

Synthesis and Micellar Characterization of CBABC Type PLGA-PEO-PPO-PEO-PLGA Pentablock Copolymers

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Poly(lactic-co-glycolic acid) (PLGA) were grafted to both ends of Pluronic® F68 ((EO)₇₅(PO)₃₀(EO)₇₅) triblock copolymer to produce poly{(lactic acid)_m-co-(glycolic acid)_n}-b-poly(ethylene oxide)₇₅-b-poly(propylene oxide)₃₀-b-poly(ethylene oxide)₇₅-b-poly{(lactic acid)_m-co-(glycolic acid)_n} (PLGA-F68-PLGA) pentablock copolymers. Molecular weights of PLGA blocks were controlled and five kinds of pentablock copolymers with different PLGA block lengths were synthesized using *in-situ* ring-opening polymerization of D,L-lactide and glycolide with tin(II) 2-ethylhexanoate (Sn(Oct)₂) catalyst. PLGA-F68-PLGA pentablock copolymers were characterized by ¹H- and ¹³C-NMR, GPC, and TGA. The numbers (2m, 2n) of repeating units for lactic acid and glycolic acid inside PLGA segments were obtained as (48, 17), (90, 23), (125, 40), (180, 59), and (246, 64), with ¹H-NMR measurement. From NMR data, the resultant molecular weights were determined in the range of 12,700-29,700, which were similar to those obtained from GPC. Polydispersity index was increased in the range of 1.32-1.91 as the content of PLGA blocks increased. TG and DTG thermograms showed discrete degradation traces for PLGA and F68 blocks, which indicate the weight fractions of PLGA blocks in pentablock copolymers can be calculated by TG profile and it is possible to remove PLGA block selectively. Hydrodynamic radius and radius of gyration of pentablock copolymer micelle were obtained in the range of 46-68 nm and 31-49 nm, respectively, in very dilute (*i.e.* 0.005 wt %) aqueous solution of THF:H₂O = 10:90 by volume at 25 °C.

Key Words : Poly(lactic acid-co-glycolic acid), Pluronic F68, Pentablock copolymer, PLGA-F68-PLGA, Ring-opening polymerization

Introduction

Amphiphilic block copolymers have been widely investigated due to its fast growing application areas in environmental, electronic, and medical technologies based on self-assembled nano-structures and aggregates formed both in solid and solution states.¹⁻⁷ Structural property and morphology of AB and ABA typed di- and triblock copolymers have been thoroughly investigated in solid phases as well as solution.¹⁻⁷ Hydrophobic (B) blocks in AB and ABA block copolymers are located at the core region and hydrophilic (A) blocks appear at the corona region in micellar solution.¹⁻⁷ Various morphologies have been reported such as sphere, rod, lamella, tube, and vesicle and so on in aqueous/organic selective solvents.^{8,9} Microphase separations of solid block copolymers have been also widely reported such as cubic, hexagonal, lamella, and gyroid phases, which is attributed to its molecular weight, volume fractions of each block, and Flory-Huggins interaction parameter (χ).¹⁰⁻¹² In these processes, the free energy is known to be balanced between the forces of minimizing interfacial area and the constituent blocks to be random coils both in bulk and solution.¹⁰⁻¹²

Pluronic poly(ethylene oxide)-b-poly(propylene oxide)-b-poly(ethylene oxide) (PEO-PPO-PEO) triblock copolymers

are well-known polymeric surfactant, which have been used as a compatibilizer in polymer blends and a nano-carrier for biomedical applications.¹³⁻¹⁵ Especially, Pluronic micelles are one of good candidates for various biomedical areas such as drug delivery and biosensor due to its biocompatibility, temperature sensitivity, and good solubility in aqueous solution.¹⁶⁻²⁸ Recently, a few kinds of PEO-PPO-PEO block copolymer have been widely used for templates of inorganic/organic-inorganic nanostructured (mesoporous) hybrid materials.²⁹⁻³¹ PEO block is a very useful unit to be linked with other polar species due to oxygen molecules with dipole moment inside the chain.²⁹⁻³¹ However, pluronic triblock copolymers are non-degradable and highly soluble in human body, which limit its versatile biomedical applications.³²⁻³⁴ Additionally, relatively low hydrophobicity of PPO block makes broad interphases between PPO and PEO blocks, which sometimes limits the application as a sustainable platform for organic-inorganic hybridization using several precursors containing bulky hydrophobic moieties.³⁵⁻³⁷

Biodegradable poly(lactic acid) (PLA) and poly(glycolic acid) (PGA) have been widely used as surgical sutures, drug delivery systems, and tissue engineering scaffolds and so on.^{32-34,38} In another sense of applications, biodegradable polymers are one of potential solutions to problems in plastic

waste management.³⁹ Interestingly, PLA polymer chain is more hydrophobic species than PPO chain and its gel state is retained longer in human body.³²⁻³⁴ Modification of PLA and PGA with PEO chains have been conducted to adjust its function to various application areas and still under investigation.^{32-34,40,41} Poly(lactic acid-co-glycolic acid) and its di- and triblock copolymers have been reported to find advanced properties.³²⁻³⁴ It is known that multiblock copolymers show more various patterns unobtainable by microphase separations of di- and triblock copolymers in solid state.^{42,43} Also, micelles of multiblock copolymers in solution have been investigated to find new structures and properties for applications.

