

Rheological Properties of Poloxamer 407 Solutions and Gels

Eun-Kyoung Park and Ki-Won Song*

Department of Organic Material Science and Engineering, Pusan National University,
Pusan 609-735, Korea (E - mail : ek31004@pusan.ac.kr)

ABSTRACT

The main objective of this work is to characterize the rheological behavior of poloxamer 407 solutions and gels in various shear flow fields.

INTRODUCTION

Water soluble triblock copolymers of poly(ethylene oxide) and poly(propylene oxide), often denoted by PEO_x - PPO_y - PEO_x, are commercially available non-ionic macromolecular surfactants commonly known as Poloxamers[®] or Pluronic[®]. Because of their surfactant properties, they have wide applications in detergency, dispersion, stabilization, foaming and emulsification. Each application can be decided by architecture of triblock, i.e., total molecular weight, relative block size and block sequence as well as thermodynamic parameters.¹

In particular, highly concentrated poloxamer solutions are widely used in numerous biomedical applications, such as drug delivery vehicles, gels for replacing biological fluids and nucleus pulposus surfactants for emulsification of food and personal care products.

Poloxamer 407, principally available in the registered trademark of Pluronic F127[®], has a molecular weight of about 12,600 (9,840-14,600), x and y are equal to 95-105 and 54-60, respectively. Poloxamer 407

aqueous solutions show thermo-reversible properties, which present great interest in optimising drug formulation.²

Reverse thermal gelation and low toxicity have been the basis of research into the use of poloxamer 407 as a possible drug delivery system in human body. It has been considered for topical delivery of lidocain, anti-cancer agents and for the covering of burnt wounds. In addition, poloxamer 407 has been studied as a potential vehicle for injectables by both the intramuscular and subcutaneous routes.³

Due to its paramount importance in pharmaceutical applications, many attempts have been made to investigate the rheological properties of poloxamer 407 during the past several decades.⁴⁻⁷ However, most of rheological investigations have been focused on steady shear viscosity and sol-gel transition phenomenon.

Based upon the above-described backgrounds, the present study has been undertaken to characterize the rheological properties of concentrated poloxamer 407 solutions and gels in various shear flow fields.

EXPERIMENTAL SECTION

Preparation of Poloxamer 407 Solutions

The poloxamer 407 (pluronic F-127)

*Corresponding Author : kwsong@pusan.ac.kr

sample used in this study is a commercially available product supplied from the Sigma - Aldrich Corporation (St. Louis, MO, USA).

In this study, poloxamer 407 solutions with different concentrations of 10 ~ 25 wt% were prepared by constant stirring using propeller-type variable-speed homogenizer for 6 hr with a rotational speed of 150 rpm at 4 °C. The sample solutions were left overnight in the water bath to ensure complete dissolution.

Rheological Measurements

The rheological properties of poloxamer 407 solutions were measured using a strain-controlled rheometer [Advanced Rheometric Expansion System (ARES), Rheometric Scientific, Piscataway, NJ, USA] equipped with a cone-plate fixture having a radius of 12.5 mm and a cone angle of 0.04 rad as well as a parallel-plate fixture having a radius of 12.5 mm and a gap size of 0.5 mm.

When adopting a parallel-plate configuration, before the samples were loaded, the two plates were covered with sandpaper in order to get rid of a wall slippage between the test material and the plates. In all measurements, a fresh sample was used and rested for 20 min after loading to allow material relaxation and temperature equilibration.

The steady shear flow properties were measured over a wide range of shear rates from 0.025 to 1000 1/s with a logarithmically increasing scale.

The sol-gel transition temperature of poloxamer 407 solutions was determined from oscillatory measurements at $\omega=1$ rad/s and $\gamma_0=0.1$ %, the temperature being increased by 0.5 °C/min from 0 to 50 °C. The transition temperature was defined as the point where the elastic modulus was half way between G' for the solution and G'' for the gel.⁸

In this study, in order not only to determine the linear viscoelastic region but also to investigate the nonlinear viscoelastic

behavior in large amplitude oscillatory shear flow fields, dynamic strain-sweep measurements were also performed for poloxamer 407 solutions. These strain-sweep tests were carried out over a strain amplitude range from 0.1 to 1000 % at several fixed angular frequencies of 0.1 ~ 50 rad/s.

