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Poly(vinyl alcohol) hydrogels: 2. Effects of processing parameters on structure and properties

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Poly(vinyl alcohol) (PVA) hydrogels were prepared by quenching solutions containing PVA polymer in pure water or an aqueous solution of dimethylsulfoxide (DMSO). Remarkably different PVA hydrogels were obtained by varying processing parameters, i.e. DMSO concentration, initial PVA concentration and quench temperature. The bulk structure of PVA hydrogels was investigated by scanning electron microscopy of samples prepared by freeze-etching. Physical and mechanical properties of the hydrogels were evaluated to determine the effects of the processing parameters. The experiments were planned according to the Box-Behnken design for surface response. PVA hydrogels prepared at low quench temperature using high DMSO and PVA concentrations exhibit low water content and significantly improved hardness, tensile strength, elongation and tear resistance strength. The best mechanical properties are obtained at the maximum DMSO concentration investigated, 75 wt%. The optical transparency of PVA hydrogels is optimized for samples prepared using 75 wt% DMSO solution containing 8 to 9 wt% PVA at a quench temperature between −20 and −35°C. An increase in DMSO and/or PVA concentrations leads to a more homogeneous and denser hydrogel structure with significantly lower equilibrium swelling. The presence of DMSO-water complexes in the medium alters the gelation mechanism and causes differences in hydrogel structure and properties.

(Keywords: hydrogels; poly(vinyl alcohol); processing)

INTRODUCTION

Synthetic hydrogels have gained increasing attention in the biomedical field due to their excellent compatibility with living tissues at high water content. Indeed, several types of hydrogels have been used in a variety of biomedical applications[1-3]. One of the most widely studied systems is poly(vinyl alcohol) (PVA) hydrogel[4-9]. PVA hydrogels have been prepared by various methods. PVA hydrogels which are chemically crosslinked, e.g. by aldehydes, may result in residues within the gel matrix that are not desirable in biomedical applications. Amorphous PVA hydrogels crosslinked by radiation show poor mechanical properties[4,5]. The mechanical properties may be improved by annealing[6], but the optical properties are poor as the hydrogels become semicrystalline[10]. Physically crosslinked PVA hydrogels prepared by repeated freezing-thawing show improved mechanical properties[11-13], but again lack optical clarity.

Knowledge of hydrogel structure is necessary for understanding the physical and mechanical properties of physically crosslinked PVA hydrogels. However, only limited results on PVA hydrogel structure were reported in previous studies[8,11,14,15]. The major difficulty in investigation of hydrogel structure by scanning electron microscopy (SEM) is due to the presence of water in the native state of hydrogels. Any attempt to remove water prior to SEM examination inevitably affects the morphology. Various techniques can be applied to study hydrogel structure[15-18]. The critical point drying technique has been used to prepare PVA xerogels for SEM examination[11,15,16]. However, freeze-etching is believed to be the most preferred method[16,17]. Recently, both freeze-etching and critical point drying techniques were applied to study PVA hydrogel structure[19]. The freeze-etching technique was demonstrated to be superior to critical point drying since it reveals a more natural structure of PVA hydrogels. Hence, the freeze-etching technique was used to study the microscopic structure of hydrogels in the present work.

Hyon *et al.*[8] reported a gelation process using an aqueous solution of dimethylsulfoxide (DMSO) and PVA. This process has been claimed to produce PVA hydrogels with improved mechanical properties as well as optical transparency. However, available information on the processing and properties of such PVA hydrogels is limited. In the present work, a similar gelation process was used to prepare PVA hydrogels and investigate the effects of processing conditions on their structure and properties. Bulk structure of PVA hydrogels were examined by SEM using the freeze-etching technique for sample preparation. Physical and mechanical properties of PVA hydrogels were evaluated to understand the effects of processing parameters.

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EXPERIMENTAL

Materials

The polymer used in this study is atactic poly(vinyl alcohol) from Air Products and Chemicals, Inc., Allentown, PA. AIRVOL 165 was selected because this commercially available grade of PVA polymer has the highest weight-average molecular weight (160 000) and degree of hydrolysis (>99.3%). The polymer was kept in a dry environment to prevent moisture absorption prior to use. Reagent grade DMSO was obtained from Aldrich Chemical Co., WI.

Experimental design

The effects of processing parameters on PVA hydrogel structure were evaluated using samples prepared under the experimental conditions shown in *Table 1*. The structure was compared between hydrogels prepared with the same processing parameters except the one under investigation.

Additional experiments to study the effects of processing conditions on hydrogel properties were planned according to the Box–Behnken design[20]. Based on preliminary results, a second-order behaviour was assumed for the PVA/DMSO/water system. This experimental design allows the mapping of the system using a minimum number of experiments. *Figure 1* depicts the 13 experimental conditions utilized in this study. DMSO concentrations used in the mixed solvent were 25, 50 and 75 wt%. The initial PVA concentration was 4, 8 or 12 wt%. Quench temperatures applied in the gelation process were 20, −20 and −60°C. Since the design requires three experimental runs for the condition of 50 wt% DMSO, 8 wt% PVA and −20°C, the total number of experiments is 15. The hydrogel properties were measured several times for each experimental condition as discussed later.

