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ORIGINAL CONTRIBUTION

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Phase conditions, hydrodynamic features and salt influence in the polymer–amphiphile interaction for the EHEC/SDS/water system

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Abstract Two fractions of ethyl(hydroxy)ethyl cellulose, EHEC, and their interactions with sodium dodecyl sulphate, SDS, have been investigated. The effect of salt on these interactions was explored. The more hydrophobic fraction exhibits a cloud point (CP) of 30 °C, and the more hydrophilic fraction has a CP around 65 °C. The properties of the systems were studied by means of hydrodynamic (viscosity), equilibrium dialysis and cloud point measurements. Dye solubilization was used to obtain indications of cluster formation on the polymer backbone. The equilibrium dialysis shows a steep binding beginning at a critical surfactant concentration indicating a cooperative effect in the EHEC/SDS/water system. It is found that when the degree of binding is moderate and only 10–20% of the value at saturation, the specific viscosity effects occur and solutions containing high polymer concentrations pass a marked maximum in viscosity. It is shown that the maximum in viscosity and the coil–coil interaction, expressed as Huggins constant, k_H, appear a composition with the same fractional amount of SDS adsorbed to both EHEC fractions. It was found that the onset of redistribution and increase in viscosity were shifted to higher SDS concentrations, although still below the normal CMC, for the EHEC fraction with a high CP. When small amounts of salt are present in the EHEC/SDS/water solutions, the CP curves develop a pronounced minimum at low SDS concentrations. The redistribution of SDS to the polymers starts immediately in the presence of salt, but the viscosity of the solutions is affected only in a very narrow composition interval.

Key words Ethyl hydroxyethyl cellulose – sodium dodecyl sulphate – interaction – sodium chloride – viscosity – equilibrium dialysis

Introduction

The interaction between uncharged water soluble polymers and anionic surfactants (amphiphiles) has attained much interest in recent years [1–9] and also been the subject of investigation in this laboratory as reported in a series of previous publications [10–14]. These studies have mainly been focused on the system ethyl hydroxyethyl cellulose (EHEC)/sodium dodecyl sulphate (SDS)/water and in particular on the properties in absence of salt and for one fraction of EHEC with a fairly low cloud point. These basic studies were initiated for two reasons. One was the specific rheological properties of these systems giving extremely high viscosities in certain composition ranges, an interesting feature for many technical applications but for which the physico-chemical explanation at the time was still largely unclear. Another reason was the importance to understand more precisely the interaction between drug molecules, often amphiphilic in nature, and polymer matrices. This is a question of increasing interest for the development of pharmaceutical formulations.

In the present paper two factors will be investigated in this perspective, the addition of salt to the system and using an EHEC with a high CP. It is shown that the two EHEC fractions interact with SDS in the same way although the observed effects are more pronounced for the polymer with a low CP. When salt is added to the system, the rheology of the respective polymer/surfactant solution differs from each other. The consequences of added salt on the polymer–amphiphile interaction has been explored up to the point of phase separation.

The main system properties studied are viscosity, dialysis equilibrium, phase separation and cloud point. In order to test for hydrophobic clusters the redistribution of dyes has also been followed.

Experimental section

Materials

The following chemicals were used as supplied: sodium dodecyl sulphate (SDS), 99.9% pure, Lot 668260, Merck, Darmstadt, Germany. Radioactive SDS, ^{35}S, Lot JC 1981, Batch B9435, Amersham, England. Sodium chloride, 99.5% pure, lot 825 KO4170404, Merck, Darmstadt, Germany. Oil Orange SS (α-Toluenazo-β-Naphtol), Tokyo Kasei Inc., Tokyo, Japan. Ethyl(hydroxyethyl) cellulose (EHEC) fraction CST-103 $M_n = 480\,000$, $MS_{eo} = 0.7$, $DS_{ethyl} = 1.5$, L920 32, and fraction E230G, $M_n \approx 5\,000\,000$, $MS_{eo} = 0.9$, $DS_{ethyl} = 0.9$, L92003, Berol Kemi, Stenungsund, Sweden. The fraction called CST-103 will hereafter be referred to as CST. The EHEC stock solution was freed from remaining salt by dialysis in tube membranes (MW cut-off approximately 10 000) from Union Carbide, Chicago IL. The stock solution of EHEC was filtered through 0.8 μm Millex-AA filters, Millipore SA, Molsheim, France. All solutions were made with MilliQ water (Millipore) as solvent.

Preparation of solutions

Stock solutions

The stock solutions of CST and E230G, respectively, were prepared according to a standard technique described elsewhere [10, 15]. The stock solutions of SDS, DBS and NaCl were prepared by dissolving the substances in water to appropriate concentrations. Radioactive SDS was dissolved in water and diluted to provide the required activity for the experiments.

Cloud point, viscosity and dye solubilization

Appropriate amounts of the EHEC stock solution were added to diluted surfactant solutions. In the solutions containing salt, small portions of NaCl stock solution was added to the SDS solutions before the polymer was added. All solutions measured at room temperature were prepared 24 h in advance to let the time-dependent processes settle [11].

Dialysis

A complete dialysis study of a certain polymer–surfactant system comprised a series of solutions, i.e., a polymer solution of a specific concentration and a set of surfactant solutions. The polymer solution was prepared by weighing EHEC stock solution into water to the desired concentration. The surfactant solutions were prepared by diluting the stock solution of SDS with appropriate amounts of water to obtain solutions with concentrations from below CMC up to several times CMC. In the dialysis experiments containing SDS, small amounts of radioactive SDS were added to the surfactant solutions until the activity equalled 50 000 dpm/ml. In the experiments with salt present, the EHEC stock solution was added to an appropriately diluted NaCl stock solution. Sodium chloride was also added to the SDS solutions so the concentration equalled that of the polymer solution.

Surface tension

A series of solutions was prepared for a surfactant by weighing the required amount of SDS stock solution into water. To determine the CMC of SDS with salt present, a series of solutions was made with constant [NaCl] and varying [SDS] for each salt concentration.

Methods

Viscosity

The viscometric measurements were carried out in ordinary Ostwald capillary viscometers with a flow time for water of approximately 100 s at 20 °C. The samples were thermostated in the viscometer, submerged in a water bath for 15 min before measurements were made. Corrections for kinetic and end effects were found to be unnecessary [16].

