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Evaluation of the accessible inclusion sites in copolymer materials containing β-cyclodextrin

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ABSTRACT

The accessible inclusion sites of insoluble copolymers containing β-cyclodextrin (β-CD) were studied in aqueous solutions by measuring the absorbance changes (decolourization) of phenolphthalein (phth) at pH 10.5. The various copolymers were reacted at different β-CD:crosslinker mole ratios with five individual types of crosslinker agents (epichlorohydrin (EP), sebacoyl chloride (SCL), terephthaloyl chloride (TCL), glutaraldehyde (GLU), and poly(acrylic) acid (PAA), respectively). The decolourization provided estimates of the 1:1 binding constants (K_1) for the β-CD monomer/phth complex. Comparable values of K_1 were measured for copolymer/phth complexes with highly accessible β-CD inclusion sites as compared with the 1:1 β-CD/phth complex. The surface accessibility of the β-CD inclusion binding sites for the polymers ranged from ~10 to 72%. The observed variability of the inclusion sites was attributed to: (i) steric effects in the annular hydroxyl region of β-CD, (ii) the degree of crosslinking of the copolymer and (iii) the accessibility of the micropore sites within the copolymers. The Gibbs free energy (ΔG°) and site occupancy (θ) of phth adsorbed to the copolymer materials was estimated independently using the Sips isotherm model. The ΔG° values ranged between −27.6 and −30.9 kJ mol^{-1} for the copolymers and are in close agreement with the value for the 1:1 β-CD/phth complexes ($\Delta G^\circ = -27$ kJ mol^{-1}) in aqueous solution.

1. Introduction

Since the "lock and key" mechanism was described by Emil Fischer in 1894 for protein–ligand interactions (Cramer, 2007) the concept has inspired researchers in supramolecular chemistry to investigate abiotic receptors that form host–guest complexes. Cyclodextrins (CDs) such as α-, β-, and γ-CD are among the most widely studied macrocyclic compounds, in part, due to their remarkable ability to form inclusion complexes with a diverse range of guest molecules in aqueous solution, the gas phase, and in the solid state (Buvári & Barcza, 1979; Cai, Tarr, Xu, Yalcin, & Cole, 2003; Eftink, Andy, Bystrom, Perlmutter, & Kristol, 1989; Georgiou, Georgiou, & Koupparis, 1995; Lebrilla, 2001; Mohamed, Wilson, Headley, & Peru, 2009; Ramirez, Ahn, Grigorean, & Lebrilla, 2000; Taguchi, 1986; Wilson, Siddall, & Verrall, 1997). CDs are cyclic compounds consisting of six (α-), seven (β-), or eight (γ-) α-D-glucopyranose units connected by α-(1→4) linkages. CDs possess a characteristic toroidal shape with a well-defined lipophilic cavity and a hydrophilic exterior that is suitable for the inclusion binding of suitably sized lipophilic compounds (Bender & Komiyama, 1978). The relatively large association constant ($K \sim 10^4$ M^{-1}) (Hamai, 1991; Harrison & Eftink, 1982; Jaime, Redondo, Sánchez-Ferrando, & Virgili, 1991; Palepu & Reinsborough, 1990) observed for 1:1 complexes of β-CD/adamantane or its derivatives are among the largest reported K values and are attributed to the optimal size-fit matching between the host and the guest, respectively.

The multi-modal noncovalent interactions between the host and the guest contribute to the favourable binding affinity and the molecular recognition observed for such host–guest complexes. The seminal NMR studies and related research by Taguchi (1986) have contributed to a better understanding of the inclusion complex formed between β-CD and phenolphthalein (phth) in aqueous solution. At pH values above its pK_a (phth), the 1:1 β-CD/phth complex resembles an illustrative example of the "*lock and key*" mechanism in supramolecular chemistry, as described by Emil Fischer (*cf.* Scheme 2; Taguchi, 1986). The formation of a well-defined inclusion complex results in a shift of the pK_a of phth due to the microenvironment effects of the β-CD macrocycle. The photophysical properties of the bound and unbound states of phth in alkaline aqueous solution have led to spectrophotometric applications of this dye for the indirect determination of binding constants between CDs and optically transparent ligands (*e.g.*, amines, surfactants, and naphthenates) (Buvári et al., 1983; Buvári, Barcza, & Kajtár, 1988; Gray, MacLean, & Reinsborough, 1995; Landy,

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Fourmentin, & Surpateanu, 2000; Meier, Luiz, Farmer, & Szpoganicz, 2001; Mohamed et al., 2009; Sasaki, Christian, & Tucker, 1989; Selvidge & Eftink, 1986; Tutaj, Kasprzyk, & Czapkiewicz, 2003; Wilson et al., 1997).

