Characterization, molecular dynamics, and encapsulation ability of β -cyclodextrin polymers crosslinked by polyethylene glycol

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Abstract¹

A series of water-insoluble cyclodextrin polymers (CDP) was prepared by crosslinking β -cyclodextrin (CD) with polyethylene glycol diglycidyl ether (PEGDE). Similarly, a reference CDP was prepared using ethylene glycol diglycidyl ether (EGDE). Increasing the feed ratio of PEGDE to CD in the reaction mixture led to high degrees of crosslinking. Relaxation measurements revealed structural homogeneity among the CDPs, which exhibited mobilities that strongly depended on the chain lengths of the crosslinking agents. In addition, all the CDPs displayed high encapsulation abilities toward bisphenol A (BPA) in aqueous media. In particular, the CDP sample with a low degree of crosslinking by PEGDE showed the highest encapsulation ability toward BPA. In contrast, the CDP crosslinked by EGDE exhibited low encapsulation ability because its highly dense structure, which results from the short chain lengths of the crosslinking agents, hinders the penetration of BPA molecules.

Keywords: cyclodextrin polymer; epoxy-functionalized PEG; molecular dynamics; encapsulation ability; **adsorption isotherm**.

¹ **Abbreviations:** AGU, anhydroglucose unit; BPA, bisphenol A; CD, β -cyclodextrin; CDP, cyclodextrin polymer; CP/MAS, cross-polarization/magic-angle spinning; DC, degree of crosslinking; DDMAS, dipolar-decoupled magic angle spinning; DP, degree of polymerization; EG, ethylene glycol; EGDE, ethylene glycol diglycidyl ether; PEG, polyethylene glycol; PEGDE, polyethylene glycol diglycidyl ether; rf, radio frequency field.

1. Introduction

β -Cyclodextrin (CD) is a cyclic oligosaccharide composed of seven α -(1 $\rightarrow$ 4)-linked anhydroglucose units (AGUs); CD possesses a hollow truncated cone structure with a hydrophobic cavity at the center and a hydrophilic outer surface (Hedges, 1998; Rekharsky & Inoue, 1998). This molecular structure makes CD capable of forming inclusion complexes, or “guest–host” compounds, with both aliphatic and aromatic molecules (Aoki, Nishikawa, & Hattori, 2003; Crini, 2005; Crini et al., 1998; Crini & Morcellet, 2002). Because CD and its derivatives can enhance the solubility and bioavailability of various hydrophobic compounds, they are used in the food, pharmaceutical, drug delivery, and chemical industries (Astray, Gonzalez-Barreiro, Mejuto, Rial-Otero, & Simal-Ga’ndara, 2009; Hedges, 1998; Kozłowski & Sliwa, 2008; Martin Dell Valle, 2004; Rekharsky & Inoue, 1998).

Several properties of CD, including its stability to pH and heat, shear forces, and its solubility, can be modified depending on the type of crosslinking agent used during its polymerization (Crini, 2005; Crini et al., 1998; Crini & Morcellet, 2002). For example, water-insoluble CD polymers (CDPs), which have gained much attention as encapsulating materials for removing organic pollutants from solvents (Cadars, Foray, Gadelle, Gerbaud, & Bardet, 2005; Gerbaud, Hediger, Gadelle, & Bardet, 2008; Gu, Tsai, & Tsao, 2006; Harada, Furue, & Nozakura, 1981; Kitaoka & Hayashi, 2002; Sreenivasan, 1996; Werner, Iannaccone, & Amoo, 1996), are generally obtained by using bifunctional crosslinking agents. Epichlorohydrin has been the most extensively utilized bifunctional crosslinking agent in CDP production; it reacts with the hydroxyl groups of CD to form inter- and intramolecular mono- and diethers (Cadars, et al., 2005; Gerbaud, et al., 2008; Gu, et al., 2006; Harada, et al., 1981; Kitaoka & Hayashi, 2002; Sreenivasan, 1996; Werner, Iannaccone, & Amoo, 1996). However, a major drawback to its use is that epichlorohydrin produces poisonous and carcinogenic byproducts under the alkaline conditions required to polymerize CD (Wester, van der Heijden, Bisschop, & van Esch, 1985).

Thus, it would be desirable to find a nontoxic crosslinking agent for CD polymerization. Consider, for instance, polyethylene glycol (PEG), which is a synthetic polymer that is amphiphilic (Bailey & Koleske, 1991, 1976) and nontoxic, and hence it can be used as an

excipient or as a carrier in different pharmaceutical formulations, foods, and cosmetics (Fuertges, & Abuchowski, 1990). PEGs are readily available in a range of molecular weights (M_w); most of those that have low molecular weights ($M_w < 10^4$) can be rapidly removed from the human body after consumption (Working, Newman, Johnson, & Cornacoff, 1997), making them widely used for biomedical research, drug delivery, tissue engineering, and surface functionalization of biomaterials (Craig, 2002; Torchilin, 2002). In addition, the wide range of available PEGs with functionalized end-groups (e.g., azides, thiols, carboxylic acids, hydroxyls, and epoxides) makes them increasingly attractive for use in biomedical and biomaterial research (Zalipsky, 1995. In particular, epoxy-functionalized PEGs are well known for their reactivity toward hydroxyl groups, and are thus used to crosslink oligo- and polysaccharides, including CD (Cesteros, Ramírez, Peciña, & Katime, 2006; Nielsen, Wintgens, Larsen, & Amiel, 2009). In these etherification reactions, the two epoxy end-units of PEG undergo successive nucleophilic attacks by two equivalents of an alkoxy anionic polysaccharide species, which is generated under basic conditions, to form the ether crosslinkage (Kono, 2014; Kono, Hara, Hashimoto, & Shimizu, 2015; Kono, Onishi, & Nakamura, 2013; Lin, Kumar, Rozman, & Noor, 2005; Rodríguez, Alvarez-Lorenzo, & Concheiro, 2003).

In this study, epoxy-functionalized PEG (polyethylene glycol diglycidyl ether, PEGDE) was used as a crosslinking agent for CD to prepare water-insoluble CDP (abbreviated as PEGCDP, Fig. 1(A)). A series of PEGCDPs were prepared by varying the feed ratio of PEGDE to CD, and a similar CDP (abbreviated as EGCDP) was prepared by using ethylene glycol diglycidyl ether (EGDE) as a crosslinking agent. Detailed structural characterization of these CDPs (Fig. 1(B)) was performed using FTIR and solid-state NMR spectroscopy. Additionally, molecular dynamics was studied by ^{13}C spin-lattice relaxation ($T_{1\rho\text{C}}$) and proton spin-lattice relaxation in the rotating frame ($T_{1\rho\text{H}}$) measurements. To demonstrate the encapsulation ability of PEGCDP and EGCDP samples, a preliminary study was conducted on the adsorption of bisphenol A (BPA), which is a well-known endocrine-disrupting chemical (von Saal, Nagel, Coe, Angle, & Taylor, 2012). The analyses in this study also demonstrate how the chain lengths of the crosslinking agents and the

degree of crosslinking (DC) affect the BPA encapsulation ability of the PEGCDP and EGCDP samples.

