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Swelling Behavior of pH-Sensitive Hydrogels Containing Degradable Poly(1,3-dioxolane) Segments

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ABSTRACT: pH-sensitive hydrogels were obtained by radical copolymerization of telechelic poly(1,3-dioxolane) (PDXLDA) with acrylic acid (AA). The copolymer networks of Poly(AA-*block*-DXL) showed pH sensitivity due to –COOH groups. They were insoluble in any solvents, but swelled in water or good solvents. The swelling behavior in both water and organic solvents is composition -dependent. The property that the hydrogel can swell in both water and organic solvents can be explained by a microphase-separated bicontinuous structure. The networks containing polyacetal segments (polyDXL) can be decrosslinked under acidic condition due to the low ceiling temperature of polyDXL. The networks structure, swelling behavior and degradation were characterized by Fourier transform infrared, differential scanning calorimetry, GC-MS analysis and swelling data.

KEY WORDS pH-Sensitive Hydrogel / Degradation / Poly(1,3-dioxolane) /

Polyacetals such as poly(1,3-dioxolane) (PDXL) provided with reactive endgroups have been used as building blocks for the preparation of macromolecular compounds with various material properties.[1] PDXL telechelic bismacromonomers can be synthesized by several methods,[2, 3] but few polymer networks have been prepared so far. Since polyDXL has a low ceiling temperature, the networks contain segments which are expected to degrade to monomer by treatment with a trace of an appropriate cationic initiator.[4] Therefore, such networks may be interesting from at least two points: first, solubilization of cross-linked polymers under mild conditions may be useful in itself; second, the possibility to study the soluble residual linear polymer chains may be used to obtain more insight in the copolymerization behavior. Among the reported networks containing polyDXL segments, including an elastic material by copolymerization with styrene, and amphiphilic polymer networks by copolymerization with methylmethacrylate (MMA) prepared by E. J. Goethals group.[5] However, no stimuli-sensitive such as pH-sensitive polymer networks containing poly(1,3-dioxolane) segment have been prepared.

In this paper, novel pH-sensitive network was prepared by copolymerization of poly(1,3-dioxolane) telechelic bismacromonomer with acrylic acid (AA). As we know, polyacrylic acid (PAA) is characterized as pH-sensitive.[6] Networks containing homopolymeric segments should give the polymer networks the same sensitivities. Due to the ease of degradation of PDXL in acid, the networks can be decrosslinked. Accordingly, these materials based on polyacetal segments have some interesting physical properties and have potential applications in biosystem, such as intelligent drug delivery system.

RESULTS AND DISCUSSION

Synthesis of PolyDXL Bismacromonomer

As reported earlier by Franta *et al.*,[7] polyDXL with primary hydroxy endgroups (HO–PDXL–OH) are obtained if the cation polymerization is carried out in the presence of a diol. This is due to a transfer reaction and /or to a propagation *via* an activated monomer mechanism.[8] Ethylene glycol was used as the diol to prepare the dihydroxylated polyDXL (macromonomer **I**). And the synthesis of polyDXL bismacromonomer was based on acrylation of **I** with acrylic acid, as shown in scheme 1.

This esterification reaction is carried out quantitatively without side reaction.[9] According to this reaction, the polyDXL bismacromonomer **II**-polyDXL diacrylate (**PDXLDA**) was produced. FT-IR spectra of the original polyDXL and the resulting PDXLDA are shown in Figure 1. The difference appears in 1638 and 1720 $\mathrm{cm^{-1}}$ attributed to the streching of C=C and C=O of the ester structure, respectively. In polyDXL, neither streching signals appear, while in PDXLDA, both signals appear due to AA end groups. Evidently, PDXLDA was an ester product of polyDXL. By comparison of number average molecular weight of PDXLDA attained from hydroxy titration with a calculated result of HNMR analysis, we got confirmed result. According to this, the functionality of terminal groups is about 2.0.

$$HO\sim\sim PDXL\sim\sim OH + CH_2{=}CH{-}COOH \xrightarrow[\text{pyridine}]{\text{DCCI}} CH_2{=}CH{-}COO\sim\sim PDXL\sim\sim OOC{-}CH{=}CH_2$$

I II

DCCI: dicyclohexylcarbodiimide

Scheme 1.

