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SHORT COMMUNICATION

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Effects of salt on the temperature and pressure responsive properties of poly(*N*-vinylisobutyramide) aqueous solutions

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Abstract We examined the effects of salt on the lower critical solution temperature (LCST) and lower critical solution pressure (LCSP) of aqueous solutions of poly(*N*-vinylisobutyramide), polyNVIBA, and compared them with those on poly(*N*-isopropylacrylamide), polyNIPAAm. We found that the addition of salt (such as Na_2SO_4, NaCl, or KCl) decreased the LCST of aqueous polyNVIBA from 45 °C to below 20 °C, almost linearly with the salt concentrations and dependent on the type of salt. We observed a similar concentration-dependent decrease in LCST for polyNIPAAm. When KI or NaSCN was added to each aqueous polymer solution, some smaller increases in LCST were observed at relatively low salt concentrations; higher concentrations of salt gave an almost linear decrease in LCST. As for LCSP, the addition of most types of salt lowered the transition pressure, but the effects were much more dependent on the type and the valence of the salt (especially of anion) in both polymers. Salt with divalent anion showed a larger decrease in LCSP, but those with mono valent anion showed a relatively small decrease, even showed a slight increase at lower salt concentrations in the case of polyNVIBA. Salt with I^- or SCN^- showed evident increases in LCSP up to 1 M and was maintained higher than the control even at 2 M. We discuss the interactions of the amide group in the side chains of polymers and water and their perturbation by ions.

Key words Poly(*N*-vinylisobutyramide – poly(*N*-isopropylacrylamide) – cloud point – salting out – thermoresponsive polymer – high pressure

Introduction

In our previous paper [1, 2] we established an effective synthesis route for *N*-vinylisobutyramide (NVIBA) and its polymer form (polyNVIBA) and found that a lower critical solution temperature (LCST) for the aqueous solutions of the polymer can be easily controlled at desired temperatures between 0 °C and 100 °C by copolymerizing with *N*-vinylalkylamides. This phenomenon is due to the changes in the hydrophilic-hydrophobic balance in the copolymers. Poly(*N*-vinylacetamide) (polyNVA) and its derivatives, such as poly(NVIBA) (that have amide groups in their side chains) are regarded as simplified polypeptide or protein model compounds. In order to study the phenomena of biopolymers and proteins in aqueous systems (in particular their structural formations and deformations), the interactions of water molecules with non-polar molecules and amide groups have received a great deal of attention from researchers [3–7]. Actually, the effect of salt on the aqueous solutions of polyNVA has been studied and the results showed a certain similarity to the denaturation of proteins in the aqueous phase [8].

In the case of aqueous polyNVA, the LCSTs were only observed in the presence of salt: the addition of salt decreases the LCST value down to an observable temperature range [8]. In regard to the so-called thermosensitive polymers, such as poly(*N*-isopropylacrylamide) (polyNIPAAm), which have LCST or volume transition in a measurable range without any addition of salts or other additives (in the case of polyNIPAAm; at around 32 °C in pure water [9, 10]), it is known that their aqueous solutions or gel forms gave a lower LCST by adding a third component of salt [11–13]. PolyNVIBA has an identical elementary compositions in the monomer unit with polyNIPAAm and an oppositely placed amide bond in the side chain. It has also been noted that these polymers have identical elementary compositions and very similar chemical group components in monomer units with homopolypeptides such as polyleucine and polyisoleucine [14, 15]. The relationship between their chemical structure and their thermo- and balo-sensitive properties (in connection to the formation and deformation of protein structures) is of great scientific interest. We have shown that aqueous solutions of polyNVIBA (and polyNIPAAm also) showed temperature- and pressure-dependent transitions [16], which can be explained by the thermodynamic equation that was drawn for protein denaturation [17].

The thermo- and balo-sensitive properties of these polymers in the presence of salt, however, has not been sufficiently studied, and, therefore, in this paper we studied the effect of salt (its type and concentrations), on the temperature and pressure transition properties of aqueous solutions of polyNVIBA and polyNIPAAm.

