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UV-assisted synthesis of super-macroporous polymer hydrogels

Petar Petrov*, Elissaveta Petrova, Christo B. Tsvetanov

Institute of Polymers, Bulgarian Academy of Sciences, "Akad. G. Bonchev" Str. 103A, 1113 Sofia, Bulgaria

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ABSTRACT

A facile method to the synthesis of polymer cryogels employing the UV irradiation technique and hydrogen peroxide as initiator is presented. Various cryogels composed of either biocompatible, biodegradable and/or temperature-responsive polymers are synthesized from polymer or monomer precursors. It is found that due to the macroporous structure, the cryogels exhibit a very rapid water uptake and, in the case of temperature-responsive polymers, ultra-rapid volume phase transition. The immobilization of Ag nanoparticles (Ag NPs) into cryogels by two different approaches allows preparation of hybrid systems possessing either very fast release of Ag NPs or very slow release of Ag^+.

1. Introduction

Polymer hydrogels are an important class materials with wide application, especially in medicine and pharmacy as drug carriers, tissue engineering matrices, membranes for biosensors, contact lenses, wound dressings, cell carriers, etc. [1–4]. Currently, there is an increasing interest in macroporous polymer gels due to their unique heterogeneous open porous structure which significantly increases their equilibrium sorption properties and allows unhindered diffusion of solutes, nano- and even micro-particles [4]. A considerable number of studies have been undertaken on the synthesis of intelligent macroporous hydrogels which are able to respond to environmental changes. Poly(*N*-isopropylacrylamide) macroporous gels seem to be the most investigated stimuli-responsive macroporous gels. These gels undergo an ultra-fast reversible volume phase transition from swollen to deswollen state at temperature about 33 °C [5–9]. Among the different methods, the cryotropic gelation is one of the most attractive techniques for preparation of macroporous hydrogels (cryogels) [4,10–17]. The process involves a moderate freezing of the system, a reaction of cross-linking and a subsequent thawing. In this process, most of the water is frozen and forms ice crystals while the non-freezable water and the soluble substances like polymer or monomer, initiator, cross-linking agent, etc. are accumulated in a non-frozen liquid microphase. The gel formation occurs in this liquid microphase and the ice crystals perform as porogens.

Recently, the first effective syntheses of cryogels of poly(ethylene oxide) and various cellulose derivatives via UV irradiation of moderately frozen systems were reported by our group [18–20]. The advantages of the UV irradiation technique are the very low capital outlay and the extremely short time for efficient gel formation. Cryogels of good quality and high gel fraction yield were prepared by UV irradiation of moderately frozen polymer systems for only 2 min at an irradiation dose rate of 5.7 J/cm^2 min by using an aromatic photoinitiator (4-benzoylbenzyl)trimethylammonium chloride (BBTMAC). In this paper, we report on the synthesis of various polymer cryogels via UV irradiation using hydrogen peroxide as initiator. Cryogels either from cross-linker free polymer solution or from monomer solution but with extremely high gel fraction yield, approaching to 100% were obtained. Such materials are composed of biocompatible, biodegradable and/or temperature-responsive polymer network and water and meet the requirements for application in biomedical areas.

2. Experimental section

2.1. Materials

Hydroxyethylcelluloses (HPC-1.150 for mol. wt. 1 150 000 and HPC-850 for mol. wt. 850 000 g/mol) were donated by Hercules Inc. (Aqualon Division, USA) and used as received. H_2O_2 (30 vol.% water solution), acrylamide, polyacrylamide (mol. wt. $= 5 \times 10^6$–6×10^6 g/mol), *N*-isopropylacrylamide, *N*-vinylcaprolactam, 2-hydroxyethyl methacrylate and poly(ethylene glycol) diacrylate (aver. mol. wt. ~575 g/mol) were purchased from Aldrich and used without purification. Aqueous dispersion of Ag nanoparticles

* Corresponding author. Tel.: +359 2 9792281; fax: +359 2 8700309.
E-mail address: ppertov@polymer.bas.bg (P. Petrov).

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(ABIO2, conc. $\sim 4.10^{-3}$ g/L) was donated by Nanoindustry Inc., Russia.