Cloud point

The cloud point of the solutions was determined by visual observation in glass tubes and taken as the temperature when the last visible sign of clouding in the solution disappeared upon cooling. Depending on whether the cloud point is determined during heating or cooling of the sample, on the rate of heating or cooling, and if the transition is detected visually or photometrically, the exact CP value may differ. Also, the actual clouding process of a polymer solution containing a surfactant may differ from that in a pure polymer solution. The most important information is the relative change in cloud point, and hence the measurements must be performed in a well standardized way.

Dye solubilization

An excess of dye was added to EHEC/SDS solutions and put on a rotating table at room temperature (Infors AG Ch-4103 Bottmingen). To separate off the dye not solubilized by the EHEC/SDS complex, the solutions were centrifuged. The absorbance of the supernatant was determined spectrophotometrically at $\lambda = 495$ nm (Spectronic Genesys 5, Milton Roy Company, New York, USA). The supernatants with an absorbance exceeding 1.3 were diluted. The results presented are all recalculated to undiluted solutions. Test experiments showed that the content of polymer and surfactant in the samples did not affect the spectral properties of Oil Orange SS.

Density

Solution densities were determined in a digital densiometer DMA 02C from Anton Paar K.G., A 8054 Graz, Austria, according to Kratky et al. [17]. The accuracy exceeds ± 0.0015 kg/m^3.

Dialysis

The equilibrium dialysis experiments were carried out in specially designed cells, with retentate and dialysate compartments separated by a SPECTRA/POR membrane (MW cut-off 12 000–14 000). The cell design was similar to the one used by Fishman and Eirich [18]. Before filling, the cells were thoroughly rinsed with deionized water. The water was then removed and the compartments were filled with the actual measuring solutions. Each series of experiments was performed with polymer solutions of constant concentration placed in the retentate compartments, but with surfactant solutions of various concentrations placed into the respective dialysate compartments. For each composition (EHEC/SDS and EHEC/SDS/NaCl) the experiments were made in triplicate. The cells were left to equilibrate in an air thermostat for a week. Results from previous [13] and present experiments showed that 3 to 4 days were sufficient, but 1 week was allowed for cells to reach equilibrium in order to be certain that reliable results were obtained. After the solutions in the dialysis cells had attained equilibrium, the concentration of surfactant was determined in the dialysate and retentate compartments respectively. The concentration of SDS was determined by scintillation counting. Test experiments showed that the presence of salt or EHEC (or both) did not cause an extinction of the scintillation.

Numerical data handling

Dialysis

The amount of surfactant redistributed to EHEC in the salt-free systems was calculated under the assumptions that the bound ions make no contribution to the ionic activities, that the degree of dissociation is 1, i.e., none of the sodium ions are condensed on the polymer bound S^- clusters, and that the contribution of the Donnan effect is given by standard equations. A chemical potential balance at equilibrium and approximating activities with concentrations gives

$$[\mathrm{Na}^+]_r[\mathrm{S}^-]_r = [\mathrm{Na}^+]_d[\mathrm{S}^-]_d\,, \tag{1}$$

where *r* and *d* denotes retentate (the compartment containing only polymer initially) and dialysate (the compartment containing only surfactant). $[\mathrm{Na}^+]_i$ is the concentration of sodium ions in solution *i*, $[\mathrm{S}^-]_i$ is the surfactant anion concentration in solution *i*. Electrical neutrality on both sides of the membrane requires

$$c_r y + [\mathrm{S}^-]_r = [\mathrm{Na}^+]_r \tag{2}$$

$$[\mathrm{S}^-]_d = [\mathrm{Na}^+]_d\,, \tag{3}$$

c_r being the concentration of EHEC in the retentate compartment expressed as g/l, *y* describes the amount of S^- redistributed to the polymer at equilibrium and expressed as moles of S^- per gram of polymer. Combining Eqs. (1–3) gives

$$[S^-]_r = [S^-]_{d^2}/C_r\,, \tag{4}$$

where

$$C_r = c_r y + [S^-]_r \tag{5}$$

is the total concentration of S^- in the retentate solution r. C_r and $[S^-]_d$ are measured directly in the experiment. Thus y is calculated from

$$y = (C_{r^2} - [S^-]_{d^2})/(c_r C_r)\,. \tag{6}$$

To simplify the writing in figures, y will in the results section be expressed as millimoles per gram of polymer. This will normally give numerical values in the range 0–8. In this calculation procedure where the degree of dissociation, α, is approximated to equal 1, the binding isotherm will contain a small error. In a previous study [13] an average value of α was determined to 0.70 for bound clusters, and 0.40 for free micelles in the bulk solution. Assuming $\alpha = 1$ introduces an error within 10% for the calculated y up to the point of maximum amount of SDS bound to the polymer [13]. The normal micelles which begin to appear in the solution at maximum binding and have a lower degree of dissociation, make it impossible to calculate a correct binding isotherm above the maximum. Since it is difficult to determine α precisely and since it was shown in previous work [13] that up to the maximum the experimentally determined $\alpha < 1$ does not introduce errors that disturb the qualitative picture, $\alpha = 1$ was assumed here. Admittedly, this is an approximation but it will still be sufficiently precise to make a comparison of results possible.

When even small amounts of salt are present in the dialysis solutions the Donnan effect is somewhat suppressed, but it still needs to be corrected for. To avoid the Donnan effect completely the sodium chloride concentration should be at least 0.1 molal [19, 20]. The electrostatic balance in the salt case would be

$$c_r y + [S^-]_r + [Cl^-]_r = [Na^+]_r \tag{7}$$

in the retentate compartment, and in the dialysate compartment

$$[S^-]_d + [Cl^-]_d = [Na^+]_d\,. \tag{8}$$

At equilibrium the chemical potential balance leads to the condition

$$[Na^+]_r[X^-]_r = [Na^+]_d[X^-]_d\,, \tag{9}$$

where

$$[X^-]_i = [S^-]_i + [Cl^-]_i \tag{10}$$

since the Cl^- and S^- ions are indistinguishable as far as their electrical charge is concerned and it will be assumed that they are distributed in the same ratio between the two compartments. This assumption leads to

$$[S^-]_r/[Cl^-]_r = [S^-]_d/[Cl^-]_d\,. \tag{11}$$

In the experiments $[S^-]_d$ and C_r are measured directly. Combining Eqs. (5, 7–11) and assuming equal volumes in the two compartments gives

$$y = \{C_r - ((-b + (b^2 - 4ac)^{1/2})/2a)/c_r\,, \tag{12}$$

where $a = C_r + [Cl^-]_{tot}$, $[Cl^-]_{tot}$ is the sum of $[Cl^-]$ in both compartments, $b = (C_r C_d - [S]_{d^2})$ and $c = -\{[S^-]_{d^3} + ([Cl^-]_{tot} \cdot [S^-]_{d^2})\}$. From this follows