(Fig. 1)

2. Experimental

2.1. Materials

CD (99.4% purity) was purchased from Wako Pure Chemical Industries, Ltd. (Japan). PEGDE and EGDE were purchased from Sigma-Aldrich Co. (USA) and Tokyo-Kasei Kogyo Co. Ltd. (Japan), respectively. All the solvents and other chemicals, which were purchased from Kanto Chemicals (Japan) and Wako Pure Chemicals (Japan), were of reagent grade and were used as received.

2.2. Preparation of CDPs

PEGCDPs **1–3** and EGCDP were prepared in a Process Station PPS-2511 organic synthesizer equipped with a magnetic stirrer and precise temperature controller (Tokyo Rikakikai Co., Ltd., Japan). PEGCDP **1** was prepared using the following procedure. CD (5.7 g, 5.0 mmol) was dissolved in a 1.5 mol L⁻¹ aqueous NaOH solution (20 mL) at 298 K and stirred at 300 rpm. PEGDE (7.8 g, 17.5 mmol) was subsequently added to the solution. The resulting mixture was stirred at 333 K for 5 h to form water-insoluble PEGCDP. After cooling to room temperature, 5% (w/v) aqueous acetic acid was added to neutralize the reaction mixture containing CDP particles. The mixture was dialyzed against distilled water for 3 days using a dialysis tube, and the white solid particles were isolated by filtration. The particles were dried in a vacuum oven at 40 °C and then cut and screened through a 20 mesh filter using a PLC-2M plastic cutting mill (Osaka Chemical Co., Japan) to obtain white granular PEGCDP **1**. The other PEGCDPs **2** and **3**, and EGCDP were similarly prepared using the corresponding initial feed amounts of CD, PEGDE, and EGDE listed in Table 1. All the CDPs were stored in a desiccator under vacuum until use.

2.3. FTIR spectroscopy

The CDP samples were diluted in the KBr powder and compressed into transparent disks. The FTIR spectra of the resulting samples were recorded at 298 K on a PerkinElmer Spectrum II FTIR spectrometer at a resolution of 4 cm⁻¹. The samples were scanned from 4000 to 500 cm⁻¹ using an average of 16 scans.

2.4. NMR spectroscopy

All the NMR experiments were performed on a Bruker AVIII spectrometer (Bruker BioSpin GmbH, Germany) at a ¹H frequency of 500.13 MHz and ¹³C frequency of 125.13 MHz.

2.4.1. Solution-state ¹H NMR

Solution-state ¹H NMR spectra were obtained in deuterium oxide at 295 K using a 2-channel 5 mm broadband observe probe, which incorporated a z-gradient coil. The ¹H excitation pulse (flip angle of 30°), data acquisition time, repetition time, and number of scans were set to 4 μs, 4 s, 2 s, and 16, respectively. The ¹H NMR chemical shifts were calibrated by referencing the methyl resonance of the internal standard 4,4-dimethyl-4-silapentane-1-sulfonic acid to 0 ppm.

2.4.2. Solid-state ¹³C NMR

Solid-state ¹³C NMR spectra were recorded at 295 K with a 4 mm dual-tuned MAS probe at 8–10 kHz. For the cross-polarization/magic-angle spinning (CP/MAS) ¹³C NMR measurements, the radio frequency field (rf) strength was set to 65 kHz for ¹³C nuclei, while a ramped shaped pulse was applied to ¹H nuclei to match the ¹H rf strength and obtain the Hartmann-Hahn condition. The contact time, acquisition time, and repetition time were set to 2 ms, 15 ms, and 4 s, respectively. The dipolar-decoupled magic angle spinning (DDMAS) ¹³C NMR spectra were recorded by setting the ¹³C excitation pulse length (flip angle of 30°), data acquisition time, and repetition time to 1.35 μs, 15 ms, and 30 s, respectively. SPINAL 64 ¹H decoupling sequences (Fung, Khitrin, & Ermolaev, 2000) with an rf strength of 75 kHz were used during the acquisition

time of the CP/MAS and DDMAS experiments. The ^{13}C NMR chemical shifts were calibrated by referencing the carbonyl carbon resonance of the external standard D-glycine to 176.03 ppm.

2.4.3. $T_{1\text{C}}$ measurements

The $T_{1\text{C}}$ measurements were carried out using the method reported by Torcha (1978). The $T_{1\text{C}}$ rates were monitored after the CP (contact time of 500 μs) had been flipped back along the static magnetic field to obtain the ^{13}C magnetization. A proper phase cycling of the flip-back 90° pulse led to an exponential decay of the ^{13}C signal intensity. ^1H nuclei were not decoupled during the following successive relaxation delays: 0.1, 0.25, 0.5, 1, 2.5, 5, 10, 20, 30, and 45 s. A total of 2048 scans were collected for each delay. The spectra were recorded at these relaxation delays, and the following ^{13}C resonance regions were integrated to obtain the $T_{1\text{C}}$ curves: C1 (106–98 ppm), C4 (88–79 ppm), C6 (65–55 ppm), and the other carbons (79–65 ppm). The resulting $T_{1\text{C}}$ curves were fitted with a mono-exponential function using the following equation (1):

$$I_t = I_0 \exp(-t / T_{1\text{C}}) \quad \text{Eq. (1),}$$

where I_t is the measured integral value and I_0 is the initial intensity of the ^{13}C magnetization. If fitting the data to the mono-exponential function resulted in over 4% error, then a di-exponential fitting function for the system containing two components (Eq. (2)) was applied:

$$I_t = I_{10} \exp(-t/T_{1\text{C}1}) + I_{20} \exp(-t/T_{1\text{C}2}) \quad \text{Eq. (2),}$$

where I_{10} and $T_{1\text{C}1}$ are the initial intensity and $T_{1\text{C}}$ values of component 1, respectively, and I_{20} and $T_{1\text{C}2}$ are the corresponding values for component 2, respectively.

