Macromol. Symp. 177, 125–138 (2002)

Graft Copolymers Composed of High Molecular Weight Poly(ethylene oxide) Backbone and Poly(*N*-isopropylacrlylamide) Side Chains and Their Thermoassociating Properties

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Summary: Novel, water-soluble thermoassociative graft copolymers based on high molecular weight (HMW) poly(ethylene oxide-co-glycidol) backbone and relatively short grafts of poly-N-isopropyl acrylamide (NIPAAm) were prepared. The copolymer precursors with two architectures (block and graft) were synthesized using Ca-amide-alkoxide initiators. The OH groups in the copolymer precursors have been utilized for grafting NIPAAm using ceric ion (Ce^{4+}) redox initiation. The idea was to imprint the "smart" properties of PNIPAAm grafts into common HMW poly(ethylene oxide). The sensitive moieties undergo reversible association transitions by changing the temperature of dilute and semidilute aqueous solutions of the copolymers. Associative properties were studied by viscosity and rheology measurements. Two types of interactions, induced by heating, depending on the copolymer concentration namely intra- and intermolecular association were observed.

1. Introduction

High molecular weight poly(ethylene oxide) (HMW PEO) is widely used as thickening, flocculating, or suspending agent. One of the advantages of HMW PEO in this application is that only very low aqueous solution concentrations are required in order to achieve dramatic effects (1). Unfortunately, aqueous solutions of HMW PEO are generally very sensitive to deformation and some mechanical degradation (loss of viscosity) can occur under high shear rate. As a result an alternative route for preparing thickeners was developed using the concept of "associative polymers".

Hydrophobically associating copolymers consist of a water-soluble polymer containing a small number of hydrophobic groups. In aqueous solution, above a certain

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polymer concentration, intermolecular hydrophobic interactions lead to the formation of macromolecular associations. As a consequence, these materials exhibit thickening properties equivalent to those observed for higher molecular weight homopolymers. The physical links between chains are disrupted under increasing shear but they reform with decreasing shear. In this way, it is possible to avoid the irreversible mechanical degradation which occurs in very high molecular weight samples when subjected to high shear stresses. However, for all these systems, the viscosity generally decreases when temperature is raised and this can be an important drawback, especially for applications over a wide range of temperatures.

N-isopropylacrylamide has been, and continues to be, the most widely used component of reversibly thermosensitive systems in water, viz. solutions of linear PNIPAAm and swollen hydrogels of crosslinked species. The unique properties of poly(ethylene glycol)-poly(N-isopropylacrylamide) block and graft copolymers in water have recently attracted a lot of attention (2-4). Part of the interest stems from the lower critical solution temperature (LCST) of PNIPAAm in water that can be tuned close to body temperature by copolymerization and may therefore be applied in the biomedical field as a stimulus-sensitive material (5). Since the hydrophilic PEG provides steric stabilization of the block copolymer in aqueous solution, the combination of the temperature-sensitive PNIPAAm and PEG should exhibit interesting thermosensitive aggregation behavior.

In the present work we undertook the synthesis and characterization of thermoassociating water soluble graft copolymer systems based on high molecular weight PEO. The idea was to imprint some "smart" properties into common PEO by introducing responsive components consisting of relatively short segments of PNIPAAm grafts. The sensitive moieties can undergo reversible association transitions by changing the environmental conditions. This approach should lead to a very complex phase transition behavior with potential applications in numerous fields including drug delivery, chemical separations, sensors, catalysis and thickening agents.

2. Experimental

2.1.Materials

Glycidol, (G) (Aldrich) was distilled under reduced pressure prior to use. N-isopropylacrylamide, (Aldrich) was recrystallized from an hexane/acetone (10:1 v/v) and vacuum dried. Ammonium cerium (IV) nitrate was purchased from Aldrich. All other chemicals were used as received.

2.2. Synthesis of precursor copolymers

The anionic precipitation polymerization of ethylene oxide (EO) and G was initiated by calcium-amide-alkoxide (6). Calcium amide modified catalyst was synthesized directly in the reaction vessel. This involved reaction of 0.5 g Ca with 0.6 ml EO in 7.5 ml heptane and 35 ml liquid NH_3 followed by thermal treatment of the catalyst suspension at 80 °C for 1 hour.