Herein, we have tried to synthesize multiblock copolymers to use as templates for specific nanostructured composite materials as well as to find more various micro- and nanophases. In this paper, as a first step, we report the synthesis and characterization of PLGA-PEO-PPO-PEO-PLGA pentablock copolymers composed of four kinds of monomers using a commercial Pluronic F68 EO₇₅PO₃₀EO₇₅ triblock copolymer. Cyclic D,L-lactide and glycolide monomers were opened using stannous octoate (Sn(Oct)₂) catalysts and grafted randomly on both ends of hydroxyl-terminated Pluronic F68. More hydrophilic glycolide monomers were incorporated into poly(lactic acid) simultaneously to make the randomly copolymerized PLGA block in which the glycolide monomer was selected to increase the flexibility and solubility of polymer chains in aqueous solution. Five kinds of pentablock copolymers were synthesized with increased molecular weight of PLGA blocks and their molecular weights and the thermal properties were investigated. Also, micellar characterization of pentablock copolymers was investigated in very dilute aqueous solution. Very recently, a similar pentablock copolymer was reported to supply more stable carrier for the anti-cancer drug delivery.⁴⁴ However, the synthesis was conducted at high temperature of 160 °C and the amount of independent PLGA units unlinked with F68 was detected as around 11 wt%.⁴⁴ Also, the synthesized pentablock copolymer was reported for only one kind of molecular weight (*i.e.* weight ratio of PLGA:F68 ≈ 4:1) while this manuscript reports different range of PLGA/F68 up to 2.57.

Experimental

Materials. D,L-Lactide (DLLA) and glycolide (GA) were purchased from Aldrich and recrystallized from ethyl acetate. The purified DLLA and GA were stored at -2 °C before use. Pluronic F68 was purchased from Aldrich and used after drying overnight under vacuum before use. Pluronic F68 is a type of poly(ethylene oxide)-*b*-poly(propylene oxide)-*b*-poly(ethylene oxide) triblock copolymer with a molecular weight of 8,500, which composed of central hydrophobic PO units of 30 and hydrophilic EO block units of 75 at both ends (Figure 1). Stannous octoate (Sn(Oct)₂) was purchased from Aldrich and used as received.

Synthesis of PLGA-F68-PLGA Pentablock Copolymers. Ring opening polymerization was employed using cyclic D,L-lactide and glycolide monomers. Simultaneously, the monomers were attached to both ends of Pluronic F68 copolymers to obtain pentablock copolymers of PLGA-F68-PLGA. The synthesis scheme is shown in Figure 1 and the synthetic procedure of a typical pentablock copolymer sample is as follows: A three neck round-bottom 1L flask with a stopcock was treated for 3 h under argon flow to remove the moisture. An adequate amount of Pluronic F68 was added with toluene of 750 mL into the flask and the mixture was stirred for 3 h at 120 °C under argon flow to remove small amount of water vapor inside F68 triblock copolymers. After cooling the mixture to room temperature, adequate amounts of D,L-lactide, glycolide, and Sn(Oct)₂ (1 wt % of D,L-lactide and glycolide) were added to the flask under argon flow. The amounts used for each reactant are summarized in Table 1. After stirring at 120 °C for 24 h under argon flow, the content was cooled to room temperature. The powder preci-

Table 1. Sample name and the corresponding amounts of reactants used in feed

Sample	D,L-Lactide (g)	Glycolide (g)	F68 (g)
P1	29.4	7.4	63.2
P2	41.5	8.4	50.1
P3	46.3	11.6	42.1
P4	53.8	13.5	32.7
P5	60.5	12.2	27.3