The frequency-sweep measurements were conducted in order to elucidate the relationship between the linear viscoelastic behavior and the microstructure of poloxamer 407 solutions under their rheological ground state. These frequency - sweep tests in small amplitude oscillatory shear flow fields were carried out over an angular frequency range from 0.01 to 100 rad/s with a logarithmically increasing scale at a constant strain amplitude of 0.0625 %

RESULTS AND DISCUSSION

Fig. 1(a) represents the shear rate dependence of the shear stress and steady shear viscosity for 17 wt% poloxamer 407 solution at 20 °C. As the shear rate is increased, the shear stress is linearly increased and thus the steady shear viscosity exhibits an almost Newtonian flow behavior.

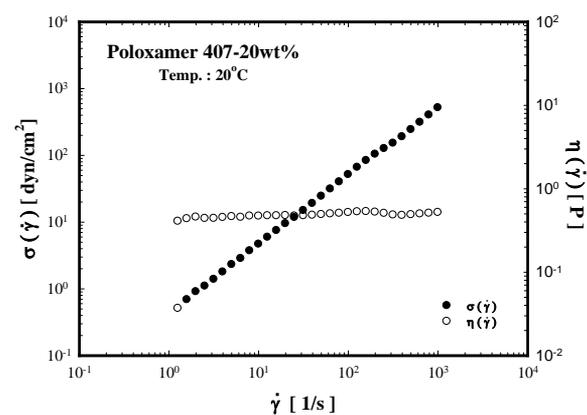


Figure 1(a). Shear rate dependence of shear stress and steady shear viscosity for 17 wt% poloxamer 407 solution at 20 °C.

Fig. 1(b) shows the shear rate dependence of the shear stress and steady shear viscosity

for 17 wt% poloxamer 407 solution at 35°C. The shear stress tends to level off and approach a limiting constant value as a decrease in shear rate toward zero at low range of shear rates, indicating that this system exhibits a finite magnitude of yield stress. In addition, while the Newtonian viscosity region is not observed at low shear rates, the steady shear viscosity is sharply decreased as an increase in shear rate, demonstrating that this system exhibits a marked non-Newtonian shear-thinning behavior.

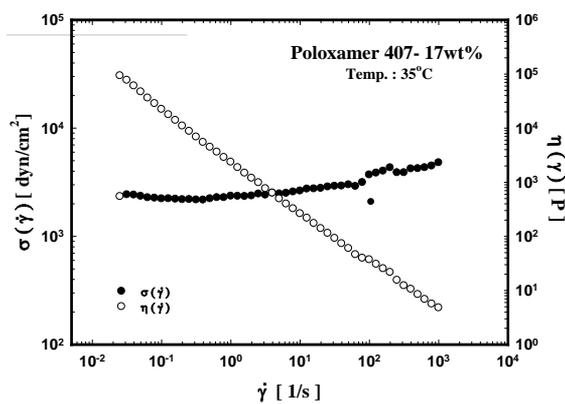


Figure 1(b). Shear rate dependence of shear stress and steady shear viscosity for 17 wt% poloxamer 407 solution at 35°C.

Poloxamer 407 has been known to show thermo-reversible gelation in aqueous media. In addition, with increasing temperature, it aggregates in micelles to minimize the free energy of solution. Upon warming, equilibrium between monomer and micelles is established, and finally aggregates are formed at higher temperature.

The sol-gel transition temperature for 17 wt% poloxamer 407 solution is displayed in Fig. 2. It can be observed that, at temperature range lower than 28°C, both the storage and loss moduli show very small magnitude but increase drastically with increasing temperature as a result of the gel forming process.

It is also interesting that an almost linear relationship is found between poloxamer 407

concentration and $T_{\text{sol-gel}}$ over a concentration range of 10 ~ 25 wt% ; the transition temperature being linearly decreased with increasing concentration, as illustrated in Fig. 3.

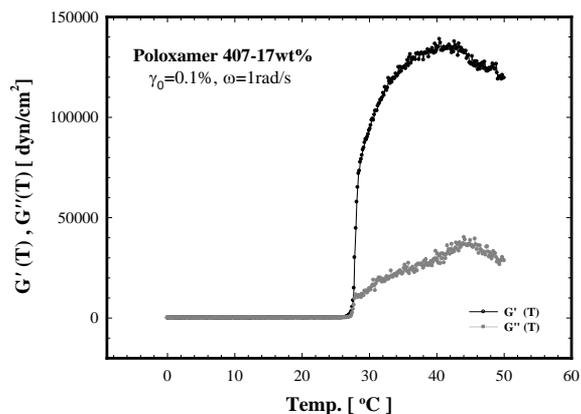


Figure 2. Temperature dependence of storage modulus and loss modulus for 17 wt% poloxamer 407 solution.