2.2.1. Poly(ethylene oxide-co-glycidol)

The copolymerization leading to random copolymers, was carried out with the calcium catalyst at 40 °C for 5 hours. After 15 min of slow bubbling of EO through the suspension formed of the modified Ca catalyst in 85 ml heptane, a certain amount (0.5-2.5 ml) G was added dropwise for 4 hours, while the bubbling of EO continued.

2.2.2. Poly(ethylene oxide-b-glycidol)

Diblock copolymers, where the first block is HMW PEO and the second block polyglycidol, were obtained by sequential anionic polymerization of EO followed by addition of G. The highly reactive hydroxyepoxide represents a latent AB_2 monomer that can be polymerized to hyperbranched polyethers with numerous hydroxyl end groups (7).

The polymer precipitates (*2.2.1* and *2.2.2)* were isolated by filtration, washed several times with heptane and the free G was then extracted with freshly distilled diethylether. The copolymers were further purified from catalyst residue and oligomers through dialysis in distilled water for a week. A dialysis cellulose membrane (Dialysis tubing, Sigma) with a cut-off value of 12000 was used. The dialyzed solution was transferred to a flask, the water was removed by evaporation at ambient temperature and the residue was dried to constant weight in a vacuum oven at 40°C.

2.3. Synthesis of PNIPAAm graft copolymers

1 g of random or block copolymer precursor was dissolved in 100 ml of deionized water under vigorous stirring and 0.5-2 g of NIPAAm was added. The solution was transferred into a 250 ml two-neck round bottom flask equipped with condenser, gas inlet/outlet, and magnetic stirrer, heated to 30°C while flushing with nitrogen for few hours. 10 ml aqueous solution of 0.11 g (0.2 mmol) cerium ammonium nitrate and 0.2 g (2 mmol) 63% nitric acid was added and the reaction was continued under stirring overnight. The reaction mixture was neutralized with an aqueous 0.25 M

NaOH. The solution was dialyzed through cellulose membrane for a week.The water was evaporated under vacuum.

3. Copolymer characterization

3.1. Spectral measurements

The copolymer structure was characterized by UV-, IR-spectroscopy and NMR. The ^1H and ^{13}C NMR spectra were recorded on a Bruker WM 250 instrument at room temperature, using D_2O, $CDCl_3$ or dry DMSO-d_6 as solvents. The compositions of the graft copolymers were determined by ^1H NMR in $CDCl_3$ from the relative intensities of the oxyethylene protons at $\delta = 3.64$ ppm and the methine protons of the isopropyl groups at $\delta = 4.00$ ppm.

3.2. Molecular mass characteristics

Molecular weights and molecular weight distributions of the samples were measured by SEC with double detection on a chromatography line consisting of a M510 pump, a U6K injector, two Ultrahydrogel columns with pore size of 120 Å and 250Å, a differential refractive index detector M 410, and a tunable absorbance detector M 486 (Waters Chromatography Division). Measurements were performed in MeOH/H_2O (15/85 v/v) solvent at 20^{0}C with a nominal flow rate of 0.8 ml/min and molecular weights were calculated by a "universal calibration" using PEO and polyethylene glycol narrow molecular weight standards.

3.3. Viscosity measurements

Solution viscosity was determined with an Ubbelohde viscosimeter having diameters of 0.45 mm at 25 °C and 40 °C. Intrinsic viscosity was measured with an initial concentration of 1.2 wt. %. The viscosity-average MW (M_v) of copolymers was calculated using the constants for pure PEO $K=1.25x10^{-4}$ and $\alpha=0.78$ (1). This relation has been established for PEO, and therefore it provides only a rough estimation of the molar mass of copolymers.

3.4. Rheological investigations

Solutions of 5, 7.5 and 10 % of PEO were prepared in distilled water. A 0.5-1 ml portion of each solution was placed on measuring sensor system type cone (d = 50 mm, 0.3°) and plate (d = 50 mm) of the Rheotron (Brabender). All experiments were carried out in the temperature range 20-60 °C, with an equilibrating time of 10 min for each temperature. The steady shear viscosity was obtained in the shear rate range from 3 to

100 s^{-1} and shear time 30 s. The dynamic oscillatory measurements were performed with frequency range of 0.01-5 Hz, amplitude in linear viscoelastic range of 0.01 rad. and 3 cycles for elipses evaluation.

