J Incl Phenom Macrocycl Chem (2008) 60:95–101
DOI 10.1007/s10847-007-9357-5

ORIGINAL ARTICLE

Inclusion complexes of cholesteryl-(ε-caprolactone)$_{\overline{10}}$ functionalized polymer with γ-cyclodextrin

Jinbao Guo · Jie Sun · Hui Cao · Huai Yang

Received: 9 April 2007 / Accepted: 25 July 2007 / Published online: 7 September 2007

Abstract An inclusion complex (IC) of γ-cyclodextrin with biodegradable cholesteryl-(ε-caprolactone)$_{\overline{10}}$ (Chol-(CL)$_{\overline{10}}$) functionalized polymer was prepared by using a general method of mixing solution. The formation of γ-CD-Chol-(CL)$_{\overline{10}}$ IC was determined by Fourier transform infrared (FTIR), ^{1}H-NMR, differential scanning calorimetry (DSC), and wide angle X-ray diffraction (WAXD), respectively. The results indicated that the oligo(ε-CL)$_{\overline{10}}$ blocks as well as the end cholesteryl moiety of the functionalized polymer were included and covered by γ-CD in a single-stranded mode in the γ-CD-Chol-(CL)$_{\overline{10}}$ ICs. Moreover, the γ-CD-Chol-(CL)$_{\overline{10}}$ ICs had a channel-type crystalline structure similar to that formed between the poly(propylene glycol) (PPG) and γ-CD. Finally, TGA revealed that the ICs had better thermal stability than their free components due to the inclusion complexation.

Keywords γ-Cyclodextrin · Inclusion complex · Cholesteryl-(ε-caprolactone)$_{\overline{10}}$ · Supramolecular structures · Thermal properties

Introduction

It is widely known that cyclodextrins (CDs) form inclusion complexes with various compounds including a great variety of small or long molecule guests without any covalent bonds [1–3]. CDs are a series of cyclic oligosaccharides, which are composed of six, seven, or eight glucose units connected by α-1,4 acetyl linkages, and called α-, β-, and γ-CD, respectively. They have a hollow truncated cone shape with a hydrophobic inner cavity and a hydrophilic outside surface [4]. CDs are water-soluble just due to hydrophilic outside surface in which much hydroxyl groups locate. However, the most remarkable feature of the CDs is their ability to incorporate guest molecules with appropriate size in their cavity [5, 6]. In general, the complexes have some different physicochemical properties compared to those of the guest molecule itself, for example, the formation of inclusion may improve the solubility and bioavailability of the guest molecule [7]. Since CDs were discovered, a large number of inclusion complexes of CDs with various low molecular weight compounds have been prepared and characterized. Meanwhile, a great number of polymeric inclusion complexes (ICs) based on CDs have been studied [8–15], especially, inclusion complexes (ICs) formed between CDs and biodegradable block copolymers have attracted much attention in recent years because of their potential application as functional biomaterials [16, 17].

In recent years, functionalized biodegradable polymers by cholesterol moiety have received a great deal of attention as the scaffold materials for drug release and tissue engineering. The cholesterol moiety was selected in the molecular design of these systems because of its high thermodynamic affinity for the cell membrane and its ability to change the membrane's permeability and fluidity [18–22]. Cholesteryl-oligo(L-lactic acid)$_{\bar{n}}$ obviously promoted cell adhesion and proliferation compared with poly(L-lactic acid), which described in detail by Stupp's group [18, 22]. There have been many other reports of functionalized polymer by cholesteryl moiety, for example, cholesteryl end-capped polycarbonates and poly(ε-CL) by a

J. Guo · J. Sun · H. Cao · H. Yang (✉)
Department of Materials Physics and Chemistry, School of Materials Science and Engineering, University of Science and Technology Beijing, Beijing 100083, P.R. China
e-mail: yanghuai@mater.ustb.edu.cn

cholesteryl moiety as drug release carrier reported by Chen et al. [19–21]. But the poor hydrophilicity of this kind of material may limit their use in many aspects. In the biomedical field, various methods have been developed to increase the solubility of the chain in water, which include incorporation hydrophilic chain into the polymer and formation complex with CD and their derivatives [7, 22].

In our investigation, we first studied the IC between the functionalized polyesters by cholesteryl moiety and γ-CD, the polymers selected for guest molecule of IC is Chol-$(CL)_{\overline{10}}$, a low molecular weight cholesteryl-$(\varepsilon\text{-CL})_{\overline{10}}$ functionalized polymer. We anticipate the hydrophilicity of functionalized polymer by inclusion can be improved. On the other hand, there exists block-selective molecular recognition and results in special block structure. Here we focused on describing the preparation and characterization of inclusion complexes of γ-CD with Chol-$(CL)_{\overline{10}}$ and the formation of the complexes was discussed in detail.