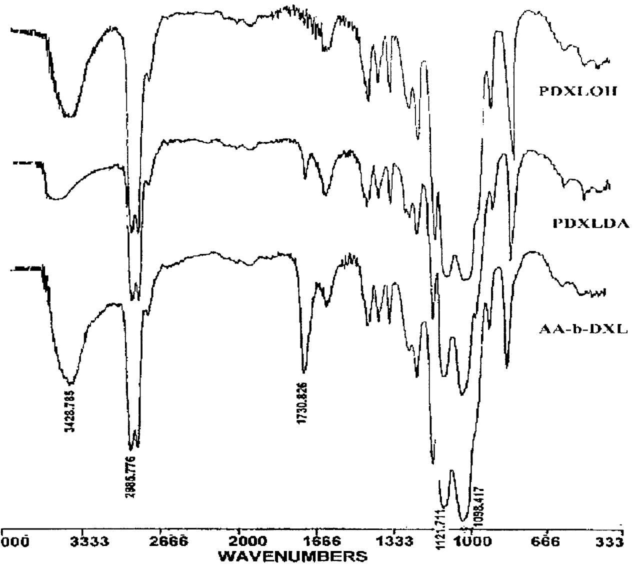

Figure 1. FT-IR-Spectrum of macromonomer 1: PDXL; 2: PDXDA; and networks 3: Poly(AA-*block*-DXL); M_n(PDXL) = 2500.

Synthesis and Characterization of pH-Sensitive Poly(AA-block-DXL) Networks

PDXLDA can copolymer with different monomers which can determine the properties of networks. If the comonomer is hydrophobic, amphiphilic networks are formed. Hydrophilic comonomer acrylic acid (AA) was selected to prepare polyacetal-based networks with some interesting physical properties. Radical copolymerization was all conducted in toluene at 70°C with 2,2′-azobis(2-methylpropionitrile) as initiator. The end products were transparent networks (**poly(AA-*block*-DXL)**) with high elasticity. From Figure 1 follows the IR-Spectrum of polymer networks (poly(AA-*block*-DXL)) in which the streching intensity of C=C bond was weakened and C=O bond was greatly strengthened by comparison with PDXLDA. The difference of the fingerprints between the PDXLDA and polymer networks also shows poly(AA-*block*-DXL) is a copolymerizaton product of PDXLDA with AA instead of a simple blend of these two constituents. The radical copolymerization of PDXLDA with AA does occur. The polymer network was dried to constant weight under vacuum and weighed and extracted with CH_2Cl_2 for 1 h to remove the unreactive monomer or residues and dried to constant weight and weighed again. The extraction ratio was about no more than 1%.

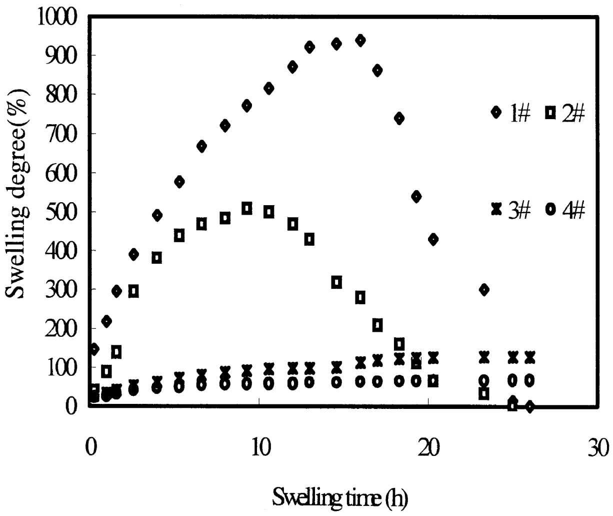

Figure 2. Swelling behavior of poly(AA-*block*-DXL) networks with different constituents in pH = 1.5 water, M_n (PDXL) = 2500, 1#: AA-*block*-95; 2#: AA-*block*-90; 3#: AA-*block*-65; 4#: AA-*block*-50.