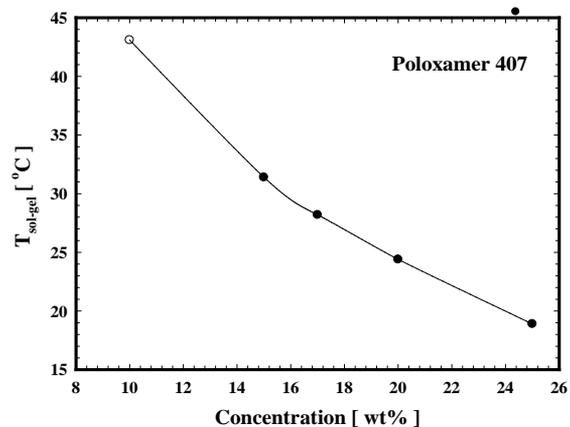


Figure 3. Concentration dependence of $T_{\text{sol-gel}}$ for poloxamer 407 solutions with different concentrations .

Fig. 4 shows the steady shear viscosity for poloxamer 407 solutions with different concentrations at 20°C. The 25 wt% solution is already changed into gel state at 20°C, while 15, 17 and 20 wt% solutions are still in sol state at the same temperature. As a consequence, the steady shear viscosity for the 25 wt% poloxamer 407 solution exhibits a significantly different flow behavior from

that for other solutions with lower concentrations.

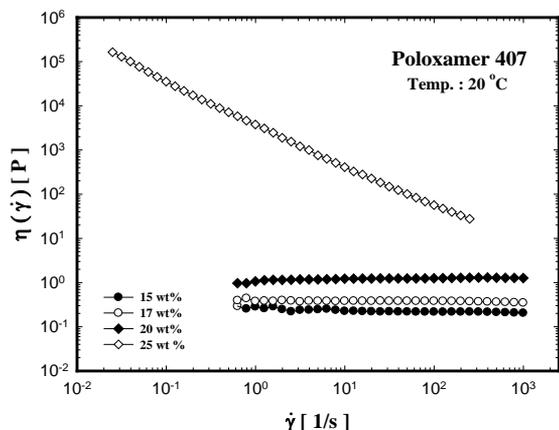


Figure 4. Concentration dependence of steady shear viscosity for poloxamer 407 solutions with different concentrations at 20 °C.

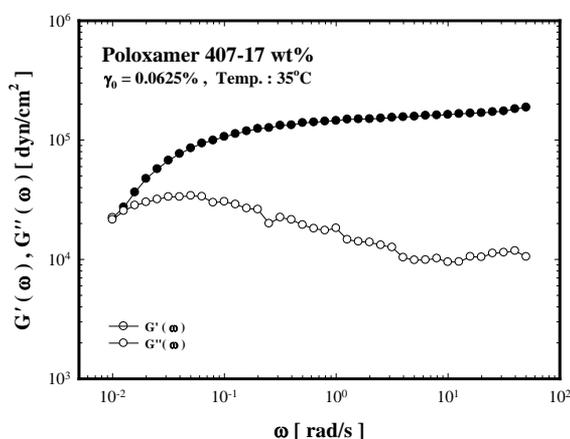


Figure 5. Storage modulus and loss modulus as a function of angular frequency for 17 wt% poloxamer 407 solution at 35 °C.

Fig. 5 shows the storage modulus and loss modulus as a function of angular frequency for 17 wt% poloxamer 407 solution at 35 °C. The storage modulus is greater than the loss modulus over an entire range of angular frequencies studied, meaning that the linear viscoelastic behavior of this system is dominated by an elastic nature. In addition, the storage modulus is found to be a weak function of angular frequency and the loss

modulus is gradually decreased as an increase in angular frequency. Such a tendency is also observed from the results obtained from dynamic strain - sweep measurements, as illustrated in Fig. 6(a) and Fig. 6(b).

Figure 6 (a) and (b) demonstrate the storage and loss moduli as a function of strain amplitude at several fixed angular frequencies of 0.1~50 rad/s for 17 wt% poloxamer 407 solution at 35 °C. It is clearly observed that the storage modulus exhibits a linear behavior within a small range of strain amplitudes ($\gamma_0 < 1\%$) and then demonstrates a sharp decrease as an increase in strain amplitude.

Furthermore, the storage modulus within a linear viscoelastic region is slightly increased as an increase in angular frequency, as matched with Fig. 5.

