC has been examined as a smart drug delivery material due to its unique reversible phase separation behaviour stimulated by external temperature [5]. Petrov’s research group [6] synthesized super-macroporous hydrogels by UV-assistance. It was found that due to the macroporous structure, the hydrogels exhibited a very rapid water uptake, and volume phase transition behavior. Mezdour [7] reported that oil/water surface rheological properties of hydroxypropylcellulose (HPC) alone and mixed with lecithin, and demonstrated that HPC is a thickening biopolymer having surface active properties both at air/water and oil/water interfaces, HPC exhibits a surface activity...
which can be observed even at low bulk concentrations. A few chains of HPC lies on the water side of the oil/water interface and contribute to a higher steric repulsion effect than lecithin alone. HPC hydrogels are well known for their phase separation near their phase transition temperature or called lower critical solution temperature (LCST). Exhibiting a sudden shrinking in volume at a temperature just above LCST, only few minutes are needed for this phase separation behaviour. Karewicz and Zasada prepared smart alginate/hydroxypropylcellulose microbeads with regular spherical shape and regular network of pore surface [8]. Yue [9] exploited the thermal responsive phase behavior of hydroxypropylcellulose to produce 3D interconnected macroporous hydrogels in aqueous. The hydrogels demonstrate a combination of interconnected macroporosity and high water content. In this paper, a series of HPC/SA hydrogels with fast temperature-response rate and heterogeneous macroporous structure are synthesized by carrying out the polymerization/crosslinking in aqueous solutions with various concentrations. Interaction hydrogen bonding between HPC and SA in resultant hydrogels is illustrated in Fig.1. Research results showed that this series hydrogels have higher swelling ratios at temperature below LCST, and exhibit fast response rate to external temperature.

![Fig. 1. Schematic representation of the hydrogen bonding between HPC and SA.](image)

**Results and discussion**

**The effect of SA amount on LCST**

The phase transition temperature of HPC/SA blend solution is measured by adding various amount of SA into HPC solution, in which theoretical content of HPC is 2%wt. The temperature at which absorbance suddenly changes is defined as the phase transition temperature. The results are displayed in Fig. 2. The phase transition temperature reduces gradually with addition of SA, and then it reaches equilibrium as SA amount is 7%wt of HPC amount. It is a result of decrease in hydrophilicity of
blends solution caused by SA viscosity; the solubility of HPC macromolecules is confined by SA macromolecular surrounding. And the action reaches the maximum when almost all the HPC macromolecules is surrounded by SA macromolecules. The extreme of SA amount is 7 %wt of HPC amount in HPC/SA hydrogels.

Fig. 2. Effect of SA amount on phase transition temperature of HPC/SA system.

The effect of temperature on swelling ratio of HPC/SA hydrogel

The effect of temperature on swelling ratio of HPC/SA hydrogel was investigated based on various concentration of HPC with addition of various SA amount. Fig. 3 displayed the results. The results indicated that swelling ratios all decrease with the temperature elevating, and swelling ratios sharply decrease when temperatures approach LCST and form turning points. However, the swelling ratios of HPC/SA hydrogels increase with the increasing of HPC.

Fig. 3. Effect of temperature on the swelling ratios of HPC/SA hydrogel.

As a result of that hydrophilicity of HPC/SA hydrogel enhance as HPC amount increase. Meanwhile, this is also a result of the interaction between hydrogel networks and solvent strengthening as more HPC are used in synthesizing HPC/SA hydrogels. Fig. 4 is the phase transition temperature result of HPC/SA blend solutions with addition of various SA into 2%wt of HPC solution. The phase transition temperatures gradually reduce with the increase of SA in HPC solution. The
temperatures at which absorbance increases sharply are shown in Fig. 4 almost similar with the temperatures at which swelling ratios reduce sharply as shown in Fig. 3. It indicates that LCST of HPC/SA blend solutions could be measured accurately by UV-vis spectrophotometer corresponding to the absorbance value.

\[ \text{Fig. 4. The LCST of HPC/SA hydrogel measured by UV-vis.} \]

**The effect of pH value on HPC/SA hydrogel**

Sodium alginate has been given considerable attention because of its pH response property, biodegradability, biocompatibility, renewability and nontoxicity [10]. It is widely used in a variety of commercial applications because of its capacity for gelatinization. The pH sensitive property of HPC/SA hydrogel was characterized, and the results are shown in Fig. 5.

\[ \text{Fig. 5. Effect of pH value on HPC/SA investigated at T=25 °C.} \]

The swelling ratios increase gradually with pH value increase, and reaches maximum at pH value of 6, except the hydrogel marked HS0. In strong acidic
mediums pH value is 1-2, -COO\(^-\) dissociated from SA is associated with H\(^+\), as – COOH which is hydrophobic. At the same time, intermolecular hydrogen bonding is formed between HPC and SA, HPC/SA hydrogel networks structure shrinks. Water molecules expel from the contraction hydrogel. So, the swelling ratio of HPC/SA hydrogel reduces.

