Rheology and Structures of EO-PO-EO Block Copolymers in Aqueous Solutions

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ABSTRACT

Aqueous solutions of a Pluronic copolymer P104 have been investigated by rheological techniques in order to characterize its gelation and its gel properties. P104 solutions have a low viscosity at low temperatures but form an elastic gel at physiological temperatures. Elastic moduli are of the order 10 kPa with a significant yield stress. Possible use of P104 to prevent flow in pipes or blood veins is discussed.

INTRODUCTION

Most materials become softer when heated and this is used in many practical applications of polymers, and in the food industry thermo-setting gels such as pectin or gelatin gels are important. Some protein solutions and suspensions of starch granulates undergo a transition from a Newtonian liquid to a solid state when heated. Boiling an egg is a good example. However, these systems are not thermo-reversible i.e. they maintain their elastic properties when cooled again. For many technical and medical applications it is desirable to have systems which are low viscosity liquids at low temperatures but form solid elastic states when heated. Such systems may be potentially useful in preventing flow in pipes at selected temperatures and block flow in blood veins during surgery or stop blood circulation to damaged organs.

Block copolymers of ethylene oxide (EO) and propylene oxide (PO) in the form of EO-PO-EO copolymers, called Pluronics or Poloxamers have some of the desired properties. They are low toxicity compounds which are approved for medical applications and used for delayed drug release. Copolymers are dissolved as single molecules, unimers, in water at low temperatures but form micelles, with a core of PO and a mantle of EO, at higher temperatures.[1,2] The hydrophobic core of PO is used to give the delayed release of hydrophobic drugs. At higher concentrations and temperatures some Pluronic solutions form thermoreversible physical gels. These gels consist of liquid crystals of packed either spherical or rod-like micelles. [1,2]

In order to block flow in a pipe a heat-setting material should have a low viscosity at low temperatures so the pipe can be filled easily. At the higher temperature of interest, 37 °C for most biomedical applications, it should form a gel with a high elastic modulus as well as a significant yield stress. If a pressure, P, is applied to a pipe of length, L, and radius, R, the stress σ exerted is given by

$$\sigma = PR/2L \tag{1}$$

To prevent flow in the pipe the material must have a yield stress which exceeds the stress due to the applied pressure.

In this paper we have investigated rheological properties of Pluronic P104 which has a composition $EO_{31}PO_{54}EO_{31}$. We are not aware of any rheological investigations of P104 in the literature. It will be shown that P104 forms gels at temperatures close to physiological temperatures and that gels have significant yield stresses which depend on the concentration of copolymer.

MATERIALS AND METHODS

Pluronic P104 was purchased from BASF and used as received. P104 was dissolved in Millipore water overnight under gentle shaking at 5 °C. Concentrations are given as w/w%.

The gelation of P104 solutions was monitored by small amplitude oscillatory deformations at 1 Hz using a Bohlin VOR rheometer with a C14 couette cell. Solutions were measured between 10 and 50 °C at a heating rate of 1°C/4min. In oscillatory experiments the storage modulus, G', and the loss modulus, G", were determined at an angular frequency, ω, and strain amplitude, γ_0, from the time dependence of the stress

$$\sigma(t)=\gamma_0\,(G'\sin\omega t + G''\cos\omega t) \qquad (2)$$

Steady shear viscosities at shear rates between 1 and 500 s^{-1} were determined by use of a Haake RS100 instrument with a Z20 couette measuring cell at 15 °C. The temperature was then increased to 37 °C and after 20 min thermal equilibration a frequency sweep between 0.1 and 40 Hz at a stress amplitude of 5 Pa was recorded. This was followed by a stress amplitude sweep at 1 Hz with increasing stress amplitudes from 1 to 440 Pa. The final test was a steady stress ramp at 37 °C with a ramp rate of 1.2 Pa/s.

RESULTS AND DISCUSSIONS

Flow curves of P104 solutions with concentrations between 20 and 30 wt% were determined at 15°C. All solutions were Newtonian in the investigated range of shear rates as seen from a shear rate independent viscosity. Viscosities were low and increased with concentration up to 77 mPas for the 30 wt% solution. Such low viscosity values ensure that cold solutions can be injected through even a small radius needle with only moderate force.

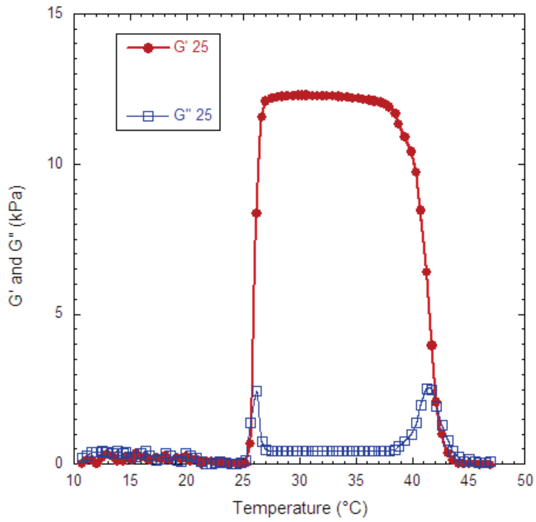

Figure 1. G'(filled circles) and G"(open squares) as a function of temperature of a 25 wt% P104 solution.