More recently, the development of copolymer materials containing CDs and suitable crosslinking agents (*e.g.*, epichlorohydrin, glutaraldehye, succinyl chloride, diisocyanates, diacid chlorides, dicarboxylic acids, and cyanuric chloride) (Crini et al., 1998; Crini, 2005; Mohamed, Wilson, Headley, & Peru, 2008; Orprecio & Evans, 2003; van de Manakker, Vermonden, van Nostrum, & Hennink, 2009; Wenz, 1994) have afforded materials with interesting physicochemical properties that extend the range of applications of native CDs. The β-CD macrocycle is a key component in designing microporous copolymers since the surface accessibility of the binding sites affects the sorption properties of such copolymer materials (Burckbuchler et al., 2008; Janus et al., 1999; Rossi, Silva, Vico, & Gonzalez, 2009; Topchieva et al., 2003; Velaz, Isasi, Sanchez, Uzquenda, & Ponchel, 2007; Wintgens & Amiel, 2005). The measurement of the accessibility of the β-CD inclusion sites is an important parameter for the development of suitable sorbent materials that involve inclusion binding. In the case of solid state materials for heterogeneous (*i.e.*, solid–gas and solid–solution) sorption processes, the physicochemical and textural properties (*i.e.*, surface area and pore structure) play an important role. The ability of CD-based copolymers to form noncovalent complexes can be attributed, in part, to the formation of well-defined inclusion complexes. On this basis, it is clear that the framework structural characteristics of the copolymers contribute substantially to the overall sorption of adsorbates for heterogeneous processes (Mohamed, Wilson, Headley, & Peru, 2011). The use of phth as an optical probe to estimate the surface accessible binding sites has been limited to a narrow range of copolymer materials such as polysiloxanes, CD functionalized polystyrene fibres, CD-epichlorohydrin polymers (Fontananova, Di Profio, Curcio, Giorno, & Drioli, 2007; Uyar et al., 2009; Velaz et al., 2007). We previously reported (Mohamed, Wilson, & Headley, 2010) the quantitative use of phth as an optical probe to map the accessible inclusion sites of β-CD based polyurethanes. The inclusion site accessibility of β-CD in the framework was largely determined by the steric bulk of the crosslinking agent and its relative crosslinking density (Mohamed et al., 2010).

In this paper, we report the results of a dye-based sorption study in aqueous solution with phth and a series of copolymer materials derived from β-CD and several types of crosslinking agents with variable molecular structure and crosslink density. The crosslinking agents include dialkyl acid chlorides (terephthaloyl and sebacoyl chloride), epichlorohydrin, glutaraldehyde, and poly(acrylic) acid. The overall goal of this study was to explore the versatility and general utility of phth as an optical probe for the evaluation of the inclusion site accessibility of a diverse class of copolymer materials (Mohamed et al., 2010).

2. Experimental

2.1. Materials

Dimethyl acetamide (DMA) DriSolv ≥ 99.8% (EMD; Edmonton, AB), methanol, chromasolv for HPLC, ≥99.9% (Sigma–Aldrich Canada Ltd.; Oakville, ON) and ethyl ether anhydrous (EMD; Edmonton, AB) were used at different stages of copolymer preparation. Phosphorous pentoxide, P_2O_5 (BDH Chemicals Canada Ltd.; Halifax, NS) was used for drying β-CD. Phenolphthalein (BDH Chemicals Canada Ltd.; Halifax, NS), sodium hydrogen carbonate (BDH Chemicals Canada Ltd.; Halifax, NS), sodium hydroxide (Alfa Aesar USA; Ward Hill, MA), and ethanol (Sigma–Aldrich Canada Ltd; Oakville, ON) were used to prepare aqueous buffer solutions containing phenolphthalein. The crosslinker agents (epichlorohydrin (EP), sebacoyl chloride (SCL), terephthaloyl chloride (TCL), glutaraldehyde (GLU) and poly(acrylic) acid; PAA (Mwt. 250,000 g/mol)) were obtained from Sigma–Aldrich Canada Ltd. (Oakville, ON) Mineral oil was obtained from EMD (Edmonton, AB). All reagents were used as received unless specified otherwise.

2.2. Copolymer preparation

A procedure for the synthesis of β-CD-based copolymers crosslinked with SCL and TCL was adapted from a previous study (Mohamed et al., 2010). The copolymers containing β-CD resulting from the reaction of SCL or TCL crosslinker agents were obtained at variable relative co-monomer mole ratios (β-CD:crosslinker) of 1:1, 1:2, and 1:3. Copolymers containing GLU were prepared at 1:3 and 1:15 ratios according to a published procedure (Xu, Liu, & Sun, 2003). The crosslinking ratio of β-CD:EP copolymers was 1:15, 1:25, and 1:35; whereas, grafting of β-CD onto PAA was done using variable β-CD:PAA mass ratios (5:1, and 10:1, w/w) (Guo & Wilson, 2009). The ratio of CD:PAA is expressed on a mass ratio (w/w), in part, because of the relatively high molecular weight and polydispersity index of PAA relative to β-CD. All copolymers were dried and sieved (40 mesh) to ensure homogeneous particle sizes.

2.3. Polymer characterization

Solid-state ^{13}C NMR spectroscopy was performed on a 500 MHz Varian Unity Inova NMR Spectrometer (Mississauga, Canada) using cross polarization (CP; $^{13}C\ \{^1H\}$) with magic angle spinning (MAS) and IR spectra were obtained in reflectance mode with a BIO-RAD FTS-40 spectrophotometer (Cambridge, USA). The characterization of the products was in agreement with published results (Bambo, 2007; Guo & Wilson, 2009; Xu et al., 2003).

2.4. Solution preparation

All solutions were prepared by volume in a 0.1 M sodium hydrogen carbonate buffer adjusted to pH 10.5 with aqueous sodium hydroxide. The concentration of phth (C_{phth}) was maintained at $\sim 3.6 \times 10^{-5}$ M for all experiments. A stock solution of phth in ethanol was made and aliquots were utilized to prepare aqueous buffer solutions of phth. The ethanol/water (0.04%, v/v) (Wilson et al., 1997), solution was used to maintain the solubility of phth. All aqueous solutions were freshly prepared and run within 24 h to minimize possible artefacts arising from instability of phth. All absorption measurements were carried out at $\lambda = 552$ nm. There was no observed change in the shape of the visible absorption band with increasing concentration of β-CD ($C_{\beta\text{-CD}}$) at this absorbance wavelength.

