

중성자 소각산란법을 이용한 전단력하에서의
PEO-PLGA-PEO 삼중블록공중합체 구조 변화 연구

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SANS Study on the Aqueous Solutions of PEO-PLGA-PEO
Triblock Copolymers Under Shear

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Introduction

Aqueous solutions of amphiphilic block copolymers in high concentration typically undergo the sol-to-gel transition with the increase in temperature[1, 2]. Poly(ethylene oxide-*b*-propylene oxide-*b*-ethylene oxide) (PEO-PPO-PEO) series have widely been investigated for the drug-delivery system (DDS) and their gelation mechanism is relatively well known by small-angle neutron scattering (SANS) experiments that the gels of PEO-PPO-PEO (4.5K-3.6K-4.5K, Pluronic F127) form through the micellar packing in close-packed (cubic) array[2,3] and the gel transition is due to the hard-sphere crystallization when the micelle concentration reaches a critical volume fraction of 0.53[4].

Recently reported poly(ethylene oxide-*b*-(DL-lactic acid-*co*-glycolic acid)-*b*-ethylene oxide) (PEO-PLGA-PEO) triblock copolymers are known to possess properties of nontoxicity and biodegradability, and also undergo the sol-to-gel transition[5]. Because the sol-to-gel boundary can be controlled by adjusting molecular characteristics such as molecular weight and hydrophilic (PEO)/hydrophobic (PLGA) balance, the PEO-PLGA-PEO triblock copolymers are considered as a promising material for DDS. Moreover, PEO-PLGA-PEO triblock copolymers stay as gels *in-vivo* more than one month even with low molecular weight, while commercial PEO-PPO-PEO and similar block copolymers can last only for a short time[6]. Based on these works, the PEO-PLGA-PEO triblock copolymers are considered to represent a different gelation mechanism compared with the gelation mechanism of the PEO-PPO-PEO.

We have studied solution behaviors and investigated the effect of shear on the gel structure of temperature sensitive triblock copolymers, PEO-PLGA-PEO, using the 8m SANS line of HANARO and the 30m NG7-SANS facility of NIST with a Couette shear cell.

Experimental

PEO-PLGA-PEOs were synthesized by ring opening polymerization in our laboratory. The molecular weights and DLLA/GA ratios in the PLGA block were summarized in Table 1.

Tube inversion method (TIM) and small-angle light scattering (SALS) was employed to construct used for phase diagrams of PEO-PLGA-PEO aqueous solutions and dynamic light scattering (DLS, BI-9000AT) equipped with a digital autocorrelator, a photon counter, and a light sources of He-Ne laser with $\lambda = 632.8$ nm was used to investigate the size distribution of PEO-PLGA-PEO in water. Rheometer RMS-800 (Rheometrics, Inc.) in a conical-cylinder geometry (cup diameter, 52 mm; bob diameter, 50 mm; bob length, 20 mm;

gap size, 0.2 mm) was used to measure the storage modulus G' of solutions as a function of temperature. Small strain was applied (2.7 ~ 5 %) to ensure linear viscoelasticity and frequency was 0.5 rad/s. Small angle neutron scattering (30m SANS-NG7, NIST) with a Couette cell (0 ~ 10,000 Hz shear rate) and circulating bath (-10 °C ~ 90 °C, ± 0.01 °C) was used to investigate the change of micelles and clusters structure upon increase in both temperature and applying shear.

Results and Discussion

Phase diagrams of aqueous PEO-PLGA-PEO solutions are represented in Figs. 1 (a) and (b). For PEO-PLGA-PEO (550-3.4K-550) containing short PEO chains hard-gels are observed, while PEO-PLGA-PEO (750-3.5K-750) having longer PEO chains soft-gels region is expanded to the hard-gels region and the lower sol-to-gel transition temperature is increased by about 20 °C. Turbidity is also observed and it is interesting to note that the turbidity depends only on the temperature not on the concentration. As noticed from Fig. 1(c), the region I shows minimum turbidity and the region II shows turbidity increase as temperature is increased. After the maximum value ($T_{\text{tur,max}}$), the turbidity again decreases in the region III and further increase in temperature in the region IV, turbidity remains almost constant before massive collapse of the copolymers from the solution.

In small angle neutron scattering we observed that the micelle aggregates became larger as temperature was increased (Fig 2.). These changes in cluster size and its distribution as a function of temperature are also confirmed by DLS as shown in Table 2. At the sol temperature the isotropic 2D pattern was observed regardless of the shear rate applied. At the hard-gel temperature, however, an anisotropic 2D pattern was observed implying that these micelle clusters are anisotropically the shaped (*i.e.*, cylindrical clusters). Moreover, these micelle clusters can align upon applying the shear (Fig 3.). At the upper sol region, an anisotropic 2D pattern which was significantly different from that of the lower sol region was still observed. Upon applying a high shear the micelles are separated from the micelle clusters due to the weak attraction among them. The behavior of the hard-gels and soft-gels is similar. However, we found that the hard-gels display a significant memory effect upon a sudden change of the shear rate.

Unlike PEO-PPO-PEO (4.5K-3.6K-4.5K, Pluronic F127), the micelles of PEO-PLGA-PEO (550-3.4K-550) in aqueous solution can not pack through the entanglement of the PEO corona chains because of the small molecular weight of PEO chains much below the entanglement molecular weight (M_e) of about 1,600. It is believed that the extensive aggregation of the copolymer due to the macroscopic liquid-liquid phase separation causes the turbidity. With increasing the temperature of the copolymer solution, the aggregation of micelles is triggered by the hydrophobic attraction in the region II and then the formation of cluster is dominant up to the maximum in turbidity. In the regions III and IV the micelle clusters are in more separated from water because PEO chains are no longer in favor of water over a certain temperature range and chains eventually collapsed from water upon further increase in temperature.

References

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