SWELLING BEHAVIOR OF HYDROGELS BASED ON N,N'-DIETHYLACRYLAMIDE

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ABSTRACT

In this work, two series of thermo-responsive hydrogels with semi-interpenetrating polymer network (semi-IPN) structure based on N,N'-Diethylacrylamide (DEA) and 2-hydroxyethyl methacrylate (HEMA) were synthesized and investigated by changing the position and content of HEMA monomer in the obtained materials, including P(DEA-co-HEMA)/PDEA (S1-structure) and PDEA/P(DEA-co-HEMA) (S2-structure). The morphological, chemical properties and swelling behaviors in pure water of the semi-IPN hydrogels were investigated. Fourier transform infrared (FTIR) spectra confirmed the polymerization ability of monomers. Scanning electronic microscopy (SEM) images showed that the pore size could be controlled by the added volume of linear polymer was in the range of 151 ± 39 ~ 340 ± 65 µm. The swelling ratio and swelling rate of the semi-IPN hydrogels increased significantly compared with that of the conventional hydrogel. In addition, the S1-structure hydrogels showed a faster swelling rate, higher swelling ratio and more thermo-sensitive than that of the S2-structure hydrogels.

Keywords: *Thermo-sensitive; swelling behavior; swelling ratio; swelling rate; semi-IPN hydrogel; N,N'-Diethylacrylamide; 2-hydroxyethyl methacrylate.*

1. INTRODUCTION

Thermo-responsive hydrogel is a three-dimensional network that is able to absorb a large amount of water without dissolving and can undergo a sharp change in volume or phase transition in response to temperature [1]. They can be molded into any form which is suitable for many potential applications in different fields such as controlled drug delivery [2], smart textile [3], biomedical [4], tissue engineering and regenerative medicine [5].

In general, the hydrogels of several N-substitued polyacrylamides show thermo-responsive behavior, such as poly(N-isopropylacrylamide) (PNIPAM) and poly(N,N'-diethylacrylamide) (PDEA) [6-8]. These hydrogels are capable of reversible phase transition at a certain temperature and is referred to as the lower critical solution temperature (LCST). Below the LCST, the hydrogel is hydrophilic and absorbs water to a swollen state, while above the LCST, it is hydrophobic and water is removed from the network to a shrunken state. This phenomenon can be explained by the inter- and intra- molecular interaction within the polymer network. At below LCST, strong hydrogen bonds between polymer network and water causes the swollen state, while at above LCSTs, the interaction within polymer network is stronger than the hydrogen bonds, leading to the shrunken state.

Most of the previous studies about thermo-responsive polymer materials were conducted with PNIPAM. However, it was reported that during hydrolysis in aqueous solution, PNIPAM-based materials were able to release toxic low molecular weight amines, then their bio-applications were limited [9]. In this case, the other hydrogels based on PDEA with the LCST of 31°C [10] can be a new attractive candidate for biomedical applications because the cytotoxicity of PDEA hydrogels is less pronounced than the

PNIPAM-based hydrogels [11]. However, the hydrogels with conventional three-dimensional structure have some disadvantages, such as low swelling ratio, and slow response rate [12]. To overcome these disadvantages, semi-interpenetrating network (semi-IPN) hydrogels is usually synthesized by introducing a linear polymer into the three-dimensional network. Generally, semi-IPN hydrogels are usually synthesized by simultaneous polymerization of a monomer system with a cross-linking agent in the presence linear polymer chains, which will be physically entangled within the polymer network [13]. Besides, a high hydrophilic thermo-responsive hydrogel can be obtained by introduced a hydrophilic segment such as acrylic acid [14], itaconamic acid [15] into the semi-IPN material. By this way the resulted hydrogels are not only high response rate but also high swelling ratio.

2-Hydroxyethyl methacrylate (HEMA) is the organic compound with a vinyl functional group which can participate in the copolymerization with another monomer. In general, when based-HEMA polymers is subjected to water, it will swell due to the molecule's hydrophilic pendant groups. Depending on the physical and chemical structure of the polymer, it is capable of absorbing from 10 to 600% water relative to the dry weight [16]. In this work, HEMA was introduced into the semi-IPN hydrogels by two methods to synthesize two structures of the thermo-responsive semi-IPN hydrogels and investigate their swelling behaviors in pure water. First, the S1-structure P(DEA-co-HEMA)/PDEA semi-IPN hydrogels were prepared by the polymerization of DEA in the presence of the linear copolymer P(DEA-co-HEMA) and the cross-linker, while the S2-structure PDEA/P(DEA-co-HEMA) semi-IPN hydrogels were synthesized by the polymerization of mixture of DEA and HEMA monomer in the presence of the linear polymer PDEA and the cross-linker. The chemical structures and morphology of hydrogels were investigated. Finally, the swelling behaviors of the obtained hydrogels were investigated in various temperatures by weighing method.

