

Comparison of rotational and oscillatory temperature sweeps for determination of the gel properties of poloxamers

Authors

T. Agnese, T. Cech, M. G. Herting, BASF SE, Ludwigshafen, Germany
F. Brandenstein, F. Soergel, Thermo Fisher Scientific, Karlsruhe, Germany

Key words

Sol/Gel transition, Gel point, Gel strength

Introduction

For the pharmaceutical application of solubilisers, the gel point can be of great importance. However, the rheological determination of the gel point and gel strength can be performed in rotational or oscillatory measurements. The purpose of this study was to determine whether these two approaches lead to the same rheological results.

Experimental methods

Materials

For this investigation, poloxamers 407 (Lutrol® F127) and 188 (Lutrol® F68), both BASF SE, Ludwigshafen, Germany were used.

Formulations

Solutions with different concentrations (10, 15 and 20 % w/w) of poloxamer 188 and 407 in water were prepared. According to common practice, "cold water" preparation was used (1). The poloxamer was stirred in using a magnetic stirrer. In order to ensure both low viscosity and homogeneous distribution, the solution was left for 2 days at refrigerated conditions (5 °C).

Equipment

To perform the rheological investigations, a Thermo Scientific™ HAAKE™ Rheometer was used, with a coaxial cylinder double gap geometry DG43Ti for rotational testing or with a 60 mm parallel plates P60Ti measuring geometry for oscillatory testing – all equipment: Thermo Fisher Scientific, Karlsruhe, Germany.

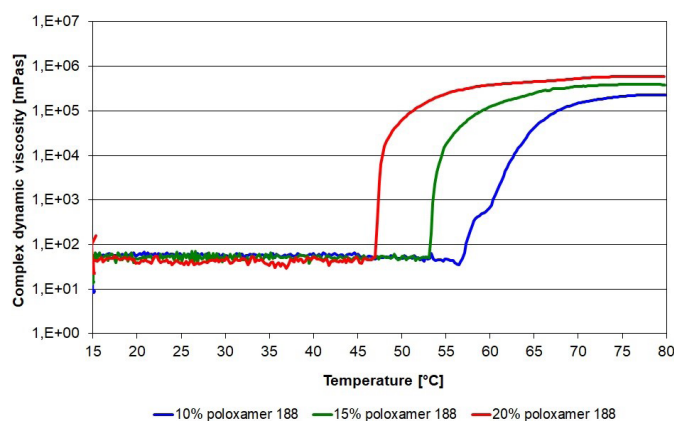


Figure 1: Complex viscosity of poloxamer 188 determined with oscillatory testing (P60Ti).

Methods

After sample loading, each sample was equilibrated at 15 °C for 3 minutes. For the investigation of the gel point, a temperature ramp (15 - 80 °C) was used with a heating rate of 2 K/min.

A shear rate of 50 s⁻¹ was set for the rotational testing. For oscillatory testing, controlled deformation (CD) mode with an amplitude of 1.0 % and a frequency of 1.0 Hz was adjusted.

Results and discussion

Poloxamer 188

Rotational testing with absolute measuring geometries provides dynamic viscosity data and requires constant shear rate across the complete measuring geometry. This is achieved either with coaxial cylinder or with plate/cone measuring geometries.

Oscillatory testing delivers complex dynamic viscosity data and is commonly conducted with parallel plates measuring geometries.

The complete rheological picture is revealed by oscillatory testing (Figure 1), delivering the gel transition temperature as a sharp onset in dependency of poloxamer concentration used (47 °C at 20 %; 53 °C at 15 % and 57 °C at 10 % polymer content). The higher the concentration of the poloxamer the lower the gel point and the higher the gel strength, indicated by the maximum viscosity.

As the increase in viscosity caused by gel formation is much smaller in rotation than in oscillation, these data are presented in linear scaling (Figure 2). Between 15 and 35 °C a thermal softening of the sol leads to a decreasing viscosity. A precise determination of the gel formation temperature is here hardly possible.

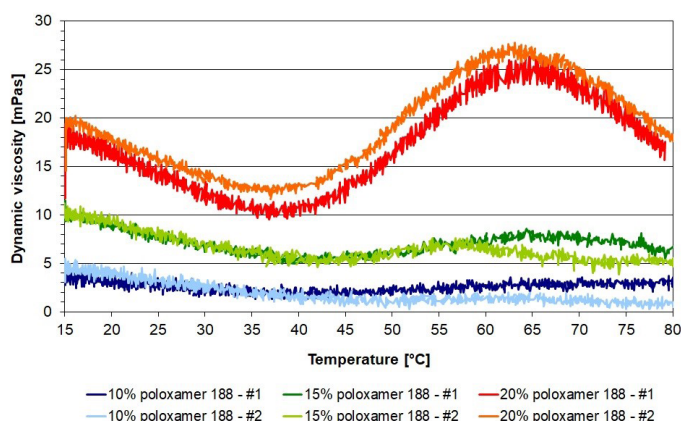


Figure 2: Dynamic viscosity of poloxamer 188 determined with rotational testing (DG43Ti).

Poloxamer 407

Compared to poloxamer 188, poloxamer 407 is forming a gel at lower temperatures.

A clear determination of the gel point is accessible from the rheological curve obtained by using oscillatory testing for all concentrations (Figure 3).

