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Thermosensitive networks based on high molecular weight polyoxyethylene and *N*-isopropylacrylamide

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Summary

γ- and UV-irradiation was successfully used for the preparation of mixed networks on the basis of high molecular weight polyoxyethylene (POE) and/or N-isopropylacrylamide and poly(N-isopropylacrylamide) (PNIPAAm). These gels preserve the swelling transition temperature of the pure PNIPAAm and shrink faster above this temperature due to the hydrophilic POE chains. It was found that in a collapsed state these gels retain alkaline organic salts from aqueous solutions.

Introduction

Polyoxyethylene (POE) gels form an important class of novel materials with numerous applications (1). In our previous publications we have reported on the synthesis of POE-based materials involving crosslinking carried out in aqueous solutions of POE by means of ionizing radiation (2) as well as photochemical crosslinking of POE films by exposure to ultraviolet irradiation (3). Our studies clearly show that POE blends of water-soluble, pH sensitive and temperature-responsive polymers can be efficiently crosslinked (4). The POE based networks retain the sensitivity of the incorporated polymers such as poly(vinylmethyl ether), poly(N-isopropylacrylamide) (PNIPAAm) or poly(2-vinylpyridine). On the other hand many of the POE properties are transferred to the conjugate. Meanwhile Bhalerao et al.(5) published their study on a thermoreversible copolymer hydrogel based on POE and PNIPAAm. Both studies (4,5) demonstrate that POE/PNIPAAm network can be formed by using the initial monomer NIPAAm, instead

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of its polymer. During the past decade a growing interest in studying N-isopropylacrylamide polymers and copolymers with POE has been registered (6). PNIPAAm is well known for its thermosensitive properties in water and therefore is widely applied. The polymer is soluble below 30.9 °C, which is its lower critical solution temperature (LCST) in water, whereas the phase separation takes place when the temperature is raised above the LCST. Crosslinked PNIPAAm demonstrates a sharp swelling transition (gel shrinking) around its LCST of 31-33°C (7). However, application of gels swollen in water is hindered by their poor mechanical properties. Furthermore, a disadvantage of the normal type of PNIPAAm gel is that upon temperature increase above the gel critical temperature it immediately shrinks forming a dense deswelling polymer layer at the gel surfase (skin layer) thus inhibiting subsequent deswelling. In recent years these unsatisfactory properties are improved by copolymerization with strongly hydrophylic monomers (8). Another approach is the formation of IPNs (9). In a mixed or IPNs with a PNIPAAm component the swelling transition temperature may be kept at the same temperature as that of the pure PNIPAAm network, regardless of the content of other components, because the PNIPAAm network may exist independently. Improved thermo-responsive properties are obtained also by grafting PEG's onto PNIPAAm gels, thus modifying the gel molecular architecture (10). Hydrophilic PEG graft chains form water paths within the skin layer, which speeds up deswelling.

The purpose of the present study was to improve our knowledge of thermoresponsive gels, based on high molecular weight polyoxyethylene and PNIPAAm. These networks are expected to combine the advantages of both polymers, resulting in an "on-off" switching material for fundamental and biomedical applications. One of the goals of this investigation was to use UV-irradiation technique along with the γ-irradiation in crosslinking.

Experimental

Materials

N-isopropylacrylamide was prepared from acryloyl chloride and i-propylamine in the presence of $(C_2H_5)_3N$ in dry ether at 0°C (11). The monomer was characterized by melting point, elemental analysis, IR- and ^{1}H-NMR-spectroscopy. PNIPAAm was prepared by free-radical polymerization in dry dioxane in inert atmosphere, using AIBN as an initiator (12). The polymer was characterized by GPC, IR- and ^{1}H-NMR

spectroscopy. Commercial POE of molecular weight 1,000,000 (Polyox N-12K, produced by Union Carbide Corp.) was used without further purification.

Preparation of Mixed Networks

Aqueous solutions of POE and PNIPAAm or NIPAAm were mixed in different ratios. After purging with argon, the solutions were irradiated (Co^{60} -gamma rays were used as an energy source) with a total dose of 5 Mrad. Two kinds of solutions were irradiated: a mixture of POE and PNIPAAm and a solution of POE, NIPAAm and N,N-methylenebisacrylamide (MBIS) which was used as a crosslinking agent. The gel fraction was determined after 10-fold washing with distilled water.

Networks in the form of films of POE/PNIPAAm cast from CH_2Cl_2 were also obtained by UV-irradiation in the presense of pentaerythritol triacrylate (PETA). The irradiation was carried out with a TQ 150 Original Hanau high-pressure 150W mercury lamp provided with a quartz tube and a cooling quartz jacket according to the procedure described in Ref.(3).. The gel fraction was established after extraction with CH_2Cl_2 and water. The gels were studied by IR- and ^{1}H-NMR spectroscopy, equilibrium swelling, swelling-deswelling kinetics, DSC and for their binding ability towards alkali salts.