When a solution of P104 is slowly heated from 10°C at low strain amplitudes and investigated by oscillatory measurements, G" dominates at low temperatures, but, at a characteristic temperature, G' increases dramatically, and a gel is formed with G' > G", as shown for a 25 wt% solution in Fig. 1. No gelation was observed at or below 23 wt%. The 24 wt% solution resulted in a very weak gel with low modulus, which shows that the gel point is between 23 and 24 wt%. The gelation profile is similar to other Pluronic systems investigated, including P94[3], P85[4], and F127[5], which all form gels of packed spherical micelles. P104 gels are, therefore, also expected to consist of packed spherical micelles.

Fig. 1 shows that a gel with G' > G" is formed between 26 and 42 °C, and the frequency sweeps showed that the gels are characterized by a virtually independent frequency dependence of G'. The rigidity and the temperature range where gels are formed depend on concentration as seen in Fig. 2. Values at 1 Hz are summarized in Table 1. The figure illustrates that an increasing concentration of P104 not only increases G', but also widens the temperature range at which gels are formed. It is also seen that gels at lower concentrations dissolve at high temperatures, as seen previously for P94[3] and P85[4]. This is believed to be due to retraction of the EO chains in the mantles of the micelles when water becomes a poorer solvent.

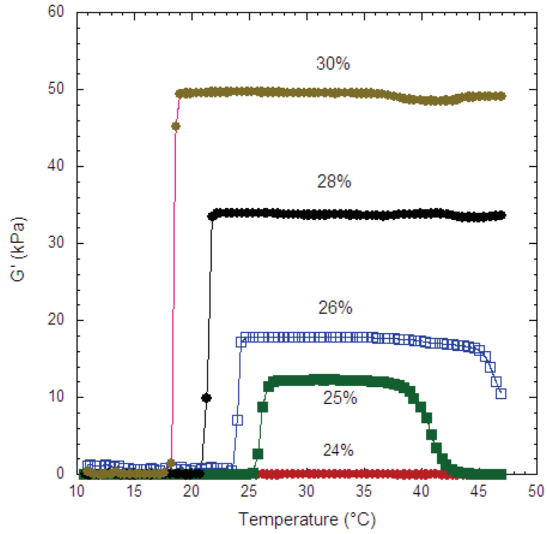

Figure 2. G' at 1 Hz as a function of temperature at the concentrations of P104 marked on the figure.

Table 1. Rheological properties of P104 gels. Gelation temperature T_{gel}, elastic modulus, cross-over strain and yield stress. at 37 °C.

Conc (wt%)	T_{gel} (°C)	G' (kPa)	γ_c	σ_y (Pa)
24	33.9	0.03	0.003	2
25	26.2	12	0.021	150
26	24.0	17	0.043	225
27	22.6	30	0.036	305
28	21.3	35	0.040	405
29	20.0	41	-	>440
30	18.6	49	-	>440

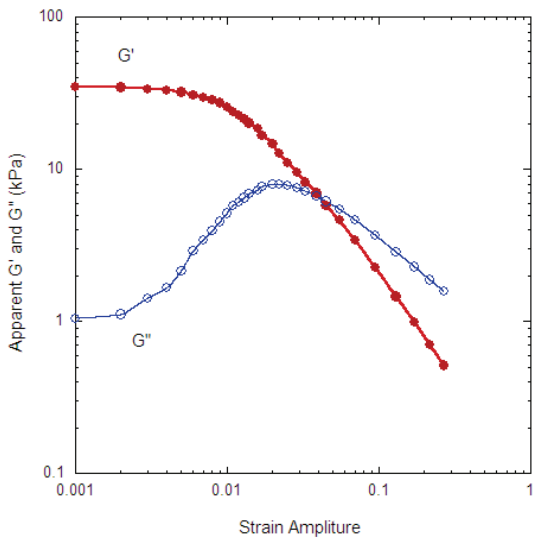

Figure 3. Apparent values of G' and G" at 1 Hz as a function of strain amplitude. Concentration of P104 is 28wt%.