2.2. Syntheses of cryogels

An appropriate amount of each polymer/monomer was dissolved in distilled water under stirring to obtain homogeneous aqueous solution (0.2–15 wt.%). Given amounts of initiator (and cross-linking agent) were added under stirring at room temperature. In the case of *N*-vinylcaprolactam, 10 vol.% ethanol was added to solubilize the monomer. The resulting homogeneous solution was poured into Teflon dishes (20 mm diameter) forming a 4 mm thick layer, which was then kept in a freezer at −20 °C for 2 h. The dishes were then quickly placed in a thermostated open chamber connected with a "Julabo" cryostat apparatus. The frozen system was irradiated with full spectrum UV–vis light with a "Dymax 5000-EC" UV curing equipment with 400 W metal halide flood lamp for 2, 5 or 10 min (irradiation dose rate = 5.7 J/cm^2 min; input power = 93 mW/cm^2). HPC cryogel with embedded Ag NPs was synthesized by dissolving HPC-1.150 in aqueous dispersion of Ag NP following the procedure described above.

2.3. Measurements of gel fraction yield and degree of swelling

Gel fraction (GF) yield and degree of swelling (DS) of the cryogels were determined gravimetrically. The GF content in the dried sample was estimated by weighing the insoluble part after extraction in distilled water for 6 days at room temperature. GF yield [%] = (weight of dried sample/initial weight of polymer) × 100. The degree of swelling was determined as follows. Disks of freeze dried cryogel were weighted and then immersed in distilled water at room temperature and an equilibrium water uptake was reached. The surface of the cryogel was blotted by filter paper prior to weighing. DS = weight of swollen sample/weight of dried sample. The experimental errors of the GF yields and the ES calculations are in the range 2–3%. In all figures, the size of the symbols roughly corresponds to the experimental error.

2.4. Rheological measurements

The measurements were performed on a Haake RheoStress 600 rheometer with a parallel plate sensor system and Peltier temperature controller. The storage modulus of the cryogels were determined by frequency sweep measurements performed in the 0.01–1 Hz frequency range at 25 °C in CD-mode (Controlled Deformation) at $\gamma = 0.005$.

2.5. Scanning electron microscopy studies

The extracted gels were quickly frozen in liquid nitrogen, fractured and freeze dried in an "Alpha 1-2 Freeze Drier" (Martin Christ) at −55 °C and 0.02 mbar for 24 h. The interior morphology of the gels was studied by using a JEOL JSM-6390 scanning electron microscope operating at 5 kV. Before observations, the gel specimens were fixed on a glass substrate and coated with gold for 60 s.

3. Results and discussion

3.1. Synthesis of cryogels from polymeric precursors

Hydroxypropylcellulose and polyacrylamide cryogels were obtained by UV irradiation of moderately frozen systems, using hydrogen peroxide as a source of radicals (5 wt.% with respect to the polymer), and subsequent thawing. H_2O_2 generates hydroxyl radicals during its photo-homolysis [21,22] which react with the polymer molecules giving rise to macroradicals. The cross-linking occurs by intermolecular recombination of two macroradicals.

Generally, the synthesis of cryogels using H_2O_2 follows the same experimental features as those reported for the water-soluble derivative of benzophenone [19,20]. It is found that the highest GF yield is reached at a freezing temperature of −20 °C and irradiation with UV light for minimum 2 min at an irradiation dose rate of 5.7 J/cm^2 min. The concentration of the initial polymer solution is very important factor to obtain cryogels of good quality. Here, one should mention that cryogels of good quality are those gels which maintain their original compactness and heterogeneous morphology when exposed to an excess of water. We found that there is a range of concentrations relating to the polymer type and molecular weight which provides the best conditions for cryostructuring and cross-linking (Table 1).

For instance, the maximum GF yield of HPC-1.150 cryogels was reached at 2 wt.% and, then at higher concentrations (≥3 wt.%) GF yield decreased due to the very viscous initial solution (physical gel) and hindered homogenization. Similar trend was observed with the PAAm precursor where the maximum GF yield was reached at 5 wt.%. As expected, the GF yield can be increased by adding small amount of cross-linking agent.

3.2. Synthesis of cryogels from monomer precursors

The UV irradiation technique was explored to synthesize polymer cryogels from aqueous solution of monomer, H_2O_2 and cross-linking agent. The polymer network is formed by free radicals polymerization/cross-linking reaction initiated by the UV light. The existence of cross-linking agent is the determining factor for obtaining a three-dimensional network instead of linear macrochains.