2. MATERIALS AND METHOD

2.1 Materials

N,N'-diethylacrylamide (DEA; $C_7H_{13}NO$) was obtained from Tokyo Chemical Industry Co., Ltd. (Japan). 2-hydroxylethyl methacrylate (HEMA, $C_6H_{10}O_3$) was received from Aldrich Chemical Corp (Saint Louis, MO, USA). Ammonium persulfate (APS; $(NH_4)_2S_2O_8$) as an initiator was purchased from Aencore Chemical Pty. Ltd. (Surrey Hills, Australia). N,N,N',N'-tetramethylethylenediamine (TEMED; $C_6H_{16}N_2$) as a catalyst and N,N'-methylenebisacrylamide (MBA; $C_7H_{10}N_2O_2$) as a cross-linker were purchased from Alfa Aesar Co. (Tewksbury, MA, USA). All reactants were used as received without any further purification.

2.2 Method

The preparation of linear copolymer P(DEA-co-HEMA) is shown in Figure 1a. It was prepared by free radical polymerization in aqueous solution of DEA and HEMA, employing APS and TEMED as an initiator and accelerator, respectively. First, DEA (1.5 g, 11.79 mmol) and 70 µL of HEMA were dissolved together in 6.0 mL of pure water by continuous stirring until homogeneous in a degassed condition by a vacuum pump, and placed the solution in an ice-water bath. Then, 2.5 mL aqueous solution of APS (0.4792 g APS/25 mL pure water) and 5.0 mL aqueous solution of TEMED (4 mL TEMED/25 mL pure water) were added to initiate the polymerization. After polymerization in the ice-water bath for 2h, the solution was ready for the synthesis of S1-structure semi-IPN hydrogels. Moreover, linear homopolymer PDEA was prepared by a similar method as described above without HEMA for the preparation of S2-structure semi-IPN hydrogels.

The preparation of the S1-structure and S2-structure semi-IPN hydrogels is illustrated in Figure 1b. S1-structure semi-IPN hydrogels were prepared by mixing the linear copolymer P(DEA-co-HEMA) solution (≈100 mg/mL) and DEA solutions (100 mg/mL, containing 3.0 mole % MBA) in a vial with various designated ratios (0:10, 1:9, 2:8, 3:7 and 4:6, v/v in an ice-water bath. The ratio 1:10 represents the conventional PDEA hydrogel. On the other hand, the S2-structure semi-IPN hydrogels were synthesized by mixing linear PDEA solution (≈100 mg/mL) with the solution of DEA (100 mg/mL, containing 3.0 mole % MBA) and HEMA in a vial with the same ratios as described above and ensured the molar ratio of DEA and HEMA in each designated ratio of two semi-IPN structures is the same. After that, the obtained mixtures were vacuumed for 30 minutes until the solution became homogeneous. In the next step, TEMED and APS solution were added as a redox initiator pair to initiate the final reaction mixture. The solution was mixed thoroughly and then quickly poured into a cylindrical glass mold with the diameter of 8.0 mm, sealed immediately, and kept at room temperature for 24 hours. The sample PDEA represents the conventional hydrogel that was synthesized without linear polymer. The obtained hydrogels were carefully removed from the mold, cut into samples with the thickness of 2.5 mm and immersed in pure water (refreshed every half-day for 1 week) to eliminate the unreacted reagents. Finally, they were dried to completely remove water for further investigation. The feed ratios are given in Table 1.

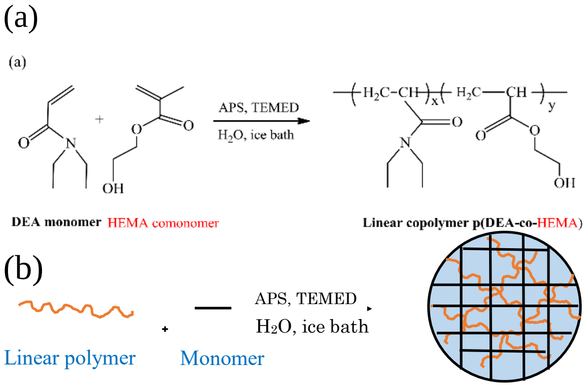


Figure 1. *Preparation scheme of (a) linear copolymer p(DEA-co-HEMA) and (b) semi-IPN hydrogels*

2.3 Characterization

Fourier transform infrared (FTIR) spectra were measured by a Perkin Elmer Spectrum RXI FTIR 10.5.2 instrument (Waltham, MA, USA) within 4000-400 cm-1 having scan resolution of 4.00 cm^{-1}. Background measurement were performed and subtracted for all the samples.

The SEM images of freeze-dried hydrogels were taken by a Hitachi TM3000 scanning electron microscope (SEM) (Hitachi, Tokyo, Japan) to investigate the interior morphology. All samples were sputter-coated with gold for 10 minutes to enhance the conductivity and SEM images were acquired at an accelerating voltage of 15.0 kV. The pore sizes and standard deviations were analyzed by ImageJ.

