

Aggregation of Modified Celluloses in Aqueous Solution: Transition from Methylcellulose to Hydroxypropylmethylcellulose Solution Properties Induced by a Low-Molecular-Weight Oxyethylene Additive

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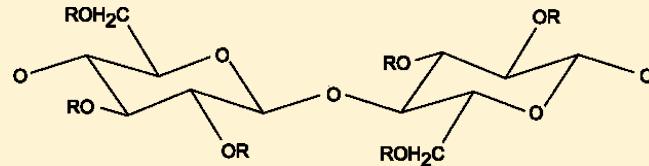
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ABSTRACT: Temperature effects on the viscosity and aggregation behavior of aqueous solutions of three different cellulose ethers—methylcellulose (MC), hydroxypropylmethylcellulose (HPMC), and ethyl(hydroxyethyl)cellulose (EHEC)—were investigated using viscosity and dynamic light scattering measurements as well as cryo-TEM. In all cases, increasing temperature reduces the solvent quality of water, which induces aggregation. It was found that the aggregation rate followed the order EHEC > HPMC > MC, suggesting that cellulose ethers containing some bulky and partially hydrophilic substituents assemble into large aggregates more readily than methylcellulose. This finding is discussed in terms of the organization of the structures formed by the different cellulose ethers. The temperature-dependent association behavior of cellulose ethers was also investigated in a novel way by adding diethyleneglycolmonobutylether (BDG) to methylcellulose aqueous solutions. When the concentration of BDG was at and above 5 wt %, methylcellulose adopted HPMC-like solution behavior. In particular, a transition temperature where the viscosity was decreasing, prior to increasing at higher temperatures, appeared, and the aggregation rate increased. This observation is rationalized by the ability of amphiphilic BDG to accumulate at nonpolar interfaces and thus also to associate with hydrophobic regions of methylcellulose. In effect, BDG is suggested to act as a physisorbed hydrophilic and bulky substituent inducing constraints on aggregation similar to those of the chemically attached hydroxypropyl groups in HPMC and oligo(ethyleneoxide) chains in EHEC.



1. INTRODUCTION

Cellulose ethers are a group of thermoresponsive polymers with several important applications in fields such as biotechnology,¹ paints,² pharmaceuticals,^{3,4} and foods,⁵ where they may be used for thickening, water binding, film formation, and controlled release. The most striking feature of cellulose ethers is that they, in contrast to unmodified cellulose, are soluble in water at room temperature. They aggregate extensively above a certain temperature because of the decrease in solvent quality. This behavior is commonly referred to as a negative temperature response, and the transition temperature, as the lower critical solution temperature (LCST). In some cases, the transition leads to gel formation. This is a common feature of methylcellulose (MC), and the gel properties are governed by the exact type of substitution.^{6,7} Hydroxypropylmethylcellulose (HPMC) and ethyl(hydroxyethyl)cellulose (EHEC) are two cellulose ethers with a certain degree of substituents with hydroxyl end groups. On increasing the temperature, aqueous

solutions of cellulose ethers may exhibit two clear viscosity transitions, where the first one is marked by a decrease in viscosity with increasing temperature and the second one that occurs at higher temperature results in a significant increase in viscosity with increasing temperature. For each type of cellulose ether, the transition temperatures depend on the degree of substitution.

The addition of different salts affects the transition temperatures of PNIPAAm and other polymers in accordance with the Hofmeister series. This does not necessarily change the transition qualitatively in terms of viscosity, phase separation, or clouding, even though a complete transition may take place over a broader temperature range and in more steps compared to when no salt is added.⁸ To affect the

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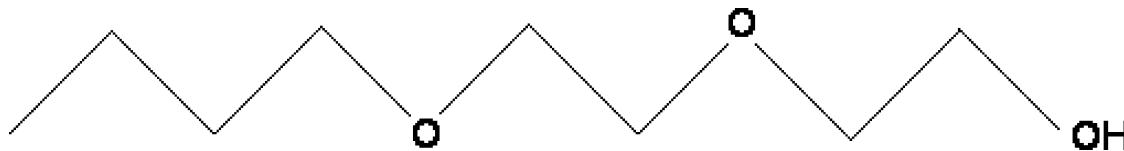


Figure 1. Structure of diethyleneglycolmonobutylether, BDG, consisting of two oxyethylene units linked to a butoxy chain.

Table 1. Substitution and Viscosity of Cellulose Ethers

sample	viscosity (Pa·s) ^a	methoxy degree of substitution	hydroxy-propyl molar substitution	ethoxy degree of substitution	hydroxy-ethyl molar substitution	M_w (kDa)
M _{1.6} C	20	1.6				530
HP _{0.12} M _{1.57} C	20	1.57	0.12			620
E _{1.3} HE _{1.5} C	4			1.3	1.5	ca. 300 ^b

^aOf 2 wt % solutions at 20 °C. ^bBased on the viscosity.

