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Synthesis and Properties of Hydrogels Based on Polyaspartamides with Various Pendants

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Summary

Hydrogels based on three kinds of polyaspartamides, i.e. non-substituted polyaspartamide, substituted polyaspartamide with sodium aspartate pendant and that with sodium sulfonate pendant, were prepared by crosslinking of polysuccinimide with ehylenediamine, followed by the hydrolysis with the corresponding amines (ammonia, sodium aspartate, and sodium 2-aminoethylsulfonate). Water absorbency and biodegradability of these products were evaluated, comparing with those of crosslinked sodium polyasparate prepared similarly. Absorbency in pure water of the three products in the present study was in the range of 70 - 150 g/g, somewhat lower than that of crosslinked sodium polyasparate, 200 g/g. Absorbency in 0.9% NaCl solution was totally lower than those in pure water and the order of the absorbency of the products was the same as the case of the pure water. On the other hand, in 3.5% NaCl solution, absorbency of crosslinked polyaspartamide containing sodium sulfonate was higher than that of crosslinked sodium polyasparate. The crosslinked polyaspartamides in the present study showed somewhat slower biodegradation speed than the crosslinked sodium polyasparate.

Introduction

In recent years, biodegradable hydrogels have received much attention, and have been extensively studied for the biomedical application such as drug delivery systems. Poly(aspartic acid) (PASP) is one of typical water soluble and biodegradable polymers, and is expected as a substitute of the conventional non-biodegradable polymers such as poly(acrylic acid). Hydrogels based on PASP have been reported as representative biodegradable superabsorbent materials by many researchers [1-3]. Poly(2-hydroxyethyl aspartamide) (PHEA), which is a derivative of PASP, is unique material exhibiting suitable properties for macromolecular prodrugs such as biodegradability, water solubility, multipoint drug attachment, and biocompatibility [4,5]. Thus hyrogel based on PHEA was studied, but water absorbency was in the range of 10 - 40 g/g, being considerably low [6,7]. On the other hand, hydrogels from other polyaspartamides have been hardly reported. In the present paper, we have prepared hydrogels based on polyaspartamides containing various pendants, and evaluated their absorbency and biodegradability. These results were compared with those of PASP based hydrogel prepared in a similar way.

Experimental

Materials

L-Aspartic acid (L-Asp), o-phosphoric acid (85%), *N*,*N*-dimethylformamide (DMF), sodium hydroxide, ammonia solution (28%), and 2-aminoethansulfonic acid (taurine) were commercially available and used without further purification.

*Preparation of PSI (**2**)*

To a 200 mL round-bottom flask was added L-Asp (26.6 g, 200 mmol), *o*-phosphoric acid (12.7 g, 200 mmol), and the flask was set on rotary evaporator. The flask was heated at 80°C for 30 min, 100 °C for 30 min, 140 °C for 60 min, and 180 °C for 180 min under reduced pressure. After cooling to room temperature, 150 mL of DMF was added to dissolve the reaction mixture. The solution was poured into a large amount of deionized water, and the precipitate was filtered, washed with deionized water, and then with methanol repeatedly until it was neutral. The solid residue was dried at 60°C for 12 h under reduced pressure.

*Preparation of crosslinked sodium polyasparate (**3a**)*

PSI (1.94 g, 20 mmol) was dissolved in DMF (18 mL) in 100 mL beaker and ethylenediamine (0.03 g, 0.5 mmol) was added to the solution under stirring at room temperature. After stirring at room temperature for 1 h, the stirring was stopped and the mixture was allowed to react for 23 h. The formed gel was moved to mortar, crushed into small pieces with pestle, and dispersed in methanol/water mixture (40 mL/40 mL) in 200 mL beaker. To the gel suspension, aqueous solution of NaOH (10 wt%, 7.6 g, 19 mmol) was added dropwise over 30 min at room temperature. After stirring overnight at room temperature, the reaction mixture was poured into methanol (100 ml). The precipitated solid was filtered off and dried under reduced pressure. The white solid was finely cut with mixer and screened through a 16-mesh sieve to give off-white granule product.

*Preparation of crosslinked polyaspartamide (**3b**)*

The procedures of **3a** were repeated except that ammonia solution (28 wt%, 1.2 g, 19 mmol) was used instead of the aqueous NaOH solution.

