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Preparation and Characterization of Polypseudorotaxanes Based on Biodegradable Poly(L-lactide)/Poly(ethylene glycol) Triblock Copolymers

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ABSTRACT: A variation of A−B−A-type triblock copolymers consisting of poly(L-lactide) (PLLA) and poly(ethylene glycol) (PEG) was synthesized and examined for complexation with α-cyclodextrins (α-CDs). Although the PLLA block has bulky methyl groups as side chains, stable polypseudorotaxanes of PLLA−PEG−PLLA triblock copolymers as well as PLLA were obtained and confirmed by ^{1}H NMR, solid-state ^{13}C CP/MAS NMR, FT-IR, and X-ray spectroscopies. From the results, it was hypothesized that the guest molecules threaded into the hydrophobic CD cavities, and they form stable pseudorotaxanes in both PEG and PLLA blocks. The α-CDs slide over the flanking bulky PLLA blocks to form an inclusion complex with PEG block; in addition, they form very stick pseudorotaxanes with the end-blocks of PLLA parts. The copolymers confined to the CD channels lost their original crystalline properties but formed a channel-type hydrophobic crystalline structure with CDs due to long chain nature of the copolymers. Such a polymeric inclusion complex can have an important role for constructing supramolecular architectures such as polyrotaxanes and molecular tubes for the use of the bioactive agent delivery system.

Introduction

Cyclodextrins (CDs) are cyclic oligosaccharides with six (α-), seven (β-), or eight (γ-)-1,4-linked glucose units, which form inclusion complexes with various guest molecules.[1] Over the past decade, polymeric inclusion complexes have attracted much attention due to their unique supramolecular architectures, such as molecular tubes or polyrotaxanes, as well as a good model for macromolecular recognition in biological systems.[2] Recently, Li et al. reported an interesting phenomenon that poly[(ethylene glycol)-*ran*-(propylene glycol)] [P(EG-*r*-PG)] could form inclusion complexes with α-CD to give polypseudorotaxanes.[3] Usually, it is assumed that PPG homopolymer could not form any crystalline inclusion complex with α-CD because the PPG chain is too bulky to penetrate into the inner cavity of α-CD. However, it seems that α-CD molecules overcome the energy barrier in passing over a PG unit or short PG segment and then form a stable inclusion complex with EG units of the copolymers. Most recently, they also reported various types of crystal structures based on inclusion complexation of triblock copolymers.[4] In their polymeric inclusion complexes, especially the reverse-type triblock copolymers of PPG−PEG−PPG and α-CDs showed a very interesting phenomenon; the smallest α-CDs slide over the flanking bulky PPG blocks to selectively form stable complexes with the middle PEG block of the triblock copolymers.[4a,b]

On the other hand, Tonelli et al. have studied some inclusion complexes of aliphatic polyesters obtained by condensation polymerizations with CDs.[5] In the aliphatic polyesters, they have been used poly(L-lactide) (PLLA) due to its controllable biodegradability, versatile mechanical properties, and relatively good biocompatibility when used in vitro and in vivo.[6] They have attempted to blend polymers as a result of forming their inclusion complexes with CDs and then coalescing the guest polymers, poly(ϵ-caprolactone) (PCL) and PLLA, from their CD inclusion complex crystals by washing with hot water.[7] In this manner, they obtained an intimately mixed blend of PCL and PLLA, which are normally immiscible. However, they did not evaluate the physical properties of their inclusion complexes, and in addition, there was no evidence that the PLLA part forms inclusion complexes with CDs. Structural analyses of such inclusion complexes are necessary to elucidate the interactions between the host (CDs) and the guest polymers and to obtain information about suitable combinations of hosts and guests.

Recently, there have been many efforts to increase the hydrophilic and other physicochemical properties of PLLA because the high crystallinity and low hydrophilicity of PLLA decreased its degradation rate and resulted in poorer soft tissue compatibility.[8] It was performed by blending PLLA with various commercial polymers, such as PCL,[9] poly(vinyl acetate),[10] and polyacrylates.[11] PEG has been also incorporated into the biodegradable polyesters to regulate the hydrophilicity of the materials as well as the nontoxic and nonimmunogenic nature by forming diblock, triblock, multiblock, and star-shaped block copolymers.[12]

In the present study, a variation of PLLA−PEG−PLLA (M_n = 12 400, 12 900, 14 200, and 16 600) copolymers was prepared by utilizing PEG as a counterpart segment to PLLA. These triblock copolymers were used as a polymeric guest for inclusion complexation with α-CDs. The PLLA block has methyl groups as side chains as same as PPG, but we could prepare stable CD inclusion complexes with the triblock copolymers as well