In this work we studied mainly the influence of the concentration of the initial monomer solution on the cross-linking efficacy. Remarkably, PNIPAAm and PAAm cryogels of extremely high GF yield (nearly quantitative monomer conversion) were obtained from 2 to 5 wt.% aqueous solutions of NIPAAm and AAm, respectively (Table 2). The as-synthesized materials do not contain undesirable monomer and cross-linking agent and, therefore, can be directly used without any extraction procedure. The conversion of HEMA to PHEMA cryogel within the studied concentration range is also very high, while VCL cannot form cryogels of high GF yield even when irradiated with UV light for 10 min. One possible reason for the low crosslinking efficacy might be the poor solubility of VCL in water. To obtain homogeneous initial monomer solution

Table 1
Formation of cryogels from polymeric precursors; temperature of freezing −20 °C, H_2O_2 – 5 wt.%.

Polymeric precursor	Polymer concentration (wt.%)	Irradiation time (min)	GF yield (%)	Swelling degree at 20 °C	Swelling degree at 60 °C
HPC-1.150	0.5	2	Traces	–	
	1	2	41	39	–
	2	2	66	22	11
	3	2	59	23	11
HPC-850	0.5	2	n	–	–
	1	2	Traces	–	–
	3	2	52	38	12
PAAm	1	5	34	–	–
	2	5	63	24	–
	5	5	71	35	–
PAAm/PEGDA[a]	5	5	94	27	–

[a] PEGDA-10 wt.%.

Table 2
Formation of cryogels from monomer precursors; temperature of freezing −20 °C, H_2O_2 – 5wt.%, PEGDA-10 wt.%.

Monomeric precursor	Monomer concentration (wt. %)	Irradiation time (min)	GF yield (%)	Swelling degree at 20 °C	Swelling degree at 50 °C
NIPAAm	2	5	>99	17	6
	5	5	>99	18	6.5
	10	5	97	17	5
	15	5	87	13	5
AAm	2	5	>99	121	–
	5	5	>99	23	–
	10	5	96	17	–
	15	5	90	11	–
HEMA	2	5	92	5.5	–
	5	5	92	5.5	–
	10	5	92	6	–
	15	5	87	5.5	–
VCL	2	10	n	–	–
	5	10	n	–	–
	10	10	25	21	19
	15	10	15	26	17

a portion of ethanol (10 vol.%) was added to the aqueous system which obviously affects the regular cryo-structuring and hinders the formation of polymer network.

3.3. Properties of cryogels

All cryogels obtained are macroporous opalescent materials with an open porous structure, which significantly increases the rate of water uptake due to the capillary effects. Since we found that the freeze-drying preserves the original morphology of cryogels [20] this method was employed in the present study for determining the swelling ratios. It should be noted that the cryogels are heterogeneous materials consisting of dense polymer walls surrounding interconnected pores filled with free water. In this case the use of the accepted for conventional hydrogels definition "equilibrium degree of swelling" is a little bit speculative, however, for evaluation of the swelling ratios the freeze dried specimens were equilibrated (until constant weight) in water. In general, more

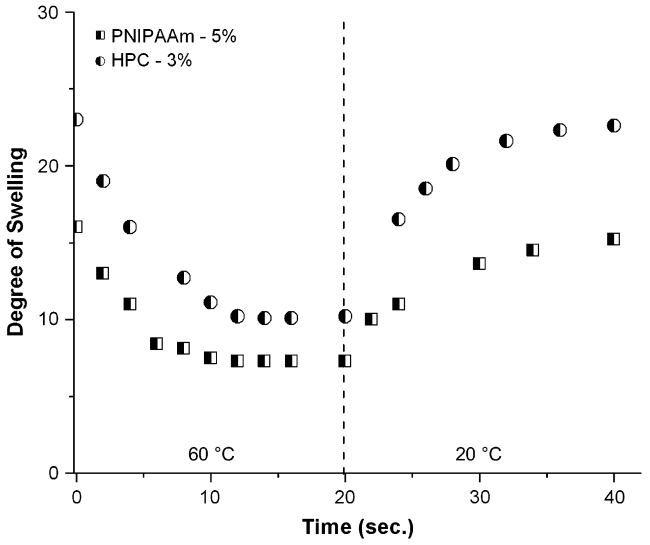

Fig. 2. Deswelling–reswelling kinetics of HPC-1.150 and PNIPAAm cryogels synthesized via UV irradiation.