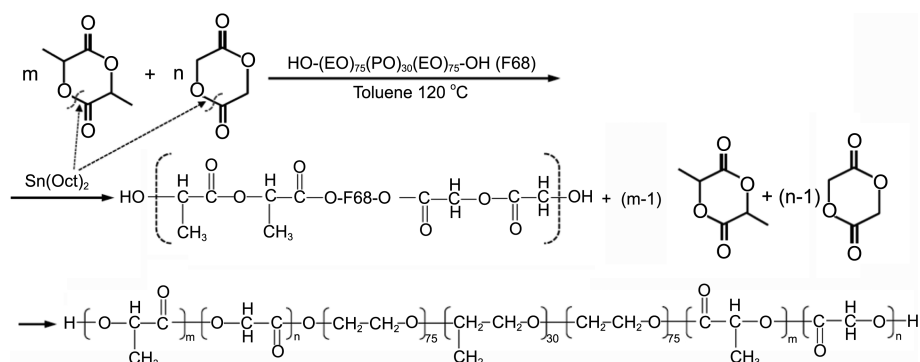


Figure 1. Chemical structure of reagents and synthesis scheme of PLGA-F68-PLGA pentablock copolymer.

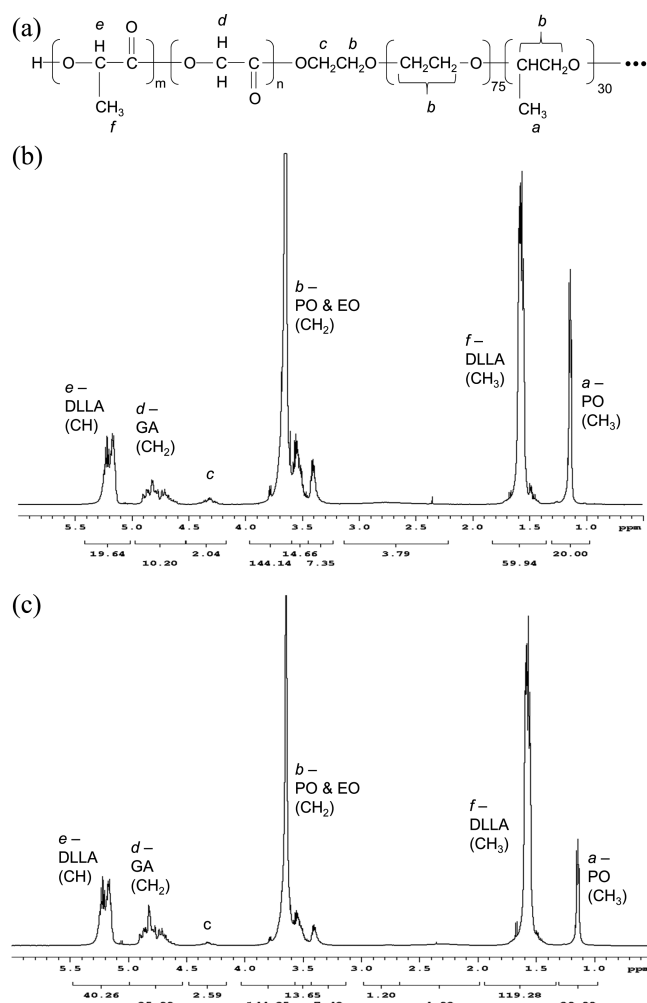


Figure 2. ^1H NMR spectra of PLGA-F68-PLGA ((b) P2 and (c) P4) pentablock copolymers in CDCl_3 .

pitations were obtained in 5000 mL of diethyl ether. The pentablock copolymer powder samples were filtered using a suction flask and dried for 30 d under vacuum.

Characterization of PLGA-F68-PLGA Pentablock Copolymers. ^1H and ^{13}C NMR Fourier transform spectrophotometer was employed to determine the structure and composition of pentablock copolymers. The NMR experiments were performed on Varian Unity (INOVA) 500 MHz system in Korea Basic Science Institute (KBSI) Daegu center. Chemical shifts for pentablock copolymer samples were obtained in ppm using tetramethylsilane (TMS) as a reference sample: ^1H NMR (500 MHz, CDCl_3 , TMS), δ 1.05–1.25 (m, $-\text{OCH}_2\text{-CH}(\text{CH}_3)\text{-}$), 1.45–1.79 (m, $-\text{O-CH}(\text{CH}_3)\text{-CO-}$ and $\text{HO-CH}(\text{CH}_3)\text{-CO-}$), 3.35–3.75 (m, $-\text{OCH}_2\text{-CH}_2\text{-}$ and $-\text{OCH}_2\text{-CH}(\text{CH}_3)\text{-}$), 4.20–4.40 (m, $-\text{CO-OCH}_2\text{-CH}_2\text{-O-}$), 4.55–5.00 (m, $-\text{OCH}_2\text{-CO-}$), 5.05–5.45 (m, $-\text{O-CH}(\text{CH}_3)\text{-CO-}$) (Figure 2). ^{13}C NMR (500 MHz, CDCl_3 , TMS), δ 16.66 ($-\text{O-CH}(\text{CH}_3)\text{-CO-}$), 17.45 ($-\text{OCH}_2\text{-CH}(\text{CH}_3)\text{-}$), 60.75 ($-\text{OCO-CH}_2\text{-}$), 68.99 ($-\text{O-CH}(\text{CH}_3)\text{-CO-}$), 70.56 ($-\text{OCH}_2\text{-CH}_2\text{-}$ and $-\text{OCH}_2\text{-CH}(\text{CH}_3)\text{-}$), 166.43 ($-\text{OCO-CH}_2\text{-}$), 169.35 ($-\text{O-CH}(\text{CH}_3)\text{-CO-}$) (Figure 3).