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Scheme 1. Synthetic Route for the Copolymers of PLLA (a) and PLLA−PEG−PLLA (b) and Proposed Structure of the Polypseudorotaxane between PLLA−PEG−PLLA Triblock Copolymers and α-CDs (c)

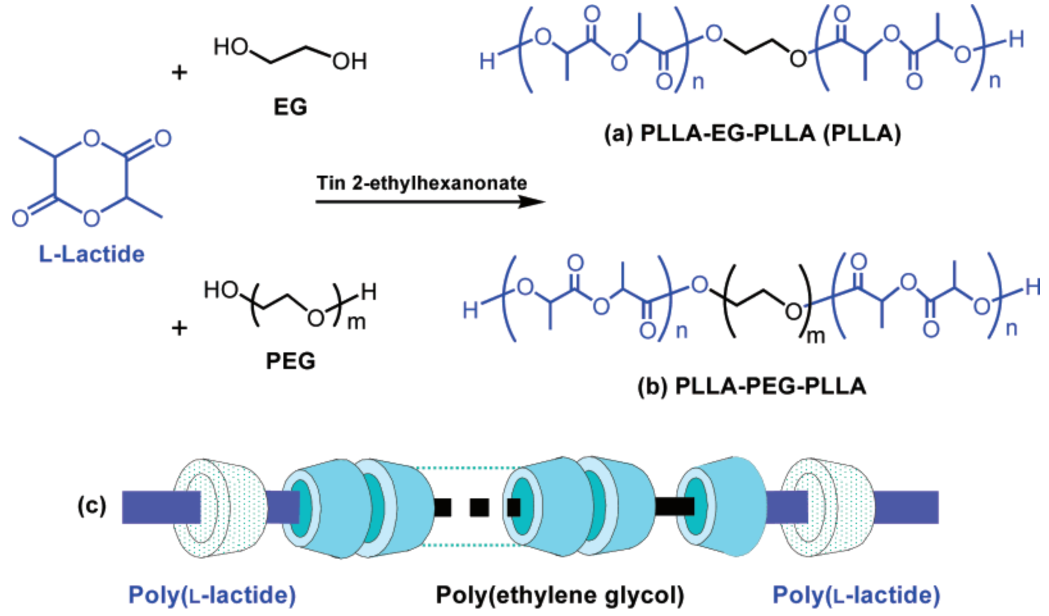

Table 1. Results of the Copolymerization of L-Lactide (LA) on PEG[a]

	LA/PEG		LA unit		M_n			
code	in feed (mol/mol)	found[b] (mol/mol)	content[c] (mol %)	M_n (g/mol)	NMR (g/mol)	GPC[d] (g/mol)	M_w/M_n	yield (%)
Tri-1	22.0	22.7	16.6	3400	13 300	12 400	1.11	92.2
Tri-2	33.0	30.5	21.1	4400	14 400	12 900	1.18	78.1
Tri-3	44.0	44.9	28.3	6400	16 500	14 200	1.28	88.3
Tri-4	56.0	54.1	32.2	7800	17 800	16 600	1.26	82.2

[a] Molar ratio of monomer to catalyst (M/cat) = 1000; cat: tin 2-ethylhexanoate. Polymerizations were carried out in bulk at 150 °C for 2 min and 115 °C for 24 h. [b] The molar ratio of L-lactide unit (LA)/PEG was determined from the integration ratio of methyne proton of the PLLA segment to the methylene proton of PEG by ^1H NMR spectroscopy (PEG $M_n = 10\ 040$; $M_w/M_n = 1.01$; $m = 228$). [c] Mol % of LA ($-OCH(CH_3)CO-$) was calculated based on *b*. [d] The number-average molecular weights of copolymers were estimated by GPC (eluent: DMF; standard: PEG).

as PLLA, which were confirmed by ^1H NMR, solid-state ^{13}C CP/MAS NMR, FT-IR, and X-ray spectroscopic methods. The thermal property of the obtained polypseudorotaxanes was performed by DSC measurement. This study provides direct evidence of the polypseudorotaxane formation between relatively bulky polymers and geometrically small cavities of α-CDs.

Experimental Section

Materials. L-Lactide (LA) supplied by Wako Pure Chemical Co. (Tokyo, Japan) was recrystallized twice from ethyl acetate before using. α-Cyclodextrin (α-CD), tin 2-ethylhexanoate, and other chemicals were purchased from Wako Pure Chemical Co. Organic solvents were purified by usual distillation methods. The other synthetic reagents were used as received without further purification.