that 80 vol.% of water is taken up by the cryogel within several seconds, and the constant weight is reached within several hours. The degree of swelling of each cryogel (Tables 1 and 2) depends on the polymer nature, pores size and the cross-linking density of the polymer walls. Specifically, in water PHEMA cryogels maintain their initial volume obtained according the synthesis procedure and no additional swelling is observed. Generally, PHEMA network is less hydrophilic compared to the other polymers and mainly the existence of macroporous morphology contributes to the apparent degree of swelling equal to 6. More interesting behavior exhibit the cryogels comprising the so-called LCST properties [23,24]. These cryogels shrink drastically at temperature above the LSCT of the corresponding polymer. The volume phase transition curves from swollen to deswollen state of two temperature-responsive cryogels, HPC and PNIPAAm, are shown in Fig. 1. HPC cryogel decreases its degree of swelling 2.5 times above 50 °C, while PNIPAAm cryogel shrinks 3 times above 35 °C.

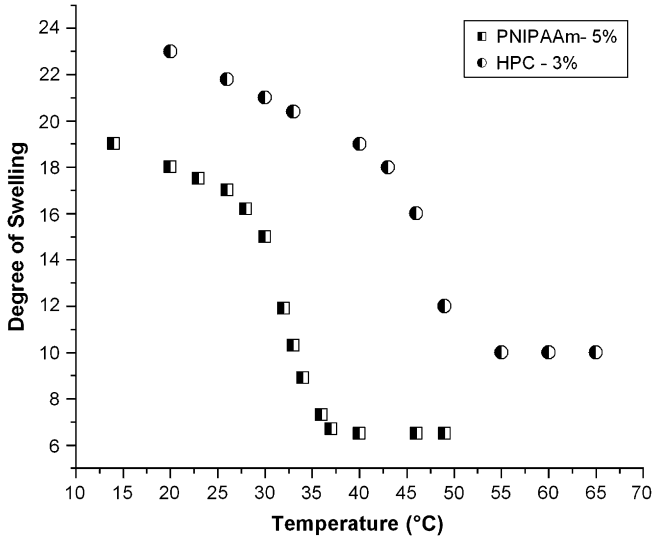

Fig. 1. Temperature dependence of the swelling properties of HPC-1.150 and PNIPAAm cryogels synthesized via UV irradiation.

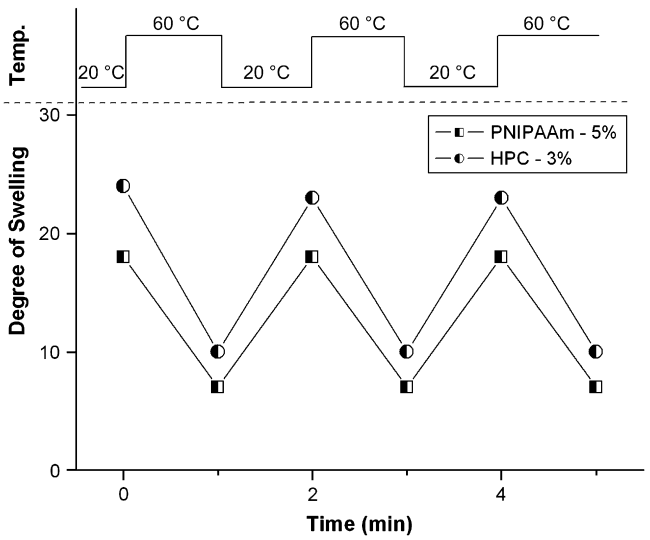

Fig. 3. Swelling–shrinking kinetics of HPC-1.150 and PNIPAAm cryogels over 1 min temperature cycles from 20 to 60 °C.