The swelling kinetics of the hydrogels were studied using gravimetric method. Dried hydrogels were immersed in pure water at 25 °C. At predetermined time points, swelling hydrogels were eliminated the excess water on the surface by filter paper and weighed by an electronic balance. The swelling ratio (SR) was calculated according to the following equation:

$$SR = \frac{W_s - W_d}{W_d} \qquad (1)$$

where Ws is the weight of the swelling hydrogel and Wd is the weight of the freeze-dried hydrogel.

The thermo-sensitive property of the hydrogels was investigated by calculation the equilibrium swelling ratio as a function of temperature. Dried hydrogels were immersed in pure water at different temperature points in the range of 20-45 °C until equilibrium. The swelling hydrogels were eliminated the excess water on the surface by filter paper and weighed by an electronic balance, and SR was calculated using the above equation.

To investigate the deswelling kinetics of the hydrogels, the dried samples were firstly immersed in DI water at 25 °C. After equilibrium swelling, the swollen hydrogels were quickly transferred to DI water at 45 °C. At predetermined time points, the shrunk hydrogels were removed, wiped off water on the surface by filter paper and weighed by an electronic balance. Water retention (WR) was calculated according to the following equation:

$$WR(\%) = \frac{W_t - W_d}{W_s - W_d} \, x \, 100 \qquad (2)$$

where Wt is the weight of the shrunk hydrogel at the specific time t at 45 °C, Wd is the weight of the dried hydrogel and We is the weight of the equilibrium swollen hydrogel at 25 °C.

3. RESULTS AND DISCUSSION

3.1 Preparation of Semi-IPN Hydrogels

Semi-IPN hydrogels were synthesized in two steps. In the first step, linear polymer PDEA and linear copolymer P(DEA-co-HEMA) was synthesized by free radical copolymerization of DEA and HEMA using APS as an initiator and TEMED as a catalyst. In the second step, DEA and linear copolymer P(DEA-co-HEMA) (for S1-structure hydrogels) or DEA, HEMA and linear polymer PDEA (for S2-structure hydrogels) were mixed together with MBA as a cross-linker and DI water in the designed ratios. Then, APS and TEMED were added to the solution to initiate the polymerization reaction and accelerate the process by facilitating homolytic scission on APS moieties [17]. Finally, three-dimensional networks were obtained with the linear copolymer-polymer chains were kept and entangled within the hydrogel network through hydrogen bonding interaction.

The FTIR spectra of DEA monomer, conventional hydrogel PDEA, S1-structure (S1-P3 sample) and S2-structure (S2-P3 sample) semi-IPN hydrogels are shown in Figure 2. In the spectrum of DEA monomer, the amide C=O stretching peak was shown at about 1700 cm^{-1}, the C–H stretching vibration band of –CH_3 and –CH_2– groups were shown at about 2924 and 2850 cm^{-1}, and the C=C stretching peak was shown at 1565 cm^{-1} [18]. After polymerization, the spectrum of conventional PDEA and semi-IPN hydrogels showed an absence of the peak at about 1590 cm^{-1}, indicating C=C was transformed into C–C in the three-dimensional hydrogels. Moreover, the C–H stretching vibration band of –CH_3 and –CH_2– groups for DEA monomer were also detected for conventional PDEA and semi-IPN hydrogels. In addition, the semi-IPN hydrogel has a distinct characteristic shoulder at 1720 cm^{-1} with a relatively low absorbance which corresponds to carbonyl group in HEMA section, indicating the successful introduction of HEMA to the semi-IPN hydrogels and linear copolymer P(DEA-co-HEMA).

Table 1. *Composition of raw materials used for the preparation of semi–IPN hydrogels*

Sample	Linear P(DEA-co-HEMA) [a] Solution, (mL)	Linear PDEA [a] Solution, (mL)	DEA (ml)	HEMA (µL)	Pure water (Ml)	MBA (mg)	APS [b] Solution (mL)	TEMED [c] Solution (mL)	Total Volume (mL)
PDEA	-	-	1.5	-	9.0	46.0	1,5	3,0	15.0
S1-P1	1.5	-	1.35	-	8.0	41.0	1.4	2.8	15.0
S1-P2	3.0	-	1.20	-	7.2	37.0	1.2	2.4	15.0
S1-P3	4.5	-	1.05	-	6.2	32.0	1.1	2.2	15.0
S2-P1	-	1.5	1.35	7.0		41.0	1.4	2.8	15.0
S2-P2	-	3.0	1.20	14.0		37.0	1.2	2.4	15.0
S2-P3	-	4.5	1.05	21.0		32.0	1.1	2.2	15.0

[a] Solution of 1 mg/10 mg DI water; [b] solution of 0.4792 g APS/25 mL DI water; [c] solution of 4 mL TEMED/25 mL DI water.