Experimentals

Materials

PolyNVIBA and polyNIPAAm were synthesized in the authors' laboratory. Our GPC analysis gave $Mn = 1.0 \times 10^4$; $Mw/Mn = 2.3$ or $Mn = 6.6 \times 10^4$; $Mw/Mn = 1.6$ for polyNVIBA, $Mn = 7.5 \times 10^3$; $Mw/Mn = 2.3$ or 4.9×10^4; $Mw/Mn = 1.8$ for polyNIPAAm (Showdex AD-80M/S column in DMF solution, standardized against PEG-PEO). Inorganic salt such as Na_2SO_4, K_2SO_4, NaCl, KCl, NaI, KI, NaSCN, and KSCN were reagent grade from Wako Pure Chemicals (Osaka, Japan) or Nacalai Tesque (Kyoto, Japan) and were used without further purifications.

Methods

The LCST was determined by the measurement of transmittance at 500 nm on a Jasco Model V-550 spectrophotometer that was equipped with a Peltier-type thermostatic cell holder coupled with a controller ETC-505T versus temperature. Temperature was controlled by PID constants using a computer at heat rates of about 1.0 °C/min and monitored by an ETC-505T with a computer. The LCST was taken as the initial break point in the resulting transmittance vs. temperature curves for each polymer solution in the heating-up process. In the measurements for balo-sensitivity, a high pressure optical cell with two sapphire windows, constructed by Teramecs Co. (Kyoto, Japan), was placed between the light source (Xe lamp) and the monochromator/photomultiplier via optical fibers and an apparent transmittance at 500 nm was recorded. The temperature of the cell was also controlled by a Peltier-type thermoregulator and was detected by a Pt resistance thermometer.

Results

When the temperature dependence of the light transmittance of the aqueous solution of two polymers on heating was measured in the presence of a constant concentration (2.0×10^{-3} mol/g aq.soln) of Na_2SO_4, KCl, or KI, the LCST of both polyNVIBA and polyNIPAAm changed significantly and the shifts in LCST were strongly dependent on the kinds of the salt used. The additions of Na_2SO_4 or KCl led to lower LCSTs for both polymers. However, the addition of KI to this concentration caused an increase in the LCST of polyNVIBA, while the LCST of polyNIPAAm was only elevated to a smaller extent.

The variations in LCST were also dependent on the concentrations of the salt; the results are shown in Figs. 1 and 2. As shown in Fig. 1, the LCST of polyNVIBA solution in the presence of Na_2SO_4, NaCl and KCl decreased almost linearly with an increase in the salt concentrations, within the range used here. A similar linear dependence was observed for polyNIPAAm. It seems to be independent of the cation species used here (Na^+ and K^+). This type of independence of a (mono) cationic species was also observed for the volume contractions of polyNIPAAm gel [12]. However, the variations in LCST were dependent characteristically on the anion species. For a divalent anion (SO_4^{2-}), the LCST drops sharply with an increase in salt concentrations and the difference from the results of KCl or NaCl can not be explained in terms of ionic strength; the slope for Na_2SO_4 is more than three times those of KCl and NaCl. LCST declined below 20 °C, more than 20 °C lower than the control, by the addition of

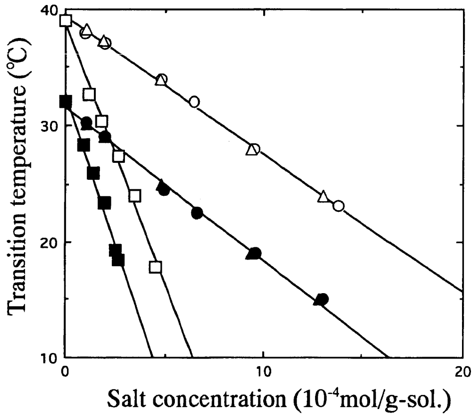

Fig. 1 Cloud point of polyNVIBA (open) and polyNIPAAm (closed) aqueous solutions as a function of the concentration of the added salt at 0.1 MPa. ○ and ●, NaCl; △ and ▲, KCl; □ and ■, Na_2SO_4. [polyNVIBA] = 0.25 wt%, [polyNIPAAm] = 0.25 wt%

