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Preparation and characterization of inclusion complexes formed by biodegradable poly(ε-caprolactone)–poly(tetrahydrofuran)–poly(ε-caprolactone) triblock copolymer and cyclodextrins

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Abstract

Inclusion complexes (ICs) formed with cyclodextrins (CDs) and polymers have been an interesting topic over the past decade. Recently, more focus has been shifted to the ICs with biodegradable polymers or copolymers because of their potential applications as novel biomaterials. This work reports the IC formation between CDs and biodegradable poly(ε-caprolactone)–poly(tetrahydrofuran)–poly(ε-caprolactone) (PCL–PTHF–PCL) triblock copolymer and the characterization of the ICs. The PCL–PTHF–PCL triblock copolymer was found to form crystalline ICs with all α-, β-, and γ-CDs. All the three ICs were prepared in high yields from aqueous medium. The ICs were characterized by X-ray diffraction (XRD), ^{13}C CP/MAS NMR, ^{1}H NMR, Fourier transform infrared, differential scanning calorimetry (DSC), and thermogravimetric analysis (TGA). The XRD studies demonstrated that all the ICs assumed a channel-type structure similar to the necklace-like ICs formed by α-CD and poly(ethylene glycol) homopolymers. Solid-state CP/MAS ^{13}C NMR studies showed that the CD molecules in the ICs adopted a symmetrical conformation due to the threading onto a polymer chain. The compositions of the ICs were studied by using ^{1}H NMR spectroscopy. From the ^{1}H NMR and DSC results, it was proposed that only the two flanking PCL blocks are included and covered by α-CD in the α-CD–PCL–PTHF–PCL IC, while the two PCL blocks as well as the middle PTHF block are included and covered by β-CD in the β-CD–PCL–PTHF–PCL IC. On the other hand, it was proposed that the PCL–PTHF–PCL copolymer is probably included and covered by γ-CD in a double-stranded mode in the γ-CD–PCL–PTHF–PCL IC. Finally, The TGA analysis revealed that the ICs had better thermal stability than their free components due to the inclusion complexation, suggesting that the complexation stabilized the copolymer included in the CD channels.

Keywords: Triblock copolymer; Cyclodextrin; Inclusion complex

1. Introduction

Cyclodextrins (CDs) are a series of cyclic oligosaccharides composed of 6, 7, or 8 D(+)-glucose units linked by α-1,4-linkages, and named α-, β-, or γ-CD, respectively (Chart 1). The doughnut-shaped geometry of CDs gives a hydrophobic cavity having a depth of ca. 8.0 Å, and an internal diameter of ca. 4.5 Å for α-, ca. 7.0 Å for β-, and ca. 8.5 Å for γ-CD, respectively [1]. They have been extensively studied in supramolecular chemistry as host molecules capable of forming inclusion complexes (ICs) with various low molecular weight guest molecules [1,2].

Over the past decade, ICs formed with CDs and polymers have attracted special interest since the finding of the first example of IC formation between α-CD and poly(ethylene glycol) (PEG) [3,4]. A large number of reports have been published on ICs formed between CD and various polymers with necklace-like supramolecular structures [5–36]. Although α-, β-, and γ-CDs have similar depth for the hydrophobic cavities (ca. 7.0 Å), their internal diameters are quite different [1]. It has been found that the size correlation between the cross-sectional areas of the polymer chains and

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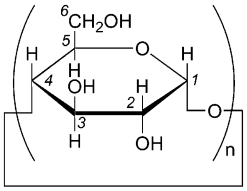

Chart 1. Structure of α-, β-, and γ-CDs ($n = 6$, 7, and 8, respectively).

the cavity internal diameters of CDs plays an important role in the IC formation [8–22].

Recently, more attention in this area has been focused on the ICs formed by CDs and block copolymers, which may involve block-selective molecular recognition and result in special block structures of great interest [23–36]. Particularly, those with biodegradable block copolymers are of special interest because of their potential applications as functional biomaterials [29–36]. For example, we reported the formation of supramolecular hydrogels induced by inclusion complexation between α-CD and Pluronics, the triblock copolymers of poly(ethylene glycol)–poly(propylene glycol)–poly(ethylene glycol) (PEG–PPG–PEG), and suggested its utility for controlled release of drugs [25]. Choi et al. recently reported the hydrogel formation between β-CD and PPG-grafted dextrans [26]. Due to the preferential inclusion, CDs can be threaded onto specific blocks of the copolymers, which may affect the morphology of the remaining blocks. Recently, an example was reported to regulate the biodegradability of poly(ε-caprolactone)–poly(L-lactide) diblock copolymers upon formation of ICs with CDs [30]. Although the size correlation between the polymer chains and the geometries of CDs is a primary factor to determine the IC formation in homopolymer systems, recently we unexpectedly found that in a triblock copolymer system, small α-CD can overcome the energy barrier to slide over a bulky PPG block into a thinner PEG block to form a stable IC [28].

Herein, we have found the biodegradable poly(ε-caprolactone)–poly(tetrahydrofuran)–poly(ε-caprolactone) (PCL–PTHF–PCL) triblock copolymer could form ICs with all α-, β-, and γ-CDs. In a previous study on IC formation between poly(ε-caprolactone)–poly(propylene glycol)–poly(ε-caprolactone) (PCL–PPG–PCL) triblock copolymer and CDs [31], it was found that only α- and γ-CDs could form ICs with the PCL–PPG–PCL copolymer. However, in our PCL–PTHF–PCL system, β-CD also formed IC, presumably due to the incentive of favorable interaction between the middle PTHF block and β-CD. In this article, we report the preparation of the ICs formed by the PCL–PTHF–PEL triblock copolymer and all α-, β-, and γ-CDs. The ICs were characterized by using X-ray diffraction (XRD), solid and liquid NMR, Fourier transform infrared (FTIR), differential scanning calorimetry (DSC), and thermogravimetric analysis (TGA). Based on our data and a comparison with other CD-polymer IC systems reported previously, the inclusion modes of the ICs are also discussed.

