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ScienceDirect
Polymer 47 (2006) 6481–6484
polymer
www.elsevier.com/locate/polymer

Polymer Communication

Cryogels of cellulose derivatives prepared via UV irradiation of moderately frozen systems

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Received 18 April 2006; received in revised form 7 July 2006; accepted 23 July 2006
Available online 9 August 2006

Abstract

Cryogels of non-ionic (hydroxypropyl)methylcellulose, 2-hydroxyethylcellulose, methylcellulose and cationic hydroxyethylcelluloses were prepared for the first time via UV irradiation of moderately frozen systems. The influence of the irradiation time, the concentration of the photoinitiator (4-benzoylbenzyl)trimethylammonium chloride, and the concentration of the polymer solution on the efficiency of the cross-linking process in moderately frozen systems was investigated. It was found that 2-min irradiation at an irradiation dose rate of 5.7 J/cm^2 min is adequate for cross-linking of 3 wt.% polymer solutions resulting in high quality cryogel.

Keywords: Cryogels; Cellulose derivatives; UV irradiation

1. Introduction

Hydrogels based on both natural and synthetic polymers have found various applications in medicine and pharmacy as drug and cell carriers, tissue engineering matrices, membranes for biosensors, contact lenses, etc. [1,2]. Cellulose derivatives have received considerable attention because of their water solubility, easy biodegradation and low costs. Hydrogels of cellulose derivatives can be obtained either by reaction with chemical reagents or by ionizing radiation [3–8]. Wach et al. have demonstrated that two processes, degradation and cross-linking, are in competition at high-energy irradiation with either electron beam or gamma rays of numerous cellulose derivatives [4,5,7]. The authors have found that when exposed to ionizing radiation at ambient temperature in solid state and in aqueous solutions of low concentration (less than 10 wt.%) the examined polymers undergo degradation, while the best results of cross-linking have been obtained at paste-like conditions (25–40 wt.% depending on the polymer). It is noteworthy that in the case of highly concentrated polymer solutions several days are required for complete dissolution of the cellulose derivative in water [4].

Recently, Doycheva et al. [9] obtained hydrogels of high molecular weight poly(ethylene oxide) by UV irradiation of both aqueous solutions and moderately frozen aqueous systems. The process of gel formation, which takes place in a frozen system, and the subsequent thawing are named cryotropic gelation and the materials obtained – cryogels [10]. The advantages of the UV irradiation are the very low capital outlay and the extremely short time for efficient gel formation.

The present paper aims at reporting on the first results for effective cross-linking of various cellulose derivatives via UV irradiation of moderately frozen systems on the basis of semidilute aqueous solutions of the polymers.

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doi:10.1016/j.polymer.2006.07.047

2. Experimental part

2.1. Materials

(Hydroxypropyl)methylcellulose (HPMC), 2-hydroxyethylcellulose (HEC), methylcellulose (MC), (4-benzoylbenzyl)trimethylammonium chloride (BBTMAC), *N*,*N*′-methylenebisacrylamide, and poly(ethylene glycol) diacrylate (M_n ca. 700) were purchased from Aldrich and used as received. Cationic hydroxyethylcelluloses (Ucare polymer JR-30M and Quatrisoft polymer LM-200) were obtained from Union Carbide Chemicals and Plastics Co.

2.2. Cryogels preparation

Each polymer (Table 1) was dissolved in an appropriate amount of distilled water to obtain semidilute solution (0.5–4 wt.%) and the sample was kept for 24 h at 5 °C to ensure complete dissolution and homogeneity. Given amount of photoinitiator, BBTMAC, (0.5–15 wt.% with respect to the polymer) dissolved in 2 ml water was added under stirring at room temperature. The resulting homogeneous solution was poured into 8 Teflon dishes (20 mm diameter) forming a 2.5 mm thick layer, which was then kept in a freezer at −30 °C for 2 h. The dishes were then quickly placed in a thermostated open chamber connected with a cryostat apparatus (“Julabo”). The frozen system was irradiated with full spectrum UV–vis light at −30 °C with a Dymax 5000-EC UV curing equipment with 400 W metal halide flood lamp for 1–5 min (input power = 93 mW/cm^2).

In some experiments cross-linking agent, *N*,*N*′-methylenebisacrylamide or poly(ethylene glycol) diacrylate (3 wt.% with respect to the polymer) was used. In this case, the concentration of the polymer solution was 3 wt.% and the amount of the photoinitiator was 2 wt.% (to the polymer mass).

In control experiments, 3 wt.% polymer solutions were irradiated with UV–vis light at room temperature.