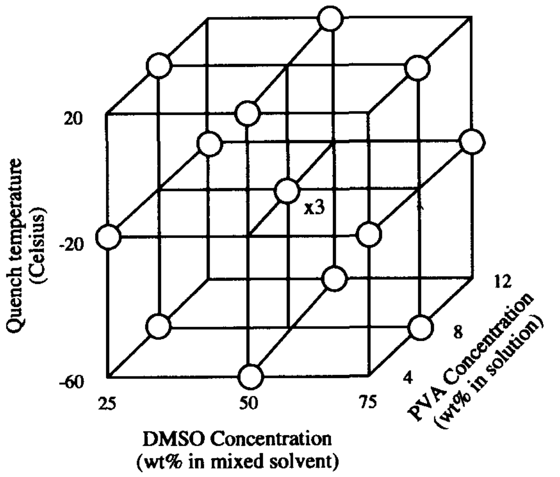


Figure 1 Box–Behnken experimental design for PVA hydrogels

The experimental data on hydrogel properties were used to calculate the mean and standard error. Comparison of the results showed statistically significant variation of properties with processing conditions. The data were then used to generate estimated response surface plots using Stratgraphics Plus software (version 6.0) from Manugistics, Inc. (Rockville, MD). To construct the response surface plots, the software requires 15 data points (one from each experimental run) for each property. Since the software allows only one data point per experimental run, the mean value of measured hydrogel properties was used. The software generated second-degree polynomials to best fit the input data. Using these equations, response surface plots of hydrogel properties were generated by keeping one of the three processing parameters.

Preparation of PVA hydrogels

Solutions were prepared by heating a mixture of PVA in the aqueous medium for 1 h at 100°C in nitrogen atmosphere. Water and DMSO vapours were recovered with a condenser during heating. After the heating step, the PVA solutions were placed in an ultrasonic bath at ~50°C for 30 min to facilitate the release of air bubbles. When all air bubbles were removed at 50°C, the solutions were cast in Petri dishes or between glass plates and quenched for 15 h at a specified temperature. For the highest quench temperature, the samples were kept at ambient conditions maintained at 20±1°C. For lower quench temperatures, samples were placed in an ultra-low temperature freezer preset at either −20 or −60°C. Decreasing quench temperature resulted in higher cooling rate and faster gelation of the samples. Following the quenching period, hydrogel discs (~35 mm in diameter and 10 mm thick) and sheets (~1 mm thick) were allowed to warm up to room temperature and then submerged in copious distilled water for at least one month to extract DMSO.

Freeze-etching and SEM

PVA hydrogel sheets of ~1 mm thickness were cut into small samples with surface area of 1 to 2 cm^2. The sample surface was always kept soaked but with a minimum of excess water. The samples were inserted vertically into a groove on the surface of a square

Table 1 Processing conditions and equilibrium swelling of PVA hydrogels

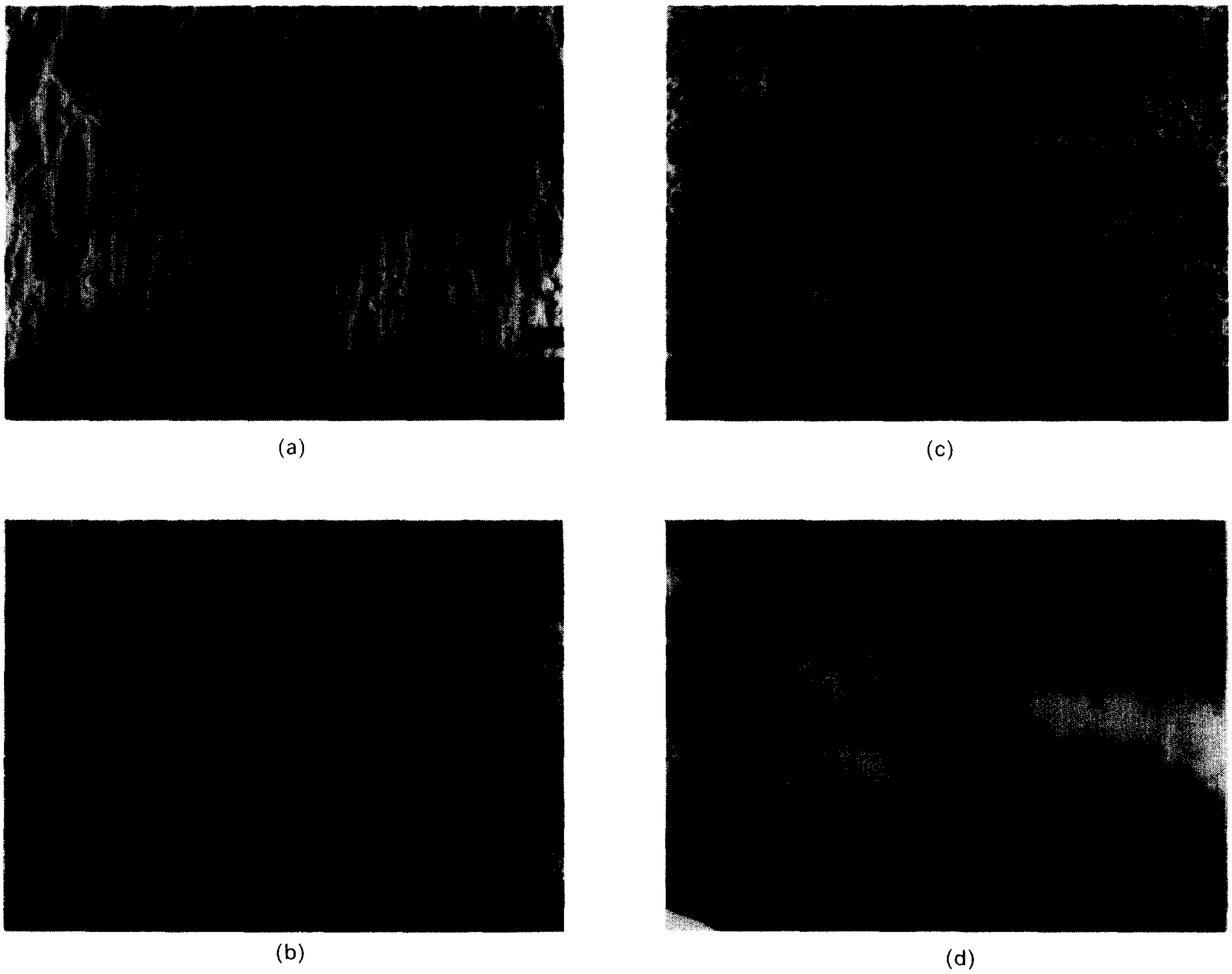
Sample	DMSO concentration in mixed solvent (wt%)	Initial PVA concentration in solution (wt%)	Quench temperature (°C)	Equilibrium swelling in water (wt%)
A	0	8	−20	95.2
B	50	8	−20	89.2
C	25	12	−20	96.3
D	75	12	−20	81.9
E	50	4	−60	94.8
F	50	8	−60	91.2