Synthesis of Triblock Copolymers. The synthesis of PLLA−PEG−PLLA triblock copolymers was performed by ring-opening polymerization of LA in bulk using PEG and tin 2-ethylhexanoate as a macroinitiator and a catalyst, respectively, according to Scheme 1. Under a nitrogen atmosphere, appropriate amounts of LA and PEG ($M_n = 10\ 040$, $M_w/M_n = 1.01$, $n = 228$) were placed into a glass tube, and a freshly prepared solution of tin 2-ethylhexanoate in anhydrous THF (3.7×10^{-2} M) was added to the tube in a glovebox (molar ratio of LA/tin 2-ethylhexanoate = 1000). The solvent was removed under vacuum for a night. The tube was purged with argon and then sealed in vacuo. The sealed tube was placed in an oil bath at 150 °C for 2 min and subsequently at 115 °C for 24 h. The obtained products were dissolved in a small amount of chloroform and precipitated in an excess amount of diethyl ether. The resulting copolymer was dried in vacuo at room temperature for 12 h.

The molar ratio of LA unit to PEG in the triblock copolymers obtained was determined by integration ratio of the ^1H NMR signals attributed to methyne proton of PLLA segment at $\delta = 4.35$ and methylene proton of PEG segment at $\delta = 3.66$.

^1H NMR(CDCl$_3$): δ (ppm) = 1.58 (d, $CHCH_3$), 3.66 (s, $-OCH_2CH_2O-$), 4.29 (t, $-OCH_2CH_2OCO-$), 4.35 (m, $CH(CH_3)$-OH), 5.15 (q, $CHCH_3$).

The synthetic results of triblock copolymers between LA and PEG (PLLA−PEG−PLLA) are summarized in Table 1. Reference polymer, PLLA (M_n = 5400, 6400, or 8100), was synthesized by the similar method described above using ethylene glycol (EG) as an initiator instead of PEG. In this paper, only one molecular weight (M_n = 5400) of PLLA was used for data arrangements.

Preparation of Polypseudorotaxane. PLLA−PEG−PLLA (0.2 g, 2.78 mmol in monomer unit) copolymer was dissolved in 5 mL of dioxane/acetone (20/80 vol %) with heating (60 °C), followed by pouring into α-CD aqueous solution (1.39 mmol). After initial stirring at 60 °C, the mixture was ultrasonically agitated and stirred for another 1 h at 60 °C. The aqueous solution became turbid, which was allowed to cool to 4 °C while continuously stirring, followed by standing at room temperature for 12 h. The precipitated product was collected by centrifugation and then washed with acetone and water to remove the free polymers and the uncomplexed α-CDs, respectively. The obtained crystal was dried at 60 °C in vacuo to give a polypseudorotaxane. In the case of the PLLA (M_n = 5400, 6400, or 8100), dioxane was used as a solvent for inclusion complexation with α-CD aqueous solution, and the same procedure was applied.[5a]

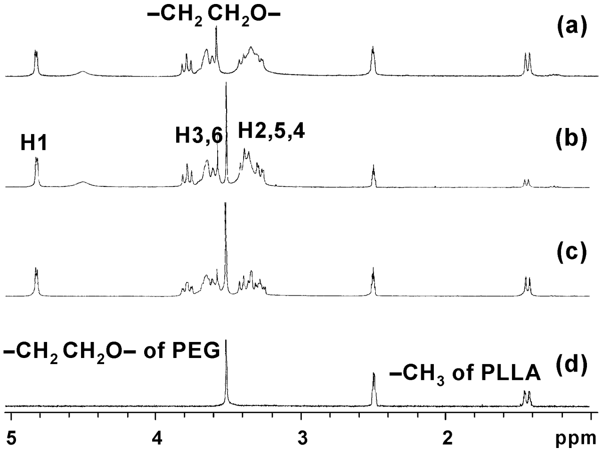

Figure 1. ^{1}H NMR spectra for inclusion complexes of PLLA (M_n = 5400)/α-CD (a), Tri-1/α-CD (b), Tri-4/α-CD (c), and Tri-4 (d) in DMSO-d_6.

Characterization. The chemical composition and molecular weight of the triblock copolymers were confirmed by ^{1}H NMR using a 400 MHz FT-NMR spectrometer (GSX-400, JEOL, Japan) and by gel permeation chromatography (GPC) using a Tosoh GPC-8020 series system with a refractive index (RI) detector (TSK Gel Multipore H_{XL}-M × 2 columns, eluent: DMF, flow rate: 1 mL/min; standard: PEG).

The solid-state ^{13}C CP/MAS NMR spectra were recorded at 100.4 MHz on a JNM-GSX 400 NMR spectrometer with a sample spinning rate of 6 kHz at 19 °C. CP spectra were acquired with a 5 ms contact time, a 10 s repetition time, and 18 000 accumulations.

