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Stimuli responsive gels based on interpenetrating network of hydroxy propylcellulose and poly(*N*-isopropylacrylamide)

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Abstract

Sequential networks made of hydroxypropylcellulose (HPC) and poly(*N*-isopropylacrylamide) (PNIPA) were synthesized by adsorption of a solution of NIPA monomer into a dried porous HPC network. NIPA polymerization inside the network allows us to obtain IPN which show, as the neat components, thermosensitive volumetric behavior. The volumetric transition temperatures range between those of HPC and PNIPA gels. Moreover, as the rate of the swelling–deswelling process is quite higher than that of PNIPA irrespective of the composition, the synthesis method appears interesting in modulated thermosensitive behavior and in the application of this kind of IPN.

Keywords: Thermally sensitive hydrogels; Blends; IPN

1. Introduction

As known, several hydrophilic polymeric gels may undergo a discontinuous volume variation upon changes in solvent composition, temperature, pH, etc. [1]. They are named 'stimuli responsive gels' and they find applications as systems for drug delivery, absorption of liquids, sensors, etc. [2–7]. High performance behavior of these gels is conditioned by two main factors: first, the temperature at which the volume transition occurs, and second, the response rate. In fact, several applications need to carry out the swelling–deswelling cycle not only at a suitable temperature, but also in a relatively short period of time. As an example, this result has been obtained by us for hydroxypropylcellulose (HPC) networks crosslinked in heterogeneous phase [8]; our method favours the formation of interconnected channels inside the structure, highly improving the swelling process characteristics. Moreover, the use of a second polymeric component which may form an interpenetrate network (IPN) with the first one could be useful to condition the balance among hydrophilic and hydrophobic groups and, consequently to improve the absorption behavior.

In this paper, we consider sequential interpenetrated networks based on HPC and poly(*N*-isopropylacrylamide) (PNIPA), both polymers being miscible with water in every proportion at room temperature. An increase in temperature up to a specific value (T_d) for each of them, causes the solution demixing in two conjugate phases with different polymer concentration. Concerning HPC, the demixing process occurs at a temperature of about 40 °C [9] which was attributed to the presence of a wide miscibility gap, characteristic of lyotropic polymer solutions when the polymer–solvent interaction parameter χ is positive and higher than about 0.05 [10]. Below 40 °C, the system is monophasic and isotropic when the HPC concentration (C_p) is lower than about 40 wt%, biphasic in the range 40–50 wt%, and completely anisotropic at $C_p > 50$ wt%.

In the case of PNIPA, T_d is generally lower than that of HPC solutions. Moreover, Afroze et al. [11] have recently demonstrated that the lowest T_d value (27 °C) corresponds to $C_p = 50$ wt%. At $C_p < 50$ wt%, T_d varies between about 31 and 34 °C, depending on the molecular weight of PNIPA. At $C_p > 50$ wt%, T_d increases around the same range, but its value is substantially independent of the polymer molecular weight. Solutions are always isotropic.

Crosslinking of aqueous solutions of HPC and PNIPA gives hydrogels which show sensitive properties. In particular, a discontinuity in the swelling curve is reported at 55 and 33 °C for HPC [8] and for PNIPA [12] hydrogels, respectively. Considering this range of transition temperature which is particularly interesting for the previously

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mentioned chemical and (or) biomedical applications, we prepared interpenetrated networks of the two polymers: the aim was to modulate the transition temperature by varying the gel composition and to improve the rate of swelling–deswelling phenomenon.

2. Experimental

2.1. Materials

HPC: it was the same sample used in a previous work [8] and was obtained from Hercules Inc. Its molecular weight is 80,000 g/mol and its molar substitution (MS) is 4.2. MS is defined as the total number of molecules of propylene oxide that have combined with the original cellulose per anhydroglucose unit. Purification of the polymer was performed by dissolution in water at polymer concentration $Cp = 25$wt%, centrifugation at 10,000 rpm for 30 min to eliminate suspended particles, and freeze drying.