aluminium holder (2.5 in × 2.5 in × 0.5 in). The aluminium holder and the samples were submerged in liquid nitrogen for ~3 to 4 min until the liquid stopped bubbling. The PVA samples were fractured in liquid nitrogen with the fractured surface facing upwards. To minimize condensation of moisture on the sample surface, the aluminium holder and the frozen samples were immediately transferred to the chamber of an AMRAY 1810 scanning electron microscope. The samples were left under vacuum in the SEM chamber for ~20 min to remove the ice on the surface which resulted from excess water or condensed moisture. The electron beam was turned on at an accelerating voltage of 10 kV. As the samples were heated by the electron beam, any ice left on the sample surface underwent sublimation, thereby revealing the PVA polymer structure.

Physical and mechanical properties

The equilibrium swelling of PVA hydrogels expressed in percentage of water content was determined using a COMPUTRAC LX10 Solid Analyzer. The solid analyser measured the wet and dry weights of the hydrogel specimen, and then calculated the percentage of water content. Three measurements of water content were performed for each hydrogel. The standard error for water content was <1%. Light transmission of PVA hydrogels was measured using an experimental set-up consisting of a Cambridge Fiber Optics Illuminator and an INX DX-10 Digital Light Meter. The relative light transmission in percentage was determined from the light intensity transmitted through the hydrogel compared with that transmitted through air. The hardness of disc-shaped PVA hydrogels was measured according to ASTM D2240[21] using a Shore OO Durometer Hardness Tester. Light transmission and hardness were measured using a minimum of five specimens for each hydrogel. The standard error for light transmission was generally <5% and around 10% for a few opaque samples. Similarly, the standard error for hardness was <5%, except for very soft hydrogels.

Tensile strength and elongation of PVA hydrogels were determined in accordance with ASTM D412[22] using a Monsanto T10 tensometer. A minimum of five dumb-bell tensile specimens were cut from the PVA hydrogel sheet using die C of ASTM D412. The specimen thickness was measured using a Panametrics Ultrasonic Thickness


(a) (c)

(b) (d)

Figure 2 SEM photographs of PVA hydrogel structure. Samples A (a) and B (b) were obtained using 8 wt% PVA in 0 and 50 wt% DMSO solutions, respectively. Samples C (c) and D (d) were obtained using 12 wt% PVA in 25 and 75 wt% DMSO solutions, respectively. All samples were prepared by quenching at −20°C

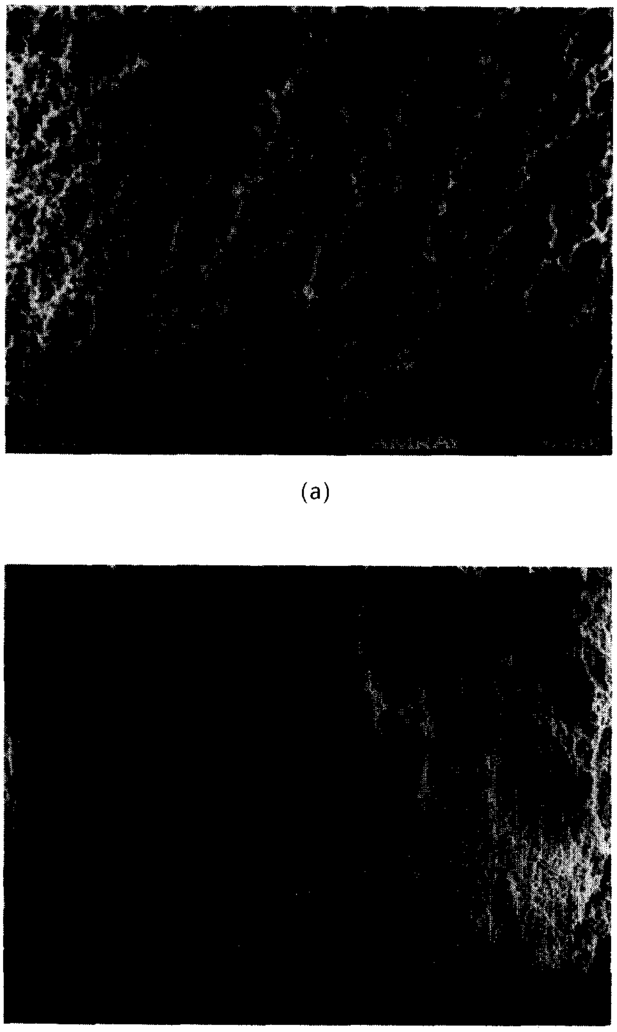
Gage, model 22DLHR. Tear resistance strength was measured according to ASTM D624[23] using a Monsanto T10 tensometer. Die C described in ASTM D624 was used to cut at least five specimens for the tear test. The specimens were extended at $20 \pm 2\,\mathrm{in\,min^{-1}}$ for both tensile and tear measurements. The standard error for mechanical properties varied from <5% for strong hydrogels to slightly >10% for weak hydrogels.