The crystallinity changes in complex formation of copolymers with α-CDs were confirmed by X-ray diffraction measurements, performed with powder diffractometry (RINT2000, Rigaku, Japan) and also image-plate photography using graphite-monochromatized Cu Kα radiation (λ = 1.542 Å).

To evaluate the chemical composition of the inclusion complexes, FT-IR spectra were recorded on a VALOR-III FT-IR spectrometer (Jasco, Tokyo, Japan) in the range between 4000 and 400 cm^{-1}, with a resolution of 2 cm^{-1} and 64 scans.

The stoichiometric number and the number-average molecular weight of the inclusion complexes were determined by the peak integration of ^{1}H NMR spectra using a 750 MHz FT-NMR spectrometer (Varian, Palo Alto, CA).

A differential scanning calorimeter (DSC821^e, Mettler Toledo) was used to measure the thermal properties of the polymeric inclusion complexes. The DSC thermograms covered the temperature range of 10−200 °C at a scanning rate of 10 °C/min.

Results and Discussion

^{1}H NMR Spectroscopy. To investigate the inclusion complexation and the stoichiometry, the ^{1}H NMR spectra of all obtained polypseudorotaxanes were measured in DMSO-d_6. NMR spectroscopic method is very useful to provide evidence for the formation of inclusion complexation in solution, since this will affect the proton environment in both the host and the guest and will hence be reflected by chemical shift variations of protons from both species. Specifically, the internal H-3 and H-5 protons in α-CDs are more sensitive to the complexation effect than the H-1, H-2, or H-4 protons located on the outside of the host cavity; therefore, the signals of the protons H-3, H-5, and H-6 are shifted upfield. The shifts of these protons to high field display increasing shielding during the complex formation with guest molecules as a result of releasing water molecules from the cavity which are replaced by the apolar alkyl chain of the guest.[13] As shown in Figure 1, the inclusion complexation in all batches was confirmed, but the stoichiometry between PLLA and α-CDs could not be calculated because the characteristic peaks of PLLA were not observed in quantitative changes in proportional to the feed ratio (data not shown). Until now, it has been believed that the cavity of α-CD is theoretically too small (ca. 4.7 Å) to include more bulky PLLA chains (ca. 5.2 Å);[14] thus, it is theoretically impossible for them to form an inclusion complex.[15] In this study, adequate solvent, ultrasonication, and heating methods were applied to reduce the activation energy barrier of the inclusion complexation between bulky guest and CDs. With an increase in the feed ratio (Tri-4/α-CD), the H-5 protons located on the smaller ring side of α-CD exhibited the largest shifts upon inclusion of Tri-4 (see Supporting Information). This result suggests that they formed very compactly locked inclusion complexes with α-CDs and the H-5 protons restricted their resonances by the neighboring guests protons. Therefore, the formed polypseudorotaxanes might be very stable like a rigid rod, and the block copolymers could not dissociate easily from the CD cavities even in DMSO-d_6. To make the inclusion complex in a fully dissociated state in the ^{1}H NMR solvents, various methods such as heating to 80 °C or changing solvents were tried; however, the largest peak shift of H-5 protons was still observed. This result suggests that partially included complexes remained in those systems.

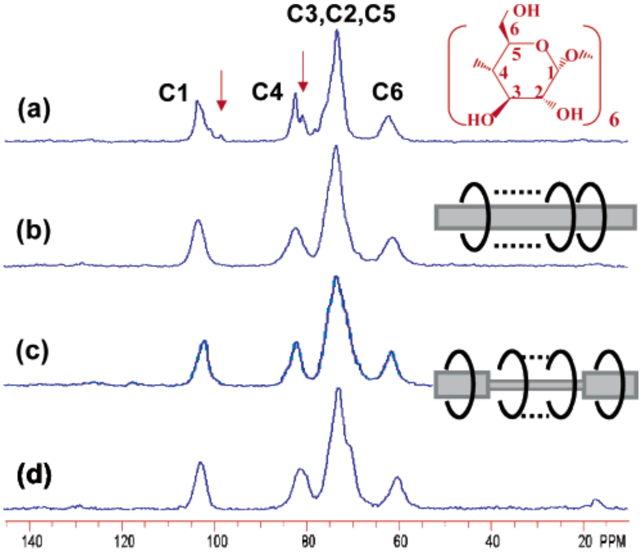

Figure 2. Solid-state ^{13}C CP/MAS NMR spectra of α-CD (a) and inclusion complexes of PLLA (M_n = 5400)/α-CD (b), Tri-1/α-CD (c), and Tri-4/α-CD (d).

