

수용성 블록공중합체의 졸-겔 전이 변화 연구

권관욱 · 박문정 · 김홍두* · 배유한** · 차국헌

서울대학교 응용화학부

경희대학교 화학과*

광주과학기술원 신소재공학과**

Rheological Behaviors of Sol-to-Gel Transition in Aqueous Solution of PEO-PLGA-PEO Block copolymers

Kwan-Wook Kwon, Moon Jeong Park, Hong Do Kim*, You Han Bae** and Kookheon Char

School of Chemical Engineering, Seoul National University, Seoul 151-742, Korea

Department of Chemistry, Kyunghee University, Yongin 449-701, Korea*

Department of Materials Science and Engineering, K-JIST, Kwang-ju 500-712, Korea**

Introduction

Block copolymers having hydrophilic chains such as PEO covalently connected to hydrophobic chains such as PPO, PBO, and PLGA can form micelles[1,2] in water when their solution concentration exceeds the critical micelle concentration (CMC)[3,4,5] or solution temperature is increased above the critical micelle temperature (CMT)[3,5,6] owing to their self-assembling nature. It is also known that aqueous solutions of these block copolymers undergo the sol-to-gel transition at high concentrations. The gels derived from these block copolymers are the physical gels formed through non-covalent associations and the gels turn into sols again when temperature is lowered below the gelation temperature; in other words, thermoreversible gelation[5,7]. Typical water soluble amphiphilic block copolymer is PEO-PPO-PEO (Pluronic®; BASF or Poloxamers®; ICI). This copolymer is commercially available as a surfactant and widely used for emulsification, detergency, dispersion stabilization and so forth[8]. It is also well known by small-angle neutron scattering (SANS) experiments that the gel of PEO-PPO-PEO (4.5K-3.6K-4.5K, Pluronic F127) forms through the micellar packing in close-packed (cubic) array[7,9] and the gel transition is due to the hard-sphere crystallization when the micelle concentration reaches a critical volume fraction of 0.53[10]. There are many factors affecting the formation of gels: molecular architecture, degree of hydrophilicity (or hydrophobicity), ratio of hydrophilic to hydrophobic blocks, molecular weight, solvency, and additives.

PEO-PLGA-PEO is another class of water soluble amphiphilic block copolymers. Moreover, because PEO-PLGA-PEO is nontoxic and biodegradable, these block copolymers are considered as good candidates for drug delivery system (DDS) taking advantage of the sol-to-gel transition. However, the gelation mechanism of the PEO-PLGA-PEO in water is not investigated in detail because these triblock copolymers are recently discovered. In present study, we investigated the gelation mechanism in aqueous solutions of PEO-PLGA-PEO triblock copolymers using tube inversion method (TIM), small-angle light scattering (SALS), dynamic light scattering (DLS) and rheological measurements and compared the behavior of PEO-PLGA-PEO with the gelation of PEO-PPO-PEO block copolymers.

Experimental

A commercial grade of PEO-PPO-PEO (4.5K-3.6K-4.5K), Pluronic F127, was kindly donated by BASF and used without further purification. The weight fraction of PEO is approximately 70 %.

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) was employed to determine the sol-gel boundaries. Vials with a 13 mm diameter were used and the vials sealed with Teflon tape were placed in a water bath which can control temperature with an accuracy of 0.01°C . To ensure equilibrium, the equilibration time for more than 10 min was allowed for each temperature and measurements were carried out every 0.5°C from 1°C to 90°C . The change from a mobile to an immobile state was determined by inverting the tube. Hard gel was defined as immobile for more than 10 min while soft gel was defined as a detection of any slow movement of the meniscus over a period of 1 min. Sol was defined to flow massively to the bottom of a tube within 1 min upon inversion.

Small-angle light scattering (SALS) was used to detect turbidity in aqueous solutions of PEO-PLGA-PEO as a function of temperature. Homemade SALS is equipped with a He-Ne laser of $\lambda = 632.8$ nm and a rotating photodiode.

Dynamic light scattering (DLS, BI-9000AT) was used to detect unimers, micelles, and clusters of both PEO-PPO-PEO and PEO-PLGA-PEO in water. DLS is equipped with digital autocorrelator and photon counter. Both light sources of He-Ne laser with $\lambda = 632.8$ nm and Ar laser with $\lambda = 488$ nm were used.

