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ORIGINAL ARTICLE

# Effects of several inter-molecular interactions on the inclusion between methyl substituted β-cyclodextrin and some linear macromolecule in supercritical carbon dioxide medium

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**Abstract** In this work, the inclusion between methyl substitute β-cyclodextrin and some linear macromolecule in supercritical carbon dioxide medium was investigated. The contributions from several factors were studied; such as the hydrogen bonding interaction between the host and guest, the hydrogen bonding interaction between the neighborhood cyclodextrin rims threaded on the polymer chain, and the matching between the host cavity and the size of the polymer axis.

**Keywords** Inclusion · Methyl substituted β-cyclodextrins · Linear macromolecules · Supercritical carbon dioxide

## Introduction

In the last 20 years, the polyrotaxane has attracted much attention due to its potential application in electronics, biomedical engineering and polymer processing. When several macrocyclic molecules are threaded on a single linear polymer chain, the pseudo-polyrotaxane is formed. The complex provides an opportunity for studying the behavior of the single polymer chain; and at the same time, it can help us to further understand the mechanism of the molecular recognition. The inclusion complex between cyclodextrin and linear polymer is one of these pseudo-polyrotaxanes.

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In most cases, the inclusion between cyclodextrin and polymer in aqueous solution was investigated [1–10], recently this investigation was focused on the selective inclusion between cyclodextrin and some block polymers [11–20]. In aqueous solution, the hydrophobic interaction between the cyclodextrin cavity and the hydrophobic part of the polymer chain is the main driving force; the molecular recognition between the host and the guest determined the extent of the complex; and the length of the polymer dominated the fraction of coverage for the polymer by the cyclodextrin rings in the complex.

There were some studies for this inclusion in other solvent. Shin et al. compared the products between some cyclodextrin and linear polymer from aqueous solution and from chloroform [21]. Jazkewitsch et al. [22] got some partial include product from dimethylformamide solution. In these organic solvent, the hydrophobic interaction between the host and the guest was eliminated and the solvent competition may interrupt the desired inclusion. There were also some studies for this inclusion in solvent-free condition. Liu et al. [23] observed that part polymer chains could thread into the cyclodextrin cavities after grinding without any solvent for some time. And Balik and co-workers found that: the crystalline structure of native α-cyclodextrin could spontaneously transform from cage stack to column stack to some extent after mixed with liquid polyethylene glycol (PEG 200 or 400) and left in static [24, 25]. In these situations, the hydrogen bonding interaction or the van der Waals interaction between cyclodextrin and the polymer was the main driving force for the inclusion. But the limited mobility of the macrocyclic molecules in solid state may restrict the inclusion, as the cyclodextrin must undergo a phase transform from cage or amorphous structure to column structure to accommodate the polymer chain [25].

Supercritical carbon dioxide ($scCO_2$), a clear medium and weak solvent compared to general organic solvent, has been successfully used in the inclusion between cyclodextrin and some small molecule compound (see Refs. [26–30]); but has not been used in the inclusion between macrocyclic molecule and linear polymer now, due to the low solubility of normal polymer and the inflexibility of some cyclodextrin matrix in this medium [31–33].

Yet it was reported in literature that: the glass transition temperature of methyl-$\beta$-cyclodextrin (MBCD, Tg = 180–182 °C) could be remarkably depressed in $scCO_2$ medium [34]; the $scCO_2$ could dissolve in some solid polymer, swell the matrix and depress the glass transition temperature of the polymer [35, 36]. And we also found that the liquefaction of MBCD provided some new approach for the inclusion between cyclodextrin and some small molecule compounds [26–28]. In $scCO_2$ medium, while the steric hindrance for substituted benzene and coumarin was strong for hydroxypropyl-$\beta$-cyclodextrin (HPBCD) in solid state, the steric effect was weak for MBCD due to the soft of this host [29, 30]. Thus for the inclusion between methyl substituted cyclodextrin and some linear macromolecule in supercritical carbon dioxide medium, the competition from the carbon dioxide molecules is weak, the host matrix is flexible, and the interactions between the polymer chains themselves can be reduced remarkably. As a result, the effect of the hydrogen bonding interaction or the van der Waals interaction on this inclusion can be demonstrated sufficiently.

Thus in this work, the inclusion between methyl substituted $\beta$-cyclodextrin and some linear macromolecules in $scCO_2$ medium was studied. Comparing the inclusion for MBCD–poly (propylene glycol) (PPO $M_w \sim 1{,}000$) with the inclusion for MBCD–poly (ethylene glycol) (PEO $M_w = 950$–$1{,}050$), the selectivity of the cyclodextrin cavity for the size of the guest molecule axis was discussed. Comparing the inclusion for MBCD–poly (propylene glycol) (PPO $M_w \sim 425$) with the inclusion for MBCD–hexatriacontane (HTC), the contribution from the hydrogen bonding interaction between the host and guest was estimated. Comparing the inclusion for MBCD-guest with the inclusion for heptakis (2,3,6-tri-O-methyl)-$\beta$-cyclodextrin (TMBCD)-guest, the effect of the hydrogen bonding interaction between the neighborhood cyclodextrin rings was derived.

## Materials

Methyl-$\beta$-cyclodextrin (1.6–2.0 methyl groups per glucose unit), TMBCD (>98.0%), poly (propylene glycol) ($M_w \sim 425$ and $M_w \sim 1{,}000$), poly (ethylene glycol) ($M_w = 950$–$1{,}050$), were purchased from Sigma-Aldrich-Fluka. HTC, AR Grade, was obtained from Aladdin-Reagent. Carbon dioxide with a purity of 99.95% was supplied by Beijing Analytical Instrument Factory.

## Methods

### Preparation of the physical mixture

According to the desired ratio for the molar number of methyl substitute $\beta$-cyclodextrin (methyl substituted BCD) to the molar number of repeated unit in the linear macromolecule (for example: $–CH_2–$ for HTC, $–CH_2–CH_2–O–$ for PEO, and $–CH_2–CH(CH_3)–O–$ for PPO), the methyl substituted BCD and linear macromolecule compound were weighted, mixed and ground in a mortar with a pestle for 3 min, then the physical mixture was obtained.

