CELLULOSE CHEMISTRY AND TECHNOLOGY

POLYACRYLAMIDE-DEXTRAN POLYMERIC NETWORKS: EFFECT OF GEL PREPARATION TEMPERATURE ON THEIR MORPHOLOGY AND SWELLING PROPERTIES

MARIA VALENTINA DINU, MARIA MARINELA PERJU, MARIA CAZACU and
ECATERINA STELA DRĂGAN

"Petru Poni" Institute of Macromolecular Chemistry, Aleea Grigore Ghica Voda 41A,
700487 Iasi, Romania

Received November 9, 2010

The study discusses the synthesis of polyacrylamide-dextran (PAAm/Dx) polymer network (semi-IPN) hydrogels, as well as the porosity and swelling capacity of these materials as a function of gel preparation temperature. The hydrogels were cross-linked with N,N'-methylenebis(acrylamide) (BAAm) and synthesized by radical polymerization at three temperatures, *i.e.* +25, +5 and -18 °C. From the weight and volume swelling ratios of hydrogels, the swollen-state porosity of the networks was estimated. The observed swollen-state porosity was about 30% for the hydrogels formed at T_{prep} = +25 and +5 °C, rapidly increasing to 94%, with decreasing the gel preparation temperature at T_{prep} = -18 °C for the PAAm/Dx semi-IPN hydrogel. By conducting the cross-linking polymerization reaction at -18 °C, PAAm/Dx semi-IPNs with a superfast responsive rate (15 s) were obtained.

Keywords: dextran, polyacrylamide, porosity, semi-IPN hydrogels, swelling kinetics

INTRODUCTION

Hydrogels are insoluble, cross-linked networks of water-soluble polymers, capable to accommodate significant amounts of water in their three-dimensional structures, without undergoing dissolution.[1] Such water retention property qualifies them as potential candidates for large-scale applications in both biomedical and pharmaceutical fields.[2-4] However, their extraordinary affinity for water also imparts poor mechanical strength and restricts their applications. Another drawback of hydrogels is the slow rate of response to external environmental changes. Thus, studies on multi-component polymers have aroused great interest, since they provide a convenient route for modifying and improving the properties of synthetic/natural polymer-based hydrogels.[5-7] For example, the formation of an interpenetrating polymer network (IPN) constitutes an important method of improving the mechanical strength of polymers, due to physical entanglements and network interactions, when compared to individual polymers.[8] If a polymer is linear and penetrates another cross-linked network without any chemical bonds between them, the IPN is called semi-IPN. If both polymers are independently cross-linked, the system is called full-IPN. Interpenetrating phases with different degradation profiles and/or different swelling responses to the environmental conditions can be used to provide multiple controls over the swelling responses of hydrogels.

The cryogelation technique is another method for preparing hydrogels with enhanced mechanical stability and superfast responsiveness to water absorption, in which the cross-linking polymerization reactions are conducted below the freezing point of the reaction solutions.[13,14] These materials, called "cryogels", are very tough and can withstand high levels of deformations, such as elongation and torsion. Previous works[15,16] show that, by conducting the copolymerization cross-linking reactions below –8 °C, hydrogels based on acrylamide (AAm), as well as on 2-acrylamido-2-methylpropane sulfonic acid sodium salt (AMPS) monomers with superfast swelling properties, could be obtained.

The present work describes the design of new superfast responsive porous semi-IPNs composed of dextran, as a physical entrapped polymer, and a network consisting of cross-linked polyacrylamide, by a combination of semi-IPN and cryogelation techniques. The influence of gel preparation temperature on the morphology and swelling properties of the PAAm/Dx hydrogels has been also evaluated.

EXPERIMENTAL

Materials

The 100 kDa Dextran (Dx) from Leuconostoc mesenteroides, purchased from Sigma-Aldrich, was used as received. Acrylamide (AAm, Fluka), N,N'-methylenebis(acrylamide) (BAAm, Sigma), ammonium persulfate (APS, Sigma-Aldrich), and N,N,N',N'-tetramethylethylenediamine (TEMED, Sigma-Aldrich) were used as received. All reagents were of analytical grade or of the highest purity available. APS and TEMED stock solutions were prepared by dissolving 0.2 g of APS and 0.625 mL of TEMED each in 25 mL of distilled water. The BAAm stock solution, prepared by dissolving 0.132 g of BAAm in 10 mL of distilled water, at 25 °C, was used for hydrogel synthesis after 24 h.