$$[S^-]_r = \{-b + (b^2 - 4ac)^{1/2}\}/2a\,. \tag{13}$$

Viscosity

When EHEC interacts with SDS the rheological properties of the polymer solution are altered. This change depends on the amount of surfactant redistributed to the polymer, y. Also the hydrodynamic volume of EHEC is affected. The intrinsic viscosity, $[\eta]$, is a measure of the hydrodynamic volume of the polymer at infinite dilution and it is obtained by extrapolating the reduced viscosity, $\eta_{red} = \eta_{sp}/c$ to zero polymer concentration, where c is the polymer concentration expressed as mass per unit volume. η_{sp} is defined by

$$\eta_{sp} = (\eta - \eta_0)/\eta_0\,, \tag{14}$$

where η and η_0 are the viscosities of solution and solvent, respectively. In order to relate the hydrodynamic volume to surfactant redistribution the reduced viscosity, η_{red}, was calculated for constant y and the corresponding values of $[\eta]$ were obtained by extrapolation to zero polymer concentration. A measure of the intensity of the polymer–polymer interactions is provided by the value of the Huggins' constant, k_H, which is obtained from the expression

$$\eta_{red} = [\eta] + k_H[\eta]^2 c + \cdots\,. \tag{15}$$

Higher order in the concentration terms have been omitted [21]. Viscosity measurements were made with sets of constant polymer concentration and varying (total) surfactant concentration. Several such sets were measured using different polymer concentrations. The equilibrium between free surfactant and polymer bound surfactant changes when the system is diluted with respect to the polymer concentration keeping the surfactant concentration constant, the reduced viscosity was therefore recalculated to constant y using the expression

$$[\mathrm{SDS}]_{\mathrm{tot}} = c_{\mathrm{r}}y + [\mathrm{SDS}]_{\mathrm{eq}}\,, \tag{16}$$

where $[\mathrm{SDS}]_{\mathrm{eq}}$ is obtained from the dialysis experiments. Thus η_{red} for constant amount of redistributed SDS was extracted from the combined dialysis and viscosity data and extrapolated to zero polymer concentration obtaining $[\eta]$ for the EHEC-SDS complex for a given y. From the same plots k_{H} was obtained for constant y [10].

Results

In order to study the effects of salt on the interactions between the nonionic cellulose derivative EHEC and the negatively charged amphiphile SDS, experiments were performed with various techniques. The measurements at salt-free conditions were made with sets of solutions containing polymer in the concentration range 0–0.40%, the amount of surfactant varying between 0 and 20 mM. The experiments with salt present were performed for a constant polymer concentration, 0.20%, with a NaCl content of 0–5 mM and varying the SDS concentration from 0 to 20 mM. To illustrate the variability of system features even within a class of very similar polymers, two fractions of EHEC were selected that from the general chemical point of view differed only in the values of degree of substitution (DS) and molar substitution (MS), see the section on "Materials". The difference in MS and DS, however, results in properties of the respective polymer that may differ considerably since the balance between hydrophobic and hydrophilic parts within the polymer is altered. This can, for instance, be observed as different values of the cloud point (CP) for the fractions of EHEC.

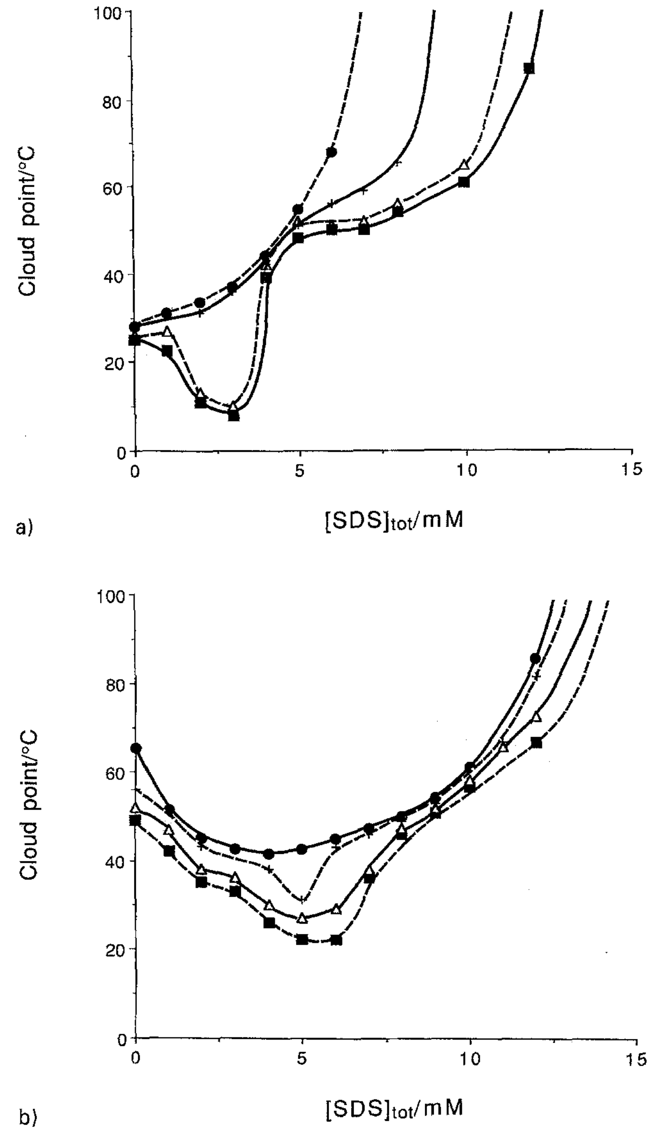

Fig. 1 Cloud point temperature versus the total SDS concentration for 0.20% EHEC with different amounts of NaCl added. (a) for CST; ● no salt added, + 1 mM NaCl, △ 3 mM NaCl, ■ 5 mM NaCl. (b) for E230G; ● no salt added, + 1 mM NaCl, △ 3 mM NaCl, ■ 5 mM NaCl