### Inclusion in $scCO_2$ medium

100 mg of the physical mixture was put into a 10 mL stainless-steel vessel; then the vessel was sealed and heated to the desired temperature; after thermal equilibrium, carbon dioxide was pumped into the vessel to the desired pressure. The content was left at the desired temperature and pressure in static for 20 h; then the carbon dioxide was rapidly discharged from the reactor within 2 min and the products in the vessel were collected. Except for some TMBCD–PEO products, the other product was directly in solid state after decompressing.

### Characterization of the product

#### *XRD characterization*

The product was characterized by XRD spectrum with a RIGAKU D/MAX 2500 X-ray diffractometer, Cu $K_\alpha$ radiation (40 kV, 200 mA), 3–60° scan rang, 8°/min scan rate. The XRD pattern of the product was compared with that of the inclusion complex reported in literature to look for the diffraction peaks from the column stack MBCD or TMBCD.

#### *Thermal analysis characterization*

The physical mixture and the product of MBCD-crystalline guest, the physical mixture and the product of TMBCD-guest, were analysis by a Perkin Elmer Diamond DSC from 25 to 200 °C with 10 °C/min heating rate and 20 mL/min nitrogen flow. The heat of melting for the crystal HTC or unbound TMBCD in the sample was determined.

*Nuclear magnetic resonance ($^1H$ NMR) characterization for MBCD–HTC*

The MBCD–HTC physical mixture at 4:1 molar ratio, the corresponding MBCD–HTC product made in 90 °C 10 MPa $scCO_2$ and the sample washed with cyclohexane, were characterized by $^1H$ NMR spectra with a Brucker Avance 400 NMR spectrometer at room temperature in $CDCl_3$. The chemical shifts were referenced to external standard TMS.

The MBCD–HTC sample washed with cyclohexane was obtained through the following treatments: 50 mg product made in 90 °C 10 MPa $scCO_2$ was dispersed in 1 mL cyclohexane, ultra-sounded for 10 s, and centrifuged for 5 min at 3,000 rpm. The cyclohexane was draw out using an injector, the left solid was dry in air and later heated at 80 °C for 2 h.

*Quantitative characterization*

For MBCD–hexatriacontane (HTC), the XRD result was coupled with the DSC analysis result for the same product, while the original HTC is in crystalline state. At first, the XRD spectrum of the physical mixture and some products were determined at the same condition; the intensity of the peak mainly from the channel structure MBCD at 17.7° relative to that from the amorphous structure MBCD at 23° in the same spectrum ($I^{\circ}_{17.7}/I^{\circ}_{23}$) was calculated. Then, the above physical mixture and the products were measured by DSC analysis. The heat for the melting of HTC in per gram of the physical mixture or the product was determined. The quantity of crystal HTC in per gram of product could be calculated. Due to the quite low solubility of MBCD and HTC in $scCO_2$ [33], the total composition of the product should be the same with that of corresponding physical mixture. Thus, the amount of dispersed HTC in per gram of the product could be derived. Let's hypothesized that the dispersed HTC molecules were all included in the MBCD cavities and the molar ratio of MBCD to $–CH_2–$ unit in HTC molecule in the inclusion complex was 1:9, then the amount of complex MBCD in per gram product could be estimated and the fraction of complex MBCD relative to the total MBCD in the product ($x$) could be calculated. With this fraction of MBCD in the corresponding product, the ($I^{\circ}_{17.7}/I^{\circ}_{23}$) in the XRD spectrum of the product was calibrated. Then Eq. 1 was obtained from the correlation between the XRD determination and the DSC analysis results for several products. The data used for this correlation was list in Table 1.

$$I^{\circ}_{17.7}/I^{\circ}_{23} = 2.91 + 0.884 \cdot [x/(1-x)] \quad (1)$$

For the other MBCD-guest product, the ($I^{\circ}_{17.7}/I^{\circ}_{23}$) in the same spectrum was calculated. Latter, the fraction of channel structure MBCD relative to the total MBCD in the same product ($x$) was derived from this relative intensity by using Eq. 1. On the assumption that the total composition of the product was the same with the corresponding physical mixture and the polymer in the complex was fully covered with the cyclodextrin rings, the complex fraction for the polymer was also estimated.

For TMBCD-guest product, the heat for the melting of crystal TMBCD in per gram physical mixture or product was directly measured by the DSC analysis, the quantity of unbound TMBCD in per gram product was calculated. Due to the low solubility of TMBCD and the guest in $scCO_2$ medium [31–33], the total composition of the product should be the same with the corresponding physical mixture, thus the fraction of complex TMBCD relative to total TMBCD in the product could be derived.

From these qualitative and quantitative analysis results, the inclusion between methyl substituted $\beta$-cyclodextrin and some linear macro-molecules in supercritical carbon dioxide medium was discussed.

## Results and discussion

The $^1H$ NMR spectrum, XRD patterns and DSC grams of the product were displayed in Figs. 1, 2, 3, 4, 5, 6, 7, 8 and 9, and the quantitative analysis results were list in Tables 2, 3 and 4.