Dimethylsulfoxide (DMSO); sodium hydroxide; *N*-isopropylacrylamide (NIPA); ammonium persulphate; *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TEMED); *N*,*N*′-methylenebisacrylamide (BIS), poly-ethyleneglicol diglycidyl ether (PEGDE), were purchased from Fluka.

2.2. Methods

HPC hydrogel preparation. HPC solution was prepared by dissolving dry frozen HPC in DMSO at room temperature, then a suitable amount of water was added and the mixture slowly stirred for 24 h to ensure uniformity. A basic solution (10% of NaOH in water) was added and the mixture stirred for 24 h. The solution composition was: HPC 9.2 wt%, DMSO 59 wt%, H_2O 30.55 wt%, NaOH 1.25 wt%. Then the crosslinker, PEGED, was added (HPC/PEGDE, wt/wt = 1), and the solution, after stirring, was thermostated at 70 °C for 2 h. After this time, the sample was poured into distilled water at room temperature to remove the unreacted HPC and crosslinker. Water was changed every 4 h over a period of 4 days, and then the crosslinked HPC was freeze dried. This sample was used in all the following experiments.

PNIPA synthesis. Purified NIPA was dissolved in distilled water at 4.76 wt%, then the initiator ammonium persulphate (2 wt% with respect to NIPA) was added. The solution temperature was maintained at 25 °C. The polymerization was accelerated by adding TEMED (2 wt% with respect to NIPA). The molecular weight of the linear polymer (18200 g/mol) was detected by viscometry at 25 °C in water, the Mark–Houwink constants [13] were $a = 0.97$, $K = 2.26 \times 10^{-4}$ (dl/g) at 25 °C.

The crosslinking reaction of PNIPA was obtained by adding *N*,*N*′-methylenebisacrylamide (3 wt% respect to NIPA) to the solution at 25 °C.

HPC/PNIPA binary systems preparation. Weighed amounts of two polymers were dissolved in water. After homogenization by stirring for at least four days to reach equilibrium conditions, the solutions were freeze dried.

Sequential IPN synthesis. An aqueous solution of NIPA, ammonium persulphate, TEMED and BIS, in the same amount used for the synthesis of crosslinked PNIPA was added, drop by drop, to a suitable amount of freeze-dried network of HPC. The system was left at low temperature, 5 °C, for 4 h to allow homogeneous swelling of the HPC gel and then warmed up to 25 °C to start the polymerization and the following crosslinking of NIPA. Different ratios of HPC–NIPA were used to modulate the IPN composition.

DSC thermal analysis. Experiments were performed using MDSC 2920 TA Instruments, under dry nitrogen atmosphere; aluminum pans were always filled with the same quantity of polymer (10 ± 1 mg). All samples were previously treated according to the following procedure to eliminate the effects deriving from previous thermal history. They were heated to 160 °C and kept at this temperature for 5 min, then cooled to −20 °C at a rate of 10 °C/min. The samples were then heated at a rate of 20 °C/min. Glass transition temperature (T_g), determined as the mid point in the shift in the baseline, and transition temperature from liquid crystalline to isotropic state (T_i), when it exists, were determined for both the homopolymers and their blends.

Thermal treatment was repeated twice for each sample. No difference between the first and the second heating treatment confirms their thermal stability.

DSC transition temperatures (T_i) were determined also by optical observations carried out with a Polivar Pol Reichert polarizing microscope equipped with a Mettler FP82 hot stage (control unit FP80).

Gel swelling. The weight swelling degree SW_T of a gel at a temperature T is defined as the ratio between the weight W_g of the swollen gel at T, and the weight W_p of the dried polymer network ($SW_T = W_g/W_p$). In order to measure W_g, a piece of gel, a cylinder of height and diameter of about 5 mm, previously dried in vacuum oven at 80 °C, was located in a stainless steel basket and put into water at constant temperature. By measuring the weight of the gel at different times t and knowing W_p, it is possible to have the trend of SW_T vs. t; the swelling generally increases to a plateau (SW_{eq} equilibrium value) in a period of time depending on the relative amount of the components. SW_{eq} measurements were performed at different temperature in the range 10–70 °C to determine the existence of volumetric phase transition.