Experimental

Materials

γ-CD were purchased from Aldrich and then dried in vacuo for 24 h at 100 °C. Cholesterol (Beijing Chemical Reagent Ltd, China) was purified by recrystallization from ethanol. ε-Caprolactone (CL, Aldrich) and toluene were distilled from CaH_2, respectively. Stannous octanoate $(Sn(Oct)_2$, Aldrich) was purified by distillation under reduced pressure and then dissolved in dry toluene prior to use. The other reagents and solvents were local commercial products and used without further purification.

Preparation of Chol-$(CL)_{\overline{10}}$ functionalized polymer

The synthesis of cholesteryl-$(\varepsilon\text{-CL})_{\overline{n}}$ functionalized polymer followed the route described by a previous paper [21]. Here, to synthesize the Chol-$(CL)_{\overline{10}}$, the cholesterol (3.86 g, 0.01 mol), ε-CL (11.4 g, 0.10 mol) and stannous octoate (17 μL, 0.05 mmol) were added into well-dried three-neck flask with a magnetic stirring bar. The reaction mixtures were stirred at 140 °C for 8 h. After the polymerization, the product was dissolved in tetrahydrofuran (THF) and precipitated in methanol. The precipitated polymer was then isolated by filtration and dried under vacuum for 24 h. For Chol-$(CL)_{\overline{10}}$, ^{1}H-NMR ($CDCl_3$): δ 0.67, 0.85, 0.87, 0.98 (–*CH*$_3$– of cholesteryl moiety), 5.34 (–*CH*=C– of cholesteryl moiety), 4.58 (–*CH*OCO– of cholesteryl moiety), 1.38 (–CH_2CH_2*CH*$_2$$CH_2CH_2$– of PCL), 1.65 (–$CH_2$*CH*$_2$$CH_2$*CH*$_2$$CH_2$– of PCL), 2.30 (–CO*CH*$_2$– of PCL), 4.05 (–*CH*$_2$OCO– of PCL), 3.64 (–*CH*$_2$OH– of PCL).

Preparation of ICs

The IC of Chol-$(CL)_{\overline{10}}$ with γ-CD was prepared as follows. Chol-$(CL)_{\overline{10}}$ functionalized polymer 0.5 g was dissolved in 30 mL of acetone and γ-CD 11.6 g was dissolved in 50 mL of distilled water. Then the Chol-$(CL)_{\overline{10}}$ solution was added dropwise to the γ-CD solution at 60 °C with vigorous stirring. After stirring at 60 °C for 3 h, the mixture was cooled to room temperature while continuously stirring overnight. The precipitated products were collected by filtration, twice washed with acetone (25 mL) to remove free polymers (stirred with a magnetic stirring bar at room temperature for 0.5 h), and then twice washed with distilled water (45 mL) to remove uncomplexed γ-CD. The white powder was then dried overnight in vacuo at 45 °C until a constant weight was obtained. The yield (wt.%) for ICs was 80%. γ-CD-Chol-$(CL)_{\overline{10}}$ IC, ^{1}H-NMR (DMSO-d_6): δ 5.73 (16H, O(7) and O(8) of γ-CD), 4.86 (8H, C(1)H of γ-CD), 4.50–4.46 (8H, O(9) of γ-CD), 3.96 (2H, –CH_2–O– of PCL), 3.60–3.50 (48H, C(5), C(6), C(3), C(2) and C(4) of γ-CD), 2.25 (2H, –C(=O)–CH_2– of PCL), 1.53–1.51 (4H, –*CH*$_2$–CH_2–*CH*$_2$–CH_2–O– of PCL), 1.21 (2H, –*CH*$_2$–CH_2–CH_2–O– of PCL), 1-0 (–*CH*$_2$– of cholesteryl moiety).

Preparation of the physical blend of Chol-$(CL)_{\overline{10}}$ and γ-CD

A physical mixture consisting of Chol-$(CL)_{\overline{10}}$ and γ-CD in the same weight ratio as the contrast complex was prepared. The Chol-$(CL)_{\overline{10}}$ and γ-CD were admixed together in a mortar and pestle for 5 min to obtain a homogeneous blend.