Rheometer RMS-800 (Rheometrics, Inc.) in a conical-cylinder geometry (cup diameter, 52 mm; bob diameter, 50 mm; bob length, 20 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.

Results and Discussion

A phase diagram of PEO-PLGA-PEO (550-3.4K-550) in water is represented in Fig. 1. Compared with the aqueous solutions of PEO-PPO-PEO (4.5K-3.6K-4.5K), the aqueous solutions of PEO-PLGA-PEO (550-3.4K-550) have a narrow temperature window for gelation. Moreover, turbidity is observed in aqueous solutions of PEO-PLGA-PEO (550-3.4K-550) and it is interesting to note that the turbidity depends only on temperature not on concentration. As noticed from Fig. 2, turbidity increases in the temperature region from (1) to (2) and again decreases from (2) to (3), indicating that the point (2) has the highest degree of turbidity. In the temperature region from (3) to (4), the turbidity is almost constant before the massive collapse of copolymers from the solution is observed at temperature (4). It is believed that the extensive aggregation of the copolymer causes the turbidity in aqueous solutions of PEO-PLGA-PEO (550-3.4K-550). With increasing the temperature of the copolymer solution, aggregation is triggered by the hydrophobic attraction from the temperature (1) and then the formation of cluster is dominant up to the temperature (2) causing the maximum in turbidity at temperature (2). It is believed that the decrease of turbidity between the temperature (2) and (3) results from the rearrangement of clusters to stabilize the system of copolymer solution. After this rearrangement of clusters, the turbidity of the copolymer solution remains constant before the copolymers collapse in water at temperature (4). These changes of cluster size and its distribution as a function of temperature are confirmed by DLS as shown in Fig. 3. While the clusters of large size ($d > 10^3$ nm) are not detected in the sol-to-hard gel transition of PEO-PPO-PEO since the lattice of the micelles is frozen in 20 wt% PEO-PPO-PEO aqueous solution, the large size clusters ($d > 10^3$ nm) are observed in agreement with the changes of turbidity in 25 wt% PEO-PLGA-PEO aqueous solution as a function of temperature. In rheological measurements, the storage modulus (G') of the aqueous solution of PEO-PLGA-PEO does not show the abrupt change at the sol-to-hard gel boundary and the behaviors of G' as a function of temperature are also similar regardless of the concentration while the absolute values of G' are proportional to the concentration of the copolymer (Fig. 4). Moreover, it is interesting to note that the

temperature showing the local maximum value of G' corresponds to the temperature showing the maximum turbidity before reaching the temperature at which the triblock copolymers collapse in water.

Unlike PEO-PPO-PEO (4.5K-3.6K-4.5K), 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 small molecular weight of PEO chains below the entanglement molecular weight (M_e) of about 1600. In aqueous solutions of the PEO-PLGA-PEO, the initial micelle structure is believed to be disrupted mainly due to the massive liquid-liquid phase separation upon heating the solution. The macroscopic phase separation causing turbidity in solution is driven by attractive hydrophobic interaction of the PLGA cores. As the concentration of the block copolymer is increased, the block copolymer clustering became more extensive and the gelation accompanied by the phase separation is induced accordingly.

References

1. M. Malmsten and B. Lindman, *Macromolecules*, **25**, 5440 (1992).
2. O. Glatter, G. Scherf, K. Schill and W. Brown, *Macromolecules*, **27**, 6046 (1994).
3. P. Alexandridis, J.F. Holzwarth and T.A. Hatton, *Macromolecules*, **27**, 2414 (1994).
4. P. Bahadur and K. Pandya, *Langmuir*, **8**, 2666 (1992).
5. G.E. Yu, Y. Deng, S. Dalton, Q.G. Wang, D. Attwood, C. Price and C. Booth, *J. Chem. Soc. Faraday Trans.*, **88**, 2537 (1992).
6. G. Wu, B. Chu and D.K. Schneider, *J. Phys. Chem.*, **99**, 5094 (1995).
7. G. Wanaka, H. Hoffmann and W. Ulbricht, *Colloid Polym. Sci.*, **268**, 101 (1990).
8. R.G. Laughin, *The Aqueous Phase Behavior of Surfactants*, Academic Press: London, 1994.
9. K. Mortensen, W. Brown and B. Norden, *Phys. Rev. Lett.*, **68**, 2340 (1992).
10. K. Mortensen and J.S. Pedersen, *Macromolecules*, **26**, 805 (1993).