Micro structural characterization. Scanning electron microscopy was performed to obtain information on the pore size and to correlate the porosity to the swelling rate of hydrogels. Small pieces of swelled gels were freeze-dried to maintain the porous structure without any collapse. Then they were plunged in liquid nitrogen and the vitrified samples were cut with a cold knife. The samples were mounted on SEM stub using silver glue and sputter-coated with gold (20 μm). The microstructure of the HPC samples

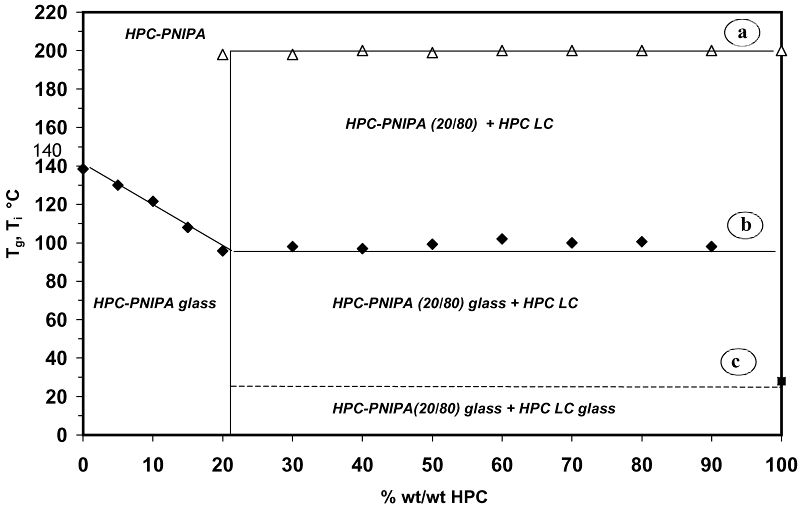

Fig. 1. Phase diagram of HPC–PNIPA system vs. polymer composition. (a) isotropization temperature T_i; (b) glass transition temperature T_g; (c) T_g of HPC in liquid crystalline phase (LC).