Swelling measurements

The irradiated POE/PNIPAAm networks after extraction were dried to constant weight under vacuum. The equilibrium degree of swelling (ES, the weight of a swollen sample divided by the weight of a dry sample) was determined at 25°C and 40°C (14).

Swelling-deswelling measurements

Samples of the dry network (50mg) were placed in a vessel equipped with a graduated ampoule for measuring the volume of the free water at 25°C untill reaching the equilibrium swelling. The volume of the free water was evaluated in an interval of 15 min. Deswelling of the same sample was registered at 40°C and the volume of the free water was evaluated every minute. This procedure was repeated two times for establishing the thermoreversible nature of the gel.

Differential Scanning Calorimetry Measurements

Samples of ca. 11.5 mg aqueous swollen gel were measured with a Perkin Elmer DSC-7

instrument in hermetically sealed stainless steel pans from 25°C to 50°C. Indium and zink were used for temperature calibration. The swollen gels were studied at a heating rate of 1.25°C/min to investigate the swelling transition temperature of the swollen networks.

Ion Binding Study

Picrate salts (PiM) were synthesized and their purity was followed spectrophotometrically. Bromophenol Blue, sodium salt (BPhB,Na) was used as received (Aldrich).

A small amount of the network (usually 50 mg) was placed in contact with 4 ml of aqueous solutions of these solutes (10^{-5} mol/l) in a special vessel equipped with fritted filter and an optical cell (1.0 cm). The system was thermostated and gently shaken until an equilibrium between the bound and the free solute was reached (24 hours, 25°C). The solution was then passed through the filter and followed spectrophotometrically. After the solution was returned back to the flask containing the network, it was thermostated at another temperature (10 min., 40°C) and the concentration of the free solute was determined again.

Results and discussion

According to GPC analysis PNIPAAm was obtained with M_n=5000 and M_w/M_n = 1.8. The signals in ^{1}H-NMR ($CDCl_3$) for olefin protones in the monomer disappear [δ 6.26dd (1H), H-1^b; 6.06dd (1H), H-2; 5.61dd (1H), H-1^a] and new signals for the homopolymer are registered [δ 2.7brs (1H), H-2; 2.1-1.4m (2H), H-1]. The content of the two polymers is calculated from ^{1}H-NMR spectra according to the equation:

$$\frac{4x + 2(1-x)}{8(1-x)} = \frac{\text{area from 2.5 to 4.5 ppm}}{\text{area from 1.0 to 2.5 ppm}}$$

where x corresponds to POE-units and (1-x) to PNIPAAm-units resp.

As seen from Table 1 networks with good yields are obtained by γ -irradiation technique. The gel fraction is higher when NIPAAm is used instead of its polymer. UV-irradiation technique turns out to be less effective. However, both the monomer and the polymer result in mixed networks with POE. Moreover, even an amount of 3-5% of PNIPAAm is able to decrease the ES twice. The mole ratio in samples 1,2,3 and 4 corresponds quite well to that in the initial polymer solutions.

Table 1. Mixed networks obtained by γ-irradiation .

Sample No	POE / NIPAAm mol % initial feeding MBIS(1%)	POE / PNIPAAm mol % initial feeding	POE / PNIPAAm mol % by NMR	Yield, %	ES^{25oC}	ES^{40oC}
1	70 : 30	-	72 : 28	84	15	6
2	-	70 : 30	73 : 27	70	13	4
3	50 : 50	-	56 : 44	83	12	4
4	-	50 : 50	57 : 43	74	18	6

Table 2. Mixed networks obtained by UV-irradiation at 25° C (a) and 70° C (b) with PETA (5%).

Sample No	POE / NIPAAm mol % initial feeding	POE / PNIPAAm mol % initial feeding	POE / PNIPAAm mol % by NMR	Yield, %	ES^{25oC}	$ES^{40\ oC}$
POE[a]	-	-	-	85	4.5	4.0
5[a]	50 : 50	-	98 : 2	37	8	6
6[a]	-	50 : 50	97 : 3	25	8	4
7[a]	-	50 : 50	96 : 4	27	9	5
7[b]	-	50 : 50	95 : 5	26	8	5

The transition temperature of a swollen network established by DSC was T_t = 33 °C. (sample 3, scanning rate 1.25°C/min). The thermogram showed an endothermic peak and reversability of the swelling-deswelling property.