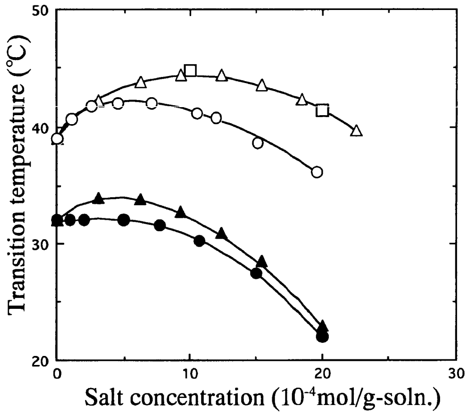

Fig. 2 Cloud point of polyNVIBA (open) and polyNIPAAm (closed) aqueous solutions as a function of the concentration of the added salt at 0.1 MPa. ○ and ●, KI; △ and ▲, NaSCN; □, KSCN. [polyNVIBA] = 0.25 wt%, [polyNIPAAm] = 0.25 wt%

approximately 5×10^{-4} mol/g-soln of Na_2SO_4. On the contrary, with the addition of I^- or SCN^-, an upward shift in LCST was first observed with an increase in the salt concentration until a certain level was attained and then a further increase produced a decrease, almost linear to the ionic concentration (Fig. 2). For polyNIPPAm, this type of characteristic effect of I^- was not evident and almost constant LCSTs were observed below 5×10^{-4} mol/g-soln. These results of these different effects (depending on the anionic species) seem to be in line with the lyotropic series or Hoffmeister series of anions. Anions with very low lyotropic numbers showed a linear decrease in LSCT and those with very high numbers showed an apparent maximum LCST with changes in the concentration.

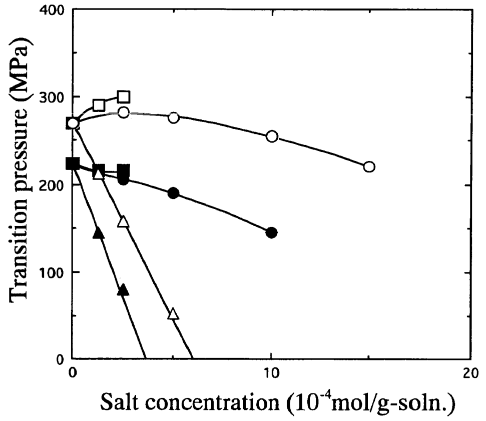

Fig. 3 Effects of salt concentration on the transition pressure of aqueous solutions of polyNVIBA (open) and polyNIPAAm (closed) at 10 °C. ○ and ●, KCl; △ and ▲, K_2SO_4; □ and ■, $MgCl_2$. [polyNVIBA] = 0.1 wt%, [polyNIPAAm] = 0.5 wt%

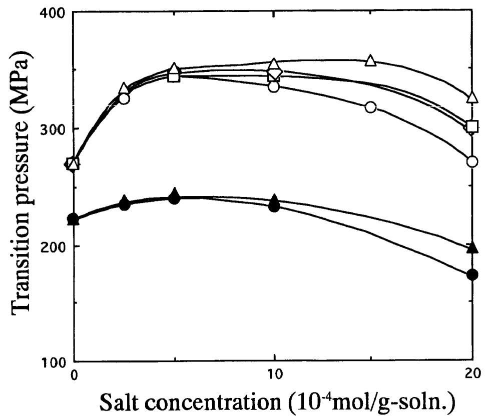

Fig. 4 Effects of the concentration of salts with lyotropic anions on the transition pressure of aqueous solutions of polyNVIBA (open) and polyNIPAAm (closed) at 10 °C. ○ and ●, KI; ◇, NaI; and ▲, NaSCN; □, KSCN. [polyNVIBA] = 0.1 wt%, [polyNIPAAm] = 0.5 wt%

The effects of the addition of these salts on the pressure behaviour (LCSP) were similar to the results on LCST, but the characteristics of the ionic species and also of the polymers were more clearly observed. The results are shown in Figs. 3 and 4. The measuring temperature was set at 10 °C, taking the lowered LCST under high salt concentrations into account. The addition of SO_4^{2-} showed a sharp and simple downward shift of transition pressure for both polymers. At 5×10^{-4} mol/g-soln, LCSP of poly NVIBA declined to almost 50 MPa, 200 MPa less than the control. The effects of salt addition on LCSP were stronger in this polymer than for polyNIPAAm. Upward shift in an intermediary concentration range was observed by KCl addition for polyNVIBA, but not for polyNIPAAm. In the latter polymer, a simple downward shift of LCSP was observed with the addition of KCl, and the differences of the slope from Na_2SO_4 could also not be explained in terms of ionic strength.