RESULTS

The microscopic structure of PVA hydrogels changed significantly with the processing parameters, which are summarized in *Table 1*. Hydrogel sample A was prepared without DMSO from 8 wt% PVA solution at −20°C quench temperature. *Figure 2a* reveals a heterogeneous and very porous structure consisting of locally oriented fibrils which are not well interconnected. The pores separating the fibrils are as large as 5 μm. On the other hand, hydrogel sample B, also prepared using 8 wt% PVA at −20°C quench temperature but from an aqueous medium of 50 wt% DMSO, shows a three-dimensional fibrillar network with no orientation, *Figure 2b*. The pore or mesh size is in the submicrometre range. The presence of DMSO during gelation of sample B eliminates the locally oriented and highly porous structure observed in sample A. As a result, the equilibrium swelling of sample B (89.2 wt% of water) is significantly lower than that of sample A (95.2 wt% of water), as shown in *Table 1*. *Figures 2c* and *d* compare the structures of samples C and D prepared using 12 wt% PVA solution at −20°C quench temperature but from aqueous media containing 25 and 75 wt% DMSO, respectively. Sample C, which has a water content of 96.3 wt%, also reveals a fibrillar network without orientation similar to sample B. However, it is more porous with mesh size of up to 3 μm. In contrast to sample C, sample D with a water content of 81.9 wt% shows a dense structure at 2000 × magnification. In general, an increase in DMSO concentration leads to a denser structure with lower water content.

The effect of initial PVA concentration on hydrogel structure can be evaluated by comparing samples E and F, prepared with initial PVA concentrations of 4 and 8 wt%, respectively. Sample E (*Figure 3a*) has a water content of 94.8 wt%, and a larger mesh size than sample F (*Figure 3b*) which has a lower water content of 91.2 wt%. The mesh size of sample E varies from <1 to ~2 μm while that of sample F ranges from submicrometre size to ~1 μm. In general, a higher initial PVA concentration leads to a less porous structure in PVA hydrogels and consequently lowers equilibrium swelling as described below.

The effects of DMSO and initial PVA concentrations on equilibrium swelling or water content are illustrated in *Figure 4a*, which shows the estimated response surface when quench temperature was kept constant at −20°C. At low DMSO and PVA concentrations, e.g. 25 wt% DMSO and 4 wt% PVA, the PVA solution formed an extremely weak and tacky gel which is highly swollen. At the other extreme, at high DMSO and PVA concentrations of 75 and 12 wt%, respectively, the equilibrium swelling is 81.9 wt%, the lowest value observed in this study. The water content of PVA hydrogels decreases with increasing DMSO concentration. This effect is more significant at higher PVA concentrations. The water content also decreases with increasing initial PVA concentration.


(a)

(b)

Figure 3 SEM photographs of PVA hydrogel structure. Samples E (a) and F (b) were obtained using 4 and 8 wt% PVA, respectively, in 50 wt% DMSO solutions. Both samples were prepared by quenching at −60°C

The estimated response surface of equilibrium swelling as a function of DMSO concentration and quench temperature for 8 wt% PVA is shown in *Figure 4b*. The water content decreases with increasing DMSO concentration, while it is estimated to decrease slightly at lower quench temperature. *Table 1* shows that sample B prepared at a quench temperature of −20°C has a slightly lower water content than sample F prepared at −60°C. This is consistent with the structure of sample B being slightly less porous than sample F. *Figure 2b* for sample B reveals a porous structure with a mesh size in the submicrometre range while *Figure 3b* for sample F shows a mesh size varying from the submicrometre range to ~1 μm. According to the estimated response surface, PVA hydrogels with the lowest equilibrium swelling are expected using the highest DMSO and PVA concentrations at the lowest quench temperature investigated. Based on the observed inverse relationship between equilibrium swelling and porosity,

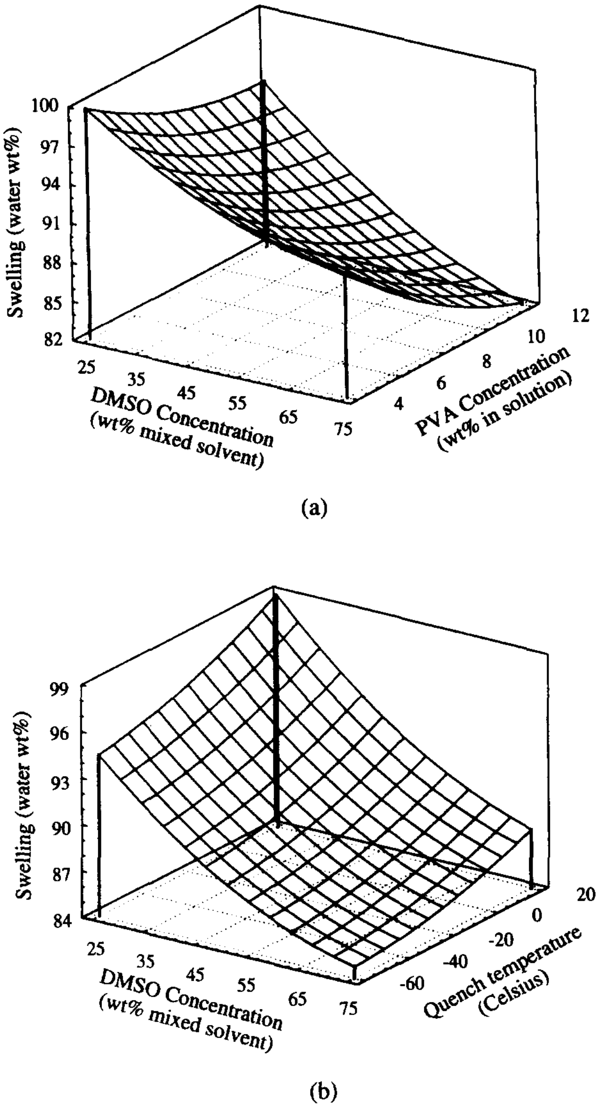


Figure 4 Response surface plots of equilibrium swelling as a function of (a) DMSO and PVA concentrations at −20°C, and (b) DMSO concentration and quench temperature at 8 wt% PVA

PVA hydrogels with the least porosity are expected at such experimental conditions.