Polyacrylic acid (PAA) is characterized as pH-sensitive hydrogel which is due to the –COOH groups. Similarly, the polymer networks with homopolymeric segments of acrylic acid should also be expected to have pH-sensitivity. Figures 2–4 testify this result. Figures 2–4 show that the swelling degree of the networks in high pH values is always higher than that of in low pH value under the same constituents. The swelling behavior of the poly(AA-*block*-DXL) networks is sensitive to pH values of water.

The swelling degree is calculated from:

$sd = (ws - wd)/wd \times 100$

ws: swelling sample; wd: dried gel sample.

The swelling degree of the hydrogels is mainly influenced by the ionization of –COOH functions in water. In pH = 1.5 (Figure 2), –COOH can hardly be ionized, thus formed strong hydrogen bonds among carbonyl groups prevent water to permeate into the networks. So it swells slowly and has the lowest equilibrium swelling degree. As shown in pH = 1.5 curve, the networks (AA-*block*-90) began to degrade in 10 h, and after 24 h the

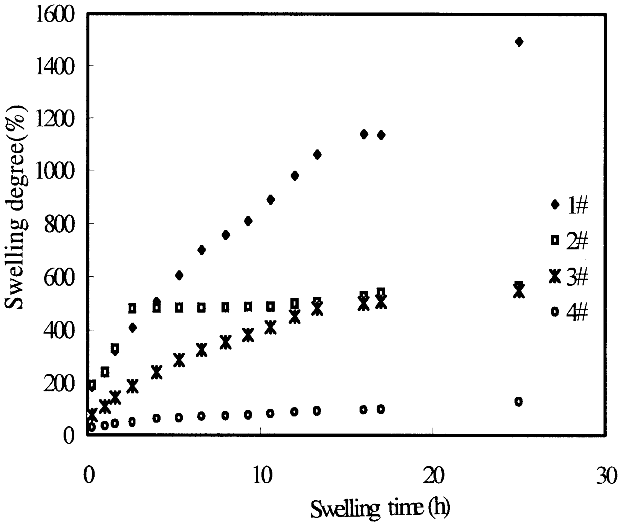

Figure 3. Swelling behavior of poly(AA-*block*-DXL) networks with different constituents in pH = 7.0 water, M_n (PDXL) = 2500, 1#: AA-*block*-95; 2#: AA-*block*-90; 3#: AA-*block*-65; 4#: AA-*block*-50.

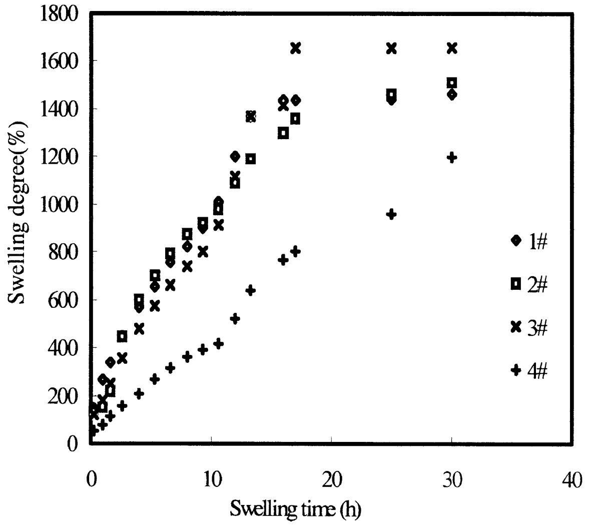

Figure 4. Swelling behavior of poly(AA-*block*-DXL) networks with different constituents in pH = 10 water, M_n(PDXL) = 2500, 1#: AA-*block*-95; 2#: AA-*block*-90; 3#: AA-*block*-65; 4#: AA-*block*-50.