*Preparation of crosslinked polyaspartamide containing disodium aspartate (**3c**)*

The procedures of **3a** were repeated except that a mixture of aspartic acid (2.53 g, 19 mmol) and aqueous solution of NaOH (10 wt%, 15.2 g, 38 mmol) was used instead of the aqueous NaOH solution.

*Preparation of crosslinked polyaspartamide containing sodium sulfonate (**3d**)*

The procedures of **3a** were repeated except that a mixture of taurin (2.38 g, 19 mmol) and aqueous solution of NaOH (10 wt%, 15.2 g, 38 mmol) was used instead of the aqueous NaOH solution.

Measurements

Reduced viscosity of PSI at a concentration of 0.5 wt% was measured in DMF at 25°C by using Ubbelode-type viscometer. IR spectra of PSI, crosslinked sodium polyaspartate and crosslinked polyaspartamides were recorded on a JASCO FT/IR-410 spectrometer.

Water absorbency of the products was measured by the tea-bag method with the reference to Japanese Industrial Standard, JIS K 7223. The tea-bag containing sample was immersed in deionized water at 25°C. After 10 min immersion, the tea-bag was picked up from the water, and excess water was drained for 5 min. The weight of tea-bag and hydrogel was then measured (W_t), and absorbency was calculated according to the following equation;

$$\text{Absorbency} = (W_t - W_b - W_p) / W_p \qquad (\mathbf{1})$$

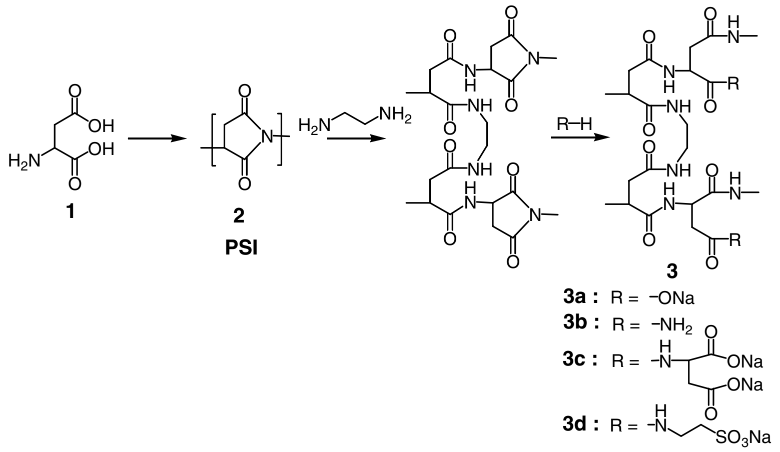
where W_b is the weight of blank tea-bag after water treatment, and W_p is the weight of dry superabsorbent hydrogel sample. Absorbency after 30 min, 1 h, 24 h, and 48 h was estimated in the same way. Further, absorbency in aqueous NaCl solution (concentration: 0.9 wt% or 3.5 wt%) was evaluated similarly. These concentrations are corresponding to those of physiological saline and seawater, respectively.

Biodegradability of the hydrogels was estimated according to the method with the reference to JIS K 6950. The activated sludge was kindly supplied from Tatara-gawa sewage-treatment plant (Fukuoka, Japan), and used as received. The biodegradability was evaluated at 25°C by monitoring the biological oxygen demand (BOD) using an OM3001 coulometer of Ohkura Electric Co.Ltd., Japan.

Results and discussion

Preparation of superabsorbent hydrogels

Hydrogels based on polyaspartamides were synthesized by three steps as shown in Scheme 1; polymerization of L-aspartic acid to form PSI (**2**), crosslinking of PSI by ethylenediamine, and ring opening reaction of PSI with amines to obtain the final product (**3b** – **3d**). Crosslinked sodium polyaspartate (**3a**) was prepared similarly.



Scheme 1. Preparation of hydrogels based on polyaspartamides.

Synthesis of PSI has been reported in several ways; reaction of maleic anhydride with ammonia [8], heating ammonium salts of maleic acid [9], and thermal polymerization of L-Asp catalyzed by acid [10]. Among them, thermal polymerization of L-Asp catalyzed by phosphoric acid has been reported to produce high molecular weight polymer [10], which was employed in the present study, because high molecular weight of the polymer is indispensable to attain high water absorbency [11,12]. Reduced viscosity of PSI obtained in the present study was 56 mL/g, which corresponds to a molecular weight of approximately 180,000 according to the empirical equation relating solution viscosity with molecular weight [4].

