

Cellular PVA Hydrogels Produced by Freeze/Thawing

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ABSTRACT: Cellular poly(vinyl alcohol) (PVA) hydrogels that exhibit enhanced swelling kinetics from an initial dry state were prepared by freezing and thawing techniques in the presence of NaCl. Gels that were dried immediately after preparation demonstrated a dual-sorption effect upon swelling. Gels that were exposed to a 10-day washing period to remove NaCl and excess PVA chains before drying showed an increased initial rate of swelling and overall water content. Freeze/thawed, cellular PVA gels showed overall enhanced swelling with increased mechanical strength over traditional gels prepared by chemical or irradiative crosslinking techniques. © 2000 John Wiley & Sons, Inc. *J Appl Polym Sci* 76: 2075–2079, 2000

Key words: poly(vinyl alcohol); swelling; freezing/thawing processes

INTRODUCTION

Hydrogels have been used and proposed for a wide variety of biomedical and drug-delivery applications. Specifically, numerous hydrogels have been implemented in controlled-release devices to achieve the appropriate delivery of a drug or protein over time. However, hydrogels often exhibit slow swelling kinetics, particularly from an initially dry state. Considerable research has focused on the development of superabsorbent hydrogels with increased swelling rates. Chen et al.¹ examined the synthesis of superporous hydrogels that contain interconnected pores within the structure. In this work, the preparation utilized a technique that captured gas bubbles inside the resulting hydrogels. Carbon dioxide gas bubbles were produced by the chemical reaction of acid and sodium bicarbonate. Different vinyl mono-

mers were investigated for the preparation of these superporous hydrogels. The gels produced were shown to have pores of 150–300 μm that were connected to form capillary channels. With the presence of such channels, the dried gels swelled to near equilibrium within minutes.

A problem commonly associated with hydrogels that possess superabsorbent properties is a rather low mechanical strength. Hydrogels prepared by traditional chemical crosslinking techniques are usually mechanically weak because they are rendered insoluble due to chemical bonds. Additional work by Chen et al.² also addressed such issues. In fact, they described the limitations involved with improving the mechanical strength without altering the superabsorbent properties. For example, they explained how increasing the crosslinking density within a hydrogel would enhance the mechanical strength but decrease the swelling capacity. In this work, they examined composite structures that resulted from the preparation of a superporous hydrogel in the presence of particulate materials which served to enhance the mechanical strength. Such materials were capable of swelling within 1 min and contained a notable improvement in the mechanical strength.

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In the present work, we investigated a different approach to prepare gels that exhibit desirable swelling characteristics and high mechanical strength. Poly(vinyl alcohol) (PVA) gels that are prepared by freezing and thawing techniques have shown many improved properties over hydrogels prepared by traditional chemical crosslinking techniques. Of particular importance in this work is the increased mechanical strength due to the existence of crystalline regions that serve as physical crosslinks. It has been shown³ that repeated cycles of freezing at -20°C and thawing at 25°C result in the formation of crystalline regions that remain intact upon being placed in contact with water or biological fluids at 37°C . These PVA hydrogels show increased mechanical strength over most hydrogels because the crystalline regions are capable of better distributing a given mechanical load or stress. Additionally, the gels show high elasticity and are capable of being extended to five or six times their initial length.⁴ Because of these characteristics, the potential for such materials for a variety of biomedical and pharmaceutical applications is quite obvious.

However, with freeze-thawed PVA gels, equilibrium swelling, particularly from the dry state, occurs at a relatively low rate. In this work, we investigated the addition of sodium chloride to produce cellular, freeze-thawed PVA gels with enhanced swelling kinetics. Prepared gels were characterized in terms of the rate of swelling as well as their equilibrium volume swelling ratios to determine if the presence of NaCl ions had a significant effect on the overall swelling properties.

EXPERIMENTAL

A 10 wt % PVA solution (control solution) was first prepared by dissolving PVA (Elvanol® HV, E.I. duPont de Nemours, Wilmington, DE, $\bar{M}_n = 64,000$, polydispersity index = 2.02, degree of hydrolysis = 99.0%) in deionized water at 90°C for 6 h. A second solution was similarly prepared with the addition of 25% sodium chloride (Mallinckrodt, St. Louis, MO) based on the weight of PVA. The sodium chloride was introduced prior to placing the solution in the oven for dissolution. Both solutions, the control and the NaCl-containing, were cast on microscope slides with thin spacers (0.7 mm) and exposed to three cycles of 8-h freezing at -20°C and 4-h thawing at 25°C . The

ensuing films were then cut into thin disks of 12-mm diameter.