Methods

Molecular weights and molecular weight distributions of the polymer were determined on a Waters HPLC system equipped with a 2690D separation module and a 2410 refractive index detector, THF as the eluent (1.0 mL/min). The differential scanning calorimetry (DSC) analysis was carried out using a Mettler DSC822e instrument under nitrogen flow (50 mL/min). All samples were first heated from 0 to 100 °C at 10 °C/min and held for 2 min to erase the thermal history, then cooled to 0 °C at 10 °C/min. Thermogravimetric analysis (TGA) was performed from room temperature to 600 °C at a heating rate of 10 °C/min under nitrogen flow (20 mL/min), using a PerkinElmer Pyris 1 instrument. Wide angle X-ray diffraction (WAXD) patterns of powder samples were obtained at room temperature on a Rigaku D_{max}-RB X-ray diffractometer with a

Cu-Kα radiation source (wavelength 0.154 nm). The supplied voltage and current were set to 40 kV and 150 mA, respectively. Samples were exposed at a scan rate of $2\theta = 2°/\text{min}^{-1}$ between $2\theta = 5°$ and 40°. Fourier transform infrared (FTIR) spectra were recorded on a Nicolet-510P spectrometer at frequencies ranging from 400 to 4000 cm^{-1}. Samples were thoroughly mixed with KBr and pressed into pellet form. The ^{1}H-NMR experiments was performed at 400.1 MHz, on a Bruker DMX-300 spectrometer. $CDCl_3$ and DMSO-d_6 were used as the deuterated solvents for the polymer and the IC, respectively.

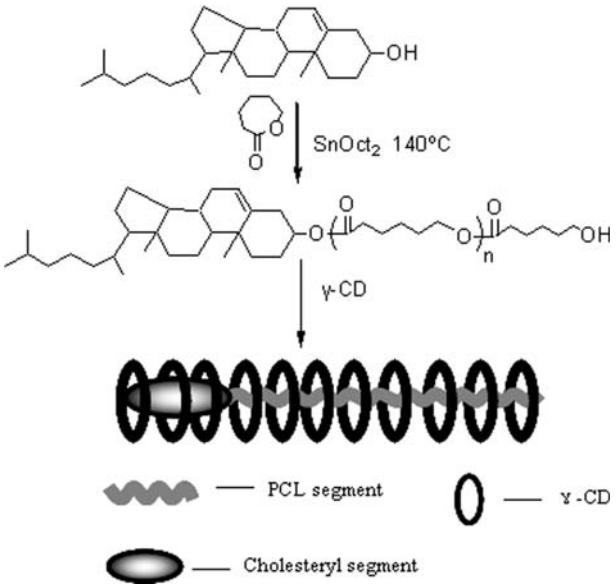
Results and discussion

Structure of Chol-$(CL)_{\overline{10}}$ functionalized polymer

The guest molecule Chol-$(CL)_{\overline{10}}$ was synthesized by the ring-opening polymerization of ε-CL using cholesterol with a hydroxyl group as an initiator. The molecular characteristics of the Chol-$(CL)_{\overline{10}}$ functionalized polymer sample were actually determined by using GPC and ^{1}H-NMR. The Mn and the molecular weight polydispersity found by GPC are 3040 and 1.64, respectively. Figure 1 shows the ^{1}H -NMR spectrum of the Chol-$(CL)_{\overline{10}}$ functionalized polymer, together with its chemical structure and the fine structures of the respective cholesterol and PCL blocks. The assignments of the ^{1}H-NMR spectrum are also shown in Fig. 1. For example, in the spectrum of Chol-$(CL)_{\overline{10}}$, the typical signals of the cholesteryl moiety and CL repeating units can be observed at 0.67, 0.85, 0.87, 0.98 ppm (cholesteryl moiety: $-CH_3$), 5.34 ppm (cholesteryl moiety: $CH = C$), 4.58 ppm (cholesteryl moiety: $-CH$OCO), 1.38 ppm (CL repeating unit: $CH_2CH_2CH_2CH_2CH_2$), 1.65 ppm (CL repeating unit: $-CH_2CH_2CH_2CH_2CH_2-$), 2.30 ppm (CL repeating unit: $-COCH_2$), 4.05 ppm (CL repeating unit: $-CH_2OCO$) and 3.64 ppm (CL repeating unit: $-CH_2OH$). Because the cholesteryl moiety is incorporated to the polymer chain after the polymerization, a new signal appears at 4.58 ppm (cholesteryl moiety: $-CH$OCO) can be found in the spectrum of Chol-$(CL)_{\overline{10}}$. These data confirm the structure and chain architecture of the Chol-$(CL)_{\overline{10}}$.

IC formation

ICs of biodegradable Chol-$(CL)_{\overline{10}}$ functionalized polymer with γ-CD was successfully prepared by mixing a solution of γ-CD with that of the Chol-$(CL)_{\overline{10}}$, followed by rigorous stirring (Scheme 1). Here, we found that the functionalized polymer formed ICs with γ-CD to give crystalline ICs in very high yields ($\approx$80%). The formation of the ICs between the Chol-$(CL)_{\overline{10}}$ functionalized polymer and γ-CD is of special interest because there involve block-selective molecular recognition. On the other hand, the most attractive characteristic of such ICs involves the control of drug release utilizing the dissociation of supramolecular structure.



