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The micellar properties of the poly(oxyethylene)–poly(oxypropylene) copolymer Pluronic F127 in water and electrolyte solution

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Summary

The micellar properties of the ABA poly(oxyethylene)–poly(oxypropylene) block copolymer Pluronic F127 have been examined in water and electrolyte solution by photon correlation spectroscopy, total intensity light scattering and viscometric techniques. The hydrodynamic micellar radius in water, as calculated from diffusion data at the critical micelle concentration, remained constant at 10.2 ± 0.1 nm, over the temperature range 35–45°C. Viscometric studies, however, showed a progressive dehydration of the micelles with temperature increase and it is clear from total intensity light scattering that this dehydration is accompanied by a concomitant increase in anhydrous volume such that the overall hydrated volume is unaffected by temperature change. Increase of solution concentration above about $10\ \text{g} \cdot \text{dl}^{-1}$ over this temperature range caused a marked increase of mean micellar size and of the polydispersity of micellar sizes, indicative of the onset of gelation. The influence of temperature on micellar size and hydration was less pronounced in the presence of $0.5\ \text{mol} \cdot \text{dm}^{-3}$ sodium chloride and gelation commenced at higher solution concentrations. The relevance of these studies to the thermal gelation of this poloxamer is discussed.

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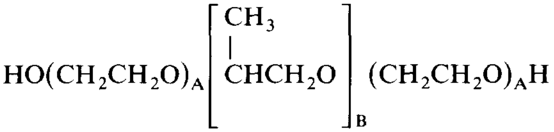
Introduction

Concentrated solutions (> 20%) of the poly(oxyethylene)–poly(oxypropylene)–poly(oxyethylene) block copolymer Pluronic F127 (Poloxamer 407) undergo reversible gelation on warming to body temperature. Recent work has been concerned with a determination of the properties of the gels and their in vitro release characteristics (Chen-Chow, 1980; Chen-Chow and Frank, 1981; Miller and Drabik, 1984). Since the gels are micellar, it is possible to elucidate the mechanism of gelation by an examination of changes in the properties of the micelles as temperature is increased. Rassing and Attwood (1983) have reported a pronounced increase of micellar aggregation number and decrease of critical micelle concentration (cmc) over the temperature range 30–40°C. Rassing and coworkers (1984) have interpreted ultrasonic relaxation and ^{13}C-NMR measurements on dilute solutions in terms of conformational changes related to alterations in the orientation of the methyl group side chains of the poly(oxypropylene) polymer chains constituting the core of the micelle. These workers have proposed that such conformational changes are accompanied by expulsion of the hydrating water from the micelles as the temperature is increased. In the present study we have investigated this proposed change in micellar hydration using photon correlation spectroscopy, light scattering and viscometric techniques and have determined the effect of added electrolyte on the micellar properties over the temperature range associated with gel formation.

Materials and Methods

Materials

Pluronic F127 was a gift from Pechiney Ugine Kuhlmann, and was used as received. F127 is an ABA block copolymer containing approximately 70% oxyethylene with a nominal molecular weight of 1.15×10^4 and general formula:



$$\mathrm{HO(CH_2CH_2O)_A}\left[\begin{array}{l}\mathrm{CH_3}\\ |\\ \mathrm{CHCH_2O}\end{array}\right]_{\mathrm{B}}\mathrm{(CH_2CH_2O)_AH}$$

Methods

Photon correlation measurements were carried out using a Malvern K7027 correlator with 26 delay channels arranged in geometric progression in conjunction with a 2 W Argon ion laser at 488 nm. All measurements were performed at an angle of 90° to the incident beam. Solutions were clarified by ultrafiltration through 0.22 μm milipore filters.

Viscosity measurements were performed using a rotational bob and cylinder method (Epprecht-Rheomat 15) and by capillary viscometry using a suspended level viscometer. Partial specific volumes were calculated from density measurements made using a digital density meter (Paar DMA O2C).

Results and Discussion

Effect of temperature on micellar properties in aqueous solution

Fig. 1 shows the concentration dependence of diffusion coefficient at low concentrations. Plots were linear at each temperature and were extrapolated to the critical micelle concentration to yield the values of limiting diffusion coefficient, D_0, given in Table 1. Hydrodynamic radii, r_h, calculated using the Stokes-Einstein equation were constant at 10.2 ± 0.1 nm. This constancy of micellar size is in marked contrast to previous results from total intensity light scattering (Rassing and Attwood, 1983) which indicated a pronounced increase of weight-average aggregation number over this temperature range. In view of the well-known variability between samples of commercially produced poloxamers, total intensity light scattering measurements were carried out on the sample under investigation to verify this temperature effect. The data are presented in Fig. 2 as plots of the light scattering intensity at a scattering angle of 90°, S_{90}, as a function of solution concentration. The angular scattering envelopes were symmetrical between scattering angles of 30° and 150° indicative of spheroidal micelles. The values of aggregation number N in Table 1 increase with temperature increase as noted in the earlier study although N values were of smaller magnitude than those of the previous sample. In order to determine the cause of the apparent discrepancy between photon correlation and total intensity light scattering results, the effects of temperature on micellar hydration was examined, since the two techniques yield hydrated and anhydrous dimensions, respectively. Rotational viscometric methods gave linear relationships between shear strain and shear stress indicating Newtonian flow properties in solutions of concentrations up to at least 5 $g \cdot dl^{-1}$. Both capillary and rotational viscometric