Examination for the quantitative characterization

In the $^1H$ NMR spectrum of MBCD–HTC physical mixture at 4:1 molar ratio (corresponding to 1:9 ratio for the molar

**Table 1** Data used in correlation the DSC analysis result and XRD result for MBCD–HTC products at 1:9 reactant ratio

| Sample | $\Delta H_m$ (HTC)[a] (J/g) | Fraction of crystal HTC[b] | Fraction of complex MBCD[c] | $I^{\circ}_{17.7}/I^{\circ}_{23}$ |
|---|---|---|---|---|
| 25.0 °C 0.1 MPa | 21.1 | 1.00 | 0.00 | |
| 100.0 °C 0.1 MPa | 19.2 | 0.91 | 0.09 | 3.0 |
| 90.0 °C 10.0 MPa | 6.9 | 0.33 | 0.67 | 4.7 |

[a] The heat for the melting of HTC crystalline in per gram product

[b] The fraction of crystalline HTC relative to total HTC in the product

[c] The fraction of complex MBCD relative to total MBCD in the product

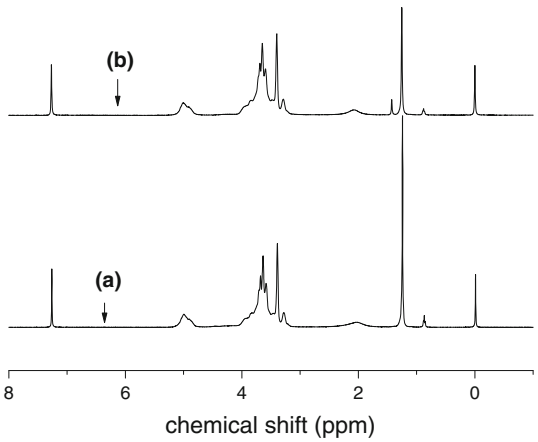


**Fig. 1** $^{1}$HNMR spectrum of MBCD–HTC: (*a*) MBCD–HTC physical mixture 1:9, (*b*) MBCD–HTC sample washed with cyclohexane

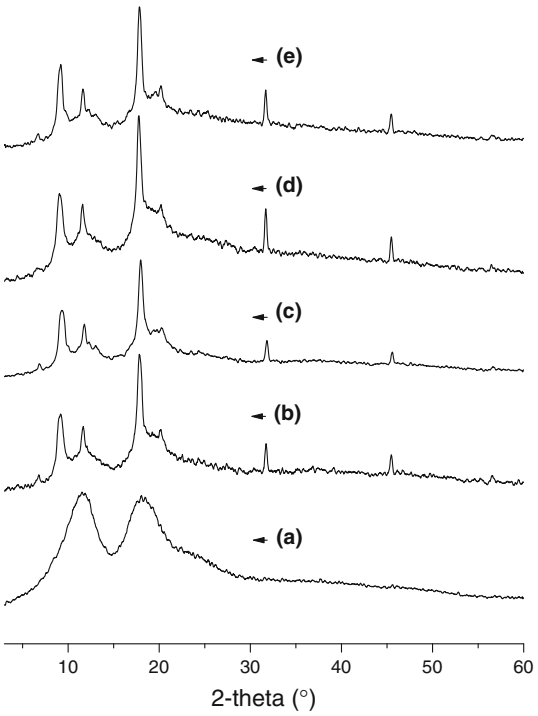


**Fig. 2** XRD spectrum of MBCD–PPO (PPO 425) and MBCD–PPO (PPO 1,000): (*a*) MBCD, (*b*) MBCD–PPO (PPO 425) 1:2 90 °C 0.1 MPa, (*c*) MBCD–PPO (PPO 425) 1:2 90 °C 10.0 MPa, (*d*) MBCD–PPO (PPO 1,000) 1:2 90 °C 0.1 MPa, (*e*) MBCD–PPO (PPO 1,000) 1:2 90 °C 10.0 MPa

number of MBCD to the molar number of $–CH_2–$ unit in HTC) (Fig. 1), the resonance at chemical shift ($\delta$) 0.87 and 1.24 was respectively belong to $CH_3$- and $–CH_2$-group in HTC molecule, the resonance around $\delta$ 4.9–5.0 was from C(1)H and O(3)H in MBCD [5]; the integral of the peak for the $–CH_2–$ is 1.68 times of that for the C(1)H and O(3)H, thus some of the H on O(3) in MBCD molecule was substituted by methyl group. In the spectrum of the original

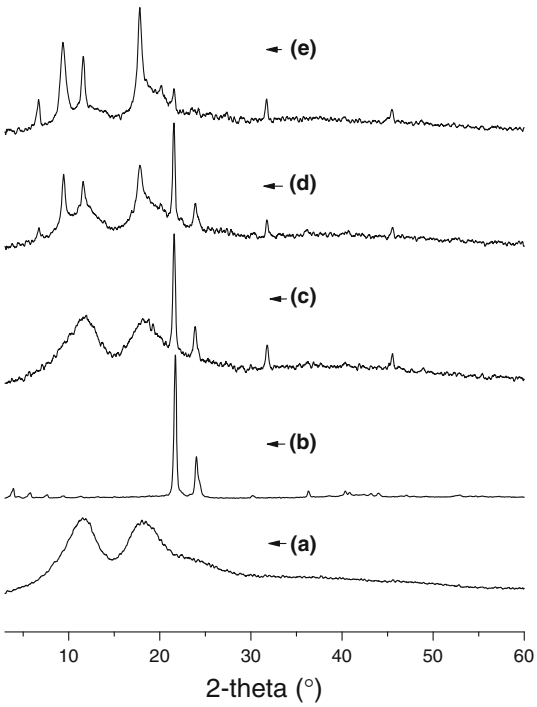


**Fig. 3** XRD spectrum for MBCD–HTC: (*a*) MBCD, (*b*) HTC 90 °C 0.1 MPa, (*c*) MBCD–HTC 1:9 90 °C 0.1 MPa, (*d*) MBCD–HTC 1:9 100 °C 0.1 MPa, (*e*) MBCD–HTC 1:9 90 °C 10.0 MPa