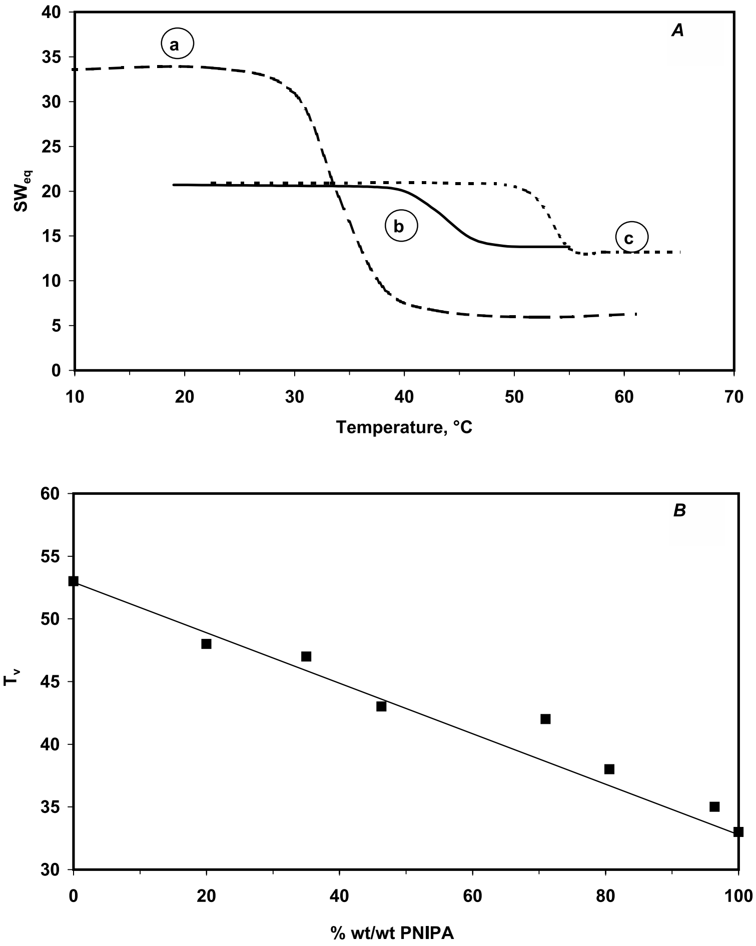

Fig. 2. (A) Equilibrium swelling degree (SW$_{eq}$) vs. temperature: (a) PNIPA; (b) HPC/PNIPA interpenetrated network (composition of 53.7/46.3 wt/wt); (c) HPC. (B) Temperatures of the volume phase transition T_v for HPC/PNIPA–IPN having different composition.

was imaged using a scanning electron microscope, Cambridge Stereoscan model 440 at 20 kV accelerate voltage.

FT-IR. Qualitative characterization of the IPN was performed by FT-IR spectra (KBr disk) using a Bruker IFS66 FT/IR spectrometer.

3. Results and discussion

3.1. HPC–PNIPA phase behavior

Miscibility between HPC and PNIPA samples at the solid state needs a specific investigation as a few factors may influence the miscibility of the two polymers. Among them we recall the molecular weight [14], the chemical HPC composition and structure, and the HPC mesogenetics which tends to rule out flexible chains from the liquid crystalline phase [15,16]. Eleven binary HPC–PNIPA blends with compositions varying from 10 to 95% wt/wt in HPC, were prepared according to the procedure reported in Section 2. The mixtures and the neat polymers were characterized by using differential thermal analysis and optical microscopy: glass transition (T_g) and isotropization temperatures (T_i) for each sample were determined (Fig. 1). A first observation concerns the neat polymers: careful determination of the HPC T_g value is very difficult, due to the continuous variation of the base line in the range −5 to 50 °C, related to the heterogeneousness of the hydroxypropyl groups' distribution. This result agrees with those reported in the literature. [17–21]. On the contrary, T_g of PNIPA, 138.4 °C, is easily determined.

Fig. 1 shows the transition temperatures T_g and T_i of binary blends as a function of the composition. When HPC is mixed with PNIPA, T_g decreases with the HPC percentage up to about 20% (Fig. 1, curve b); then its value remains constant ($T_g = 100$ °C) for further increments of the HPC amount. If we look at the isotropization temperature (Fig. 1, curve a), we observe that T_i is constant in the same range of the T_g constancy and it is no longer detectable when the HPC content is lower than 20%. If we consider the area corresponding to the 20–100% (wt/wt) range of HPC at low temperature the system consists of a 20/80 (wt/wt) HPC/PNIPA blend, in the glassy phase and glassy liquid-crystalline HPC. The dotted line is arbitrarily drawn at $T = 25$ °C, at about the middle of the temperature variation in the T_g range. Immediately above, in the area delimited by T_g of the HPC in the glassy liquid crystal phase, we found HPC liquid crystals and a 20/80 HPC/PNIPA mixture in the glassy phase. The area, which follows at higher temperature, refers to the same components except that the 20/80 (wt/wt) blend is in the rubbery phase. Over the T_i line, the situation changes for HPC which is no longer a liquid crystal, but an amorphous polymer completely miscible with PNIPA.

Finally, the left part of the diagram gives the trend of T_g vs. composition for the homogeneous blend having a HPC content lower than 20%.

Therefore, the immiscibility between the neat components in a wide range of ratio of composition and temperature is assessed.

To confirm these results, optical observation of samples under crossed nicols showed anisotropy with decreasing brightness between 100 and 20 HPC percentage and with increasing temperature. Optically determined T_i values, agree with the values in Fig. 1.