2. Experimental

2.1. Materials

Poly(ε-caprolactone)–poly(tetrahydrofuran)–poly(ε-caprolactone) (PCL–PTHF–PCL) triblock copolymer with indicative M_n of 2000 in total and 500 for each PCL block, was purchased from Aldrich. In this study, we actually determined the molecular characteristics of the triblock copolymer sample using gel permeation chromatography (GPC) and ^{1}H NMR spectroscopy. Poly(ethylene glycol) (PEG, $M_n = 1000$) and poly(propylene glycol) (PPG, $M_n = 1000$) homopolymers were also supplied by Aldrich. α-CD, β-CD, and γ-CD were supplied by Tokyo Kasei, Inc., Japan. DMSO-d_6 (99.9%) and $CDCl_3$ (99.8%) used as solvents in the NMR measurements were obtained from Aldrich.

2.2. Preparation of inclusion complexes

The general procedure for all ICs with α-, β-, and γ-CDs is as follows. Certain amount of bulk PCL–PTHF–PCL triblock polymer was added into excess of CD aqueous solution in a test tube at 60 °C. The mixture was sonicated in an ultrasonic waterbath for 10 min, followed by vortexing at room temperature for 10 min. The IC was gradually formed as white crystalline precipitate. To ensure that there was no free PCL–PTHF–PCL copolymer left with the IC, the reaction mixture was allowed to stand for t min, and then V ml of the supernatant was removed, and the same volume of the CD aqueous solution (V ml) was added. The mixture was heated again at 60 °C, followed by sonication and vortexing. The same procedures were repeated twice, and then the reaction mixture was allowed to stand overnight. Finally, the white precipitate was collected by suction filtration, washed with a limited amount of water, and dried under vacuum.

2.2.1. α-CD–PCL–PTHF–PCL IC

PCL–PTHF–PCL triblock copolymer (40 mg) and saturated α-CD aqueous solution (12.4 ml, 0.145 g ml^{-1}) were used, while $t = 10$ min, and $V = 3.0$ ml. Yield, 130 mg (65%). ^{1}H NMR (400 MHz, DMSO-d_6, 22 °C): δ 5.52 (d, ca. 61H, O(2)H of CD), 5.44 (d, ca. 61H, O(3)H of CD), 4.79 (d, ca. 61H, H(1) of CD), 4.48 (t, ca. 61H, O(6)H of CD), 3.98 (m, ca. 23H, *e* and *i′* of PCL–PTHF–PCL), 3.75 (t, ca. 61H, H(3) of CD), 3.62 (m, ca. 122H, H(6) of CD), 3.58 (m, ca. 61H, H(5) of CD), 3.25–3.40 (m, ca. 188H, *f*, *f′*, *i*, and *e′* of PCL–PTHF–PCL, and H(2) and H(4) of CD), 2.27 (m, ca. 23H, *a* and *a′* of PCL–PTHF–PCL), 1.51 (m, ca. 113H, *b*, *b′*, *d*, *d′*, *g*, *g′*, *h*, and *h′* of PCL–PTHF–PCL), 1.28 (m, ca. 23H, *c* and *c′* of PCL–PTHF–

PCL). IR (KBr, cm^{-1}): 3368 (vs, br, −OH), 2931 (s, C−H), 2867 (s, C−H), 1736 (s, C=O), 1153 (vs, C−O), 1177 (vs), 1030 (vs), 752, 704, 574. Anal. Calcd for $C_{134}H_{248}O_{40}$·10.1-$C_{36}H_{60}O_{30}$·15H_2O: C, 47.45; H, 7.07. Found: C, 47.80; H, 7.47.

2.2.2. β-CD–PCL–PTHF–PCL IC

PCL–PTHF–PCL triblock copolymer (40 mg) and β-CD aqueous solution (80 ml, 0.022 g ml^{-1}) were used, while $t = 30$ min, and $V = 16$ ml. Yield, 247 mg (78%). ^{1}H NMR (400 MHz, DMSO-d_6, 22 °C): δ 5.57 (d, ca. 101H, O(2)H of CD), 5.68 (d, ca. 101H, O(3)H of CD), 4.82 (d, ca. 101H, H(1) of CD), 4.46 (t, ca. 101H, O(6)H of CD), 3.98 (m, ca. 23H, *e* and *i′* of PCL–PTHF–PCL), 3.63 (m, ca. 303H, H(3) and H(6) of CD), 3.56 (m, ca. 101H, H(5) of CD), 3.27–3.37 (m, ca. 269H, *f*, *f′*, *i*, and *e′* of PCL–PTHF–PCL, and H(2) and H(4) of CD), 2.27 (m, ca. 23H, *a* and *a′* of PCL–PTHF–PCL), 1.51 (m, ca. 113H, *b*, *b′*, *d*, *d′*, *g*, *g′*, *h*, and *h′* of PCL–PTHF–PCL), 1.28 (m, ca. 23H, *c* and *c′* of PCL–PTHF–PCL). IR (KBr, cm^{-1}): 3367 (vs, br, −OH), 2928 (s, C−H), 1733 (s, C=O), 1157 (vs, C−O), 1180 (vs), 1030 (vs), 757, 705, 578. Anal. Calcd for $C_{134}H_{248}O_{40}$·14.4$C_{42}H_{70}O_{35}$·38H_2O: C, 45.45; H, 6.88. Found: C, 45.75; H, 7.30.

2.2.3. γ-CD–PCL–PTHF–PCL IC

PCL–PTHF–PCL triblock copolymer (30 mg) and γ-CD aqueous solution (9.3 ml, 0.192 g ml^{-1}) were used, and $t = 30$ min, and $V = 5.0$ ml. Yield, 219 mg (79%). ^{1}H NMR (400 MHz, DMSO-d_6, 22 °C): δ 5.76 (m, ca. 243H, O(2)H and O(3)H of CD), 4.88 (d, ca. 122H, H(1) of CD), 4.53 (t, ca. 122H, O(6)H of CD), 3.98 (m, ca. 23H, *e* and *i′* of PCL–PTHF–PCL), 3.52–3.62 (m, ca. 486H, H(3), H(6), and H(5) of CD), 3.27–3.39 (m, ca. 310H, *f*, *f′*, *i*, and *e′* of PCL–PTHF–PCL, and H(2) and H(4) of CD), 2.27 (m, ca. 23H, *a* and *a′* of PCL–PTHF–PCL), 1.51 (m, ca. 113H, *b*, *b′*, *d*, *d′*, *g*, *g′*, *h*, and *h′* of PCL–PTHF–PCL), 1.28 (m, ca. 23H, *c* and *c′* of PCL–PTHF–PCL). IR (KBr, cm^{-1}): 3367 (vs, br, −OH), 2929 (s, C−H), 1733 (C=O), 1158 (vs, C−O), 1180 (vs), 1028 (vs), 755, 703, 576. Anal. Calcd for $C_{134}H_{248}O_{40}$·15.2$C_{48}H_{80}O_{40}$·46H_2O: C, 45.01; H, 6.81. Found: C, 45.41; H, 7.43.