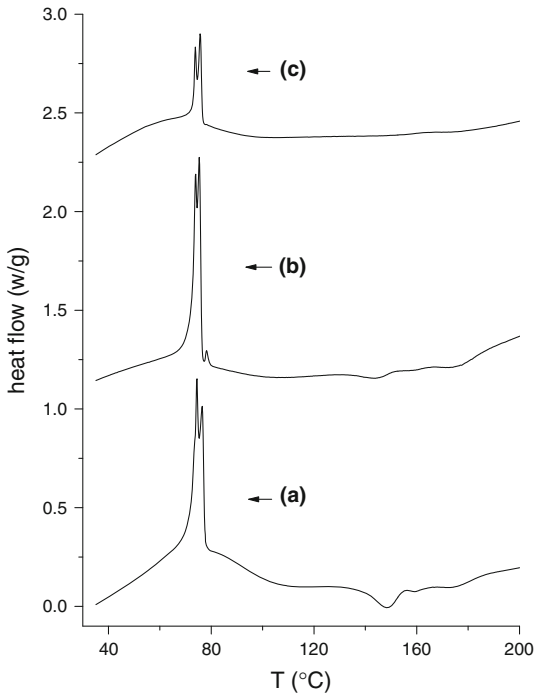


**Fig. 4** DSC grams for MBCD–HTC: (*a*) MBCD–HTC 1:9 mix, (*b*) MBCD–HTC 1:9 100 °C 0.1 MPa, (*c*) MBCD–HTC 1:9 90 °C 10.0 MPa

MBCD–HTC product made in 90 °C 10 MPa $scCO_2$ at 1:9 reactant ratio, the integral of the peak for $–CH_2–$ in HTC is 1.71 times of that for C(1)H and O(3)H in MBCD, thus the

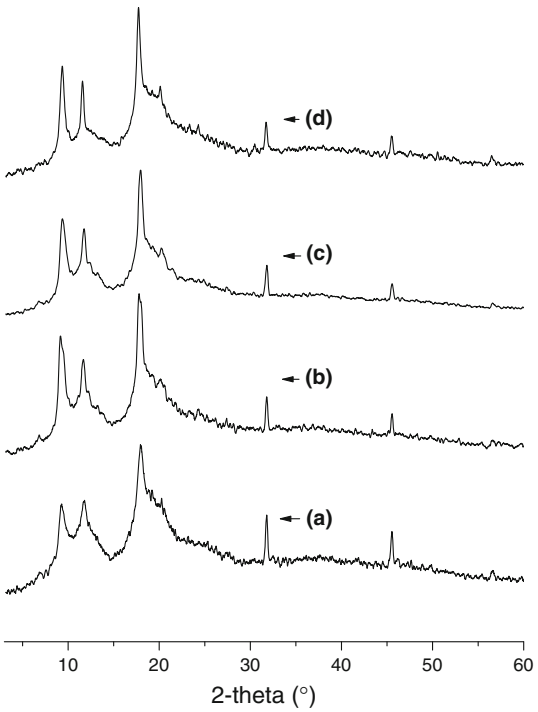


**Fig. 5** XRD spectrum of MBCD–PEO (PEO 1,000): (*a*) MBCD–PEO 1:2 50 °C 10.0 MPa, (*b*) MBCD–PEO 1:2 90 °C 0.1 MPa, (*c*) MBCD–PEO 1:2 90 °C 7.0 MPa, (*d*) MBCD–PEO 1:4 90 °C 0.1 MPa

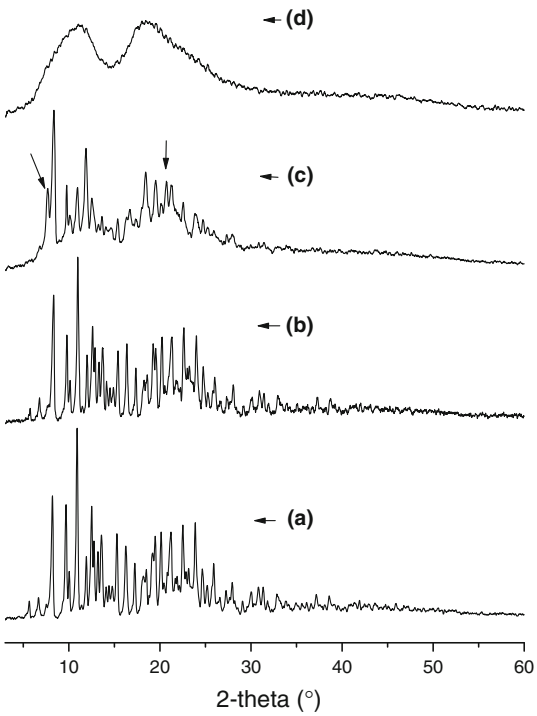


**Fig. 7** XRD spectrum for TMBCD–PEO (PEO 1,000): (*a*) TMBCD–PEO 1:3 mix, (*b*) TMBCD–PEO 1:3 50 °C 0.1 MPa, (*c*) TMBCD–PEO 1:3 90 °C 0.1 MPa, (*d*) TMBCD–PEO 1:3 90 °C 7.0 MPa

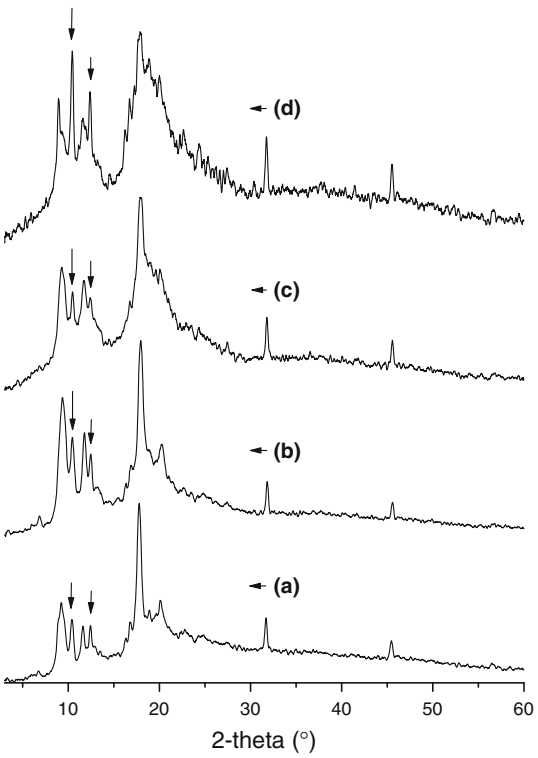


**Fig. 6** XRD spectrum for MBCD–PEO with cage crystalline MBCD: (*a*) MBCD–PPO (PPO 1,000) 1:2 110 °C 12.0 MPa, (*b*) MBCD–PEO (PEO 1,000) 1:2 90 °C 10.0 MPa, (*c*) MBCD–PEO (PEO 1,000) 1:4 90 °C 7.0 MPa, (*d*) MBCD–PEO (PEO 1,000) 1:4 90 °C 10.0 MPa