Solid-State ^{13}C CP/MAS NMR Spectroscopy. Because the formed inclusion complexes did not dissolve enough in the solvents for ^{1}H NMR spectroscopy, solid-state NMR spectra were measured to evaluate the formation of polypseudorotaxanes. Figure 2 shows solid-state ^{13}C CP/MAS NMR spectra for the polypseudorotaxanes of PLLA/α-CD, Tri-1/α-CD, and Tri-4/α-CD compared with that of α-CD. The spectrum of α-CD in the uncomplexed state shows strong splitting for all C_{1-6} resonances, indicating that α-CD molecules are in a rigid, less symmetric cyclic conformation.[16,17] On the other hand, the CD inclusion complexes showed less splitting for each glucose carbon, which indicates that α-CDs in the inclusion complexes have adopted more symmetric cyclic conformations.[18] In addition, the peaks characteristic of the glycoside linkage at 98 and 80 ppm

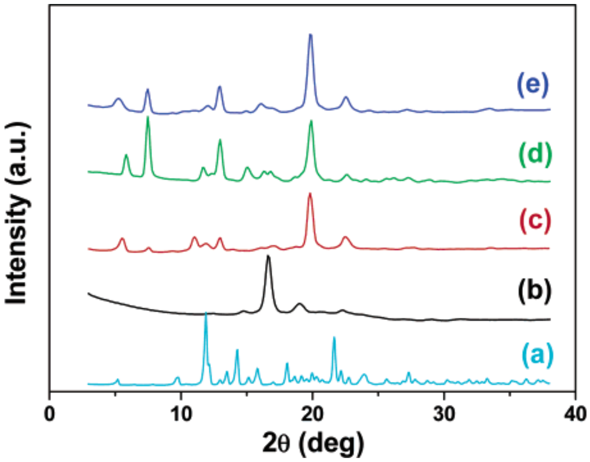

Figure 3. X-ray diffraction patterns for α-CD (a), PLLA (M_n = 5400) (b), PEG/α-CD inclusion complex (c), PLLA (M_n = 5400)/α-CD inclusion complex (d), and Tri-1/α-CD inclusion complex (e).

disappeared in the spectra of both the PLLA/α-CD and the triblock/α-CD inclusion complexes. These results indicate that the α-CD molecules include both PLLA and PEG chains in the copolymers to form channel-structured inclusion complexes.

X-ray Diffraction Spectroscopy. Figure 3 shows wide-angle X-ray diffraction patterns of α-CD, PLLA copolymers, and their inclusion complexes. The diffractograms of both the PLLA/α-CD and the Tri-1/α-CD inclusion complexes showed a pattern quite different from those of the host CDs or the guest copolymers. Reflections observed at $2\theta = 7.60°$ (d = 11.6 Å), 13.0° (d = 6.80 Å), and 20.0° (d = 4.44 Å) were explained by a hexagonal unit cell with lateral dimension a = 13.6 Å, which was the same as reported for the PEG/α-CD inclusion complex (Figure 3c).[19] The strong 210 reflection is a typical peak of the inclusion complexes with α-CD, suggesting the electron density distribution of the core of α-CD molecules with radius ~5 Å. As a result, it is concluded that α-CD can form inclusion complexes with all the PLLA copolymers examined and have a columnar crystalline structure.

FT-IR Spectroscopy. Another strong evidence of the inclusion complexation was obtained by the FT-IR spectra of triblock copolymers, α-CD, and inclusion complexes of triblock copolymers with α-CD. As shown in Figure 4, the extremely broad band between 4000 and 3000 cm^{-1} is normally assigned to the symmetric and asymmetric O−H stretching modes. The center of this band for pure α-CD is 3389 cm^{-1} and is shifted to higher frequency 3420 cm^{-1} when it forms the inclusion complex with triblock copolymers. This shift is likely due to association of the O−H groups of CDs with the included polymeric chain.[20]

The bands observed in the 3000−2500 cm^{-1} region for α-CD (Figure 4b) and the PLLA/α-CD complex (Figure 4c) are slightly different. PLLA has several strong bands due to the C−H stretching mode around 3002 and 2952 cm^{-1}, while α-CD has a band around 2940 cm^{-1}. A broad shoulder around 2886 cm^{-1}, as well as shifted C−H stretching mode of α-CD at 2943 cm^{-1}, appeared in the PLLA/α-CD spectra (Figure 4c), which were probably attributed to the included PLLA segments in their inclusion complexes.

