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Swelling characteristics of a blend hydrogel made of poly(allylbiguanido-*co*-allylamine) and poly(vinyl alcohol)

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A hydrogel was prepared by mixing poly(allylbiguanido-*co*-allylamine) hydrochloride (PAB) with poly(vinyl alcohol) (PVA) and by repeatedly freezing and thawing the blend. The swelling behaviour of the gel was studied as a function of the pH and ionic strength of the medium. The performance of the gel was compared to that of a blend hydrogel made from poly(allylamine) hydrochloride (PAA) and PVA. In a salt-free aqueous medium, the PAB/PVA hydrogel displayed a remarkable pH response: a drastic reduction in size was observed above pH 9 and below pH 3, but the size was little affected in the pH range 3–9. In a medium of constant ionic strength ($\mu = 0.1$), the hydrogel's pH response was much different: it was significantly reduced in size above pH 10, but the size was affected only moderately below pH 10. When the ionic strength of the medium was varied at a fixed pH, the size change of the hydrogel was gradual. For instance, in sodium chloride solutions (at a pH of 6.0), the hydrogel shrank by about 30% as the electrolyte concentration was raised from 10^{-6} to $2\,mol\,l^{-1}$. All these phenomena could be understood by observing that: (i) PAB is subject to multiple acid–base equilibria (with widely spaced pK_a values); and (ii) the electrostatic interactions among the charges on the polymer backbone are shielded by the added electrolyte as the ionic strength of the medium is raised.

(Keywords: cationic PAB/PVA hydrogel; swelling characteristics; pH response)

INTRODUCTION

Polymer gels that are responsive to external stimuli such as pH[1–3], chemical[4–7] and biochemical compounds[8–10], heat[11–16], light[17] and electric fields[18] have been extensively studied in recent years. It was reported that physically crosslinked poly(vinyl alcohol) (PVA) hydrogels could be prepared by repeated freezing and thawing[19]. These hydrogels, which display a high elastic modulus even though their water content is very high, form a useful material for a variety of biomedical applications. We have already reported that blend-hydrogel membranes made by mixing poly(allylbiguanido-*co*-allylamine) hydrochloride (PAB) with PVA promoted cell growth and adhesion[20]. Prior to that we also reported that PAB with positively charged biguanido groups was prepared by the reaction of poly(allylamine) hydrochloride (PAA) and guanyl-*O*-methylisourea[21].

It is well known that the swelling behaviour of hydrogels containing either positively or negatively charged groups show pH response in the acidic or basic regions, respectively. We expected the swelling behaviour of the PAB/PVA hydrogel to be more sensitive than that of the PAA/PVA hydrogel in the acidic region. The PAB/PVA hydrogel, however, displays a pH response in both acidic and basic regions.

In this paper, the effects of pH and ionic strength on the swelling behaviour of PAB/PVA hydrogel are described.

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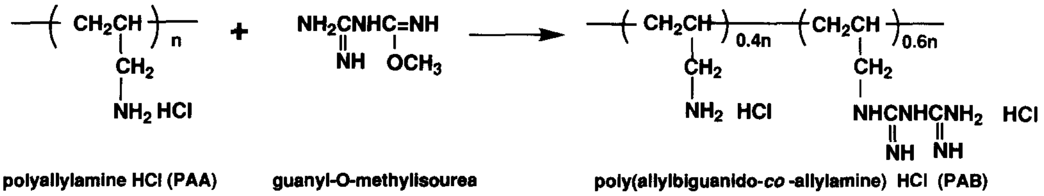
EXPERIMENT

Materials and methods

Poly(vinyl alcohol) (PVA) was purchased from Wako Pure Chemical Industries Co. (Japan). The degree of polymerization of the PVA was about 2000 and the degree of saponification was over 98% (sample code 167-03065). Poly(allylamine) hydrochloride (PAA) ($MW = 7500-11\,000$) was purchased from Nitto Boseki Co. (Japan) (sample code PAA-HCl-3S). Poly-(allylbiguanido-*co*-allylamine) hydrochloride (PAB) was synthesized as shown in *Scheme 1* by the reaction of PAA with guanyl-*O*-methylisourea in methanol solution under a nitrogen atmosphere[21]. After reaction, PAB contained 60% allylbiguanido groups.

