

The effect of external stimuli on the equilibrium swelling properties of poly(*N*-vinyl 2-pyrrolidone/itaconic acid) poly-electrolyte hydrogels

Murat Şen^{1,*}, Ömer Kantoğlu², Olgun Güven¹

¹Hacettepe University, Department of Chemistry, 06532 Beytepe, Ankara, Turkey

²Turkish Atomic Energy Authority, Ankara Nuclear Research and Training Centre, İstanbulyolu, 30. İm, Sınav, 06105 Ankara, Turkey

Received 17 February 1998; revised 17 April 1998; accepted 17 April 1998

Abstract

Hydrogels with varying crosslink densities and ionic moieties were prepared from the ternary systems *N*-vinyl 2-pyrrolidone/itaconic acid/water by irradiation with γ rays at ambient temperature. The influence of external stimuli such as pH, temperature and ionic strength of the swelling media and the type of buffer on the equilibrium swelling properties were investigated. Hydrogels showed typical pH response and temperature responses, such as high-pH and low-temperature swelling and low-pH and high-temperature deswelling. A change in the ionic strength of the swelling solution from 0.01 to 0.20 caused a decrease in the equilibrium degree of swelling of hydrogels. Oscillatory swelling behaviour was also observed and investigated in response to changes in the pH of the solution. © 1998 Elsevier Science Ltd. All rights reserved.

Keywords: Hydrogel; Swelling; Poly(*N*-vinyl 2-pyrrolidone/itaconic acid)

1. Introduction

As early as 1950 attempts were made for the development and use of environmental sensitive materials in biomedical and biotechnological applications. Most of the initial studies on the ionizable polymeric systems have been due to Katchalsky [1,2] and Dusek and coworkers [3,4], and further work was done by Tanaka [5], Peppas [6] and Siegel [7,8] and their collaborators.

Temperature and pH have been the solution variables in typical physiological and chemical systems [9,10]. Recently Gudeman and Peppas [11] synthesized and characterized pH sensitive interpenetrating networks of Poly(vinyl alcohol) and monoprotic acrylic acid. They investigated the influence of molecular weight between crosslinks on the equilibrium degree of swelling and oscillatory swelling behaviours of hydrogels. It was found that as the molecular weight between crosslinks increased the equilibrium degree of swelling value increased and yielded faster swelling and deswelling rates. A change in pH from 3 to 6 caused an ionization of the hydrogel and an increase in the weight swelling ratio, with greater increase exhibited by interpenetrated networks with a higher ionic content.

During the last decade a number of studies have been

performed with Poly(*N*-isopropylacrylamide) (PiPAAm), poly(2-dimethylamino ethyl methacrylate) (PDMAEM) and Poly(vinyl methyl ether)(PVME) and their copolymers with monoprotic acids and bases and well defined their temperature and pH sensitivities in different swelling conditions [12–15]. Bertran et al. synthesized and characterized negatively ionizable gel PiPAAm copolymerized with sodium acrylate and positively ionizable gel PiPAAm copolymerized with 2-(dimethylamino ethyl methacrylate) [12]. They investigated the influence of temperature on the swelling behaviours and transition temperatures of hydrogels. It was found that with increasing ionization, the temperature range over which the gel volume change is greatest becomes larger and shifts to higher temperatures.

In more recent years a series of papers has been published by Saraydın, Karadağ and Güven who synthesized new hydrogels from the copolymers of acrylamide and diprotic itaconic acid and maleic acid and showed that these hydrogels are biocompatible [16–18]. These authors also published that these hydrogels are potential adsorbents for biological agents and dyes and heavy metal ions from aqueous solutions [19–21].

In this study, we report the effect of external stimuli such as pH, ionic strength, temperature and type buffer on the equilibrium swelling of hydrogels of *N*-vinyl 2-pyrrolidone (VP)/itaconic acid (IA) copolymers. Equilibrium and

* Corresponding author.

oscillatory swelling behaviours have also been investigated in response to changes in the pH of the swelling media.

2. Experimental

2.1. Chemicals

The two monomers used in this study, VP and IA were obtained from Fluka and BDH respectively. KH_2PO_4 , K_2HPO_4 and H_3PO_4 used to prepare phosphate buffers and tri-sodium citrate, sodium dihydrogen citrate and citric acid used to prepare citrate buffers were obtained from BDH.