Methods

Semi-IPN hydrogels of PAAm and Dx were prepared by free radical cross-linking copolymerization in aqueous solution at three temperatures (T_{prep}), *i.e.*, +25, +5 and -18 °C. The initial concentration of monomers (AAm + BAAm), C_o, as well as the cross-linking ratio, X, which is the mole ratio of cross-linker BAAm to monomer AAm, were kept constant. APS (3.51 mM) and TEMED (0.25 mL/100 mL reaction solution) were used as a redox initiator system. To illustrate the synthesis procedure, the preparation of hydrogels at C_o = 5 wt% and X = 1/80 is presented below.

Typically, 0.4868 g AAm, 7 mL Dx solution (1 wt%), 1 mL BAAm and 1 mL TEMED stock solutions were first mixed in a 10 mL graduated flask. The solution was cooled at 0 °C in an ice-water bath, purged with nitrogen gas for 20 min, after which the APS stock solution (1 mL) was added. 2 mL portions of this solution were transferred to 4 mm in diameter glass tubes; the glass tubes were sealed, immersed in a thermostated bath at T_{prep} and polymerization was conducted for one day.

After preparation, the hydrogel samples in the form of rods (4 mm in diameter and about 10 mm long) were placed in a large excess of water for 48 h, to wash out any soluble polymers, unreacted monomers and the initiator, changing the washing water from time to time (on the average, at about 2 h). Further on, the swollen hydrogel samples were carefully deswollen in a series of water-acetone mixtures, increasing the acetone contents. Each sample was dehydrated stepwise in water-acetone mixtures: 20% (3 h) → 40% (3 h) → 60% (3 h) → 80% (3 h) → 100% (12 h). This solvent exchange process facilitated the final drying of the hydrogel samples, at 40 °C up to constant weight.

The equilibrium volume (q_v) and equilibrium weight swelling ratios (q_w) of the hydrogels were calculated as:

$$q_v = \left(\frac{D_w}{D_{dry}}\right)^3 \quad (1)$$

$$q_w = \frac{m_w}{m_{dry}} \quad (2)$$

where D_w and D_{dry} are the diameters of the equilibrium swollen and dry gels, measured by a calibrated digital compass, m_w and m_{dry} are the weights of gels after equilibrium swelling in water and after drying, respectively.

Surface morphology and internal structure of dry semi-IPNs were observed on a Quanta 200 type Environmental Scanning Electron Microscope (ESEM), operating at 30 kV with secondary electrons, in the low-vacuum mode. Cross-sections of the samples were prepared using a sharp blade to reveal their internal structures.

The swelling properties were studied by the conventional gravimetric procedure.[17] The swelling behavior of dried hydrogels was determined by immersing the completely dried (40 °C for 24 h) hydrogel samples in double-distilled water at 25 °C. The swollen gels were weighed by an electronic balance at predetermined time points, after wiping the excess surface liquid by filter paper. The swelling ratio (SR) was defined by Equation (3):

$$SR = \frac{(W_t - W_d)}{W_d}, \ g \cdot g^{-1} \quad (3)$$

where W_d is the weight (g) of the dried sample, and W_t is the weight (g) of the swollen sample at time t. Measurements were performed in three replicates and average data were used for calculating the swelling ratio.

The water retention capacity (*WR*) was determined in an oven at 25 °C, according to a previously presented method.[7]

Thus, equilibrium swollen hydrogels, in an amount of 0.1 g, were maintained, at 25 °C, and the decrease of their weight was measured as a function of time. The values of WR were calculated by Equation (4):

$$WR\ (\%) = \left(\frac{W_t}{W_{eq}}\right) \times 100 \quad (4)$$

where W_t is the weight (g) of the sample at the time of keeping in the oven, t, and W_{eq} is the weight (g) of the equilibrium swollen sample.

