Solubilization Properties of *N*-substituted Amphiphilic Acrylamide Copolymers

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ABSTRACT: Amphiphilic copolymers of sodium 2-acrylamido-2-methylpropanesulfonate (AMPS) and dodecylmethacrylamide (DodMAAm) were synthesized. The ratio of the reduced viscosities of these copolymers in water and in 0.2 mol/L NaCl solution shows that these copolymers containing from 50 to 66 mol % of DodMAAm have a relatively small and constant hydrodynamic size. Viscometric and static light scattering measurements indicated that the copolymers shrinked and intermolecularly associated, forming interchain aggregates in water through hydrophobic interactions. These copolymers solubilize $dl - \alpha$ -tocopherol acetate, giving a transparent solution; but the solution became turbid in a month due to increasing intermolecular association. To suppress this excess intermolecular association, polymers with four different crosslinking ratios were synthesized. The polymer of a crosslinking ratio of 0.5 mol % showed a strong solubilization property, resulting in transparent solution with an improved stability. The fluorescence spectra of pyrene in the polymer solution proved that these copolymers could form strong hydrophobic domains, which solubilize a hydrophobic compound, in less than 30 w/w % ethanol solution. These copolymers could have an excellent function of sustained release of perfume as a novel function. © 1999 John Wiley & Sons, Inc. J Appl Polym Sci 73: 2447-2453, 1999

Key words: solubilization; amphiphilic polymer; interchain aggregates; fluorescence; turbidity

INTRODUCTION

Polysoaps, amphiphilic polyelectrolytes, were synthesized by Strauss and Jackson¹ in 1951 by quaternizing poly(2-vinylpyridine) with *n*-dodecyl bromide and were confirmed to adopt a highly compact conformation due to the aggregation of the long aliphatic side chains in water. Ferry et al.² reported that the copolymers of maleic acid and styrene formed a highly compact conformation in aqueous solution at low degrees of ionization 3 due to the hydrophobic aggregation of phenyl groups.⁴

Since a hydrophobic association competes with electrostatic repulsion in amphiphilic polyelectrolytes, no interchain aggregates are formed at low contents of hydrophobic units. On the other hand, amphiphilic polyelectrolytes containing a sufficient number of hydrophobic units form interchain aggregates in which hydrophobic units form interchain aggregates and hydrophilic segments form outer layers in aqueous solution.^{5–11} The interchain aggregates are rigid and static in nature as compared with the highly dynamic nature of conventional surfactants micelles.^{7,11} The stability of

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the interchain aggregates depends on its size, shape, and mole fraction of hydrophobic residues in amphiphilic polyelectrolytes.^{11–13} The formation and structure of the interchain aggregates of amphiphilic polymer were energetically investigated recently by static and dynamic laser light scattering.^{14–17} Li et al. reported that the formation of randomly carboxylated polystyrene ionomer particles involves the collapse of the hydrophobic backbone chains, the interchain aggregation, and the transfer of the carboxyl groups toward the particle surface. The density and size of these particles were varied by the degree of carboxylation and ionomer concentration.¹⁶

In this study, we investigated the solubilization properties of amphiphilic polyelectrolytes, aiming at an application of the interchain aggregates. Molecular design is important for developing a new useful material, which can show remarkable functions, such as highly solubilizing ability. Polymers that have solubilization ability should have the following three characteristics: (1) polymers should be amphiphilic and be miscible with water; (2) polymers should have an enough amount of hydrophobic parts to form hydrophobic domains which can take up solubilizates; (3) polymers should be able to wrap or surround solubilizate. For these essential characteristics, polymers should contain hydrophilic groups, such as sulfonic acid groups, carboxyl groups, hydroxyl groups, or amide linkages. Sulfonic acid groups are better than carboxyl groups because of their highly dissociating properties. As hydrophobic, C8-C18 may be suitable. To incorporate solubilizates, aliphatic carbon chains may be preferable over aromatic carbons because the former is more flexible than the latter. This article shows the solubilization properties of N-substituted amphiphilic acrylamide copolymers consisting of sodium 2-acrylamido-2-methylpropanesulfonate (AMPS) and dodecylmethacrylamide (DodMAAm).