Scheme 1 Preparation of supramolecular ICs of Chol-$(CL)_{\overline{10}}$ with γ-CD

The formation of the IC was strongly supported by wide angle X-ray diffraction (WAXD) studies. Harata and coworkers reported that the crystal structures of CD complexes are classified mainly into three types: channel, cage, and layer [8]. In Fig. 2, the WAXD pattern of the γ-CD-Chol-$(CL)_{\overline{10}}$ IC is compared with that of free γ-CD. The pattern for the γ-CD-Chol-$(CL)_{\overline{10}}$ IC resembles that of the IC formed by γ-CD and PPG as well as PCL as reported previously, which are known to display a channel type structure as showed in Fig. 3a [13, 17], and differs from that of γ-CD. And the characteristic peak at 7.6° is clearly observed in Fig. 2, which is the key feature serving as a fingerprint for the channel-type structure of ICs formed between γ-CD and polymers [13, 17]. The 7.6° peak characteristic of channel structure γ-CD-IC not present in the diffraction pattern of pure γ-CD, because it adopts a cage structure as shown in Fig. 3b. These results indicate that Chol-$(CL)_{\overline{10}}$ and γ-CD have formed IC with a channel structure in which at least the oligo(ε-CL)$_{\overline{10}}$ blocks of the Chol-$(CL)_{\overline{10}}$ chain are include inside the γ-CD channels. On the other hand, from Fig. 2, it can also be seen that preferable resolved pattern implies that the γ-CD-Chol-$(CL)_{\overline{10}}$ IC has high crystallinity which is very similar to that of γ-CD-PPG IC [17], it may be because the

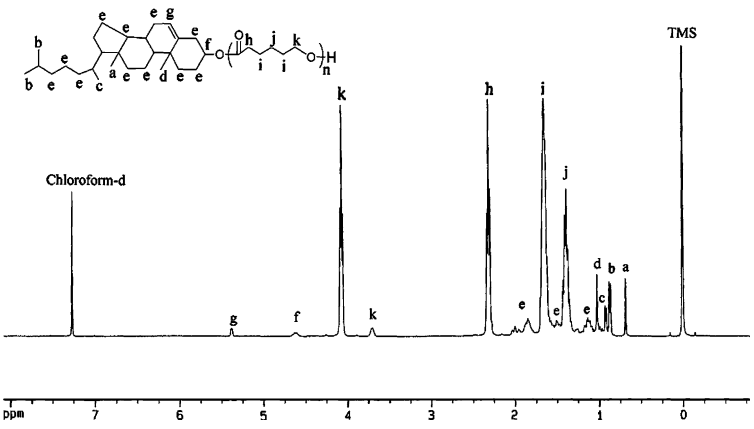


Fig. 1 The 400-MHz ^{1}H-NMR spectrum of the Chol-$(CL)_{\overline{10}}$ functionalized polymer in $CDCl_3$

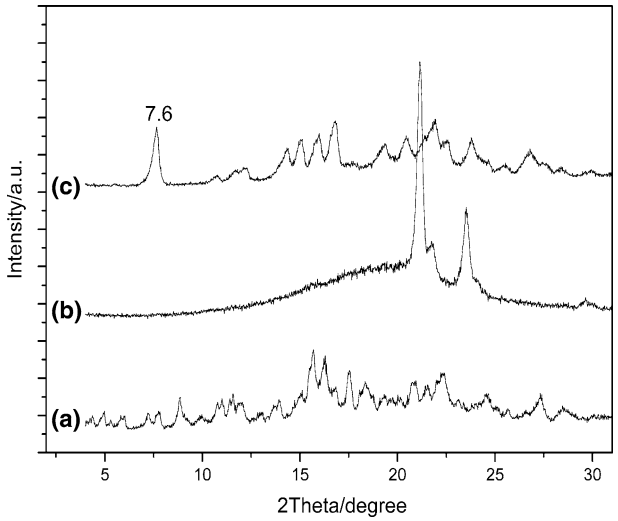


Fig. 2 WAXD thermograms of (a) γ-CD, (b) Chol-$(CL)_{\overline{10}}$, and (c) γ-CD-Chol-$(CL)_{\overline{10}}$ ICs

Chol-$(CL)_{\overline{10}}$ is included by γ-CD in a single-stranded mode, while the bulkier PPG chain is included by γ-CD in a single strand.