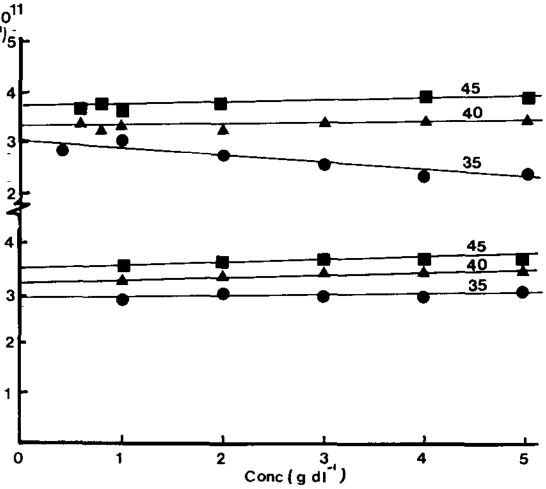


Fig. 1. Diffusion coefficient, D, as a function of solution concentration in water (upper graphs) and 0.5 $mol \cdot dm^{-3}$ sodium chloride (lower graphs) at the temperatures indicated.

TABLE 1

EFFECT OF TEMPERATURE ON THE MICELLAR PROPERTIES OF PLURONIC F127 IN WATER AND ELECTROLYTE SOLUTION

Temperature (°C)	Solvent	D_0 (10^{11} $m^2 \cdot s^{-1}$)	$[\eta]$	r_h (nm)	r_a (nm)	Aggregation number N
35	H_2O	3.1	20.8	10.1	4.8	3.2
	0.5 M NaCl	2.9	16.7	10.6	5.4	9.3
40	H_2O	3.4	18.5	10.3	5.1	9.4
	0.5 M NaCl	3.2	15.5	10.4	5.4	15.6
45	H_2O	3.8	14.0	10.2	5.3	12.0
	0.5 M NaCl	3.5	14.0	10.7	5.8	15.6

techniques were used in the determination of the intrinsic viscosity $[\eta]$ at each temperature. Data were plotted according to:

$$\eta_{sp}/c = [\eta] + [\eta]^2 K_H c$$

where η_{sp} is the specific viscosity, K_H the Huggin's constant and c the concentration ($g \cdot dl^{-1}$) (see Fig. 3). Micellar hydration, δ, was calculated from the viscosity data using the Oncley equation, $[\eta] = \nu(\bar{v} + \delta v^0)$; a value of 2.5 being assigned to the viscosity increment ν assuming micellar sphericity. The partial specific volume, $\bar{v}$, was determined from density measurements. Hydration levels (See Fig. 4) are far higher than can be accounted for solely by hydrogen bonding to ether oxygens of the poly(oxyethylene) chains and indicate considerable mechanical entrapment of water by these chains. Temperature increase causes pronounced micellar dehydration, in

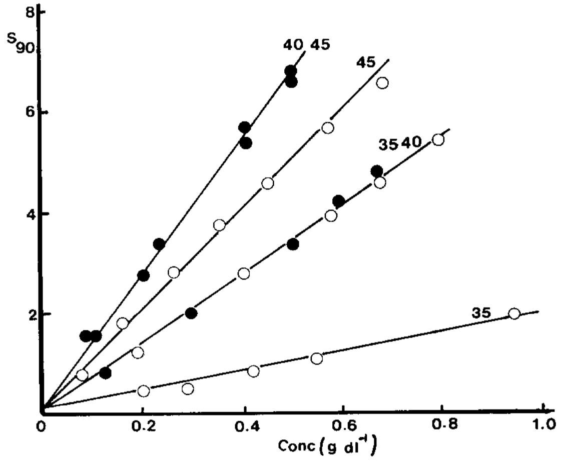


Fig. 2. Concentration dependence of the light scattering ratio, S_{90}, in (○) water and (●) in 0.5 mol·dm^{-3} sodium chloride at the temperatures indicated.