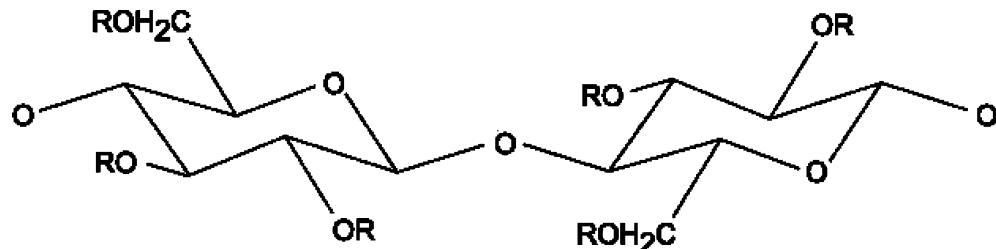


Figure 2. Structure of modified cellulose in methylcellulose ($R = H$ or CH_3), in hydroxypropylmethylcellulose ($R = H$, CH_3 , or $CH_2CH(OR')CH_3$), and in ethyl(hydroxyethyl)cellulose ($R = H$, CH_2CH_3 , or CH_2CH_2OR'). Substituent R' represents a new R group.

viscosity of polymer solutions, other types of additives such as alcohols or surfactants may be used. Glycol ethers are low-molecular-weight solvents with very good, in many cases complete, miscibility with water. They may consist of one to three oxyethylene units and an aliphatic chain with one to six carbon atoms.⁹ The amphiphilic structure of glycol ethers with one lipophilic and one hydrophilic part, as illustrated in Figure 1, gives them surfactant-like properties in water mixtures, where they decrease the surface tension¹⁰ and enhance the wetting of nonpolar substrates.⁹ Glycol ethers are good solvents for cellulose ethers. Two glycol ethers—diethyleneglycolmonobutylether (also called butyldiglycol and abbreviated BDG; structure shown in Figure 1) and triethyleneglycolmonobutylether (butyltriglycol, BTG)—are commonly used for cellulose ether preparation in paint applications. They are known to counteract the association between hydrophobically modified cellulose ethers in aqueous solutions, where they act as less-polar solvents compared to water.² Previously, EHEC was studied in water/BDG mixtures at room temperature, comparing the effect of the additive using unmodified or hydrophobically modified EHEC samples with different side-chain lengths and densities.^{11,12} In this study, we have explored the temperature response of cellulose ethers in a novel way by studying the effect of BDG on the aggregation properties of MC solutions and compared the behavior to that of HPMC and EHEC aqueous solutions in the absence of BDG. This allows us to present a molecular view of how BDG affects the aggregation of MC by acting as a physisorbed substituent. We also demonstrate that the aggregation rate increases when hydrophilic substituents are added to cellulose ethers, either by grafting or physisorption, and this finding is discussed in terms of changes in aggregate structure due to the presence of these substituents.

2. MATERIALS AND METHODS

2.1. Polymers. Freeze-dried samples of methylcellulose, hydroxypropylmethylcellulose, and ethyl(hydroxyethyl)cellulose, identified as M115, HPM116, and Bmc PR, respectively, were obtained from Akzo Nobel, Stenungsund, Sweden. The polymers were purified from a possible byproduct by first dissolving them in water to a concentration of around 1 wt %. The solutions were then centrifuged at ca. 7000g for 60 min to remove water-insoluble material. Water-soluble impurities such as salt and glycols were removed through the dialysis of the supernatants against excess Millipore water for 7 days. Spectra/Por membrane tubing with an M_w cutoff of 6000–8000 was used for the dialysis. The Millipore water in the water tank was exchanged once a day. After dialysis, the polymers were freeze-dried. The molecular weight was obtained from size-exclusion chromatography at 30 °C with a 2 × TSK G6000 PWXL 7.8 × 300 mm column, a precolumn, and a mobile phase of 0.04 M sodium acetate and 0.02% sodium azide at pH 6. Refractive index, light scattering (at 7 and 90°), and viscosity measurements were employed in the analysis.

To highlight the degrees of substitution of the cellulose ethers, we will refer to the MC, HPMC, and EHEC samples as M_{1.6}C, HP_{0.12}M_{1.57}C, and E_{1.3}HE_{1.5}C, respectively, throughout this report. The compositions of the three cellulose ethers, their molecular weights, and the viscosities of their 2 wt % solutions in water are summarized in Table 1, and their structures are detailed in Figure 2. M_{1.6}C and HP_{0.12}M_{1.57}C have a very similar methoxy content of ca. 1.6 substituents per anhydroglucose unit. The hydroxypropyl substituents are very important, even though the molar substitution in HP_{0.12}M_{1.57}C is only 0.12 mol of hydroxypropyl groups per mole of anhydroglucose.