2.5. Copolymer sorption

7 mL of buffered aqueous solution containing phth ($\sim 3.6 \times 10^{-5}$ M) were added to vials containing variable masses of sorbent (*e.g.*, β-CD, glucose, glucose copolymer and CD copolymers). The mixtures were shaken for 24 h, centrifuged with Precision Micro-Semi Micro Centricone, Precision Scientific Co. (Chicago, USA) at 1550 rpm, and the absorbance of the supernatant was measured using a Varian CARY 100 double beam spectrophotometer (Mississauga, Canada) at room temperature ($22 \pm 0.5\ ^\circ C$) to monitor the absorbance changes at λ_{max} of 552 nm.

2.6. Data analysis

A non-linear least squares (NLLS) fitting procedure was used to determine the 1:1 equilibrium binding constants (K_1) between

β-CD and phth, as outlined previously (Wilson et al., 1997). The method utilizes the Beer–Lambert law and the assumption that the molar absorptivity of the β-CD/phth complex is zero (Buvári et al., 1983; Eftink et al., 1989; Taguchi, 1986). The formation of the 1:1 complex for β-CD and phth at equilibrium in aqueous solution, and the mass-balance relations are given below. The mole content of β-CD in the copolymer materials is treated in a similar fashion with respect to native β-CD in Eq. (1):

$$\beta\text{-CD} + \text{phth} \overset{K_1}{\rightleftharpoons} \beta\text{-CD/phth} \tag{1}$$

$$[\text{phth}]_o = [\text{phth}] + [\text{CD–phth}] = [\text{phth}](1 + K_1[\text{CD}]) \tag{2}$$

$$[\text{CD}]_o = [\text{CD}] + [\text{CD–phth}] \tag{3}$$

The terms $[CD]_0$, [CD], and [CD–phth] refer to the total, unbound, and 1:1 complexed forms of β-CD, respectively. The 1:1 equilibrium binding constant (K_1) for β-CD and phth is expressed as follows:

$$[\text{CD–phth}] = [\text{phth}]_o \left(1 + \frac{1}{K_1[\text{CD}]}\right)^{-1} \tag{4}$$

The values for [CD–phth] and [phth] were obtained using the Beer–Lambert law for phth and Eqs. (2) and (3). The criterion utilized for the best fit for the NLLS procedure involved the minimization of the sums of the squares of the residuals (SSR) according to the relation, $\text{SSR} = \sum_i [(A_{\text{calc}})_i - (A_{\text{expt}})_i]^2$, where A_{calc} and A_{expt} are the respective calculated and experimental absorbance values at each value of $[CD]_o$.

The site occupancy (θ) for phth onto the polymer framework and the ΔG° values for sorption (complex formation) was determined independently from the calculated model parameters (*i.e.*, Q_m and K_{eq}) derived from the Sips isotherm (Liu & Liu, 2008; Sips, 1948) (*cf.* Eq. (5)). The Sips model accounts for the heterogeneity of the adsorbent surface and the adsorbent-adsorbate interactions. The Sips model is versatile since it accounts for Freundlich and Langmuir behavior; and reaffirms that the non-inclusion and inclusion sites may contribute to the overall sorption process. The non-inclusion copolymer/phth interactions are not considered to contribute significantly. However, such effects are taken into account with the Sips heterogeneity parameter (n_s) in Eq. (5):

$$Q_e = Q_m \frac{K_{eq} C_e^{n_s}}{1 + K_{eq} C_e^{n_s}} \tag{5}$$

Q_e is the amount of phth adsorbed by the copolymer (mol phth/g copolymer), Q_m is the maximum amount of phth adsorbed within the copolymer monolayer, C_e is the equilibrium amount of phth in aqueous solution (M), K_{eq} is the 1:1 equilibrium binding constant (M^{-1}), and n_s is the Sips heterogeneity constant. The Sips model describes behavior depicted by the Langmuir model when n_s is equal to unity and confers a homogenous sorbent surface. The accessibility of the CD inclusion sites (*i.e.*, % bound phenolphthalein) of the copolymer materials is related to the decolourization of phenolphthalein in the presence of copolymer by Eq. (6):

$$\left(\frac{C_o - C_e}{C_o}\right) \times 100\% \tag{6}$$

where C_o is the total concentration of phth and C_e is defined as in Eq. (5). The error contributions for C_o and C_e are related to uncertainties in absorbance of the dye. Therefore, it is necessary to differentiate Eq. (6) with respect to each concentration parameter (*i.e.*, C_o and C_e). Thus, the total error for the site accessibility is described by the following expression:

$$\frac{\partial}{\partial C_o}\left(\frac{C_o - C_e}{C_o}\right) + \frac{\partial}{\partial C_e}\left(\frac{C_o - C_e}{C_o}\right) = 2\left|\frac{-C_e}{C_o^2}\right| \Delta C_o + 2\left|\frac{-1}{C_o}\right| \Delta C_e \tag{7}$$

where ΔC_o and ΔC_e are the standard errors, respectively. It should be noted that there is both a positive and negative error contribution with respect to each data point, as depicted by the scaling factor which precedes the absolute value of each quantity in Eq. (7).