3.5. Turbidimetry

The transmittance of 3 wt. % aqueous polymer solutions was measured by UV-VIS Specord (Carl-Zeiss-Jena, Germany) at 500 nm in the temperature range of 30 ÷ 40 ^{0}C equipped with a thermostated cell. The temperature was increased at a 0.2 ^{0}/min rate. The sample was allowed to equilibrate for at least 15 min at each temperature. Thus, the cloud point of copolymer solutions was defined.

4. Results and Discussion

4.1. Synthesis of copolymer precursors

The base-catalyzed ring-opening polymerization of glycidol was recently studied intensively by Frey and Muelhaupt (8). Intra- as well as intermolecular transfer steps subsequent to the ring-opening reaction can lead to the formation of primary alkoxide as active site, which further propagates resulting in branched structure (9). Co-polymerization of EO and G using ionic coordinative initiators by precipitation polymerization could be an easy way of getting functionalized high molecular weight PEO. Heterogeneous polymerization systems usually do not follow the pattern established in homogeneous polymerization. The two monomers have different distribution coefficients in the two phases present in the polymerization mixture. They can copolymerize in a random or blockwise fashion. This consideration imply that the percentage of the functional monomer may vary substantially in the polymer fractions formed at different time intervals. It is also possible that one of the monomers may homopolymerize with little or no incorporation of the other.

Copolymerizations of EO and G monomers were carried out in hexane using anionic coordination mechanism. In all cases low MW products with predominant content of G occurred during the reaction: NMR spectra of the copolymers before and after dialysis differ significantly in the G content. The mole fraction of G incorporated in the copolymer was calculated from the phenyl group content after reaction of the polymer with phenyl isocyanate (PhNCO). The result presented in Table 1 clearly show that only a small fraction of G was incorporated in the HMW copolymer. Thus it was possible to compare the intrinsic viscosity of PEO derivative with those of pure PEO.

Table 1. Synthesis and properties of copolymer precursors.
Catalyst: 0.5g Ca as amide-alkoxide; reaction temperature 40 °C; hexane 80 ml; reaction time 5hrs.

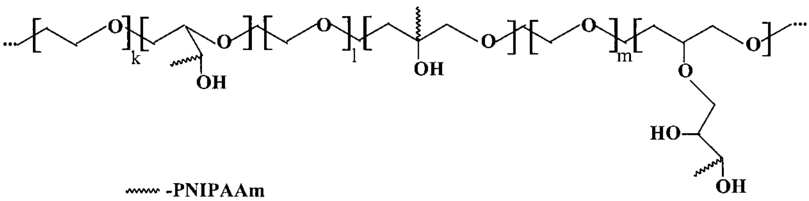
№	Type of copolymer	Glycidol ml	Yield g	$[\eta]^{30}_{H20}$	Mv .10^6	-[EO]-/-[G]-*
P1	Poly(EO-co-G) statistical	2	22	7.3	1.3	25
P2		2	12**	5.8	0.9	150
P3		1.5	22	6.4	1.1	20
P4	***Poly(EO-b-G)	1.5	50	7.6	1.4	50

* The ratio was determined by reaction of polymer with PhNCO, followed by twofold polymer precipitation in ether and UV analysis described in detail in (10)
** Reaction time 2 hours
*** Sequential polymerization: 4 hours blowing of EO followed by addition of glycidol in small portions for another 2 hours (10)

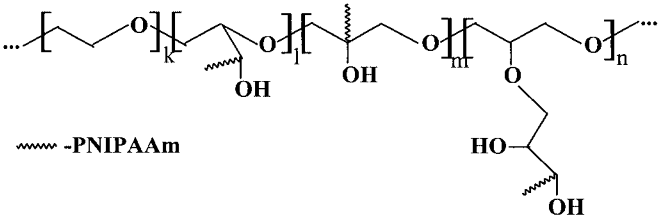
4.2. Grafting of NIPAAm onto copolymer precursors

The use of the ceric-cerous redox system to initiate graft copolymerization of vinyl monomers with cellulose has been reported by a number of investigators (11, 12). The mechanism of the copolymerization reactions has been reported to be a free-radical process in which the transfer of electrons from the hydroxyl groups of the cellulose to the ceric ion results in the formation of a free radical on the cellulose molecule (13). Due to its ease of application as well as its grafting efficiency, the Ce^{IV} ion method has gained considerable importance in the grafting reaction with other polymers bearing hydroxyl groups.