A new band appeared at 1762 cm^{-1} in the spectra of Figure 4c, which was absent in the spectrum of α-CD (Figure 4a). It is most probably due to the carbonyl stretching from amorphous PLLA phases. The small change of the 1493 and 1453 cm^{-1} bands was also observed in the PLLA/α-CD samples. These characteristic bands suggest that the PLLA polymer chains are included inside the channels of α-CDs.

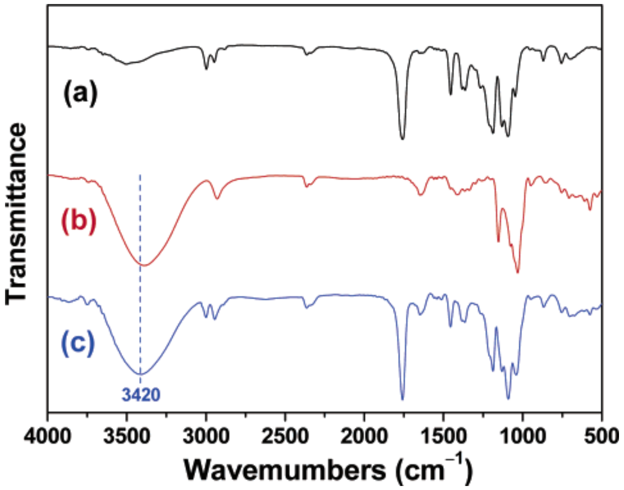

Figure 4. FT-IR spectra of PLLA (M_n = 5400) (a), α-CD (b), and their inclusion complex (c).

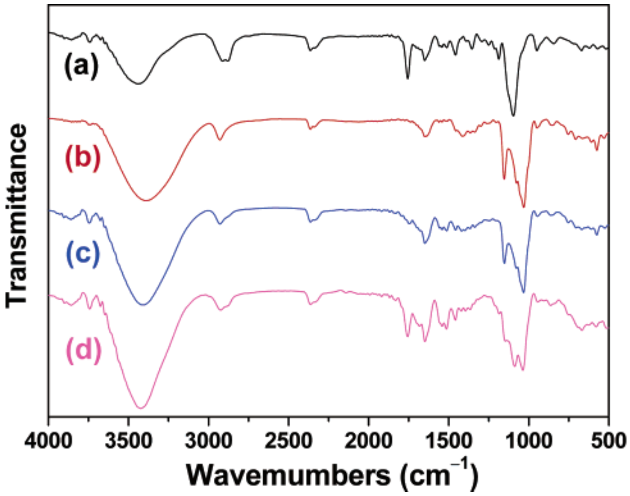

Figure 5. FT-IR spectra of Tri-1 (a), α-CD (b), Tri-1/α-CD inclusion complex (c), and Tri-4/α-CD inclusion complex (d).

The bands observed in the 1200−800 cm^{-1} region of the PLLA/α-CD complex were referred to as stretching modes of the glucosidic group (C−O−C, at 1189 cm^{-1}) coupled with C−C (1092 cm^{-1}) and C−O (1042 cm^{-1}) stretching modes, which were very similar for those of α-CD.[21]

There were no significant differences in the spectra of the inclusion complexes between PLLA/α-CD and triblock copolymers/α-CD (Figure 5). In the case of the inclusion complexes based on triblock copolymers, the center for O−H stretching modes shifted to higher frequency. New bands appeared at 2947 cm^{-1} with a shoulder at 2887 cm^{-1} for both the Tri-1/α-CD and Tri-4/α-CD inclusion complexes, which are different from α-CD. An obvious new band at 1762 cm^{-1} due to C=O can also be observed.

Stoichiometry of the Polypseudorotaxanes. Because the stoichiometry of all the obtained polypseudorotaxane was not calculated by ^{1}H NMR spectroscopic method, inclusion complexes were prepared with different ratios of copolymers/α-CDs in feed without the

Table 2. Thermal Properties of Polypseudorotaxanes between PLLA−PEG−PLLA Triblock Copolymers and α-CDs

code	PLLA in copol[a] (wt %)	PEG segment		PLLA segments			
		T_m[b] (°C)	ΔH[c] (kJ/mol)	T_c[d] (°C)	ΔH[e] (kJ/mol)	T_m[f] (°C)	ΔH[g] (kJ/mol)
Tri-1	25.4	52.9	6.9	92.2		148.8	0.1
Tri-2	30.6	51.4	5.2	95.6	−0.1	151	0.4
Tri-3	39.0	50.1	5.3	99.1	−0.4	161.0	0.9
Tri-4	43.8	48.8	4.2	100.8	−0.8	163.0	1.1
PLLA5K	98	56.8[h]	0.1	91.2	−1.0	156.7	2.6

[a] Weight ratio of PLLA to PEG−PLLA−PEG triblock copolymers. [b,f] Melting temperatures of PEG and PLLA for triblock copolymers, respectively. [c,g] Heat capacity of PEG and PLLA in melting, respectively. [d] Crystallization temperature of PLLA for triblock copolymers. [e] Heat capacity of PLLA in crystallization. [h] Glass-transition temperature of PLLA with a M_w of 5000.

