Responsive Gelation of Hydrophobized Linear Polymer

Claus Greve Madsen[1], Joachim Toeth[1], Lene Jorgensen[1] Sami Hietala[2] and Stefanía Baldursdottir[1]

[1] Department of Pharmacy, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark

[2] Laboratory of Polymer Chemistry, Department of Chemistry, University of Helsinki, Finland

ABSTRACT

In this study we present the rheological properties of a physically linked polymer network, composed of linear hydrophilic chains, modified with hydrophobic moieties in each end. Solutions of the polymer in ethanol-water mixtures showed Newtonian behaviour up to about 99 % ethanol, with the highest viscosity observed in a 1:1 mixture of ethanol and water. In pure ethanol, the polymer forms a thermo-responsive, non-Newtonian gel, which collapses upon addition of as little as 1 % water or heating to about 40 °C.

INTRODUCTION

Responsive polymers are a mainstay of modern medicine. A recent review on the subject estimated that the number of publications on the subject had increased ten-fold over the last decade[1], and with good reason. The use of responsive polymers allow pharmaceutical developers to target drug delivery, reduce adverse effects or increase the storage time of the drug in question. Traditional examples include tablet coatings which are chemically stable at low pH values, but degrade at high pH, allowing acid liable drugs to pass safely through the stomach[2], and pseudoplastic gels which allow storage of formulations which would otherwise segment, while still being easy to apply because of their decreased viscosity with stress upon spreading on the area to effect[3]. More advanced examples include implanted hydrogels which react to increased levels of glucose in the blood stream by releasing insulin[4], and tumour-targeting systems which releases its drug cargo when in proximity of cancer cells due to changes in various physiological parameters[5].

Traditionally, gels are made of relatively high molecular weight polymer chains, which form a three dimensional network, thereby creating a highly viscous, solid-like material containing mostly solvent (or air, in the case of an aerogel[6]). The network can be connected either chemically (e.g. by covalent bonding) or physically (e.g. by electrostatic interactions, hydrophobic interactions etc.). In responsive gels the network is either created or collapsed in response to stimulation. The methods by which the network is created or collapsed are manifold, and a complete reiteration is outside the scope of this work. The interested reader is instead recommended the following review on the subject[7].

In this study, we present the changes in rheological properties of a system created from various ratios of water-ethanol (EtOH) mixtures and relatively short, linear polymer chains which have been hydrophobically

modified in either end, thereby allowing a network to be formed by hydrophobic interactions between the termini.

MATERIALS AND METHODS
Polymer and solvents

The polymer used in this study was a linear, hydrophilic main-chain, with a hydrophobic moiety at each terminus. The ratio of main-chain to hydrophobic moiety was about 24:1. The polymer was dissolved in either ultrapure water, ethanol (EtOH) [99.9 % J.T. Baker, Avantor Performance Materials, B.V.] or mixtures of water-EtOH in different ratios.

Sample preparation

Solutions were obtained by adding ultrapure water, pure EtOH or mixtures of water-EtOH to the powered polymer (2.5 % w/v), and leaving to dissolve at room temperature for at least 1 hour. Solutions contained 100, 75, 50, 25, 5, 1 and 0% (v/v) water.

Rheological measurements

All measurements were conducted on an AR-G2 rheometer [TA Instruments]. Measurements were performed with a 40 mm steel cone with a 1 ° angle and 33 μm truncation gap. Measurement parameters varied with sample: Solutions with 100-1 % v/v water were measured with 2 minute conditioning at 25 °C, followed by a steady shear measurement with shear rates of 0.01-1000 s^{-1}. Maximum point time was set to 1 minute. The sample containing 100 % v/v EtOH was measured with a conditioning step at 40 °C (ensuring even plate distribution) for 2 minutes. A time sweep was then performed for 30 minutes, where the temperature was lowered to 25 °C during the first 2 minutes, with angular frequencies of 6.283 rad/s – 62.83 rad/s. The power law exponent, n, was calculated from the frequency sweeps measured during the evolvement of the gel within a timeframe of

1 min, where: $G' \propto G'' \propto \omega^n$. This was followed by strain sweeps performed with 0.01 – 100 % strain and an angular frequency of 6.283 rad/s. All the oscillatory shear measurements were conducted within the linear viscoelastic region and were excluded if inertia dominance was detected. Finally, another conditioning for 1 minute and a steady shear measurement was performed at shear rates of 0.01-1000 s^{-1}, and a maximum point time of 1 minute.

RESULTS AND DISCUSSION

The viscosity of the samples was investigated at different volume fractions of water. All the samples showed Newtonian behaviour up to 99 % v/v water content. The viscosity increased with decreased water content up to 50 % v/v, at which point the solution displayed its maximum viscosity (Fig. 1).
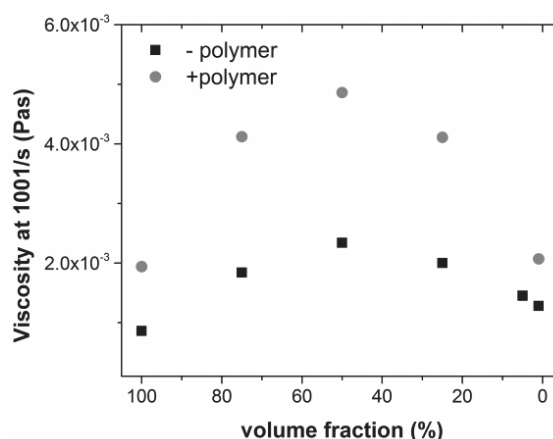

Figure 1. Viscosity, at shear rate of 100 s^{-1}, as a function of volume fraction of water, in water-ethanol mixtures. Circles and squares represent solvent mixtures in the presence and absence of the polymer, respectively.