For the rotational measurements with Poloxamer 407 solutions, the DG43Ti could not be used for 15 and 20 % polymer content, as the viscosity of the gel was found to be too high. Therefore, P60Ti geometry was also used for the rotational measurements.

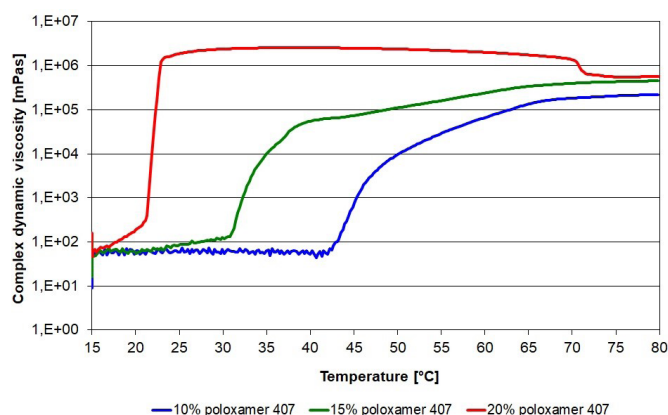


Figure 3: Complex viscosity of poloxamer 407 determined with oscillatory testing.

In rotational testing, only the 20 % concentration resulted in a clear viscosity onset (Figure 4). However, the determined gel formation temperature was considerably higher than with oscillatory testing. In rotation, a forming network is partly destroyed through applied shear rate, hence, the gel formation requires higher temperatures to build up a stable gel network. This offset is dependent on the heating rate. The lower the heating rate the smaller the offset.

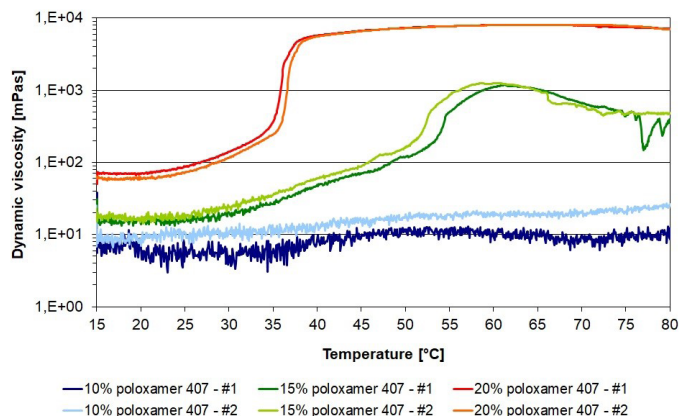


Figure 4: Dynamic viscosity of poloxamer 407 determined with rotational testing (P60Ti).

To evaluate the influence of heating rate and shear rate, rotational tests with a heating rate of 1 K/min with various shear rates (20, 50, 100 and 500 s⁻¹) were performed using 20 % poloxamer 407 solution. The obtained results were compared to oscillatory results for the same concentration (Figure 3). This comparison is displayed in Figure 5.

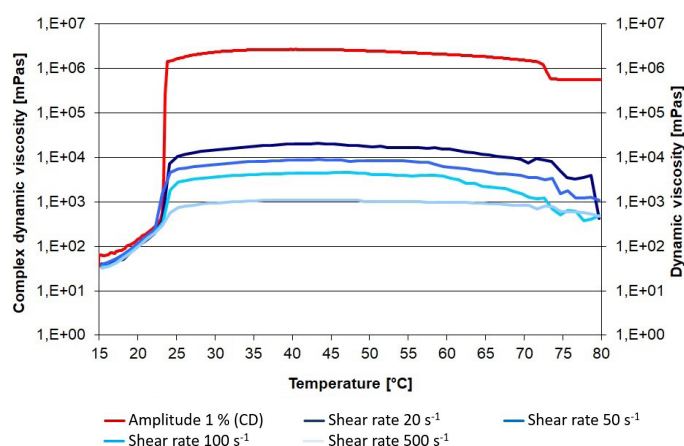


Figure 5: Comparison of complex and dynamic viscosity of poloxamer 407 (20 %) using oscillatory testing in CD mode with a heating rate of 2 K/min (red) and rotational testing with different shear rates and a heating rate of 1 K/min (blue) (P60Ti).

By applying a lower heating rate (1 K/min) in rotation, the same gel point could be found as in oscillation. However, the maximum viscosity measured, was clearly depending on the shear rate applied. The lower the shear rate the higher is the maximum viscosity. Lower shear rates than 20 s⁻¹ would be required to shift the maximum viscosity closer to the gel strength obtained in oscillation.

Conclusion

In general, the rheological results are depending on the measuring method used. While in oscillation the gel formation is not disturbed, in rotation the forming gel network is partly disrupted by the shear rate applied.

This results in lower maximum gel viscosities in rotation compared to oscillation. As a consequence, the shear rate should be adjusted as low as possible to come close to the results found in oscillation.

The gel formation temperature in rotation is occurring at higher temperatures than in oscillation. However, in the case of low heating rates, this effect can be reduced and the results are comparable with the temperatures found in oscillation.

Applying all these suggested improvements for rotational measurements will only result in comparable results if the poloxamer concentration is high.

However, for all poloxamers in all examined concentration, a detailed rheological characterisation was possible using oscillating measuring method (2, 3).

Reference

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