The ^{1}H-NMR spectrum of γ-CD-Chol-$(CL)_{\overline{10}}$ IC was given in Fig. 4. It can be clearly seen that both γ-CD and Chol-$(CL)_{\overline{10}}$ functionalized polymer components existed in the IC. It is well known that γ-CD molecules adopt the conformation of a torus in which the H-3 and H-5 protons are located inside the cavity. Some information about the ICs can be obtained with the change of chemical shift of H-3 and H-5 protons [3, 4]. From the Fig. 4, it can be observed that the H-3 and H-5 protons (δ = 3.61 and 3.50 ppm) shifted upfield comparing the original position of H-3 and H-5 protons (δ = 3.65 and 3.56 ppm) in γ-CD in DMSO-d_6. In principle we can guess that ICs formed between Chol-$(CL)_{\overline{10}}$ and γ-CD. In general, by comparing the integral of peak for CD (1H) with that of the oligo(ε-CL)$_{\overline{10}}$ methylene groups, the host–guest stoichiometry of ICs can be calculated by the molar ratio of the monomeric repeating unit of oligo(ε-CL)$_{\overline{10}}$ to CDs [23], herein, it could be calculated that the stoichiometry is approximately 1 (γ-CD:CL) in γ-CD-Chol-$(CL)_{\overline{10}}$ IC. Based on this data, firstly, considering the above WAXD result, we can confirm that the Chol-$(CL)_{\overline{10}}$ is included by γ-CD in a single-stranded mode, although PCL (M_w <

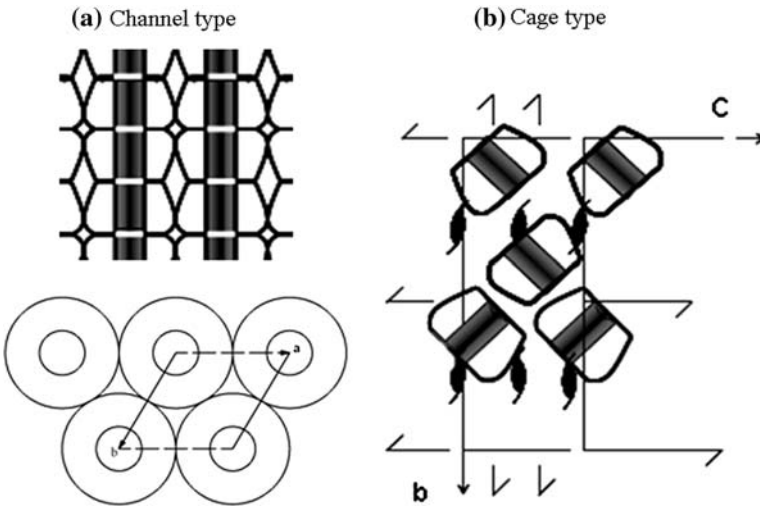


Fig. 3 Schematic description of: (**a**) channel type and (**b**) cage type, crystal structures formed by crystalline CD inclusion complexes

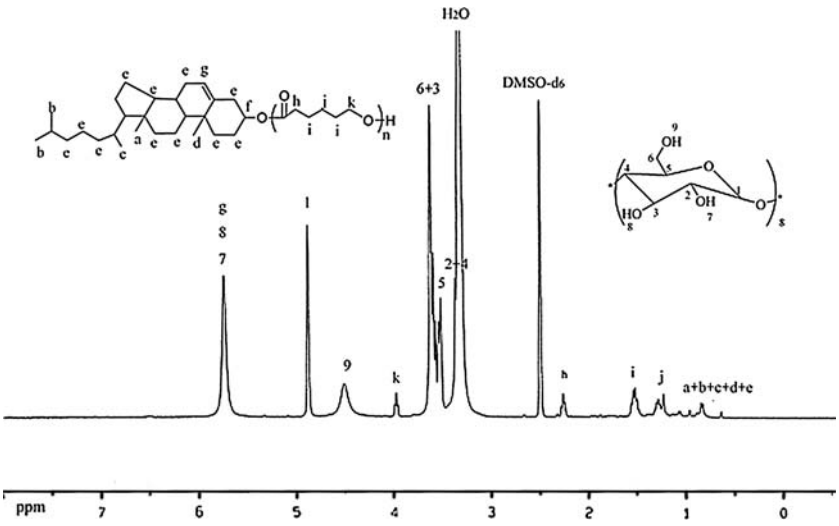


Fig. 4 ^{1}H-NMR spectrum (DMSO-d_6) of γ-CD-Chol-$(CL)_{\overline{10}}$ ICs formed between Chol-$(CL)_{\overline{10}}$ and γ-CD

2000) is covered in the double-stranded mode by γ-CD [13]. Furthermore, it can be concluded that both oligo(ε-CL)$_{\overline{10}}$ blocks and the end cholesteryl moiety of the functionalized polymer are included and covered by γ-CD. If only the PCL blocks are included and covered by γ-CD as showed in Scheme 1, the rate is not equal to 1, this is because that PCL at higher molecular weights ($M_w >$ 2000) cannot form stoichiometric (γ-CD:CL $\approx$ 1) inclusion complexes with γ-CD. It is due to the low dispersibility of PCL at higher molecular weight in aqueous solution [13]. On the other hand, as reported previously [24], cholesterol can form stable inclusion complex (IC) with γ-CD, what's more, the polymer chain is threaded from two ends, cholesteryl moiety is also included inside the γ-CD channels. So we can say the ratio is approximately 1 just due to cholesteryl moiety is included by γ-CD channels.