Gel permeation chromatography (GPC) was performed on an EcoSEC HLC 8320 GPC (Tosoh Co.) equipped with a

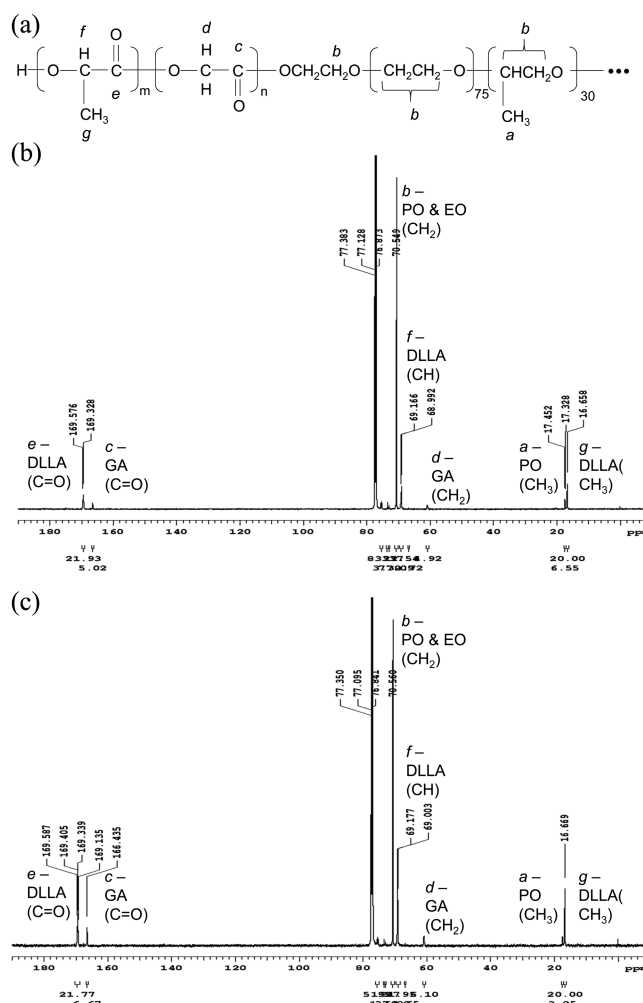


Figure 3. ^{13}C -NMR spectra of PLGA-F68-PLGA ((b) P2 and (c) P4) pentablock copolymers in CDCl_3 .

differential refractometer as a detector at Korea Polymer Testing and Research Institute (KOPTRI). The block copolymer samples were fully dissolved in tetrahydrofuran (THF) as a same concentration of 3 mg/mL and filtered with 0.45 μm PTFE syringe filter. 10 μL of block copolymer solution were injected into the GPC column with a flow rate of 0.35 mL/min at 40 $^\circ\text{C}$. The molecular weights were obtained by fitting on calibration curve of standard polystyrene reference samples.

Thermogravimetric (TG) and differential TG (DTG) analysis were performed on TA Q50 TGA system. TG and DTG profiles were recorded up to 500 $^\circ\text{C}$ in flowing nitrogen (100 mL/min) with a heating rate of 5 $^\circ\text{C}/\text{min}$.

Micellar Characterization of PLGA-F68-PLGA Pentablock Copolymers.

Sample Preparation: PLGA-F68-PLGA pentablock copolymers were initially dissolved to prepare dilute polymer solution of 0.05 wt % in tetrahydrofuran (THF). Distilled water was added dropwise to the polymer solutions under stirring using a syringe pump at a constant rate of 1 mL/min. The final concentration of the polymer solutions was 0.005 wt % and the water/THF solvent composition was 90/10

(v/v). For light scattering experiment, the polymer solutions were filtered through a PVDF filter of 0.45 μm pore size.

Light Scattering Experiment: Light scattering experiment was carried out with a Brookhaven static and dynamic light scattering system. 16 mL vials were used as sample cell, and they were cleaned by filtered toluene and dried before use.

