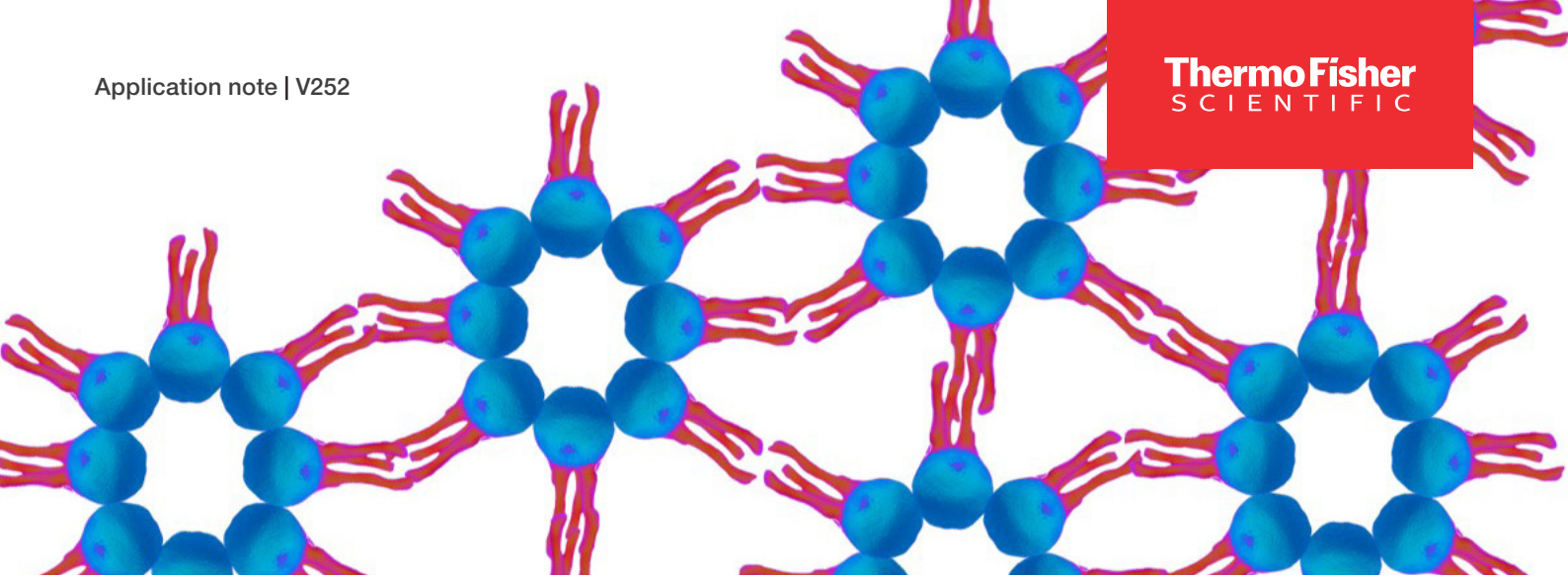

Determination of sol/gel transition temperature and gel properties of poloxamer blends with oscillatory measurements

Authors

T. Agnese, T. Cech, M. G. Herting, BASF SE, Ludwigshafen, Germany

F. Soergel, Thermo Fisher Scientific, Karlsruhe, Germany

Key words

Sol/Gel Transition, Gel Point, Gel Strength, Molecular Weight

Introduction

Poloxamer 407 is a standard surfactant for liquid pharmaceutical applications. As regards specific dosage forms it is suggested to use the temperature-initiated gel formation properties of this product to achieve high viscosities (e.g. contact with the skin of the human body).

Depending on the active pharmaceutical ingredient, high poloxamer concentrations are necessary for solubilisation. However, the sol/gel transition temperature of an aqueous poloxamer 407 solution depends on its concentration. A higher poloxamer concentration lowers the gel point temperature (GPT) (1). This can be a problem and may raise the need for an adjustment. Earlier investigations showed that poloxamer 188 offered a distinctively higher GPT than poloxamer 407 (1, 2, 5).

The aim of this study was the rheological characterization of the gel formation dynamics of aqueous solutions containing mixtures of the poloxamers 188 and 407. For the investigation oscillatory testing was applied (3). Particular focus was laid on GPT and strength of the formed gel to answer the question to which extend those parameters can be tailored to the regarding application by mixing poloxamers with different molecular weights.

Materials and methods

Materials

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

Formulations

Aqueous solutions of poloxamer 188 and 407 were characterized in a previous work (#1 to #6) (1) and these results were compared with those of various poloxamer mixtures (#7 to #13) which were investigated in this study (Table 1).

According to common practice, “cold water“ preparation was used (4). The poloxamer was stirred in using a magnetic stirrer. In order to ensure both, low viscosity as well as homogeneous distribution, the solution was left for 2 days at refrigerated conditions (5 °C).