FT-IR is a very useful tool to verify the presence of both host and guest components in IC crystals and it can also give more information about the formation of ICs, as shown in Fig. 5. The free Chol-$(CL)_{\overline{10}}$ polymer is characterized by distinct carbonyl stretching bands at 1724 cm^{-1} in Fig. 5b. The spectrum of γ-CD shows a broad band at 3385 cm^{-1}due to the symmetric and antisymmetric O–H stretching mode in Fig. 5a. The spectrum of the physical blend shown in Fig. 5c showed no significant differences from the respective spectra of each of the pure components as seen in Figs. 5a and b. However, some significant differences could be seen in the spectrum of the inclusion complex as displayed in Fig. 5d. It can be seen that the C=O band of Chol-$(CL)_{\overline{10}}$ at 1724 cm^{-1} is shifted to higher frequency at 1734 cm^{-1} in γ-CD- Chol-$(CL)_{\overline{10}}$ IC which is the C=O stretching band for amorphous bulk phases of oligo(ε-CL)$_{\overline{10}}$ blocks. Meanwhile the broad O–H band of γ-CD at 3385 cm^{-1} is also up shifted at 3404 cm^{-1}. These further indicate that the ICs of Chol-$(CL)_{\overline{10}}$ with γ-CD successfully formed. Moreover, the characteristic shifts in

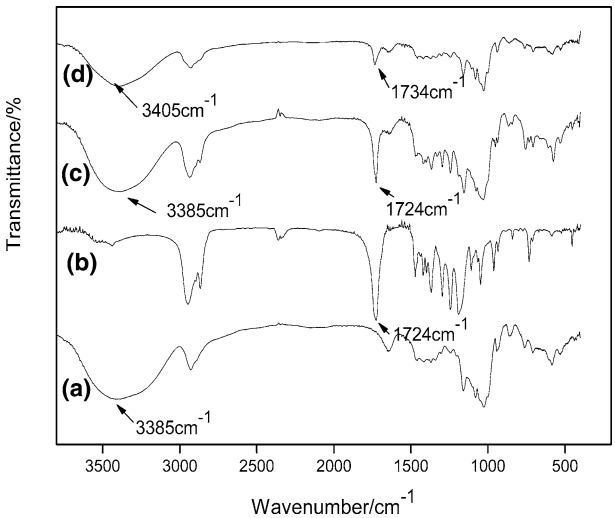


Fig. 5 FT-IR spectra of (a) γ-CD, (b) Chol-$(CL)_{\overline{10}}$, (c) γ-CD and Chol-$(CL)_{\overline{10}}$ physical blend, and (d) γ-CD-Chol-$(CL)_{\overline{10}}$ ICs

ICs are probably due to the formation of hydrogen bonds, which mainly occur between the hydroxyl groups of CDs and the carbonyl groups of oligo(ε-CL)$_{\overline{10}}$ blocks of Chol-$(CL)_{\overline{10}}$ polymer [23].

Thermal properties of ICs

The melting behavior and cold-crystallization behavior of the functionalized polymer and the ICs are shown in Fig. 6. The melting peak and the crystallization peak were observed in the curve of the pure Chol-$(CL)_{\overline{10}}$ functionalized polymer, but no melting peak and crystallization peak were detected for γ-CD and the ICs. This fact confirmed further that no free functionalized polymer existed in γ-CD-Chol-$(CL)_{\overline{10}}$ IC, the crystallization of Chol-$(CL)_{\overline{10}}$ was remarkably suppressed in the γ-CD cavity, and the

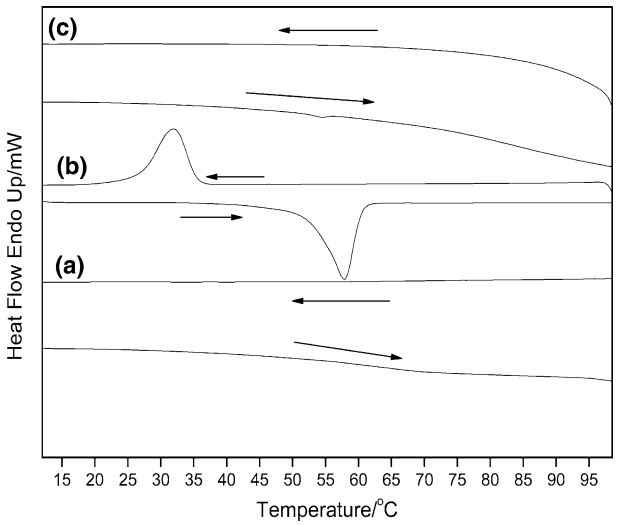


Fig. 6 The heating and cooling DSC curves of (a) γ-CD, (b) Chol-$(CL)_{\overline{10}}$, and (c) γ-CD-Chol-$(CL)_{\overline{10}}$ ICs

original crystalline properties of the functionalized polymer were almost lost.