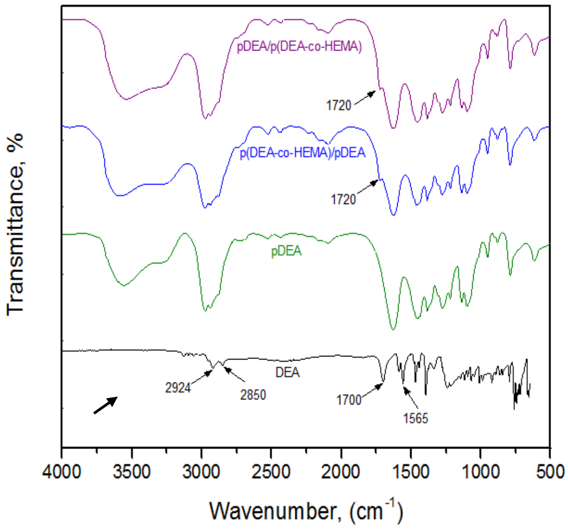


Figure 2. *FTIR spectra of DEA monomer, conventional PDEA hydrogel, S1-structure (S1-P3 sample) and S2-structure (S2-P3 sample) semi-IPN hydrogels.*

3.2 Interior Morphology

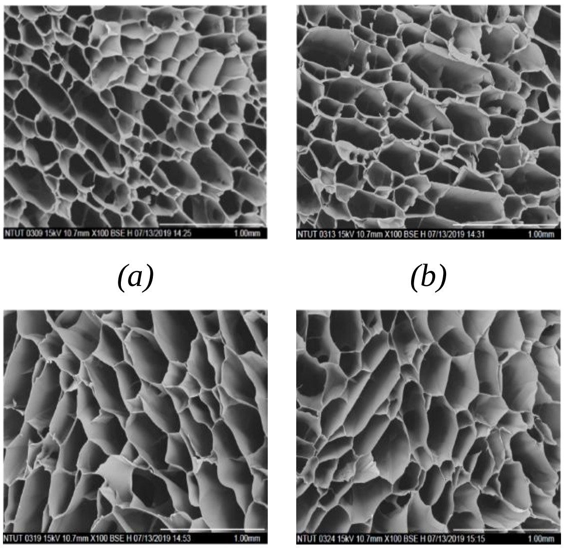
(a) (b) (c)

Figure 3. *Optical images of (a) conventional PDEA, (b) S1-structure (S1-P1 sample) and (c) S2-structure (S2-P1 sample) semi-IPN hydrogels.*

Figure 3(a–c) shows photographs of conventional PDEA, S1-structure and S2-structure semi-IPN hydrogels, respectively. The semi-IPN hydrogels were more opaque and elastic than conventional hydrogel, showing a successful synthesis of the novel hydrogel. The transmittance of three samples is different, indicating that the linear polymer had altered the structural state of the obtained semi-IPN hydrogels. This may be related to the hydrophobicity of HEMA in poor-water condition. Moreover, HEMA in three-dimensional structure is more strongly influenced in linear copolymer. Similar observations have been previously reported for salecan/pNIPAM semi-IPN hydrogels [19] and hydrogels based in HEMA and NIPAM [20].

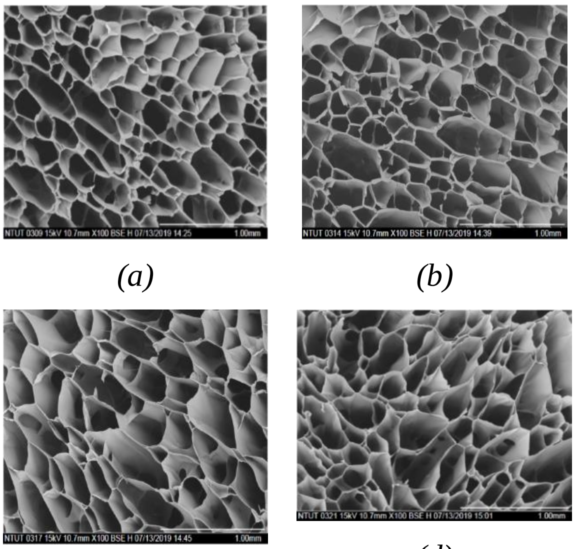
Table 2. *Pore sizes of conventional pNIPAM and semi-IPN hydrogels.*

Sample	**Pore size (µm)**	**Sample**	**Pore size (µm)**
PDEA	151 ± 39		
S1-P1	178 ± 56	S2-P1	162 ± 45
S1-P2	228 ± 45	S2-P2	220 ± 64
S1-P3	247 ± 61	S2-P3	228 ± 47



(a) *(b)* *(c)* *(d)*

Figure 4. *SEM images of conventional PDEA and semi-IPN hydrogels: PDEA (a), S1-P1 (b), SN1-P2 (c) and S1-P3.*



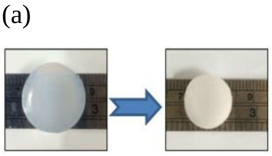
(a) *(b)* *(c)* *(d)*

Figure 5. *SEM images of conventional PDEA and semi-IPN hydrogels: PDEA (a), S2-P1 (b), SN2-P2 (c) and S2-P3.*