Determination of pK_a *values of the cationic polymers*

Two of the pK_a values of PAB (pK_a 2.0, 12.6) were obtained spectroscopically using the absorption peak at 233 nm by means of Hirt's method[22]. U.v. spectra were



Scheme 1 Synthesis of PAB

measured in the wavelength region of 200 to 300 nm with a Hitachi model 330 spectrophotometer equipped with a 1 cm path-length quartz cell. U.v. spectrograms were obtained for PAB solutions of different pH values ranging from 1 to 7.7 and from 11.7 to 13. The pH of the solution was adjusted by suitable concentrations of hydrochloric acid or sodium hydroxide under constant ionic-strength conditions ($\mu = 0.1$). Sodium chloride was used to fix the ionic strength.

The other pK_a of PAB (pK_a 9.6) was obtained by the potentiometric titration method as described before[21]: PAB (144.2 mg, 1.06 mmol; as degree of substitution = 0.60) and sodium chloride (145.0 mg) were dissolved in a mixture of N/10 hydrochloric acid (10.00 ml) and distilled water (about 15 ml) in a 25 ml volumetric flask, and then titrated by 1 N sodium hydroxide ($f = 0.996$) under a nitrogen atmosphere at 25°C by using an automatic titrator (GT-05 type, Mitsubishi Kasei Co.). Two inflection points were observed at pH values of about 5.5 and 10.8, respectively.

The u.v. spectrum of PAA did not show any absorption peak in the wavelength range 200–300 nm. The potentiometric titration of PAA, however, revealed an inflection point at a pH of about 4.4.

Preparation of PVA blend-hydrogel membranes

A polymer blend (PAB/PVA) was prepared at 30/70 monomer molar ratio. The mixture of PAB/PVA and distilled water (10% wt/vol) was autoclaved at 120°C for 30 min. This treatment gave a completely transparent solution. The solution was poured onto a glass plate, spread out, cooled slowly to room temperature, and subsequently stored at −18°C. The hydrogel membrane thus prepared was subjected to 10 freezing–thawing cycles, a process that significantly improved the membrane's mechanical strength[19].

A PAA/PVA hydrogen membrane with monomer molar ratio = 10/90 was also prepared in a similar manner.

Effect of pH on the swelling of the hydrogel

No added salt. Test pieces of these hydrogel membranes were cut off with dimensions ca. 5 mm wide, ca. 0.2 mm thick and ca. 10 cm long. The pH of the aqueous medium was adjusted to the desired value by 0.1 N hydrochloric acid and 0.1 N sodium hydroxide. No other electrolyte was present in the medium. The degree of elongation (D) of a hydrogel that was immersed in a solution of known pH under a nitrogen atmosphere at 20°C was calculated by measuring the length of the equilibrated and starting hydrogel specimens:

$$D = [(L - L_0)/L_0] \times 100 \qquad (1)$$

In the above equation, L and L_0 are the length of the equilibrated and starting hydrogel specimens, respectively. In all the experimental runs, the starting length L_0 is the length of the specimen immersed in pure distilled water under nitrogen atmosphere at 20°C.

After equilibrating the specimen at a given pH and ionic strength and measuring the equilibrated length, the specimen was washed with distilled water, immersed in N/100 hydrochloric acid for 10 min, washed with distilled water again, and then immersed in pure distilled water for 30 min. The length of the hydrogel was measured again now to ensure that it has regained its initial dimension L_0 before proceeding with the next run.

Solutions of constant ionic strength. The degree of elongation with pH was also evaluated under a constant ionic strength ($\mu = 0.1$) by a similar method. The ionic strength was held fixed using sodium chloride.

Effect of ionic strength on the swelling of the hydrogel

The degree of elongation at various concentrations of sodium chloride was also evaluated using a procedure similar to that described above.