For comparison, ICs of PEG with α-CD and PPG with β-CD and γ-CD were prepared according to previous reports [4,12].

2.3. Measurements and characterization

The ^{1}H NMR spectra were recorded on a Bruker AV-400 NMR spectrometer at 400 MHz at room temperature. The ^{1}H NMR measurements were carried out with an acquisition time of 3.2 s, a pulse repetition time of 2.0 s, a 30° pulse width, 5208-Hz spectral width, and 32K data points. Chemical shifts were referred to the solvent peaks ($\delta = 7.30$ and 2.50 ppm for $CDCl_3$ and DMSO-d_6, respectively). The ^{13}C NMR spectra were recorded on a Bruker AV-400 NMR spectrometer at 100 MHz at room temperature. The ^{13}C NMR measurements were carried out using composite pulse decoupling with an acquisition time of 0.82 s, a pulse repetition time of 5.0 s, a 30° pulse width, 20,080-Hz spectral width, and 32K data points. Chemical shifts were referred to the solvent peaks ($\delta = 77.16$ ppm for $CDCl_3$). The solid-state ^{13}C CP/MAS NMR spectra were measured on a Bruker AV-400 NMR spectrometer at 100 MHz with a sample spinning rate of 5000 Hz at room temperature. CP spectra were acquired with a 4-ms proton 90° pulse, a 1-ms contact time, and a 5-s repetition time. Chemical shifts were referred to external standard adamantane.

XRD measurements were carried out using a Simens D5005 diffractometer using Ni-filtered Cu Kα (1.542 Å) radiation (40 kV, 40 mA). Powder samples were mounted on a sample holder and scanned from 5 to 35° in 2θ at a speed of 0.6°/min.

DSC measurements were performed using a TA Instruments 2920 differential scanning calorimeter equipped with an auto-cool accessory and calibrated using indium. The following protocol was used for each sample: quenching the sample from room temperature to −160 °C, then heating from −160 to 200 °C at 20 °C min^{-1}. Data were collected during the heating run. Transition temperatures were taken as peak maxima. TGA was made using a TA Instruments SDT 2960. Samples were heated at 20 °C min^{-1} from room temperature to 800 °C in a dynamic nitrogen atmosphere (flow rate = 70 ml min^{-1}).

FTIR spectra were recorded on a Bio-Rad 165 FTIR spectrophotometer; 64 scans were signal-averaged with a resolution of 2 cm^{-1} at room temperature. Samples were prepared by dispersing the complexes in KBr and compressing the mixtures to form disks.

GPC analysis was carried out with a Shimadzu SCL-10A and LC-8A system equipped with two Phenogel 5μ 50 and 1000 Å columns (size: 300 × 4.6 mm^2) in series and a refractive detector. THF was used as eluent at a flow rate of 0.30 ml min^{-1} at 40 °C. Monodispersed poly(ethylene glycol) standards were used to obtain a calibration curve.

3. Results and discussion

3.1. Structure of PCL–PTHF–PCL triblock copolymer

The molecular characteristics of the PCL–PTHF–PCL triblock copolymer sample were actually determined by using GPC and ^{1}H NMR. The M_w, M_n, and the molecular weight polydispersity found by GPC are 2980, 2450, and 1.21, respectively. Fig. 1 shows the ^{1}H NMR spectrum of the PCL–PTHF–PCL triblock copolymer, together with its chemical structure and the fine structures of the respective PCL and PTHF blocks. The assignments of the ^{1}H NMR spectrum are also shown in Fig. 1, which confirms the structure and chain architecture of the PCL–PTHF–PCL

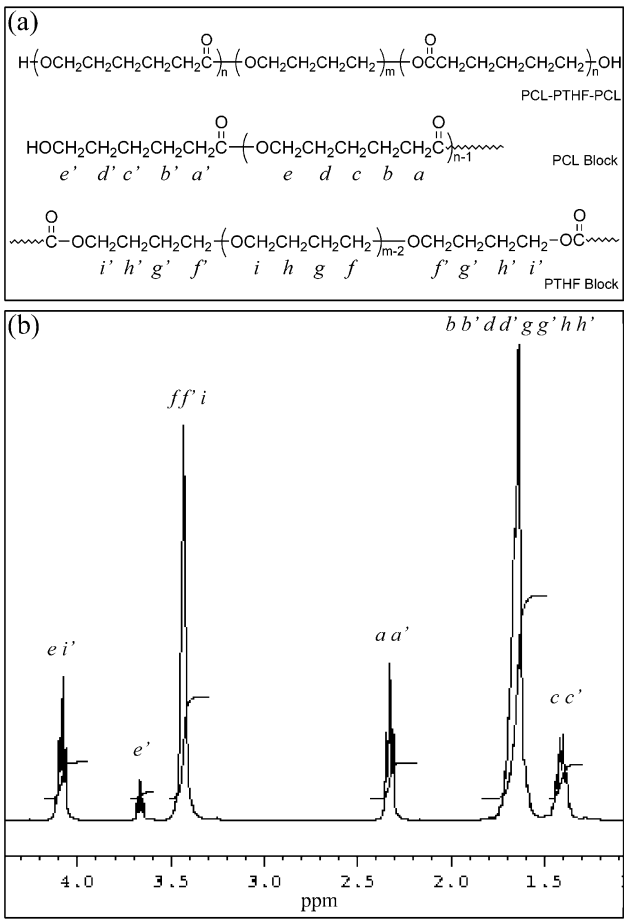

Fig. 1. (a) The structure of the PCL–PTHF–PCL triblock copolymer and the fine structures of the PCL and PTHF blocks. (b) The 400-MHz ^{1}H NMR spectrum of the PCL–PTHF–PCL triblock copolymer in $CDCl_3$. The molecular weight and block lengths determined by the ^{1}H NMR spectrum are as follows: $M_n = 2500$, $2n = 11.4$, $m = 16.8$.

triblock copolymer. From the integral intensities of the peaks, the composition and each block length of the block copolymer can be calculated, and the results are as follows: $M_n = 2500$, $2n = 11.4$, $m = 16.8$. The results obtained from the ^{1}H NMR spectrum are in good agreement with those from GPC.