The OH groups in the EO/G copolymer precursors have been utilized for grafting NIPAAm using ceric ion (Ce^{4+}) redox initiation. A series of water-soluble graft copolymers composed of poly(EO-co-G) or poly(EO-b-G) backbones and PNIPAAm grafts were obtained under the conditions described in the Experimental Section.(Scheme 1 and Scheme 2)



Scheme 1.Poly(EO-co-G-g-NIPAAm)



Scheme 2.Poly(EO-b-G-g-NIPAAm)

It is useless to compare the molecular-weight characteristics of the graft copolymers with those of the starting material, since employing nitric acid in the graft copolymerization causes some cleavage of the polyether macromolecules. As a result of this side reaction the molecular weights of grafted with NIPAAm copolymers changed with one order of magnitude as shown in Table 2.

Table 2. Synthesis of grafted with NIPAAm copolymer: 1g copolymer precursor dissolved in 100 ml distilled H_2O; reaction time 16 hrs; reaction temperature 30 °C; $(NH_4)_2Ce(NO_3)_6$ - 0.2 mmol.

№	Copolymer precursor*	NIPAAm g	Yield g	$[\eta]^{25oC}_{H2O}$	Mn .10^5	MWD	-[EO]-/-[NIPAAm]-	
							IR	^{1}H NMR
	Poly(EO-co-G)							
P5**	P1	1	1.1	0.93	1.1	2.8	63	57
P6**	P2	2	1.15	0.87	1	2.5	26	21
P7	P2	1	1.2	2.00	1	2.3	5.3	4,6
P8	P3	0.5	1.12	1.80	0.9	2.2	4.8	4.2
P9	P3	2	1.4	2.13	1.2	2.4	4.8	4.2
	Poly(EO-b-G)							
P10	P4	0.5	1.08	3.75	1.7	3.1	13	10
P11	P4	0.8	1.15	4.10	1.8	3.2	16	12
P12	P4	1.5	1.37	3.90	2.1	3.4	14	10

* Samples of precursors, see Table 1.

** Reaction time 8 hrs; reaction temperature 60 °C.

Figure 1 shows the ^1H NMR spectrum of the graft copolymer in D_2O. The phase transition of the graft copolymers is associated with the decrease of the PNIPAAm chain mobility. This process is clearly shown in Fig. 1.

The chemical shift assignments for all the carbons are summarised in Table 3.

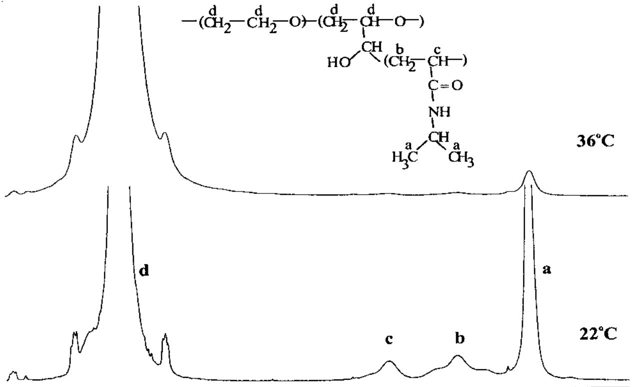


Fig. 1. ^1H NMR spectrum of poly(EO-co-G-g-NIPAAm) (P8) in D_2O. Effect of temperature on the intensities of the oxyethylene backbone protons and the protons of the PNIPAAm grafts.

It is extremely difficult to consider the mechanism of grafting, since different OH groups are present in the starting material (see Scheme 1 and 2), which additionally causes broadening of the graft copolymer polydispersity.

Table 3. Chemical shift assignments for ^{13}C peaks in the graft copolymer P11

Type of carbon	Chemical shift (ppm)
- CH_3 (PNIPAm)	22.79
- CH_2 (PNIPAm)	34.68
- CH (PNIPAm)	42.97
- CH_2 (PEO)	70.79
- C=O (PNIPAm)	176.6

4.3. Phase transition

The transmission curves for the statistical and block graft copolymers are compared in Figure 2. When the temperature reaches the cloud point temperature (T_{cp}), an abrupt increase in turbidity is observed for all samples.