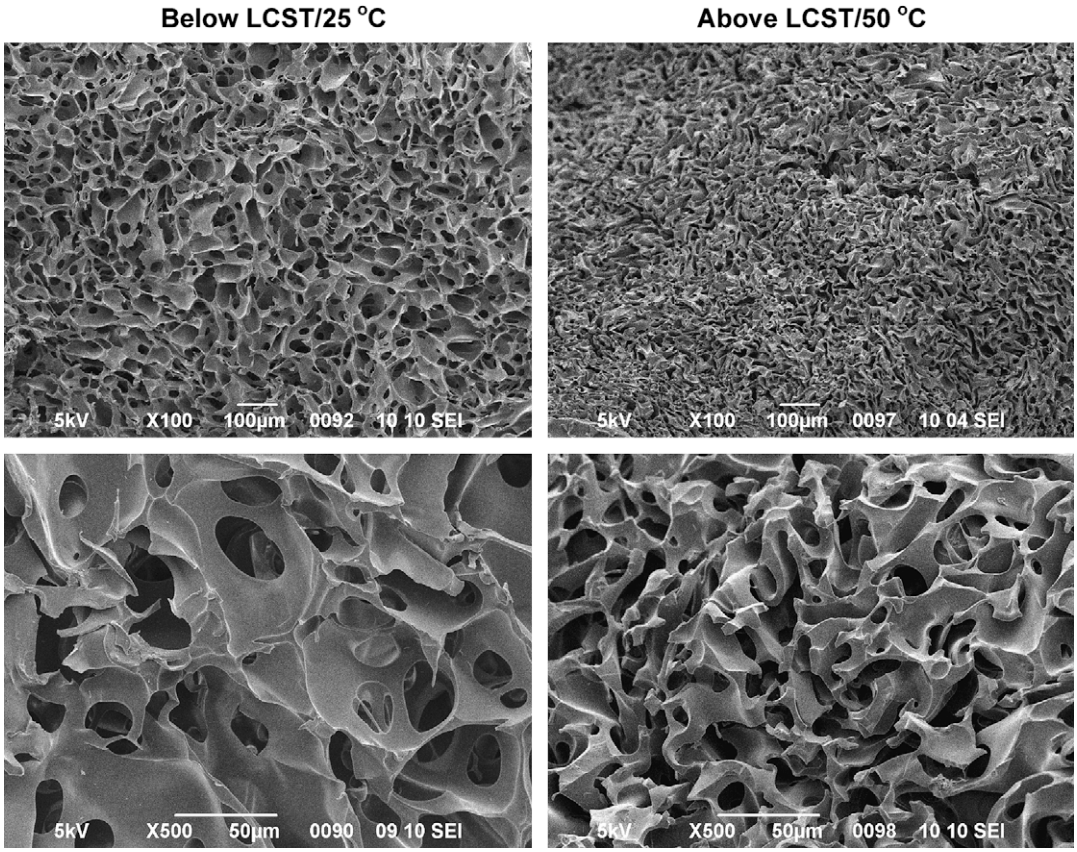

Fig. 4. SEM micrographs of PNIPAAm cryogel (5 wt.% solution, frozen at −20 °C, H_2O_2 – 5 wt.%, PEGDA-10 wt.%) at 25 °C (left) and 50 °C.

Very important characteristic of the temperature-responsive cryogels is the time for transition from swollen to deswollen state and vice versa. The HPC and PNIPAAm cryogels synthesized via the UV irradiation technique show an ultra-rapid response to changes in the temperature of water and reach equilibrium when transferred from 20 to 60 °C in 5–10 s (Fig. 2).

Furthermore, immersed again in water at 20 °C both cryogels uptake within the first 15–20 s approximately 90 vol.% of water amount calculated at equilibrium state. Ultra-rapid response to changes in temperature is characteristic of super-macroporous hydrogels and, on the other hand, is not observed for the conventional hydrogels composed of the same polymers [7]. Concerning their potential applications, not less important is the capability of cryogels to reversibly reach their nearly equilibrium states at given temperature in a reproducible way. The deswelling–reswelling of HPC and PNIPAAm cryogels for three cycles switching from 20 to 60 °C is shown in Fig. 3. Definitely, both cryogels exhibit remarkably reversible properties within the studied time interval.

The main role for such properties plays the specific structure of the material, i.e. the combination of very thin polymer walls with huge interconnected pores containing free water. The interior morphologies of PNIPAAm cryogel (5 wt.%) at temperatures below and above the LCST are shown in Fig. 4. At 25 °C the PNIPAAm cryogel is swollen and has a super-macroporous structure with round-shaped interconnected pores (50–100 μm) surrounded by thin walls (ca. 1–2 μm). The phase transition of PNIPAAm registered above 35 °C causes a drastic decrease of the volume of cryogel resulting in much smaller pores (Fig. 4, right). Notably, in deswollen state the cryogel does not lose its open-cell structure.