Static Light Scattering (SLS) – Static light scattering (SLS) was used to measure the aggregation number and radius of gyration (R_g) of the aggregates. Angular and concentration dependence of the scattered light was analyzed by the following Zimm plot.

$$\frac{K_c}{R_\theta} = \left(1 + \frac{q^2 R_g^2}{3}\right) \left(\frac{1}{M_w} + 2A_2c\right) \quad (1)$$

where, the Rayleigh ratio, $R_\theta = I_{A,\theta} \sin\theta R_T n_0^2 / (I_T n_T^2)$; $K = 4\pi^2 n_0^2 (dn/dc)^2 / N_A \lambda^4$; scattering vector, $q = 4\pi n_0 \sin\theta / \lambda$; c is concentration of polymer solution. dn/dc was used as 0.135 for PEO in water solution, and the reflective index of water, 1.333 was used as n_0 . Cell temperature was kept constant at 25 °C, the wavelength of the laser light, λ was 641.1 nm. In dilute solution, $2A_2c$ term is negligibly small, then the angular dependency of the scattered light can be analyzed by the following Eq. (2),

$$\frac{K_c}{R_\theta} = \frac{1}{M_w} \left(1 + \frac{q^2 R_g^2}{3}\right) \quad (2)$$

From the y axis intercept and slope of this plot, M_w and R_g of the aggregates are obtained.

Dynamic Light Scattering (DLS) – Dynamic light scattering was used to measure the hydrodynamic radius (R_h) of the aggregates. In DLS theory, Stoke-Einstein equation is used as follows.

$$R_h = kT / 6\pi\eta D \quad (3)$$

where, D is translational diffusion coefficient, η is viscosity of the solvent. Decay rate, Γ was determined from the auto-correlation function of the scattered light. Since $\Gamma = Dq^2$, diffusion coefficient D was obtained from the slope of the plot Γ vs. q^2 . Cell temperature was 25 °C and the viscosity of the solvent was used as 0.894 cp.

Transmission Electron Microscopy (TEM): TEM images were obtained with a FEI TECNAI G² F30 ST operated at an accelerating voltage of 200 kV. The polymer solution was prepared as a concentration of 0.005 wt % in water/THF mixed solvent composed of 90/10 (v/v). The polymer solution was dropped onto porous carbon film on a copper grid and then dried. A drop of osmium tetroxide (OsO_4) (2.5 wt %) in 2-methyl-2-propanol was placed on the copper grid and dried at room temperature.

Results and Discussion

Five kinds of PLGA-F68-PLGA block copolymers with different compositions were synthesized by ring opening polymerization of cyclic D,L-lactide and glycolide monomers

in the presence of stannous octoate as a catalyst. Ring-opened monomers were added to the both ends of hydroxyl-terminated Pluronic F68 ($\text{EO}_{75}\text{PO}_{30}\text{EO}_{75}$) and the reaction mechanism is known to be a kind of coordination polymerization supported by $\text{Sn}(\text{Oct})_2$ catalyst.⁴⁰ Molecular weight and block compositions were controlled by the amount of D,L-lactide and glycolide monomers added in the reactants as shown in Table 1. Polymer samples were named as P-x listed in Table 1 and Table 2.

The chemical compositions and molecular weights of pentablock copolymers were characterized by ¹H- and ¹³C NMR spectrophotometry. Figure 2 shows the representative ¹H NMR spectra of P2 and P4 pentablock copolymers in CDCl_3 . The degree of polymerizations (m, n) of PLGA blocks in poly{(lactic acid)_m-co-(glycolic acid)_n}-b-poly(ethylene oxide)₇₅-b-poly(propylene oxide)₃₀-b-poly(ethylene oxide)₇₅-b-poly{(lactic acid)_m-co-(glycolic acid)_n} copolymer were calculated from the peak intensity ratios of methyl (-O-CH(CH_3)-CO-, δ 1.45-1.79) or methylene (-OCH₂-CO-, δ 4.55-5.00) protons of PLA and PGA based on the number of PPO unit (-OCH₂-CH(CH_3)-, δ 1.05-1.25) in the F68 triblock copolymer. The small peak appeared at 4.20-4.40 ppm is attributed to methylene protons (-CO-O-CH₂-CH₂-O-) in PEO block linked with ester group in D,L-lactide or glycolide as shown in Figure 2(a), which clearly indicates the chemical linkage is formed successfully between F68 copolymers and cyclic LA and GA monomers. As shown in Figure 2(b) and Figure 2(c), the relative peak intensity ratio (f/a) representing the repeating-unit ratio of PLA/PPO in P4 was increased compared with that of P2 copolymer, which indicates the amount of PLA block in P4 is more than that in P2 copolymer. Similarly, d/a ratios are different both in P2 and P4 samples, which is related with the unit ratio of PGA/PPO block. Figure 3 shows the representative ¹³C NMR spectra of P2 and P4 pentablock copolymers in CDCl_3 . The peaks at 17.45 and 70.56 ppm are attributed to PPO and PEO blocks in F68 polymer. The peaks at 16.66, 68.99, and 169.45 ppm are for PLA and those at 60.75 and 166.43 ppm are for PGA, respectively. The degree of polymerizations (m, n) of PLGA blocks were simply obtained from the respective peak intensity ratios and the results showed nearly the same with those obtained from the analysis of ¹H NMR. From the NMR results for all five pentablock copolymers (Figure S1 and S2 in Supporting Information), the number average molecular weights and the weight ratios of each block were calculated and summarized in Table 2.