Table 1. Molecular weight of PEO-PLGA-PEO triblock copolymers used in present study

Block Copolymer	¹ H-NMR		GPC		
	M _n	DLLA/GA (mole ratio)	M _n	M _w	PDI
PEO-PLGA-PEO	550 - 3400 - 550	80/20	5980	8060	1.35
	750 - 3500 - 750	80/20	6400	8400	1.31
	2000 - 2100 - 2000	79/21	7550	9690	1.28

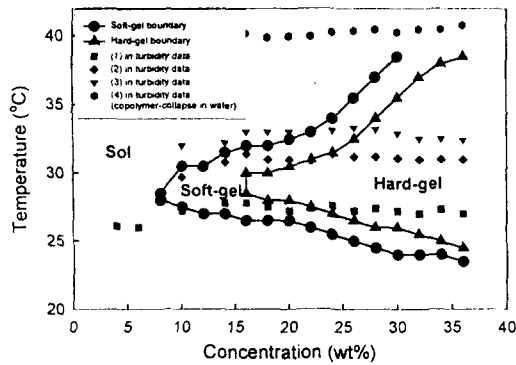


Figure 1. Phase diagram of PEO-PLGA-PE (550-3.4K-550) in water by tube inversion method.

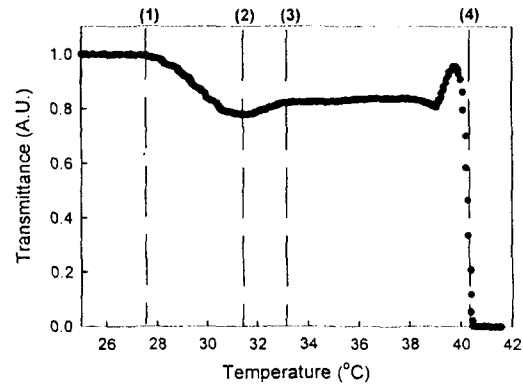


Figure 2. Turbidity change in aqueous solution of PEO-PLGA-PEO (550-3.4K-550) as a function of temperature. Concentration is 24 wt% and heating is 0.5 °C/min.

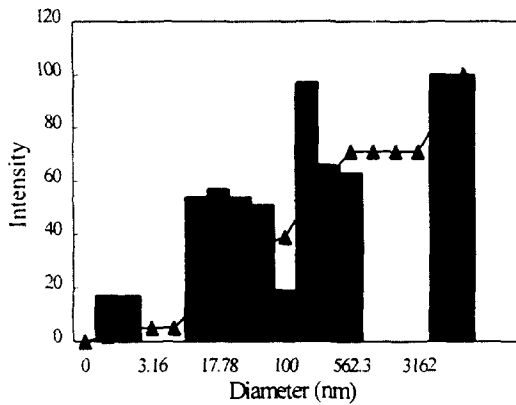


Figure 3. DLS measurement of PEO-PLGA-PE (550-3.4K-550) in water. c = 25 wt% and T = 30 °C

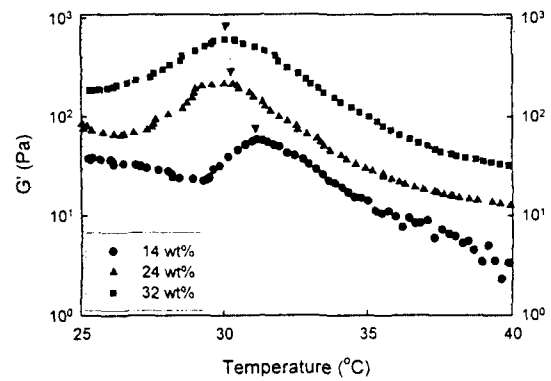


Figure 4. Change of G' as a function of temperature in aqueous solutions of PEO-PLGA-PEO (550-3.4K-550). $\omega = 0.5$ rad/s, $\gamma = 0.05$, and heating rate = 0.5 °C/min.