Optimal density of crosslinking is another essential factor to attain high water absorbency. If the crosslinking is insufficient, most of polymers will dissolve out. Excess crosslinking, on the contrary, will restrict the chain expansion in water and then restrict high water absorbency also. In the present study, ethylenediamine, one of the simplest aliphatic diamine, was employed as crosslinker. The feed amount of ethylenediamine was kept at 2.5 mol% of PSI, because it was a minimal amount to form a gel during the crosslinking reaction with good reproducibility.

Figure 1 is the IR spectra of PSI (**2**), crosslinked sodium polyaspatate (**3a**), and crosslinked polyaspartamides (**3b** – **3d**). Absorption bands due to imide ring are observed at 1750 cm^{-1}and 1170 cm^{-1} in the spectrum of **2**. In the spectra of **3a** – **3d**, these absorptions are absent, and instead, absorptions at 3400 - 3200 cm^{-1} due to N-H and absorptions due to the introduced side groups are seen. These results indicate that the ring opening of PSI by amines proceeded successfully, and the products have chemical structures as shown in Scheme 1.

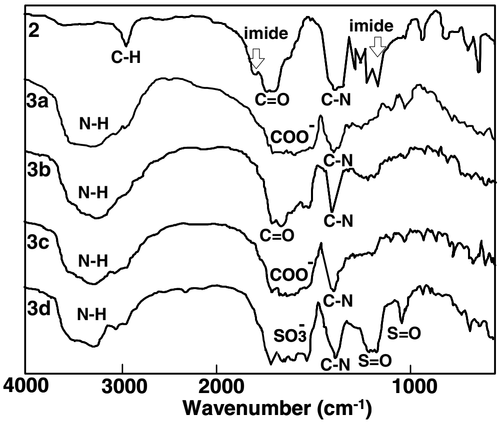


Figure 1. IR spectra of PSI and crosslinked polyaspartamides.

Water absorbency

Figure 2 shows time dependence of absorbency in pure water of hydrogels based on polyaspartamides (**3b** – **3d**). Absorbency of crosslinked sodium polyaspartate (**3a**) is also listed for comparison. **3a** absorbed water rapidly; its absorbency almost saturated in 10 min, and its maximum absorbency was 200g/g. Absorption speed of **3b** – **3d** was somewhat slower than that of **3a**; their absorption saturated after 1 h water treatment. Among **3b** – **3d**, **3c** absorbed most water at 160 g/g, lower than that of **3a**.

Slower absorption of **3b** – **3d** might be due to their hydrogen bonding of amide group in side group which might prevent polymer chain from expanding rapidly.

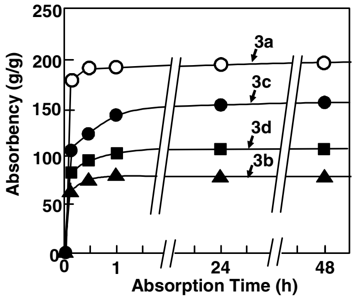


Figure 2. Absorbency of hydrogels based on polyaspartamides in pure water.

Absorbency in 0.9 % NaCl solution was totally lower than that in pure water; it is a general tendency of superabsorbent hydorgels based on sodium polyacrylate [11,12]. The order of absorbency was the same as that in pure water, i.e., **3a** > **3c** > **3d** > **3b**, as shown in Figure 3.

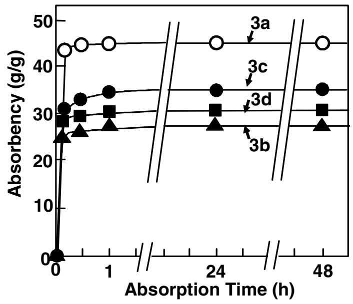


Figure 3. Absorbency of hydrogels based on polyaspartamides in 0.9 % NaCl solution.

In 3.5% NaCl solution, absorbency of **3d** was the highest among those examined including **3a** (Figure 4). This high absorbency might be due to high water affinity of sulfonate group. This result should be emphasized because superabsorbent hydrogels should absorb aqueous NaCl solution in many applications. Further, absorbency of **3b** and **3c** is very close to that of **3a**.

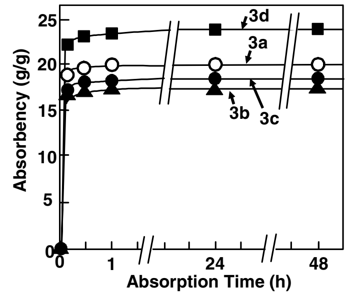


Figure 4. Absorbency of hydrogels based on polyaspartamides in 3.5 % NaCl solution.