Fig. 6. The SEM image of HPC/SA hydrogel (a) surface morphology; (b) cross-section morphology from HS3.

However, at pH value of 6, a large amount of -COOH dissociate completely, and become -COO\(^-\), macromolecular chains fully extend because of electrostatic forces; osmotic pressure enhancing within the hydrogel network referenced Zhang [11].
Water molecules diffuse into hydrogel more easily. Greatest swelling ratio generate pH value of 6. While, when pH value is more than 6, the swelling ratio decreases caused by increasing ionic strength and shrinking of hydrogel network structures at the pH value condition.

*The surface and cross-section morphology examined with SEM*

Fig. 6 (a) is the surface morphology and Fig.6 (b) is the cross-section morphology respectively. Phase domain increases with the increasing of SA amount in HPC, and this contributes to the rough surface morphology. Macro porous hydrogel observed from Fig.6 (b) is another cause that a series of HPC/SA hydrogel has faster temperature responsive characteristic and larger equilibrium swelling ratio than HS0 hydrogel.

**Conclusions**

A series of HS hydrogel which are both sensitive to temperature and pH value, were synthesized from HPC and SA by solution polymerization. The LCST of HPC/SA hydrogels reduce gradually with the increasing of SA in HPC from 43.7 °C to 36.8 °C. The swelling ratios reach maximum at pH of 6 by addition of pH sensitive material SA.

**Experimental part**

*Materials*

The HPC employed in this study was kindly donated by Hercules Inc. (Wilmington, DE, USA). Its molecular weight was 80,000g/mol, and its molar substitution (according to the manufacturer) was between 3.4 and 4.4. Reagent grade SA was purchased from Sigma-Aldrich. Biochemical reagents glutaraldehyde (25% pure) as the crosslinking agent of HPC and SA, and analytical reagent hydrochloride of crosslinking reaction catalyst, were both purchased from Sinopharm Chemical Reagent Company Shanghai China respectively. Experimental water was deionized water.

*Approach*

HPC sample and SA were dried in vacuum at 45 °C for 12 h to remove the free water from samples before use. The double sensitive hydrogels composed of HPC and SA were prepared as follows: HPC and SA were dissolved in aqueous solution firstly based on the desired concentrations respectively. Secondly, crosslinking reaction of HPC was carried out with magnetic stirring by added glutaraldehyde as crosslinking agent and a few drops of hydrochloric acid as catalyst under nitrogenous atmosphere at 25 °C for reacting 6 h. After this, by instilling SA solution into pre-crosslinking HPC system, the reaction was continued for 12 h at 25 °C. Resulting hydrogels were cut with puncher to form the same disc, and marked HS0, HS1, HS3, HS5 and HS7 according to SA amount in HPC. Such as HS3 represents the weight ratio of SA in hydrogel is 3%wt of HPC amount. The phase transition temperature of blend solution with 0.1 %wt of total material concentration was tested by a PE Lambda-650 UV-VIS spectrophotometer at λ=500 nm in the temperature range from 20 °C to 60 °C at 0.3 °C /min. The blend solution was prepared by mixing HPC solution and SA solution according to set materials amount. Swelling ratios were investigated by weighting...
methods under various temperature and pH value conditions. The swelling ratio was calculated using Eq. (1).

\[ SR = \frac{(m_t - m_d)}{m_d} \]

where SR defined as swelling ratio does not change with time. \( m_t \) swelling hydrogels’ mass as it reaches swelling equilibrium state in medium solutions by measuring every 10 min, and swelling equilibrium time is 500-600 min. \( m_d \) is dry hydrogels’ mass after it was dried in vacuum. The surface and cross-section morphology were examined with a JEOL JSM-5600LV scanning electron microscope at an accelerating voltage of 15KV. The images were taken at magnifications of 50, 100 and 200 times after samples were coated with a gold-palladium target using a vacuum evaporator for 30 min.

Acknowledgements

This work was supported by Special Foundation for the Natural Science of the Shaanxi Province Department of Education, Grant No.09JK351 and 09JK346, by Chinese National Natural Science Foundation, Grant No. 20906058, by Natural Science Foundation of the Shaanxi Province, Grant No. 2010JQ4020 and by Scientific Research Foundation for Doctor of Shaanxi University of Science and Technology, Grant No. BJ09-02.

References