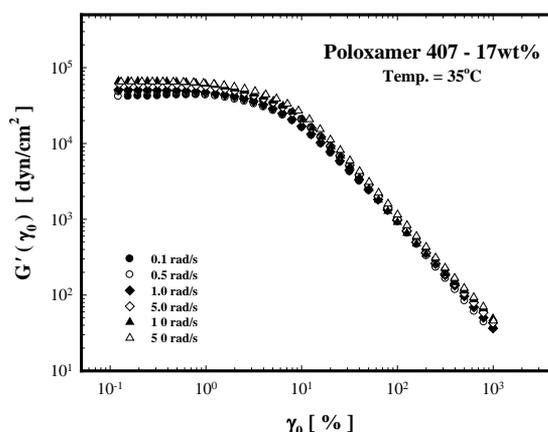


Figure 6(a). Storage modulus as a function of strain amplitude for 17 wt% poloxamer 407 solution at various angular frequencies at 35 °C.

In contrast to the storage modulus, the loss modulus within a linear viscoelastic region is gradually decreased as an increase in angular frequency and does not exhibit a clear linear behavior except at extremely small angular frequencies.

Especially, this system represents an exceptional nonlinear behavior at strain amplitude range larger than 0.1% where the loss modulus is first increased up to a

certain strain amplitude ($\approx 10\%$), beyond which followed by a decrease in loss modulus with increasing strain amplitude, indicating a so-called strain-overshoot phenomenon.

In addition, the degree of strain-overshoot is increased as an increase in angular frequency.

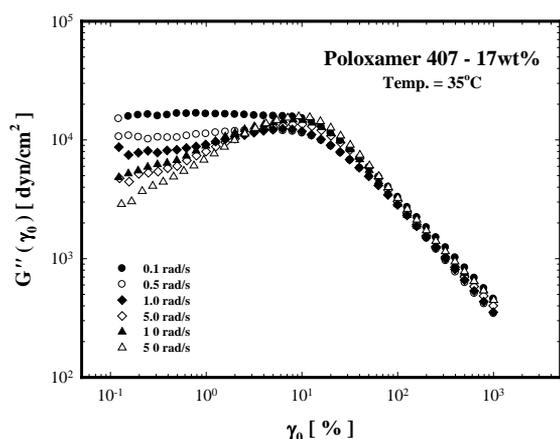


Figure 6(b). Loss modulus as a function of strain amplitude for 17 wt% poloxamer 407 solution at various angular frequencies at 35 °C.

ACKNOWLEDGEMENTS

This work was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (Grant Number : 2010 - 0011027).

REFERENCES

1. Cabana, A., Aït-Kadi, A. and Juhász, J. (1997), "Study of the Gelation Process of Polyethylene Oxide_a-Polypropylene Oxide_b-Polyethylene Oxide_a Copolymer (Poloxamer 407) Aqueous Solutions", *J. Colloid and Int. Sci.*, **190**, 307-312.
2. Dumortier, G., Grossiord, J. L., Agnely, F. and Chaumeil, J. C. (2006), "A Review of Poloxamer 407 Pharmaceutical and

Pharmacological Characteristics", *Pharm. Res.*, **23**, 2709-2728.

3. Ricci, E. J., Bentley, M. V. L. B., Farah, M., Bretas, R. E. S. and Marchetti, J. M. (2002), "Rheological Characterization of Poloxamer 407 Lidocaine Hydrochloride Gels", *Euro. J. Pharm. Sci.*, **17**, 161-167.

4. Escobar-Chávez, J. J., Lopez-Cervantes, M., Naik, A., Kalia, Y. N., Quintanar – Guerrero, D., and Ganem – Quitanar, A. (2006), "Applications of Thermoreversible Pluronic F – 127 Gels in Pharmaceutical Formulations", *J. Pharm. Pharmaceut. Sci.*, **9**, 339-358.

5. Cho, H. J. , Balkrishnan, P., Park, E. K., Song, K. W., Hong, S. S., Jang, T. Y., Kim, K. S., Chung, S. J., Shim C. K., and Kim, D. D. (2011), "Thermoreversible Gel for Intranasal Deliver of Fexofenadine Hydrochloride", *J. Pharm. Sci.*, **100**, 681-691.

6. Edsman, K., Carlfors, J., and Petersson, R. (1998), "Rheological Evaluation of Poloxamer as an in-situ Gel for Ophthalmic Use", *Euro. J. Pharm. Sci.*, **6**, 105-112.

7. Fusco, S., Borzacchiello, A., and Netti, P. A. (2006), "Perspectives on : PEO – PPO - PEO Triblock Copolymers and Their Biomedical Applications", *J. Bioactives and Compatible Polymers*, **21**, 149-164.

8. Jiang, J., Li, C., Lombardi, J., Colby, R. H., Rigas, B., Rafailovich, M. H. and Sokolov, L. C. (2008), "The Effect of Physiologically Relevant Additives on the Rheological Properties of Concentrated Pluronic Copolymer Gels" , *Polymer*, **49**, 3561-3567