EXPERIMENTAL

Monomers

Dodecylmethacrylamide (DodMAAm) was synthesized as reported previously.¹¹ 2-Acrylamido-2-methylpropanesulfonic acid (AMPS) (Merck, Schuchardt, Germany) was used without further purification.

Copolymers

In a three-neck flask, 1.4094 g (6.80 mmol) of AMPS, 3.3453 g (13.20 mmol) of DodMAAm, 0.0165 g (0.10 mmol) of 2,2'-azobis(isobutyronitrile) (AIBN) (Nacalai Tesque, Kyoto, Japan), and 10 mL of distilled N,N'-dimethylformamide (DMF) (Wako) were placed under nitrogen atmosphere. The polymerization was carried out at 70°C for 22 h. To precipitate the polymer, the mixture was poured into a large excess of diethylether. The copolymer was purified by reprecipitating from methanol into a large excess of diethylether three times. The polymer was then dissolved in 11 mol/L aqueous sodium hydroxide. The solution was dialyzed against pure water for a week and freeze-dried. The yield of the copolymer was 67%. The copolymer composition was determined by the S/C ratio in elemental analysis.

Crosslinked Polymers

In a three-neck flask, 1.4923 g (7.20 mmol) of AMPS, 3.2441 g (12.80 mmol) of DodMAAm, 0.0165 g (0.10 mmol) of AIBN, 0.0078 g (0.05 mmol) of N,N'-methylenebisacrylamide (Kanto Chemical, Tokyo), and 10 mL of distilled DMF were placed under nitrogen atmosphere. Polymerization and purification were carried out in a manner similar to above.

Measurements

The reduced viscosities of copolymers (0.5 g/dL aqueous solution) were measured at 25°C by using a conventional Ubbelohde viscometer. Turbidity was measured with an integration spherical turbidimeter (Japan Precision Optics, Tokyo). Weight-average molar mass of the polymer was determined by a static light scattering spectrophotometer equipped with a He–Ne laser at 25°C (DLS-7000, Otsuka Electronics, Osaka). The hydrodynamic radius was measured by a dynamic light scattering spectrophotometer equipped with Ar laser at 25°C (DLS-7000). Absorption spectra were recorded on a JASCO V-550 spectrophotometer. Fluorescence spectra were recorded on a Shimadzu RF-5300PC spectrofluorophotometer at room temperature.

Solubilization of *dl*-α-Tocopherol Acetate

The copolymer (0.1 g), dl- α -tocopherol acetate (0.05 g), and 4-hydroxybenzoic acid methyl ester

(as an antiseptic 0.1 g) were dissolved in ethanol (1 g) and then mixed with water (98.75 g).

Solubility Measurement of Methyl Cinnamate

Two stock solutions were prepared, that is, the first solution consisting of the copolymer (0.1 g), ethanol (1.0 g), and water (98.9 g), and the second solution consisting of ethanol (1.0 g) and water (99.0 g). To 10 g of each solution, 0.2 g of methyl cinnamate (Kanto Chemical) was added. After the solution was stirred for a predetermined period of time at room temperature, insoluble methyl cinnamate was filtered by a 0.2- μ m syringe filter. One gram of filtrate was diluted to 50 mL with methanol. The concentration of methyl cinnamate in the methanol solution was determined by its absorbance at 276.2 nm.