3.2. IC formation

When testing the IC formation between CDs and the PCL–PTHF–PCL triblock copolymer, we found that the copolymer formed ICs with α-CD as well as β- and γ-CDs to give crystalline ICs in very high yields (65–79%). The formation of the ICs between the PCL–PTHF–PCL triblock copolymer and CDs is of special interest because there were very few cases that a polymer could form ICs with all three types of CDs [5–36].

3.3. XRD studies

The formation of the CD–PCL–PTHF–PCL ICs was strongly supported by XRD studies. Fig. 2 shows the XRD patterns of the three CD–PCL–PTHF–PCL ICs in comparison with the pure PCL–PTHF–PCL triblock copolymer, and ICs of CDs with other polymers or small molecules. In Fig. 2(a), from top to bottom are shown the XRD patterns of the pure PCL–PTHF–PCL copolymer, free α-CD, the α-CD–propionic acid IC, the α-CD–PEG ($M_n = 1000$) IC, and the α-CD–PCL–PTHF–PCL IC. The pattern of the α-CD–propionic acid IC represents a cage-type structure of α-CD ICs [37,38], while the pattern of the

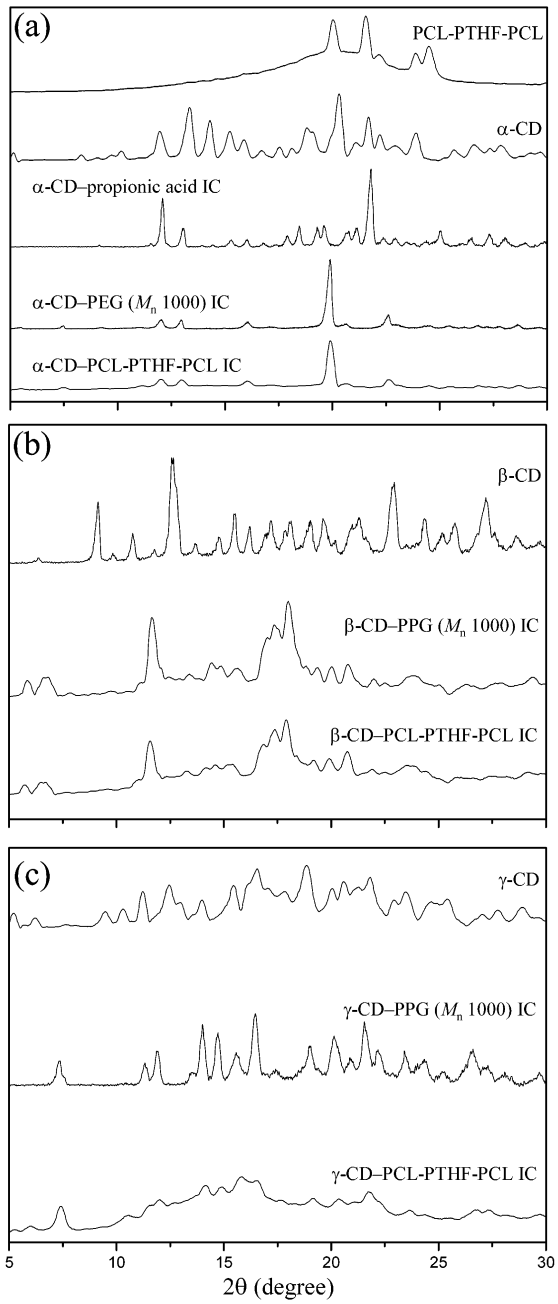

Fig. 2. XRD patterns of (a) α-CD–PCL–PTHF–PCL IC, (b) β-CD–PCL–PTHF–PCL IC, and (c) γ-CD–PCL–PTHF–PCL IC in comparison with the pure PCL–PTHF–PCL triblock copolymer, and ICs of other polymers or small molecules with α-CD, β-CD, or γ-CD.

α-CD–PEG IC with a number of sharp reflections and the main one at $2\theta = 19.4°$ ($d = 4.57$ Å) represents the channel-type structure of crystalline necklace-like ICs of α-CD and PEG [4]. The pattern of the α-CD–PCL–PTHF–PCL IC is similar to that of the α-CD–PEG IC, but totally different from those of the pure PCL–PTHF–PCL copolymer, free α-CD, and the α-CD–propionic acid IC, suggesting that the α-CD–PCL–PTHF–PCL IC is isomorphous with the channel-type structure formed by the α-CD–PEG IC, which is a typical structure of ICs formed by multi α-CD molecules threaded on a polymer chain.

In Fig. 2(b), the XRD pattern of the β-CD–PCL–PTHF–PCL IC is compared with those of free β-CD and the β-CD–PPG ($M_n = 1000$) IC. The pattern of β-CD–PPG IC is different from that of β-CD where the β-CD molecules take a cage-type structure [39]. The β-CD–PPG IC has been previously proven to take a channel-type structure [12]. The pattern of the β-CD–PCL–PTHF–PCL IC is similar to that of the β-CD–PPG IC. Therefore, the β-CD–PCL–PTHF–PCL IC can be also considered to take a channel-type crystalline structure, in which the PCL–PTHF–PCL copolymer chain is included by β-CD molecules.