The addition of anions with very high lyotropic numbers (such as I^- and SCN^-) resulted in a distinct increase in transition pressure (as shown in Fig. 4) and, at concentrations of 5×10^{-4} or 1×10^{-3} mol/g-soln, the transition pressure of polyNVIBA solution became almost 350 MPa, more than 80 MPa higher than the control. Even at 2×10^{-3} mol/g-soln of these ions, LCSP was not below the control. Here, a slight dependence on cation species was observed; sodium ion gave lower LCSP at 2×10^{-3} mol/g-soln that potassium ion, which is compatible to the Hoffmeister series.

Discussion

The transitions of these thermoresponsive polymers occur by the dehydration process and the strengthening of hydrophobic interactions among side chains. They are also related to the structural deformation of water around the hydrophobic groups. Thus, the effects of salts on transition temperature and pressure could be related to many possible factors that are included in these processes. In general, the effects of salt on aqueous polymer and biopolymer systems may originate from their effects on the polymer skeleton, the direct interactions of salt (ions) with the side chain polar groups (such as amide or carboxyl) and/or the effects on the hydrogen-binding ability of water [17]. In many different cases, from oligopeptides or proteins to synthetic water-soluble polymers, the effectiveness of salt addition (especially that of anions) more or less follows the Hoffmeister or the lyotropic series [3–5, 18]. The results are not easily related to the simple physicochemical variables such as ionic strength; the contrasting results of K_2SO_4 and $MgCl_2$ in Fig. 3 indicate this clearly. The Hoffmeister series for the presently used anions is $SO_4^{2-} > Cl^- > I^- > SCN^-$, and lyotropic numbers for them are 2, 10, 12.5 and 13.3 (N), respectively [19]. Some researchers have explained the results by the B coefficient of viscosity [12], which is an indicator of ion–water interaction [20]. B coefficient values for SO_4^{2-}, Cl^-, and I^- are 0.208, -0.007 and -0.068 (mol^{-1}), respectively. In a study of higher-order structures of proteins, such as ribonuclease A, it was shown that anions with higher lyotropic numbers (salting-in ions) lead to the denaturation of proteins into coil-like structures and those with lower numbers (salting-out ions) induced native and ordered structures (globule state) [21].

The present results can be explained in a similar context. Salting-in anions or anions (which have rather large and negative B-coefficients) may break the structure of bulk water and, as a result, stabilize hydrophobic hydration; the coil-like structure is favored in these solutions, such as SCN^- or I^-. However, slating-out anions or those that have positive or less negative B-coefficients function as structure makers for water and, as a result, they strengthen hydrophobic interactions among the side chains in order to promote the formation of the globular structures (collapse-state) of the polymers. In other words, the hydration of the side chains of the polymer was weakened by the addition of slating-out ions and was unchanged or slightly strengthened by the addition of salting-in ions. These kinds of effects are more evidently observed in the pressure-dependence.

In general, hydrophobic interactions between (or among) alkyl chains show slightly positive volume changes and it was estimated around $+1$ to $+2$ ml/mol per methylene group [22]; the hydrophobically hydrated water has a smaller partial molar volume than does the bulk water, and thus the antagonism of temperature and pressure effects was observed on the stability of coil structures at relatively low pressure [16]. However, the compressibility of bulk water is larger than the former and the above situation is inverted by increasing pressure. Above 200 MPa, hydrophobic interactions (not those of rather electric interactions among aromatic residues) among alkyl chains are favored. Thus, the turning point in the T and P dependence of the cloud point was observed for both polymer solutions [16]. As for ionic solutions, the relative volumetric situation of hydrated water and bulk water should be modified. Salting-out ions will promote this type of inversion of the situation and salting-in ions will not change or maintain the situation. Thus, the transition pressure becomes lower when the system contains anions with lower lyotropic numbers.