2.2. Preparation of hydrogels

Three components were used in the preparation of VP/IA hydrogels, namely VP, IA and water. Aqueous solutions of monomers of 2 ml VP and 60, 120 and 180 mg IA were prepared in 1 ml of pure water in different compositions (VP/IA mole ratios, 100.0/0.0, 97.6/2.4, 95.3/4.7, 93.2/6.8). Monomer solutions thus prepared were placed in the PVC straws of 4 mm diameter and irradiated by 25 kGy in air at ambient temperature in Gammacell 220 type γ irradiator at a fixed dose rate of 0.44 kGy h^{-1} . Hydrogels obtained in long cylindrical shapes were cut into pieces 3–4 mm long and stored for later evaluations.

2.3. Swelling studies

Dried hydrogels were left to swell in a solution of desired pH (2–9), ionic strength, I (0.01–0.20 M), and temperature (4.0–65.0°C). Swollen gels removed from the swelling media at regular intervals were dried superficially with filter paper, weighed and placed in the same bath. The measurements were continued until a constant weight was reached for each sample. The weight fraction of polymer in swollen gel, w , was used to calculate the volume fraction v_{2m} and equilibrium degree of swelling (EDS), Q , of the gel sample equilibrated in the buffer solution.

$$v_{2m} = [1 + \rho/\rho_w(w^{-1} - 1)] \quad (1)$$

where ρ and ρ_w are the densities of swollen gel and water. The EDS was defined as $Q = 1/v_{2m}$.

3. Results and discussion

3.1. Preparation of hydrogels

When pure VP and VP/IA/water mixture have been irradiated with γ rays, polymerization and crosslinking reactions take place simultaneously. The total dose required for the onset of gelation for pure VP, the sensitizing effect

Table 1

Mol% of IA in the feed and in the gel systems and % gelation

Gel name	Mol% IA		% Gelation
	In feed	In gel	
PVP	0.0	0.0	92.5
P(VP/IA)-1	2.4	2.0	87.7
P(VP/IA)-2	4.7	3.0	85.4
P(VP/IA)-3	6.8	3.2	82.7

of water and the influence of IA on the gelation of VP monomer were very well demonstrated in our previous studies [22,23]. Percentage gelation, i.e. percentage conversion of monomers into insoluble network, was based on the total weight of the diprotic acid and monomer in the initial mixture. The amount of IA in the monomer, polymer and/or copolymer form was determined by titration of extract against NaOH (0.05 N) to phenolphthalein end point. The mol% of IA in the initial mixtures and in the copolymeric gels and percentage gelation are summarized in Table 1.

3.2. pH-responsive characteristics

In order to follow the pH response of the P(VP/IA) hydrogels, dry samples are allowed to swell to equilibrium in phosphate buffers of varying pH at fixed ionic strength ($I = 0.1$) and temperature ($T = 25.0^\circ\text{C}$). Fig. 1 shows the change in the EDS of VP hydrogels containing various mole ratios of IA with changing pH values. The curves display single steps with a broadened S shape, which can be compared to the swelling curves of monoprotic acid containing systems. The broadening is due to overlapping of the dissociation of the first and second acids (nominal $\text{p}K_{a1}$ 3.85 and $\text{p}K_{a2}$ 5.44) [24] of the IA in these pH ranges.

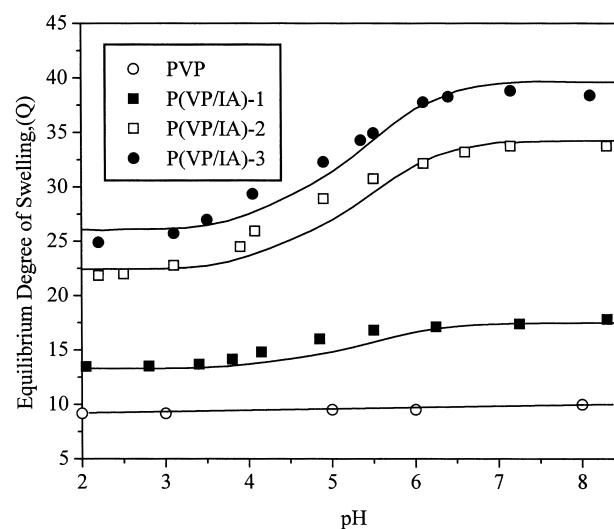


Fig. 1. Effect of pH on the equilibrium degree of swelling values of PVP and P(VP/IA) hydrogels. Solid curves are theoretical predictions.