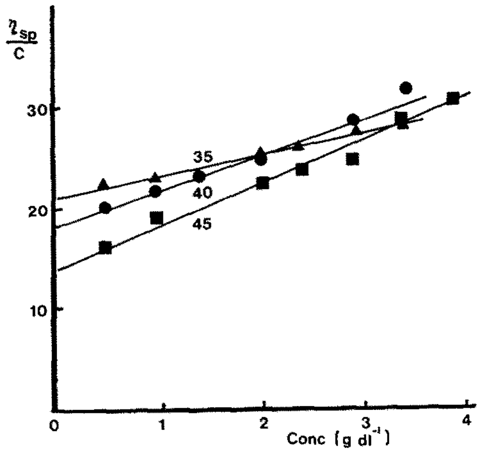


Fig. 3. Variation of reduced viscosity with concentration in aqueous solution at the temperatures indicated.

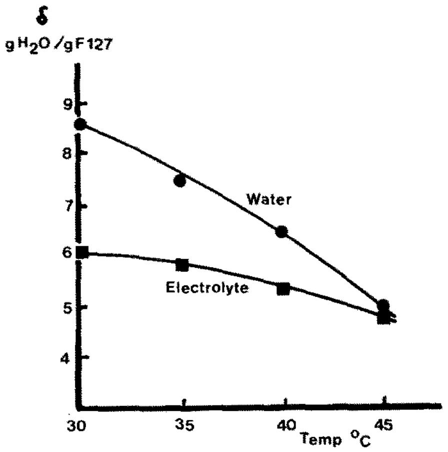


Fig. 4. Variation of micellar hydration, δ, with temperature in water and 0.5 mol·dm^{-3} sodium chloride.

agreement with the findings of Rassing et al. (1984). Estimated values of the anhydrous radius, r_a, from a combination of the r_h values from photon correlation studies and the hydration values from viscosity are included in Table 1. The increase in the r_a values with temperature is in qualitative agreement with the increase in the anhydrous micellar size as determined from total intensity light scattering studies. Clearly, temperature increase is causing a simultaneous decrease in micellar hydration and increase in aggregation number such that the hydrodynamic micelle is remaining constant in size.

Effect of concentration on micellar properties in aqueous solution

Photon correlation studies on solutions of higher concentration showed a pronounced apparent decrease in diffusion coefficient as the concentration exceeded 10 $g \cdot dl^{-1}$. Interpreting these changes exclusively in terms of micellar growth, i.e. ignoring the effect of micellar interaction on the magnitude of D, we obtained the variation of r_h with concentration shown in Fig. 5. At concentrations in excess of 20 $g \cdot dl^{-1}$, evidence of gel formation was visibly apparent in the solutions. Two theoretical approaches were used to asses the polydispersity of micellar sizes in these solutions. The interpretation of photon correlation data for polydisperse systems involves the direct inversion of the equation:

$$g(\tau) = \int_0^{\infty} G(\Gamma)\exp(-\Gamma\tau)\mathrm{d}\Gamma \qquad (1)$$

in order to derive the distribution function $G(\Gamma)$. In Eqn. 1, $g(\tau)$ is the measured correlation function: $\Gamma = D_{app} \cdot q^2$; D_{app} is the apparent translational diffusion coefficient; q is magnitude of the scattering vector and τ is the correlation decay time. In the method of cumulant expansion (Koppel, 1972), Eqn. 1 is expanded about $\bar{\Gamma}$, the mean of $G(\Gamma)$ giving:

$$g(\tau) = \exp(-\bar{\Gamma}\tau)\left(1 + \frac{\mu_2\tau^2}{2!} - \frac{\mu_3\tau^3}{3!} + \ldots\right) \qquad (2)$$

where $\mu_2 = \int(\Gamma - \bar{\Gamma})^2 \cdot G(\Gamma)\mathrm{d}\Gamma$, represents the second moment about $\bar{\Gamma}$. It may be

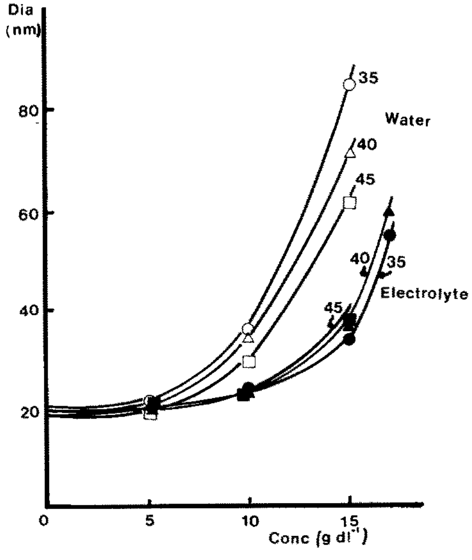


Fig. 5. Apparent micellar diameter as a function of concentration in water and 0.5 $mol \cdot dm^{-3}$ sodium chloride at the temperatures indicated.

