

## Cyclodextrin-based Dendritic Supramolecules; New Multivalent Nanocarriers

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### Additional information

#### Materials

Triphenylphosphine was purchased from Merck and recrystallized in methanol prior use. Iodine and sodium methoxide were purchased from Aldrich and used without further purification.  $\beta$ -Cyclodextrin was provided from Fluka and dried prior use. Ferrocene, palladium (II) chloride, sodium borohydride (NaBH<sub>4</sub>), 2-ethyl-2-oxazoline, methanol, diethyl ether, tetrahydrofuran (THF), aniline and diethanolamine were purchased from Merck. DMF was purchased from Merck and distilled from CaH<sub>2</sub>. Multi-wall carbon nanotubes (MWNTs) were prepared by chemical vapor deposition procedure in the presence of Co/Mo/MgO as catalyst at 900 °C. The outer diameter of MWCNT was between 20-40 nm.

#### Instruments

The transmission electron microscopy (TEM) images were obtained using a LEO 912AB electron microscope with accelerating voltage of 200 kV. A Shimadzu UV-visible 1650 PC spectrophotometer was used for recording absorption spectra in solution using a cell of 1.0 cm path length. Infrared (IR) spectra were recorded by a Nikolt 320 FT-IR. Differential scanning calorimetry (DSC) thermograms were recorded using TA-60 WS differential scanning calorimeter under air atmosphere. Samples about 1 mg were placed in the aluminium type pans and were heated at the rate of 13 °C/min to 500 °C. <sup>1</sup>H NMR spectra were recorded in D<sub>2</sub>O solution on a bruker DRX 400 (400 MHz) apparatus with the solvent proton signal for reference. Dynamic light scattering (DLS) diagrams were obtained using a Malvern-zs 20.4. The molecular weight distributions were determined by gel permeation chromatography (GPC) using Pump 1000 using PL aquagel-OH mixed- H 8 mm column connected to a differential refractometer, RI with water as the mobile phase at 25 °C. Pullulan standard samples were used for calibration.

## Experimental Procedures

### Synthesis of per-7-iodo- $\beta$ -cyclodextrin (CD-I)

Per-7-iodo- $\beta$ -cyclodextrin (CD-I) was synthesized according to reported procedure in literature [1]. Iodine (20.25 g, 80 mmol) was added to a solution of triphenylphosphine (20.2 g, 80 mmol) in dried DMF (70 ml) under continuous stirring. Afterward, dried  $\beta$ -cyclodextrin (5.8g, 5 mmol) was added into the reaction flask and mixture was stirred at 70 °C under N<sub>2</sub> atmosphere for 18 h. The reaction solution was then concentrated at 60 °C by reduced pressure to half volume. The pH was adjusted to 9-10 by addition sodium methoxide in methanol (3 M) while mixture was cooling to room temperature simultaneously. The mixture was kept at room temperature to destroy the formate esters formed in the reaction, after 1 h it was poured into methanol to obtain a precipitate. The precipitate was separated from methanol by filtration. Then it was washed with methanol and dried by vacuum oven to obtain the final product as white powder (45% yield).

### Synthesis of $\beta$ -cyclodextrin-poly(2-ethyl-2-oxazoline) having aniline termination moieties (CD-POX-A)

2-ethyl-2-oxazoline (2.25 ml, 22 mmol) was added to a solution of CD-I (0.3 g, 0.157 mmol) in dried DMF (10 ml) at 25 °C under continuous stirring. The reaction solution was then stirred at 140 °C under N<sub>2</sub> atmosphere for 24 h. Afterward the temperature of reaction was reduced to 80 °C and a solution of aniline (excess) in dried DMF was injected into the reaction flask and it was stirred for 12 h at the same temperature. After filtration and evaporation of solvent, the product was precipitated in diethyl ether and dried by vacuum oven at 50 °C for 1 h.