PVA hydrogels become more transparent when prepared using increased DMSO concentration in the medium. *Figure 5a* shows an increase in relative light transmission with increasing DMSO concentration. The opposite trend was observed for the variation of equilibrium swelling with DMSO concentration. Hence, water content affects optical transparency. Highly swollen hydrogels are considerably less transparent due to the large mesh size of their heterogeneous structure. In contrast, the excellent transparency of hydrogels with low water content is attributed to their homogeneous structure which has a small mesh size. A similar effect of hydrogel structure on optical transparency was previously suggested by Hyon *et al.*[8]. The relative light transmission also changes significantly with polymer content and appears to be maximized between 8 and 9 wt% PVA. Quench temperature also shows a strong influence on the transparency of PVA hydrogels, *Figure 5b*. Opaque gels were produced at room temperature even at high DMSO concentration. Hydrogel transparency is improved as the quench temperature is lowered until an optimum temperature is reached, below which hydrogels become less transparent. Relative light transmission appears to be maximum for hydrogels quenched between −20 and −35°C, depending upon DMSO concentration.

The hardness increases when the hydrogels are prepared using more DMSO and PVA, *Figure 6a*. The increase in hardness is steep at high DMSO or PVA concentration. With reference to *Figure 4a*, hardness is inversely related to equilibrium swelling. Hydrogels which have low water content are harder than highly swollen ones. The hardness changes only slightly with quench temperature according to *Figure 6b*. A lower quench temperature results in slightly harder hydrogels. Based on the estimated response surface, the hardest hydrogels are expected using the highest DMSO and PVA concentrations at the lowest quench temperature investigated.

Figure 7a shows that the tensile strength of PVA hydrogels increases with increasing DMSO concentration in the medium, except at low PVA concentrations near 4 wt%. Similarly, the tensile strength increases with

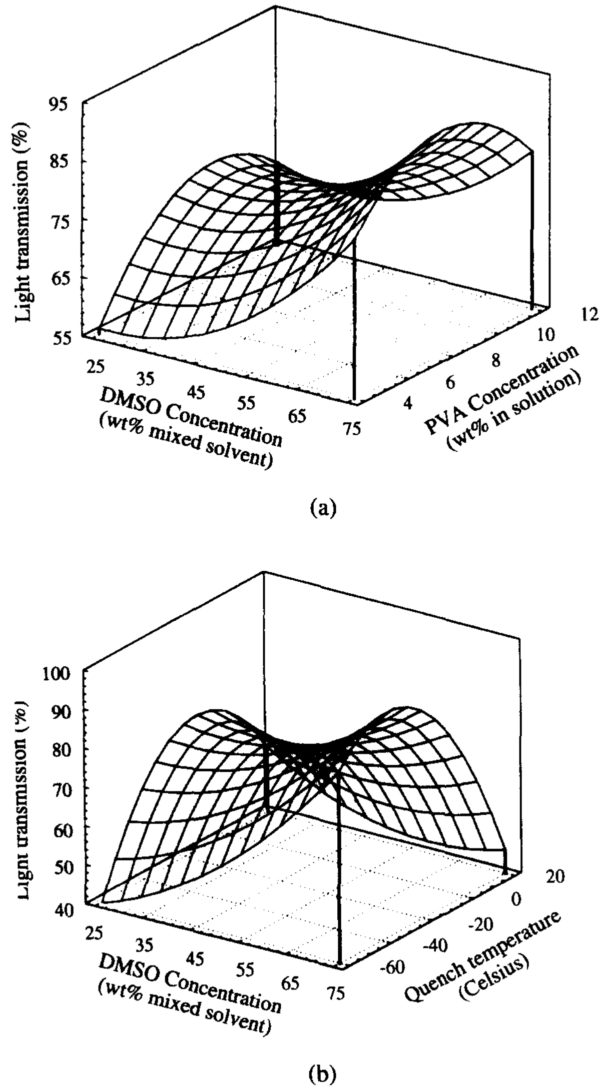


Figure 5 Response surface plots of relative light transmission as a function of (a) DMSO and PVA concentrations at −20°C, and (b) DMSO concentration and quench temperature at 8 wt% PVA