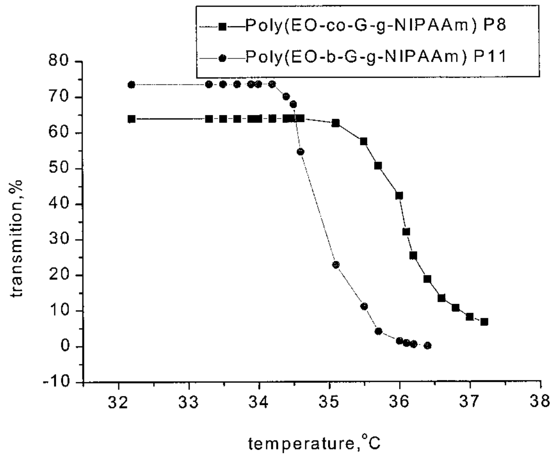


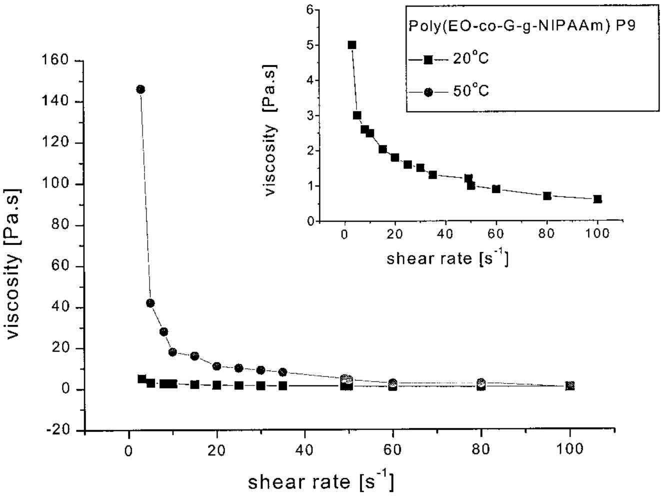
Fig. 2. Cloud point of a 3 % aqueous solution of EO/G copolymers with different architecture, grafted with NIPAAm.

The origin of this turbidity behavior arises because PNIPAAm sequences can self-assemble in aqueous solutions in micellar-like structures, stabilized by the HMW PEO blocks. It is worth noting that all copolymers do not form two well-separated phases even at temperatures much higher than T_{cp}. Instead, they appear in the form of turbid suspensions, stable for several hours. The microscopic phase separation, detected by the appearance of turbidity, is shifted to higher temperatures compared to the LCST of the PNIPAAm homopolymer (33°C). The onset of transmission curves depends on the copolymer architecture. Thus, the cloud point temperature of the random copolymer is higher than that of the blockcopolymer.

4.4. Rheological properties

4.4.1. Semi-dilute solution properties

The viscosities of semidilute graft copolymer solutions were found to decrease with shear rate which is typical for non-Newtonian systems. This kind of shear-thinning flow behavior is well known from aqueous associating polymers (14). Figure 3 shows the viscosity as a function of shear rate of a 5 wt.% solutions of poly(EO-co-G-g-NIPAAm) and poly(EO-b-G-g-NIPAAm). The viscosity of the studied systems displays a remarkable decrease up to $\gamma \approx 10\ s^{-1}$ and at higher shear rates the changes are not significant.



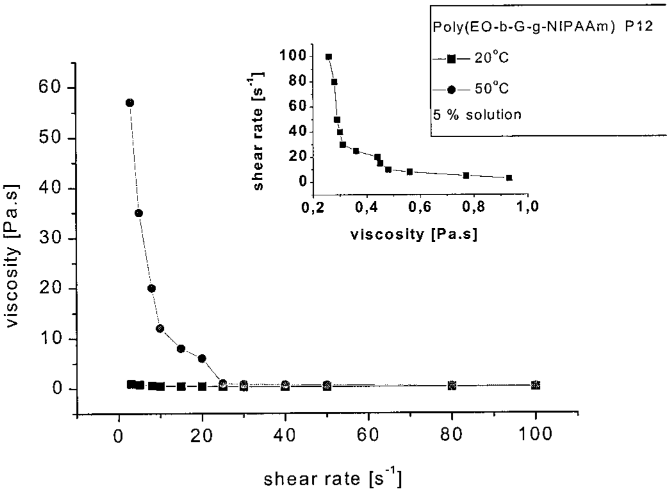


Fig. 3. Variation of the viscosity with shear rate for 5 wt.% solutions of poly(EO-co-G-g-NIPAAm) and poly(EO-b-G-g-NIIPAAm).