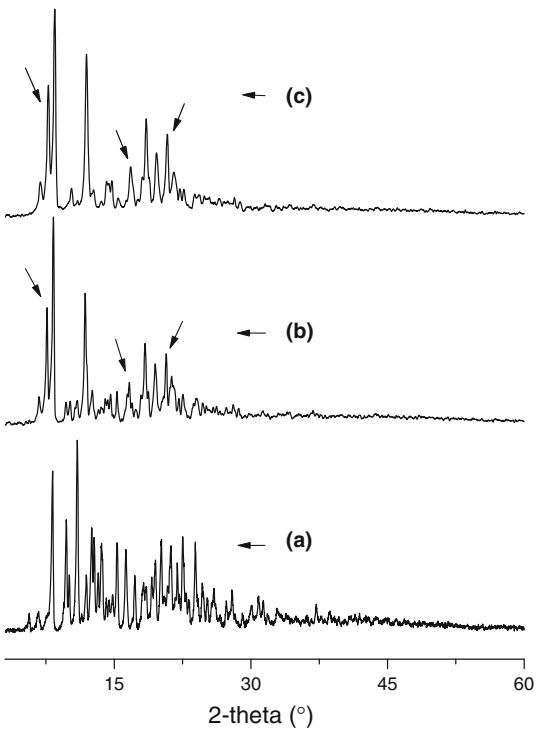


**Fig. 8** XRD spectrum for TMBCD–HTC: (*a*) TMBCD orig., (*b*) TMBCD–HTC 1:9 90 °C 0.1 MPa, (*c*) TMBCD–HTC 1:9 90 °C 10.0 MPa

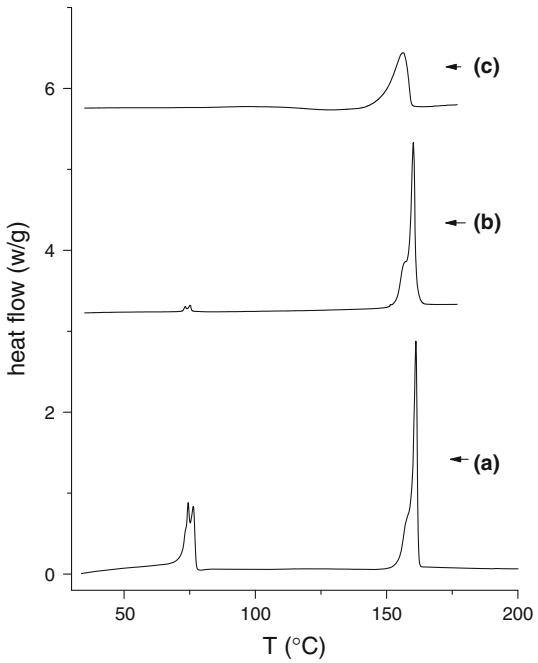


**Fig. 9** DSC grams for TMBCD–HTC: (*a*) TMBCD–HTC 1:9 mix, (*b*) TMBCD–HTC 1:9 90 °C 0.1 MPa, (*c*) TMBCD–HTC 1:9 90 °C 10.0 MPa

composition of the product was indeed the same with the corresponding physical mixture.

The dissolution of HTC in cyclohexane was test. 5.0 mg HTC solid was put in 0.5 mL cyclohexane and ultrasounded for 2–3 s, the solid was all dissolved; even after centrifuged for 5 min at 3,000 rpm, no solid was found. In our previous work, the MBCD was not dissolved in cyclohexane [26–29]. Thus during the washing process, the unbound HTC in the above product should all be dissolved in the cyclohexane and be removed from the sample, the unbound MBCD and the complex was left. In the $^1$H NMR spectrum of the sample washed with cyclohexane, the resonance at $\delta$ 1.42 was from the cyclohexane residue, the integral of the peak for $-CH_2-$ in HTC is 1.16 times of that for C(1)H and O(3)H in MBCD, thus about 70% HTC in the original product was complex with MBCD molecule. And from the DSC analysis results show in Table 1, about 67% HTC in the original product was dispersed; thus in the original product, the dispersed HTC was all included in the MBCD cavity.

The above results strongly supported the assumptions in the quantitative characterization. In the ideal inclusion complex of αCD-PEO, the ratio between the molar number of αCD to the molar number of $-CH_2-CH_2-O-$ unit in PEO chain should be 1:2; but due to the delocalization for cyclodextrin ring on the polymer chain, this ratio may range from 1:2.2 to 1:2.7 [9]. On the average, the molar ratio for αCD ring to PEO repeated unit in the real