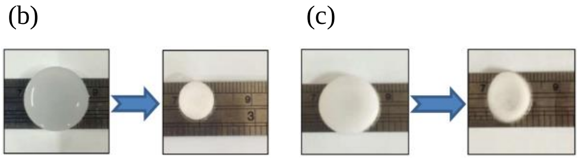
SEM images of the freeze-dried hydrogels are presented in the Figure 4(a–d) and Figure 5 (a-d) for S1-structure and S2-structure, respectively, indicating a clear porous structure with uniform pore size. In the conventional hydrogel network, the thick wall could be observed with the pore size of about 151 ± 39 µm. The thick wall of conventional hydrogels based on DEA was also reported by Zhang et al. [21] and Chen et al. [22]

The SEM images clearly showed the dependence of interior morphology on the linear copolymer content introduced into the semi-IPN hydrogels. They are listed in the Table 2. For S1-structure semi-IPN hydrogel, the average pore sizes were 178 ± 56, 228 ± 45 and 247 ± 61 for S1-P1, S1-P2 and S1-P3 sample, respectively. Besides, table 2 also showed the pore sizes of S2-P1, S2-P2 and S2-P3 sample were 162 ± 45, 220 ± 64 and 228 ± 47 µm, respectively. This result shows that the morphology of the two structures are quite similar and only depends on the content of linear polymer and hydrophilic pedant groups introducing from HEMA section.

3.3 LCST Behavior



pDEA at 25 °C pDEA at 45 °C



S1-P3 at 25 °C S1-P3 at 45 °C S2-P3 at 25 °C S2-P3 at 45 °C

Figure 6. *Photographs of the hydrogels in the swollen state at 25 oC and the shrunken state at 45 ^{o}C in pure water: (a) PDEA, (b) S1-P3 and (c) S2-P3.*

Figure 6 shows the images of pDEA, S1-P3 and S2-P3 samples in the swollen state at 25 oC (below LCST) and 45 ^{o}C (above LCST). At the beginning, the diameter of all samples were 17 mm. After being immersed about 12 h in DI water at 45 ^{o}C, the diameter reduced to 14.0, 9.5 and 12.0 for pDEA, S1-P3 and S2-P3 sample, respectively. The change in the diameter of the conventional and other semi-IPN hydrogels was listed in the Table 3. This result confirmed that the semi-IPN hydrogel was more thermo-responsive than the conventional pDEA hydrogel. Moreover, this result also showed that the S1-struture hydrogel was more thermo-responsive than S2-structure hydrogel. The results can be explained by the more heat conduction and thermal sensitivity of linear copolymer p(DEA-co-HEMA) than homopolymer pDEA. These linear polymers acted as a thermal conductor, which helped the heat transfer in the semi-IPN hydrogels take place faster than in the conventional pDEA hydrogel.

3.4 Swelling behavior

3.4.1 Swelling Kinetics and Equilibrium Swelling Ratio

Figure 7(a, b) shows the swelling kinetic curves of S1- and S2-structure semi-IPN hydrogels in pure water at 25 ^{o}C. It can be found that the swelling rate and equilibrium swelling ratio of the hydrogel increased from S1-P1 to S1-P3 and S2-P1 to S2-P3 for S1-1 and S2-structure, respectively. These values of semi-IPN hydrogels were also higher than that of conventional pDEA hydrogel. These results can be explained by the molecule's hydrophilicity pedant groups of HEMA which were introduced into semi-IPN hydrogels such as carbonyl and hydroxyl groups. When the HEMA content increased, the semi-IPN hydrogels possessed more hydrophilicity groups and absorbed more water, leading to a higher equilibrium swelling ratio. Besides, the linear polymers have supported the water molecules to move more easily from outside into the hydrogel network, leading to an increased swelling rate [23]. In the comparison about the equilibrium swelling ratio between S1-structure and S2-tructure semi-IPN hydrogel, it shows that the equilibrium swelling ratio of S1-based hydrogels were higher than (that of) S2-based hydrogels (with the same HEMA content). This result may be due to the fact that the hydrophilic activity of HEMA segment in the linear copoplymer was higher than in the three-dimensional structure.