Fluorescence Spectra Measurement

The pyrene was dissolved in ethanol-water of varying ratios at 5.9×10^{-6} mol/L. The copolymer (0.1 g) was dissolved in the ethanol-water solution (99.9 g). Pyrene fluorescence spectra were measured with excitation at 340 nm. The ratio of the first to third vibrational fine structures (*I*1/*I*3) of pyrene fluorescence was calculated. It is known that the ratio of the first to third vibrational fine structures (*I*1/*I*3) of pyrene fluorescence reflects the local environmental polarity. The *I*1/*I*3 ratio is higher in polar media (e.g., in water *I*1/*I*3 = 1.81), and the I1/I3 ratio becomes lower in less-polar media.¹⁸ When pyrene is solubilized in surfactants micelles, the *I*1/*I*3 ratio is 1.12.¹⁹

Perfume Intensity Measurement

The solubilizer (0.1 g), limonene (0.01 g), and 4-hydroxybenzoic acid methyl ester (0.1 g) were dissolved in ethanol (1 g) and then mixed with water (98.79 g). A few drops of the solution were placed on a filter paper (diameter 70 mm). The intensity of the perfume vapored from the filter paper were measured by using a perfume intensity meter (Alabaster EKW-8603, B&H, Osaka) at room temperature. The measurements were done at 0, 20, and 40 min after the application.

RESULTS AND DISCUSSION

To satisfy those necessary properties stated introduction, we chose 2-acrylamido-2-methylpropane sulfonic acid (AMPS) as a hydrophilic monomer and dodecylmethacrylamide (DodMAAm) as a hydrophobic monomer. Although there are many types of copolymers (e.g., random, block, and graft copolymers), we chose random copolymers in this study because the synthesis is simple. The copolymer composition (AMPS : DodMAAm) = (p mol % : q mol %) is abbreviated as poly(AMPS–Dod-MAAm) = p : q (Fig. 1).

Reduced viscosities of poly(AMPS-DodMAAm) of varying p:q ratios were measured in water and in 0.2 mol/L NaCl. The ratio of the reduced viscosities in water and in 0.2 mol/L NaCl are plotted against the DodMAAm content of the copolymer (Fig. 2). The reduced viscosity reflects the hydrodynamic size of polymer occupied in solution. The hydrodynamic size of copolymer containing less than 40 mol % of DodMAAm decreases gradually with increasing DodMAAm content. When the DodMAAm content is lower than 20 mol %, the polymer chains are extended. In a DodMAAm content region between 40 to 66 mol %, the hydrodynamic size becomes small and almost constant, regardless of its copolymer composition. This suggests that the hydrodynamic size can keep its own specific size. The polymer containing more than 67 mol % of DodMAAm can be larger in size. A sharp increase in the viscosity at >67 mol % DodMAAm may indicate an extensive intermolecular association. Since the polymers containing from 40 to 66 mol % DodMAAm show an almost constant hydrodynamic size, we chose a polymer (64 mol % DodMAAm) for conformational analysis using the static light scattering method. Because this polymer is soluble not only in water but also in ethanol, the measurements were done in both the solvents. The weight-average molar mass (M_w) is 4.0×10^4 and the radius of gyration is 25 nm in ethanol; however, the



Figure 1 Poly(AMPS–DodMAAm).



Figure 2 Relationship between the ratio of reduced viscosities in water and in 0.2 mol/L NaCl and the DodMAAm content in poly(AMPS-DodMAAm). Polymer concentration is 0.5 g/dL at 25°C.

apparent M_w is 4.8×10^5 , the radius of gyration is 23 nm, and the average hydrodynamic radius (R_h) is 25 nm in water. These result show that (1) the molar mass in water was 12 times as large as that in ethanol; (2) the radius of gyration in water was almost the same as that in ethanol; and (3)the ratio of the radius of gyration to the hydrodynamic radius was 0.92. Therefore, it was suggested that the polymer was random coil in ethanol and that the polymer in water shrinked and associated with each other, thus forming interchain aggregates. The density of the aggregates ρ $= M_w/[(4/3)\pi N_A R_h^3]$ is 0.01 g/cm³, where N_A is Avogadro's number. So that the packing of the interchain aggregates is relatively loose.^{15–17} A conceptual illustration of polymer conformation in both solutions is shown in Figure 3.