GPC analysis was performed to obtain the number- and the weight-average molecular weights and molecular weight distribution of pentablock copolymers (Figure S3 in Supporting Information). Figure 4 shows the variation of GPC traces for the weight-average molecular weights of five pentablock copolymers. Molecular weight and distributions were increased as the added PLGA amount is increased. Molecular weight dispersity was obtained in the range of 1.32-1.91 as listed in Table 2. It is known that dispersity is related with the amount of catalyst and the reaction temperature. The low dispersity is attributed to a mild reaction temperature of 120 °C even

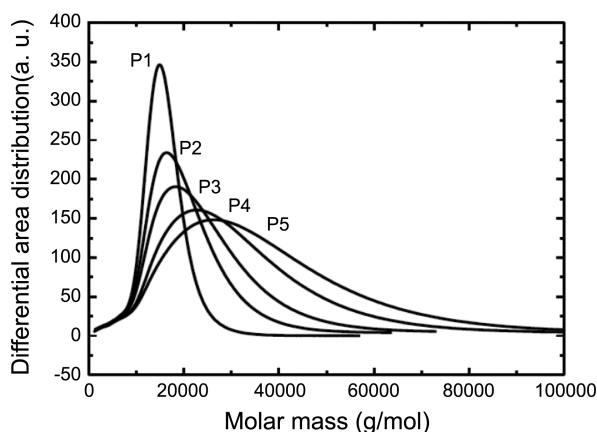


Figure 4. GPC chromatogram of PLGA-F68-PLGA pentablock copolymers.

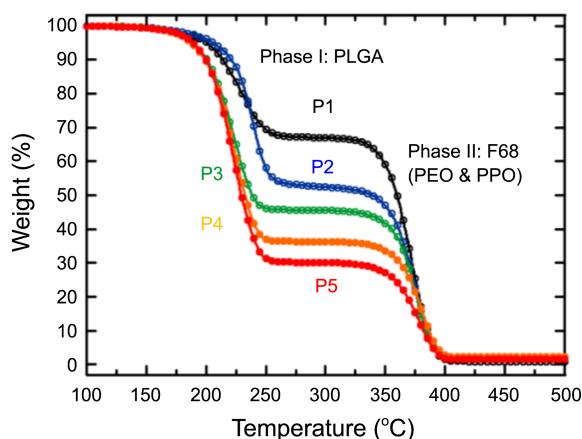


Figure 5. TGA thermograms of PLGA-F68-PLGA pentablock copolymers.

though high amount (*i.e.* 1 wt % of the monomers) of catalyst was used.

TGA thermogram was obtained to investigate the thermal property of pentablock copolymers. Figure 5 shows the weight change for five kinds of pentablock copolymers up to 500 °C under nitrogen atmosphere. Thermal degradation shows distinct two-step transition composed of the first phase (phase I) from 160 °C to 260 °C and the second phase (phase II) from 320 °C to 400 °C. The degradation from 100 °C to 160 °C was not observed which clearly represents there

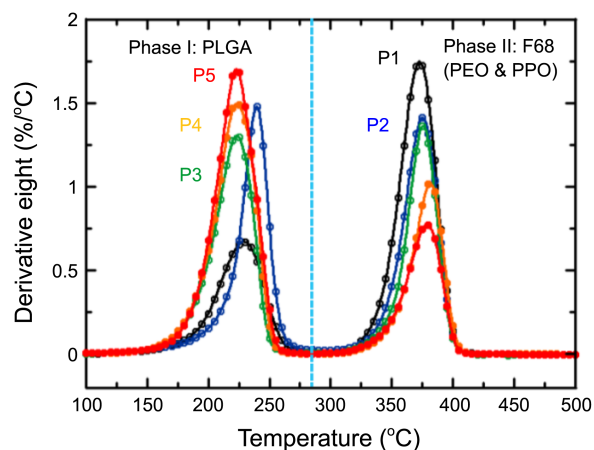


Figure 6. Differential TGA profiles of PLGA-F68-PLGA pentablock copolymers.

is no free PLGA chains polymerized independent of F68 polymer chains.⁴⁴ The weight percent at the end point of phase I (*i.e.* 260 °C) were measured as 67.7, 53.9, 45.9, 36.5, and 30.4, which correspond to P1, P2, P3, P4, and P5, respectively. The removed weights were nearly equal to the weight percent of PLGA blocks in five pentablock copolymers listed in Table 2, which clearly indicates the most parts of PLGA blocks are degraded up to 260 °C. Figure 6 is the DTG traces for five pentablock copolymers and clearly shows an identical degradation pattern with two phases. The TGA results suggest that it is possible to remove PLGA blocks selectively as well as to estimate the weight ratio of PLGA block in the block copolymers.