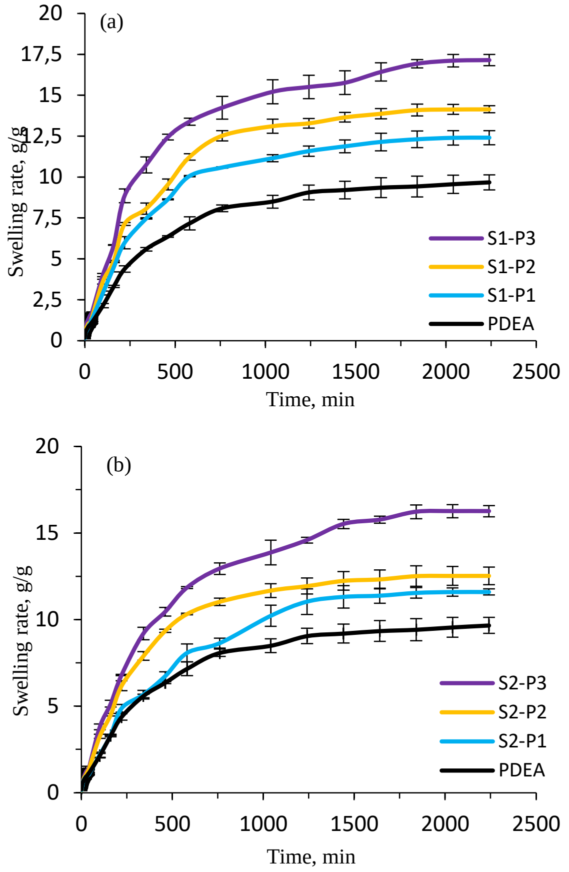


Figure 7. *Swelling kinetic curves in pure water at 25 °C of (a) S1-structure; (b) S2-structure semi-IPN hydrogels.*

3.4.2 Deswelling Kinetics

Figure 8(a, b) shows the deswelling kinetics of the S1- and S2-structure semi-IPN hydrogels hydrogels. It was measured by transferring the equilibrium swollen hydrogels in DI water from 25 °C to 45 °C. As mention above, when the temperature was higher than LCST, the hydrogel networks were collapsed since the absorbed water moved out. In Figure 8(a, b), the semi-IPN samples show the faster shrinking rate compared to conventional PDEA hydrogel. Moreover, most of water inside the semi-IPN hydrogels was removed when their structure collapsed, while the conventional pNIPAM hydrogel was only 32%.

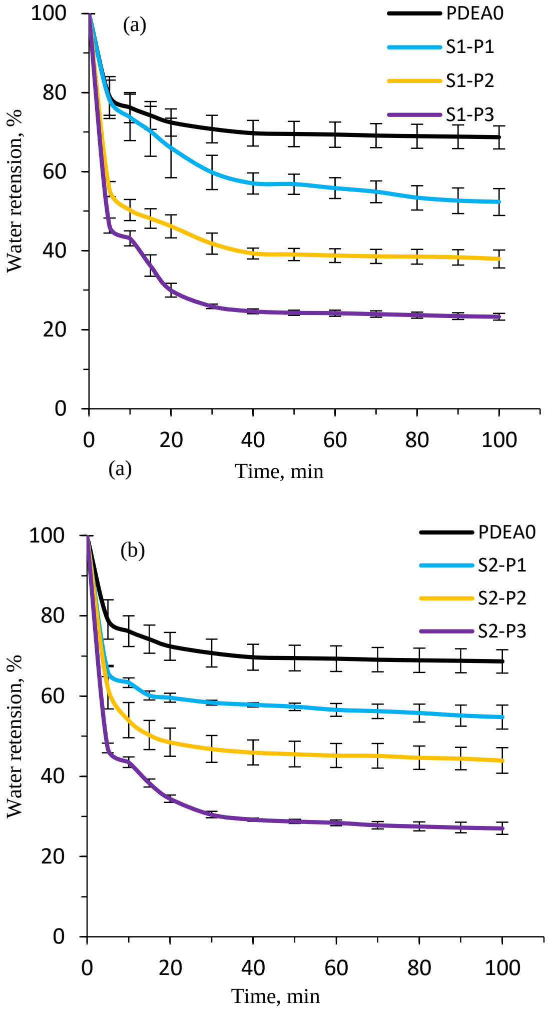


Figure 8. Deswelling kinetic curves as *temperature changes from 25 to 45 °C in pure water of (a) S1-structure and (b) S2-structure semi-IPN hydrogels.*

The water retention of semi-IPN hydrogels was influenced by the linear polymer/copolymer. For example, after immersing in DI water at 45 °C about 100 minutes, the water retention values were 52.3% and 23.3% for S1-P1 and S1-P3 samples; were 54.7% and 27.0% for S2-P1 and S2-P3 samples, respectively. In general, the conventional PDEA hydrogel formed from dense walls which may prevent water molecules from running out when it was immersed into the higher LCST condition. For the semi-IPN hydrogels, the hydrophilic linear copolymer provided good channels and water molecules easily moved out when their structure collapsed.