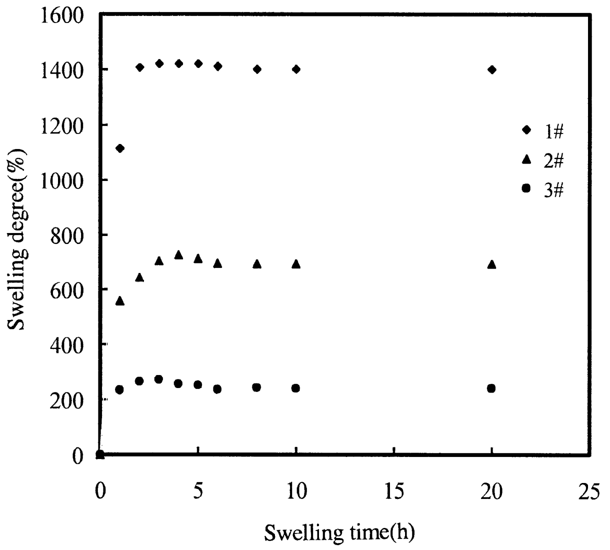

Figure 5. Swelling behavior of networks with different constituents in CH_2Cl_2, 1#: AA-*block*-95; 2#: AA-*block*-65; 3#: AA-*block*-50; M_n(pDXL) = 2500.

networks dissolved completely in water. At pH > 7.0 (present = 10.0), the –COOH functions can be easily ionized by reaction with OH^-. The networks swell fast and then reach the highest equilibrium swelling degree. While at pH ≥ 7.0, the networks can only swell untill reaching equilibrium swelling, but not be decrosslinked in water. With higher basicity, the networks can reach higher equilibrium swelling degree.

In the networks of poly(AA-*block*-DXL), AA homopolymeric segments are connected by the polyDXL segments. Figures 2–4 also show that the swelling degree of the hydrogel is dependent on the ratio of the two constituents. AA-*block*-95 means the ration of PDXL content in the networks is 95% (wt%). In Figure 2 (pH = 1.5), with decrease of PDXL content in the networks, the swelling degree decreases. The networks with high PDXL content degrade more easily and faster than networks with low PDXL content. Figure 4 shows the swelling kinetics of the hydrogels with different ratio of the two constituents in pH = 10.0. The equilibrium swelling degree increases with the AA content, but the swelling rate decreases with AA content. PDXL segments thus play a role in the swelling rate of the networks in water. This means that PDXL contributes more than PAA segments to swelling behavior in water.

The networks prepared swell in organic solvents. In CH_2Cl_2, the networks swell fast and has the highest equilibrium swelling degree, then in H_2O, THF, CH_3OH in turn. With increase of PAA content in networks, the swelling degree in organic solvents is also greatly influenced. Figure 5 support this. In CH_2Cl_2, the swelling degree decreases with increase of AA content contrary to the situation of in CH_3OH in which the swelling degree increases with AA content. The swelling behavior of the networks depends on a comprehensive effect of polarity, solubility parameters of the solvents. As a result, the swelling behavior of the networks is solvent-dependent and composition-dependent.

That the networks swell in water and organic solvents is interesting because it behaved like an amphiphilic networks. This behavior can be explained by a microphase-separated bicontinuous structure.[10] DSC analysis gives further support for a microphase-separated structure. Table I shows DSC analysis of the PDXL and polymer networks of poly(AA-*block*-

DXL) under the same heating process. Both of them show an endotherm at about 50°C which is due to the melting of the crystalline PDXL. In networks, another endotherm at 20°C appeared due to the copolymerization with PAA, because the PDXL segments act as crosslinking agent in the networks and the two chain segments of PDXL and PAA possess different flexibility. In the networks AA-*block*-90, the melting temperature of PDXL segments (53.8°C) has an increase than that of the PDXL macromonomer (46.1°C). This is also because the PAA chain segment is more rigid than the PDXL chain segment. The rigidity of the networks is increased so as to increase the melting temperature. The polymer networks show a microphase-separated interconnecting structure.