Cloud point

The cloud point curves of CST and E230G, containing various NaCl concentrations, are given in Fig. 1 as a function of the total SDS concentration, $[\mathrm{SDS}]_{\mathrm{tot}}$. For the CST sample with no salt present, the value of CP increases continuously with added SDS, and the curve displays a strong upward curvature beginning at $[\mathrm{SDS}]_{\mathrm{tot}} \approx 2.5$ mM. For the E230G sample, on the other hand, CP first decreases considerably towards a minimum around 42 °C for $[\mathrm{SDS}]_{\mathrm{tot}} \approx 4$ mM and then increases. Both EHEC samples show the same CP value, 42 °C, at $[\mathrm{SDS}]_{\mathrm{tot}} \approx 3.5$ mM. If salt is added the response is similar for the two samples and a "bulging" minimum in CP develops for such low salt concentrations as 1 to 3 mM NaCl, as seen in Figs. 1a and 1b. It is to be noted that the addition of salt shifts the CP minimum to higher surfactant concentrations but affects the CMC of SDS in the opposite direction, as determined by surface tension measurements. The same pattern is observed for higher polymer concentrations [22]. For E230G the value of CP decreases fairly continuously as salt is added. For CST no change is observed until the salt content is above 1 mM but then the lowering of CP comes rather suddenly. The lowering of CP derives from the change in free energy of the complex polymer–cluster system and its state of solvation in a medium containing an electrolyte. The CP curves for all salt concentrations come together, like in an isobestic point, in a narrow [SDS] region at [SDS] $\approx$ 4.5 mM for CST and [SDS] $\approx$ 8 mM for E230G. The cloud point of pure CST is not affected when salt is added, but for E230G it is lowered markedly.

Viscosity

Figure 2a shows viscosity results in the form of η_{red} vs. $[\mathrm{SDS}]_{\mathrm{tot}}$ for a set of CST concentrations in the range 0.05–0.25%. The values of η_{red} were calculated according to Eq. (14) using the correspondent SDS/water solution as solvent viscosity. The results show that the effect of SDS can be divided into three regions. For SDS concentrations below about 2.5 mM there is no effect on the viscosity. In a middle region between 2.5 and 7 mM the viscosity shows a considerable maximum if the polymer concentration is high enough. For low polymer concentrations there is rather a decrease. It appears as if a transition to viscosity increase occurs at polymer concentration between 0.10 and 0.15%. Others have shown that a considerable increase in viscosity of uncharged polymers can be brought about by the addition of SDS [23–28]. Similar experiments have been performed on the E230G/SDS/water system. Figure 2b presents viscosity data for E230G in terms of η_{red} for sets of constant polymer concentration extending from 0.05 to 0.40% (thus exceeding the concentration of critical overlap, $c_{\mathrm{p}}^{*} \approx 0.26\%$ for the pure polymer) as a function of SDS concentration. The η_{red} curves for the E230G/SDS/water system can also be divided into three parts, each qualitatively similar to those of the CST sample. However, there are important differences. The increase in viscosity is shifted to higher SDS concentrations and the maximum, which is not as pronounced as for CST, occurs in the vicinity of the normal CMC. The viscosity increase is considerably less for the E230G sample with added SDS than for the CST sample. The viscosity measurements with solutions containing EHEC and SDS with added salt can be seen in Figs. 2c and 2d. Compositions with a cloud point below 20 °C were omitted. The concentration 0.20% of EHEC was chosen since this is just sufficient for both CST and E230G to develop a clear viscosity maximum upon addition of SDS. A similar increase in η_{red} of solutions with higher EHEC concentrations upon addition of SDS in the presence of salt have been reported by others [23, 29]. η_{red} for each EHEC/SDS/NaCl/water solution was calculated according to Eq. 14 using as "solvent" viscosity the corresponding SDS/NaCl/water solution. The viscosity first increases for the CST sample with SDS as salt is added, reaches a maximum for about 3 mM NaCl and then decreases as more salt is added, as seen in Fig. 2c. A decrease in η_{red} with added salt for SDS-polymer solutions have been observed by others [30]. There is a slight decrease in η_{red} for the CST samples with low SDS concentrations and 1 mM NaCl. For the E230G sample, on the other hand, the viscosity maximum decreases continuously as salt is added and eventually the maximum disappears and a minimum develops instead, as seen in Fig. 2d. The composition which shows the lowest cloud point and is on the verge of phase separation, gives this minimum in viscosity.

Equilibrium dialysis

The equilibrium dialysis results are presented in Fig. 3 as a plot of y, millimoles of SDS bound per gram of polymer, versus $[\mathrm{SDS}]_{\mathrm{eq}}$, the equilibrium concentration of SDS. The redistribution curves of CST as function of $[\mathrm{SDS}]_{\mathrm{eq}}$ without salt, as can be seen in Fig. 3a, display a foot point at $[\mathrm{SDS}]_{\mathrm{eq}} \approx 2.5$ mM where the onset of redistribution occurs (sometimes referred to as T_1 [9]). The foot point is followed by a steep increase in y up to a maximum in y indicating a cooperative mechanism [9, 31]. At the maximum in y the polymer is assumed to be saturated (this point is sometimes called T_2 [9]). After the maximum in y desorption seems to occur at $[\mathrm{SDS}]_{\mathrm{eq}} \approx 6.5$ mM, i.e., when ordinary micelles begin to form in the bulk solution. The redistribution curves obtained from the dialysis equilibrium experiments of the E230G/SDS/water system show qualitatively similar characteristics as those of the corresponding CST system, although the onset of redistribution occurs at higher SDS concentrations, as seen in Fig. 3b. The redistribution starts at $[\mathrm{SDS}]_{\mathrm{eq}} \approx 5$ mM (as compared to 2.5 mM for CST) and increases almost linearly in a fairly steep way, implying a cooperative mechanism [9, 31], up to a maximum which is lower than that for CST. After the maximum at $[\mathrm{SDS}]_{\mathrm{eq}} \approx 8$ mM, desorption begins. For both EHEC fractions the maximum in y decreases with increasing polymer concentration, and the concentration $[\mathrm{SDS}]_{\mathrm{eq}}$ for which maximum in y occurs decreases with increasing EHEC concentration. Furthermore, the function y vs $[\mathrm{SDS}]_{\mathrm{eq}}$ becomes steeper the higher the polymer concentration, which reflects the increasing cooperativity.