Solutions were prepared by dispersing the freeze-dried polymers in water at high temperature (80–90 °C) under stirring and then cooling to room temperature under continuous stirring. Finally, the solutions were stirred in an ice bath for at least 30 min. Diethyleneglycolmonobutylether (Fluka, ≥99%), which is referred to as BDG throughout this report, was added to the aqueous polymer solutions to obtain solvent mixtures with weight proportions of 90:10, 95:5, and 97.5:2.5 between water and BDG. The maximum BDG content was chosen on

the basis of the observation that 1 wt % M_{1.6}C did not dissolve in water/BDG 80:20.

2.2. Rheology. An AR-G2 rheometer (TA Instruments) equipped with a bob and cup system was utilized for oscillation strain control measurements. A temperature sweep was carried out starting at 10 °C, heating to 85–90 °C, and then cooling to 10 °C again. Heating/cooling rates of between 0.1 and 1.5 °C/min were used. The temperature control was assured by Peltier concentric cylinders, which allow a maximum heating rate of 13 °C/min. Four heating elements are placed in contact with the lower cup geometry, providing efficient heat transfer up the walls of the cup. The elements are held in place by an insulated jacket. A platinum resistance thermocouple is placed close to the top of the cup, ensuring accurate temperature measurement and control.

2.3. Light Scattering. Light-scattering measurements were conducted with a Brookhaven Instruments (USA) device, which consists of a BI-200SM goniometer and a BI-9000AT digital autocorrelator. A water-cooled argon-ion laser, Lexel 95 model 2, was used as the light source. It was used at a wavelength of 514.5 nm and emitted vertically polarized light at a maximum power of 840 mW. In DLS mode, the signal analyzer was used in a multi- τ mode (i.e., the time axis was logarithmically spaced to span the required correlation time range). The autocorrelation functions were measured at an angle of 90° in 218 channels using a 200 μm pinhole. A 0.2 μm filter (Anopore aluminum oxide filters from Whatman Int. Ltd.) was used to remove some large aggregates present in solution.

The measured scattering intensity for a dilute polymer solution can theoretically be given as

$$I(q) = KM\phi P(q) S(q) = \frac{4\pi^2 n_0^2 (\mathrm{d}n/\mathrm{dc})^2}{N_A \lambda_0^4} M\phi P(q) S(q) \quad (1)$$

where n_0 is the refractive index of the solvent, $\mathrm{d}n/\mathrm{dc}$ is the refractive index increment, λ_0 is the wavelength of the laser beam in vacuum, N_A is Avogadro's number, M is the weight-averaged mass of the polymer, and c is the polymer mass concentration. Parameter q is the modulus of the scattering vector, and $q = 4\pi n_0 \sin(\theta)/\lambda$, where 2θ is the angle between the incident and scattered beams and λ is the wavelength of the light. $P(q)$ is the polymer-normalized form factor ($P(q=0)=1$). The structure factor $S(q)$, which for very dilute solutions is $S(q)=1$, describes concentration effects. Thus, if aggregation occurs without a change in the scattering contrast ($\mathrm{d}n/\mathrm{dc}$), then the scattering intensity at small q values will increase because of the increase in M . We use this fact to follow the aggregation in dilute polymer solutions.

The scattering intensity from 0.02 wt % cellulose ether solutions was recorded at a fixed angle of $2\theta = 90^\circ$ during a stepwise increase in temperature. The intensity of the scattered light was recorded for about 30 min at each temperature. The onset of aggregation is identified by an increase in scattering intensity, and the change in scattering intensity with time at a given temperature is a qualitative measure of the aggregation rate. Note that the intensity can also be influenced by changes in $P(q)$, which in general will decrease if the particles are homogeneous and increase in size.

The effective hydrodynamic diameter was determined from the intensity autocorrelation function using the non-negatively restricted least-squares (NNLS) method and Gaussian fitting of the size distributions. From the last 10 measurements at each temperature, average sizes were obtained. The choice of analysis method was based on the fact that the polydispersity was high, in the range of 0.3–0.6 as found using cumulant analysis with a quadratic fit.

2.4. Cryo-Transmission Electron Microscopy. The cryo-TEM specimens were prepared in a custom-built climate chamber with controlled humidity and temperature. A pair of tweezers hanging inside the chamber was used to hold the microscopy Cu grid, which had been covered first by a perforated polymer film (made from cellulose acetate butyrate) and second by thin evaporated carbon layers on both sides. After the specimens were heated and kept at the selected temperature for 30 min, a small drop of the sample solution was placed on the grid. The drop was blotted with filter paper to form a thin sample layer spanning the holes in the film. Thereafter, the grid

was rapidly plunged into the cryogen (i.e., liquid ethane held at a temperature just above its freezing point (−182 °C)). The grid with the vitrified sample was then transferred to the Zeiss Libra 120 TEM (Germany) using a Gatan CT3500 (U.K.) cryo-transfer apparatus. The specimen was kept at a temperature below −165 °C during both transfer and examination.¹³

3. RESULTS

3.1. Rheology. At low temperatures, the viscosity of aqueous solutions of cellulose ethers decreases smoothly with increasing temperature, in correspondence with the viscosity of water (Figure 3a,b). For HPMC and EHEC, above a critical