In Fig. 2(c), the XRD pattern of the γ-CD–PCL–PTHF–PCL IC is compared with those of free γ-CD and the γ-CD–PPG ($M_n = 1000$) IC. Similar to the observation with β-CD, the pattern for the γ-CD–PCL–PTHF–PCL IC resembles that of the IC formed by γ-CD and PPG ($M_n = 1000$), i.e. the γ-CD–PPG IC, which is known to display a channel-type structure [12], and differs from that of γ-CD, a cage-type structure [39]. Although the pattern for the γ-CD–PCL–PTHF–PCL IC is less resolved than that of the γ-CD–PPG IC, the characteristic peak at 7.5° is clearly observed, which is the key feature serving as a fingerprint for the channel-type structure of ICs formed between γ-CD and polymers [17,18,31]. The less resolved pattern implies that the γ-CD–PCL–PTHF–PCL IC has lower crystallinity than the γ-CD–PPG IC, which may be because the PCL–PTHF–PCL is included by γ-CD in a double-stranded mode, while the bulkier PPG chain is included by γ-CD in a single strand [12].

3.4. Solid-state NMR studies

The formation of ICs between the PCL–PTHF–PCL copolymer and CDs was also supported by the solid-state NMR studies. Fig. 3 shows the ^{13}C CP/MAS NMR spectra of the CD–PCL–PTHF–PCL ICs in comparison with the free α-CD, β-CD, and γ-CD, respectively. The spectrum of α-CD in the uncomplexed state shows multiple resolved resonances for C_1 and C_4. Especially, resonances for C_1 and C_4 adjacent to a single conformationally strained glycosidic linkage are observed in the spectrum (shown by arrows) [40,41]. The results indicate that the α-CD assumes a less symmetrical conformation in the crystalline uncomplexed state. In contrast, for the α-CD–PCL–PTHF–PCL IC, all C_1–C_6 of α-CD shows a single unresolved resonance,

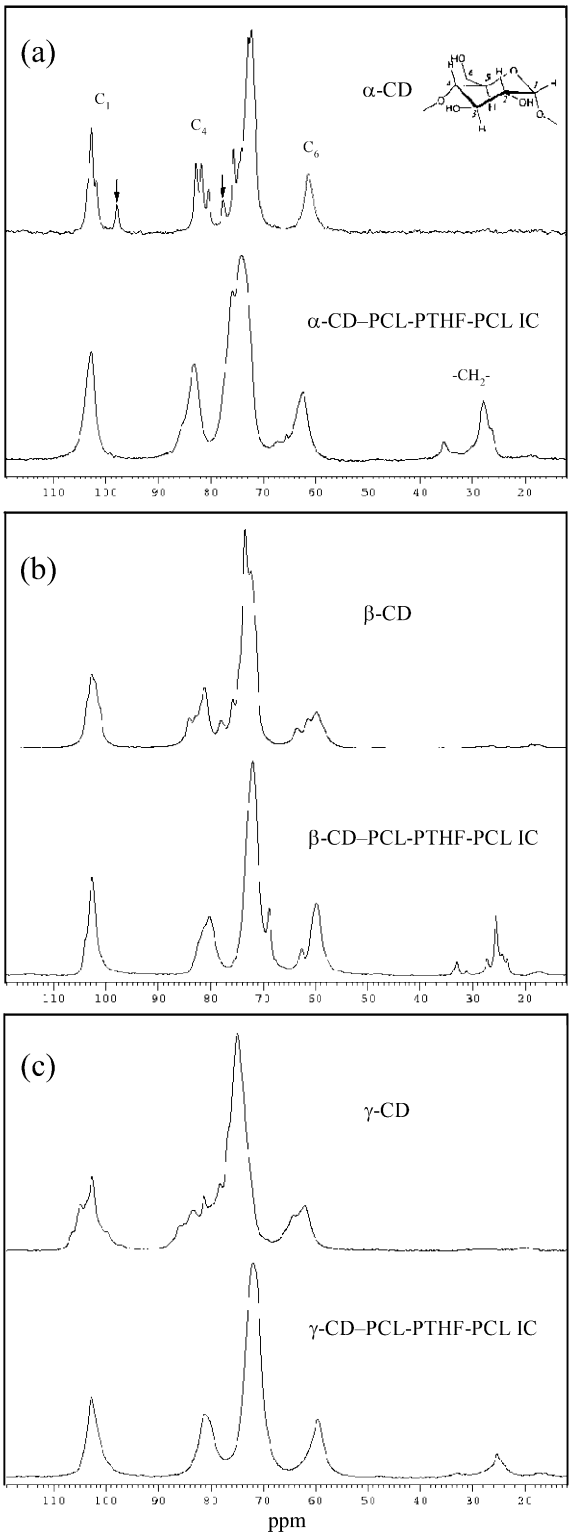

Fig. 3. ^{13}C CP/MAS NMR spectra of (a) α-CD(PCL–PTHF–PCL IC, (b) β-CD–PCL–PTHF–PCL IC, and (c) γ-CD–PCL–PTHF–PCL IC in comparison with free α-CD, β-CD, and γ-CD, respectively. The arrows show the resolved resonances for C_1 and C_4 adjacent to a single conformationally strained glycosidic linkage in free α-CD.

indicating that α-CD adopts a more symmetric conformation and each glucose unit of α-CD is in a similar environment in the IC. Similar results, which are believed to support the formation of ICs between CDs and polymers, have been previously observed in the solid state ^{13}C CP/MAS NMR spectra of various crystalline ICs [5–22].

Similar to the case of the α-CD–PCL–PTHF–PCL IC, the ^{13}C CP/MAS NMR spectra of β-CD–PCL–PTHF–PCL and γ-CD–PCL–PTHF–PCL ICs also show less resolved resonance for all C_1–C_6 of each glucose unit of β-CD or γ-CD, than those in the free β-CD or γ-CD, respectively. The results further support that the ICs are formed between the PCL–PTHF–PCL copolymer and β-CD or γ-CD.

In addition, the resonances for the PCL–PTHF–PCL triblock copolymer are also clearly observed in the spectra of the CD–PCL–PTHF–PCL ICs, at 20–40 ppm for methylene carbons, and at 170–180 ppm for carbonyl carbons (data not shown in the figure), while those for the methylene oxide carbons are found to overlap with those of the CD carbons at the region of 65–80 ppm. The results strongly suggest the existence of the PCL–PTHF–PCL triblock copolymer in the ICs.