As seen in Fig. 3c compared to Fig. 3a the presence of salt displaces the redistribution to lower surfactant concentrations; both the onset of redistribution as well as the maximum in y occur at lower SDS concentrations than for

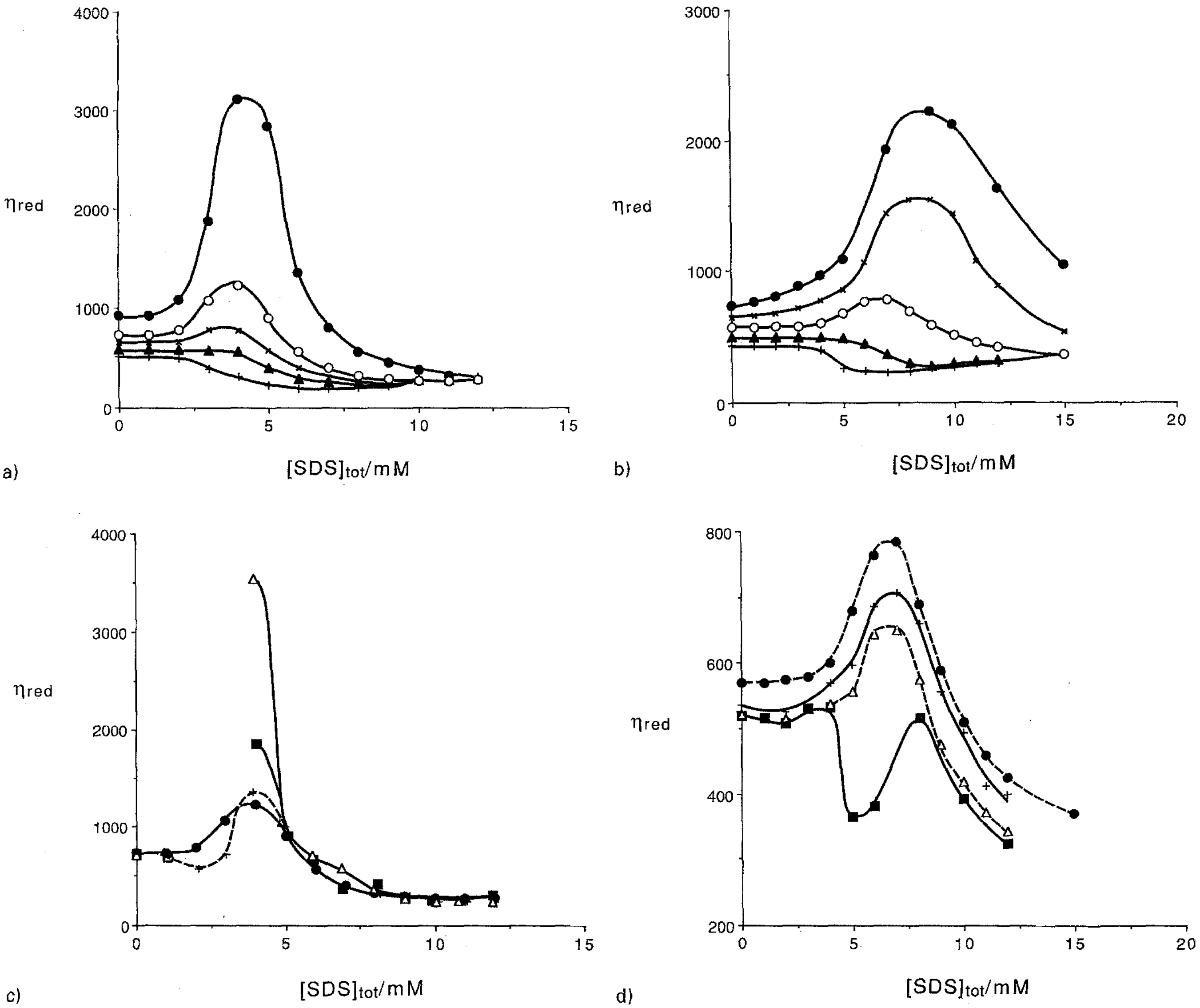

Fig. 2 Reduced viscosity (ml/g) as a function of total SDS concentration for (a) various CST-103 concentrations at 20 °C; + 0.05% CST, ▲ 0.10% CST, × 0.15% CST, ○ 0.20% CST, ● 0.25% CST. (b) various E230G concentrations; + 0.05% E230G, ▲ 0.10% E230G, ○ 0.20% E230G, × 0.30% E230G, ● 0.40% E230G. (c) for 0.20% CST-103 at 20 °C with different amounts of NaCl added; ● no salt added, + 1 mM NaCl, △ 3 mM NaCl, ■ 5 mM NaCl. (d) for 0.20% E230G at 20 °C with different amounts of NaCl added; ● no salt added, + 1 mM NaCl, △ 3 mM NaCl, ■ 5 mM NaCl

salt-free conditions. The dialysis curves for CST/SDS/NaCl/water system can be divided into three parts: The first part describes how the redistribution starts immediately and progresses slowly at low SDS concentrations. At the beginning of the curves representing 0.20% CST with 3 and 5 mM NaCl added respectively, there is a small part where phase separation occurs. Then a "breakpoint" appears (between the foot point (cac) and the maximum) followed by the second part where the redistribution proceeds in a steep way up to a maximum. The third part of the dialysis curve, after the maximum, shows a decrease in redistribution similar to the salt free systems, cf. the discussion below. The dialysis curves for the E230G/SDS/NaCl/water system, as seen in Fig. 3d, display the same shape as those for CST in Fig. 3c, with a lower maximum of binding.

To be able to discuss the polymer–surfactant as well as the polymer–polymer interactions in quantitative terms in the salt-free systems, the viscosity data combined with the results from the equilibrium dialysis experiments were