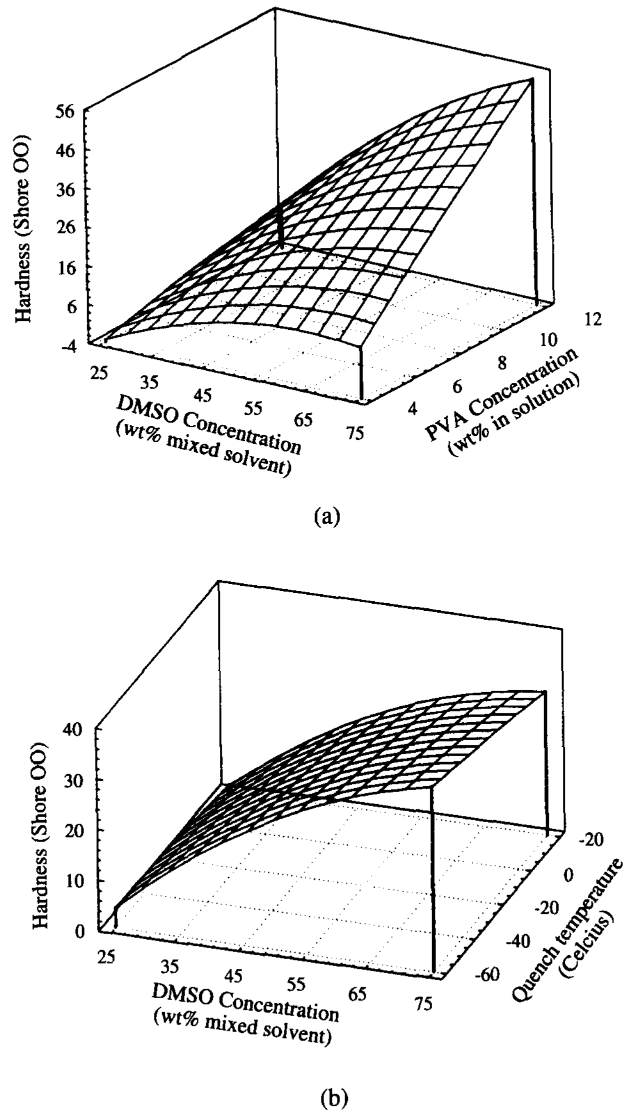


Figure 6 Response surface plots of hardness as a function of (a) DMSO and PVA concentrations at -20°C, and (b) DMSO concentration and quench temperature at 8 wt% PVA

increasing PVA concentration, except at low DMSO concentrations near 25 wt%. As with hardness, the increase in tensile strength is more pronounced at high PVA concentrations. Referring to *Figure 4a*, there is a significant effect of water content and corresponding hydrogel structure on tensile strength of PVA hydrogels. *Figure 7b* shows that higher tensile strength is obtained at lower quench temperature. The effect of temperature on tensile strength is more significant at higher DMSO concentration. The highest tensile strength is obtained for hydrogels prepared using the highest DMSO and PVA concentrations at the lowest quench temperature investigated.

Figure 8a shows an increase in elongation of PVA hydrogels with increasing DMSO and PVA concentrations. Unlike tensile strength, elongation depends strongly on DMSO concentration at low PVA concentrations near 4 wt%. Elongation also varies significantly with PVA concentration at low DMSO concentrations near 25 wt%. The effect of quench temperature on elongation is less significant than that of DMSO concentration. The highest elongation is expected for hydrogels prepared using the highest DMSO and PVA concentrations independent of quench temperature.

Similar to tensile strength, the tear resistance increases with increasing DMSO concentration except at low PVA concentrations near 4 wt%, *Figure 9a*. It also increases with increasing PVA concentration except at low DMSO concentrations near 25 wt%. Like hardness and tensile strength, tear resistance increases more rapidly at higher DMSO and PVA concentrations. As shown in *Figure 9b*, the tear resistance increases almost linearly with DMSO concentration while it exhibits a maximum in its dependence on quench temperature. The tear resistance is expected to be maximum for hydrogels prepared near -30°C using the highest DMSO and PVA concentrations in the medum.

DISCUSSION

PVA hydrogels exhibiting very different properties were obtained by varying the processing parameters, i.e. DMSO concentration, initial PVA concentration and

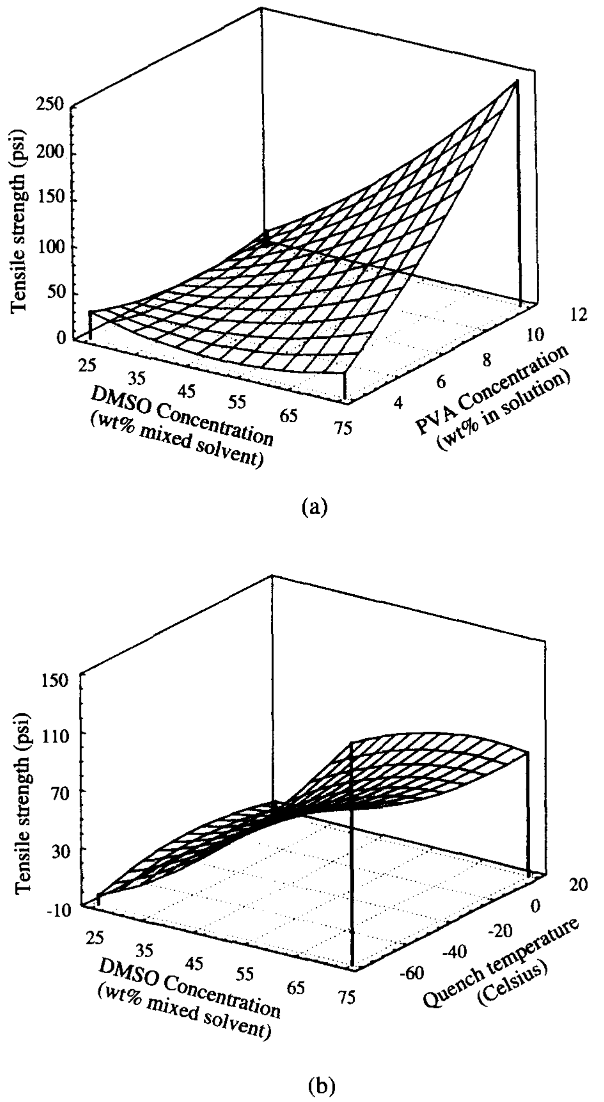


Figure 7 Response surface plots of tensile strength as a function of (a) DMSO and PVA concentrations at -20°C, and (b) DMSO concentration and quench temperature at 8 wt% PVA