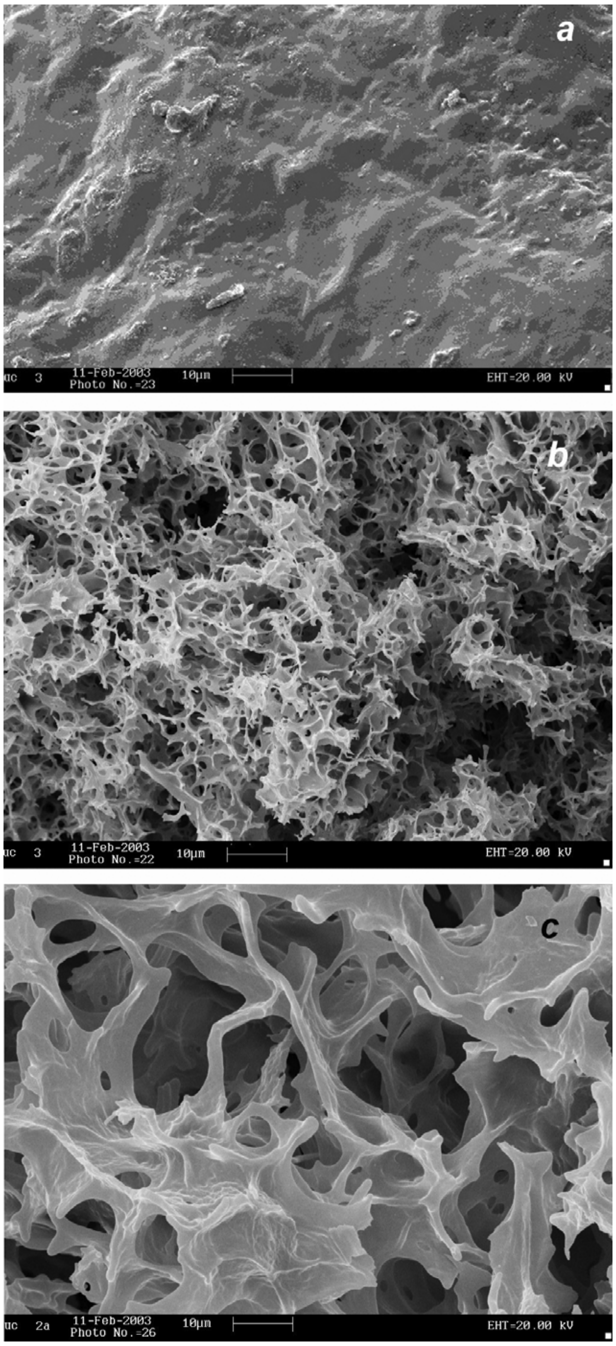

Fig. 3. SEM micrographs of freeze-dried gels. Samples a, b, c are the same as that of Fig. 2A.

3.2. Synthesis of IPN

HPC and PNIPA samples were separately crosslinked according to the procedure described in Section 2. A known amount of each sample was put into water at room temperature and left to up to constant weight. Then, this procedure was repeated by increasing the temperature from 5 to 60–70 °C. The trend SW_{eq} vs. temperature was reproducible even in cooling course in the examined range of temperature. Volume transition temperature (T_v) was taken as the temperature corresponding to the inflection point of the curve SW_{eq} vs. temperature. Thermosensitive behavior was observed in both cases, as shown in Fig. 2A (curves a and c). Curve c, which refers to HPC network, shows a volumetric transition at about 53 °C. PNIPA network, curve a) shows a similar transition at about 33 °C. Moreover, it is evident that the extent of the transition from the swelled to the shrunken state is different in the two cases. A further aspect, probably the most interesting, is that HPC gel needs no more that an hour to achieve its maximum swelling starting from the dry network, while PNIPA gel needs about 5 days. SEM microscopy of sections of the two networks, Fig. 3, shows that HPC morphology is noticeably porous, while that of PNIPA is very compact. In a previous work, we reported that HPC hydrogels obtained from heterogeneous conditions show a porous structure with interconnected channels characterized by high solvent adsorption rate, while the gels obtained from homogeneous solutions show a compact structure and low adsorption rate. Therefore, the differences in swelling rate may be explained on this basis even for the present case. This behavior, the different temperature of volumetric transition (T_v), the volumetric transition extent and the swelling rate, suggest that, besides the method of the chemical modification of the neat polymers, modulated behavior could be obtained by using interpenetrated networks of the two polymers (IPN).