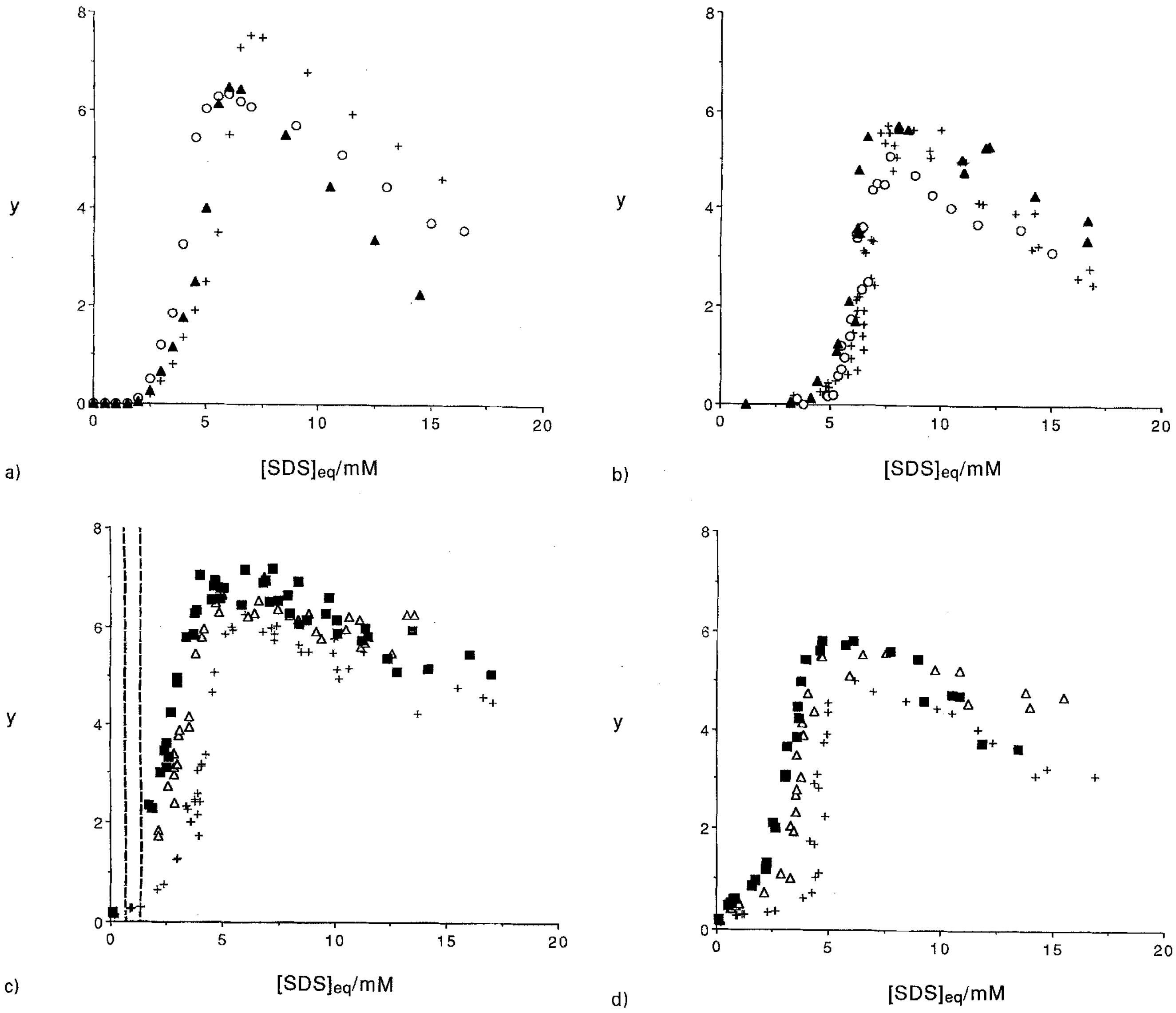

Fig. 3 y (millimoles of SDS redistributed per gram of EHEC) versus $[\mathrm{SDS}]_{\mathrm{eq}}$ for (a) different CST concentrations at 20 °C; + 0.05% CST, ▲ 0.10% CST, ○ 0.20% CST. (b) for different E230G concentrations at 20 °C; + 0.05% E230G, ▲ 0.10% E230G, ○ 0.20% E230G. (c) for 0.20% CST with different amounts of NaCl added. The region between the dotted lines represents the CST/SDS compositions containing either 3 or 5 mM NaCl, which have phase separated; + 1 mM NaCl, △ 3 mM NaCl, ■ 5 mM NaCl. (d) for 0.20% E230G with different amounts of NaCl added at 20 °C; + 1 mM NaCl, △ 3 mM NaCl, ■ 5 mM NaCl

recalculated to η_{red} for constant amount of SDS redistributed to CST using Eq. (16). Thus the intrinsic viscosity, $[\eta]$, and Huggins' constant, k_{H}, could be obtained for constant y according to the procedure described in "Numerical data handling". In Fig. 4 are shown $[\eta]$ and k_{H} as a function of y for CST and E230G respectively. The intrinsic viscosity of CST decreases markedly at very low values of y, and then continues to flatten out, and k_{H} passes through a maximum as seen in Fig. 4a. For E230G the result is comparable with the difference that k_{H} passes through a sharper maximum and $[\eta]$ increase slightly at higher y as seen in Fig. 4b.

Dye solubilization

To provide more information about the SDS redistributed to E230G, dye solubilization experiments were performed on the E230G/SDS/water system. Several investigators have reported solubilization of hydrophobic dyes by

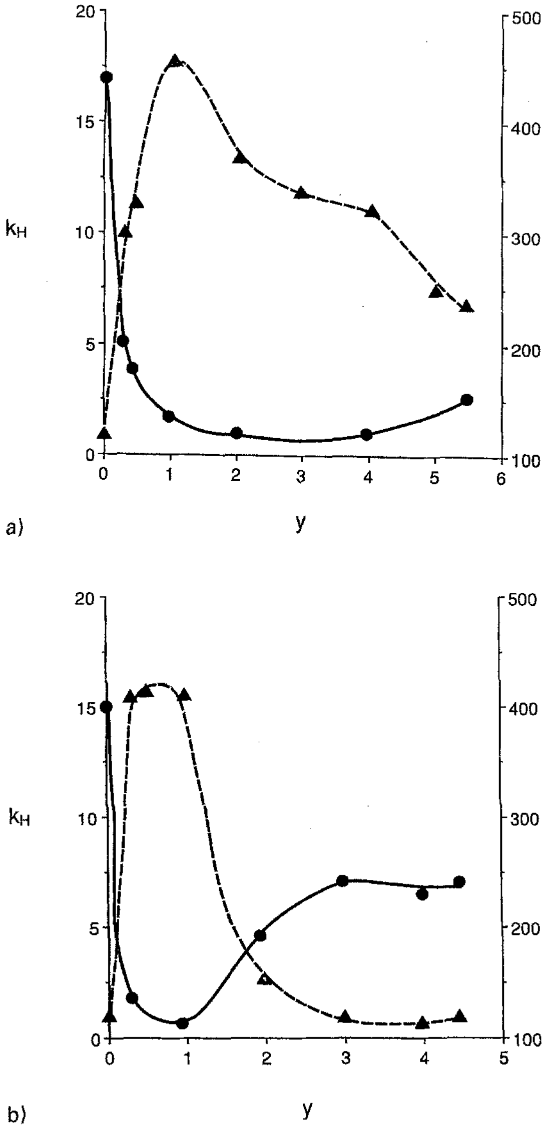

Fig. 4 Intrinsic viscosity, $[\eta]$ (ml/g), and Huggins' constant, k_H, as a function of y (millimoles of SDS redistributed per gram of EHEC) for (a) CST at 20 °C; ● $[\eta]$, ▲ k_H. (b) for E230G at 20 °C; ● $[\eta]$, ▲ k_H