2.4.4. $T_{1\text{pH}}$ measurements

The $T_{1\text{pH}}$ measurements were carried out by inserting variable delays of 0.1, 0.2, 0.5, 1, 2, 3, 4, 5, 7.5, 10, and 15 ms prior to CP. During these delays, ^1H magnetization was irradiated with an rf strength of 70 kHz and then transferred to the neighboring ^{13}C spins by CP. A short contact time of 400 μs was set to avoid ^1H spin diffusion during CP. ^1H was decoupled during the acquisition time by the SPINAL 64 decoupling, and 2048 scans were collected for each delay. ^{13}C NMR spectra were recorded at these delays and the $T_{1\text{pH}}$ values for the ^{13}C resonance

regions at 106–98, 88–79, 79–65, and 65–55 ppm were determined using the fitting function shown in Eq. (3) in a method similar to the one used to measure the T_{1C} values:

$$I_t = I_0 \exp(-t/T_{1\rho H}) \quad \text{Eq. (3),}$$

where I_t and I_0 are defined as described for Eq. (1).

2.5. Encapsulation of BPA

The abilities of the CDP samples to encapsulate BPA as a guest molecule were estimated by the following procedure. Each CDP sample (20 mg) was placed into a 50 mL centrifuge tube containing 20 mL of 0.1 mM aqueous BPA solution, and the tube was placed in a shaker under 120 rpm oscillation at 298 K. At different time intervals, the mixture was filtered through a membrane filter with a pore size of 0.45 μm . The filtrate was analyzed on an Epoch 96 well micro-volume spectrophotometer (BioTek Instruments, Inc., USA); the absorbance of the sample was measured at 275 nm and the BPA concentration was determined using a calibration curve previously prepared by our group (Kono & Nakamura, 2013). The encapsulation ability of each CDP toward BPA (q) was calculated using Eq. (4):

$$q_t = V (C_{\text{ini}} - C_t) / w \quad \text{Eq. (4),}$$

where q_t (mmol g^{-1}) is the encapsulation ability at contact time t , V is the volume of the BPA solution (L), C_{ini} is the initial concentration of BPA (mmol L^{-1}), C_t is the concentration of BPA at contact time t (mmol L^{-1}), and w is the weight of CDP (g) in the sample. The effects of contact time t and C_{ini} on the encapsulation ability of each CDP were investigated.

3. Results and Discussion

3.1. Preparation of CDPs

Prior to preparing the PEGCDPs, the average degree of polymerization (DP) of the ethylene glycol (EG) repeating units in PEGDE was first determined by solution-state ^1H NMR spectroscopy. As shown in Fig. S1, the area of the ^1H resonance corresponding to the EG repeating units (3.7 ppm) integrates to 14.4, while those of the other ^1H resonances integrate to

1. Based on these values, the average DP of the EG repeating units and the average M_w of PEGDE were calculated to be 7.2 and 447 g mol⁻¹, respectively.

A series of PEGCDPs **1–3** was prepared by setting the molar feed ratios of PEGDE to CD to 3.5:1, 5:1, and 7:1, respectively (Table 1). Additionally, the reference sample EGCDP was analogously prepared by setting the molar feed ratio of EGDE (in which the DP of the EG repeating units is 1) to CD to 7:1. All the crosslinking reactions were conducted in NaOH solutions at 333 K. Upon heating, each reaction mixture gradually changed in appearance from transparent to turbid within 30 min. As the reactions proceeded further, small white solid particles precipitated from the reaction mixtures. After 5 h, the mixtures were neutralized, dialyzed, and filtered to isolate the white solid particles, which were dried and subsequently screened through a 20 mesh sieve to obtain white granular CDP particles. The isolated yields of PEGCDPs **1–3** were 59, 63, and 74%, respectively, while the yield of EGCDP was 65%. These results indicate that higher initial concentrations of PEGDE result in higher yields of water-insoluble PEGCDPs due to increased DC. Meanwhile, the low yield of water-insoluble EGCDP was attributed to a less fully developed network structure (compared to PEGCDP **3**), which is due to the short chain length of EGDE; this instead resulted in the formation of water-soluble EGCDP.

3.2. Structural characterization

3.2.1. FTIR spectroscopy

The FTIR spectra of CD, PEGCDP **3**, and EGCDP are depicted in Fig. 2, and are normalized based on the intensity of the glucopyranose ring stretch at 1646 cm⁻¹ (Kono, Onishi, & Nakamura, 2013). Aside from the band at 1646 cm⁻¹, these spectra similarly displayed peaks corresponding to OH stretching vibrations between 3750 and 3100 cm⁻¹, an asymmetric stretching vibration for the aliphatic CH₂ groups at 2960 cm⁻¹, and the vibration of the α -(1→4) glucopyranose ring at 942 cm⁻¹ (Kono, Onishi, & Nakamura, 2013). As expected, the asymmetric aliphatic CH₂ adsorptions of PEGCDP **3** and EGCDP were higher than that of CD. Additionally, the PEGCDP **3** and EGCDP spectra exhibited the following adsorption bands: symmetric stretching vibration of CH₂ at 2892 cm⁻¹, scissoring bending vibration of CH₂ at 1462 cm⁻¹, and bending vibration of

CH at 1354 cm^{-1} (Kono, Onishi, & Nakamura, 2013). The presence of these new adsorption bands indicates that PEGDE and EGDE reacted with the hydroxyl groups of CD to form ether crosslinkages. Further, the intensities of the adsorptions at 2960, 2892, 1462, and 1354 cm^{-1} are greater in the PEGCDP **3** spectrum than in the EGCDP spectrum. This observation arises from the high number of EG repeating units in PEGCDP **3** compared to EGCDP, which was confirmed by the solid-state NMR characterization of these CDPs (Section 3.2.2).

(Fig. 2.)

3.2.2. Solid-state ^{13}C NMR spectroscopy

The CP/MAS ^{13}C NMR spectra of CD, PEGCDPs **1–3**, and EGCDP are shown in Figs. 3(A) and 3(B), and are normalized based on the intensity of the C1 resonances of the CD units. The ^{13}C linewidths of the CD units in the spectra of PEGCDPs **1–3** and EGCDP were broad compared to those of unmodified CD, indicating the polymerization of the CD units and esterification of the CD hydroxyl groups at the 2, 3, and 6 positions with the crosslinking agents (Kono & Nakamura, 2013). The most notable difference between the ^{13}C NMR spectrum of CD and those of the CDPs was the presence of the ^{13}C resonance corresponding to the EG repeating units at 72 ppm in the spectra of all PEGCDPs. The intensity of this resonance was greater in samples that contained higher initial feed amounts of PEGDE. In the ^{13}C NMR spectrum of EGCDP, the EG repeating units appeared as shoulders of the ^{13}C resonances corresponding to C2, C3, and C5 in the CD units. In addition, the ^{13}C resonances at 48 ppm corresponding to the epoxy end-groups in the crosslinking agents (Kono, Onishi, & Nakamura, 2013) were not detected in the ^{13}C NMR spectra of the CDPs. This provides additional evidence that most of the epoxy groups in the crosslinking agents reacted with the hydroxyl groups of CD.