Upon preparing the control and NaCl-containing samples, several swelling experiments were performed to characterize the effect of NaCl on the overall swelling properties. The swelling of thin disks of the gels was characterized first from an initial "relaxed state" in which the gels were allowed to swell immediately after the last freezing period. These gels already contained a significant amount of water prior to swelling. Swelling of gels from an initial dry state was also examined. Such gels were allowed to dry immediately after the last freezing period. Experiments were also conducted with gels that were washed immediately after the last freezing period to remove NaCl and excess PVA chains that did not participate in the formation of stable crystals. These samples were washed in 50 mL of deionized water at 37°C for 10 days. During that time, the washing medium was replaced with 50 mL of fresh water each day. After this washing period, the gels were allowed to dry before swelling.

For all swelling experiments, each disk of initial thickness of 0.7 mm was allowed to swell in 50 mL of deionized water at 37°C . At various times during the first 10 h of swelling, the samples were blotted and weighed in air and heptane (using the buoyancy principle) to determine the volume swelling ratio as reported by us before.⁵ In addition, the swelling medium was sampled at each time interval to determine the amount of PVA dissolved from each disk during swelling. At each time interval, 5 mL of the solution was withdrawn and each jar was filled with a fresh 50 mL of deionized water. The dissolution of PVA was determined by complexing each 5-mL sample of aqueous PVA withdrawn with 2.5 mL of a 0.65M boric acid solution and 0.3 mL of a 0.05M $\text{I}_2/0.15\text{M}$ KI solution and then diluting to 10 mL with deionized water at 25°C . The absorbance of visible light at 671 nm was then measured to determine the concentration of complexed PVA in solution. Therefore, for each sample, the volume swelling ratio and fractional dissolution of PVA was calculated as a function of swelling time.

Scanning electron microscopy (SEM) was also implemented to more closely study the structure of such gels for the presence of pores. Gels that were first washed after preparation and then dried to remove NaCl and excess PVA chains were studied in terms of their inner structures. These dried gels were exposed to liquid nitrogen

and fractured to examine the inner surfaces with SEM.

RESULTS AND DISCUSSION

The prepared PVA gels were first examined in terms of their swelling from an initial relaxed state. The volume swelling ratio of the control gels and gels prepared in the presence of 25% NaCl is shown over a period of 10 h in Figure 1. It is apparent that the gels initially contained large fractions of water with volume swelling ratios of approximately 11. Upon being placed in contact with water, both gels immediately swelled to a high extent. However, the rate of swelling of gels prepared in the presence of NaCl was much higher. In fact, the initial rate of swelling for the gels prepared in the presence of NaCl was calculated as 0.23 min^{-1} compared to a rate of swelling for the control gels of 0.13 min^{-1} . Both gels reached a maximum in the swelling ratio at 3–4 h. At longer times, there was still considerable variation due to instabilities of the gel structure. It is likely that chain-dissolution effects and changes in the crystalline structure inhibited the gels from maintaining a swelling equilibrium. However, it does appear that the presence of NaCl contributed to enhanced uptake of water during the initial swelling process.

Upon more closely examining chain-dissolution effects from initial relaxed gels in Figure 2, some important conclusions could be made: It is apparent that there was considerable PVA dissolution from both samples over a swelling period of 10 h. In fact, approximately 23% of PVA dissolved from

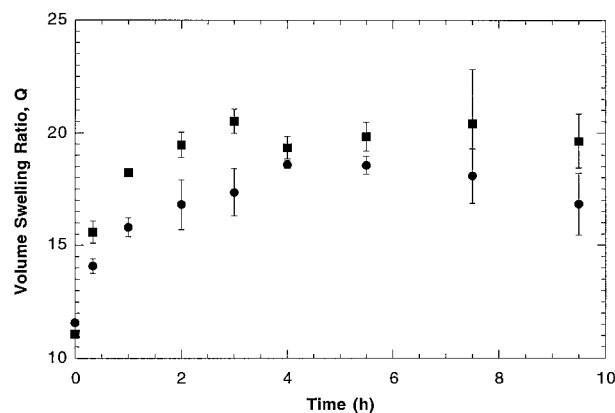


Figure 1 Swelling of (■) cellular, freeze/thawed PVA gels and (●) control gels from an initial relaxed state.

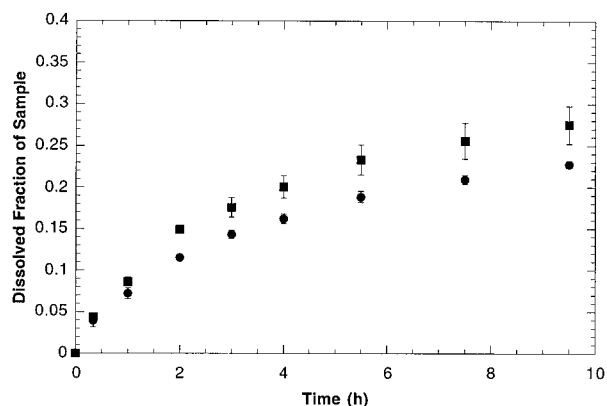


Figure 2 Fractional PVA dissolution from (■) cellular, freeze/thawed PVA gels and (●) control gels when swollen from an initial relaxed state.

the control samples and 27% from gels prepared with NaCl. Therefore, it appears that by incorporating NaCl during the preparation a slightly lower fraction of PVA was incorporated into the overall stable crystalline structure. Freezing and thawing in the presence of NaCl may be altered in terms of the decreased physical crosslinking. This would likely explain the increase in the initial rate of swelling as well.