The thermal properties of γ-CD-Chol-$(CL)_{\overline{10}}$ IC complexes were investigated with TGA. As shown in Fig. 7, the physical blend of γ-CD and Chol-$(CL)_{\overline{10}}$ had two decomposition temperatures which belong to those of pure Chol-$(CL)_{\overline{10}}$ (Fig. 7b) and pure γ-CD (Fig. 7a), respectively in Fig. 7c at the temperature of 250 °C and 296 °C. However, the thermal properties of γ-CD-Chol-$(CL)_{\overline{10}}$ IC is very different from that of physical blend, it presented a two-step thermal degradation (Fig. 7d) which is very similar to that of other polymer ICs [16, 17, 23]. The first step can be mainly attributed to the decomposition of γ-CD, while the second step is mainly that of the guest Chol-$(CL)_{\overline{10}}$ polymer. It further validated the formation of the complex. Additionally, the decomposition temperature for both γ-CD and the guest Chol-$(CL)_{\overline{10}}$ in γ-CD-Chol-$(CL)_{\overline{10}}$ ICs is 320 °C and 361 °C,

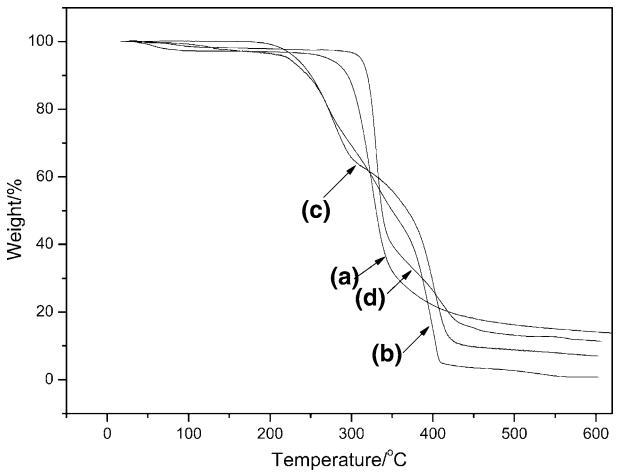


Fig. 7 TGA thermograms of (a) γ-CD, (b) Chol-$(CL)_{\overline{10}}$, (c) Chol-$(CL)_{\overline{10}}$ and γ-CD physical blend, and (d) γ-CD-Chol-$(CL)_{\overline{10}}$ ICs

while both the free γ-CD and the free Chol-$(CL)_{\overline{10}}$ decomposed at the temperature of 296 °C and 250 °C, respectively. After complexation, the initial decomposition of γ-CD-Chol-$(CL)_{\overline{10}}$ IC were higher than those of pure Chol-$(CL)_{\overline{10}}$ and γ-CD, and this indicated that complexation with γ-CD enhanced the thermal stability of the Chol-$(CL)_{\overline{10}}$ and γ-CD.

Conclusions

Supramolecular ICs of biodegradable Chol-$(CL)_{\overline{10}}$ functionalized polymer with γ-CD was successfully prepared by mixing a solution of γ-CD with that of the polymer. The ICs of Chol-$(CL)_{\overline{10}}$ functionalized polymer with γ-CD formed through γ-CD threading onto oligo(ε-CL)$_{\overline{10}}$ block as well as the cholesteryl moiety of functionalized polymer, whose original crystalline properties were completely suppressed in the hydrophobic γ-CD cavities. Moreover, the ICs of Chol-$(CL)_{\overline{10}}$ functionalized polymer with γ-CD had a channel-type crystalline structure similar to that formed between the poly(propylene glycol) (PPG) and γ-CD. Further more, the TGA results showed that the inclusion complexation between the Chol-$(CL)_{\overline{10}}$ functionalized polymer and γ-CD enhanced the thermal stability of the guests.