Consistent with poly-electrolyte systems, swelling of these gels is strongly dependent on pH. An increase in pH from 2 to 8 caused a significant increase in the equilibrium degree of swelling of hydrogels with higher IA contents. In all compositions maximum extents of swelling were reached at pH 7, this being due to complete dissociation of acidic groups of IA at this pH value.

The value of the equilibrium degree of swelling of an ionic network very much depends on the concentration of ionizable groups in the network. Increase in the ionic comonomer IA produced swelling degree that increase dramatically at all pH values especially with gels P(VP/IA)-2 and P(VP/IA)-3 where the concentration of ionic comonomer is relatively high. Also notable is the fact that the addition of only minute amount of IA comonomer (0.2 mol%) radically changes the swelling behaviour of the gel P(VP/IA)-3, (mole ratio 96.8/3.2) over P(VP/IA)-2, (mole ratio 97.0/3.0). The contribution of various factors such as polymer-based, solution-based and polymer-solvent combination type parameters on the EDS of these hydrogels are very well elaborated in our previous study [25].

3.3. Ionic strength-responsive characteristics

The effect of external ionic strength on the equilibrium degree of swelling of VP/IA copolymeric hydrogels at 25°C is given in Fig. 2. Solution pH was fixed at 3.0 and 8.0 to obtain minimum and maximum swelling for each gel, thereby allowing ionic strength effects to be observed most clearly. An increase in ionic strength generally decreased the swelling, because the difference in concentration of mobile ions between the gel and solution is reduced causing a decrease in the osmotic swelling pressure of these mobile ions inside the gel. It is seen from Fig. 2 that with increasing ionic strength of the swelling solution the

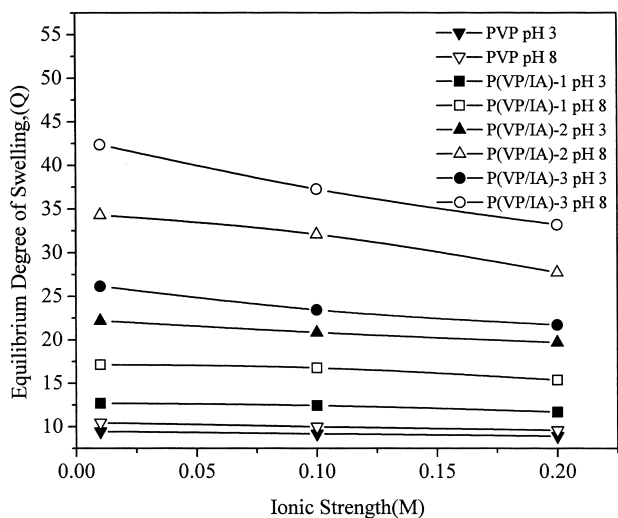


Fig. 2. Effect of ionic strength on the equilibrium degree of swelling values of PVP and P(VP/IA) hydrogels.

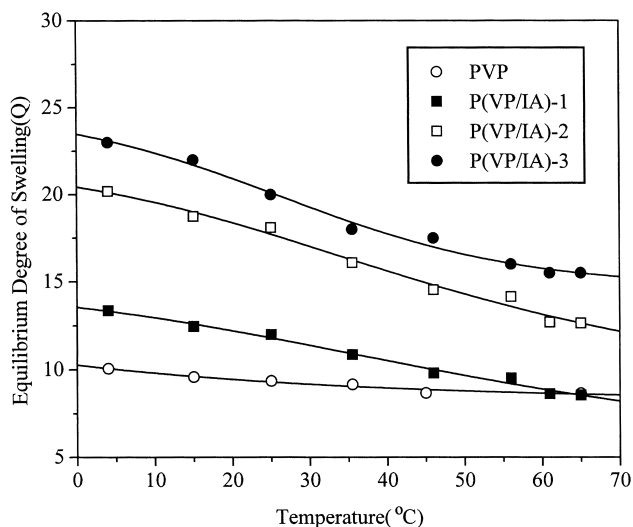


Fig. 3. Effect of temperature on the equilibrium degree of swelling values of PVP and P(VP/IA) hydrogels at pH 3.