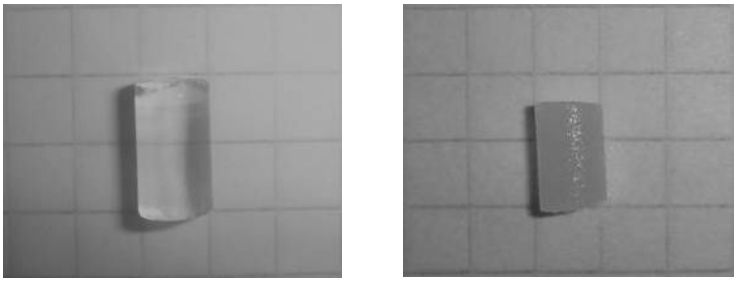
RESULTS AND DISCUSSION

Effect of gel preparation temperature on morphology of PAAm/Dx semi-IPNs

Semi-IPN hydrogels based on PAAm and Dx were synthesized by cross-linking copolymerization reactions at 3 temperatures, *i.e.*, +25, +5 and -18 °C, for 24 h. During polymerization, the first step was the reaction between APS and TEMED, in which TEMED catalyses the decomposition of the persulfate ion, to give sulfate free radicals, which initiate polymerization of AAm. In the presence of a cross-linking agent, BAAm, the cross-linking reaction occurs and a three-dimensional network of PAAm is finally obtained. The Dx chains interdiffuse and get physically entangled within this PAAm 3D network. On the other hand, by conducting the cross-linking polymerization reactions in the frozen reaction system (cryopolymerization), at T_{prep} = -18 °C, PAAm/Dx semi-IPN cryogels are generated. In these cryogelation systems, although no phase separation occurs during network formation, the frozen zones (ice crystals) of the reaction system act as a template during gelation, leading to a porous structure by thawing at the end of gel preparation. The PAAm/Dx semi-IPNs formed below the freezing point of water (T_{prep} = -18 °C) were opaque, indicating that these hydrogels have separate domains in a spatial scale of submicrometer to micrometer, while those formed at +25 °C were semi-transparent, with a smooth slippery surface (Fig. 1).

ESEM analysis of the dried semi-IPN networks revealed the presence of bicontinuous morphologies. The PAAm/Dx semi-IPNs prepared at +25 °C have a porous structure with irregular spherical pores about 3 μm in diameter (Fig. 2A), while those formed at -18 °C exhibit a heterogeneous morphology consisting of polyhedral pores with sizes of about 80 μm (Fig. 2B). The interconnected character of the pores is also evident in the PAAm/Dx semi-IPNs prepared at -18 °C.

Information on the internal structure of all hydrogels in a swollen state was obtained from the relative values of the equilibrium weight (q_w) and volume swelling ratios (q_v). During swelling, the pores located inside the network are rapidly filled with the solvent; at the same time, the polymer region takes up the solvent from the environment, whose extent depends on the attractive force between the solvent molecules and the polymer segments.[18] The equilibrium weight swelling ratio q_w includes the amount of solvent taken by both processes, *i.e.*, q_w includes the solvent in the gel, as well as in the pore regions of the network. On the contrary, if we assume isotropic swelling, *i.e.*, pore volume remains constant upon swelling, the equilibrium volume swelling ratio q_v of the porous networks is caused only by the hydration of the network chains. Accordingly, the higher the difference between q_w and q_v, the higher the volume of the pores in the network sample. The values of the equilibrium weight swelling ratio (q_w) and equilibrium volume swelling ratio (q_v) of the PAAm/Dx semi-IPNs, synthesized at different temperatures, are presented in Figure 3. For the hydrogels formed at +25 or +5 °C, the values of q_v and q_w are very close to each other, their values ranging from 22 to 30, while for those formed at -18 °C, decreases down to 2.619. These results demonstrate the occurrence of macropores in the hydrogel matrices prepared at -18 °C.