**Table 2** Estimated fraction of column structure MBCD relative to total MBCD in MBCD-line macromolecule product

| $Mol_{MBCD}$:$Mol_{guest\ unit}$ in reactants | $T$ (°C) | $P$ (MPa) | $I_{17.7^\circ}/I_{23^\circ}$ | $x$ | $y$ |
|---|---|---|---|---|---|
| MBCD–PPO (PPO $M_w$ = 425) | | | | | |
| 1.00:2.00 | 50 | 0.1 | 3.8 | 0.5 | 0.6 |
| 1.00:2.00 | 50 | 7.0 | 4.9 | 0.69 | 0.86 |
| 1.00:2.00 | 50 | 10.0 | 4.8 | 0.68 | 0.85 |
| 1.00:2.00 | 90 | 0.1 | 3.8 | 0.5 | 0.6 |
| 1.00:2.00 | 90 | 7.0 | 4.6 | 0.66 | 0.83 |
| 1.00:2.00 | 90 | 10.0 | 4.8 | 0.68 | 0.85 |
| 1.00:4.00 | 90 | 0.1 | 5.4 | 0.74 | 0.46 |
| 1.00:4.00 | 90 | 7.0 | 5.7 | 0.76 | 0.48 |
| 1.00:4.00 | 90 | 10.0 | 5.1 | 0.71 | 0.44 |
| MBCD–PPO (PPO $M_w$ = 1,000) | | | | | |
| 1.00:2.00 | 50 | 0.1 | 2.8 | 0 | 0 |
| 1.00:2.00 | 50 | 7.0 | 3.1 | 0.2 | 0.2 |
| 1.00:2.00 | 50 | 10.0 | 3.1 | 0.2 | 0.2 |
| 1.00:2.00 | 90 | 0.1 | 3.5 | 0.4 | 0.5 |
| 1.00:2.00 | 90 | 7.0 | 3.7 | 0.5 | 0.6 |
| 1.00:2.00 | 90 | 10.0 | 4.0 | 0.5 | 0.7 |
| 1.00:2.00 | 110 | 0.1 | 4.2 | 0.6 | 0.7 |
| 1.00:2.00 | 110 | 7.0 | 4.2 | 0.6 | 0.7 |
| 1.00:3.00 | 90 | 0.1 | 4.4 | 0.63 | 0.53 |
| 1.00:3.00 | 90 | 7.0 | 5.7 | 0.76 | 0.63 |
| 1.00:3.00 | 90 | 10.0 | 6.5 | 0.80 | 0.67 |
| 1.00:4.00 | 90 | 0.1 | 6.6 | 0.81 | 0.50 |
| 1.00:4.00 | 90 | 7.0 | 5.9 | 0.77 | 0.48 |
| 1.00:4.00 | 90 | 10.0 | 6.0 | 0.78 | 0.49 |
| MBCD–HTC | | | | | |
| 1.00:9.00 | 90 | 0.1 | 2.6 | 0 | 0 |
| 1.00:9.00 | 90 | 7.0 | 2.7 | 0 | 0 |
| 1.00:9.00 | 90 | 10.0 | 4.7 | 0.67 | 0.67 |
| 1.00:9.00 | 100 | 0.1 | 3.0 | 0.1 | 0.1 |
| 1.00:9.00 | 100 | 7.0 | 4.5 | 0.65 | 0.65 |
| 1.00:9.00 | 100 | 10.0 | 4.8 | 0.68 | 0.68 |
| MBCD–PEO (PEO $M_w$ = 1,000) | | | | | |
| 1.00:2.00 | 50 | 0.1 | 2.7 | 0 | 0 |
| 1.00:2.00 | 50 | 7.0 | 3.1 | 0.2 | 0.2 |
| 1.00:2.00 | 50 | 10.0 | 2.7 | 0 | 0 |
| 1.00:2.00 | 90 | 0.1 | 3.6 | 0.4 | 0.5 |
| 1.00:2.00 | 90 | 7.0 | 3.8 | 0.5 | 0.6 |
| 1.00:3.00 | 90 | 0.1 | 3.9 | 0.5 | 0.4 |
| 1.00:3.00 | 90 | 7.0 | 4.1 | 0.6 | 0.5 |
| 1.00:4.00 | 90 | 0.1 | 3.4 | 0.4 | 0.2 |

*x*: estimated fraction of MBCD in column structure relative to total MBCD in the product

*y*: estimated fraction of included guest relative to total guest in the product

[a] The deviation for typical experiments is within 10% of the determined one

**Table 3** The XRD intensity of cage and column structure MBCD in product

| $Mol_{MBCD}$:$Mol_{poly.unit}$ in reactant | $T$ (°C) | $P$ (MPa) | $I_{10.4}°/I_{9.0}°$ |
|---|---|---|---|
| MBCD–PPO (PPO $M_w = 725$) | | | |
| 1.00:2.00 | 110 | 10.0 | 0.62 |
| 1.00:2.00 | 110 | 12.0 | 0.95 |
| MBCD–PPO (PPO $M_w = 1{,}000$) | | | |
| 1.00:2.00 | 110 | 10.0 | 0.66 |
| 1.00:2.00 | 110 | 12.0 | 0.67 |
| MBCD–PEO (PEO $M_w = 1{,}000$) | | | |
| 1.00:2.00 | 90 | 10.0 | 0.54 |
| 1.00:4.00 | 90 | 7.0 | 0.45 |
| 1.00:4.00 | 90 | 10.0 | 1.35 |

αCD-PEO inclusion complex is about 1:2.5. Estimated from this value, 1 MBCD ring should include 7.5 $–CH_2–$ unit in MBCD–HTC complex. As the interaction between MBCD and HTC is weak than the interaction between αCD and PEO, the shift distance of the delocalization for MBCD ring on the HTC chain may be longer. Thus the hypothesis that the ratio for the molar number of MBCD to the molar number of $–CH_2–$ unit in HTC molecule is 1:9 for the MBCD–HTC complex is reasonable.

## Inclusion of MBCD–PPO (PPO $M_w \sim 425$) and inclusion of MBCD–HTC

The pure MBCD has an amorphous structure even after treated in $scCO_2$ medium [26–30] and PPO was a thick or viscous liquid. The crystal diffraction at 9.1°, 11.6° and 17.7° could clearly be observed for MBCD–PPO (PPO $M_w \sim 425$) product (Fig. 2), the position and the pattern of these three peaks were the same with those of the channel structure inclusion complex between 2,6-dimethyl-β-cyclodextrin (2,6-DMBCD) and poly (tetrahydrofuran) [5]. As 2,6-DMBCD was the main composition in random substituted MBCD [27], thus some column inclusion was already formed between the host and the guest in our product. At 1:2 molar ratio between MBCD and PPO repeat unit (reactant ratio), the complex fraction was low in 0.1 MPa air. After some carbon dioxide was added into the reactor, the inclusion was somewhat improved. As some PPO ($M_w \sim 425$) molecules may dissolve in $scCO_2$ medium [31, 32] and not contacted with the MBCD matrix, the real reactant ratio may be lower for the inclusion at 1:2 initial ratio. At 1:4 reactant ratio, more than 70% MBCD was threaded onto the polymer chain in the product (Table 2). While excess amount of PPO exist, the complex fraction or MBCD–PPO (PPO $M_w \sim 425$) was approximate to that for MBCD–PPO (PPO $M_w \sim 725$) in our previous work.