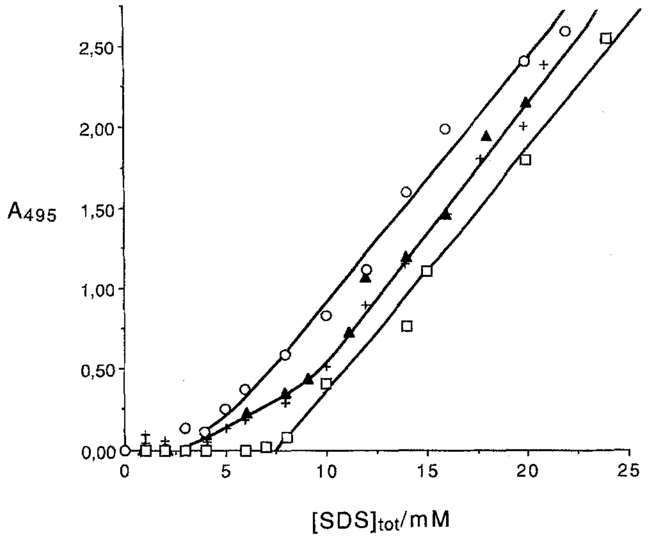

Fig. 5 The absorbance at $\lambda = 495$ nm of solubilized Oil Orange SS, A_{495}, as a function of $[SDS]_{tot}$ for E230G/SDS/water solutions. □ 0.00% E230G, + 0.05% E230G, ▲ 0.10% E230G, ○ 0.20% E230G

association complexes of water soluble polymers and ionic surfactants [32–36]. In Fig. 5 the absorbance at $\lambda = 495$, A_{495}, from the dye solubilization experiments is given as a function of SDS concentration. Regression calculation on the data of the SDS/water system gives a CMC at 7.5 mM, a value consistent with the one obtained from fluorescence quenching measurements [12]. It is known that different methods tend to give somewhat different CMC for a surfactant [24, 37]. When E230G is present in the surfactant solutions the solubilization of dye starts at a concentration below CMC, supporting the equilibrium dialysis results of redistribution. The fact that the dye added to an E230G-SDS solution is solubilized below the normal CMC, together with the observed cooperative manner of redistribution lead to the conclusion that the redistributed SDS forms clusters similar to ordinary micelles. There appears to be some solubilization of dye even below $[SDS]_{tot} = 5$ mM. This suggests that very small amounts of SDS redistribute to E230G though the main onset of the effect occurs at $[SDS]_{tot} \approx 5$ mM. In pure polymer solutions without surfactant only minute traces of solubilized dye were detected and it can be concluded that no dye is redistributed to or solubilized by the polymer since for 0.2% polymer a value of only $A_{495} = 0.007$ was obtained. The same experiments on the CST/SDS/water system were made in a previous study [12] verifying the foot point in binding of 2.5 mM SDS and cluster formation of SDS bound to CST.

Discussion

It has for a long time been well known that certain additives and especially those of an amphiphilic nature give remarkable rheological properties to solutions of polysaccharide derivatives [1–6]. This has been particularly recognized for the cellulose ethers since those play such an important role in pharmaceutical and food industries. From the broad spectrum of investigations published, one can also conclude that the macroscopic properties are sensitive to the detailed structure of the polymer and to the chemical properties of the amphiphile [1–6].

The two EHEC fractions studied, CST and E230G, have been found to behave quite differently in the physico–chemical sense, clearly indicating the need for very careful batch characterization in applications. Recently, similar observations were made in a special study from this laboratory on the general problem of characterization of water-soluble polymers, especially cellulose ethers [38]. In the analysis of experimental results, one may being with the cloud point curves for salt-free conditions as seen in Fig. 1. The increase in cloud point for CST with added SDS, induced by interaction between the surfactant and the polymer, leads to the conclusion that the CST sample is continuously solubilized by adding SDS. The E230G sample, on the other hand, displays a minimum with increasing SDS concentration, first becomes less soluble and only after a sufficient amount of SDS has been added does the solubility increase. Both samples are EHEC derivatives but the difference in substitution, and perhaps also substituent distribution, is sufficient to make the samples behave in this quite different way, cf. [38]. At $[\mathrm{SDS}]_{\mathrm{tot}} \approx 2.5$ mM the cloud point curve for the CST/SDS/water shows a steeper increase, and this correlates well with the onset of binding as seen in Fig. 3a. At this composition the viscosity starts to increase. This increase, given as an increase in η_{red}, is presumably due to a combination of several effects such as electrical charging as a result of redistribution of a charged surfactant, network formation due to two or several polymer coils "sharing" clusters on the polymer backbone and conformational effects [9, 25]. The foot point is followed by a steep binding isotherm up to a maximum. After the maximum in y desorption seems to occur at $[\mathrm{SDS}]_{\mathrm{eq}} \approx 6.5$ mM, i.e., when ordinary micelles begin to form in the bulk solution. These compositions occur where the curve of η_{red} display very low viscosities. Most likely the polymer is solubilized by normal micelles and there will be competing equilibrium. Observations much along the same lines have been published by others although a complete explanation is yet to be offered [27, 39–41]. It should be noted that the amount of SDS bound to CST depends on the polymer concentration, Fig. 3a. For instance the shift in coil–coil interaction may result in a difference in availability of hydrophobic binding sites, and when a surfactant is present in the solution, in the sharing of one cluster by two or more polymer coils.

The E230G/SDS/water system shows a resemblance to that of CST/SDS/water. The composition that gives the lowest cloud point, just before the CP starts to increase more steeply, corresponds to the foot point of the binding isotherm as well as the composition where the viscosity increase begins to develop. With its higher cloud point, E230G can be expected to give a much weaker redistribution of SDS than CST. Hence the foot point will occur at a higher SDS concentration and the maximum in reduced viscosity is less pronounced. Furthermore, the variation of η_{red} with added SDS in the concentration range of $[\mathrm{SDS}]_{\mathrm{tot}}$ between 6 and 11 mM is not as sensitive to polymer concentration as for the CST/SDS/water system, a fact which is also in accord with the model proposed.