(A) D_{sw} = 6.03 mm

(B) D_{sw} = 4.88 mm

Figure1: Optical microscopic pictures of PAAm/Dx semi-IPN hydrogels in swollen state prepared at T_{prep} = +25 °C (A) and T_{prep} = -18 °C (B)

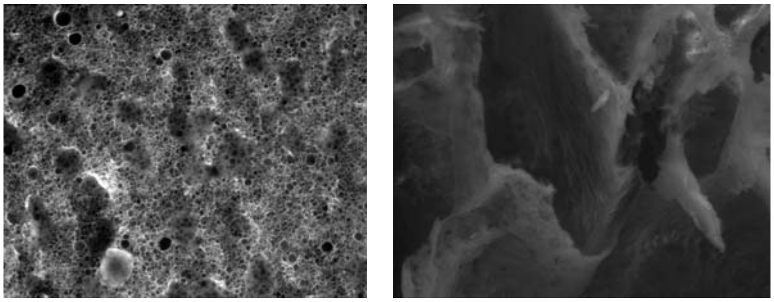

(A) (B)

Figure 2: ESEM images of PAAm/Dx semi-IPN hydrogels prepared at +25 (A) and -18 °C (B). The scaling bars are 100 μm. Mag. = 1000x

From the weight and volume swelling ratios of hydrogels, the swollen-state porosity of the networks, P_s, was estimated using Equation (5):

$$P_s = \left[1 - q_v\left(1 + \frac{(q_w - 1)d_2}{d_1}\right)^{-1}\right]\times 100 \qquad (5)$$

where d_1 and d_2 are the densities of solvent (water) and polymer, respectively. The values of swollen-state porosities, P_s, calculated with Equation (5), are plotted as a function of T_{prep} in Figure 4.

Swollen-state porosity, P_s, was of about 30% for the hydrogels formed at T_{prep} = +25 and +5 °C, while it rapidly increased up to 94% with decreasing the preparation temperature for the PAAm/Dx semi-IPN hydrogel, at -18 °C. Moreover, Figure 4 presents the dry-state porosities, P, of the networks calculated from polymer densities, by Equation (6):

$$P = \left(1 - \frac{d_0}{d_3}\right)\times 100 \qquad (6)$$

where d_0 is the density of the networks in a dried state and d_3 is the density of the networks in a swollen state, calculated according to Equations 7 and 8.

$$d_0 = \frac{m_{dry}}{(\pi D_{dry}^2 l_{dry}/4)},\ g\cdot mL^{-1} \qquad (7)$$

$$d_3 = \frac{m_w}{(\pi D_w^2 l_w/4)},\ g\cdot mL^{-1} \qquad (8)$$

The two different techniques used to estimate the porosity of networks, one starting from the swelling ratios and the other from polymer densities, gave similar results for the PAAm/Dx semi-IPN hydrogel prepared at -18 °C. Dry-state porosity, P, was slightly lower than swollen-state porosity, P_s, for the samples prepared at +5 and +25 °C, probably due to the partial collapse of the pores during drying. The results obtained by porosity measurements agree with those of the ESEM analysis of the hydrogel networks morphology in a dry state (Fig. 2).

The total volume of pores, V_p, of all hydrogels was estimated from the uptake of cyclohexane. V_p was found to be around 7.73 $mL\cdot g^{-1}$ for the PAAm/Dx semi-IPN hydrogel prepared at -18 °C, while those formed at higher temperatures exhibited negligible pore volumes.

Effect of gel preparation temperature on swelling properties of PAAm/Dx semi-IPNs

The PAAm/Dx semi-IPNs were swollen in water, at 25 °C and pH = 5.5. The results of the swelling measurements of the hydrogels obtained at +25 and +5 °C are presented in Figure 5, while those obtained for the hydrogels prepared at -18 °C are summarized in Figure 6.

As shown in Figure 5, the PAAm/Dx semi-IPNs obtained at +25 °C showed higher swelling ratios, *SR*, than those obtained at +5 °C. Moreover, the hydrogels formed at -18 °C attain the equilibrium state in water within 15 s, by either weight (Fig. 6) or volume (Fig. 7). The images from Figure 7 were taken during the swelling process of a hydrogel sample formed at -18 °C. The accelerating swelling rates of hydrogels prepared at -18 °C are due to the stable pore structure, which cannot collapse during drying or deswelling, as well as to the large water channels (pores – Fig. 2B), which enable the fast diffusion of water in the hydrogel network.