Table 1: Compositions tested – listed, the amount of poloxamer (w/w) present in the individually formulated aqueous solution

	Poloxamer 188	Poloxamer 407
Formulation #01	10 %	
Formulation #02	15 %	
Formulation #03	20 %	
Formulation #04		10 %
Formulation #05		15 %
Formulation #06		20 %
Formulation #07	5 %	10 %
Formulation #08	5 %	20 %
Formulation #09	10 %	10 %
Formulation #10	10 %	20 %
Formulation #11	20 %	5 %
Formulation #12	20 %	10 %
Formulation #13	20 %	20 %

Equipment

To perform the rheological investigations, complex dynamic viscosity from oscillatory testing was determined using a Thermo Scientific™ HAAKE™ Rheometer, with a 60 mm parallel plate measuring geometry – all equipment: Thermo Fisher Scientific, Karlsruhe, Germany.

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. For oscillatory testing, controlled deformation mode with an amplitude of 1.0 % and a frequency of 1.0 Hz was adjusted.

Results and discussion

By means of oscillatory testing, a distinct GPT could be determined for all formulations tested.

In regard to poloxamer 188, the GPT clearly depended on its concentration in water – the higher the poloxamer content, the lower the temperature which was required to initiate the gel formation. It was found that an increase of the polymer concentration in the solution by 5 % reduced the GPT by about 5 K (Figure 1).

Regarding poloxamer 407, the GPT was found at markedly lower temperatures. The dependency of the GPT on the poloxamer concentration was even more pronounced – an increase in polymer content by 5 % resulted in a GPT reduction of 10 K. Furthermore, it could also be seen, that the sol/gel transition was less sharp, particularly at higher concentrations (Figure 1). This can be explained by the bimodal distribution of the molecular weight of this product (Figure 2). Within the single components, the highest gel strength was measured for sample #6 between 20 and 70 °C. Above 70 °C, both 20 % samples (#3 and #6) show the same level of complex dynamic viscosity (Figure 1).

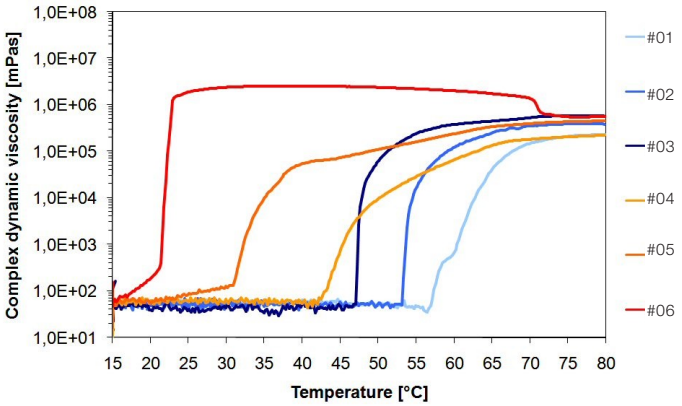

Figure 1: Complex dynamic viscosity and gel formation as function of temperature – different concentrations of individual poloxamers 188 (blue) and 407 (red) (1).

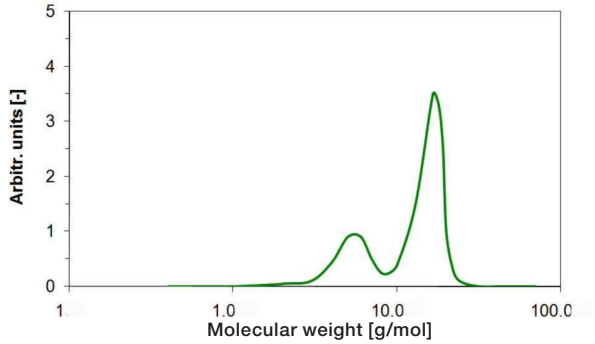

Figure 2: Molecular weight distribution of poloxamer 407.

By adding 5 % poloxamer 188 to solutions of 10 and 20 % poloxamer 407 (#7 and #8), the resulting GPTs were higher than the GPTs for the single component solutions with 10 and 20 % poloxamer 407 (#4 and #6). Comparing sample no. 8 to the single components, the sol viscosity below 20 °C as well as the gel strength above 35 °C (and even above 70 °C) was found to be distinctively higher (Figure 3).