The site occupancy of the adsorbate and the corresponding ΔG° of complex formation are defined as follows:

$$\theta = \frac{Q_e}{Q_m} \tag{8}$$

$$\Delta G^\circ = -RT \ln K_{eq} \tag{9}$$

R is the gas constant ($J\,mol^{-1}\,K^{-1}$), T is temperature in K, and K_{eq} is defined by Eq. (5). The Sips model parameters are forthwith interpreted in the same manner as the formation of the 1:1 β-CD/phth inclusion complexes (*cf.* Eq. (1)); where $K_{eq} \approx K_1$.

3. Results and discussion

3.1. Synthesis

For brevity, the nomenclature adopted for the crosslinked copolymers is described according to the type of crosslinker used and the co-monomer mole ratio (β-CD:crosslinker agent). For example, the 1:15 β-CD:EP copolymer designation is referred to as EP-*X* (*X* = 15 moles of EP) and the molar quantity of β-CD is unity. The nomenclature for β-CD grafted onto PAA is defined on a weight basis where the weight of PAA is assumed to be unity relative to the mass of β-CD. Therefore, PAA-5 refers to a β-CD:PAA co-monomer weight ratio of 5:1 (w/w). The use of weight ratios for the β-CD:PAA is more appropriate than mole ratios due to the comparatively large molecular weight of PAA relative to β-CD.

3.2. Sorption of phth with β-CD crosslinked copolymers

The phth decolourization increased as the relative amount of copolymers increased whilst the value for C_{phth} was maintained constant. Attenuated removal of phth occurs as the crosslinking increases (*cf.* Fig. 1a and b). This is evident according to the estimates of the accessible β-CD (%) for the 1:1 (72.4%), 1:2 (67.9%), and 1:3 (12.1%) for TCL-based copolymer materials; and 1:1 (54.3%), 1:2 (33.1%), and 1:3 (12.9%) for the SCL-based copolymer materials. The greater removal of phth at low levels of crosslinking implies that phth forms well-defined 1:1 complexes with the β-CD inclusion sites in the polymer framework, thus contributing to decolourization of the dye. As discussed previously (Mohamed et al., 2010), increasing the crosslink density generally attenuates the sorption properties of the copolymer materials for two likely reasons: (i) steric crowding of the hydroxyl annular region of β-CD and (ii) reduced access to the micropore framework and the β-CD inclusion sites. According to the space filling models of Taguchi (1986), inclusion of the benzenoid form of phth (*cf.* Scheme 2; Taguchi, 1986) and H-bonding between the phenolate anions with the hydroxyl groups of β-CD contribute to the formation of the transparent 1:1 β-CD/phth dianion inclusion complex. Increased substitution in the annular hydroxyl region of β-CD inhibits favourable H-bonding with phth and decreases the inclusion binding of this host–guest complex. Thus, the expected steric effects are consistent with the attenuated decolourization of phth for highly crosslinked copolymers, as observed in Fig. 1a and b. In addition, copolymers with greater levels of crosslink density result in reduced access of phth to the microporous domains of the copolymer framework. Consequently, reduced decolourization of phth is observed because of steric restrictions in the annular hydroxyl region of β-CD, as described above.

In Fig. 1a, the TCL-1 copolymer displayed the greatest removal of phth; whereas, TCL-2 and -3 copolymers show reduced removal of phth from solution. A comparison of TCL and SCL indicates that

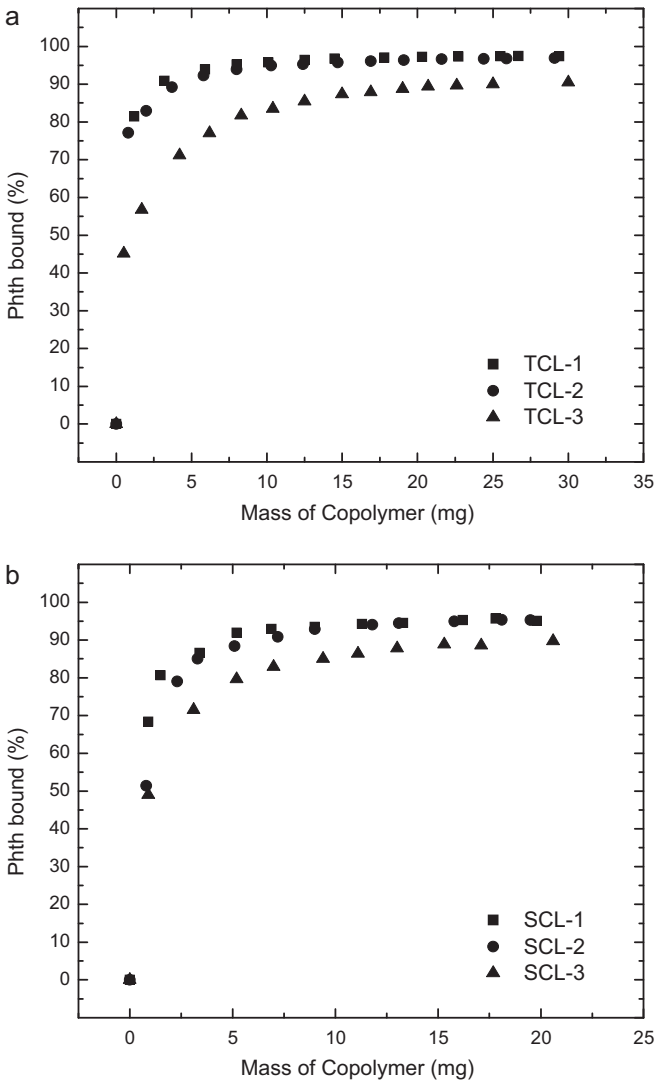


Fig. 1. Percentage of bound phenolphthalein from aqueous solution with copolymer materials in 0.1 M $NaHCO_3$ buffer at pH 10.5 and 295 K at the crosslinking ratio β-CD:crosslinker of 1:1, 1:2 and 1:3: (a) terephthaloyl chloride (TCL) and (b) sebacoyl chloride (SCL).