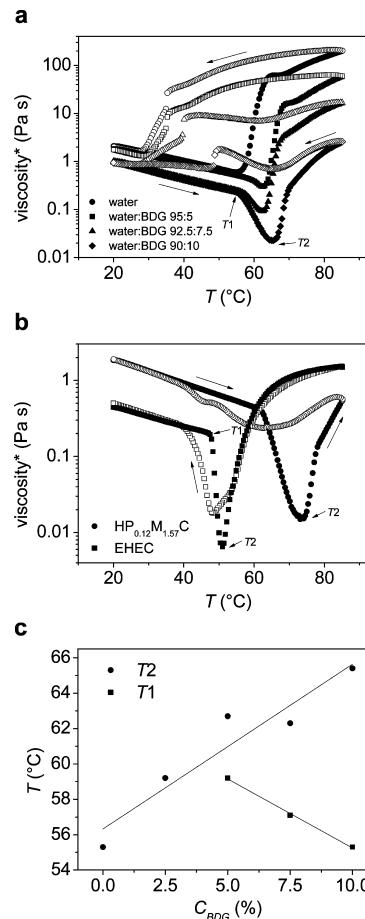


Figure 3. Complex viscosity (defined as $\mu^* = (G'^2 + G''^2)^{1/2}/2\pi f$, where G' and G'' are the storage and the loss moduli, respectively, and f is the frequency)¹² as a function of temperature (sweep rate 1 °C/min) for (a) 1 wt % M_{1.6}C in water (●), water/BDG 95:5 (■), water/BDG 92.5:7.5 (▲), and water/BDG 90:10 (◆) and (b) 1 wt % aqueous HP_{0.12}M_{1.57}C (●) and E_{1.3}HE_{1.5}C (■) solutions. Filled and unfilled symbols correspond to data obtained on heating and cooling, respectively. Arrows along the curve indicate the direction of the temperature sweep. The T₁ and T₂ temperatures are also marked. (c) T₁ and T₂ temperatures vs BDG concentration for 1 wt % solutions of M_{1.6}C. Linear fits are used as guides for the eye.

temperature denoted T₁ in Figure 3b, the viscosity drops sharply. At a slightly higher temperature, referred to as T₂ in Figure 3b, a significant viscosity increase is observed for aqueous solutions of these cellulose ethers. For aqueous MC solutions, the T₁ transition is absent and only the T₂ transition is observed (Figure 3a). In most cases, the viscosity increase is

much more dramatic for MC solutions than for solutions of HPMC or EHEC.

The data presented in Figure 3a illustrate how the complex viscosity of 1 wt % aqueous $M_{1.6}C$ solutions is affected by the addition of the BDG cosolvent. There are three main effects of BDG addition. First, the T_2 temperature is shifted to higher values. Second, at BDG concentrations at and above 5 wt % a T_1 transition is also observed. Third, the value of the complex viscosity at high temperatures is significantly decreased (note the log scale of the y axis in Figure 3a). Thus, when the solvent is changed from pure water to a mixture of water and BDG the viscosity behavior of the $M_{1.6}C$ solution shifts toward that of a typical aqueous HPMC solution. In these measurements, the temperature sweep rate was 1 °C/min, which shifts the transition temperatures upward by a few degrees compared to an extrapolated zero sweep rate value.^{14,15}

The effect of BDG concentration on the transition temperatures observed in MC solutions is summarized in Figure 3c. The T_2 transition temperature increases close to linearly with BDG content, from about 55 °C in water to around 65 °C when 10 wt % BDG is present. In the solvents with 5 wt % or more of BDG, a T_1 transition, which moved to lower temperature with increasing BDG concentration (Figure 3c), was also observed. At 10 wt % BDG, the T_1 temperature was similar to the T_2 temperature of $M_{1.6}C$ dissolved in pure water (i.e., around 55 °C). With increasing BDG content, the T_1 transition became more pronounced and the T_2 transition became less dramatic.

For comparison, the behavior of 1 wt % aqueous solutions of $HP_{0.12}M_{1.57}C$ and $E_{1.3}HE_{1.5}C$ is shown in Figure 3b. Both solutions show T_1 and T_2 temperatures, but the viscosity increase observed above T_2 is much less dramatic than for $M_{1.6}C$. The viscosity hysteresis observed at higher temperature is very large for $M_{1.6}C$, clearly noticeable for $HP_{0.12}M_{1.57}C$, and minor for the $E_{1.3}HE_{1.5}C$ solution.