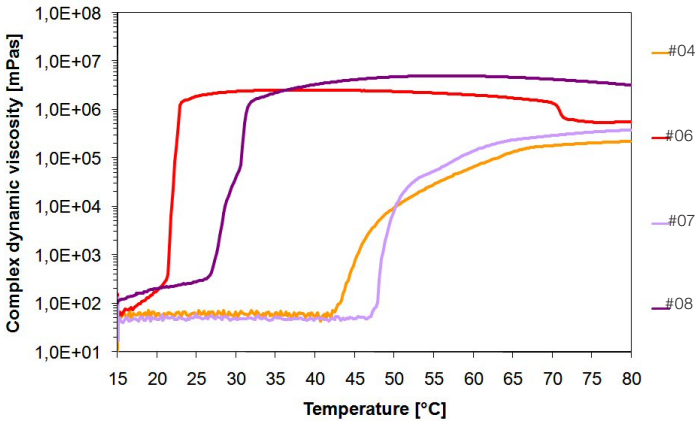

Figure 3: Complex dynamic viscosity and gel formation as function of temperature – 5 % poloxamer 188 as basic formulation.

In the next step, 10% poloxamer 188 was added to solutions of 10 and 20 % poloxamer 407. Interestingly, the GPTs of these two formulations (#9 and #10) were still located between the GPTs of the individual polymers (#1, #4 and #6). Again, the sol viscosity below 20 °C as well as the viscosity level of the gel above 35 °C were higher for the higher concentrated formulation (#10) (Figure 4).

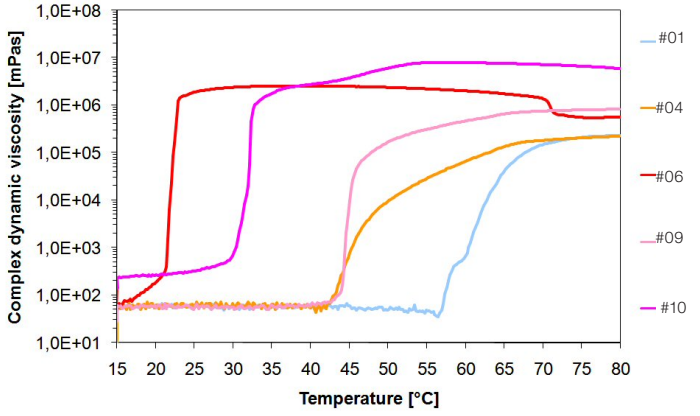

Figure 4: Complex dynamic viscosity and gel formation as function of temperature – 10 % poloxamer 188 as basic formulation.

In a last step, 5, 10 and 20 % poloxamer 407 were added to a solution of 20% poloxamer 188 (#11, #12 and #13). Again, the GPTs for all these formulations were found between the individual polymers (#3, #4 and #6). The sol viscosity below 20 °C as well as the gel strength was found to be elevated again (Figure 5).

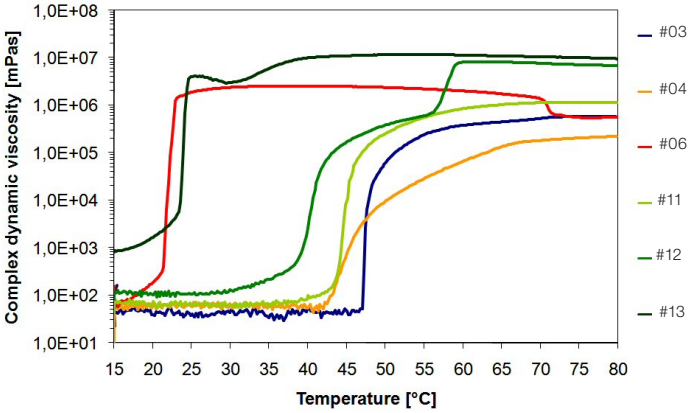

Figure 5: Complex dynamic viscosity and gel formation as function of temperature – 20 % poloxamer 188 as basic formulation.

Conclusion

The addition of poloxamer 188 to an aqueous solution of poloxamer 407 elevated the gel point temperature (GPT). Interestingly, the GPTs were always located between those of the single polymers independent of the individual concentration. Furthermore, mixtures of the two poloxamers yield higher gel strength than solutions of the single solubilizes.

References

1. T. Cech, M.G. Herting, F. Soergel, et al.; Comparison of rotational and oscillatory temperature sweeps for determination of the gel properties of poloxamers; Thermo Fisher Scientific Application note V250
2. Dumortier, et al.; A review of poloxamer 407 pharmaceutical and pharmacological characteristics; Pharm. Research, Vol. 23, No.12, 2006
3. G. Schramm; A practical approach to rheology and rheometry; 2nd edition; 2004; Thermo Fisher Scientific; Karlsruhe, Germany
4. T. Agnese, T. Cech, M.G. Herting, F. Soergel; Influence of preparation method on viscosity of different poloxamers; Thermo Fisher Scientific Application note V249
5. T. Agnese, T. Cech, M.G. Herting, F. Soergel; Influence of sodium chloride concentration on gel temperature and gel properties of poloxamer blends; Thermo Fisher Scientific Application note V253

For more information, please visit
thermofisher.com/rheometers