3.4.3 Temperature Dependence

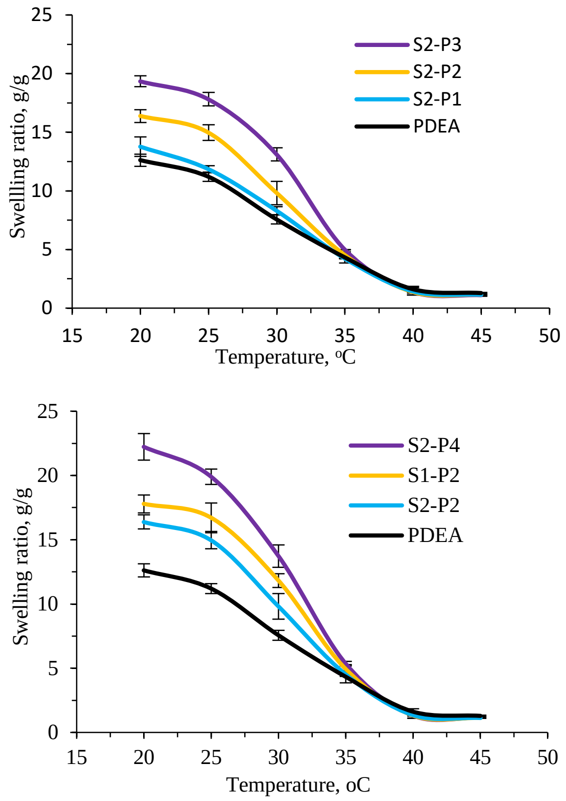


Figure 9. *Swelling ratio values in water as a function of temperature from 20-45 °C of (a) S1-structure and (b) S2-structure semi-IPN hydrogels*.

Figures 8(a-b) indicated the thermo-sensitive property of the semi-IPN hydrogels. High swelling ratios were found in the temperature of 20-30 oC. while there was a significant decreasing in swelling ratios found in the range of 30-40 °C. These results showed the strong influence of temperature on the phase transition of semi-IPN hydrogels which shrunk above the LCST and swelled below the LCST. Moreover, in the range of 40-45 °C (above their LCST) shows no significant differences in the swelling ratios and it may be due to all hydrogel samples retracted to form the same tight structure. The phase transition of semi-IPN hydrogels as a function of temperature in this work proves that it can be used as a drug delivery system or an absorbing material. Finally, it also shows that, in the range of 20 – 35 °C, the swelling ratio of S1-structure hydrogel is always higher than that of S2-structure hydrogel with the same HEMA content. These results may be related to the higher hydrophilicity of linear copolymer p(DEA-co-HEMA) than linear polymer pDEA as discussed above.

4 CONCLUSION

In this work, two series of semi-IPN hydrogels based on DEA and HEMA were synthesized and investigated. The S1-structure hydrogel p(DEA-co-HEMA)/pDEA was prepared by introducing comonomer HEMA into linear polymer, while the S2-structure pDEA/p(DEA-co-HEMA) hydrogel was received by introducing HEMA into three dimensional network. The chemical structure was confirmed by FTIR spectra. A uniform porous structure of the semi-IPN hydrogels was conformed by SEM. The equilibrium swelling ratios were influenced by the content of HEMA introducing into hydrogel network: increasing the HEMA content leading to an increased the swelling ratio. With the same HEMA content introducing into network, S1-structure hydrogels exhibited higher swelling ratios and swelling rate than S2-structure hydrogels. Moreover, this work also confirmed that the semi-IPN and S1-struture hydrogel were more thermo-responsive than that of the conventional pDEA and S2-structure hydrogel, respectively. Further application of semi-IPN hydrogels based on DEA and HEMA are in progress.

REFERENCES

[1] Zhao, Z.X.; Li, Z.; Xia, Q.B.; Bajalis, E.; Xi, H.X.; Lin. Y.S. Swelling/deswelling kinetics of PNIPAAm hydrogels synthesized by microwave irradiation. *Chemical Engineering Journal* **2008**, 142, 263-270.

[2] Li, Y.; Guo, H.; Gan, J.; Zheng, J.; Zhang, Y.; Wu, K.; Lu, M. Novel fast thermal-responnsive poly(N-isopropylacrylamide) hydrogels with functional cyclodextrin interpenetrating polymer networks for controlled drug release. *J. Polym. Res*. **2015**, 22, 91.

[3] Huang, Z.S.; Shiu, J.W.; Way, T.F.; Rwei, S.P. A thermo-responsive random copolymer of poly(NIPAm-co-FMA) for smart textile applications. *Polymer* **2019**, 184, 121917.

[4] Erol, O.; Pantula, A.; Liu, W.; Gracias, D.H. Transformer hydrogels: a review. *Adv. Mater. Technol*. ***2019***, 4, 1900043.

[5] Mantha, S.; Pillai, S.; Khayambashi, P.; Upadhyay, A.; Zhang, Y.; Tao, O.; Pham, H.M; and Tran, S.D. Smart Hydrogels in tissue engineering and regenerative medicine. *Materials* ***2019***, 12, 3323; doi:10.3390/ma12203323.

[6] Inomata, H.; Goto, S.; Saito, S. Phase transition of N-Substituted acrylamide gels. *Macromolecules* **1990**, 23, 4887-4888.