Examination of the swelling from an initial relaxed state gave some initial insight as to the effect of incorporating NaCl into freeze/thawed PVA gels. However, of increased importance, particularly for many release applications, is the swelling of freeze/thawed PVA gels from an initial dry state. To investigate such properties, gels were dried in air at room temperature (25°C) immediately after the last freezing period. The swelling of these initially dried gels in water at 37°C over 10 h is shown in Figure 3.

We can see that the gels swelled to a high extent in the first 15 min. We cannot accurately conclude from these results how fast this initial uptake occurred. However, no further swelling occurred during the next few hours. Then, at 4 h of swelling, both gel types swelled to a higher extent. After this time, there is considerable variation in the swelling ratio. The behavior observed can be described as a dual-sorption effect. Initially, the dry gels swelled to a certain extent, accommodating the maximum water possible. During this initial sorption stage, the structure exhibited changes due to the uptake of water. In the presence of the initial amount of water, polymer chains underwent a period of relaxation over several hours. After that period of time, the gels

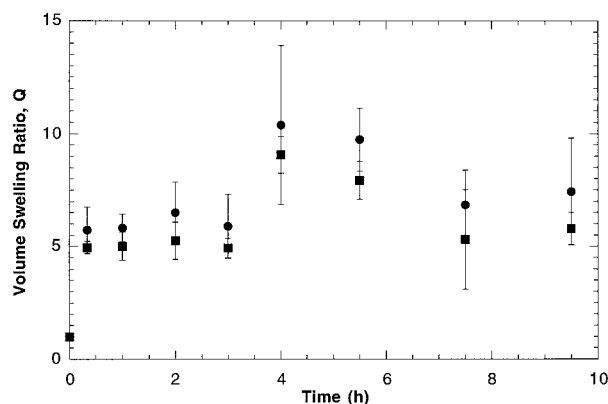


Figure 3 Swelling of (■) cellular, freeze/thawed PVA gels and (●) control gels from an initial dry state.

were capable of accommodating more penetrant and exhibited a further increase in the swelling ratio. However, with the freeze/thawed PVA system, a second equilibrium swelling ratio was not maintained because of the additional instabilities present as the gels swell to a higher extent. An increase in the amount of water likely caused increased rearrangement of the structure. With increase in the free volume and mobility in a more swollen structure, there is increased rearrangement due to secondary crystallization. This likely explains the decrease in the swelling ratio at longer times of swelling. However, it is important to note that when examining the swelling of the gels from an initial dry state no significant change in the swelling properties occurred with the addition of NaCl during preparation.

It was also of interest to examine the corresponding PVA dissolution behavior of these initially dried gels. The dissolved fraction of PVA over 10 h of swelling is shown in Figure 4. For both gel types, an overall low amount of PVA was lost during the swelling process. Approximately 3–8% of PVA dissolved after 10 h of swelling. This was much lower in comparison to the dissolution behavior observed in Figure 2 for the initially relaxed gels (23–27%). These results emphasize the presence of a dual-sorption effect when swelling freeze/thawed gels from the dry state. The disentanglement and subsequent dissolution of PVA was slowed down considerably when swelling from the dry state. It is likely that an increase in the dissolution of PVA may occur at longer times as the presence of the additional water in the gels increases the rate of disentanglement and dissolution. No conclusive results can be drawn concerning the difference between the con-

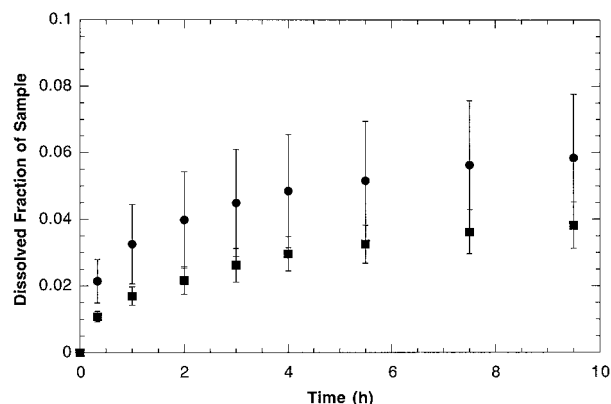


Figure 4 Fractional PVA dissolution from (■) cellular, freeze/thawed PVA gels and (●) control gels when swollen from an initial dry state.

trol gels and gels prepared in the presence of NaCl.