3.2. Aggregation Properties. 3.2.1. Aqueous Solutions.

The aggregation process of $M_{1.6}C$, $HP_{0.12}M_{1.57}C$, and $E_{1.3}HE_{1.5}C$ in 0.02 wt % aqueous solutions was studied using light scattering. We note that the polymer concentration used in the light-scattering study by necessity is lower than that used for viscosity measurements. It has previously been shown that the viscosity T_1 and T_2 transition temperatures for aqueous HPMC solutions are insensitive to the bulk concentration, whereas a close to linear increase in T_2 with decreasing concentration is observed for aqueous MC solutions, giving an increase in T_2 by about 5 °C when extrapolated from 1 wt % to close to 0 wt%.^{14,15} The viscosity transition temperatures are also affected by the sweep rate.^{14,15}

For the $M_{1.6}C$ solution, the development of the scattered light intensity and the hydrodynamic diameter upon increasing the temperature is shown in Figure 4a. The size and intensity correlate well because the solution is dilute. The hydrodynamic diameter of the scattering objects was found to be in the range of 60–70 nm at 50 °C and increasing with increasing temperature. The aggregation rate is initially slow but increases steadily with increasing temperature, and, as judged from the change in scattering intensity, it becomes more pronounced from 52 to 53 °C. In the case of $HP_{0.12}M_{1.57}C$ and $E_{1.3}HE_{1.5}C$, the aggregation undergoes a more pronounced transition with a significant increase in scattering intensity from around 53 and 48 °C, respectively. For $E_{1.3}HE_{1.5}C$, this corresponds to the T_1 temperature in viscosity measurements, and it also coincides with the macroscopic cloud point.² The difference in

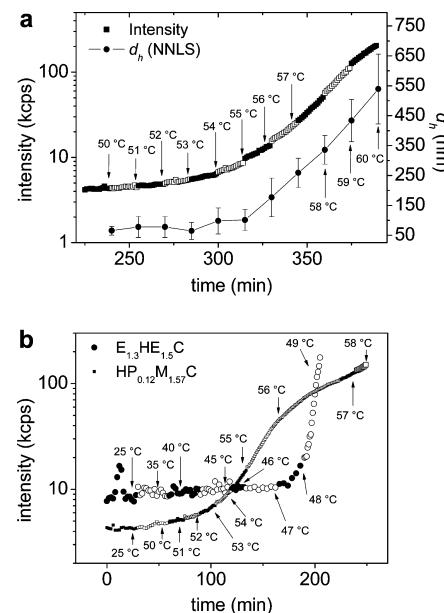


Figure 4. (a) Intensity of light (■) scattered at 90° by a 0.02 wt % $M_{1.6}C$ aqueous solution during heating from 50 to 60 °C and average hydrodynamic diameter (● with error bars showing the standard deviation) of the scattering objects at each temperature calculated using the non-negatively restricted least-squares (NNLS) method. (b) Intensity of light scattered at 90° by a 0.02 wt % $E_{1.3}HE_{1.5}C$ aqueous solution (●) during heating from 25 to 49 °C and for a 0.02 wt % $HP_{0.12}M_{1.57}C$ aqueous solution (■) during heating from 25 to 58 °C. The scattered light was recorded for around 30 min at each temperature as illustrated by the experimental time scale shown on the abscissa.

aggregation behavior between MC and HPMC was also noted in an earlier study.¹⁴

3.2.2. MC Solutions in Mixtures of Water and BDG. The intensity of light scattered by 0.02 wt % $M_{1.6}C$ dissolved in different mixtures of water and BDG was recorded during a stepwise increase in temperature from below to above the T_2 transition. The addition of BDG induced small peaks at short correlation times. These peaks were also seen in water/BDG mixtures without polymer and thus were assigned to density fluctuations in the solvent mixture, and they were therefore not included in the data analysis. The scattering intensity for $M_{1.6}C$ in the water/BDG 95:5 mixture is shown in Figure 5. The

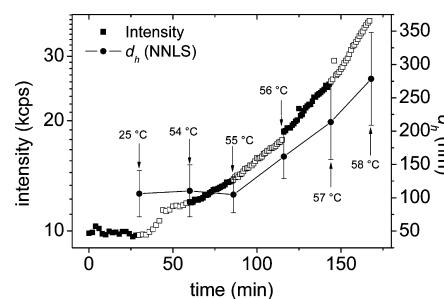


Figure 5. Intensity of light (■) scattered at 90° by a 0.02 wt % $M_{1.6}C$ solution in water/BDG 95:5 during heating from 25 to 58 °C and average hydrodynamic diameter (● with error bars showing the standard deviation) of the scattering objects at each temperature calculated from the non-negatively restricted least-squares (NNLS) method.

scattering intensity increases smoothly with temperature, and both the intensity and the size of the scattering objects were very similar in the absence and presence of 5 wt % BDG (cf. Figures 4 and 5). However, at room temperature the scattering objects in the water/BDG mixture are somewhat larger, about 100 nm, compared to the 60–70 nm size found when pure water was used as the solvent. The standard deviation of the size of the objects was also found to be larger in the water/BDG 95:5 mixture than in pure water. An increase in the BDG content to 10 wt % induced a clear transition at 55 °C as shown in Figure 6, and the hydrodynamic diameter increased faster than in water or water/BDG mixtures with lower BDG content.