2.3. Measurements of gel fraction yield and equilibrium degree of swelling

Gel fraction (GF) yield and equilibrium degree of swelling (ES) of the cryogels were determined gravimetrically. GF content in the dried sample was estimated by weighing the insoluble part after extraction in distilled water for 7 days at room temperature. GF yield [%] = (wt. of dried sample/initial wt. of polymer) × 100. ES was determined at room temperature. Disks of dried cryogel were immersed in distilled water and an equilibrium water uptake was reached (at least 72 h). The surface of the cryogel was blotted by filtration paper prior to weighing. ES = wt. of swollen sample/wt. of dried sample.

Table 1
Characteristics of non-ionic and cationic cellulose derivatives as specified by the suppliers

Cellulose derivative	DS[a]	MS[b]	DQ[c]	Approximate mol. weight (g/mol)
HEC	1	2	–	250,000
HPMC	1.1–1.6	0.1–0.3	–	120,000
MC	1.5–1.9	–	–	88,000
JR-30M	–	–	0.4	900,000
LM-200	–	–	0.08	250,000

[a] Degree of substitution.
[b] Molar degree of substitution.
[c] Molar degree of substitution of quaternary ammonium moiety.

2.4. Dynamic rheological measurements

Dynamic rheological measurements of the cryogels were performed on a Haake RheoStress 600 rheometer with a parallel plate sensor system (20 mm diameter) and Peltier temperature controller. Disks of the cryogels were extracted for 7 days and the dynamic storage (G') and loss (G'') moduli were measured in the 0.1–10 Hz frequency range at 25 °C in CD-mode ($\gamma = 0.005$).

3. Results and discussion

Semidilute solutions of non-ionic (hydroxypropyl)methylcellulose, 2-hydroxyethylcellulose, methylcellulose and cationic hydroxyethylcellulose (JR-30M), and hydrophobically modified cationic hydroxyethylcellulose (LM-200) were irradiated with UV–vis light in both frozen state (−30 °C) and at room temperature. The frozen-thawed samples were opaque spongy materials, while all samples irradiated at RT were still liquid. Fig. 1 shows the storage and loss moduli in the 0.1–10 Hz frequency range of 3 wt.% aqueous HEC solutions irradiated at the above mentioned conditions. The apparent values of G' and G'' of the sample obtained by UV irradiation of the frozen aqueous systems exhibit little dependence on the frequency (f) and $G' > G''$ over the entire f range explored. The observed results are consistent with the typical behavior of a polymer gel [11] and indicate that cross-linking reactions

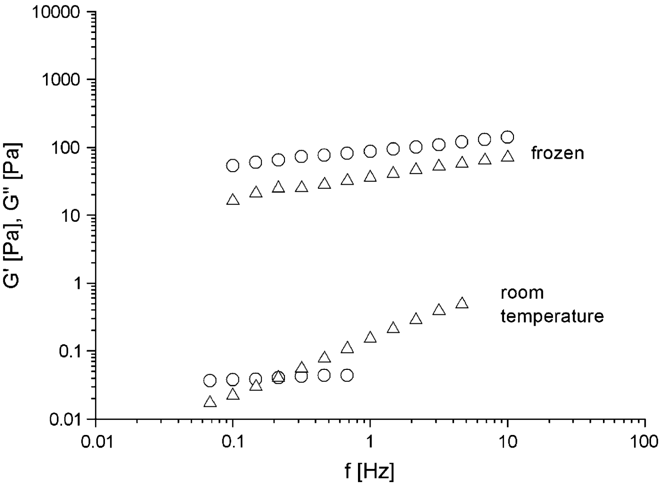

Fig. 1. Variation of elastic (○) and loss (△) moduli in the 0.1–10 Hz frequency range of 3 wt.% aqueous HEC solutions irradiated with UV–vis light at room temperature and in frozen state; 5 wt.% BBTMAC; irradiation time: 2 min.

occur predominantly under the chosen experimental conditions. In contrast, the sample irradiated at room temperature exhibits quite a different behavior. G'' is strongly dependent on f and a cross-over at ca. 0.2 Hz was observed. The values of G' and G'' are orders of magnitude lower than the moduli of the frozen-thawed sample. Moreover, the viscosity (η) of the initial solution is higher than η of the solution after irradiation at room temperature, which is an evidence for degradation of HEC macromolecules.