In order to get insight into the properties of materials of given polymer obtained via different approaches, polyacrylamide cryogels were synthesized from 5 wt.% monomer solution (P.AAm) containing cross-linking agent (PEGDA, 10 wt.% with respect to the monomer) and from 5 wt.% polymer solutions without PEGDA (PAAm) and with 10 wt.% PEGDA (PAAm/PEGDA), respectively.

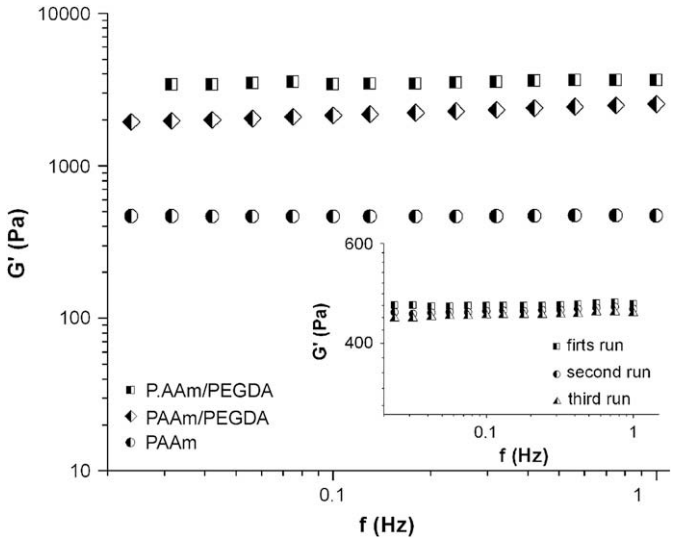

Fig. 5. Elastic moduli of PAAm cryogels formed from 5 wt.% AAm solutions (P.AAm/PEGDA) and 5 wt.% PAAm solutions without cross-linking agent (PAAm) and containing 10 wt.% PEGDA (PAAm/PEGDA); temperature of freezing −20 °C, H_2O_2 – 5 wt.%; irradiation time: 5 min.