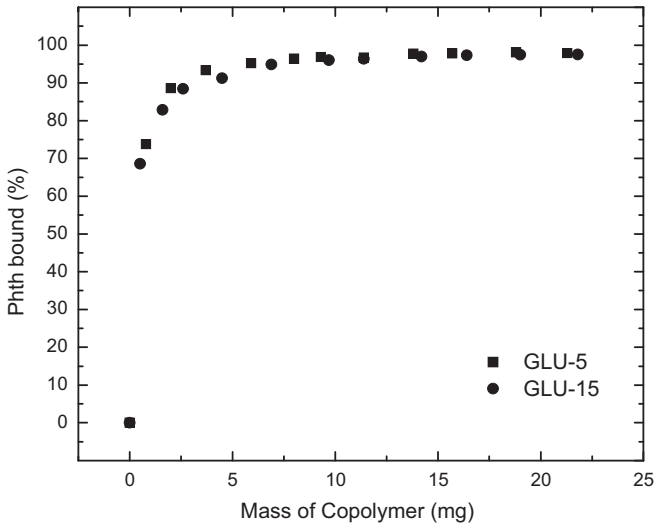


Fig. 2. Percentage of bound phenolphthalein from aqueous solution with β-CD crosslinked with glutaraldehyde (GLU) in 0.1 M $NaHCO_3$ buffer at pH 10.5 and 295 K at the crosslinking ratio β-CD:GLU of 1:5 and 1:15, respectively.

the latter is a bulkier linker molecule with a greater surface-to-volume ratio, and the observed steric effects of SCL, are more pronounced as compared with TCL (Fig. 1b). Fig. 2 depicts the removal efficiency for copolymer materials containing a crosslinker with reduced molecular weight (GLU) relative to TCL and SCL. The observed decolourization and the relative size of the crosslinker provide support that steric hindrance plays a significant role in the accessibility of the β-CD inclusion sites of such copolymer materials. β-CD crosslinked with GLU at the 1:3 and 1:15 mole ratios reveal similar accessibility values of 68.7% and 64.6%, respectively. Although GLU is a smaller moiety relative to TCL and SCL (*cf.* Fig. 3), the steric effects are less pronounced at elevated levels of crosslinking. For example; GLU-15 exhibits comparable accessibility of the β-CD sites as compared with TCL-2 (*i.e.*, 65% *vs.* 68%).

Fig. 4a–c illustrates changes in absorbance (Abs) of phth *vs.* $C_{\beta\text{-CD}}$ for copolymers containing β-CD at a fixed concentration of phth (C_{phth}). The solid lines through the experimental data represent the calculated Abs values according to the NLLS fitting routine as described by Eq. (4). The decrease in Abs as $C_{\beta\text{-CD}}$ increases is more gradual as the crosslinker content increases for each of the copolymers studied. In the case of TCL and GLU (*cf.* Fig. 4a and c), the steep falloff is more evident when compared with SCL (*cf.* Fig. 4b). Lower levels of crosslinking indicate that inclusion binding of phth is favoured for this system. Pronounced attenuation of phth binding is observed for copolymers with the highest crosslinker mole content among the copolymer materials. The steric effect appears to further correlate with the relative size of the linker. The decolourization of phth for each respective copolymer is listed in descending order as follows: SCL > TCL > GLU. This observation suggests that the relative size of the linker plays a steric role by affording variable accessibility to the inclusion sites of β-CD, the hydrophile–lipophile balance of the linker in the copolymer framework, and its relative solvent accessibility. The effect of increasing substitution in the annular hydroxyl region of β-CD with bi-functional crosslinkers at greater levels of crosslinking was previously described (*cf.* Scheme 3; Mohamed et al., 2010). As steric crowding occurs at the narrow end of the β-CD annulus, crosslinkers react at the wider secondary annular region until the degree of substitution approaches ~3 at each annular face (Mohamed et al., 2010). A previous study (Glazyrin, Grachev, Kurochkina, & Nifant'ev, 2004) of various modified forms of β-CD indicate that a 4-fold to 40-fold decrease in the 1:1 binding constant was observed for acetylated and hydroxypropyl substituted β-CD when the average degree of substitution

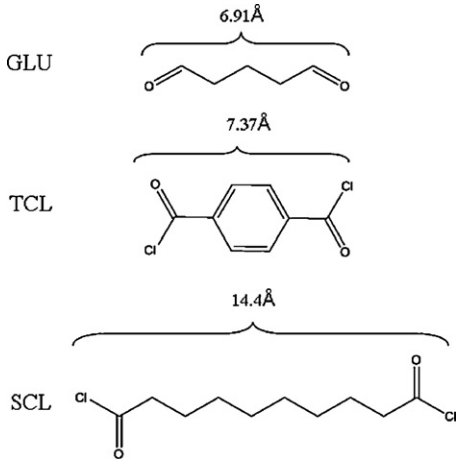


Fig. 3. Size of glutaraldehyde (GLU), terephthaloyl chloride (TCL) and sebacoyl chloride (SCL) calculated using Spartan'08 V1.2.0.