The general features of the cryotropic gelation as well as the similarities and differences when compared to gelation under positive temperatures were recently reviewed by Lozinsky [10]. According to the accepted model, a system obtained by moderate freezing of multi-component systems (including polymers) consists of polycrystals of the frozen solvent and a non-frozen liquid microphase (NFLMP). It is noteworthy that the soluble substances are accumulated in the NFLMP. In addition, it was found that after crystallization of the main bulk of the solvent, a certain fraction of the solvent is not incorporated into the solid phase. Due to the non-freezable solvent molecules the non-frozen microphase retains liquid and thus the solutes accumulated into NFLMP possess sufficient molecular or, in the case of polymers, segmental mobility. Moreover, due to the cryoconcentration effect and some other factors (for example, increased dielectric constant of the medium upon cooling) an acceleration of chemical reactions is observed within a defined range of negative temperatures for the solvent used. Based on the theory for cryotropic gelation, we suggest that during freezing of semidilute water solutions of cellulose derivatives the major portion of the solvent forms crystals, whereas polymer, the photoinitiator and the water molecules connected to the polymer through hydrogen bonds (non-freezable solvent) form a non-frozen liquid microphase. Obviously, the polymer concentration in NFLMP is very high (cryoconcentration effect) and the reaction conditions closely resemble the conditions in the paste-like state. Therefore, during UV irradiation the reactions of cross-linking prevail over the chain scission reactions and a cryogel is formed. The mechanism of photochemical cross-linking induced by BBTMAC photoinitiator has been discussed elsewhere [9]. The cross-linking occurs by hydrogen atom abstraction from the polymer chains and subsequent intermolecular recombination of two macroradicals. The difference between the samples irradiated at room temperature and those irradiated at −30 °C can be explained by the fact that the low yield of intermolecular recombination in semidilute solutions is caused by insufficient number of chains in close vicinity to each other. Therefore, the scission is the predominant reaction in the samples irradiated at room temperature. In contrast, due to the cryoconcentration effect in the frozen sample, the cross-linking reactions are favored and gels of cellulose derivatives were obtained.

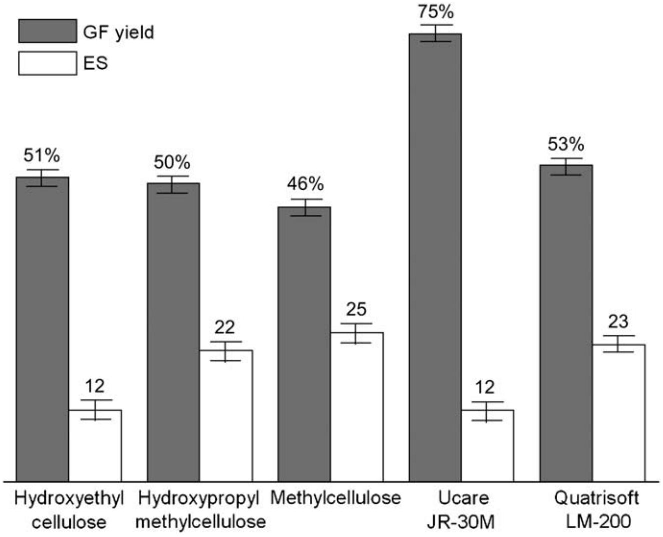

Fig. 2. Cryogels via UV−vis irradiation of moderately frozen systems prepared on the basis of 3 wt.% solutions of different non-ionic and cationic cellulose derivatives; 5 wt.% BBTMAC; irradiation time: 2 min.

Cryogels of non-ionic HPMC, HEC, MC, of cationic HEC and of hydrophobically modified cationic HEC were successfully prepared by UV irradiation of frozen systems for 2 min (dose = 11.4 J/cm^2). Gel fraction yields between 46 and 75% and equilibrium degrees of swelling between 12 and 25 times were estimated gravimetrically (Fig. 2). Importantly, cryogels of cellulose derivatives are opaque materials and a significant part of water can be separated easily by compression at low mechanical loads. This observation is in a good agreement with the theory of cryostructuration [10]. According to this theory, the cryogels are macroporous and usually spongy non-transparent materials. The crystals of the frozen solvent act as a porogen. After thawing the capillary-bound solvent can be easily separated by compression.

The influence of the most important factors for the process of gel formation, such as irradiation time, concentration of photoinitiator, concentration of polymer solution, on the cross-linking process in moderately frozen HPMC aqueous systems was investigated.

Aqueous solutions (3 wt.%) containing 5 wt.% photoinitiator (with respect to the polymer) were frozen and then irradiated with UV−vis light within the 1−5 min interval (5.7−28.5 J/cm^2). A gel forms even at the initial stage of irradiation and the GF yield increases with the irradiation time in the first 2 min. Then GF yield reaches a constant value and no significant changes are observed in the studied time interval.