In the XRD diffraction pattern of MBCD–HTC product at 90 °C 0.1 MPa (Fig. 3), the crystalline peak at 21.7° and 24.0° from the free HTC was strong and the crystal diffraction from the column stack MBCD was not found. As the reaction temperature was raised, the diffraction from free HTC was a little reduced and the diffraction from column stack MBCD appeared. After carbon dioxide was introduced in the reactor up to 10 MPa, the diffraction from free HTC was almost cut down and the diffraction from column stack MBCD was evidently sharpen for the product. In addition to this, there was also some evidence from the DSC analysis for the inclusion between MBCD and HTC in the product (Fig. 4). In the DSC gram, a couple of peak was observed at 74–76 °C due to the melting of free HTC in the product [37, 38]. After treated in $scCO_2$ medium, the heat for the melting of free HTC in per gram sample was evidently decreased (Table 4). As the solubility of MBCD and HTC in $scCO_2$ medium was quite low [33], the total composition of the product was the same with that of the corresponding physical mixture. In dry air, the inclusion between MBCD and HTC was quite weak; this was the same with the phenomena reported in literature [25]. In $scCO_2$ medium, the complex fraction for MBCD–HTC at 90–100 °C was lower than the complex fraction for MBCD–PPO (PPO $M_w \sim 425$) at 90 °C. In HTC

**Table 4** DSC analysis results for crystal HTC or TMBCD in modified BCD-HTC

| $Mol_{mBCD}$:$Mol_{guest\ repeat\ unit}$ in reactant | $T$ (°C) | $P$ (MPa) | $\Delta H_m$ (HTC) (J/g)[a] | $\Delta H_m$ (TMBCD) (J/g)[b] | Fraction of free[c] |
|---|---|---|---|---|---|
| MBCD–HTC | | | | | |
| 1.00:9.00 | 25 | 0.1 | 21.1 | | 1.00 |
| 1.00:9.00 | 100 | 0.1 | 19.2 | | 0.91 |
| 1.00:9.00 | 90 | 10.0 | 6.9 | | 0.33 |
| TMBCD–HTC | | | | | |
| 1.00:9.00 | 25 | 0.1 | | 41.8 | 1.00 |
| 1.00:9.00 | 90 | 0.1 | | 36.9 | 0.88 |
| 1.00:9.00 | 90 | 7.0 | | 36.1 | 0.86 |
| 1.00:9.00 | 90 | 10.0 | | 31.6 | 0.76 |

[a] The heat for the melting of HTC crystalline in per gram product

[b] The heat for the melting of TMBCD crystalline in per gram product

[c] The fraction of crystal HTC to total HTC in the product or the fraction of crystal TMBCD to total TMBCD in the product

molecule, there was no oxygen atom, therefore no hydrogen bonding between the host and the guest; in PPO molecule, there was some oxygen atom linked in the chain, there must be some hydrogen bonding interaction between cyclic MBCD rims and PPO chain threaded in the MBCD cavity. Thus the hydrogen bonding interaction between the host and the guest must have an important contribution to the inclusion in $scCO_2$ medium, as the complex fraction was much higher for MBCD–PPO than for MBCD–HTC at the same condition.

### Inclusion of MBCD–PPO (PPO $M_w \sim 1{,}000$) and inclusion of MBCD–PEO (PEO $M_w \sim 1{,}000$)

The sharp diffractions from the column stack MBCD was also observed in the XRD pattern of MBCD–PPO (PPO $M_w = 1{,}000$) product prepared at temperature down to 90 °C (Fig. 2). At 50 °C, the complex fraction was low; as the reaction temperature was raised, the inclusion was improved. For reaction at 90 °C and 1:2–1:3 reactant ratio, introducing carbon dioxide into the reactor promoted the inclusion. While the initial reactant ratio was adjusted to 1:4, the inclusion for MBCD was remarkably enhanced. In the product, the MBCD ring threaded on the polymer chain could be 80% of the total MBCD; and 70% polymer chain could be included in the MBCD cavity, on the assumption that the molar ratio between MBCD and PPO repeat unit in the inclusion complex was 1:2.5 [9].

The crystal diffraction from the column stack MBCD was also observed for MBCD–PEO product (Fig. 5). The peak was broaden at 50 °C and was sharpen at higher temperature or higher reactant ratio. At 1:2 reactant ratio, the complex fraction for MBCD–PEO was closed to that for MBCD–PPO with similar length. At 1:3 reactant ratio, the fractional conversion of MBCD from amorphous state to column structure could be 0.5–0.6 for MBCD–PEO; which was lower than that for MBCD–PPO at corresponding condition. Adding some carbon dioxide to the reactor or adjusting the reactant ratio to 1:4 has slight influence on the inclusion. Thus in $scCO_2$ medium, while polymer existed in slightly excess amount, MBCD could include both PPO chain and PEO chain; but a little prefer PPO chain to PEO chain with similar length, due to the matching between the MBCD cavity and the diameter of the polymer axis.

Harada et al. has ever studied the inclusion of methyl substituted BCD-PPO and the inclusion of methyl substituted BCD-PEO in aqueous solution [4]. Methyl substituted BCD could form stable inclusion complex with PPO and the complex could precipitate from the solution; but the inclusion between methyl substituted BCD and PEO was not found, and no solid complex was obtained. Comparing the results in aqueous solution and in $scCO_2$ medium, the selectivity of methyl substituted BCD for the guest in aqueous solution was not from the choice of the host cavities to the size of the guest axis, but was mainly from the difference on the hydrophobic property of the guests.