TABLE 2

EFFECT OF CONCENTRATION ON THE POLYDISPERSITY OF MICELLAR SIZE AS EXPRESSED BY THE PUSEY Q FACTOR AND SIZE DISTRIBUTION CURVES DERIVED FROM THE EXPONENTIAL SAMPLING TECHNIQUE

Concentration ($g \cdot dl^{-1}$)	Q			Peak half-widths (nm)		
	35°C	40°C	45°C	35°C	40°C	45°C
0.4	0.16	–	0.09	24	–	–
0.8	–	0.13	–	–	25.5	29
10.0	0.27	0.21	0.19	43.5	33	34
20.0	0.54	0.52	0.49	58	55	50.5

shown that $\bar{\Gamma}$ gives the mean decay constant and the normalised variance of the distribution may be approximated to,

$$Q = \mu_2/\bar{\Gamma}^2 \qquad (3)$$

Values of Pusey Q factor are given in Table 2 and indicate an increasing polydispersity of micelle size with increase of concentration at each temperature.

An alternative inversion technique has been proposed by Ostrowsky et al. (1981) in which $G(\Gamma)$ is expressed in terms of eigenfunctions and eigenvalues of the Laplace transform. This method of analysis is particularly suited to the exponential sampling method used in this investigation. Fig. 6 shows typical size distribution curves derived by this technique for concentrations of 0.4 and 20 $g \cdot dl^{-1}$ over the temperature range studied. For the sake of clarity, curves for intermediate concentrations are not shown. As may be seen from this figure and from the half-peak widths of Table 2, there is a marked broadening of the curves with increase of concentration at each temperature.

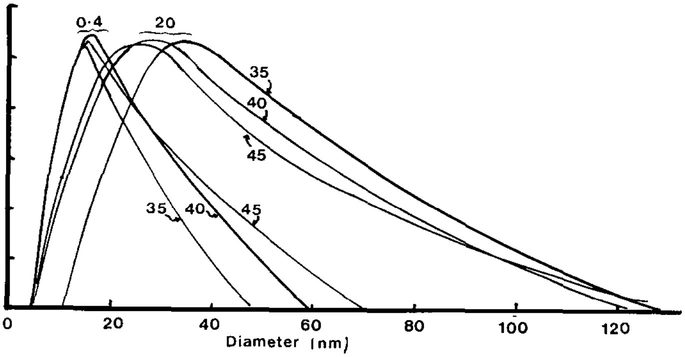


Fig. 6. Micellar size distribution curves for aqueous solutions of concentrations 0.4 and 20 $g \cdot dl^{-1}$ at the temperatures indicated.

Effect of electrolyte on micellar properties

A linear variation of D with solution concentration in the presence of 0.5 $\text{mol}\cdot\text{dm}^{-3}$ NaCl was noted over the temperature range 35–45°C (Fig. 1) with D_0 values as given in Table 1. Hydrodynamic radii were constant with a mean value of 10.6 nm; about 4% higher than the mean value in the absence of electrolyte.

The influence of electrolyte on the temperature dependence of the micellar hydration, δ, was determined by capillary viscometry. δ values, calculated from the intrinsic viscosities of Table 1 are plotted as a function of temperature in Fig. 4. Comparison with the analogous graph in the absence of electrolyte shows that although an increase of temperature results in dehydration of the micelles in the electrolyte solution, this effect is much less marked than that noted in water.

Analysis of the light scattering curves in 0.5 $\text{mol}\cdot\text{dm}^{-3}$ NaCl (Fig. 2) showed a much less pronounced temperature effect on anhydrous micellar size than was noted in water. (Table 1). Hence, we conclude that the effect of the added electrolyte is to reduce the influence of temperature on both micellar size and hydration.

The consequences of these differences in micellar properties on the gelation process is seen from photon correlation measurements in more concentrated solutions. Fig. 5 shows that the very pronounced increase of micellar size which corresponds to the onset of gelation occurs at higher solution concentration in the presence of electrolyte.

Conclusion

Our studies provide a further insight to the process of gelation of this block copolymer. Temperature increase has been shown to result in micellar dehydration. This is in agreement with the earlier ultrasonic velocity and ^{13}C-NMR studies of Rassing et al. (1984) who have attributed the cause of dehydration to conformational changes in the poly(oxypropylene) chains leading to expulsion of hydrating water. Our investigations have shown that this dehydration is accompanied by a concomittant increase in the anhydrous volume of the micelle such that the overall hydrated volume is not significantly altered by temperature increase. Increase of solution concentration over this temperature range leads to an apparent dramatic increase of micellar size and polydispersity. It is suggested that such changes are a consequence of interactions between poly(oxyethylene) chains of adjacent micelles which, as a result of their dehydration, experience increased friction with a resulting tendency to form multimolecular units leading eventually to gel formation. Although Pluronic F127 will form gels in the presence of added electrolyte, gelation commences at higher solution concentrations than observed in water.

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