(Fig. 3.)

The DDMAS ^{13}C spectra of PEGCDPs **1–3** and EGCDP are shown in Fig. 3(C). It is worth noting that the measurements from the DDMAS experiments provide quantitative estimates of all resonances in the samples regardless of the mobility of the segments (Tuzi, Naito, & Saitô, 1996). In contrast, measurements from the CP/MAS experiments enhance the resonances of the rigid segments such as the crystalline and high density regions, while suppressing the resonances of the flexible segments such as the amorphous and low density regions; this is due to the use of CP to produce ^{13}C magnetization. The ^{13}C resonances at 72 ppm, which correspond to the EG repeating units of the PEGCDPs, were strongly enhanced in the DDMAS spectra compared to those in the CP/MAS spectra. This observation indicates that the EG repeating units exhibit higher molecular flexibility than the CD units in the PEGCDPs. The areas of the C1 resonances (I_{C1}) and the other carbon resonances (I_{others}) in the DDMAS spectra (Table 2) were integrated and the values were used to estimate the amounts of the crosslinking agents that reacted with CD in the CDP samples. Based on the I_{others} value of each sample, the average DC, which was defined as the average number of crosslinking agents that reacted with one CD molecule in each CDP, was calculated using Eq. (5):

$$\text{DC} = 7 \times (I_{\text{others}} - 5) / n \quad \text{Eq. (5),}$$

where constants 7 and 5 pertain to the number of AGUs per CD molecule and the number of carbon nuclei in one AGU **except for C1**, respectively, and n is the number of carbons per crosslinking agent ($n = 20.8$ for PEGDE and $n = 8$ for EGDE). The DC for PEGCDPs **1–3** were determined to be 4.22, 5.11, and 5.76, and correspond to **the average molecular weights of CDPs per CD unit** (M_{wrep}) of 3022, 3420, and 3712 g mol^{-1} , respectively. For EGCDP, the DC was estimated to be 6.21 and M_{wrep} was calculated to 2216 g mol^{-1} . These results indicate that high initial concentrations of PEGDE facilitate the formation of the PEGCDP network structures and the reactivity of EGDE toward CD is greater than that of PEGDE.

3.3. Molecular dynamics

3.3.1. $T_{1\rho}$ measurements

T_{1C} values provide localized information on the molecular dynamics of different chemical sites within a molecule and are measured by ^{13}C solid-state NMR spectroscopy. Owing to the low natural abundance of the ^{13}C isotope (1.1 %), spin diffusion between ^{13}C nuclei is negligible. Consequently, the dynamic information contained in T_{1C} values is obtained at a localized molecular level and reflects the averaged dynamics over a larger molecular domain (Hediger, Emsley, & Fischer, 1999). Molecular dynamics in the MHz range influences the T_{1C} values.

The series of ^{13}C spectra shown in Fig. 4(A) was obtained from T_{1C} measurements on CD, PEGCPD **3**, and EGCDP. These experiments were performed by setting 10 relaxation delays ranging from 0.1 to 45 s (detailed in Section 2.4.3). The peaks in the following regions were integrated: C1 (107–97 ppm), C4 (90–79 ppm), C6 (66–54 ppm), and the other carbon resonances (79–66 ppm). The resulting series of integrated values for each region was fitted by the mono-exponential function denoted in Eq. (1). All the regions of CD were successfully fitted to the mono-exponential function. The T_{1C} values of the following regions were in the range of 33.8–21.8 s: C1, C4, and the overlap of C2, C3, and C5. Meanwhile the C6 region exhibited faster relaxation ($T_{1C} = 4.1$ s) due to the conformational flexibility about the C5–C6 axis (Gerbaud, Hediger, Gadelle, & Bardet, 2008). The relaxation behaviors of the C1, C4, and C6 regions in PEGCDP **3** were also fitted using the mono-exponential decay function, and their measured T_{1C} values were 19.1, 10.4, and 0.81 s, respectively. On the other hand, the regions between 79 and 68 ppm that correspond to the EG carbons and the overlap of C2, C3, and C5 in the CD units were fitted to the diexponential function denoted in Eq. (2). The results revealed T_{1C} values of 0.42 and 11.8 s for the fast and slow relaxation components, respectively. PEG is generally expected to exhibit a faster relaxation time than CD (Domján, Bajdik, & Pintye-Hódi, 2009), and the T_{1C} of the slow component is almost equivalent to that of C4. Therefore, the slow component was attributed to the relaxation behavior of the overlap of C2, C3, and C5 in the CD units, while the fast component was attributed to the EG repeating units. As summarized in Table 3, the T_{1C} values of the EG repeating units are significantly lower than those of the CD unit, indicating that the PEG chains in the PEGCDPs are highly mobile in the MHz regime compared to the CD units. It is also worth noting that all the T_{1C} values of the CD units in PEGCDP **3** are

lower than those of unmodified CD. This is attributed to a decrease in the intermolecular hydrogen bonding interactions between the CD hydroxyl groups in PEGCDP, since the PEG chains separate the CD units from each other. Moreover, esterification of the CD hydroxyl groups with the PEGDE epoxy-end groups decreases the amount of intra- and intermolecular hydrogen-bonding interactions. These factors enhance the mobility of the CD units in PEGCDP and yield lower T_{1C} values. In contrast, there are more intra- and intermolecular hydrogen-bonding interactions between unmodified CD units, making the molecular mobility of unmodified CD relatively restricted (Avakyan, Nazarov, Alfimov, Bagatur'yants, & Voronezhcheva, 2001).

(Figs. 4 and 5.)

In the case of EGCDP, the T_{1C} values for the C1, C4, and C6 regions were 49.8, 27.9, and 4.6 s, respectively. The T_{1C} behaviors of these regions were fitted by the mono-exponential function. For the other carbon regions between 79–65 ppm, the relaxation behaviors contained two components similar to the analogous regions in PEGCDP **3**: the slow relaxation component ($T_{1C} = 30.1$ s) was attributed to the overlap of C2, C3, and C5 in the CD units, and the fast component ($T_{1C} = 2.3$ s) was attributed to the EG units. The EG groups in EGCDP are less mobile than those in PEGCDP **3**, which exhibit a T_{1C} of 0.42 s. The difference in the T_{1C} values between the EG groups of PEGCDP **3** and EGCDP reflects the difference in chain lengths between these EG units. Additionally, the T_{1C} values for the CD units in EGCDP are higher than those of unmodified CD, indicating that the molecular mobility of the CD units in EGCDP are severely restricted despite the decrease in the number of intramolecular hydrogen-bonding groups in the CD units (a result of esterification crosslinking). Therefore, EGCDP presumably possesses a highly dense structure in which short chains of EGDE promote a relatively high DC. Out of the three samples, EGCDP exhibited the highest T_{1C} value for its CD units.