The interaction pattern between SDS and the two EHEC fractions display similar tendencies and the main features may be summarized as follows. When small amounts of SDS are added to a water solution of EHEC there is a slight change in CP. To observe the onset of major interaction in terms of redistribution of surfactant and increase in reduced viscosity, η_{red}, the solutions must have a sufficient SDS concentration. The amount of SDS needed depends on the chemical properties of the EHEC fraction, the more hydrophilic E230G chain requires a higher SDS concentration than CST. It is interesting to note that when the amount of SDS redistributed equals 1 millimole per gram EHEC, i.e., $y = 1$, this corresponds for both polymers to the maximum in η_{red}, the hydrodynamic maximum in interaction as expressed by k_{H}, and the minimum in intrinsic viscosity, $[\eta]$, as seen in Figs. 4a and 4b. Also, the foot points observed in the redistribution curves, as discussed above, coincide with the beginning of the increase in η_{red} for both EHEC fractions. These facts support the view that the mechanism of interaction giving rise to the considerable increase in viscosity observed is identical for the two polymers. It also shows that in order to reach maximum in the viscosity effect the polymer chain should be far from "saturated" ($y \approx 1$ corresponds to about 10–20% of the maximum binding). In both systems the redistributed SDS forms clusters on the polymer backbone, as seen in Fig. 5 and reported in [12]. This suggests that the increase in viscosity is caused by two or more polymer coils sharing one cluster thus creating a network. Such a mechanism should depend on polymer concentration. In very dilute polymer solutions the hydrodynamic volume decreases remarkably (i.e., $[\eta]$ decreases) for low values of specific binding, y, and for probability reasons the interactions are overwhelmingly intermolecular. When the polymer concentration increases the probability of intermolecular interaction becomes dominant when a concentration in the vicinity of critical overlap is reached ($c^* \approx 1/[\eta]$) and a three-dimensional "network" can form. The increase in intermolecular interaction up to unusually high values as y increases to about 1 is experimentally supported by the remarkable increase in k_{H}. At still higher SDS concentrations the polymer becomes more and more saturated and k_{H} decreases. Thus the tendency to share clusters must finally vanish and the network disintegrates. The hydrophobic parts of the polymer may also be solubilized in normal micelles formed in the bulk, which would explain the almost identical reduced viscosities for all polymer concentrations at high SDS concentrations. From the presentation above it is clear that the interaction of SDS with the two different EHEC fractions is qualitatively rather similar although there are differences that reflect the chemical substitution difference and also lead to a different macroscopic behavior.

As mentioned earlier, the CP curves for all salt concentrations come together, like in an isobestic point, in a narrow [SDS] region at [SDS] $\approx$ 4.5 mM for CST and [SDS] $\approx$ 8 mM for E230G, a region which is identical to the one where the reduced viscosity for the polymers with various NaCl concentrations drops down after the maximum and all curves join, as seen in Figs. 2c and 2d. By and large the effects in this respect are more pronounced for the CST sample than for the E230G sample. Obviously, this would fit the general model just proposed. As more surfactant is added to the EHEC solution the tendency of intermolecular interaction has been found to decrease and the polymer contribution to the system properties would approach that of the polymer/solvent system. There is a viscosity increase for the CST sample with SDS as salt is added, which reaches a maximum for about 3 mM NaCl and then decreases as more salt is added, as seen in Fig. 2c. There is a slight decrease in η_{red} for the CST samples with low SDS concentrations and 1 mM NaCl. For the E230G sample, on the other hand, the viscosity maximum decreases continuously as salt is added and eventually the maximum disappears and a minimum develops instead, as seen in Fig. 2d. The composition which shows the lowest cloud point and is close to phase separation, gives this minimum in viscosity. All these experimental facts from the hydrodynamic studies support the general model of interaction discussed above. It should be noted that the intrinsic viscosity of the CST sample in water without surfactant is independent of salt concentration, whereas for E230G the intrinsic viscosity decreases slightly. The effect is not large but outside experimental error limits and indicates a sensitivity to added electrolyte also supporting the general model. A second fact that exposes how markedly salt affects pure E230G in solution is the lowering of CP upon addition of salt as seen in Fig. 1b. The sensitivity of pure E230G to added salt has been observed earlier in a study by Nilsson et al. [38], where aggregation is indicated for a polymer in a solution containing 5 mM NaCl. Similar studies of the effect of added electrolyte on properties of uncharged polymers in water solution have reported considerable differences in hydrodynamic volume for NaCl concentrations as high as 0.1–0.4 M [42, 43]. The onset of the lowering of CP for salt compositions the EHEC/SDS/water system is in fair agreement with the onset of binding, as can be seen from the dialysis equilibrium results, Figs. 3c and 3d. The dialysis curves for the E230G/SDS/NaCl/water system, Fig. 3d, display the same shape as those for CST in Fig. 3c, and can be related to the CP results for E230G. The onset of redistribution corresponds to the initial decrease in cloud point. The "breakpoint" in the dialysis curves occurs in this system at $[\mathrm{SDS}]_{\mathrm{tot}} \approx 5$ mM SDS and coincides with the minimum in the CP curves for 3 and 5 mM NaCl respectively. This is in accord with the redistribution model proposed earlier for the thermodynamic binding equilibrium [13]. The lowest value of CP when salt is added occurs at a total SDS concentration where $y \approx 1.5$ for E230G, i.e., at a binding value almost identical to that giving maximum in hydrodynamic interaction for salt-free conditions.

This points to a mechanism where the partially saturated chain ($y \approx 1.5$) is in a state where it tends to aggregate, i.e., to reduce the overall free energy it prefers a hydrophobic surrounding. It is on the verge of being salted out. A similar mechanism might explain the cloud point results of E230G, Fig. 1b, which also show a minimum when only SDS is added to the polymer solutions. This minimum could be the result of a "salting-out" effect due to free surfactant ions and counterions which are present in the solution [44]. The fact that elevated temperatures result in a higher population of the non polar conformers of the polymer which prefer to interact with themselves, and less of the polar ones which prefer to interact with water, may contribute to the decrease in CP for E230G with added SDS [45].

The complexity of the quaternary systems studied is partially due to the large number of components but perhaps mainly due to the intricate interaction of a charged surfactant with an uncharged polysaccharide backbone with hydrophobic substituents of different character distributed along the chain contour. The fourth component, salt, tends to alter the solvation and clustering equilibrium, especially at elevated polymer concentrations, and an intricate phase behavior is observed. The aim of the present study has been to explore the main features of the systems at hand to identify properties essential for the applications. The results also indicate that substituted cellulose derivatives of a fairly similar overall structure still may interact with amphiphiles in a very specific way. A conclusion for applications, where for instance the systems should be used as controlled release reservoirs in pharmaceutical formulations, is that the multicomponent systems are very sensitive to even minute changes in composition and chemical structure. As a consequence a careful characterization will always be needed.

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