PVA gels prepared in the presence of NaCl and control PVA gels were also exposed to a 10-day period of washing to remove NaCl and excess PVA chains that did not participate in the crystallization process. At that time, the gels were allowed to dry before beginning the swelling process. Figure 5 shows the corresponding swelling of such gels that were washed and then dried. It is apparent that both gel types experienced enhanced initial swelling rates due to the 10-day washing period. Particularly, the gels prepared in the presence of NaCl exhibit a much higher initial swelling rate of 0.44 min^{-1} when compared to the control gels (0.16 min^{-1}). The gels prepared in the presence of NaCl were capable of reaching a volume swelling ratio of nearly 14 after 1 h of swell-

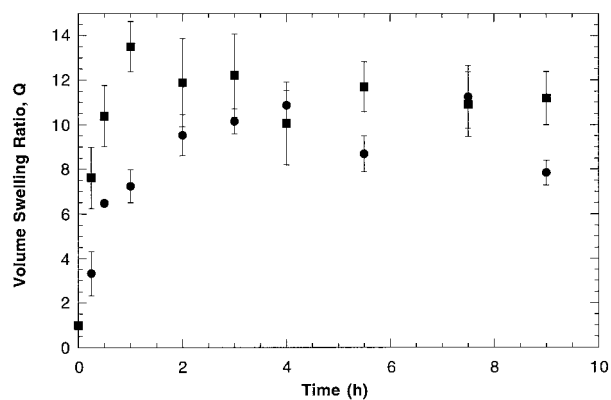


Figure 5 Swelling of (■) cellular, freeze/thawed PVA gels and (●) control gels from an initial dry state after a period of washing.

ing. It is also worth noting that with the swelling of these gels no significant amount of PVA dissolution occurred, as shown by the boric acid technique. Thus, the washing period did serve to remove residual PVA chains. A combination of the incorporation of NaCl during preparation techniques as well as an adequate washing period served to enhance the swelling rate and overall water content of freeze/thawed PVA gels.

SEM was also used with the previously described gels. However, no conclusive results were obtained to show increased pore size due to the incorporation of NaCl. The difficulties likely arose due to the gel-drying techniques. More conclusive evidence concerning the gel structure may be obtained using a more recently developed technique, cryogenic SEM, in which a gel structure can actually be examined in its swollen state.

CONCLUSIONS

PVA gels prepared by freezing and thawing techniques show increased mechanical strength over most hydrogels due to the presence of crystalline regions that serve as the physical crosslinks. However, such gels also exhibit relatively slow swelling kinetics, specifically from the dry state. This work examined the preparation and characterization of cellular, freeze/thawed PVA hydrogels. Such gels were prepared in the presence of NaCl. The effect of NaCl ions on the rate of swelling and overall water content was examined. Gels that were dried immediately after preparation exhibited a dual-sorption effect during swelling. However, by exposing the gels to a 10-day period of washing, NaCl and excess PVA chains that did not participate in the crystallization process were removed. When these gels were dried after this washing period, overall enhanced swelling was noted. Both the initial rate of swelling and the

overall water content were increased with gels prepared in the presence of NaCl. Although SEM did not conclusively confirm increased porosity, the swelling results provide initial promise into the further development of such gels. Indeed, other SEM techniques, specifically cryogenic SEM, may be employed to better examine the structure. However, it was shown that a combination of the incorporation of NaCl during preparation techniques and an adequate washing period did enhance the overall swelling kinetics of freeze/thawed PVA gels.

This work was essentially a feasibility study to determine parameters that may affect the swelling behavior of such gels. By also varying such parameters as the amount of NaCl, the initial aqueous concentration of PVA, PVA molecular weight, and freezing and thawing conditions, we can likely further enhance the swelling of freeze/thawed PVA hydrogels. Such gels with enhanced swelling and mechanical strength show promise for a variety of applications in the biomedical and pharmaceutical areas.

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REFERENCES

1. Chen, J.; Park, H.; Park, K. *J Biomed Mater Res* 1999, 44, 53.
2. Chen, J.; Park, H.; Park, K. *Proceed Int Symp Control Rel Bioact Mater* 1998, 25, 60.
3. Stauffer, S. R.; Peppas, N. A. *Polymer* 1992, 33, 3932–3936.
4. Tamura, K.; Ike, O.; Hitomi, S.; Isobe, J.; Shimizu, Y.; Nambu, M. *Trans Am Soc Artif Organs* 1986, 32, 605.
5. Peppas, N. A.; Wright, S. L. *Eur J Pharm Biopharm* 1998, 46, 15–29.