EDS values show a continuous decrease, and this effect becomes more pronounced at pH 8 than at pH 3.

The effect of relative amounts of IA in the gel system can be clearly seen by comparing the ionic strength dependence of the equilibrium degree of swelling of P(VP/IA)-3. The changes were observed most clearly at the fully ionized state (pH 8). When the ionic strength of the medium was increased from 0.01 to 0.20 M the equilibrium degree of swelling was observed to decrease by 10% for P(VP/IA)-1 and 27% for P(VP/IA)-3 at pH 8.

3.4. Temperature-responsive characteristics

Figs 3 and 4 represent the influence of temperature on the equilibrium degree of swelling of P(VP/IA) hydrogels in phosphate buffer solution at pH 3 and pH 8 respectively.

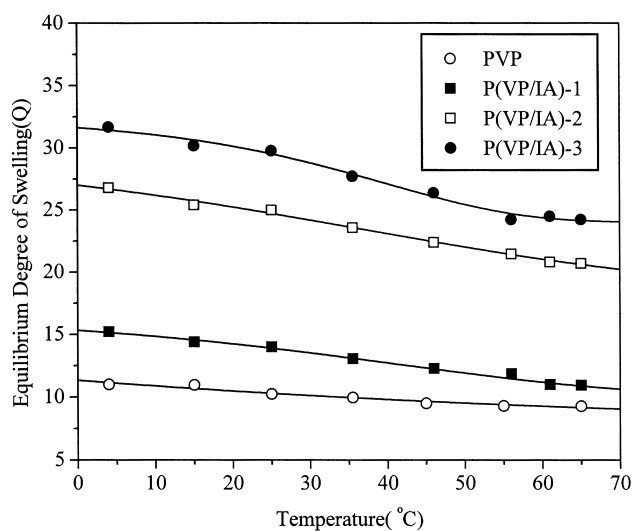


Fig. 4. Effect of temperature on the equilibrium degree of swelling values of PVP and P(VP/IA) hydrogels at pH 8.

Table 2
The transition temperatures of hydrogels

Gel name	Transition temperature (°C)	
	pH 3	pH 8
PVP	–	–
P(VP/IA)-1	35.0	41.8
P(VP/IA)-2	32.5	41.0
P(VP/IA)-3	32.0	40.0

The equilibrium degrees of swelling of non-ionic PVP hydrogels in pH 3 and pH 8 phosphate buffers are also included in Figs 3 and 4 for comparison. As can be seen from these figures, P(VP/IA) hydrogels exhibit large continuous changes in water content as a function of temperature. These changes are due to volume collapse upon warming. It has been shown that a number of hydrogels demonstrate nearly continuous volume transition and associated phase transition from a low temperature, highly swollen gel network to a collapsed, high temperature phase near their critical points [26,27]. The phase transition is analogous though fundamentally distinct from the lower critical solution phase transition (LCST). Güner and Ataman [28] have found that un-crosslinked PVP exhibits an LCST between 35 and 40°C, depending on the salt type in the aqueous solution, and thus the polymeric gels rich in VP monomer can be expected to exhibit volume collapse upon warming.

However, due to the slight decrease of EDS of PVP hydrogels a sharp volume transition was not observed at both pH values in the temperature range of 4–65°C. The EDS value of PVP hydrogels are 10.1 and 11.0 at 0°C in the pH 3 and pH 8 buffer solutions respectively. These values decreased slightly with a rise in temperature up to 65°C to 8.9, and 9.3 at pH 3 and pH 8 respectively. In this temperature range the desorption of water from the hydrogel becomes generally difficult, suggesting that water remaining in the hydrogel mostly consists of the binding water, referred to as uncontrollable water. However, water adsorbed in the P(VP/IA) hydrogels is both controllable

and uncontrollable water, of which controllable water had a characteristic swelling–deswelling ability with change in temperature closely related to the IA content in the gel system. From a comparison of Figs 3 and 4 it has been observed that the temperature range where the volume change is greatest (the transition region) is slightly shifted to higher temperatures and is broadened due to more continuous transition as the gel ionization increases at higher pH. The transition temperatures of P(VP/IA) hydrogels were determined from the first derivative of EDS versus temperature curves in Figs 3 and 4 and the results are given in Table 2. Table 2 indicates that the transition temperature is dependent not only on the pH of the swelling solution but also on the gel composition. The slight shift may be attributed to the lower transition temperature of PIA as compared to that of PVP.