3.3.2. $T_{1\rho H}$ measurements

The $T_{1\rho\text{H}}$ values characterize molecular motion in the kHz regime. In contrast to the $T_{1\text{C}}$ values, which probe molecular motion in localized regions, the $T_{1\rho\text{H}}$ values are averaged by spin-diffusion over a distance spanning about 2–3 nm. Therefore, the $T_{1\rho\text{H}}$ values can provide an insight into the homogeneity of a compound within a volume of about $\sim 20 \text{ nm}^3$ (Hediger, Emsley, & Fischer, 1999). A material with structural homogeneity will produce equivalent $T_{1\rho\text{H}}$ values and its entire structure can be considered as a unique proton spin bath. However, a material with two different domains will yield two groups of $T_{1\rho\text{H}}$ values, provided that the domain dimensions are larger than the space averaged by spin diffusion. In such a case, two distinct proton spin baths are observed (Domján, Bajdik, & Pintye-Hódi, 2009).

Fig. 4(B) shows the ^{13}C NMR spectra obtained from $T_{1\rho\text{H}}$ experiments on CD, PEGCPD **3**, and EGCDP. The experiments were conducted by setting 11 relaxation delays ranging from 0.1–15 ms (detailed in Section 2.4.4). By a similar method used to obtain the $T_{1\text{C}}$ values, the four main regions in the ^{13}C NMR spectra depicted in Fig. 4(B) were integrated, and the series of integration values for each region was plotted over the relaxation delays as displayed in Fig. 6. The relaxation behaviors of all the regions were fitted by the mono-exponential decay function expressed in Eq. (3), and the calculated $T_{1\rho\text{H}}$ values of each sample were almost all equivalent (Table 3). These data indicate that each sample has structural homogeneity and a unique proton spin bath. Additionally, the molecular motions that were characterized in the MHz regime by the $T_{1\text{C}}$ experiments did not appear to affect the homogeneous slow motions that were determined from the $T_{1\rho\text{H}}$ experiments. Interestingly, the $T_{1\rho\text{H}}$ values of the three samples were determined to be ranked in the following order: CD (3.4 ms) > EGCDP (1.9–2.0 ms) > PEGCPD **3** (1.1–1.2 ms). This indicates that PEGCPD **3** undergoes the largest scale of spatial averaging by spin diffusion out of these samples, revealing that crosslinking agents with long chains strongly affect the slow motions of the entire PEGCDP molecule.

(Fig. 6.)

3.4. Encapsulation ability toward BPA

3.4.1. Kinetics studies

The encapsulation ability of PEGCDPs 1–3 and EGCDP toward guest molecules was evaluated using BPA, which is a known endocrine disruptor in aqueous media (von Saal, Nagel, Coe, Angle, & Taylor, 2012). BPA has two hydrophobic hydroxyphenyl groups in its structure that can be encapsulated within the CD cavity of the PEGCDPs and EGCDP (Aoki, Nishikawa, & Hattori, 2003; Kitaoka & Hayashi, 2002).

Contact time is an important parameter because it reflects the encapsulation kinetics of the CDPs for a given initial concentration of guest molecules (Salmaso et al., 2007). Fig. 7(A) shows the effect of contact time on the encapsulation ability of the CDPs toward BPA. Elevated encapsulation rates were observed at the beginning of the experiments, and saturation levels were gradually achieved over the course of 2 h for EGCDP and 6 h for PEGCDPs 1–3. Because each CDP has a distinct molar amount of CD units per unit mass (Table 2), the encapsulation efficiency toward BPA was defined as the percentage of CD units that encapsulated BPA out of all the CD units in each CDP over time (Fig. 7(B)). The BPA encapsulation efficiencies of the CDPs at equilibrium are ranked in the following order: PEGCDP 1 > PEGCDP 2 > PEGCDP 3 > EGCDP. This order is the reverse of that for the DC of the CDPs (Table 2).

(Fig. 7)

Several kinetics models can be used to describe the kinetics of encapsulation by CD-based materials (He, Qui, Qin, Yan, & Yang, 2014; Valente, & Söderman, 2014; Zhao, Lin, and Yao, 2012). In this study, two common models, namely the pseudo first-order model (Ho, & McKay, 1998) and the pseudo second-order model (Ho, & McKay 1999), were used to analyze the experimental data in order to examine the mechanism by which the encapsulation process is controlled. The pseudo first-order model was suggested by Lagergren for describing adsorption in solid/liquid systems (Lagergren, 1898), and it was further developed by Ho and McKay to analyze kinetic data (Ho, & McKay, 1998). The Lagergren linear form of the pseudo first-order model can be expressed as follows (Eq. (6)).

$$\ln (q_e - q_t) = \ln q_e - k_1 t \quad \text{Eq. (6).}$$

The pseudo-second order kinetic model proposed by Ho and McKay can be expressed as follows (Eq. (7)).

$$t / q_t = 1 / (k_2 q_e^2) + t / q_e \quad \text{Eq. (7),}$$

where q_t and q_e are the encapsulation abilities at contact time t and at equilibrium (mg g^{-1}), respectively, and k_1 and k_2 are the rate constants of the pseudo-first order and pseudo-second order models for the encapsulation process.

The curve-fitting plots of the pseudo-first and pseudo-second order models obtained based on Fig. 7(A) are shown in Fig. 7(C) and 7(D), respectively. These plots provide the kinetic parameters for the two models determined from the curve-fitting plots (k_1 , k_2 , and $q_{e,cal}$), which represent the BPA encapsulation ability at equilibrium. These values are summarized in Table 4. The $q_{e,cal}$ values obtained from the pseudo-first order model were lower than the experimentally determined q_e values ($q_{e,exp}$) and were, therefore, not reasonable. On the other hand, the $q_{e,cal}$ values obtained from the pseudo second-order model almost completely agreed with the $q_{e,exp}$ values. In addition, the correlation coefficients (R^2) for the pseudo-second order kinetic model were 1, while the R^2 values for the pseudo-first order model were considerably lower in the range 0.315–0.785. These results suggest that the pseudo-second order adsorption mechanism was predominant in the encapsulation of BPA by the PEGCDPs and EGCDP prepared in this study. Similar kinetic behaviors of the CD-based materials have been reported for the adsorption of cationic dyes (Crini, 2008, Crini, Peindy, Gimbert, & Robert, 2007), heavy metal cations (Badruddoza, Shawon, Tay, Hidajat, & Uddin, 2013), and pesticides (Liu, Cai, Wang, & Chen, 2011). Therefore, it is possible to predict the BPA encapsulation behavior by these CDPs over the entire range using the pseudo-second order model (Ho, & McKay 1999).