References

1. Szejtli J.: Cyclodextrin, Their Inclusion Complexes, pp. 95–140. Akademiai Kiado, Budapest, Hungary (1982)
2. Wenz, G., Han, B.H., Müller, A.: Cyclodextrin rotaxanes and polyrotaxanes, Chem. Rev. **106**, 782 (2006)
3. Szejtli, J.: Cyclodextrin Technology, pp. 48–58. Kluwer Academic, Dordrecht, The Netherlands (1988)
4. Bender, M.L., Komiyama, M.: In: Hafner,K., Lehn, J.M., Rees, C.W., Schleyer, P.R., Trost, B.M., Zahradnik, R. (eds.) Cyclodextrin Chemistry, pp. 2–9. Springer, New York (1978)
5. Pedersen, M., Bjerregaard, S., Jacobsen, J., Søensen, A.M.: A genuine clotrimazole γ-cyclodextrin inclusion complex-isolation, antimycotic activity, toxicity and an unusual dissolution rate, Int. J. Pharm. **176**, 121 (1998)
6. Li, S., Purdy, W.C.: Cyclodextrins and their applications in analytical chemistry, Chem. Rev. **92**, 1457 (1992)
7. Wang, B., He, J., Sun, D., Zhang, R., Han, B.X.: Utilization of supercritical carbon dioxide for the preparation of 3-hydroxyflavone and β-cyclodextrin complex, J. Incl. Phenom. Macrocycl. Chem. **55**, 37 (2006)
8. Harada, A., Kamachi, M.: Complex formation between poly (ethy1ene glycol) and α-Cyclodextrin, Macromolecules **23**, 2821 (1990)
9. Harada, A., Li, J., Kamachi, M.: Molecular necklace: A rotaxane containing many threaded α-cyclodextrins, Nature **356**, 325 (1992)
10. Harada, A., Li, J., Kamachi, M.: Synthesis of a tubular polymer from threaded cyclodextrins, Nature **364**, 516 (1993)
11. Rusa, C.C., Bullions, T.A., Fox, J.: Inclusion compound formation with a new columnar cyclodextrin host, Langmuir **18**, 10016 (2002)

12. Huh, K.M., Cho, Y.W., Chung, H.: Supramolecular hydrogel formation based on inclusion complexation between poly(ethylene glycol)-modified chitosan and α-cyclodextrin, Macromol. Biosci. **4**, 92 (2004)
13. Kawaguchi, Y., Nishiyama, T., Okada, M., Kamachi, M., Harada, A.: Complex formation of poly(ε-caprolactone) with cyclodextrins, Macromolecules **33**, 4472 (2000)
14. Shin, K.M., Dong, T., He, Y., Inoue, Y.: Effect of methylated cyclodextrins on the crystallization of poly(3-hydroxybutyrate), Macromol. Chem. Phys. **207**, 755 (2006)
15. Choi, H.S., Yui, N.: Design of rapidly assembling supramolecular systems responsive to synchronized stimuli, Prog. Polym. Sci. **31**, 121 (2006)
16. Lu, J., Shin, I.D., Nojima, S., Tonelli, A.E.: Formation and characterization of the inclusion compounds between poly(ε-caprolactone)-poly(ethylene oxide)-poly(ε-caprolactone) triblock copolymer and α- and γ-cyclodextrin, Polymer **41**, 5871 (2000)
17. Li, J., Chen, B., Wang, X., Goh, S.H.: Preparation and characterization of inclusion complexes formed by biodegradable poly(ε-caprolactone)–poly(tetrahydrofuran)–poly (ε-caprolactone) triblock copolymer and cyclodextrins, Polymer **45**, 1777 (2004)
18. Klok, H.A., Hwang, J.J., Iyer, S.N., Stupp, S.I.: Cholesteryl-(L-lactic Acid)*n*j building blocks for self-assembling biomaterials, Macromolecules **35**, 746 (2002)
19. Wan, T., Zou, T., Cheng, S.X.: Synthesis and characterization of biodegradable cholesteryl end-capped polycarbonates, Biomacromolecules **6**, 524 (2005)
20. Yu, L., Zhang, H., Cheng, S.X., Zhuo, R.X., Li, H.: Study on the drug release property of cholesteryl end-functionalized poly(ε-caprolactone) microspheres, J. Biomed. Mater. Res. Part B: Appl. Biomater. **77B**, 39 (2006)
21. Zhang, L., Wang, Q.R., Jiang, X.S., Cheng, S.X., Zhuo, R.X.: Studies on functionalization of poly(ε-caprolactone) by a cholesteryl moiety, J. Biomater. Sci. Polym. Ed. **16**, 1095 (2005)
22. Klok, H.A., Hwang, J.J., Hartgerink, J.D., Stupp, S.I.: Self-assembling biomaterials: L-lysine-dendron-substituted cholesteryl-(L-lactic acid)*n*, Macromolecules **35**, 6101 (2002)
23. Wang, J.L., Wang, Dong, C.M.: Supramolecular inclusion complexes of star-shaped poly(ε-caprolactone) with α-cyclodextrin, J. Polym. Sci.: Part A: Polym. Chem.**43**, (4271) 2005
24. Cserháti, T., Forgács, E.: Modification of the apparent lipophilicity of steroidal drugs with gamma-cyclodextrin, Eur. J. Pharm. Biopharm. **46**, 153 (1998)