3.5. Buffer type-responsive characteristics

For the investigation of the type of buffer effect on the swelling properties of hydrogels, the EDS values in citrate buffer were compared with the swelling values in phosphate buffer. The variation of EDS values of hydrogels with the ionic strength of citrate buffer at pH 3 and pH 8 are given in Table 3. From a comparison of Q values especially for P(VP/IA) hydrogels at each pH, it has been observed that, at any ionic strength, phosphate buffer permits greater swelling ratios than citrate buffer and this effect is more pronounced at low ionic strength (0.01 M) and for a completely ionized state of hydrogel (pH 8). The effect of buffer type on the EDS of hydrogels can be explained by considering the distribution of polyvalent anions in the citrate and phosphate buffer solutions. The pK_a s for citrate are 3.15, 4.78, and 6.40, while those for phosphate are 2.15, 7.10, and 12.12. At any pH below 8 there will be more di- and trivalent anions in citrate buffer than the phosphate buffers and increase of the polyvalent anions increase the Donnan effect. Thus, at constant ionic strength, phosphate buffer should permit greater swelling than citrate buffer, as was observed in this work.

Table 3
The EDS values of hydrogels in phosphate and citrate buffer solutions

Gel name	Phosphate buffer			Citrate buffer		
	Ionic strength 0.01 M	Ionic strength 0.10 M	Ionic strength 0.20 M	Ionic strength 0.01 M	Ionic strength 0.10 M	Ionic strength 0.20 M
pH 3						
PVP	9.9	9.2	8.9	9.6	9.1	8.9
P(VP/IA)-1	12.7	12.4	11.7	10.8	10.3	9.2
P(VP/IA)-2	22.2	20.8	19.7	20.0	19.2	18.6
P(VP/IA)-3	26.1	23.4	21.7	24.0	21.5	19.8
pH 8						
PVP	10.4	10.0	9.6	9.6	9.3	9.2
P(VP/IA)-1	17.1	16.8	15.4	16.2	15.4	13.8
P(VP/IA)-2	34.3	32.1	27.8	30.1	27.2	22.4
P(VP/IA)-3	42.4	37.3	33.2	38.0	35.0	30.0

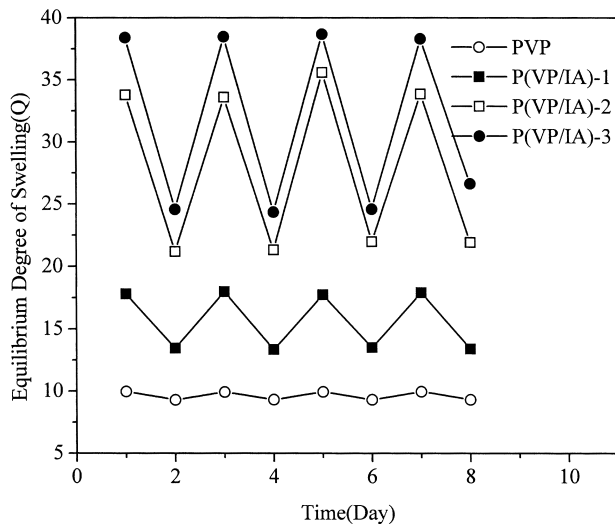


Fig. 5. Oscillatory swelling behaviours of PVP and P(VP/IA) hydrogels with pH alternating between 3 and 8. Lower and upper points correspond to pH 3 and pH 8 respectively.