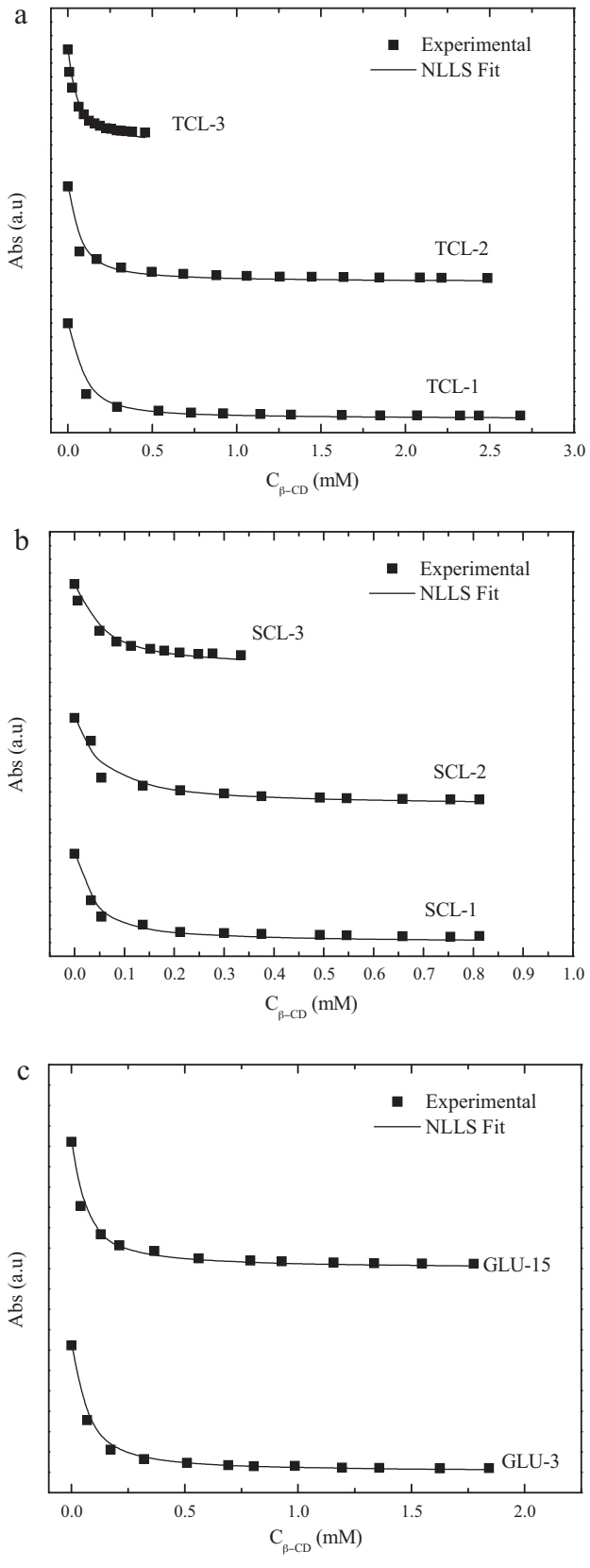


Fig. 4. Absorbance changes for phenolphthalein as a function of increased mole content of β-CD ($C_{\beta\text{-CD}}$) for insoluble copolymers at variable mole ratios at pH 10.5 in 0.1 M $NaHCO_3$ and 295 K: (a) β-CD:TCL, (b) β-CD:SCL, (c) β-CD:GLU, and (d) β-CD:EP. The solid line refers to the NLLS best-fit according to Eq. (4) $K_1 = 2.66 \times 10^4\ M^{-1}$ and the fraction bound of β-CD (CD–phth) is an adjustable parameter between 0 and 100 mol%.

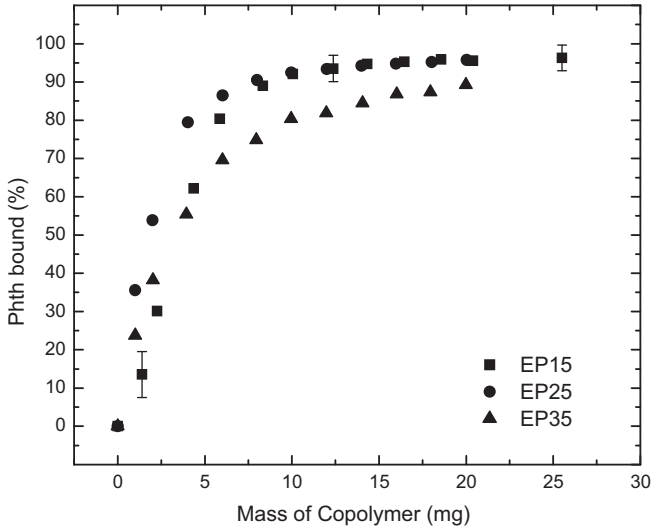
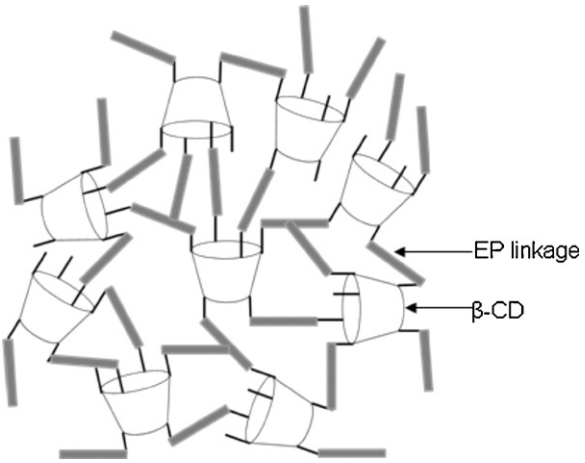