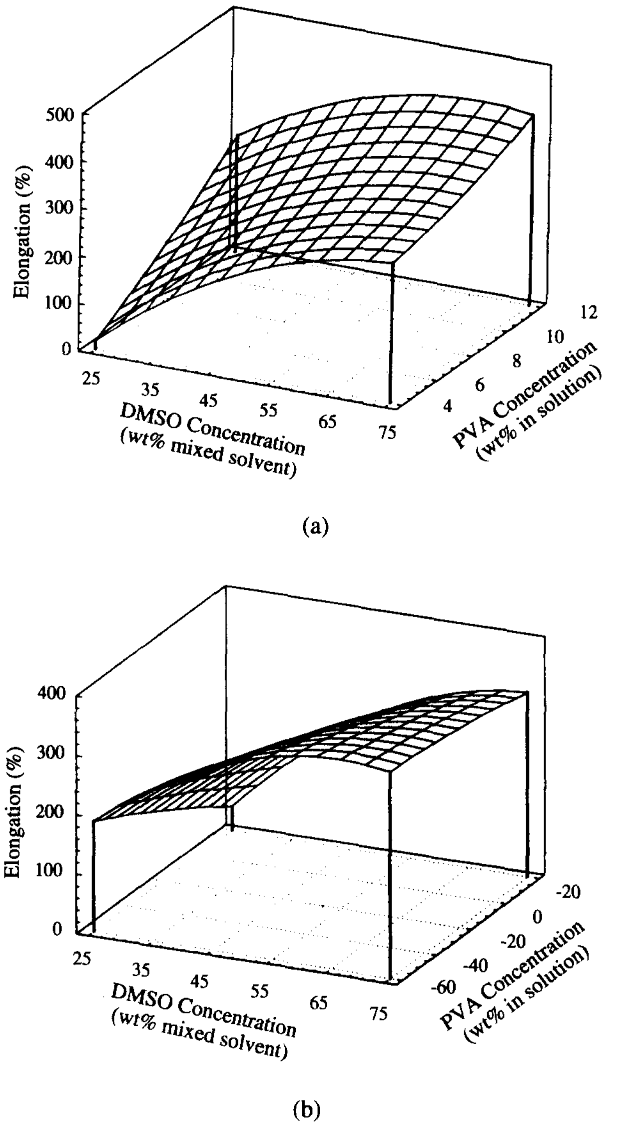


Figure 8 Response surface plots of elongation as a function of (a) DMSO and PVA concentrations at −20°C, and (b) DMSO concentration and quench temperature at 8 wt% PVA

quench temperature. The hydrogels varied from being weak and soft to tough and rubbery. For instance, gelation of a 4 wt% PVA solution in 50 wt% DMSO aqueous medium at 20°C for 15 h resulted in a very weak, soft and highly swollen gel. On the contrary, gelation of a solution containing 12 wt% PVA in 75 wt% DMSO solution at −60°C for 15 h led to a tough and rubbery gel with a significantly lower water content. Under certain processing conditions, gelation may not occur at all. This was the case for 8 wt% PVA in 25 wt% DMSO solution quenched at 20°C for 15 h. Hydrogel appearance also changed significantly with the processing conditions, varying from opaque and translucent to transparent.

The wide variations in physical and mechanical properties of PVA hydrogels are closely associated with differences in the microscopic structure. *Figures 2* and *3* reveal significant differences in porosity and mesh size, which are directly related to the density of junctions in the PVA network. A decrease in mesh size or increase in junction density generally leads to harder, stronger and more transparent hydrogels with lower equilibrium swelling. The variations in hydrogel structure are influenced by the gelation mechanism which depends on processing conditions.

As previously mentioned, PVA hydrogel prepared without DMSO (*Figure 2a*) has a heterogeneous and porous structure with local orientation. This morphology suggests phase separation during the quenching period. This sample was prepared below both spinodal and sol–gel transition curves, according to the phase diagram reported by Komatsu *et al.*[24]. Therefore, phase separation due to spinodal decomposition is expected. However, at −20°C quench temperature phase separation due to freezing occurred rapidly, before significant spinodal decomposition took place. As a result, oriented structure was formed due to directional growth of ice crystals as the solution froze. This phenomenon has been previously reported for the formation of anisotropic ice–agar composites[25] and PVA hydrogel[26].

Interactions between DMSO and water in aqueous solutions have been widely studied[27–30]. Various complex structures of DMSO and water were reported, the