3.6. Oscillatory swelling behaviour

The oscillatory swelling behaviour of hydrogels at 25°C with pH alternating between 3 and 8 was investigated to confirm the reversibility of the swelling process. Fig. 5 shows swelling–deswelling changes of PVP and P(VP/IA) copolymeric hydrogels under alternating pH values. As shown in Fig. 5, hydrogels possess regularly reversible pH-responsive characteristics when cycled between pH 3 and pH 8 at 24 h intervals and maintain their physical properties on repeated use. The geometrical shapes and forms of the gels were observed to be retained during these cycles. The time domains mentioned in these swelling–deswelling experiments are significantly controlled by the size and shape of the hydrogels investigated. The smaller the size and larger the surface areas, the shorter become the oscillation periods.

4. Conclusion

In this study, the effect of external stimuli on the equilibrium swelling properties of P(VP/IA) polyelectrolyte hydrogels has been investigated. The swelling studies show that, pH, temperature, ionic strength and the type of the swelling solution are the basic parameters affecting the equilibrium degree of swelling of P(VP/IA)

hydrogels. Also notable is the fact that addition of only a few percent IA comonomer radically changes the swelling behaviour of PVP and it becomes completely a responsive polymer by this modification.

Acknowledgements

The authors gratefully acknowledge the support provided by the International Atomic Energy Agency through the Research contract No: 9076/R1

References

- [1] Katchalsky A, Lifson S. *J Polym Sci* 1955;15:69.
- [2] Katchalsky A. *Pure and Applied Science* 1971;26:327.
- [3] Dusek K, Janacek J. *J Appl Polym Sci* 1975;19:3061.
- [4] Hasa J, Ilavsky M, Dusek K. *J Polym Sci, Polym Phys Ed* 1997;13:253.
- [5] Tanaka T. *Encyclopedia of Polymer Science and Engineering* 1987;7:514.
- [6] Peppas NA, Nicos AG. In: Peppas NA, editor. *Hydrogels in medicine and pharmacy*. Boca Raton, FL: CRC, 1986.
- [7] Siegel RA. *Advances in Polymer Science* 1993;109:233.
- [8] Siegel RA, Firestone BA. *Macromolecules* 1988;21:3254.
- [9] Kaetsu I, Uchida K, Morita Y, Okubo M. *Radiat Phys Chem* 1992;40:157.
- [10] Kaetsu I, Morita Y, Otori A, Naka Y. *Artificial Organs* 1990;14:237.
- [11] Gudeman LF, Peppas NA. *J Appl Polym Sci* 1995;55:919.
- [12] Bertran S, Baker JP, Hooper HH, Blanch HW, Prausnitz JM. *Macromolecules* 1991;24:549.
- [13] Firestone BA, Siegel RA. *Polymer Communications* 1988;29:204.
- [14] Yu H, Grainger DW. *J Appl Polym Sci* 1993;49:1553.
- [15] Katayama S, Hirokawa Y, Tanaka T. *Macromolecules* 1994;17:2641.
- [16] Karadağ E, Saraydın D, Öztöp HN, Güven O. *Polym for Adv Technol* 1994;5:664.
- [17] Karadağ E, Saraydın D, Çetinkaya S, Güven O. *Biomaterials* 1996;17:67.
- [18] Saraydın D, Karadağ E, Güven O. *Polym for Adv Technol* 1994;6:719.
- [19] Saraydın D, Karadağ E, Öztöp HN, Güven O. *Biomaterials* 1994;15:917.
- [20] Karadağ E, Saraydın D, Güven O. *Sep Sci and Technol* 1995;30:3747.
- [21] Saraydın D, Karadağ E, Güven O. *Sep Sci and Technol* 1996;31:423.
- [22] Güven O, Şen M. *Polymer* 1991;32:2491.
- [23] Şen M, Güven O. *Polymer* 1998;39:1165.
- [24] Weast RC, editor. *Handbook of chemistry and physics*, 53rd edn. Ohio: The Chemical Rubber Co., 1972.
- [25] Şen M, Güven O. *Polymer*, in press.
- [26] Hirotsu S, Hirokawa Y, Tanaka T. *J Chem Phys* 1987;87:1392.
- [27] Bae YH, Okano T, Kim SW. *J Polym Sci B* 1990;28:923.
- [28] Güner A, Ataman M. *Colloid and Polym Sci* 1994;272:175.