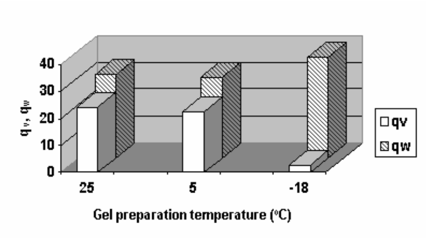


Figure 3: Equilibrium volume (q_v) and equilibrium weight swelling ratios (q_w) of PAAm/Dx semi-IPN hydrogels shown as a function of gel preparation temperature (T_{prep})

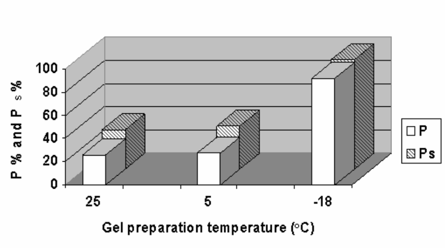


Figure 4: Swollen-state porosity, P_s, and dry-state porosity, P, of semi-IPN PAAm/Dx hydrogels plotted as a function of gel preparation temperature (T_{prep})

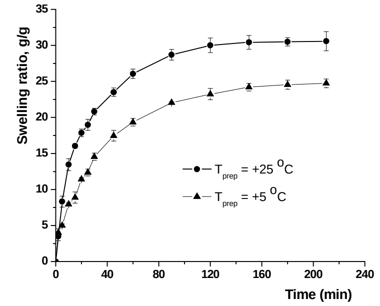


Figure 5: Swelling ratio as a function of time for PAAm/Dx semi-IPN hydrogels prepared at +25 and +5 °C

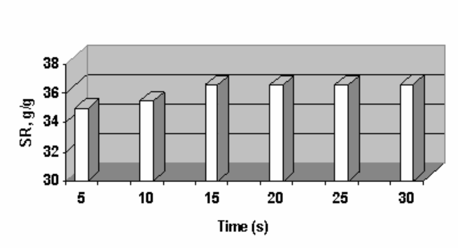
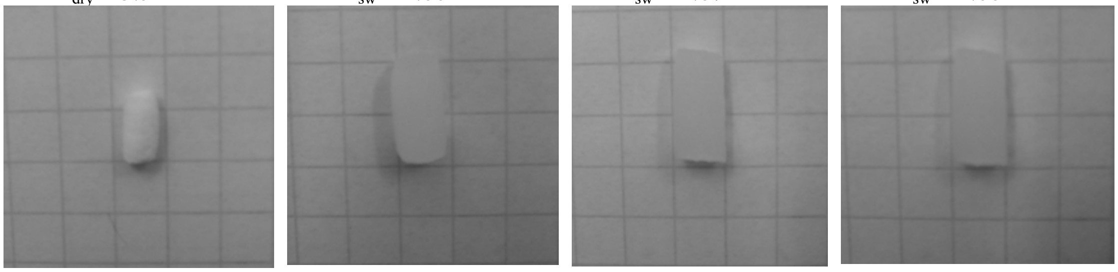


Figure 6: Swelling ratio as a function of time for PAAm/Dx semi-IPN cryogel prepared at -18 °C

D_{dry} = 3.54 mm D_{sw} = 4.86 mm D_{sw} = 4.87 mm D_{sw} = 4.88 mm



Time = 0 5 s 10 s 15 s

Figure 7: Optical microscopic images taken during swelling of PAAm/Dx semi-IPN hydrogels prepared at -18 °C. The diameter of the gel samples and the swelling times are given. C_o = 5 w/v%, X = 1/80

In contrast to this superfast swelling feature of the hydrogels formed from frozen monomer solutions, those prepared at +25 or +5 °C required about 180 min to attain the equilibrium swollen state starting from the dry state (Fig. 5).

The slow swelling rate of these hydrogels is mainly due to the partial collapse of their porous structure, because of the cohesional forces between the solvated polymer chains. Thus, the polymerization reaction conducted below the freezing point of water (T_{prep} = -18 °C) resulted in the formation of superfast responsive semi-IPNs.

To analyze the sorption mechanism of water in PAAm/Dx semi-IPNs, the diffusion phenomenon was analyzed by the empirical equation proposed by Franson and Peppas:[19,20]

$$M_t/M_\infty = kt^n \tag{9}$$

where M_t and M_∞ represent the amount of water uptake at time t and at equilibrium, respectively, k is a characteristic constant of the hydrogel, and n is a characteristic exponent describing the mode of the penetrating transport mechanism. The values of diffusional exponent n and the related transport mechanism depend on the geometry of the samples. For a cylinder, n is defined as follows: $n < 0.45$ (Case-I, Fickian diffusion); $0.45 < n < 0.89$ (Anomalous transport); $n = 0.89$ (Case-II transport).[20]

The equation proposed by Franson and Peppas could not be applied to describe the sorption mechanism of water in hydrogels prepared at -18 °C, due to their superfast responsive rate.