Degradation of the Networks

All polymer networks prepared degrade completely in acid solution. Degradation of Poly(AA-*block*-DXL) is shown in Figure 2. At pH = 1.5 water, the networks contain high content of PDXL segments can degrade completely in 24 h. The solvents had great influence on degradation. From Table II solvents such as CH_2Cl_2 in which the networks swell fast make the networks degrade fast. With the addition of isopropyl alcohol, the degradation was retarded because the hydroxy functions, due to the higher basicity, reduce the protonation of the acetal groups and hence the rate of degradation. After 1 h degradation (incompletely) of this networks (with $[CF_3SO_3H]= 0.01$ mol L^{-1}) in CH_2Cl_2, there were still some residues left in the bottle, most fragments solved in CH_2Cl_2. Both of them were determined respectively. Figure 6 was FT-IR spectra of the degraded residues. Only peaks of PAA was found in later, no signals in 1024–1120 cm^{-1} which belonged to C–O–C functions of polyDXL. This shows that the networks in which polyDXL acts as polymeric crosslinking agent were decrosslinked. By GC-MS of the degraded solution in CH_2Cl_2, the substance of 1,3-dioxolane, 1,3,5-trioxepane and 1,3,6-trioxocane were found in degraded solution. This is shown in Table III and proved that degradation does occur.

Table I. DSC analysis of Poly(AA-*block*-DXL) networks(AA-*block*-90) and polyDXL. M_n(pDXL) = 2500

Polymer	T_g/°C	T_m/°C	
PDXL	−60.0	–	–
PAA	106.0	–	–
PDXLDA	–	53.8	–
AA-*block*-90	–	46.1	20.0

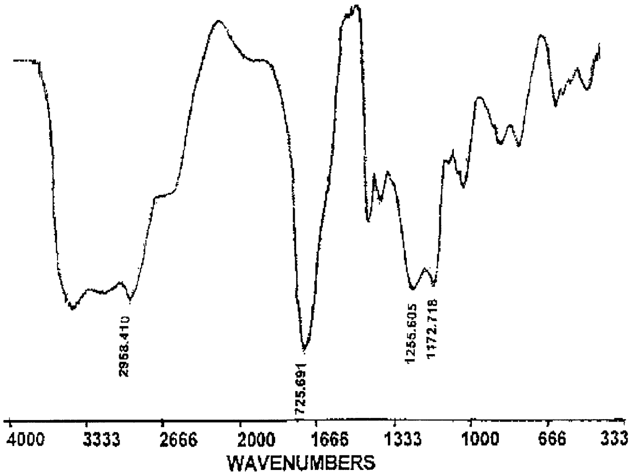

Figure 6. FT-IR spectrum of degraded residues of polymer networks AA-*block*-90; M_n(pDXL) = 2500.

EXPERIMENTAL

Reagents

1,3-Dioxolane, Acros Organics, was purified by distillation over CaH_2 and dried on sodium wire under reflux in the presence of a trace of benzophenone until a blue color was obtained. The monomer was distilled just before use (bp 74°C). Dichloromethane was distilled twice over CaH_2. The solvent was distilled just

Table III. Analysis of degraded solution in CH_2Cl_2 by GC-MS

Peak#	RT(min)	ID	Quality /%	Area /%
1	1.48	Chloromethane	91	3.66
2	1.55	Ethyl chloride	96	0.95
3	1.72	Methylene chloride	96	73.55
4	1.97	1,3-Dioxolane	91	19.81
5	3.47	1,3,5-Trioxepane	64	1.78
6	4.10	1,3,6-Trioxocane	91	–

RT: retention time. ID:identification.