3.5. ^1H NMR studies and stoichiometry

The compositions of the CD–PCL–PTHF–PCL ICs were quantitatively studied using ^1H NMR spectroscopy. Fig. 4 shows the ^1H NMR spectra of the PCL–PTHF–PCL triblock copolymer, α-CD, and the ICs of the PCL–PTHF–PCL copolymer with α-, β-, and γ-CDs in DMSO-d_6. A comparison between the integral intensities of peaks for CDs and those for the PCL–PTHF–PCL copolymer gives the compositions and CD contents of the CD–PCL–PTHF–PCL ICs. The numbers (x) of CD in a single IC supramolecule and the CD contents of the ICs are listed in Table 1. The compositions determined from ^1H NMR spectroscopy were also found to be in good agreement with the elemental analysis results.

As shown in Table 1, the number of CD molecules per PCL–PTHF–PCL copolymer chain is 10.1 and 14.4 for the α- and β-CD–PCL–PTHF–PCL ICs, respectively. The

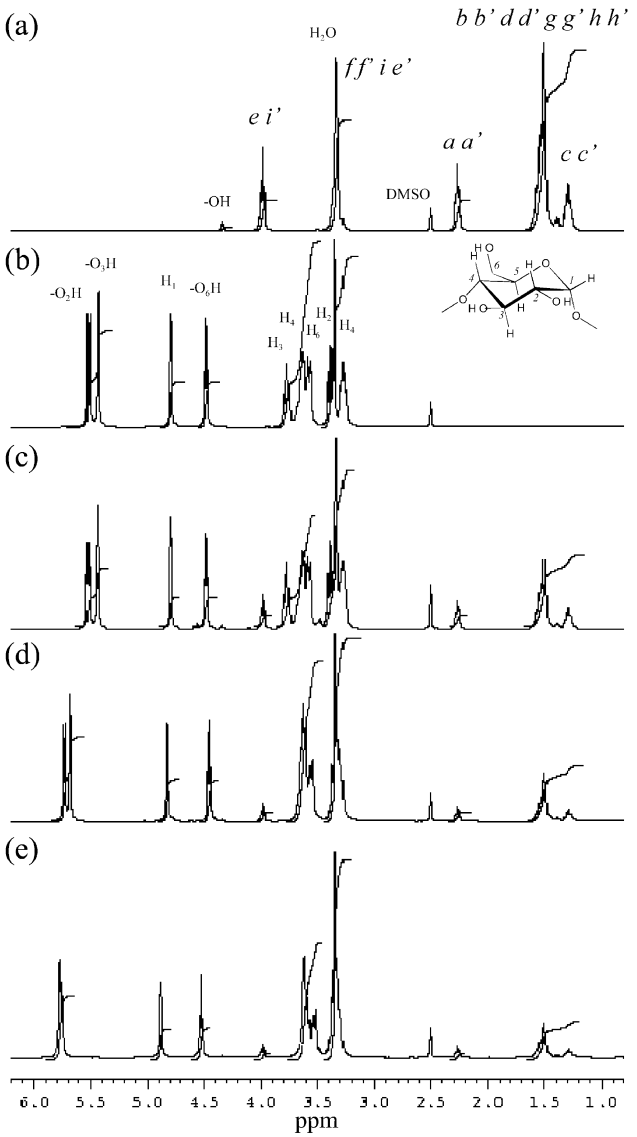

Fig. 4. The 400-MHz ^1H NMR spectra of (a) PCL–PTHF–PCL triblock copolymer, (b) α-CD, (c) α-CD–PCL–PTHF–PCL IC, (d) β-CD–PCL–PTHF–PCL IC, and (e) γ-CD–PCL–PTHF–PCL IC in DMSO-d_6. The proton assignments of PCL–PTHF–PCL copolymer are shown in Fig. 1(a).

Table 1
Compositions of the CD–PCL–PTHF–PCL ICs and the CD contents estimated from ^1H NMR and TGA, and the decomposition temperatures (T_d) of the ICs in comparison with their free components

Inclusion complex	x[c]	CD content (wt%)		$T_{d(free)}$[a] (°C)		$T_{d(IC)}$[b] (°C)	
		^1H NMR	TGA	CD	PCL–PTHF–PCL	CD	PCL–PTHF–PCL
α-CD–PCL–PTHF–PCL	10.1	83	72	320	364	338	388
β-CD–PCL–PTHF–PCL	14.4	89	78	336	358	332	392
γ-CD–PCL–PTHF–PCL	15.2	91	77	319	360	326	386

Temperatures at which 10% of mass loss has occurred from TGA curves.
[a] T_d for free CD and free PCL–PTHF–PCL triblock copolymer.
[b] T_d for each component in the ICs.
[c] The number of CD molecules in a single IC supramolecule determined by ^1H NMR.

total M_n of the PCL–PTHF–PCL copolymer is 2500, while the respective block length are $2n = 11.4$ and $m = 16.8$. If the whole PCL–PTHF–PCL copolymer chain is fully included and covered by α- or β-CD molecules in single strand where the polymer chain is fully extended, similar to the case of the α-CD–PEG ICs [4], there would be about 28 α- or β-CD molecules in the α- or β-CD–PCL–PTHF–PCL ICs.

As for α-CD–PCL–PTHF–PCL IC, there may be a few possible structures since the number of CD cannot closely and fully cover the whole polymer chain of the triblock copolymer: (1) only the two flanking PCL blocks are included and covered by α-CD; (2) only the middle PTHF block is included and covered by α-CD; and (3) the polymer chain is sparsely cover by α-CD. Considering the triblock chain architecture and the facts that the polymer chain is threaded from two ends and the IC is crystalline, it is thought that most likely only the two flanking PCL blocks are included and covered by α-CD, where the PCL blocks are closely covered by α-CD to form crystalline IC domains.