New crystal diffractions appeared at 10.4° and 12.4° for MBCD–PPO (PPO $M_w \sim 1{,}000$) product (Fig. 6) obtained at 110 °C and carbon dioxide pressure down to 10 MPa, which was from the cage structure crystalline of the free 2,6-DMBCD [5]. This phenomena was also observed for MBCD–PPO (PPO $M_w \sim 725$) product treated in $scCO_2$ medium, because 2,6-DMBCD was the main composition in the MBCD [27] and the unbound 2,6-DMBCD in the product could crystallize by using the column stack structure of the inclusion complex as the template [39]. This crystalline was also formed in MBCD–PEO product obtained even at lower temperature and lower carbon dioxide pressure (90 °C, 7.0 MPa); at 1:4 reactant ratio, the intensity of these diffractions were further increased, and this was opposite to the tendency for MBCD–PPO (PPO $M_w \sim 725$). The intensity for diffraction at 10.4° from the cage structure of the free MBCD relative to that at 9.0° from the column structure of the complex MBCD was summarized in Table 3. As the cage stack structure may compete with the column stack structure for MBCD rings, the crystalline of free MBCD into cage structure may interrupt the desired inclusion between MBCD and the polymer.

### Inclusion of TMBCD–PEO (PEO $M_w \sim 1{,}000$) and inclusion of TMBCD–HTC

In contrast with MBCD, the pure TMBCD was a crystalline with a melting point at about 170 °C; in its molecule, the hydroxyl groups in $\beta$-cyclodextrin were almost all replaced by the methoxyl group. The inclusion of TMBCD–PEO (at 1:3 molar ratio for TMBCD: $–CH_2–CH_2–O–$ unit) and the inclusion of TMBCD–HTC (at 1:9 molar ratio for TMBCD: $–CH_2–$ unit) was test in $scCO_2$ medium.

After heated at 50 °C for 20 h, the crystalline structure of TMBCD in the TMBCD–PEO product was the same with that in the physical mixture, thus there was no interaction between the host and guest in this situation. When the reaction temperature was raise to 90 °C, two new crystal diffractions appeared and the relative intensity of the original diffractions was totally altered (Fig. 7). After left in 7.0–10.0 MPa carbon dioxide for 20 h, then the carbon dioxide was discharged, the product was in liquid state. Later the product was solidified after natural cooling. In the XRD pattern of these solidified product, no crystal diffraction was found, thus the product was fully amorphous.

After heated in air or $scCO_2$ medium, there was only two crystal XRD diffraction respectively at 21.7° and 24.0° for pure HTC. Similar to that for TMBCD–PEO product at 90 °C 0.1 MPa, new peaks and the relative intensity

changes were also found in the XRD spectrum of TMBCD–HTC product; the diffraction peaks were even broaden for product obtained in 10 MPa $scCO_2$ medium (Fig. 8). And the XRD patterns of our product was also different from that of the solid inclusion complex between TMBCD and poly (tetrahydrofuran) (PTHF); in the spectrum of that inclusion complex, there was only one sharp and strong crystal diffraction at about 8° [4, 5]. In the DSC gram, the original TMBCD has a melting peak at 160 °C. After treated in $scCO_2$ medium, the melting point for TMBCD in the product was shift down to 156 °C and the peak was remarkably broaden (Fig. 9). Moribe et al. ever studied the inclusion between TMBCD and flurbiprofen in $scCO_2$ medium [40]; the melting peak around 150–160 °C belonged to the unbound TMBCD and a new melting peak appeared at 170–180 °C for the inclusion complex. If TMBCD rings were threaded on the polymer chain and re-crystallized into column stack structure, the crystallinity of the product should be reinforced and the melting point of the inclusion complex should be higher than that of the original TMBCD. Thus the melting peak at 156 °C in the DSC gram of the product also belonged to the unbound TMBCD crystal. The quantitative result was summarized in Table 4; more than 75% TMBCD in the products was unbound, although the XRD pattern of the TMBCD–HTC product was remarkably different from that of the physical mixture.

Harada et al. investigated the interaction between methyl substituted cyclodextrin and some polymer in aqueous solution. Under the driving of the hydrophobic interaction between the cyclodextrin and the polymer chain, DMBCD could increase the aqueous solubility of poly (tetrahydrofuran) (PTHF) or PPG diamine and formed solid inclusion complexes; TMBCD only formed solid inclusion complex with PTHF [4, 5]. Takata and co-workers investigated the inclusion between TM-CD and some linear polymers under continue grinding without solvent [23]. TM-αCD could partly form inclusion complex with PTHF, and TM-βCD formed partial inclusion complex with PTHF or PEO with low efficiency, even under the action of external mechanical press. In $scCO_2$ medium, DMBCD formed column inclusion complex with the linear macromolecules, TMBCD–PEO was totally amorphous and most TMBCD was left free in the TMBCD–HTC products. Thus in non-aqueous medium, without the assistant of the hydrogen bonding interaction between the neighborhood cyclodextrin rims, the cyclodextrin rings was difficult to thread onto the linear macromolecule chain by themselves.

## Conclusions

In $scCO_2$ medium, the inclusion between methyl substituted β-cyclodextrins and some linear macromolecules were investigated. While polymer existed in slightly excess amount, MBCD could include both PPO chain and PEO chain; but a little prefer PPO chain to PEO chain with similar chain length, due to the matching between the MBCD cavity and the diameter of the polymer axis. As the complex fraction was much higher for MBCD–PPO (PPO $M_w \sim 425$) than that for MBCD–HTC at the same condition, the hydrogen bonding interaction between the host and the guest molecule has an important contribution to the inclusion. While DMBCD could form column inclusion complex with the linear macromolecule chain, TMBCD–PEO product was totally amorphous and most TMBCD was left free in the TMBCD–HTC products; thus the hydrogen bonding interaction between the neighborhood cyclodextrin rims threaded on the polymer chain was the key factor to stabilize the inclusion complex.

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