Figure 5 summarizes absorbency of various hydrogels. As shown above, **3a** absorbed much pure water; its absorbency was as high as ca. 200 g/g. The decrease of absorbency of **3a** by NaCl was remarkable; as is the case of conventional superabsorbent hydrogels [11]. Hydorgel based on polyaspartamide containing sodium aspatate (**3c**) showed similar absorption behavior. On the other hand, hydrogel based on unsubstituted polyaspartamide (**3b**) and that containing sodium sulfonate (**3d**) absorbed less pure water but their decrease by NaCl was considerably small. Thus it has been proved that the appropriate choice of side group of hydrogels based on polyaspartamides is very important to attain high water absorbency either in pure water or NaCl solution.

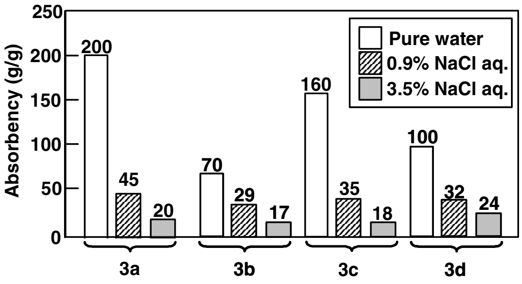


Figure 5. Comparison of absorbency of hydrogels based on polyaspartamides.

Biodegradability

Figure 6 shows biodegradability of various materials measured by continuous BOD method. Cellulose was used as the standard material to check the biodegradation activity of the activated sludge. The activated sludge degraded ca. 80 % of cellulose and 50 % of **3a** for 20 days. On the other hand, 30 - 40 % of **3b** – **3d** were degraded by this activated sludge, irrespective of kinds of side groups. Thus it was found that the introduction of various amide pendants suppressed the biodegradation speed of crosslinked polyaspartate to some extent, but hydrogels based on polyaspartamides kept biodegradable character to some extent, as shown in Figure 5. Side group containing amide bond seems to remain during the evaluation and restrict the biodegradation. Further study on relationship between structure of hydrogels including side group and biodegradability is still on progress.

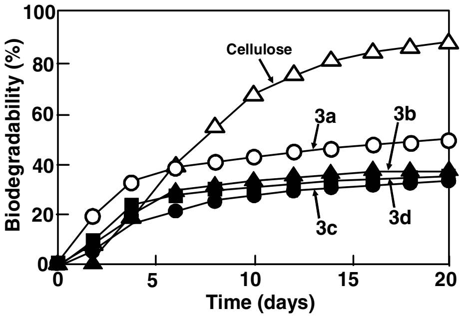


Figure 6. Biodegradability of various materials measured at 25°C.

Conclusion

We have prepared superabsorbent hydrogels based on polyaspartamides with various pendant groups. Among them, hydrogel containing sodium sulfonate exhibited high water absorbency even in NaCl solution at high concentration. Further, they are environmentally friendly material because they exhibited biodegradability. Applications of these hydrogels in the field of drug delivery system and tissue engineering are potentially expected.

References

1. Tomida M, Yabe M, Arakawa Y, Kunioka M (1997) Polymer 38: 2791
2. Chang CJ, Swift G (1999) J. Macromol. Sci., Pure Appl. Chem. A36: 963
3. Min SK, Kim JH (2001) Korean Polym. J. 9: 143
4. Neri P, Antoni G, Benvenuti F, Cocola F, Gazzei G (1973) J. Med. Chem. 16: 893
5. Caliceti P, Quarta SM, Veronese FM, Cavallaro G, Pedone E, Giammona G (2001) Biochim. Biophys. Acta 1528: 177
6. Yoon SW, Chung DJ, Kim JH (2003) J. Appl. Polym. Sci. 90: 3741
7. Pitarresi G, Palumbo FS, Giammona G, Casadei MA, Moracci FM (2003) Biomaterials 24: 4301
8. Wood LL (1994) USP 5,288,783
9. Harada K (1959) J. Org. Chem. 24:1662
10. Nakato T, Kusuno A, Kakuchi T (2000) J. Polym. Sci., Polym. Chem. Ed. 38: 117
11. Buchholz FL, Graham AT (1998) Modern Superabsorbent Polymer Technology, Wiely-vch, New York