When we studied the IC formation between PEG and CDs, the β-CD with a larger cavity could not form IC with PEG because the PEG chain is too thin to fill into the β-CD cavity [4]. However, we found the β-CD–PCL–PTHF–PCL IC was formed in high yield, although the PCL–PTHF–PCL copolymer chain has similar cross-sectional area to PEG. Considering the size correlation between the cavity of β-CD and the cross-sectional area of PCL–PTHF–PCL copolymer in extended structure, there may be little possibility that β-CD covers an extended chain of PCL–PTHF–PCL copolymer. Therefore, we propose that the larger channel formed by β-CD may be filled by a slightly contracted PCL–PTHF–PCL chain, since there are only 14 β-CD involved in the β-CD–PCL–PTHF–PCL IC. In a previous study on IC formation between PCL–PPG–PCL triblock copolymer and CDs [31], only α- and γ-CDs were found to form ICs with the PCL–PPG–PCL copolymer. Therefore, the PTHF block may play an important role in the formation of the β-CD–PCL–PTHF–PCL IC. This implies that the PTHF block must be involved in the IC formation and is favorably included by β-CD. This can be understood from the fact that pure PTHF polymer tends to form stable IC with β-CD. It is interesting that a 'slight' difference in block structure may lead to quite different character of a block copolymer in IC formation with CDs.

As for the γ-CD–PCL–PTHF–PCL IC, the number of CD molecules per PCL–PTHF–PCL copolymer chain is 15.2 as shown in Table 1. Since the γ-CD channel can include double strands of polymer chains such as PEG [11], if two PCL–PTHF–PCL triblock copolymer chains are fully included and covered by γ-CD molecules, there would be about 28 γ-CD molecules in the IC. The number of γ-CD molecules per PCL–PTHF–PCL copolymer chain is 15.2 (Table 1). In other words, the number of γ-CD molecules per two PCL–PTHF–PCL copolymer chains is about 30. Therefore, it is thought that the whole double strands of the two PCL–PTHF–PCL copolymer chains are included and covered by γ-CD, where the two polymer chains take a extended structure similar to that of PEG in the γ-CD–PEG IC as reported previously [11]. Although there may be possibility that γ-CD sparsely covers a single PCL–PTHF–PCL chain, it is unlikely because of the big difference in size between the cavity of γ-CD and the polymer chain. Another evidence for the double-stranded mode of the γ-CD–PCL–PTHF–PCL IC is that the IC has lower crystallinity, which is similar to the case of the double-stranded γ-CD–PEG IC [11], while the single-stranded γ-CD-PPG IC has very high crystallinity (Fig. 2(c)) [12].

3.6. DSC studies

Our hypothesis regarding the inclusion modes of the CD–PCL–PTHF–PCL ICs was further supported by the DSC studies of the ICs. The DSC curves of pure PCL–PTHF–PCL copolymer and its ICs with α-, β-, and γ-CDs are shown in Fig. 5. As shown in Fig. 5(a), there are two partially overlapped endothermic peaks at 16 and 26 °C in the DSC curve of pure PCL–PTHF–PCL copolymer, corresponding to crystal fusion of the triblock copolymer. Both PCL and PTHF homopolymers with similar chain lengths to those in the triblock copolymer have melting temperatures at the similar temperature range, so it is hard to identify which peak corresponds to which block, or the two peaks are due to a melting–recrystallization phenomenon. It should be noted that pure α-CD does not show any thermal transitions during the course of heating. The stoichiometric α-CD–PEG and β-CD–PPG ICs studied previously also present no thermal transitions before decomposition because every single polymer chain is closely included in the channels formed by CDs in those ICs [4,12]. Upon formation of ICs, the endothermic peaks are largely

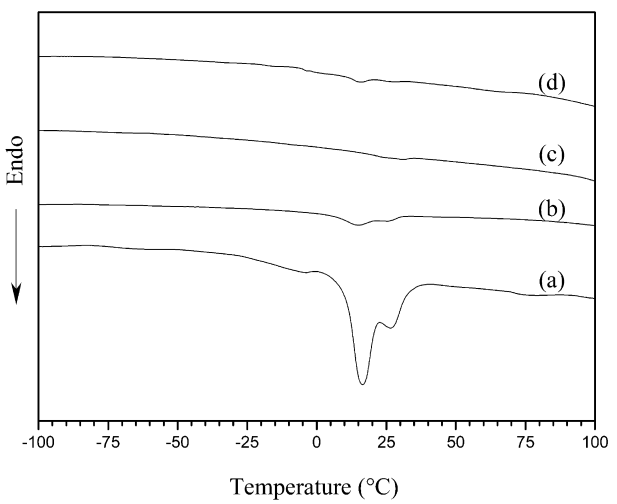

Fig. 5. DSC thermograms (first heating run at 20 °C min^{-1}) for: (a) the PCL–PTHF–PCL triblock copolymers; (b) α-CD–PCL–PTHF–PCL IC; (c) β-CD–PCL–PTHF–PCL IC; and (d) γ-CD–PCL–PTHF–PCL IC.

compressed in the thermogram of the α-CD–PCL–PTHF–PCL IC, while they are almost absent in the thermograms of β- and γ-CD–PCL–PTHF–PCL ICs. This is in accordance with our hypothesis that the PTHF block is free of inclusion in the α-CD–PCL–PTHF–PCL IC, which can still form some crystalline phase of PTHF, while both PCL and PTHF blocks are fully included and covered by CD molecules in the β- and γ-CD–PCL–PTHF–PCL ICs.

3.7. Thermal stability

The thermal stability of the CD–PCL–PTHF–PCL ICs was evaluated using TGA and compared with their CD precursors and the pure PCL–PTHF–PCL copolymer. Fig. 6 shows the weight loss curves of the ICs and their precursors upon heating up to 600 °C. The ICs undergo two-step thermal degradation. The first step can be mainly attributed to decomposition of CD, while the second one mainly to the PCL–PTHF–PCL copolymer. Although the ICs and free CD start to decompose at similar temperatures ranging from 290 to 300 °C, the course of weight loss for the complexed CD is obviously slower than free CD, particularly in the cases of α- and γ-CD–PCL–PTHF–PCL ICs. We use the temperature at which 10% of mass loss has occurred after a certain component starting decomposition as the decomposition temperature (T_d) to quantitatively evaluate the thermal stability [42], and the results for all three ICs are listed in Table 1. The T_d values for the PCL–PTHF–PCL copolymer in the ICs increased by 13–19 °C, as compared with the free copolymer. Therefore, the PCL–PTHF–PCL triblock copolymers was stabilized by the formation of the ICs. In addition, the two-step weight loss behavior can be used to estimate the ratio between CD and the copolymers in the ICs [28]. Although the TGA method may not be as accurate as the ^{1}H NMR due to the partially overlapping of the two weight loss steps, the CD contents estimated from the TGA results are in quite good agreement with those determined by ^{1}H NMR spectroscopy, as shown in Table 1.