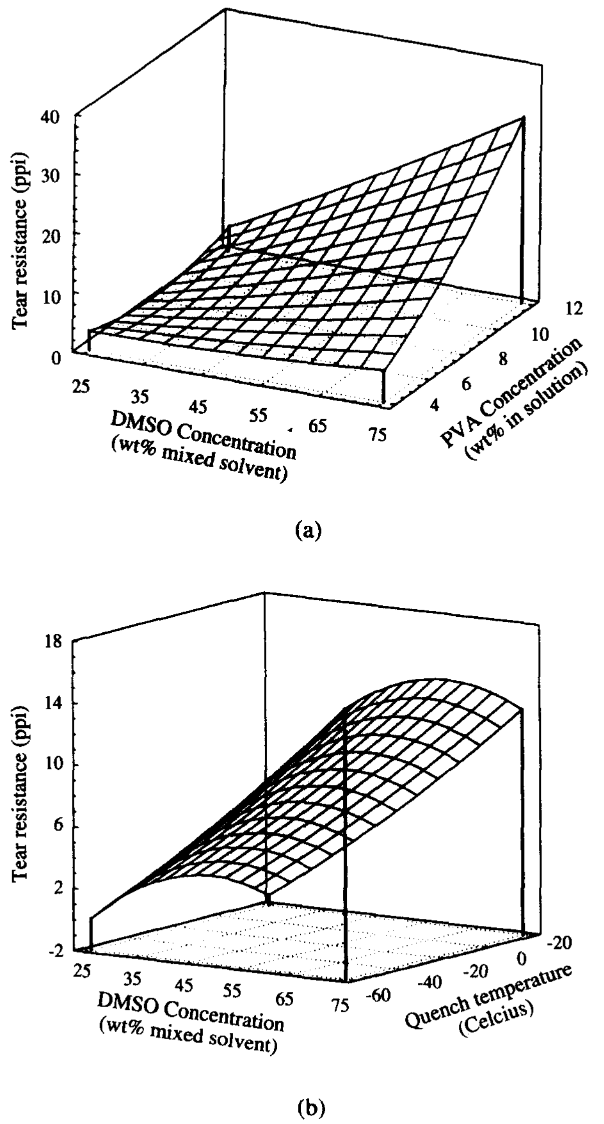


Figure 9 Response surface plots of tear resistance as a function of (a) DMSO and PVA concentrations at −20°C, and (b) DMSO concentration and quench temperature at 8 wt% PVA

most common being DMSO.2H_2O. The interesting cryoprotective property of DMSO–water complexes appears to play an important role in the gelation of PVA hydrogels. Rasmussen and MacKenzie[28] reported a phase diagram of the water–DMSO system which illustrates a dramatic effect of DMSO on freezing depression. In the present study, similar freezing depression was observed for the aqueous solutions of PVA with DMSO. Freezing depression allows PVA in DMSO solution to form a gel at a low temperature without experiencing phase separation which is normally caused by freezing. Furthermore, quenching at a low temperature leads to a high cooling rate which induces rapid gelation before significant liquid–liquid phase separation occurs due to spinodal decomposition. Upon further cooling, vitrification occurs while the system is still in a highly dispersed state and phase separation does not proceed[31]. Thus, gelation of PVA in the presence of sufficient DMSO results in a more homogeneous structure than without DMSO.

The phase diagram presented by Rasmussen and MacKenzie[28] indicates the presence of a solid phase (water) beside a liquid phase, presumably of DMSO–water complexes, below the freezing curve for low DMSO concentration. The presence of solid water causes phase separation as temperature falls below the freezing curve. On the other hand, the simultaneous presence of liquid DMSO–water complexes perhaps disrupts the normal growth of ice crystals. Furthermore, it was observed that gelation occurred before freezing which most likely obstructs the directional phase separation of PVA. This explains the absence of local orientation in the extremely porous and heterogeneous structure of sample C, *Figure 2c*.

Initial PVA concentration also plays an important role in determining the properties of hydrogels. As stated earlier, higher PVA concentration generally leads to stronger and harder gels with more homogeneous structure and lower water content. To evaluate the effect of PVA concentration, it is necessary to consider the critical gelation concentration (*CGC*) of polymer solutions. The polymer is capable of forming a continuous network due to chain overlap above the *CGC*. However, a gel may be formed from a heterogeneous solution even though its macroscopic average concentration is lower than the *CGC* because the concentration in the polymer-rich phase may exceed the *CGC*[32]. This may explain the porous and heterogeneous structure of PVA hydrogels prepared from solutions with low PVA concentration. In the absence of DMSO, the PVA/water phase diagram reported by Komatsu *et al.*[24] shows that the sol–gel transition temperature curve rises with PVA concentration, and exceeds the spinodal temperature curve at approximately 15 wt%. Phase separation due to spinodal decomposition occurs prior to gelation for solutions with PVA concentration below 15 wt% PVA. Above this concentration, a gel can be formed without phase separation. This suggests that a denser and more homogeneous structure can be obtained as PVA concentration is increased. A similar effect of PVA concentration is observed for PVA hydrogels prepared in the presence of DMSO.

The estimated response surface plots suggest that harder and stronger PVA hydrogels with lower water content are produced at higher DMSO and PVA concentrations and at lower quench temperature. However, PVA hydrogels with maximum transparency are obtained at the highest DMSO concentration (75 wt%), between 8 and 9 wt% PVA concentration, and between −20 and −35°C quench temperature. Based on these results, additional experiments beyond 75 wt% DMSO are necessary for an improved understanding of the behaviour of PVA hydrogels. A more detailed investigation of the gelation behaviour over a wider range of DMSO concentration is in progress. The results will be reported separately[33].

SUMMARY

PVA hydrogels with remarkably different structures and properties were obtained by varying DMSO concentration, initial PVA concentration and quench temperature. The estimated response surface analysis shows significant improvements in optical transparency, hardness, tensile strength, elongation and tear resistance of PVA hydrogels when the equilibrium swelling decreases with increasing DMSO and PVA concentrations. Quench temperature has a relatively small influence on the mechanical properties and equilibrium swelling, but significantly affects the optical transparency of PVA hydrogels. For the range of experimental parameters investigated, PVA hydrogels with the lowest equilibrium swelling and the highest hardness, tensile strength and elongation are obtained using the highest DMSO (75 wt%) and PVA (12 wt%) concentrations at the lowest quench temperature (−60°C). Tear strength is maximum for hydrogels prepared near −30°C. The hydrogels are most transparent when prepared using the highest DMSO concentration (75 wt%) with 8 to 9 wt% PVA. The quench temperature should be between −20 and −35°C depending upon the DMSO concentration. A dense and homogeneous microstructure corresponds to a tough and rubbery hydrogel with low water content and good optical transparency. On the other hand, a weak and soft hydrogel which is highly swollen and relatively opaque has a heterogeneous and porous surface. The formation of DMSO–water complexes in the medium affects the rate and mechanism of PVA gelation, leading to different structure and properties of the hydrogels.

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