RESULTS AND DISCUSSION

Figure 1 shows the u.v. spectra of PAB solution (concentration 10^{-4} mol l^{-1}) of varying pH under constant ionic-strength ($\mu = 0.1$) conditions. From these spectrograms we determined by Hirt's method[22], using the absorption peak at 233 nm, that two of the pK_a values of PAB are located at 2.0 and 12.6, respectively. The potentiometric titration[23] of PAB solution with 1 N NaOH solution (*Figure 2*) revealed that PAB also has

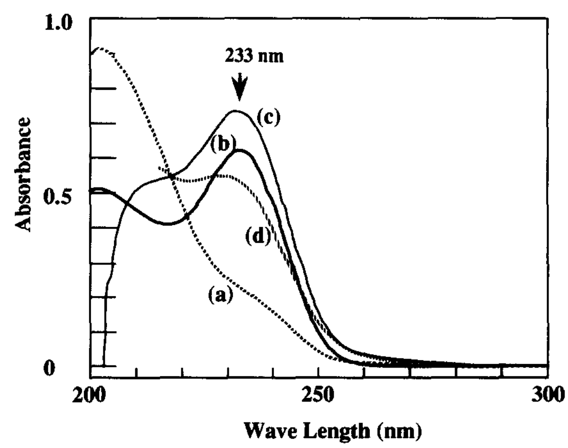


Figure 1 U.v. spectra of PAB at a fixed ionic strength ($\mu = 0.1$): (a) 0.1 N HCl (pH 1.0), (b) 0.1 M NaCl (pH 7.7), (c) 0.005 N NaOH/NaCl (pH 11.7) and (d) 0.1 N NaOH (pH 13.0). Ionic strength is adjusted with NaCl when necessary. Curves (a), (b), (c) and (d) correspond to formulae of *Scheme 2*

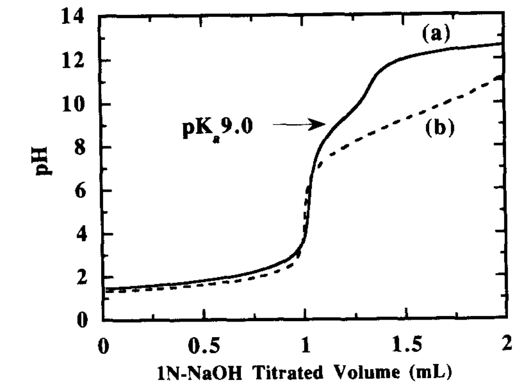


Figure 2 Potentiometric titration curves of (a) PAB and (b) PAA

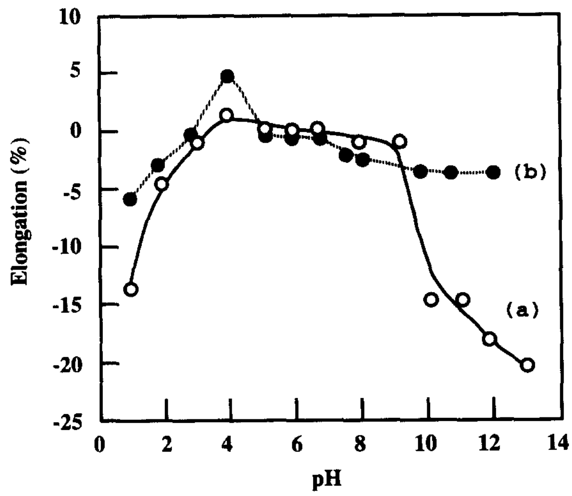
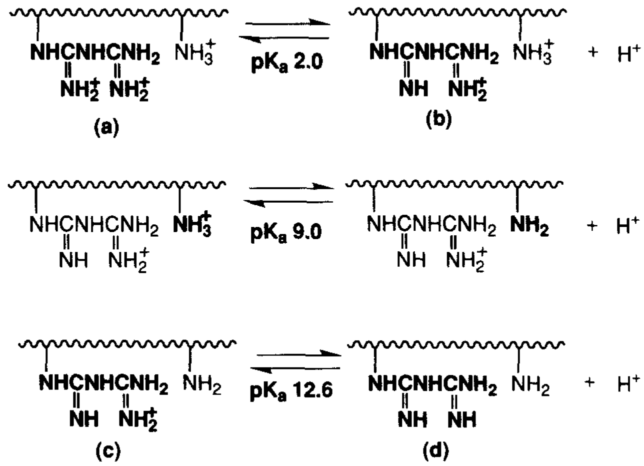


Figure 3 Elongation of hydrogels with pH in a salt-free medium: (a) PAB/PVA hydrogel, (b) PAA/PVA hydrogel

another pK_a at 9.0. In the case of PAA, which is known to be a monoprotic base, the potentiometric titration curve shows an inflection point at a pH of about 4.4 (*Figure 2*)[24,25]. It is, however, not possible to make an accurate determination of pK_a from the curve.