Static and dynamic light scattering were employed to study the aggregation behavior of PLGA-F68-PLGA pentablock copolymers in THP-containing water solution. The aggregation behavior of the pentablock copolymers was characterized at the concentration of 0.005 wt % in water/THF (90/10 by volume) mixed solvent. Figure 7 shows a partial Zimm plot for five pentablock copolymers in aqueous solution. The M_n , R_g , and the aggregation number (N_{agg}) of polymer aggregates can be calculated by obtaining y intercepts and slopes from the Eq. (2) for each polymer solution, which are listed in Table 3. The aggregation number was calculated by M_w (aggregates)/ M_w (polymer chains). As the molecular weight of PLGA block increases, R_g and N_{agg}

Table 2. Characterization of PLGA-PEO-PPO-PEO-PLGA pentablock copolymers^a

Sample	¹ H- & ¹³ C-NMR			GPC					
	No. of repeating unit		molecular formula	M_n (g/mol)	W_{LG}^b feed	W_{LG}^c product	M_n (g/mol)	M_w (g/mol)	PDI
	DLLA	GA							
P1	48	16.5	(L ₂₄ G ₈)F68(L ₂₄ G ₈)	12,700	0.369	0.345	10,700	14,100	1.32
P2	90	23	(L ₄₅ G ₁₂)F68(L ₄₅ G ₁₂)	16,100	0.499	0.483	11,500	17,100	1.48
P3	125	40	(L ₆₂ G ₂₀)F68(L ₆₂ G ₂₀)	19,700	0.579	0.575	12,000	19,400	1.61
P4	180	59	(L ₉₀ G ₂₉)F68(L ₉₀ G ₂₉)	24,700	0.673	0.663	13,400	24,900	1.85
P5	246	64	(L ₁₂₃ G ₃₂)F68(L ₁₂₃ G ₃₂)	29,700	0.727	0.720	14,100	27,100	1.91

^aRepeating units of EO are calculated as 150 based on PO block of 30 units for all samples. ^bThe weight ratio of (DLLA+GA)/(F68+DLLA+GA) added in feed. ^cThe weight ratio of PLGA/(F68+PLGA) calculated in product.

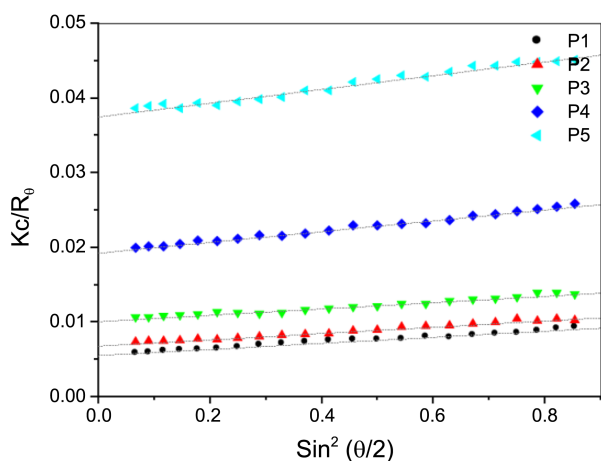


Figure 7. Static light scattering data of PLGA-F68-PLGA pentablock copolymers.

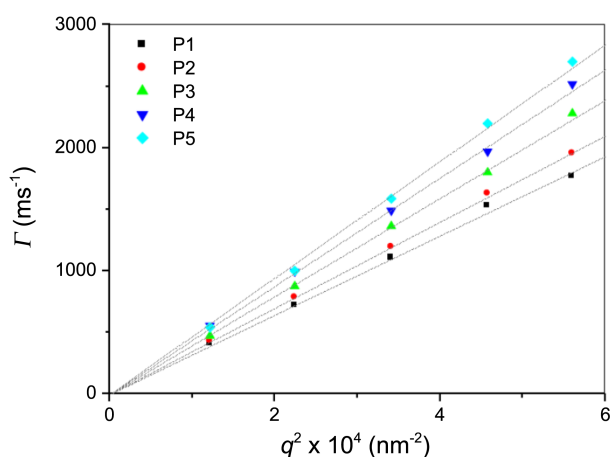


Figure 8. Dynamic light scattering data of PLGA-F68-PLGA pentablock copolymers.