Figure 4 shows the reduced viscosity versus temperature plots for aqueous solutions of both copolymer structures at a shear rate of 3s^{-1}. The viscosity increases at temperatures higher than 40 °C. Typical thermothickening behavior was observed with maximum at 50 °C. The magnitude of the thermothickening effect obtained with poly(EO-co-G-g-NIPAAm) is much greater then that observed with poly(EO-b-G-g-NIPAAm). The magnitude of thickening is almost 3 decade of viscosity for poly(EO-co-G-g-NIPAAm), and 2 decade of viscosity for poly(EO-b-G-g-NIPAAM). The onset of the thermo-thickening behavior, or the transition temperature (T_{ass}) which corresponds to the self-assembling of PNIPAAm grafts, does not fully agree with the value issued from the turbidity measurements. When the temperature reaches T_{ass}, the PNIPAAm side chains start to self-aggregate while the PEO backbone stabilize the PNIPAAm phase at the microscopic level. In semi-dilute solutions, the PNIPAAm microdomains are connected through the highly soluble PEO chains into a physical 3-dimensional network with the expected viscoelastic properties. The macroscopic transition, i.e. viscosity, proceeds continuously with increasing temperature. At T > 50°C, the viscosity decreases upon heating obviously due to inverse solubility-relationship of PEO chains. We have verified the reversibility of the thermothickening process by comparing the two plots obtained on heating and cooling. The two curves are very similar and we can conclude that in our experimental conditions, each step of the association process results in a true thermodynamic equilibrium.

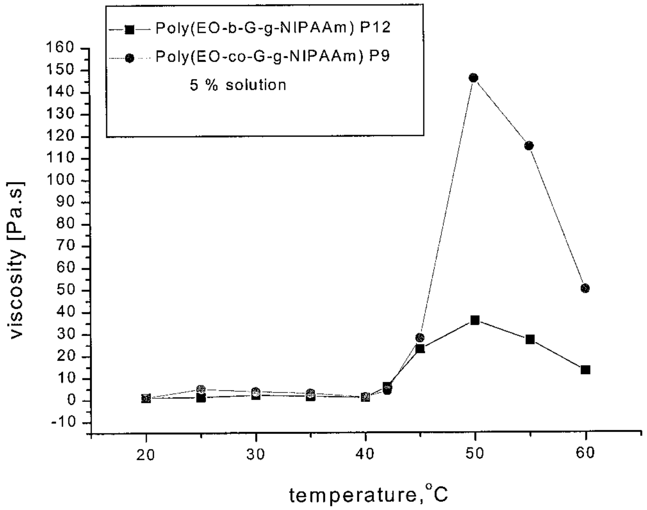


Fig. 4. Typical variation of steady flow viscosity of 5 % aqueous solutions of poly(EO-b-G-g-NIIPAAm) (P12) and poly(EO-co-G-g-NIPAAm) (P9); shear rate 3 s^{-1}.

The evaluation of the dynamic moduli provides important information about the balance between viscous and elastic forces as well about the structural changes after long relaxation periods (15). Dynamic oscillatory experiments show that at higher concentrations (7.5 wt.%) of aqueous solutions the studied systems demonstrate viscoelastic behavior. Figure 5 shows the typical frequency dependence of the dynamic moduli for the aqueous solutions of poly(EO-co-G-g-PNIPAAm).