Six IPN having an HPC/PNIPA composition of 3.6/96.4, 19.4/80.6, 29/71, 53.7/46.3, 65/35, 80/20 (wt/wt) were synthesized. The method consists of adding a suitable amount of the solution of NIPA, initiator and crosslinker to a known amount of dried HPC network, as explained previously. After a period of about 24 h at a temperature of 25 °C, the polymerization and crosslinking reactions inside the swollen gel are practically over. The IPN gels, after purification by washing were analyzed by FT-IR, obtaining confirmation of the PNIPA presence. Absorption bands at 1280 and 1456 cm^{-1}, characteristic of C–N and N–H groups were observed.

Fig. 2A curve b reports, as an example, the variation of SW_{eq} with the temperature for the sample HPC/PNIPA having composition 53.7/46.3 (wt/wt): only one volumetric transition temperature (43 °C) was observed. Taking into account that PNIPA and HPC are miscible in the solid state only in a narrow composition range (less than 20% wt of HPC), we could expect two volumetric transitions, while the results evidence only one volumetric transition for all IPN samples. We believe that this behavior is strictly correlated to the syntheses method: IPN made of an intimate mixture of the two polymers which behaves as 'homogeneous' system were obtained.

Fig. 2B shows the results for the all the IPN prepared. T_v varies linearly between 33 °C (PNIPA) and 55 °C (HPC). It is therefore possible to obtain a hydrogel with a specific T_v by a simple variation of the interpenetrated network composition.

Moreover, SEM micrographs of the samples a, b, c of

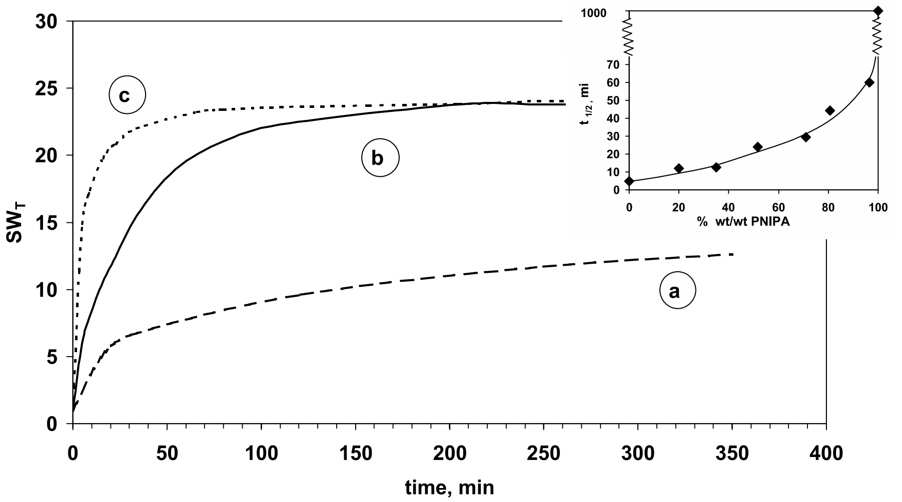

Fig. 4. Swelling degree (SW_T) vs. time, samples a, b, c are the same as that of Fig. 2. The insert gives the time necessary to obtain half of the equilibrium swelling ($t_{1/2}$) as a function of the IPN composition.