### Synthesis of $\beta$ -cyclodextrin-poly(2-ethyl-2-oxazoline) having diethanolamine termination moieties (CD-POX-D)

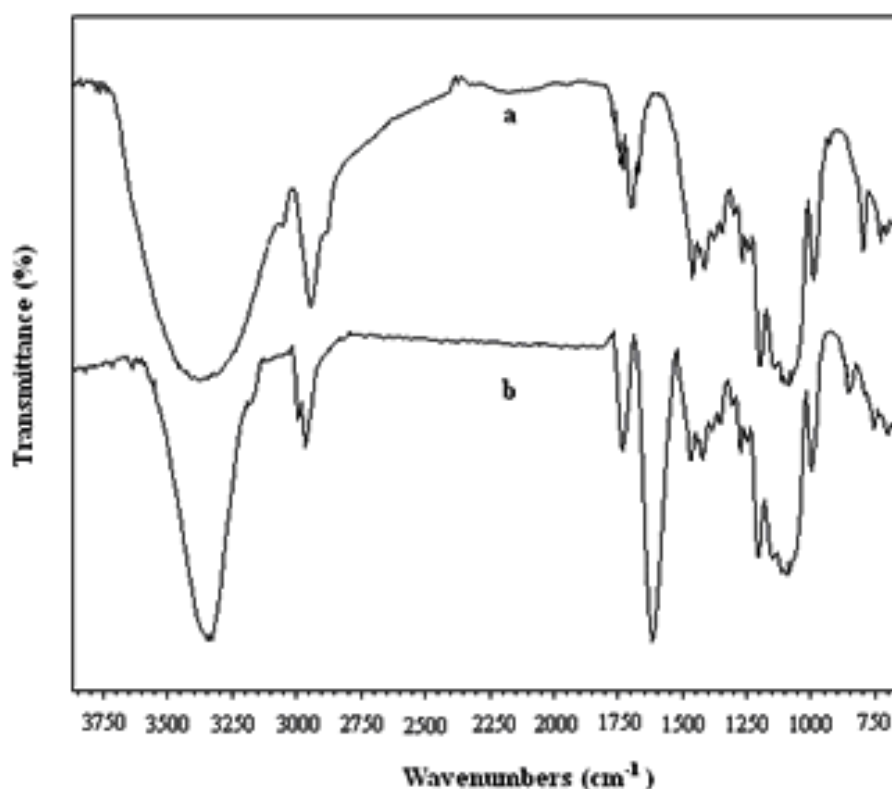
(CD-POX-D) was prepared in the same manner that was used to produce CD-POX-A except that diethanolamine was used instead of the aniline.

### Opening of MWCNTs

Multi-walled carbon nanotubes (MWNTs) were opened according to reported procedure in literature [2]. Briefly, MWNTs (2g) were added to 30 mL of H<sub>2</sub>SO<sub>4</sub> and HNO<sub>3</sub> mixture (3:1) in a reaction flask and refluxed at 120 °C for 24 h. The mixture was cooled and diluted by distilled water and then it was filtered. The product (MWNTs-COOH) was washed by distilled water and dried by vacuum oven.