However, the effects of the direct interaction of anions with amide groups in the side chain, as was suggested in the case of polyNIPAAm gel [13], could not be totally excluded at this level of study, since this type of interaction could also perturb the hydration or interaction of water with this polar group (which has lower entropy and also a smaller partial volume), and as a result the change in the entropy and volume of the transition would be reduced. The non-linearity of the concentration dependence, especially for the cases of salting-in ions, could be given by the balance among the effects on water structure, on hydration and on more direct dipolar interactions.

The differences in the two types of polymers are related to the strength of the hydration. At 0.1 MPa, polyNVIBA shows higher LCST than polyNIPAAm. In contrast to the temperature response, however, the pressure reponse of these polymers is much more affected by the molecular weight of the used polymers, but even when compared with similar molecular weights, polyNVIBA shows a higher LCSP at 10 °C (Kunugi et al., unpublished results). This means that the intermolecular interactions and also the intramolecular interactions among the collapsed domains on one polymer chain (the molecular weights of the polymers used here are well above the predicted unit domain of the collapsed region; about 10^4 [14, 15]) play more important roles in the pressure induced aggregations of the collapsed chains. The structural differences in the two polymers are in the direction of the amide bond of the side chains. This may cause a significant effect on the interaction (positive or negative) of the hydrophobic hydration shell and the water bound to the amide group of the side chain; this type of interaction seems stronger in polyNIPAAm.

In conclusion, we found that changes in LCSP, as well as LCST, that are caused by the addition of inorganic salt can be explained in terms of salting-out and salting-in effects and, consequently, the LCSP and LCST of aqueous polyNVIBA and of polyNIPAAm can be easily controlled by changing the kinds and the concentrations of salt.

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References

1. Suwa K, Wada Y, Kikunaga Y, Morishita K, Kishida A, Akashi M (1997) J Polym Sci Part A: Polym Chem Ed 35:1763
2. Suwa K, Morishita K, Kishida A, Akashi M (1997) J Polym Sci Part A: Polym Chem Ed 35:3087
3. von Hippel PH, Schleich T (1969) Acc Chem Res 2:257
4. von Hippel PH, Wong K (1964) Science 145:577
5. Robinson DR, Jencks WP (1965) J Am Chem Soc 87:2470
6. Nandi PK, Robinson DR (1972) J Am Chem Soc 94:1299
7. Schrier EE, Schrier EB (1967) J Phys Chem 71:1851
8. Hong JS, Nakahara T, Maeda H, Kikunaga Y, Kishida A, Akashi M (1996) Colloid Polym Sci 274:1013
9. Heskins M, Guillet JE (1968) J Macromol Sci Chem A2:1441
10. Schild HG (1992) Prog Polym Sci 17:163
11. Schild HG, Tirrell DA (1990) J Phys Chem 94:4352
12. Inomata H, Gogo S, Take K, Saith S (1992) Langmuir 8:687
13. Park TG, Hoffmann AS (1993) Macromolecules 26:5045
14. Tiktopulo EI, Bychkova VE, Ricka J, Ptitsyn OB (1994) Macromolecules 27:2879
15. Tiktopulo EI, Uversky VN, Lushchik BB, Klenin SI, Bychkova VE, Ptitsyn OB (1995) Macromolecules 28:7518
16. Kunugi S, Takano K, Tanaka N, Suwa K, Akashi M (1997) Macromolecules 30:4499
17. Hawley SA (1971) Biochemistry 10:2436
18. Ataman M (1987) Colloid Polym Sci 265:19
19. McBain JW (1954) In: Colloid Science. DC Heath & Co., Boston
20. Gurney RW (1953) In: Ionic Processes in Solution. Dover Pub Inc
21. von Hippel PH, Wong KY (1965) J Biol Chem 240:3909
22. Suzuki K, Taniguchi Y, Watanabe T (1973) J Phys Chem 77:1918