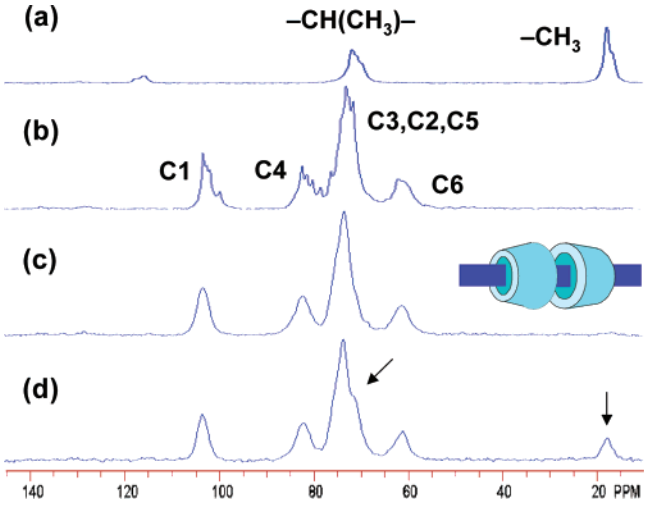

Figure 6. ^{13}C CP/MAS NMR spectra of the PLLA (M_n = 5400)/α-CD inclusion complexes with a molar feed ratio of 1:0 (a), 1:1 (b), 2:1 (c), and 4:1 (d).

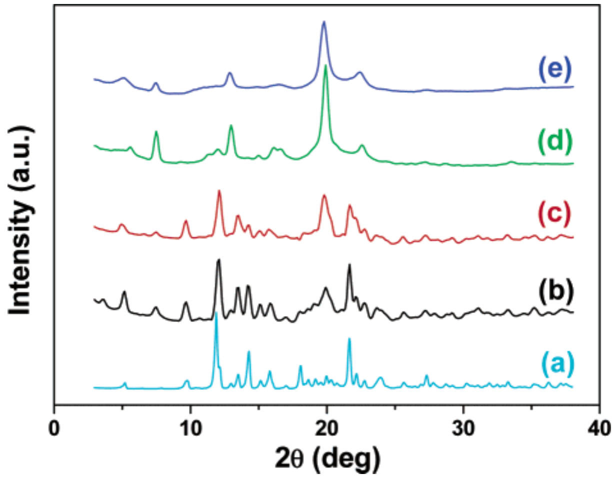

Figure 7. X-ray diffraction patterns for the Tri-4/α-CD inclusion complexes with a molar feed ratio of 0 (a), 0.5 (b), 1.0 (c), 2.0 (d), and 4.0 (e).

washing process, physical states of which were observed by solid-state ^{13}C CP/MAS NMR and X-ray diffraction spectroscopic methods. To obtain accurate analysis data, the same amount of polypseudorotaxanes was applied to all batches in the sampling process. Figure 6 shows the solid-state ^{13}C CP/MAS NMR spectra of the PLLA/α-CD inclusion complexes with various molar feed ratios. The molar feed ratio was based on each repeating unit of triblock copolymers, [EG] and [LA]. The inclusion complex with a 2:1 feed ratio (Figure 6c) has adopted most symmetric cyclic conformations compared with other spectra. The spectrum with an excess amount of the copolymers (Figure 6d, feed ratio 4:1) shows uncomplexed guest peaks besides the inclusion complex peaks. In the case of the Tri-1/α-CD and the Tri-4/α-CD inclusion complexes, similar results were obtained (data not shown).

To confirm these results, X-ray diffraction spectra were measured for all triblock copolymers as well as PLLA. As shown in Figure 7, the polypseudorotaxane of Tri-4/α-CD with feed ratio 2:1 showed the maximum characteristic peaks of inclusion complex. More feeding of the guests to the inclusion system (Figure 7d) resulted in broadening and decreasing some characteristic peaks of inclusion complex ($2\theta = 7.60°$, 13.0°, and 20.0°). This result is well coincident with that of the solid-state ^{13}C CP/MAS NMR spectroscopic study on the polypseudorotaxanes. In the case of other polypseudorotaxanes based on various triblock copolymers, the same result was obtained (data not shown). From these results, it is concluded that the stoichiometry for the complex formation between PLLA and α-CD is to be about 2:1.