To investigate an effect of polymer composition on solubilization properties, the solubilization of dl- α -tocopherol acetate (as a solubilizate) was checked. Polymers containing less than 50 mol % of DodMAAm were unable to solubilize dl- α -tocopherol acetate. This result suggests that the contents of hydrophobic parts that surround dl- α -tocopherol acetate are poor. On the other hand, the polymer containing 50 to 70 mol % of DodMAAm could solubilize dl- α -tocopherol acetate. The polymers encapsulated dl- α -tocopherol acetate in their hydrophobic domains of interchain aggregates. Poly(AMPS–DodMAAm) = 36 : 64 gave the most transparent solution.

To investigate that the quantity of a solubilizate solubilized in the poly(AMPS-DodMAAm) = 36 : 64, the solubility of methyl cinnamate was



Figure 3 A conceptual illustration of polymer conformation: (a) the polymer in ethanol, and (b) the polymer in water. The spoonlike symbol (—) represents DodMAAm.

measured. Since dl- α -tocopherol acetate was unsuitable for this experiment because of its extremely low solubility, methyl cinnamate, which is more hydrophilic and more soluble in water, was employed as a solubilizate in this experiment. The relationship between the concentration of methyl cinnamate and the stirring time is shown in Figure 4, which shows that methyl cinnamate rapidly dissolved in 1 w/w % ethanol solution. It is found that the methyl cinnamate concentration in solution in the presence of the polymer is higher than that in its absence. It is considered that a difference in the methyl cinnamate concentrations with and without the poly-



Figure 4 The time course of methyl cinnamate concentration at room temperature. The closed circle (\bigcirc) and the open circle (\bigcirc) represent methyl cinnamate concentration in 1 w/w % ethanol with and without poly(AMPS-DodMAAm), respectively.



Figure 5 Relationship between the I1/I3 ratio and the ethanol concentration. The closed circle (\bigcirc) and the open circle (\bigcirc) represent the I1/I3 ratio of solution with and without poly(AMPS-DodMAAm), respectively. Pyrene concentration is 5.9×10^{-6} mol/L.

mer in 1 w/w % ethanol indicates solubilizing ability of the polymer. It was found that 0.1 g of the polymer can solubilize 0.01 g of methyl cinnamate.

To investigate the effect of ethanol on the solubilizing ability of poly(AMPS-DodMAAm) = 36: 64, pyrene was added into a mixture of the polymer, ethanol, and water. The fluorescence spectra of pyrene were measured because the fluorescence spectra can provide useful information about the nature of local environments. Figure 5 shows the relationship between the I1/I3 ratio and the ethanol concentration in aqueous solutions. The I1/I3 ratio of ethanol solution without the polymer decreases with an increase in the ethanol concentration. On the other hand, the I1/I3 ratio of the solution with the polymer is 1.08 in pure water and gradually increases to 1.46 at 30 w/w % ethanol, and the ratios are almost the same as those of the solutions without the polymer at >40 w/w % ethanol. The polymer can form the interchain aggregates at ethanol content < 30w/w %, showing low I1/I3 ratios (<1.46), but the polymer may not be able to form the interchain aggregates at >40 w/w % ethanol.

The stability of solubilized solutions containing dl- α -tocopherol acetate prepared from poly-(AMPS–DodMAAm) = 36 : 64 were investigated. Figure 6 shows that the time course of the solution turbidity at various temperatures. If the solution was stored at 50°C, the turbidity showed a constant value for 4 weeks. This means that the interchain aggregates formed from the polymer could disperse completely. If the solution was



Figure 6 Turbidity change of solubilized solution. The components in the solution are poly(AMPS–DodMAAm) (0.1 g), dl- α -tocopherol acetate (0.05 g), antiseptic (0.1 g), ethanol (1 g), and water (98.75 g). The circle (\bullet), the triangle (\blacktriangle), and the square (\blacksquare) represent the turbidity of the solution, at 0°C, room temperature, and 50°C, respectively.