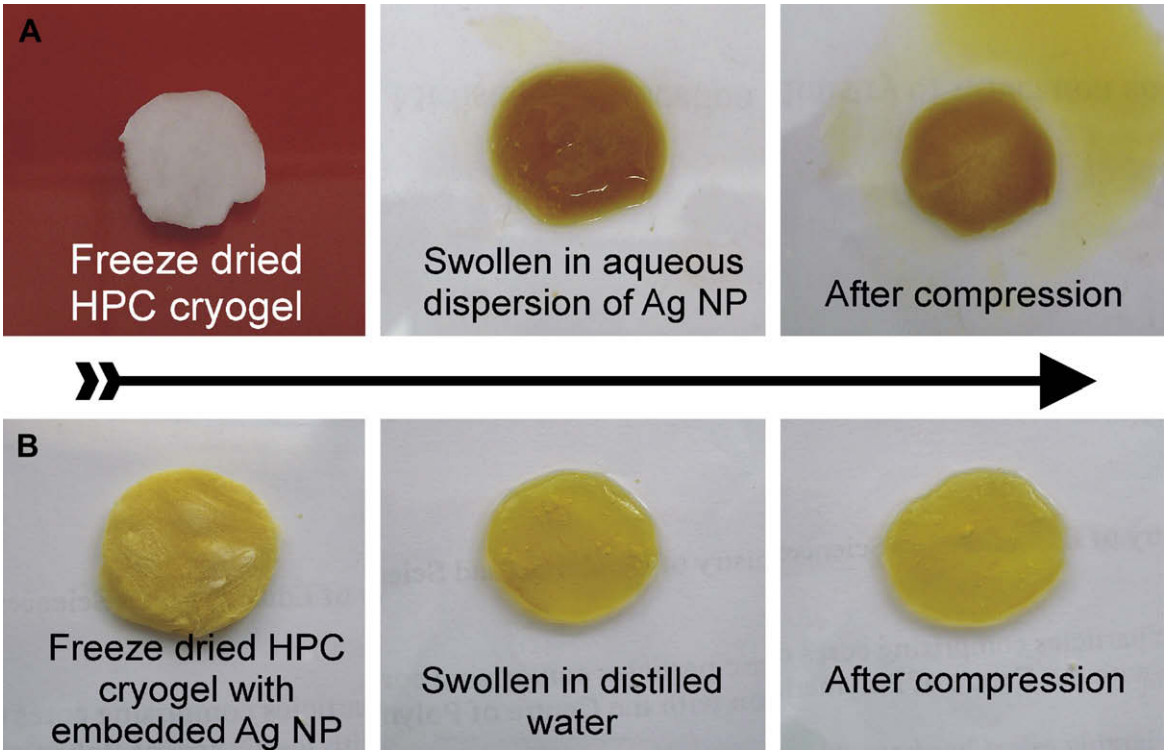

Fig. 6. Ag nanoparticles immobilized into (A) the pores of HPC-1.150 cryogel and (B) the walls of HPC-1.150 cryogel.

Apparently, PAAm cryogels obtained without cross-linking agent are softer and more swollen compared to P.AAm gels. Dynamic rheological measurements (Fig. 5) reveal that PAAm cryogels has an elastic modulus, G', approximately three times lower compared to the gels synthesized with 10 wt.% PEGDA. On the other hand, there is no significant difference in the viscoelastic properties of cryogels formed by two different mechanisms but containing equal amount of PEGDA.

It should be mentioned that such measurements do not change the macroscopic properties of the samples and no squeezed water after three runs of the same sample was observed at the experimental conditions applied (Fig. 5 – inset). However, these measurements aim only at comparing the different PAAm cryogels. It is obvious that the incorporation of cross-linking agent increases the stiffness of material, probably due to increased cross-linking density of the polymer network.

3.4. Immobilization of Ag nanoparticles into the cryogels

Various species like yeast cells, biomass from microbial sources, and silver nanoparticles were successfully immobilized in the cryogels synthesized via the UV irradiation technique. In this work we selected Ag NP (mean diameter ca. 20 nm; see Figs. S1and S2 in the Supporting information) as a model system to demonstrate the unique ability of cryogels to accommodate species via two different ways, into the cryogel walls or into the cryogel channels. Ag NPs were immobilized in the channels of the gel by immersing a freeze-dried HPC cryogel in aqueous dispersion of Ag NPs. As mentioned above, the freeze-drying process does not change the macroporous, spongy-like structure of materials and thus the dispersion fills the channels (interconnected pores) of the dry cryogel in a few seconds (Fig. 6A). The second approach includes mixing of the Ag NPs dispersion and polymer followed by freezing and subsequent cross-linking (Fig. 6B). Due to the cryostructuration effect this method leads to incorporation of Ag NPs into the polymer matrix.

Noteworthy, both types of materials exhibit completely different properties. The cryogels containing Ag NPs only in the channels can release them immediately by compression (Fig. 6A) or, in the case of temperature-responsive polymers, by switching to temperatures above the corresponding LCST (Fig. S3 in the Supporting information). In addition, when placed in a large excess of water the cryogels containing Ag NPs in the pores release the particles in several hours, while the cryogels with Ag NPs embedded in the walls exhibit a slow release of Ag^+ for months. In the last case, Ag NPs are physically entrapped within the dense polymer network which does not allow NPs to escape the polymer matrix. Thus, by different loading of Ag NPs one can obtain cryogel/Ag NPs hybrid systems with different release profile suitable, for instance, for antibacterial applications [25]. The two immobilization techniques described above are not restricted to Ag NPs only and can be applied to any water-soluble species and water-dispersible particles up to certain limit in the size.

4. Conclusions

The UV irradiation technique is a facile method for the synthesis of super-macroporous polymer cryogels from both polymer and monomer precursors. The combination of H_2O_2 initiator and the nearly quantitative conversion of monomers allows preparation of green materials consisting of biocompatible polymer network and water without any additional purification. All cryogels obtained possess macroporous structure, which impart a very rapid water uptake and, in the case of temperature-responsive polymers, ultra-rapid volume phase transition. In general, different nano- and micro-sized particulates can be immobilized within the cryogels pores and/or walls.

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Appendix. Supporting information

Supporting information associated with this article can be found in the online version, at doi:10.1016/j.polymer.2008.12.039.

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