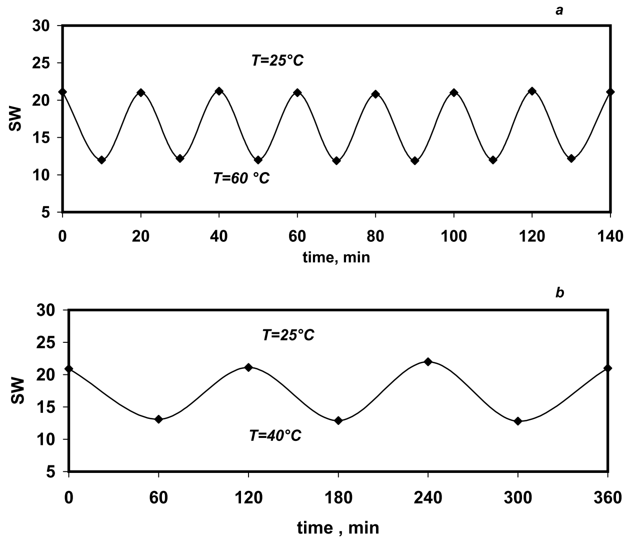

Fig. 5. Trend of SW as a function of time by varying the temperature from 60 to 25 °C (neat HPC sample a) and from 40 to 25 °C (HPC/PNIPA–IPN sample b of Fig. 2A).

Fig. 2A reveal that the presence of HPC (Fig. 3b) confers a much higher porosity to the IPN than that of neat PNIPA (Fig. 3a). Comparison of Fig. 3a and b obviously suggests qualitatively a great difference in the water diffusion rate inside the hydrogels and therefore a correlation between the swelling rate and the HPC contents. This aspect will be discussed in the following.

Fig. 4 shows the trend of SW_T at fixed temperature, $T = 25$ °C, as a function of time for the neat polymers PNIPA curve a, HPC curve c and for the IPN HPC/PNIPA 53.7/46.3 (wt/wt), curve b. The abscissa stops at about 400 min but curve a crosses the other two curves at higher time and reaches a constant value only after about 6000 min. The insert in Fig. 4 shows a more impressive image of HPC role on the rate of the swelling–deswelling process: the time necessary to obtain half of the equilibrium swelling ($t_{1/2}$) is reported as a function of the network composition; what is particularly remarkable is the decrease of $t_{1/2}$ from 1000 min for neat PNIPA to 60 for IPN containing as little as 3–4% of HPC. Of course, $t_{1/2}$ continues to decrease by about 10 times by increasing the HPC amount until the characteristic value of neat HPC network.

Considering that the swelling is reversible, it is possible to study a thermal cycle characterized by alternating swelling and deswelling processes even for sequential IPN. These gels are an example of ‘thermal sponges’ as the release as the absorption of the solvent is not due to a mechanical action (squeezing and desqueezing) but to an increase and decrease in temperature. Obviously better results can be obtained the lower the deswelling temperature and the faster the process.

In a previous work, we reported the cycle obtained with a hydrogel made of neat HPC [4]. Fig. 5a illustrates the behavior of the sample subjected to a thermal cycle between 25 and 60 °C, remaining at each temperature for about 10 min, a short time correlated to the high porosity of the hydrogels. Fig. 5b shows the result obtained with an IPN sample 96.4/3.6 where the temperatures for the swelling and deswelling processes were 25 and 40 °C, respectively; the time necessary to observe a significant variation of volume was 60 min. A very good reproducibility of the swelling and deswelling phenomena after the first cycle was observed. The IPN hydrogel, being less porous, needs a longer time. However a lower temperature may be used for the deswelling process, due to the lower T_v for the IPN of 35 °C, compared to 55 °C for the neat HPC.

4. Conclusion

Sequential IPN based on HPC and PNIPA were prepared by swelling pre-crosslinked HPC with known amounts of a solution of NIPA, BIS, TEMED, ammonium persulphate. After NIPA polymerization and crosslink, the IPN should reasonably differ mainly in the polymer content, that is the HPC/PNIPA ratio. This hypothesis is supported by some behavior like the volumetric transition: in fact, T_v has a linear trend when plotted vs. PNIPA percentage, as shown in Fig. 2B. Thus, we have obtained IPN containing the same chemical groups, even if in different proportion, and T_v variable from 33 to 55 °C. This range of transition temperature could be of great interest for bio application of IPN hydrogels. A further point, often neglected, is the rate of swelling–deswelling process. A dependence of the rate on the porosity of hydrogel is obvious, but what is not so obvious is the high porosity which characterizes all the IPN (Fig. 3b) even at high PNIPA content. It follows that the rate of the volumetric transition at a suitable temperature is noticeable for all networks, being the highest for the neat crossed HPC and the lowest for neat crossed PNIPA.

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