Fig. 5. Percentage of bound phenolphthalein from aqueous solution with β-CD epichlorohydrin copolymers in 0.1 M $NaHCO_3$ buffer at pH 10.5 and 295 K at the crosslinking ratio β-CD:EP of 1:15, 1:25 and 1:35. Error bars are shown according to Eq. (7) where sample errors are shown a low, intermediate, and high mass values of copolymer material. The errors correspond to 6.03%, 3.45%, and 3.35%, respectively.

reaches ~3.8–3.6. Thus, the binding of β-CD and some of its water-soluble derivatives may form complexes with phth depending on the structure, site of substitution (i.e., 2-, 3-, and 6-hydroxyl positions), and the degree of substitution of β-CD, respectively.

3.3. Sorption of phth with β-CD epichlorohydrin copolymers

Similar to TCL-, SCL- and GLU-based copolymers, the EP-based materials show comparable decolourization of phth as the relative amount of the copolymer was increased whilst the value for C_{phth} was constant. The decolourization results provide support that phth forms 1:1 inclusion complexes between phth and β-CD within the copolymer framework. Fig. 5 illustrates the bound phth *vs.* the mass of EP-based copolymers along with error bar estimates of the bound phth (*cf.* Eq. (6)) according to Eq. (7). The error bar estimates are listed in brackets for low (3.35%), intermediate (3.45%), and high (6.03%) mass values of copolymer. The errors presented in Fig. 5 are representative of such plots and are not shown elsewhere for the sake of clarity. The results show a more gradual change in decolourization as the mass of the copolymer increases, indicating that the materials attenuate the formation of β-CD/phth complexes. The relative accessibility of the EP-based copolymers are given in descending order: EP-25 (33.0%) > EP-15 (21.8%) > EP-35 (15.5%). The estimates indicate that EP-25 has less steric hindrance whereas EP-35 had the greatest. This observation could be due to the fact that EP-35 favoured formation of an A-B_n type copolymer as opposed to the A-B type copolymer, *i.e.*, at higher values of EP. Beyond the 1:21 (β-CD:EP) mole ratio, one may predict that the excess EP results in extensive crosslinking between EP chains and/or the formation of EP oligomer domains. This is a consequence of the fixed number of hydroxyl groups (*i.e.*, 21) of β-CD available for reaction with EP. Therefore, the occurrence of extensive crosslinking (*cf.* Scheme 1) inhibits access of phth to the inclusion and micropore adsorption sites. The relatively high crosslinking ratios employed herein for the β-CD:EP copolymers yields insoluble materials in aqueous solution; whereas, CD:EP copolymers with co-monomer ratios ≤ 1:10 are known to be water soluble (Orprecio & Evans, 2003).



Scheme 1. Highly crosslinked β-CD:EP copolymer. For purpose of clarity the copolymer framework is depicted at low levels of crosslinking relative to the conditions (*i.e.*, 1:15–1:35) employed in this study.

3.4. Sorption of phth with β-CD PAA grafted copolymers

Fig. 6 illustrates results observed for bound phth *vs.* the mass of β-CD:PAA copolymer. Similar to the EP-based copolymers, a gradual increase in the amount of bound phth with increasing mass of the copolymer is observed for both PAA-5 and PAA-10. The results indicate the materials are less effective at sequestering phth from aqueous solution. PAA-5 had a similar number of accessible sites

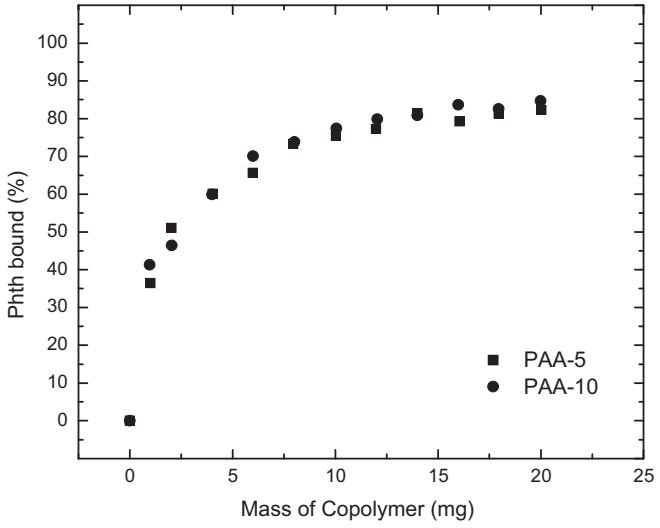


Fig. 6. Percentage of bound phenolphthalein from aqueous solution with β-CD crosslinked with epichlorohydrin in 0.1 M $NaHCO_3$ buffer at pH 10.5 and 295 K at the crosslinking ratio β-CD:PAA of 5:1 and 10:1.

Table 1
Phenolphthalein based estimates (%) of the surface accessible β-CD site in the macrocycle-based materials, fractional coverage, θ[a], at 1 mg of the copolymer and Gibbs free energy change[b], ΔG complex formation with phth in aqueous solution at pH 10.5 and 295 K.