3.4.2. Encapsulation isotherms

Next, the effect of C_{ini} on the q_e was investigated and the results are displayed in Fig. 8(A). Overall, the q_e values of the CDPs increased as C_{ini} increased. Encapsulation and adsorption are usually described through isotherms, i.e., the amount of adsorbate on the adsorbent as a

function of pressure (in the case of a gas) or concentration (in the case of a liquid) at constant temperature (Crini, 2008). The adsorption isotherm is important for describing the interaction of the adsorbates on the adsorbents and for optimizing the use of adsorbents. The Langmuir and Freundlich models, which are the most popular isotherm equations, were tested in this study (Crini, 2008; Dalaran, Emik, Güçlü, İyim, & Özgümüş, 2011).

(Fig. 8)

The basic assumption of the Langmuir model is that adsorption occurs at specific homogeneous sites on the adsorbent. It is further assumed that once an adsorbate occupies a site, no further adsorption can take place at the site (Dalaran, Emik, Güçlü, İyim, & Özgümüş, 2011). Thus, the linear form of the Langmuir equation can be expressed by Eq. (8).

$$1 / q_e = 1 / (K_L q_{max} C_e) + 1 / q_{max} \quad \text{Eq. (8),}$$

where q_{max} is the maximum amount of BPA encapsulated by each CDP, C_e is the BPA concentration at equilibrium, and K_L is the Langmuir constant, also known as the binding constant for the encapsulation system (Chase, 1984). The equilibrium parameter constant, R_L , which is an essential characteristic of the Langmuir isotherm, can be expressed as a dimensionless constant and is defined by Eq. (9),

$$R_L = 1 / (1 + K_L C_0) \quad \text{Eq. (9),}$$

where C_0 is the saturated BPA concentration of the system at 298 K, which was determined to be 1.078 mmol L⁻¹. Based on the R_L values, the adsorption process can be categorized as unfavorable ($R_L > 1$), linear ($R_L = 1$), favorable ($0 < R_L < 1$), or irreversible ($R_L = 0$). On the other hand, the linearized form of the Freundlich equation is given by Eq. (10),

$$\ln q_e = \ln K_F + n^{-1} \ln C_e \quad \text{Eq. (10),}$$

where K_F is the Freundlich constant, which is a comparative measure of the adsorption capacity of the adsorbent, and n^{-1} is an empirical constant, which gives valuable information on the isotherm shape (Crini, 2008). Based on the n^{-1} values, the adsorption process may be classified as irreversible ($n^{-1} = 0$), favorable ($0 < n^{-1} < 1$), or unfavorable ($n^{-1} > 1$).

Linear plots corresponding to the Langmuir and Freundlich isotherm models are presented in Figs. 8(B) and 8(C), respectively, and the linearized isotherm coefficients of these models determined from the plots are summarized in Table 5. As observed in the figures and table, the R_L values obtained from the Langmuir model indicate favorable adsorption. Additionally, the n^{-1} values, in the case of the Freundlich model, lie in the range 0–1, indicating favorable encapsulation of BPA by the PEGCDPs and EGCDP. However, the R^2 values for the Langmuir model are considerably higher than those for the Freundlich model, implying that the BPA encapsulation by the CDPs follows a Langmuir-type adsorption mechanism.

As shown in Table 5, the maximum efficiencies of the PEGCDPs decreased as the DC increased in these samples. This indicates that an increase in DC results in increased spatial blocking of the CD cavities in the CDPs by the PEG chains and/or other CD units, and thus results in lower efficiencies. In addition, all the CDPs exhibited high K_L values ranging between 25–64 mmol L⁻¹, indicating that all the CDPs formed stable inclusion complexes with BPA molecules. However, EGCDP exhibited a relatively low K_L value of 25 mmol L⁻¹ compared to the PEGCDPs, which exhibited K_L values ranging from 50–64 mmol L⁻¹. The difference between the K_L values of EGCDP and the PEGCDPs was attributed to the difference in the chain lengths of their crosslinking moieties, as discussed in section 3.4.3.

3.4.3. Encapsulation mechanism

Several other differences between the BPA encapsulation abilities of the PEGCDPs and EGCDP are worth noting. For instance, it took approximately 6 h for the PEGCDPs to reach equilibrium during BPA encapsulation, while EGCDP reached equilibrium within only 2 h (Fig. 7(A)). Further, the PEGCDPs achieved maximum efficiencies ranging from 82–97% during BPA encapsulation, while EGCDP achieved a relatively lower value of 76% (Table 5). These observations suggest that the highly dense structure of EGCDP, which was determined from the relaxation measurements, inhibits BPA molecules from penetrating the inner CD units of the particles. Instead, BPA molecules are encapsulated both on and near the surface of the CD units, making them more susceptible to dissociation. This consequently results in a low K_L value for the

EGCDP system (Table 5). On the other hand, the PEGCDPs have spatial structures that are considerably more flexible, since both the inner and outer CD units are loosely connected through a network of long PEG chains. Such structures are consistent with the findings of the relaxation measurements. Therefore, most of the CD units in the PEGCDPs are able to encapsulate BPA molecules; this structural explanation accounts for the high K_L values and BPA encapsulation efficiencies of the PEDGCDPs, despite their lower $q_{\max}$ values and maximum efficiencies (Table 5).

In addition, the encapsulation of BPA by the CDPs is fitted by using the Langmuir isotherm model. It is well known that the Langmuir isotherm is constructed based on the following four assumptions (Duff, Ross, & Vaughan, 1988):

1. The surface of the adsorbent is uniform, i.e., all the adsorption sites are equivalent.
2. The adsorbed molecules do not interact with each other.
3. All the molecules are adsorbed by the same mechanism.
4. At maximum adsorption, only a monolayer is formed. In other words, the adsorbate molecules do not deposit on previously adsorbed molecules on the adsorbent.

Therefore, based on the fact that our data fit well to the Langmuir isotherm model, we suggest that the BPA molecules were encapsulated in the cavities of the CD units in the CDPs and that there were no BPA molecules encapsulated within the network formed by the PEG chains in the CDPs. If the BPA molecules were encapsulated in the PEG networks as well as in the cavities of CD, the adsorption data should fit to the Freundlich model, which is generally employed to describe heterogeneous adsorption systems (Crini, 2008).