The values of M_t/M_∞ as a function of time for the PAAm/Dx semi-IPNs prepared at +25 and +5 °C were plotted in Figure 8.

The portion of curves with a fractional water uptake M_t/M_∞ below 0.7 has been analyzed with Equation (10). According to literature, Equation (10) is only valid for M_t/M_∞ below 0.7, because, in this portion, a linear time dependence of the fractional water uptake for all geometries is obtained.[19,20] Constants *n* and k were calculated from the slopes and intercepts of the $\log M_t/M_\infty$ plots as a function of $\log t$ (inset of Fig. 8), their values being listed in Table 1.

$$log(M_t/M_\infty) = logk + nlogt \qquad (10)$$

As shown in Table 1, the value of *n* (0.384 ± 0.044) found for the PAAm/Dx semi-IPNs prepared at +25 °C shows that the water sorption in this network was diffusion-controlled (Case-I, Fickian diffusion), while for those prepared at +5 °C, the value of *n* = 0.66 ± 0.016 indicates that swelling was controlled by a non-Fickian mechanism. The non-Fickian or anomalous diffusion (0.45 < *n* < 0.89) occurs when the rates of diffusion and polymer relaxation are comparable, being connected to the transition region between the two limiting situations of Case I and Case II.[21] The results obtained showed that the gel preparation conditions affected the transport mechanism, *i.e.*, the values of *n*. It is also evident from Table 1 that all correlation coefficient values are over 0.99, indicating a small estimated standard error and a high precise linear regression equation.

Water retention capacity, *WR*, that is the capacity of hydrogels to lose water, was determined with Equation (4), being measured as a function of time. The kinetic curves of *WR* (%) of the PAAm/Dx semi-IPNs are plotted in Figure 9.

Table 1

Parameters *n* and *k* for PAAm/Dx semi-IPN hydrogels prepared at +25 and +5 °C

Sample	T_{prep}	*n*	*k*	R^2
PAAm/Dx semi-IPNs	+25 °C	0.384 ± 0.044	0.183 ± 0.021	0.995 ± 0.026
	+5 °C	0.66 ± 0.016	0.053 ± 0.020	0.996 ± 0.006

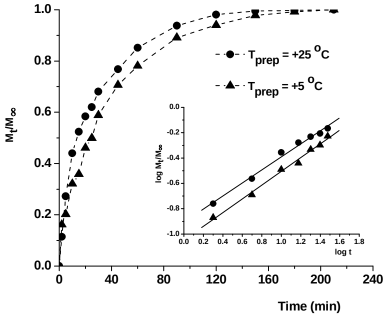


Figure 8: M_t/M_∞ as a function of time for PAAm/Dx semi-IPN hydrogels prepared at +25 and +5 °C

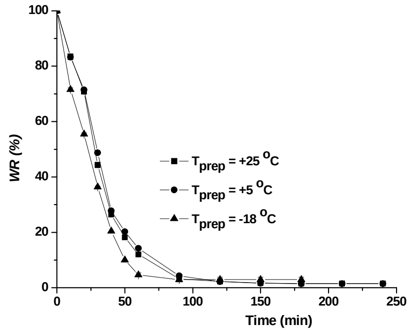


Figure 9: Water retention capacity (*WR*, %) of PAAm/Dx semi-IPNs at 25 °C as a function of time

Figure 9 shows that the rate of water loss at 25 °C was clearly influenced by the hydrogel preparation temperature. In the case of PAAm/Dx semi-IPNs prepared at +25 or +5 °C, and -18 °C, water retention leveled off at about 1.5 wt% within 100 min, and at 3 wt% within 60 min, respectively. Such differences in the rate of water loss could be correlated with the porous structure, with pores of about 3 µm, for hydrogels prepared at +25 °C (Fig. 2A), and polyhedral pores of sizes of about 80 µm for those prepared at -18 °C, respectively (Fig. 2B).