[7] Liu, H.; Liu, M.; Jin, S.; Chen, S. Synthesis and characterization of fast responsive thermo- and pH-sensitive poly[(N,N-diethylacrylamide)-co-(acrylic acid)] hydrogels. *Polym. Int.* **2008**, 57, 1165-1173.

[8] Cai, W.; Gupta, R.B. Poly(N-ethylacrylamide) Hydrogels for lignin separation. *Ind. Eng. Chem. Res.* **2001**, 40, 3406-3412.

[9] Kostanski, L.K.; Huang, R.; Ghosh, R.; Filipe, C.D.M. Biocompatible poly(N-vinyllactam)-based materials with environmentally-responsive permeability. *J. Biomater. Sci. Polymer Edn.* **2008**, 19, 275-290.

[10] Idziak, I.; Avoce, D.; Lessard, D.; Gravel, D.; Zhu, X.X. Thermosensitivity of Aqueous Solutions of Poly(N,N-diethylacrylamide). *Macromolecules* **1999**, 32, 1260-1263.

[11] Hanykova, L.; Spevacek, J.; Radecki, M.; Zhigunov, A.; Kourilova, H.; Sedlakova, Z. Phase transition in hydrogels of thermoresponsive semi-interpenetrating and interpenetrating networks of poly(N,N-diethylacrylamide) and polyacrylamide. *European Polymer Journal* **2016**, 85, 1-13.

[12] Liu, Y.; Zhang, K.; Ma, J.; Vancso, G.J. Thermoresponsive semi-IPN hydrogel microfibers from continuous fluidic processing with high elasticity and fast actuation. *ACS Appl. Mater. Interfaces* **2017**, 9, 901-908.

[13] Chen, J.; Liu, M.; Liu, H.; Ma, L.; Gao, C.; Zhu, S.; Zhang, S. Synthesis and properties of themo- and pH sensitive poly(diallyldimethylammonium chloride)/poly(N,N-diethylacrylamide) semi-IPN hydrogel. *Chemical Engineering Journal* **2010**, 159, 247-256.

[14] Liu, H.; Liu, M.; Ma, L.; Chen, J. Thermo- and pH-sensitive comb-type grafted poly(N,N-diethylacryl amide-co-acrylic acid) hydrogels with rapid response behaviors. *European Polymer Journal* **2009**, 45, 2060-2067.

[15] Rwei, S.P.; Tuan, H.N.A.; Chiang, W.Y.; Way, T.F. Synthesis and characterization of pH and thermo dual-responsive hydrogels with a semi-IPN structure based on N-isopropylacrylamide and itaconamic acid. *Materials* **2018**, 11, 696; doi:10.3390/ma11050696.

[16] Ahmed, E. M., Hydrogel: Preparation, characterization, and applications: A review, Journal of Advanced Research, **2015**, 6, 105–121.

[17] De Feng, X.; Guo, X.Q.; Qiu, K.Y. Study of the initiation mechanism of the vinyl polymerization with the system persulfate/**N,N,N***'*,**N***'*-tetramethylethylenediamine. **Makromol. Chem. 1988**, **189**, 77–83.

[18] Liu, D.; Liu, H.; Hu, N. pH-, sugar-, and temperature-sensitive electrochemical switch amplified by enzymatic reaction and controlled by logic gates based on semi-interpenetrating polymer networks. *J. Phys. Chem. B* **2012**, 116, 1700-1708.

[19] W. Wei, X. Hu, X. Qi, H. Yu, Y. Liu, J. Li, J. Zhang, W. Dong, A novel thermo-responsive hydrogel based on salecan and poly(N-isopropylacrylamide): Synthesis and characterization. *Colloids Surface B Bioinertfaces* **2015**, 125, 1–11.

[20] Tuan, H.N.A. and Dat, N.T. Semi-IPN Hydrogels Based on N-isopropylacrylamide and 2-Hydroxyethyl Methacrylate. *Journal of Technical Education Science* **2020**, 56, 64-71.

[21] Zhang, N.; Liu, M.; Shen, Y.; Chen, J.; Dai, L.; Gao, C. Preparation, properties, and drug release of thermo- and pH-sensitive poly((2-dimethylamino)ethyl methacrylate)/poly(N,N-diethylacrylamide) semi-IPN hydrogels. *J. Mater. Sci*. **2011**, 46, 1523-1534.

[22] Chen, J.; Liu, M.; Zhang, N.; Dai, P.; Cao, C.; Ma L.; Liu, H. Influence of the grafted chain length on responsive behaviors of the grafted poly(DEA-co-DMAEMA) hydrogel. *Sensor and Acuators B: Chemical* **2010**, 149, 34-43.

[23] W. Wei, X. Qi, Y. Liu, J. Li, X. Hu, G. Zuo, J. Zhang, Synthesis and characterization of a novel pH-thermo dual responsive hydrogel based on salecan and poly (N, N-diethylacrylamide-co-methacrylic acid). *Colloids Surface B Biointerfaces* **2015**, 136, 1182–1192.

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