The influence of the photoinitiator content (0.5−15 wt.% with respect to the polymer) on the cross-linking efficiency showed similar behavior. At BBTMAC concentrations lower than 2 wt.% the GF yield increases with the increase of the photoinitiator, while between 2 and 15 wt.% the amount of photoinitiator does not affect the content of the gel fraction in the samples studied. It seems that 2 wt.% BBTMAC is a sufficient concentration for effective cross-linking, however, 5 wt.% BBTMAC was used in most of our experiments.

Table 2 shows the influence of the initial concentration of HPMC aqueous solution on the cross-linking efficiency. The GF yield and the cross-linking density increase (ES decreases) with increasing the concentration and reach a maximum at polymer concentration of 2 wt.%, followed by a decrease at

Table 2
Influence of the polymer concentration on the cross-linking efficiency in moderately frozen HPMC systems; 5 wt.% BBTMAC; irradiation time: 2 min

Concentration of HPMC solution wt.%	GF yield (%)	ES in H_2O
0.5	44 ± 2	33 ± 3
1	63 ± 2	14 ± 2
2	64 ± 2	15 ± 2
3	50 ± 2	22 ± 2
4	39 ± 2	26 ± 3

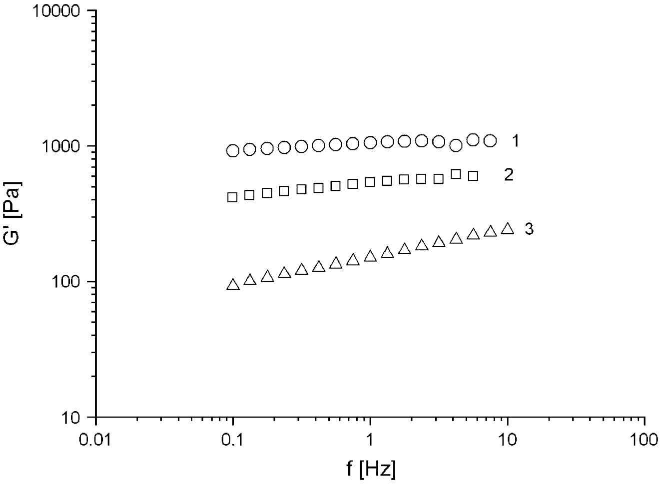

Fig. 3. Elastic moduli of cryogels prepared by UV–vis irradiation of moderately frozen systems based on 3 wt.% aqueous HPMC solutions containing 3 wt.% *N*,*N*′-methylenebisacrylamide (1), 3 wt.% poly(ethylene glycol) diacrylate (2), and without cross-linking agent (3); 2 wt.% BBTMAC; irradiation time: 2 min.

higher concentrations. Obviously, the best conditions for cross-linking of the studied HPMC solutions are in the 1–2 wt.% concentration interval. At concentration >3 wt.% the mixtures become highly viscous, which possibly hinders the process of regular cryostructuration resulting in lower yield of gel fraction and higher values of ES.

The GF yield of HPMC cryogels was further improved by addition of cross-linking agent to the initial aqueous solution. Two different bifunctional water soluble cross-linking agents, *N*,*N*′-methylenebisacrylamide and poly(ethylene glycol) diacrylate, were tested. As expected, the GF yield increased from 50 to 67% when MBAAm was used and to 63% in the case of PEGDA.

The incorporation of cross-linking agent into the cryogel has an impact on the viscoelastic properties of the material obtained. Fig. 3 shows the apparent elastic moduli of HPMC cryogels prepared with MBAAm, PEGDA and without cross-linking agent. The two cryogels containing cross-linking agents exhibit much higher G' compared to the sample without a cross-linking agent. This could be due to the increased cross-linking density and the type of incorporated segments. It should be mentioned that water loss during the measurements was not taken into account, however, we did not observe significant difference between the amounts of squeezed water of the samples studied. The rheological data do not exactly characterize the real physicomechanical properties of the gel phase in spongy cryogels, but it shows that by incorporating cross-linking reagents into the cryogels, materials with different properties can be produced.

4. Conclusions

UV irradiation is applied for the first time for successful cross-linking of various non-ionic and cationic cellulose derivatives in moderately frozen state. The main advantages of this method are the relatively fast preparation of homogeneous semidilute solution of polymer and photoinitiator and the extremely short irradiation time required for obtaining high quality cryogels. Importantly, cryogels of cellulose derivatives are opaque materials and a part of the solvent can be separated easily by compression. The gel fraction yield and the elastic properties of the cryogels can be improved by the addition of a small amount of cross-linking agent.

Acknowledgement

The preliminary experiments of this work were supported by VIRSOL (Paris, France). The authors gratefully acknowledge the financial support by ''Alexander von Humboldt Stiftung'' for the rheometer RheoStress 600 and SONY International for the Dymax UV-light curing system.

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