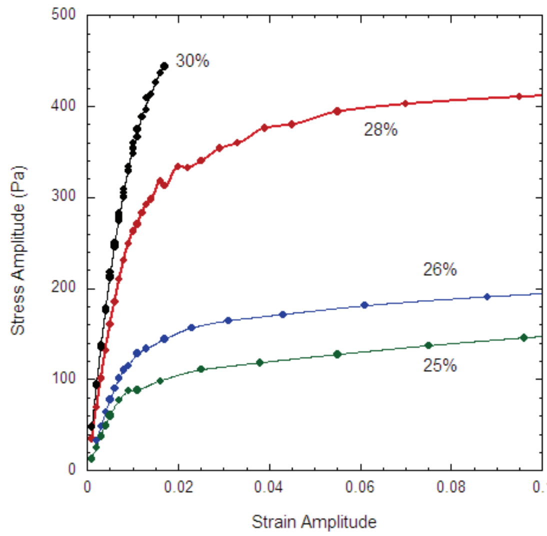

Figure 4. Magnitude of stress amplitude against apparent strain amplitude at 1Hz at the concentrations indicated.

Colloidal physical gels often show a very restricted linear range, i.e. strain range where G' and G" are independent of strain amplitude. This is also the case for P104 gels as shown in Fig. 3. It is seen that G' decreases rapidly at strain amplitudes above 1% where the meaning of G' and G" are not strictly well defined. At higher strain amplitudes the apparent values of G" exceed G′. The cross-over strain values, γ_c, where G' equals G" are summarized in Table 1.

These values mark maximal strain deformation at which elastic properties dominate and values are only about 0.04.

The same data can also be plotted as stress amplitude, σ_0, against magnitude of strain amplitude, γ^*. These magnitudes are related through the complex shear modulus G^* as

$$\sigma_0 = G^* \gamma^* \quad (3)$$

In the linear range, stress is proportional to strain amplitude as seen in Fig.4. Above a certain stress, strain increases more rapidly. This maximal stress is seen to increase from about 150 Pa for the 25 wt% gel to more than 400 Pa for the 28 wt% gel. An even higher stress is needed for the 30 wt% gel. These stresses are an indication of the yield stresses. However, the yield stress can also be estimated by applying a stress ramp to the gels, as shown in Fig.5.

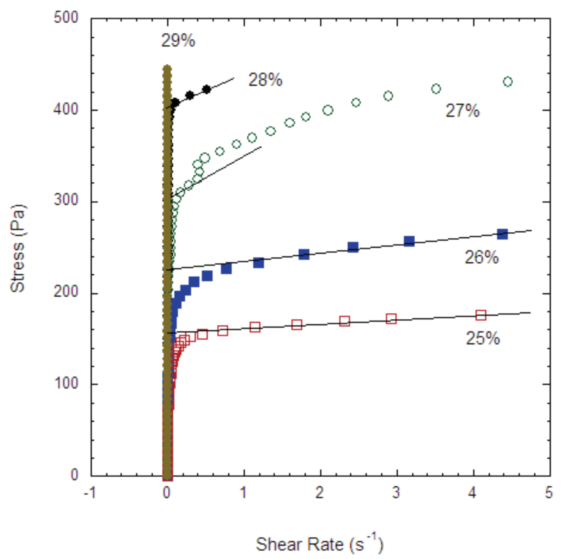

Figure 5. Stress against measured shear rate in stress ramp experiments on P104 gels at 37 °C at the concentrations marked.

Fig. 5 shows that the relationship between stress and shear rate follow the Bingham model well in which

$$\sigma = \sigma_y + \eta_b \dot{\gamma} \quad (4)$$

In this equation, σ_y is the yield stress and η_b is the Bingham or plastic viscosity. Flow only occurs when a stress greater that the yield stress is applied to the sample. Values obtained by a linear extrapolation to vanishing shear rates are summarized in Table 1. These values are seen to be in quite good agreement with the maximum stress amplitudes in Fig. 4. Both figures indicate that P104 gels have significant yield stresses with values from 100 Pa for a 25 wt% solution to more than 400 Pa at higher concentrations.

In order to prevent flow in a pipe, gels must have yield stresses greater than the applied stresses given by Eq. 1. If a pressure of 1 bar is applied to a 1m pipe with a radius of 1cm a yield stress greater than 500 Pa is needed and will necessitate P104 concentrations of the order of 30 wt% or more. In order to stop bleeding or flow in a 10 cm blood vein with a radius of 1 mm at a typical pressure of 0.1 bar, Eq. 1 predicts a necessary yield stress of at least 50 Pa.

P104 seems to be an excellent choice for blocking flow at physiological temperatures. Other Pluronics copolymers may be more useful at other temperatures. Pluronics with a longer PO block will form gels at a lower temperature. The magnitude of the yield stress is important for prevention of flow but in some cases slip effects may occur at lower pressures or stresses. Further studies are needed to test the applicability of such systems under practical conditions.

CONCLUSIONS

It has been shown that P104 solutions are fairly low viscosity Newtonian liquids at low temperatures. Such solutions form thermo-reversible gels at P104 concentrations above 24 wt%. These gels have high moduli of the order 10 kPa with yield stresses above 100 Pa. It is argued that these gels should be considered when it is desired to prevent flow in pipes and in blood veins.

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