CONCLUSIONS

Porous semi-IPNs based on PAAm and Dx were prepared by cross-linking copolymerization reactions, at different temperatures. The gel preparation temperature was found to be the key factor determining the porous structure of networks. The inner network structures of the newly reported semi-IPNs prepared at -18 °C exhibit a heterogeneous morphology consisting of pores with sizes around 80 µm, while those formed at +5 or +25 °C have pores with sizes around 3 µm. The swelling kinetics of hydrogels in water showed higher swelling ratios for PAAm/Dx semi-IPNs prepared at +25 °C. Moreover, by conducting the cross-linking polymerization reaction at -18 °C, PAAm/Dx semi-IPNs with a superfast responsive rate (15 s) were obtained. The swelling mechanism and the rate of water loss of the investigated hydrogels at 25 °C were clearly influenced by the hydrogel preparation temperature. Water retention leveled off after 100 min in the case of PAAm/Dx semi-IPNs prepared at +25 or +5 °C, and after 60 min, respectively, for PAAm/Dx semi-IPNs prepared at -18 °C.

ACKNOWLEDGEMENTS: The financial support of this research by the European Social Fund "Cristofor I. Simionescu" Postdoctoral Fellowship Programme (ID POSDRU/89/1.5/S/55216), Sectorial Operational Programme for Human Resources Development, 2007-2013, is gratefully acknowledged.

REFERENCES

[1] M. E. Byrne and V. Salian, *Int. J. Pharm.*, **364**, 188 (2008).
[2] T. R. Hoare and D. S. Kohane, *Polymer*, **49**, 1993 (2008).
[3] N. Bhattarai, J. Gunn and M. Zhang, *Adv. Drug. Deliv. Rev.*, **62**, 83 (2010).
[4] A. Guiseppi-Elie, *Biomaterials*, **31**, 2701 (2010).
[5] D. L. Merlin and B. Sivasankar, *Eur. Polym. J.*, **45**, 165 (2009).
[6] W. Wang and A. Wang, *Carbohydr. Polym.*, **80**, 1028 (2010).
[7] E. S. Drăgan and M. M. Perju, *Soft Mater.*, **8**, 49 (2010) .
[8] D. Myung, D. Waters, M. Wiseman, P. E. Duhamel, J. Noolandi and C. N. Ta, *Polym. Adv. Techn.*, **19**, 647 (2008).
[9] L. C. Yin, L. K. Fei, F. Y. Cui, C. Tang and C. H. Yin, *Biomaterials*, **28**, 1258 (2007).
[10] S. F. Li, Y. J. Yang, X. L. Yang and H. B. Xu, *J. Appl. Polym. Sci.*, **105**, 3432 (2007).
[11] P. Chivukula, K. Dusek, D. Wang, M. Duskova-Smrckova, P. Kopeckova and J. Kopecek, *Biomaterials*, **27**, 1140 (2006).
[12] Y. X. Zhang, F. P. Wu, M. Z. Li and E. J. Wang, *Polymer*, **46**, 7695 (2005).
[13] V. I. Lozinsky, *Russ. Chem. Rev.*, **71**, 489 (2002).
[14] P. Arvidsson, F. M. Plieva, V. I. Lozinsky, I. Y. Galaev and B. Mattiasson, *J. Chromatogr. A*, **986**, 275 (2003).
[15] M. V. Dinu, M. M. Ozmen, E. S. Dragan and O. Okay, *Polymer*, **48**, 195 (2007).
[16] M. M. Ozmen, M. V. Dinu, E. S. Dragan and O. Okay, *J. Macromol. Sci.*, *A*, *Pure Appl. Chem.*, **44**, 1195 (2007).
[17] B. Vazquez, J. S. Roman, C. Peniche and M. E. Cohen, *Macromolecules*, **30**, 8440 (1997).
[18] O. Okay, *Prog. Polym. Sci.*, **25**, 711 (2000).
[19] B. Kim, K. La Flamme and N. A. Peppas, *J. Appl. Polym. Sci.*, **89**, 1606 (2003).
[20] P. L. Ritger and N. A. Peppas, *J. Control. Release*, **5**, 37 (1987).
[21] J. Chen, M. Liu and S. Chen, *Mater. Chem. Phys.*, **115**, 339 (2009).