Thermal Properties of the Polypseudorotaxanes. Figure 8e shows a typical DSC thermogram of a quenched triblock copolymer sample by rapid freezing after high-temperature annealing. From the lower temperature region, a step, an endotherm, an exotherm, and an endotherm were observed, which correspond to the melting temperature (T_m) of PEG segment and the crystalline temperature (T_c) and the T_m of the PLLA segments, respectively. The glass transition temperature (T_g) of PLLA was not clearly observed in the thermogram because it may overlap the endotherm accompanying the melting of crystallized PEG segments.

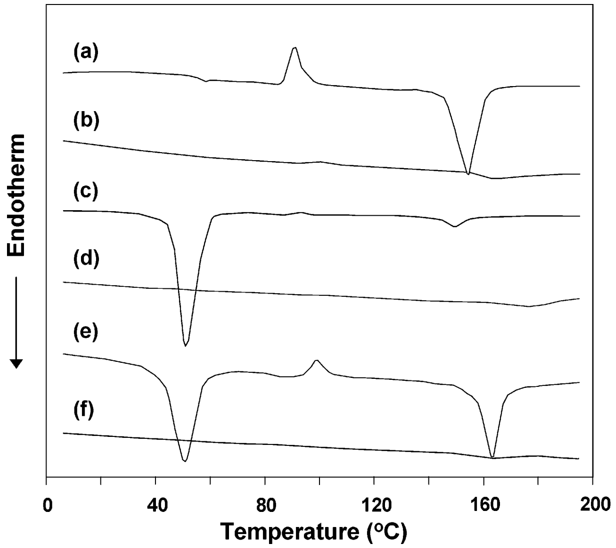

Figure 8. DSC thermograms of PLLA (a), PLLA (M_n = 5400)/α-CD (b), Tri-1 (c), Tri-1/α-CD (d), Tri-4 (e), and Tri-4/α-CD (f). The feed ratio of guest/host for all inclusion complexes is 2.

The results of DSC measurements containing T_m and ΔH values are summarized in Table 2. Nevertheless, the heat capacity of crystallized PEG in melting decreased with an increase in the weight fraction of PLLA segments;[22] those values of T_c and T_m of PLLA segments increased gradually. When the total length of the two PLLA blocks was close to that of the PEG block (Tri-4), neither the PEG nor the PLLA blocks could crystallize spontaneously. In addition, T_m values of PLLA crystalline phases varied from 148 to 163 °C with increasing the PLLA ratio from 25.4 to 43.8 wt %. Such a melting behavior may be explained by reaching an equilibrium length of block segments which restrict crystallization and, therefore, result in poorly ordered crystalline phases and lower crystalline content. The melting transitions for these crystalline phases were influenced by the copolymer compositions and the average block lengths. On the other hand, there were no corresponding melting peaks for all the inclusion complexes with a stoichiometry 2:1, such as Tri-1/α-CD, Tri-4/α-CD, and PLLA/α-CD inclusion complexes (Figure 8). These results are coincident with the X-ray diffraction and solid-state ^{13}C CP/MAS NMR spectroscopic measurements, which means that all the guest copolymers chains, both PEG and PLLA segments, participate in the formation of new channel-type crystalline structures with α-CD molecules.[17a]

Conclusion

Polymeric inclusion complexes between CDs and PLLA−PEG−PLLA were successfully prepared and characterized quantitatively with various analytical methods. The obtained results suggest that the PLLA chains were included inside the channels formed by α-CDs. To our best knowledge, it is the first report to clarify the inclusion complexation and stoichiometry of the amphiphilic biodegradable PLLA copolymers. From the results of X-ray diffraction and solid-state ^{13}C CP/MAS NMR spectroscopic methods, these copolymers confined to the CD channels lost their original crystalline properties but formed a channel-type crystalline structure with CDs due to long chain nature of the copolymers. The stoichiometric number of [LA] monomer unit and [CD] was found to be 2:1, which was observed in the polypseudorotaxanes of triblock copolymers as well as PLLA. These results strongly suggest that the PLLA copolymers are fully complexed by α-CDs; α-CDs slide over the flanking bulky PLLA blocks to form an inclusion complex with PEG block, and in addition, they formed rigid-rod-like pseudorotaxanes with the bulky end-blocks of PLLA parts. Such a polymeric inclusion complex can be promising for constructing supramolecular architectures such as polyrotaxane and molecular tube for the use of biodegradable materials in the field of drug delivery and tissue engineering.

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Supporting Information Available: ^{1}H NMR spectra for inclusion complexes between Tri-4 and α-CD with various feed ratios in DMSO-d_6. This material is available free of charge via the Internet at http://pubs.acs.org.

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