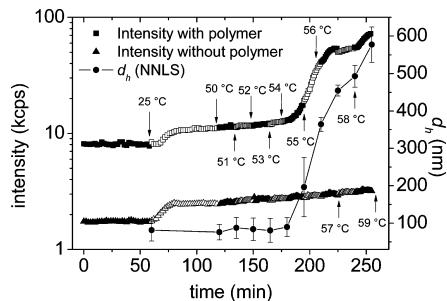


Figure 6. Intensity of light scattered at 90° by a 0.02 wt % M_{1.6}C solution in water/BDG 90:10 (■) and by water/BDG 90:10 (▲) during heating from 25 to 59 °C and average hydrodynamic diameter (● with error bars showing the standard deviation) of the scattering objects at each temperature calculated from the non-negatively restricted least-squares (NNLS) method.

Glycol ethers mixed with water may phase separate at high temperatures,⁹ but in our 10 wt % BDG mixture, we did not observe phase separation up to 60 °C. However, with 5 or 10 wt % BDG in the solvent, the scattered light intensity was considerably higher at 50 °C compared to that at 25 °C (Figures 5 and 6), demonstrating the increased importance of density fluctuations. In Figure 6, the intensity increase up to 50 °C is similar for the mixture with 10 wt % BDG without polymer compared to that for M_{1.6}C dissolved in the same solvent and thus is primarily due to density fluctuations in the solvent mixture.

3.3. Aggregate Structure. Cryo-TEM was employed to capture images of 0.02 wt % M_{1.6}C bulk solutions in pure water and in a mixture of water and 10 wt % BDG. The solution temperature was, for different experiments, held at temperatures below and above the transition points during at least 30 min, after which samples of the solutions were frozen and imaged. The results obtained for solutions above the transition points are shown in Figure 7. In the pure water solution, a clear transition was observed when changing from 50 to 60 °C. Similarly to what was found in an earlier study for another MC in water solution,¹⁴ increasing the temperature in the M_{1.6}C aqueous solution above the T₂ temperature induced the formation of fibrils that form a network as shown in Figure 7. The formation of this network is the reason for the high increase in viscosity above the T₂ temperature.

Figure 7 also shows an image of the solution of M_{1.6}C in 10 wt % BDG held at 70 °C, which is above the bulk transition temperatures, T₁ and T₂. No fibril formation was observed. The darker areas in the TEM image can be interpreted as diffuse aggregates. We obtained similar images using cryo-TEM in our earlier study on aggregation in an HPMC aqueous solution above T₂, but in that case, some large elongated fibrils were formed at higher HPMC concentrations.¹⁴

4. DISCUSSION

4.1. Temperature-Induced Aggregation of MC, HPMC, and EHEC in Aqueous Solution. Structurally, MC differs from HPMC in that the only substituent that is present is the weakly hydrophobic, small methoxy group, whereas HPMC also includes the more hydrophilic, bulkier hydroxypropyl substituent. EHEC differs from both MC and HPMC in that it includes ethoxy substituents that are more hydrophobic and larger than the methoxy group as well as oligo(ethyleneoxide) side chains that are larger and more hydrophilic than the hydroxypropyl group. For all three polymers, an increase in temperature reduces the solvent quality of water, and extensive aggregation will occur at sufficiently high temperature. In this work, we studied the aggregation process with dynamic light scattering and found that the aggregation of MC and HPMC with similar degrees of methoxy substitution and similar molecular weights was initiated at similar temperatures (Figure 4). However, the aggregation rate is significantly higher for

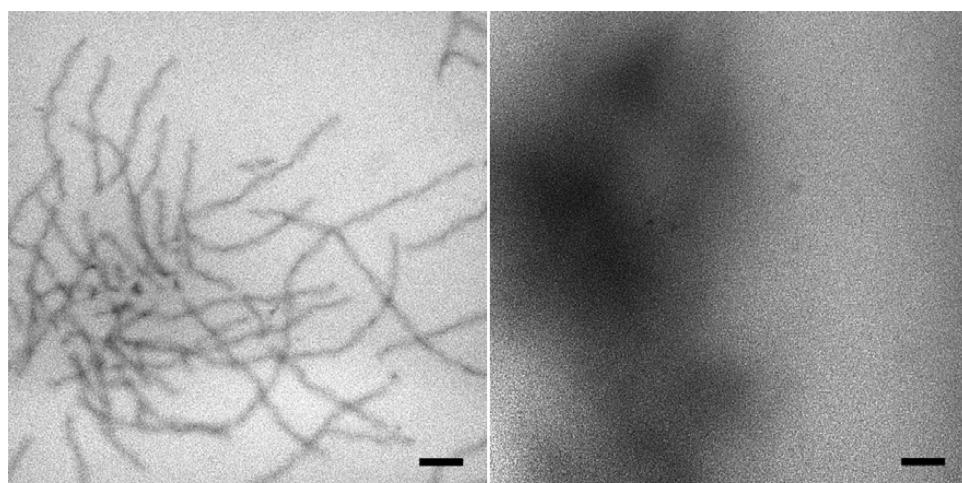


Figure 7. Cryo-TEM images from (left) a 0.02 wt % M_{1.6}C aqueous solution at 60 °C and (right) 0.02 wt % M_{1.6}C in a water/BDG 90:10 mixture at 70 °C. The scale bars are 100 nm.