Table II. Degradation of Poly(AA-*block*-DXL) networks (AA-*block*-90) under different conditions at 25°C (M_n(PDXL) = 2500)

Solvents	$[H^+]^a$/mol L^{-1}	$[OH]^b$/mol L^{-1}	Degradation time/h
CH_2Cl_2	0.01	0	2
CH_2Cl_2	0.005	0	2.5
CH_2Cl_2+isopropyl alcohol	0.01	0.01	2.5
CH_2Cl_2+isopropyl alcohol	0.01	0.1	12
THF	0.01	0	4
H_2O	0.01	0	25

[a] CF_3SO_3H content. [b] Isopropyl alcohol content.

before use. Triflic acid was purified by distillation. Acrylic acid was distilled in a trace of benzoquinone. Dried pyridine was obtained by distillation in KOH.

*Synthesis of α,ω-Dihydroxylated PolyDXL (**I**)*

15 µL CF_3SO_3H in 10 mL of CH_2Cl_2 solution placed in a 50 mL flask provided with stirring and an inlet for dry nitrogen. 0.2 mL ethylene glycol was added. With stirring, 20 mL dioxolane dropwise added to the system. The mixture was stirred for 3 h and thermostated at 50°C. Excess *tert*-butylamine was added to stop the reaction. The reaction mixture was poured out into beaker and precipitated in cold ether and washed several times with ether. Then the precipitate was dried under vacuo. 15.5 g (yield 80%) of **I** with $M_n = 2500$ was obtained.

Synthesis of PolyDXL Bismacromonomer

Ten grams OH–PDXL–OH ($M_n = 2500$) and 10 mL of pyridine were placed in a flask with stirring and an inlet for dry nitrogen. One milliliter acrylic acid was introduced. Two grams dicyclohexacarbodiimide in 5 mL CH_2Cl_2 solution dropwise added. The mixture was thermostated at 25°C for 2 h. The mixture was washed with cold ether several times. The precipitate was dried under vacuum. Eight point five grams PDXL diacrylate (PDXLDA) (yield 85%) were obtained.

Polymer Networks Synthesis

Ten milliliter of toluene, 1 g PDXLDA, 5 mg of 2,2′-azobis(2-methylproprionitrile), a certain amount of comonomer were placed in a 20 mL test tube. The tube was sealed under vacuum at 70°C for 16 h. A gel was obtained. To remove unreacted monomers, the product was sequentially extracted with dichloromethene, ethanol. After drying under vacuum, the gel was cut into round thin slims and characterized of its swelling degree and its degradation in acid.

Swelling Degree Measurements

Dry discs of 10–20 mm diameter were immersed in distilled water or other solvents and equilibrated for at least 24 h, removed from the solvent, blotted with filter paper and weighed every 30 or 60 min.

Degradation in Acid Solution

Two grams polymer networks were placed in 10 mL of a 0.01 mol L^{-1} triflic acid solution in CH_2Cl_2or other solvents. Degradation time was measured time necessary to dissolve the material completely.

DSC Measurements

DSC curves were obtained at a standard heating and cooling rate of 10°C min^{-1}. Samples were run in an argon atmosphere at −100°C to 150°C.

CONCLUSION

Polymer networks containing polyacetal segments with pH-sensitivity or other special physical properties can be prepared by copolymerization of polyDXL bismacromonomer with different monomers which determine the properties of networks. The networks as these two segments possess two important physical properties: swelling and degradation. The swelling behavior of polymer networks was pH-sensitive, solvent-dependent, and composition-dependent. Degradation is also influenced by solvents, acid concentration etc. After degradation, the linear segments of polyDXL became cycled molecules. Based on this study, more attention could be paid to these materials for potential application to biosystem.

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