Figure 3 shows the degree of elongation of PAB/PVA and PAA/PVA hydrogels in the pH range 1–13 in a medium where there is no added electrolyte. The size of the PAB/PVA hydrogel was little affected by pH changes in the pH range 3–9. However, the membrane shrank appreciably below pH 3 and above pH 9, and showed a reduction in size of about 15% at pH 1 and 20% at pH 13. These observations on the elongation behaviour can be correlated with the pK_a values of PAB (2.0, 9.0 and 12.6) determined above, and the ionic-strength variations that take place inevitably when the pH of the medium is adjusted by the addition of HCl and/or NaOH.

The location of the pH relative to the pK_a values determines the extent of protonation of the various ionizable units on the biguanido and the amine pendent groups (*Scheme 2* shows the different acid–base equilibria involved). The degree of protonation of these groups, in turn, determines the extent of swelling of the gel due to electrostatic repulsions among these charges. In other words, it is assumed that the attainment of a degree of protonation is approached within each p$K_a \pm 0.5$ pH. It is estimated that the pK_a



Scheme 2 Acid–base equilibria in PAB

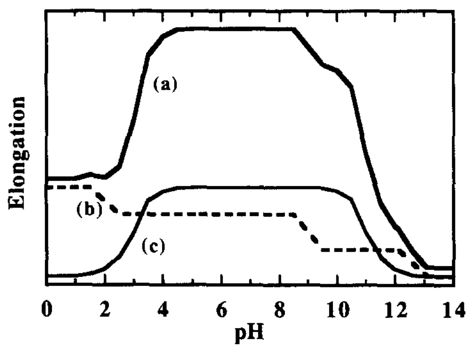


Figure 4 Schematic diagram of the elongation model: (a) net elongation; (b) elongation component due to electrostatic repulsion; (c) elongation component due to ionic strength ($a = 2$ in equation (2))

values associated with biguanido groups are 2.0 and 12.6 and that of amino groups is 9.0 owing to their organic compounds[26,27] (*Scheme 2*). It is estimated that the extents of swelling of the gel due to electrical repulsions are: 100% below pH 1.5, 50% between pH 2.5 and pH 12.1, and 0% over pH 12.9 by the biguanido group; and 100% below pH 8.5, and 0% over pH 9.5 by the amino group. The relative magnitude of the swelling by biguanido groups is estimated to be 60% owing to the substitution of the biguanido group in PAB polymer, and that of the amino group is 40%. The swelling behaviour of the total electrical repulsion (D electric) may be indicated by a curve such as b in *Figure 4*.

The process of maintaining the pH of a medium (by adding NaOH and/or HCl) from extremely low to high values, say from 1 to 13, makes the ionic strength of the medium go through a minimum. In other words, the ionic strength vs. pH profile will have its minimum value at a neutral pH of 7, about which pH the profile will be symmetric. In the case of the pH range from 0 to 7, the ionic strength reduces with the decrease of hydrogen-ion concentration similar to the salt effect that was found by Tanaka *et al.*[28]. Therefore, the elongation component due to the ionic strength (D_{ionic}) displays a curve such as c in *Figure 4*. The degree of *net* elongation (D_{net}) will be constituted as follows:

$$D_{net} = aD_{ionic} + D_{electric} \qquad (2)$$

where a is the proportion of the two components. *Figure 4* illustrates schematically how the two components contribute to the net elongation (curve *a* in *Figure 4*), namely (1) the component due to the changing degree of ionization of the acid–base groups and (2) the component representing the shielding of electrostatic repulsions by the ionic strength of the medium, vary as the pH of the medium is raised. It is easy to understand from the figure how these components will add up to the net elongation behaviour experimentally observed (*Figure 3*).

In contrast to PAB/PVA hydrogel, PAA/PVA hydrogel showed a maximum in elongation at pH 4 and less dramatic changes in membrane dimensions with pH variations (*Figure 3*). The observed differences in the elongation vs. pH profiles of PAB/PVA and PAA/PVA hydrogels result from the presence of biguanido groups in the former gel.