With regard to the complexation of BPA with CD, the existence of synergistic effects between a BPA molecule and two CD units belonging to the same macromolecular chain ((i.e., the formation of 1:2 inclusion complexes) has been proposed (Yang, Chen, & Liu, 2008; Wang, Zeng, Wei, & Lin, 2006). If 1:2 inclusion complexes are formed in the PEGCDPs and EGCDP, the maximum efficiency of BPA encapsulation would be expected to be less than 50%. However,

in this study, the maximum encapsulation efficiencies of the CDPs were in the range 94.6 %, suggesting that most of the BPA encapsulated by the CDPs formed 1:1 inclusion complexes. The difference in the complexes formed by the BPA and CD units is considered to be a result of the DC value as well as the molecular flexibility of the crosslinking agents used for the preparation of the CDPs. Low DC and/or the use of a crosslinking agent with a long chain will permit the formation of 1:2 inclusion complexes, whereas high DC and/or the use of a crosslinking agent with a short chain will lead to the formation of a 1:1 complex, as in the case of the PEGCDPs and EGCDP prepared in this study. Therefore, using PEGDE with a longer chain may allow the formation of the more stable 1:2 complex with BPA.

With regard to the composite materials prepared from the CD and PEGs, water-swollen hydrogels were prepared by the reaction of hexamethylene isocyanate-activated CD with PEG of average M_w of $1.9 \times 10^3 \text{ g mol}^{-1}$. Both the end groups of PEG were amine-activated (Salmaso et al., 2007). The hydrogels obtained exhibited swelling behavior in aqueous solutions and the water-uptake increased logarithmically with decrease in the CD/PEG ratio. Swelling allows the loading of lysozyme as well as small compounds of β -estradiol and quinine. In this study, swelling of the PEGCDPs or EGCDP in aqueous media was not observed in the BPA encapsulation experiments. We hypothesize that the CDPs did not swell in water because the average M_w of PEGDE used in this study (447 g mol^{-1}) was considerably lower than that of the amine-activated PEG used for the preparation of the hydrogels ($1.9 \times 10^3 \text{ g mol}^{-1}$). If PEGDE with a higher average M_w is used for the preparation of PEGCDPs, large molecules such as proteins and nucleic acids could be encapsulated in the structure of PEGCDPs. Such structures may be useful as carrier materials for controlled protein drug delivery.

4. Conclusion

Several water-insoluble CDPs were produced by crosslinking reactions between CD molecules and different amounts of PEGDE in aqueous solutions. Detailed structural characterization, solid relaxation measurements, and investigation of the encapsulation ability of

the CDPs for the removal of BPA from aqueous solutions were performed. The following conclusions were drawn from the study:

1. Increasing the feed ratio of PEGDE to CD in the reaction mixture led to high DC.
2. PEGCDPs and EGCDP were structurally homogeneous and the mobilities of these CDPs strongly depended on the chain lengths of the crosslinking agents.
3. All the CDPs exhibited high BPA encapsulation abilities in aqueous media. The encapsulation ability strongly depended on the DC and chain length of crosslinking agents. Lower DC and higher chain length of the crosslinking agent allowed effective penetration of BPA.
4. The results obtained suggest that the encapsulation of BPA onto the CDPs occurred predominantly by the pseudo-second order adsorption mechanism.
5. The encapsulation of BPA onto the CDPs followed the Langmuir adsorption isotherm.

Based on these findings, it was concluded that the CDPs synthesized in this study were highly capable of encapsulating BPA guest molecules and may be suitable adsorbents that can readily accommodate guest–host interactions. In addition, since the syntheses of the CDPs do not require highly toxic reagents and solvents, they are considered to be both biologically safe and biocompatible, which allow them to be used in pharmaceutical applications such as matrices for controlled drug delivery.

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Appendix. Supplementary data

Supplementary data associated with this article can be found, in the online version, at
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Figure captions:

Fig. 1. (A) Scheme for the syntheses of PEGCDP and EGCDP from the polymerization of CD using crosslinking agents PEGDE and EGDE, respectively. (B) A schematic illustration of the structures of PEGCDP and EGCDP.

Fig. 2. FTIR spectra of CD, PEGCDP **3**, and EGCDP.

Fig. 3. Solid-state ^{13}C NMR spectra of CD, PEGCDP **1–3**, and EGCDP that were normalized based on the intensity of the C1 resonance in the CD units. (A) Effect of crosslinking agents on the CP/MAS ^{13}C NMR spectra. (B) Effect of the initial feed amounts of PEGDE on the CP/MAS ^{13}C NMR spectra. (C) DDMAS ^{13}C spectra of PEGCDPs **1–3** and EGCDP. Integration values of the C1 resonance in the CD units at 107–97 ppm (I_{C1}) and those for the other carbon resonances at 90–54 ppm (I_{others}) of the DDMAS spectra are summarized in Table 2.

Fig. 4. Series of ^{13}C NMR spectra recorded for CD, PEGCDP **3**, and EGDE with relaxation delays in the $T_{1\text{C}}$ (A) and $T_{1\text{pH}}$ (B) experiments. Integration of the peak areas in the following four regions were performed on all spectra, and the integral values in terms of the delays are plotted in Figs. 5 and 6: C1 (107–97 ppm), C4 (90–79 ppm), C6 (66–54 ppm), and the other carbon resonances (79–66 ppm).

Fig. 5. $T_{1\text{C}}$ decay curves for the following regions in the ^{13}C spectra of CD, PEGCDP **3**, and EGCDP: C1; C4; overlapped C2, C3, C5, and EG repeating unit; and C6. The relative intensities for all regions were obtained from the spectra displayed in Fig. 4(A). The regions containing the overlapped C2, C3, C5, and EG units of PEGCDP **3** and EGCDP were fitted with the di-exponential function expressed in Eq. (2). Each exponential decay of the two components in these regions is depicted by a dotted line. All other decay curves were fitted by the mono-exponential decay function expressed in Eq. (1). The $T_{1\text{C}}$ values are summarized in Table 3.

Fig. 6. $T_{1\text{pH}}$ decay curves for the following regions in the ^{13}C spectra of CD, PEGCDP **3**, and EGCDP: C1; C4; overlapped C2, C3, C5, and EG repeating units; and C6. The relative intensities for each region were obtained from the spectra displayed in Fig. 4(B). All the regions were fitted by the mono-exponential decay function as expressed in Eq. (3). $T_{1\text{pH}}$ values are summarized in Table 3.

Fig. 7. (A) Time dependency of BPA encapsulation in PEGCDPs **1–3** and EGCDP. The BPA encapsulation experiments were performed under the following conditions: CDP content (dried) = 20 mg; $C_{\text{ini}} = 500 \mu\text{mol L}^{-1}$; encapsulation medium and volume = 20 mL of distilled water; and temperature = 298 K. (B) Time dependency of the BPA encapsulating efficiency for PEGCDPs **1–3** and EGCDP. The efficiency was defined as the percentage of CD units that encapsulated BPA molecules out of all the CD units in each CDP. (C) Pseudo-first order kinetic plot and (D) pseudo-second order kinetic plot for the encapsulation of BPAs in the CDPs.