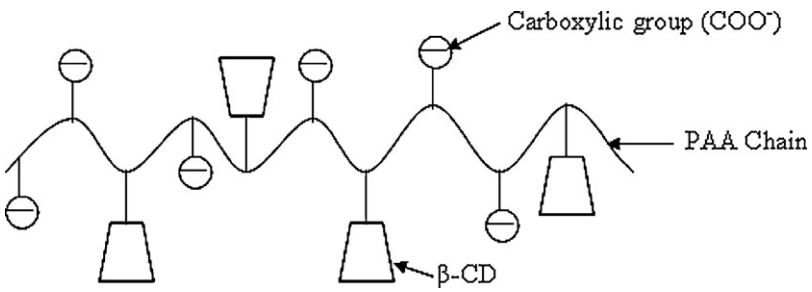
Material	% accessible	θ	ΔG° (kJ mol^{-1})[b]
TCL-1	72.4	0.476	−29.4
TCL-2	67.9	0.636	−29.8
TCL-3	12.1	0.362	−25.3
SCL-1	54.3	0.723	−29.9
SCL-2	33.1	0.918	−30.9
SCL-3	12.9	0.891	−29.6
GLU-3	68.7	0.585	−30.0
GLU-15	64.6	NR[c]	NR[c]
EP-15	21.8	0.0513	−30.5
EP-25	33.0	0.126	−27.6
EP-35	15.5	0.0541	NR[c]
PAA-5	16.0	NR[c]	NR[c]
PAA-10	12.6	NR[c]	NR[c]

[a] θ: refer to Eq. (6).
[b] ΔG°: refer to Eq. (7).
[c] NR: not reported because the surface accessibility was too low resulting in poor fits according to the Sips isotherm model (*cf.* Eq. (5)).

(16.6%) compared with PAA-10 (12.6%), and these types of grafted copolymer materials have the lowest number of accessible sites among the four types of materials studied. The low accessibility is attributed to the Coulombic repulsion of the ionized carboxylic groups of the PAA (*cf.* Scheme 2) with the phth dianion at these conditions. The repulsive interactions with the ionized carboxylate groups on the PAA backbone retard the formation of inclusion complexes with the β-CD-PAA copolymer. Similar observations were made in a recent sorption (Guo & Wilson, 2009) for -CD-PAA copolymer materials with the *p*-nitrophenolate anion at pH = 9.0 in aqueous solution.

3.5. Standard Gibbs free energy and site occupancy

Table 1 shows the Gibbs free energy change of complex formation (ΔG°) and provides independent support for the 1:1 binding constants between phth and native β-CD and copolymer materials containing β-CD. Relative to the Langmuir model (*cf.* Eq. (5) where $n_s = 1$) model, the unrestricted Sips model provides a better description of the results and may indicate that the linkers affect the decolourization of phth in a limited fashion. However, the formation of the 1:1 inclusion complexes between β-CD based copolymers with phth is the predominant mechanism responsible for the observed decolourization. In Table 1, the site occupancy does not show well-defined trends that correlate with the co-monomer mole ratios of the copolymers. This is attributed to the nature of the crosslinker, as described above. As well, the experimental conditions cover a limited range of copolymer/phth ratios which limit the accuracy of the modeling and the respective Q_m values obtained. As evidenced in Table 1, the Gibbs free energy change depends on the site occupancy of the β-CD sorption sites since



Scheme 2. PAA chain with deprotonated carboxylic groups at pH 10.5 (*i.e.*, pH > pK_a) at those conditions. *Note*: phth exists as a dianion species at these pH conditions.

the magnitude of the equilibrium binding constant is directly proportional to the relative accessibility of the inclusion binding site of β-CD. Moreover, the magnitude of ΔG° for the copolymers is slightly more favourable than the value for the 1:1 β-CD/phth complexes ($\Delta G^{\circ} = -25\,kJ\,mol^{-1}$) (Mohamed et al., 2009; Wilson et al., 1997). Notwithstanding the potential steric effects arising from the crossslinking effects of the framework, the small differences in ΔG° may be related to differences in hydration of the copolymer and surface effects (Glazyrin et al., 2004).

This dye-based sorption method represents a facile, versatile, and relatively low cost analytical method for the evaluation of the inclusion site accessibility of β-CD based copolymer materials. In particular, this approach offers a high degree of molecular inclusion selectivity towards phenolphthalein and provides useful insight about the sorption properties of sorbent materials containing β-CD. This method is relatively sensitive and molecular selective for copolymers containing β-CD. This method is anticipated to have extensive analytical applications for materials researchers who wish to design advanced functional sorbent materials containing β-CD (i.e., beads, thin films, fibres, etc.) for sorption-based applications.

4. Conclusions

Accessibility of the β-CD inclusion sites was determined using a dye-based study of water insoluble copolymer materials containing β-CD in aqueous solution at pH 10.5 and 295 K. This study illustrates the versatility and general applicability of phth as a molecular selective probe for the determination of the surface accessible β-CD sites for a wide range of copolymer materials. The decolourization results support that the formation of 1:1 β-CD/phth inclusion complexes occur for solid-solution equilibria. The Gibbs free energy change for the formation of 1:1 complexes between phth and β-CD copolymer materials ranged from −27.6 to $-30.9\,kJ\,mol^{-1}$, according to the Sips isotherm. The copolymers display behavior comparable to the 1:1 β-CD/phth complex in aqueous solution. In general, the accessibility of the β-CD sites decrease as the co-monomer ratio increases. The decolourization results reveal that the β-CD:PAA copolymer materials have much lower inclusion site accessibility. The attenuated inclusion site accessibility is attributed to the Coulombic repulsions between the phth dianion species and the PAA carboxylate anion sites.

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