Figure 5 shows the degree of elongation of PAB/PVA hydrogel with pH (2–12) at a *constant* ionic strength ($\mu = 0.1$). The hydrogel exhibits a small shrinkage in the pH ranges 2–3 and 7–8, but a steep shrinkage above pH 10. As could be noted from the acid–base equilibria shown in *Scheme 2*, below pH 2, each biguanido group in PAB binds two protons, and the amino groups are also protonated. As a result, the number of positive charges in the gel has the highest value. On the other hand, in the pH range from 3 to 7, biguanido groups bind only one proton each, and hence the net charge of the gel has a somewhat smaller value. This approximately constant net charge keeps the degree of swelling of the gel also fairly constant in this pH range (*Figure 5*). Upon further increasing the pH, first the amino groups are deprotonated above a pH of 9, and subsequently the biguanido groups are also deprotonated above a pH of 13. Thus in this pH range, the electrostatic repulsions gradually disappear and the gel collapses, as seen in *Figure 5*. In this case, unlike in *Figure 3*, the shape of the elongation vs. pH curve is not affected by the ionic strength, since it is held fixed. These phenomena suggested that the degree of elongation was affected by the electrostatic repulsions. The difference of the change in area of the elongation vs. pH curve between PAB/PVA hydrogel and pK_a values of PAB is considered to be due to the different ways of measuring the states, namely the former were held in the hydrogel state and the latter were given freely in aqueous solution.

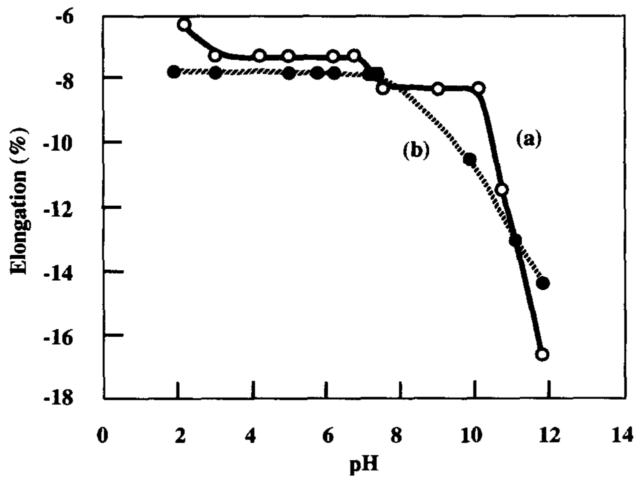


Figure 5 Elongation of hydrogels with pH at a fixed ionic strength ($\mu = 0.1$): (a) PAB/PVA hydrogel, (b) PAA/PVA hydrogel

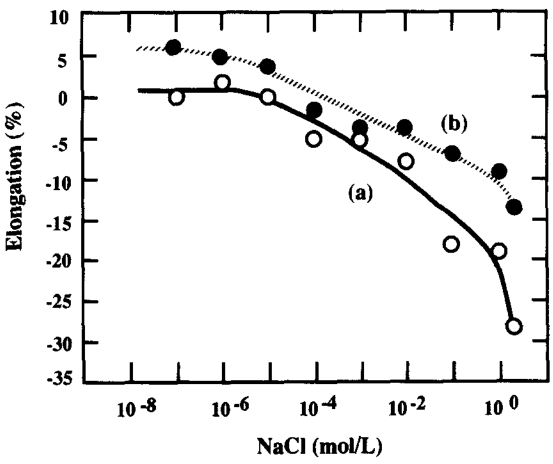


Figure 6 Elongation of hydrogels as a function of NaCl concentration at a fixed pH of 6.0: (a) PAB/PVA hydrogel, (b) PAA/PVA hydrogel

Figure 6 shows the degree of elongation of PAB/PVA and PAA/PVA hydrogels as a function of the concentration of sodium chloride added to the medium while holding its pH constant at 6.0. Increased concentration of sodium chloride resulted in a decrease in the elongation of both hydrogels. These results display the profound effect that the ionic strength has on the degree of swelling of both the hydrogels.

CONCLUSION

In summary, the swelling characteristics of PAB/PVA hydrogels display a more pronounced pH and ionic strength response compared to PAA/PVA hydrogels. When no added salt is present in the medium, the swelling of the PAB/PVA gel is affected both by the degree of ionization of the basic groups in PAB (biguanido and amino groups) and by the ionic-strength changes that accompany the process of adjusting the pH of the medium. In strongly acidic and basic solutions, such ionic-strength effects are large enough to cause appreciable shrinkage of the gel, whereas in the vicinity of neutral pH the net swelling is dominated by the electrostatic repulsions among the protonated basic groups on the PAB backbone.

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