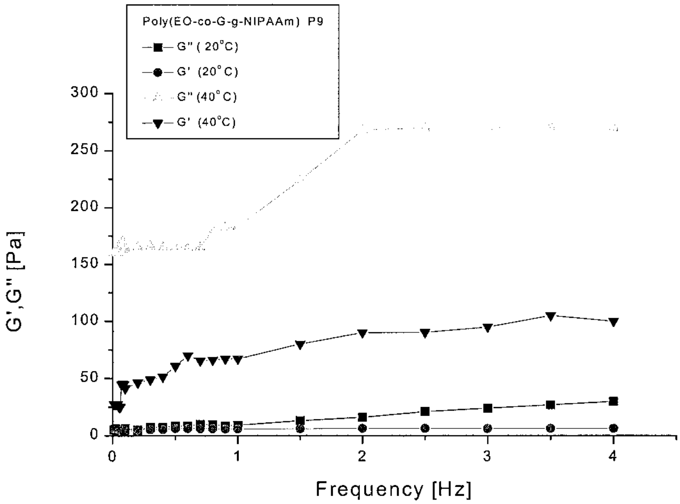


Fig. 5. Frequency dependence of the dynamic moduli of 7.5 % aqueous poly(EO-co-G-g-NIPAAm).

At 20 °C the loss modulus G'' increases with frequency when the storage modulus G' reaches a plateau after ω = 0.5 Hz. At 40 °C G' and G'' reach plateau after ω = 2.0 Hz with significant increase of their value. These results indicate that the interchain association of the copolymers is favored by temperatures higher than 40 °C.

4.4.2. Dilute solution properties

The drastic viscosity decrease in the dilute aqueous polymer solutions at 40 °C and beyond 0.5-0.7 wt. % (concentrations below the critical for coil overlapping) can be ascribed to the intrachain self-assembled association.The viscosity results plotted in Figure 6 can be compared to the monomolecular micellization where the hydrophobic PNIPAAm grafts are clustered towards the center of the shrunk coil and the hydrophilic

PEO backbone is the corona-forming moiety. Thus the polymer coils adopt a rather compact conformation, due to the formation of intrachain aggregates.

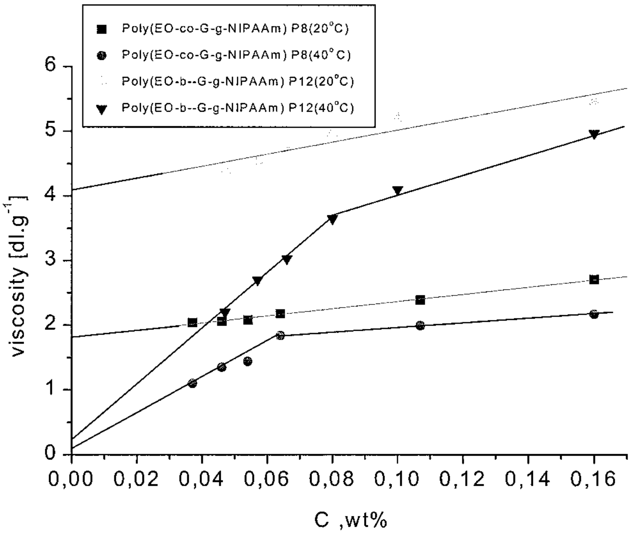


Fig. 6. Intrinsic viscosity [η] as a function of copolymer concentration at temperatures below and above the LCST of PNIPAAm grafts.

6. Conclusions

In this paper we reported the synthesis and solution properties of novel thermoassociative water-soluble graft copolymers comprising high molecular weight poly(ethylene oxide) grafted with poly(N-isopropylacrylamide) side chains.

The synthesis of thermoassociative graft copolymers has been described through a two-step procedure: 1) the synthesis of copolymer precursors of functional HMW PEO carrying OH-groups with two architectures : poly(EO-co-G-g-NIPAAm) and poly(EO-b-G-g-NIPAAm); 2) the grafting of NIPAAm onto these precursors using Ce^{IV} initiators.

From the set of PNIPAAm grafted PEO copolymers in aqueous solution we can separate two types of interactions, induced by heating, depending on the copolymer concentration that is to say intra- and intermolecular association.

In semidilute conditions, aqueous solutions of PEO copolymers start to exhibit associative properties at temperatures slightly higher than the LCST of PNIPAAm grafts. In this aggregation regime, PNIPAAm side chains begin to self-assemble forming loose clusters which behave as physical crosslinks. From the viscoelastic point of view both the number of elastically active chains of the physical network and the life time of the stickers increase.

Acknowledgements

Financial support from the National Fund "Scientific Research" (project X-808) is gratefully acknowledged. The authors thank to Prof. A.H.E. Mueller, University of Bayreuth, for helpful discussions.

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