It is known (15) that a large difference is observed in deswelling kinetics of crosslinked PNIPAAm at 33°C (two days) and 40°C (about two months) due to the quick formation of a "skin layer". The deswelling of our mixed networks is achieved only in 5 min. at 40°C (Fig. 1).

Obviously, POE hinders the formation of a dense structure and allows water to be expelled from the gel even at higher temperatures than T_t. This statement is supported also from the values for the equilibrium swelling bellow and over the T_t of PNIPAAm (Tables 1 and 2). The ion binding ability of mixed POE/PNIPAAm networks showed that contrary to pure POE gels they capture alkali picrates in a collapsed state (Fig. 2) The process is reversible and suggests that alkali cations could be removed from aqueous solutions. The binding of BPhB,Na (Fig. 3) clearly shows the tendency for a possible uptake of anions from a preswollen gel. Preliminary results for drug release show that a burst of a loaded drug can be achieved by a local hypothermia.

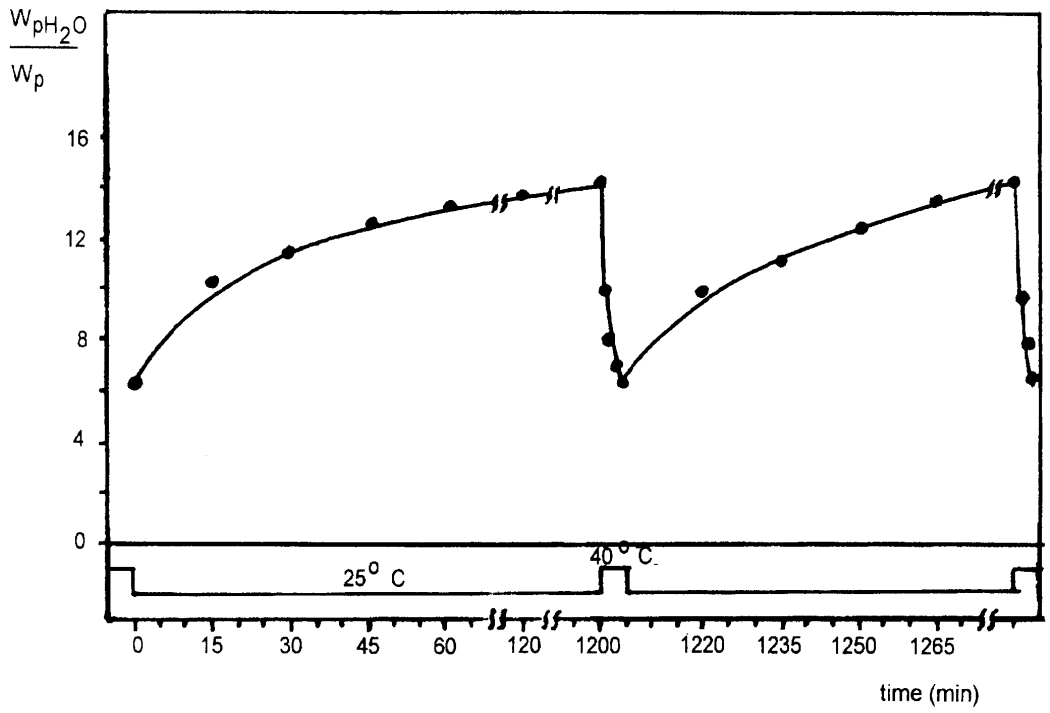

Fig.1 Swelling-deswelling kinetics of POE/PNIPAAm network

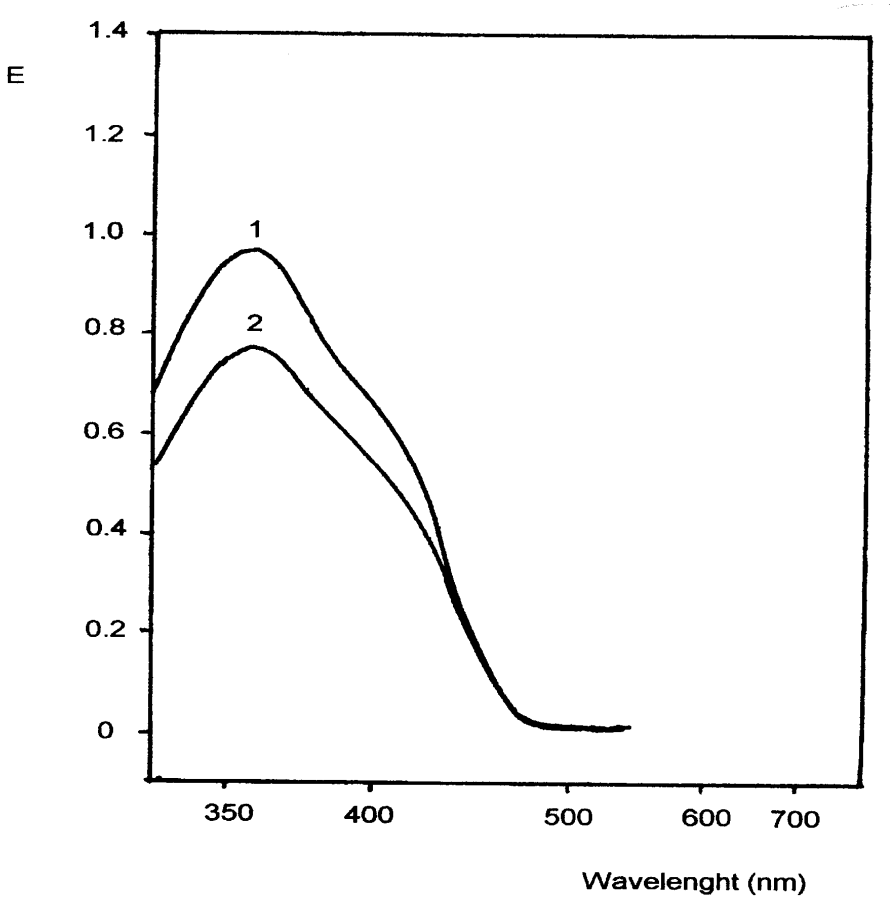

Fig.2 Binding of aqueous NaPi to POE/PNIPAAm network:1-25°C (no binding); 2-binding at 40°C

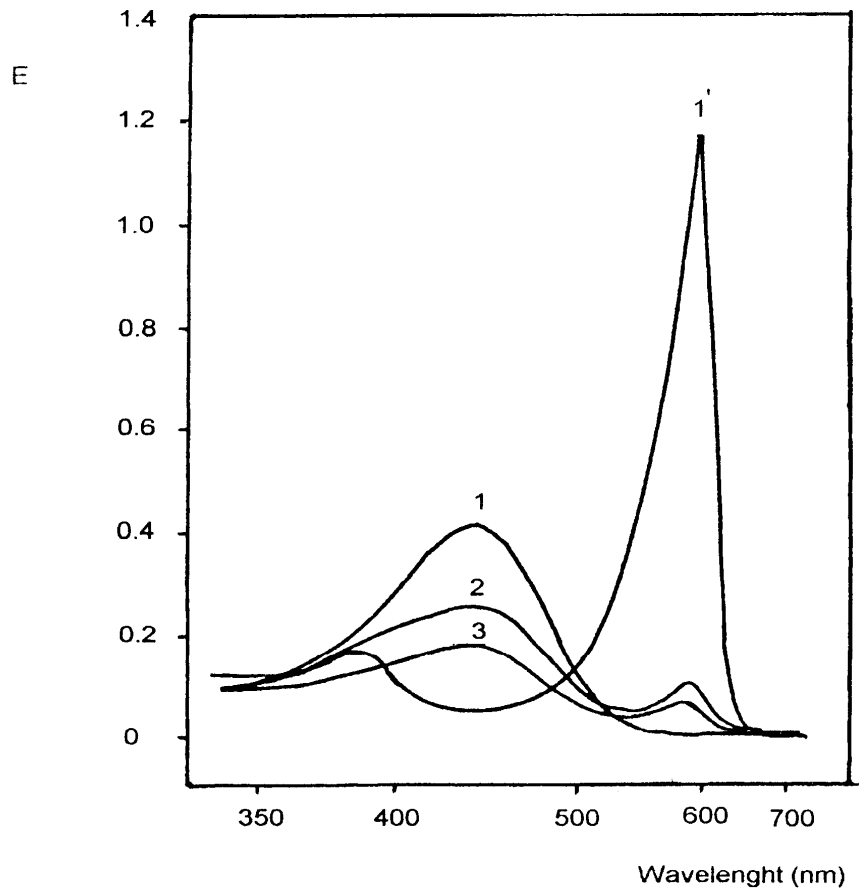

Fig.3 Binding of aqueous BPhB,Na to POE/PNIPAAm network:1'- Initial solution of BPhB,Na ; 1- The same (acidified);2- Binding at 25°C ; 3- Binding at 40°C

Conclusion

Mixed networks based on high molecular POE and PNIPAAm prepared either by γ - or by UV-irradiation retain the LCST of pure PNIPAAm. An amount of 3-5% of PNIPAAm is sufficient to decrease the ES twice. The second component, POE, prevents the quick formation of a "skin layer". Their ability for a reversible binding of ions suggests the possibility of usage in medicine and pharmacy.

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