were decreased. This is consistent with the general trend observed in block copolymer micelles, but one has to be careful to interpret the result quantitatively. For the analysis of copolymers or aggregates, the simple light scattering theory developed for homo-polymers (eq. (1)) does not work in rigorous sense since they are not homogeneous scattering entities. Therefore the static light scattering results must be appreciated with proper caution. Diffusion coefficient (D) was obtained by plotting Γ versus q^2 to finally determine

Table 3. Light scattering result of PLGA-F68-PLGA pentablock copolymers

Sample	R_h (nm)	R_g (nm)	R_g/R_h	M_w (aggregates)	N_{agg}^a
P1	68	49	0.721	1.8×10^8	1.3×10^4
P2	62	46	0.742	1.5×10^8	8.5×10^3
P3	55	39	0.709	9.9×10^7	5.2×10^3
P4	50	38	0.760	5.2×10^7	2.2×10^3
P5	46	31	0.674	2.7×10^7	9.9×10^2

^a $N_{agg} = M_w$ (aggregates)/ M_w (polymer chains)

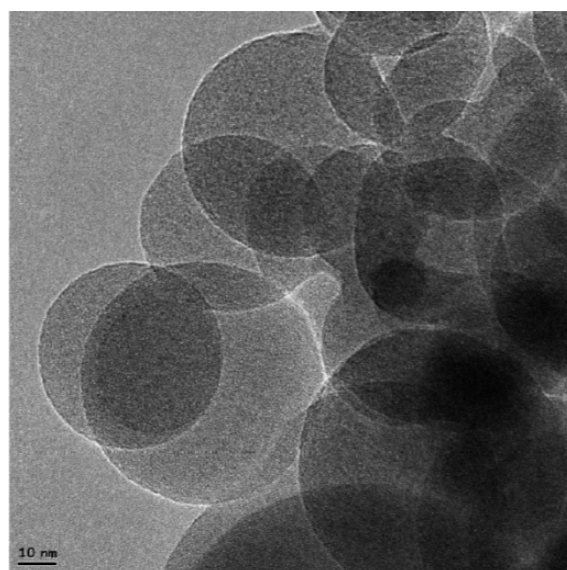


Figure 9. TEM image for P3 PLGA-F68-PLGA pentablock copolymer.

hydrodynamic radius (R_h) of micellar aggregates. Figure 8 shows the difference of slope (*i.e.* diffusion coefficient) for respective pentablock copolymers in dilute solution which is obtained by dynamic light scattering. Static and dynamic light scattering results are summarized in Table 3. It is known that the value of R_g/R_h is related to the conformation and architecture of polymer chains in solution and the crosslinking density distribution of the microgels.^{45,46} For instance, the value of around 1.5 corresponds to linear and flexible polymer chains, while 0.775 for uniform hard spheres. The ratios of R_g/R_h for pentablock copolymers were calculated in the range of 0.67–0.76, which represents the micellar aggregates is close to hard spheres. To confirm the micellar structure for the pentablock copolymer, TEM measurement was employed as shown in Figure 9. Figure 9 clearly shows the spherical shape of micellar aggregates, as predicted by the R_g/R_h ratio.

Conclusions

PLGA-F68-PLGA pentablock copolymers composed of four kinds of polymers such as poly(propylene oxide), poly(ethylene oxide), poly(lactic acid), and poly(glycolic acid) were successfully synthesized by ring opening polymerization of cyclic D,L-lactide and glycolide monomers to Pluronic F68 block copolymer and stannous octoate as a catalyst. The molecular weight and the weight fraction of each block were controlled by the amounts of D,L-lactide and glycolide monomers in reactants. Chemical bond between the hydroxyl-terminated PEO in F68 block copolymer and the monomers of ring-opened lactide and glycolide was confirmed by ^1H NMR analysis. The varied chemical compositions and the number average molecular weights were also verified with ^1H - and ^{13}C NMR analysis. The weight average molecular weight and distribution were measured

by GPC method. Molecular weight dispersity was obtained in the range of 1.32-1.91 and the values were increased as the content of PLGA block increased. TG and DTG profiles showed a clear discrete two-step trace for PLGA block and PEO-PPO-PEO copolymer, respectively. DLS analysis showed hydrodynamic radius of PLGA-F68-PLGA pentablock copolymer micelles were in the range of 46-68 nm in very dilute aqueous solution (*i.e.* 0.005 wt %) of THF:H₂O = 10:90 by volume at 25 °C. The radius of gyration were calculated in the range of 31-49 nm by SLS analysis. TEM image showed the micellar aggregates are in spherical shape.

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