Fig. 8. (A) Effect of C_{ini} on q_e for PEGCDPs **1–3** and EGCDP. The BPA encapsulation experiments were performed under the following conditions: CDP content (dried) = 20 mg; encapsulation medium and volume = 20 mL of distilled water; temperature = 298 K; and encapsulation time = 24 h. (B) Langmuir isotherm and (C) Freundlich isotherm for the encapsulation of BPA in the CDPs.

Table 1. Initial feed amounts of CD and crosslinking agents used in CDP synthesis reactions and the corresponding yields.

CDP sample	Initial feed amount			Yield / g (%) ^b
	CD / g (mmol)	PEGDE / g (mmol) ^a	EGDE / g (mmol)	
PEGCDP 1	5.7 (5.0 mmol)	7.8 (17.5 mmol)		8.9 (59)
PEGCDP 2	5.7 (5.0 mmol)	11.2 (25.0 mmol)		10.7 (63)
PEGCDP 3	5.7 (5.0 mmol)	15.7 (35.1 mmol)		13.7 (74)
EGCDP	5.7 (5.0 mmol)		6.2 (35.4 mmol)	7.2 (65)

^a Molar amount of PEGDE was calculated by the following equation:
(Molar amount of PEGDE/mmol) = (amount of PEGDE/g) / 447 g mol⁻¹,
where 447 g mol⁻¹ was the average molecular weight of PEGDE because the average degree of polymerization of ethylene glycol repeating units in PEGDE was 7.2.

^b Yield of each CDP was determined based on the molar amount of CD in each CDP, which was calculated by the following equation:
(Yield, %) = [(Yield / g) × 10³ / (M_{wrep} of each CDP / g mol⁻¹)] × 100 / (Initial feed amount of CD / mmol),
where the M_{wrep} was the average molecular weight of each CDP per one mole of CD unit. M_{wrep} values of CDPs are summarized in Table 2.

Table 2. Structural parameters for each CDP measured by solid-state ^{13}C NMR spectroscopy.

CDP sample	Peak integration values in NMR		Structural data		
	I_{C1}^a	I_{others}^a	DC ^b	M_{wrep}^c /g mol ⁻¹	CD content ^d mmol/g
PEGCDP 1	1	17.3	4.22	3022	0.331
PEGCDP 2	1	19.9	5.11	3420	0.292
PEGCDP 3	1	21.8	5.76	3712	0.269
EGCDP	1	12.1	6.21	2216	0.451

^a I_{C1} is the integration value of the ^{13}C resonance for C1 in the CD units, and I_{others} is the sum of the ^{13}C resonances of each CDP (minus the C1 resonance). I_{C1} was set to 1 for each CDP.

^b Degree of crosslinking defined as the average number of crosslinking agent per CD unit.

^c The average molecular weight per one mole of CD unit in each CDP, which was determined by the following equation:

$$M_{wrep} / \text{g mol}^{-1} = 1135 / \text{g mol}^{-1} + \text{DC} \times 447 / \text{g mol}^{-1},$$

where 1135 g mol⁻¹ and 447 g mol⁻¹ are the molecular weight of CD and the average molecular weight of PEGDE, respectively. For EGCDP, M_{wrep} was determined by the following equation:

$$M_{wrep} / \text{g mol}^{-1} = 1135 / \text{g mol}^{-1} + \text{DC} \times 174 / \text{g mol}^{-1},$$

where 174 g mol⁻¹ is the molecular weight of EGDE.

^d Molar amount of CD units per 1 g of CDP, which was calculated by the following equation:
(CD content / mmol g⁻¹) = $1 \times 10^3 / (M_{wrep} / \text{g mol}^{-1})$.

Table 3. T_{1C} and $T_{1\rho H}$ values for CD, PEGCPD **3**, and EGCDP.

Sample	C1 region (107–97 ppm)	C4 region (90–79 ppm)	C2, C3, C5, EG region (79–66 ppm)	C6 region (66–54 ppm)
	T_{1C} / s			
CD	33.8	26.6	21.8	4.1
PEGCDP 3	19.1	10.4	11.8 0.42	0.81
EGCDP	49.8	27.9	30.1 2.3	4.6
	$T_{1\rho H}$ / ms			
CD	3.4	3.4	3.4	3.4
PEGCDP 3	1.1	1.2	1.2	1.1
EGCDP	1.9	1.9	2.0	1.9

Table 4. Kinetic parameters for the encapsulation of BPA by CDPs.

Sample	$q_{e,exp}^a$ /mmol g ⁻¹	Pseudo first-order model			Pseudo second-order model		
		k_1 / min ⁻¹	$q_{e,cal}^b$ / mmol g ⁻¹	R^2	k_2 / mmol ⁻¹ g min ⁻¹	$q_{e,cal}^c$ / mmol g ⁻¹	R^2
PEGCDP 1	0.283	0.197	0.0571	0.654	3.51	0.285	1.000
PEGCDP 2	0.244	0.293	0.0586	0.785	4.03	0.248	1.000
PEGCDP 3	0.210	0.243	0.0318	0.724	4.74	0.211	1.000
EGCDP	0.278	0.145	0.0106	0.315	3.61	0.277	1.000

^a Amount of BPA encapsulated by one gram of the CDP at equilibrium.

^b Calculated amount of BPA encapsulated by one gram of the CDP at equilibrium, determined from the curve fittings using the pseudo first-order model (Fig. 7(C)).

^c Calculated amount of BPA encapsulated by one gram of CDP at equilibrium, determined from the curve fittings using the pseudo second-order model (Fig. 7(D)).

Table 5. Langmuir and Freundlich isotherm coefficients for the encapsulation of BPA by CDPs.

Sample	Langmuir isotherm					Freundlich isotherm		
	q_{max} / mmol g ⁻¹	Maximum efficiency / mol %	K_L / mmol ⁻¹ L	R_L	R^2	K_F / mmol L ⁻¹	n^{-1}	R^2
PEGCDP 1	0.313	94.6	51.3	0.0178	0.994	0.501	0.307	0.933
PEGCDP 2	0.260	89.2	50.3	0.0181	0.991	0.377	0.272	0.928
PEGCDP 3	0.216	80.2	63.9	0.0143	0.995	0.296	0.229	0.940
EGCDP	0.344	76.4	25.0	0.0358	0.997	0.574	0.398	0.949

(A)

(B)

Fig. 2

Fig. 4

Fig. 5

Fig. 6