HPMC, and an even higher aggregation rate is observed for EHEC. Thus, we reach the counterintuitive conclusion that the aggregation rate increases when hydrophilic substituents are introduced, and more so with oligo(ethyleneoxide) groups than with hydroxypropyl groups. To rationalize these findings, we consider the structure of the aggregates formed.

4.2. Aggregate Structure of MC, HPMC, and EHEC in Aqueous Solutions at High Temperatures. The cryo-TEM images reported here (Figure 7) as well as in a previous report¹⁴ demonstrate that the aggregation of MC leads to the formation of fibrils. This indicates intimate contact between the aggregated MC chains and efficient shielding of the methoxy groups from the aqueous solution, a view that is supported by NMR measurements that show that the methoxy groups become largely immobilized.^{16,17} A consequence is that further aggregation requires the reorganization of already formed aggregates, which is a slow process and reduces the aggregation rate into larger objects.

The bulky hydroxypropyl group present in HPMC counteracts but does not completely prevent fibril formation. Thus, the aggregates formed are more open. The substituents present in HPMC are less shielded from water than in MC (and more mobile as demonstrated by NMR measurements¹⁶), which facilitates further aggregation and explains the higher aggregation rate of HPMC as compared to that of MC. This difference in aggregate structure between MC and HPMC has also recently been used to rationalize why HPMC adsorption to nonpolar surfaces increases significantly above T2, whereas hardly any increase in MC adsorption is observed when the T2 temperature is passed.¹⁵

EHEC with its bulky oligo(ethyleneoxide) chains has not been reported to form fibrils and is expected to have the hydrophobic groups even less shielded from water in the aggregates that do form above the cloud point than is the case for HPMC. Thus, the aggregation rate for EHEC is even higher than for HPMC.

4.3. Viscosity Hysteresis at High Temperatures. Rheology data show that the viscosity hysteresis between heating and cooling is very large for MC, significant for HPMC, and minor for EHEC (Figure 3). This is also a consequence of the difference in aggregate structure. The compact fibrils formed by MC are slow to form and slow to disrupt, explaining the predominance of kinetically trapped states. The aggregation of HPMC leads to less-compact aggregates and less-extensive fibril formation, and these aggregates form more quickly and disentangle more rapidly. The formation and disruption of the aggregates formed in non-fibril-forming EHEC solutions is a comparatively rapid process, explaining the minor viscosity hysteresis.

4.4. Aggregation, T1, and T2 Temperatures. In this section, we compare transition temperatures obtained from viscosity and light-scattering data. It should be noted that different concentrations had to be used in the two types of measurements. Thus, it is important to note that it previously has been shown that the viscosity T1 and T2 transition temperatures for aqueous HPMC solutions are insensitive to the bulk concentration, whereas a close to linear increase in T2 with decreasing concentration is observed for aqueous MC solutions, giving an increase in T2 of about 5 °C when extrapolated from 1 wt % to close to 0 wt%.^{14,15} The viscosity transition temperatures are also affected by the sweep rate.^{14,15} In the light-scattering experiments, the temperature change is slow and best compared to the transition temperatures

obtained by extrapolation to zero sweep rate. For M_{1.6}C, the T2 transition extrapolated to zero sweep rate is about 51 °C (for a 0.75 wt % solution, data not shown), and if this is further extrapolated to very low concentrations, a transition at around 55 °C is expected. For HP_{0.12}M_{1.57}C, the T1 transition extrapolated to zero sweep rate occurs at 61 °C.

For EHEC solutions, which has the fastest aggregation kinetics of the cellulose ethers investigated in this study, we find a perfect correlation among the T1 temperature associated with a sharp drop in viscosity, the onset of aggregation as determined by dynamic light scattering, and the macroscopic cloud point. We have previously shown that for a different HPMC the onset of aggregation as determined by dynamic light scattering closely coincided with the T2 temperature extrapolated to zero sweep rate.¹⁴ This is clearly not the case for the HPMC used in the present investigation. Here we find that the aggregation starts at a temperature (52 to 53 °C) that is even lower than the T1 temperature extrapolated to zero sweep rate.¹⁵ Thus, it appears that one cannot specify the relation between the onset of aggregation and the T1 temperature more precisely than stating that the T1 temperature reflects a significant decrease in the total hydrodynamic volume of the HPMC molecules and that this volume can decrease because of either intramolecular coiling or aggregation leading to a less-expanded conformation. The absence of a T1 temperature for MC reflects that fibril formation is preferred over the formation of less-extended aggregate structures.