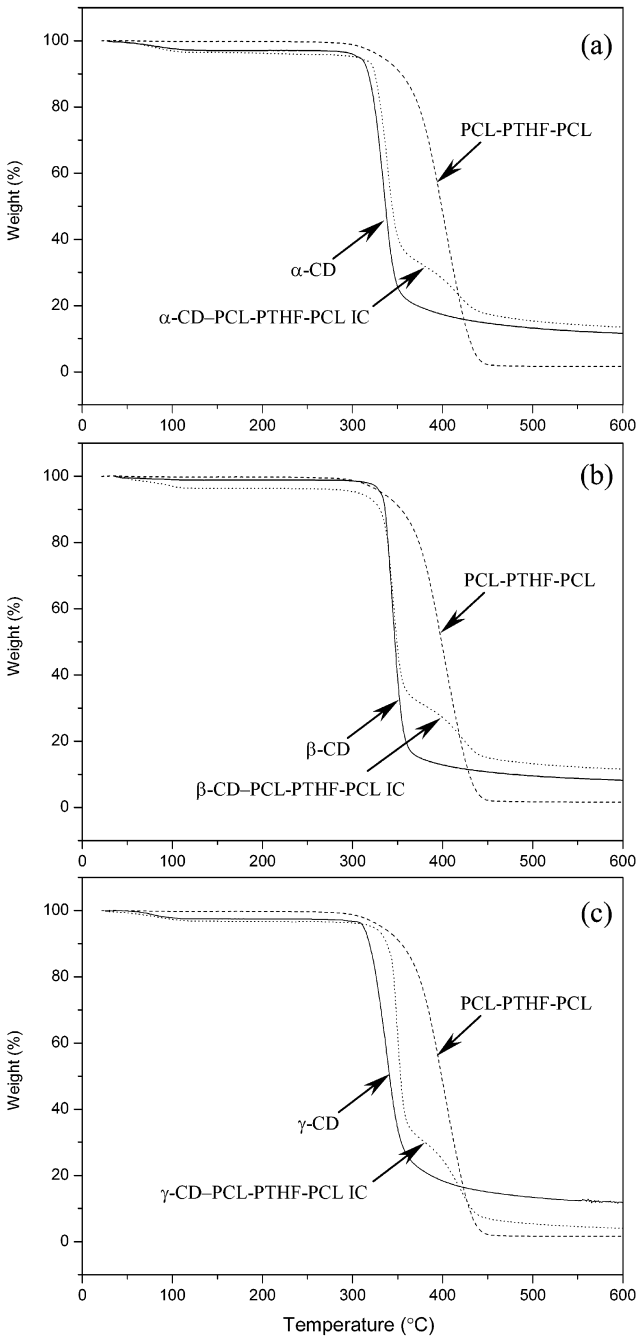

Fig. 6. TGA curves of (a) α-CD–PCL–PTHF–PCL IC, (b) β-CD–PCL–PTHF–PCL IC, and (c) γ-CD–PCL–PTHF–PCL IC in comparison with the pure PCL–PTHF–PCL triblock copolymer, and the free α-CD, β-CD, or γ-CD, respectively.

4. Conclusions

Biodegradable PCL–PTHF–PCL triblock copolymer was found to form ICs with all α-CD, β-CD, and γ-CD from aqueous medium in high yields ranging from 65 to 79%. The XRD studies showed that all the CD–PCL–PTHF–PCL ICs assume a channel type structure. The formation of the CD–PCL–PTHF–PCL ICs was also confirmed by solid-state ^{13}C CP/MAS NMR studies. The ^{1}H NMR studies gave the numbers of CD molecules in a single complex supramolecule. From both ^{1}H NMR and DSC results, we propose that only the two flanking PCL blocks are included and covered by α-CD in the α-CD–PCL–PTHF–PCL IC (Fig. 7(a)), while the two PCL blocks as well as the middle PTHF block are included and covered by β-CD in the β-CD–PCL–PTHF–PCL IC, where the PCL–PTHF–PCL copolymer chain takes a contracted structure so as to fit into the larger space of the channel formed by β-CD (Fig. 7(b)). It is of special interest that the PCL–PTHF–PCL copolymer forms IC with β-CD, since a similar PCL–PPG–PCL copolymer was not found to form IC with β-CD in a previous report [31]. It is also proposed, from our NMR, DSC, and XRD data, and a comparison with the literature, that two PCL–PTHF–PCL copolymer chains are included

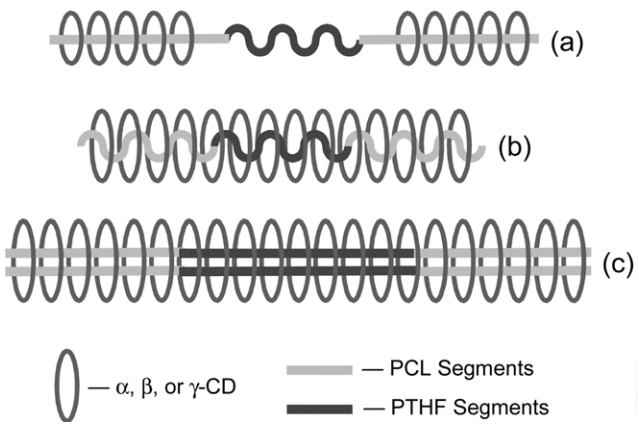

Fig. 7. The proposed structures of (a) the α-CD–PCL–PTHF–PCL IC, (b) the β-CD–PCL–PTHF–PCL IC, and (c) the γ-CD–PCL–PTHF–PCL IC.

and covered by the largest γ-CD in a double-strand mode in the γ-CD–PCL–PTHF–PCL IC (Fig. 7(c)). Finally, the TGA results showed that the PCL–PTHF–PCL triblock copolymer in the ICs has better thermal stability, therefore, the complexation stabilizes the copolymer included in the CD channels.

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