The difference between solution and solvent viscosity also increased up to this point, at which the solution had double the viscosity of the pure solvent (approximately $4.0 \cdot 10^3$ Pas compared to $2.0 \cdot 10^3$ Pas at shear rates of 100s^{-1}, respectively). Increasing the fraction of water above 50 %

v/v decreased the viscosity, as well as the viscosity difference between the solution and the solvent (Fig. 1). The solution of 100 % water was approximately as viscose as the solution containing 1 % v/v water (approximately $2.0 \cdot 10^3$ Pas compared to $2.1 \cdot 10^3$ Pas at shear rate of 100s^{-1}, respectively). The difference in polymer solution and solvent viscosity was however, greater for solutions of 100 % v/v water than solutions containing 1 % v/v water.

Interestingly, at 100 % EtOH the sample formed a gel, and with as little as 1 % v/v of water present the gel collapsed into a solution, with a viscosity near that of the solvent alone (approximately $2.1 \cdot 10^3$ Pas compared to $1.3 \cdot 10^3$ Pas at shear rate of 100 s^{-1}, respectively, Fig. 2).
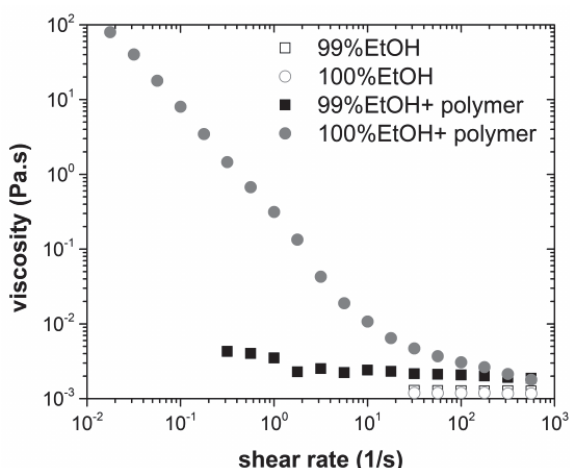

Figure 2. Shear rate dependency of polymer samples in 99 % (squares) and 100 % (circles) ethanol (EtOH). Samples without the polymer are presented as a reference (open symbols).

Figure 2 shows the shear rate dependency of the viscosity of the polymer gel, and polymer solution with 1 % v/v added water, and the solvent mixture is included for comparison. As expected, both the water-EtOH mixture and the pure EtOH showed Newtonian behaviour and the polymer solutions with 1 % v/v added water showed only minor shear thinning properties (going from approximately 0.03 Pas to 0.01

Pas). However, in pure EtOH the polymer showed a strong shear thinning behaviour (from 100 Pas to 0.01 Pas) at shear rates between 0.01 s^{-1} and 10 s^{-1}, after which it slowly reached the 2nd Newtonian plateau where the viscosity decrease only slightly (going from 0.01 Pas to 0.001 Pas at shear rates between 10 s^{-1} and 1000 s^{-1}).

The results confirm the absences of a major network in the presences of water, as there where little or no change in viscosity upon shear rate change (Fig. 2).

Oscillatory shear measurements were conducted on the 100 % EtOH sample that showed a build-up of a strongly elastic structure of the network during the first 10 min of the measurement (Fig. 3). This is supported by the decreasing of the power law exponents (n).
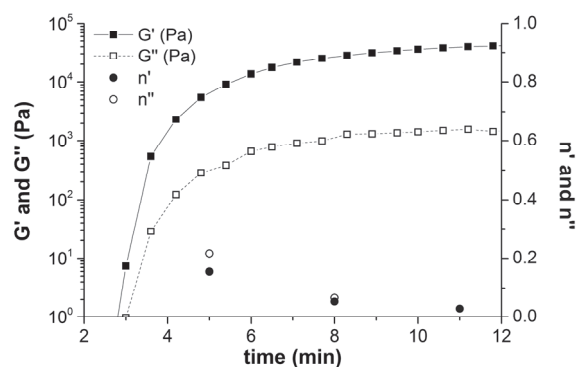

Figure 3. Development of the elastic and viscous moduli (left axis) and the power law exponents n' and n'' (right axis) over time after cooling from 40 °C to 25 °C (the first 2 min), at frequency of 6.283 rad/s and the oscillation strain of 0.1 %.

The results indicate that a network which spans the total solvent volume is only formed in pure EtOH.

The polymer may, primarily, be affected by water in two ways: As the terminal ends of the polymer are hydrophobic, the clustering of these groups together will become more thermodynamically favourable

as the content of water increases[8]. In pure EtOH this effect would be considerably smaller, allowing the grouping of fewer terminal ends and thereby a wider network. Additionally, as the main-chain is hydrophilic it will be hydrated as water content increases, thereby increasing the distance that the main-chains repel each-other[9].

CONCLUSIONS

In water-EtOH mixtures the polymer formed a Newtonian solution from 100 to 1 % water. The highest viscosity for the solution was observed in 1:1 EtOH-water mixtures. In pure EtOH the polymer formed a non-Newtonian gel. While shear thinning was observed for polymer solutions containing 1 % v/v added water, this was very weak, confirming a total loss of network at this water content. Oscillatory shear measurements showed that the gel contained a strong elastic structure.

The observed effects are ascribed to the addition of water making clustering of the hydrophobic terminals and dissipation of the hydrophilic main-chain more favourable, thereby causing a loss of the macroscopic network structure.

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