stored at room temperature, the turbidity increased in the first 2 weeks and showed a constant value for the next 2 weeks. This means that the interchain aggregates could aggregate moderately, showing an increase in the turbidity for 2 weeks. If the solution was stored at 0°C, the turbidity increased over a period of 4 weeks. This means that the polymers could aggregate for 4 weeks without reaching the constant value. To suppress the time-dependent intermolecular association, the polymer was weakly crosslinked. The structure of crosslinked poly(AMPS–DodMAAm) = 36: 64 is shown in Figure 7. The crosslink ratios of the polymer were 0.25, 0.5, 1.0, or 1.5 mol %. The solubilized solutions were prepared with these crosslinked polymers, and the solution turbidities were monitored for a month. Figure 8



Figure 7 Crosslinked poly(AMPS-DodMAAm).

exhibits time course of the turbidity in the presence of the crosslinked polymers. The crosslinked polymers improved the stability of dl- α -tocopherol acetate solubilized solutions and gave more transparent solutions than that with the without crosslinking (Fig. 1).

Surfactant molecules in conventional micelles are rapidly replaced with free surfactant molecules in the solution, thus forming so-called "dynamic micelles." On the other hand, micelles formed from amphiphilic polymers, such as poly-(AMPS-DodMAAm), are not dynamic micelles but "static micelles."^{7,11} It is speculated that solubilizates encapsulated in static micelles can be released gradually. Hence, we examined sustained release properties of the static micelles using a perfume (limonene) solubilized in hydrophobic domains of the micelles. In this experiment, the release rate of the perfume from the interchain aggregates of poly(AMPS-DodMAAm) was compared with that from the micelles of nonionic surfactant polyoxyethylene(60) hydrogenated castor oil. Changes in the perfume intensity with time are exhibited in Figure 9. The initial perfume intensity is assumed to be 1.0. Although the polymer and the surfactant have almost the



Figure 8 The time course of the turbidity of the solubilized solution with the crosslinked poly(AMPS–DodMAAm) at room temperature. The components in the solution are crosslinked poly(AMPS–DodMAAm) (0.1 g), dl- α -tocopherol acetate (0.05 g), antiseptic (0.1 g), ethanol (1 g), and water (98.75 g). The closed triangle (\blacktriangle) represents the turbidity of the solution with polymer with 0% crosslinked ratio; the open circle (\bigcirc), that with 0.25%; the closed circle (\blacklozenge), that with 0.5%; the closed square (\blacksquare), that with 1.0%; the open square (\Box), that with 1.5%.



Figure 9 The time course of the perfume intensity at room temperature. The components in the solution are solubilizer (0.1 g), limonene (0.01 g), antiseptic (0.1 g), ethanol (1 g), and water (98.79 g). The closed bar (\blacksquare) represents the perfume intensity from the solubilized solution with poly(AMPS-DodMAAm); the open bar (\Box), that with polyoxyethlene(60) hydrogenated castor oil.

same perfume intensity at initial, the perfume intensity of solution with the polymer is stronger than that of solution with the surfactant at 40 min. This result suggests that poly(AMPS–Dod-MAAm) shows an excellent function of sustained releasing perfume, which was delivered from the static micelles.

CONCLUSIONS

To develop a new polymer that can solubilize cosmetic ingredients, amphiphilic polyelectrolytes were synthesized. It was found that poly(AMPS-DodMAAm) synthesized with AMPS (a hydrophilic monomer) and DodMAAm (a hydrophobic monomer) can show an excellent solubilizing ability. The results of the static light scattering measurement unveiled that the polymer dispersed in ethanol and formed the interchain aggregates due to their intermolecular association through hydrophobic interaction each other in water. The mechanism of solubilization with poly(AMPS-DodMAAm) can show that solubilizates were encapsulated in hydrophobic domain inside the interchain aggregates. The pyrene fluorescence experiment showed that poly(AMPS-DodMAAm) had strong hydrophobic domains in lower than 30 w/w % ethanol aqueous solution. Although the solubilized solution became turbid with time due

to intermolecular association, the moderately crosslinked poly(AMPS–DodMAAm) had an excellent solubilization properties and improved the stability of solution than noncrosslinked polymer because of its suppressing ability for the excess amount of intermolecular association. It was found that poly(AMPS–DodMAAm) has an excellent function of sustained perfume as a novel characteristic of polymer solubilizer.

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