The T2 temperature reflects the onset of formation of a network spanning the solution volume. In the case of MC, the network is formed by interconnected fibrils¹⁴ and has significant strength as seen by the large increase in viscosity. The presence of hydroxypropyl groups in HPMC leads to a higher T2 transition temperature, a less-dense fibrillar network, and a less-dramatic increase in viscosity. In EHEC solutions intermolecular entanglements also occur as evidenced by an increase in viscosity, but the network structure is weak.

4.5. Effect of BDG on MC Solutions. BDG has amphiphilic character consisting of a short (C4) hydrocarbon chain and a two-units-long ethyleneoxide chain (Figure 1) and accumulates at hydrophobic interfaces. Mixing water with BDG leads to a sharp decrease in surface tension from a value of 72 mN/m in pure water to around 30 mN/m at a BDG concentration of 10 wt %,¹⁰ which is equal to 0.62 M and higher than the critical micelle concentration (cmc) of about 0.54 M.¹⁸ At higher BDG concentrations, the surface tension levels out. Thus, it is plausible to suggest that BDG will preferentially accumulate close to the hydrophobic regions of MC and act as a physisorbed substituent. If this picture is correct, then the hydrophobic interactions between MC chains will be diminished and the free-energy change required to displace BDG from the MC chain will counteract aggregation into a compact fibrillar structure. This scenario implies that MC in a water/BDG mixture will behave as HPMC in an aqueous solution. Indeed, this is what is observed. The T2 temperature increases, the viscosity increases at temperatures above T2, the viscosity hysteresis is less pronounced with increasing BDG content, and a T1 temperature appears when 5 wt % BDG (or more) is present in the solution as shown in Figure 3. Furthermore, the onset of aggregation as determined by dynamic light scattering is largely unaffected by the BDG content, but the aggregation rate increases with increasing BDG concentration. This implies that the formation of fibrils is counteracted, and indeed no fibrils are detected by cryo-TEM

(Figure 7). In fact, our $M_{1.6}C$ sample in a water/BDG 90:10 mixture behaves very similarly to $HP_{0.12}M_{1.57}C$ in aqueous solutions. The concentration of BDG needed to induce a qualitative change in the solubility of MC in water is, according to our results, well correlated with the concentration needed to reach a surface tension of less than half of that of pure water. Such a correlation can be seen in light of other studies on the relation between the interfacial tension and miscibility differences in a glycol ether–water mixture.¹⁹

5. CONCLUSIONS

The aqueous solution behaviors of three cellulose ethers—methylcellulose (MC), hydroxypropylmethylcellulose (HPMC), and ethyl(hydroxyethyl)cellulose (EHEC)—have been compared. The three cellulose ethers are similar in the sense that an increase in temperature reduces the solvent quality of water for all three polymers, and thus above a critical temperature significant aggregation into extended structures occurs. Despite this, the properties of aqueous solutions of these polymers differ significantly, and these differences are all due to the presence of hydrophilic, bulky substituents in HPMC and EHEC. The primary effect of these bulky, hydrophilic substituents is that aggregation into condensed fibrils is counteracted. Thus, fibrils are formed extensively only in aqueous solutions of MC, which explains the high viscosity of MC solutions above T_2 . Some fibrils are also formed in HPMC solutions whereas no such structures have been reported for EHEC.

The hydrophobic methyl groups are more efficiently shielded from the aqueous phase in the fibrillar aggregates formed by MC than is the case in the less-condensed aggregates favored by HPMC and EHEC. This counteracts the kinetics of the self-assembly into large aggregates, explaining that the aggregation kinetics just above the T_2 transition follows the order EHEC > HPMC > MC. In contrast, the onset temperature of aggregation is found to be similar for MC and HPMC with similar degrees of methyl substitution and similar molecular weights.

For EHEC solutions, which display the fastest aggregation kinetics, the T_1 transition coincides with the onset of aggregation and the macroscopic cloud point. For the MC and HPMC samples investigated here, the onset of aggregation occurred at temperatures below the viscosity transition points, but different results have been obtained for other MC and HPMC samples. Thus, for MC and HPMC the T_1 transition is associated with the shrinkage in the total hydrodynamic volume that can occur by a combination of intrachain contraction and aggregation into less-extended structures, and the appearance of this viscosity feature does not correspond exactly to the onset of aggregation.

In water/BDG mixtures with at least 5 wt % of the amphiphilic cosolvent, the solution behavior of methylcellulose is changed to mimic that of HPMC in water. The rational for this is that BDG accumulates in hydrophobic regions of MC and acts as a physisorbed hydrophilic, bulky substituent. As a consequence, the aggregation into fibrils is suppressed and instead more open aggregate structures are formed. This effect of BDG addition, which has not been reported previously, results in more rapid aggregation into large structures, increased T_2 temperature, a slower viscosity increase above T_2 , and reduced viscosity hysteresis.

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Notes

The authors declare no competing financial interest.

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