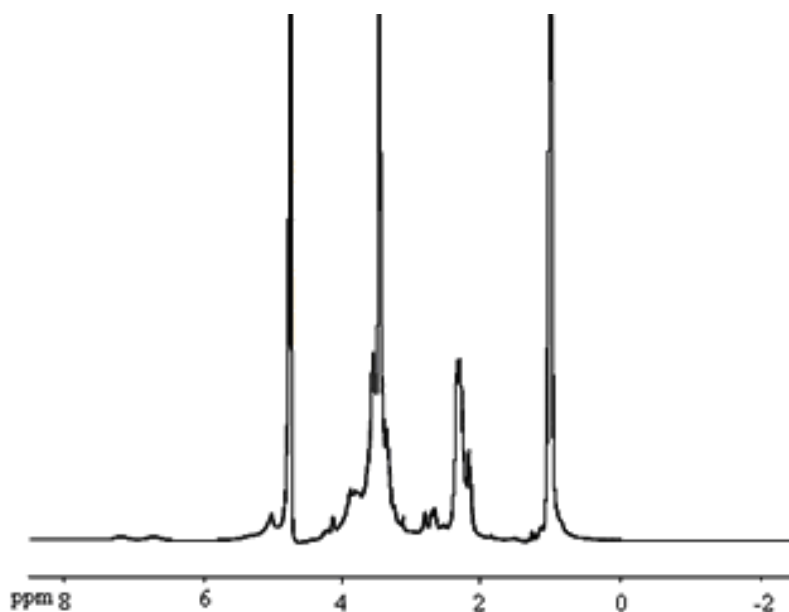
## Discussion

IR spectroscopy was used in order to investigate the structure of synthesized materials. Figure ESI1a shows the IR spectrum of CD-I. In this figure, absorbance bands at 3380, 2920, 1151, 1039 and 670 cm<sup>-1</sup> can be attributed to the O-H, C-H, C-O-C, C-OH and C-I stretching vibrations respectively. Appearance of the absorbance band of C-I in this spectrum confirms the iodination of cyclodextrin. As it can be seen the absorbance band of the C-I bond which had been appeared at 670 cm<sup>-1</sup> for CD-I is disappeared in the IR spectrum of CD-POX-A and a new peak at 1630 cm<sup>-1</sup> is appeared. This result shows that a nucleophilic reaction between 2-ethyl-2-oxazoline monomer and CD-I has been occurred and iodide has been substituted by nitrogen of 2-ethyl-2-oxazoline. On the other hand appearance of an absorbance band at 1630 cm<sup>-1</sup> is assigned to the amide bond of polyoxazoline, confirming the cationic ring opening polymerization of 2-ethyl-2-oxazoline and conjugating of polyoxazoline arms to cyclodextrin (Fig. ESI1b).



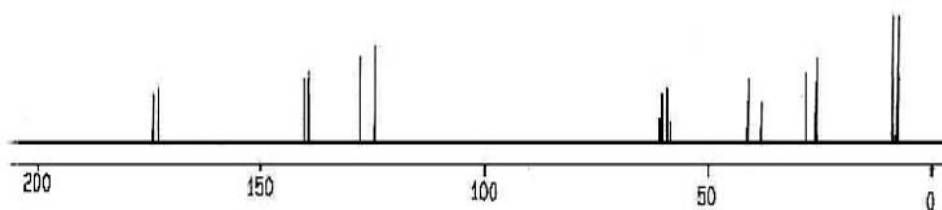
**Fig. ESI1** FT-IR spectra of (a) CD-I and (b) CD-POX-A.

Signals of all segments of CD-POX-A hybrid material, CD core, POX arms and aniline termination moieties, can be found in the  $^1\text{H}$ -NMR spectrum of this compound (Fig. ESI2). Signals at 3.4-5 ppm are assigned to the protons of  $\beta$ -CD core. Two signals appeared at 1.1 and 2.3 ppm are attributed to  $\text{CH}_3$  and  $-\text{CO}-\text{CH}_2-$  groups of POX arms. Signal of  $-\text{NCH}_2$  has overlapped with those for  $\beta$ -CD at 3.45 ppm. Protons of aromatic ring of termination aniline moieties can be observed at 6.7 and 7.1 ppm. A significant signal at 5.1 ppm is appeared in this spectrum which is attributed to the anomeric proton of cyclodextrin core. This signal proves attachment of the polyoxazoline arms to the cyclodextrin core.



**Fig. ESI2**  $^1\text{H}$  NMR spectrum of CD-POX-A in  $\text{D}_2\text{O}$ .

$^{13}\text{C}$  NMR spectrum of CD-POX-A is displayed in the Fig. ESI3. Signals of  $\beta$ -CD segments are appeared at 58-61 ppm. Signals of POX are appeared at 41.45, 26.1 and 8.7 ppm for  $-\text{NCH}_2$ ,  $-\text{CO}-\text{CH}_2-$  and methyl groups, respectively. Signals at 173 and 174 ppm are assigned to the different carbonyl groups of POX chains. Signals at 124-141 ppm are attributed to the carbons of aniline segments.



**Fig. ESI3**  $^{13}\text{C}$  NMR spectrum of CD-POX-A in  $\text{D}_2\text{O}$ .

Figure ESI4 shows the DSC thermograms of  $\beta$ -CD, CD-I, CD-POX-A and CD-POX-D. As can be seen in this figure, thermograms of CD-POX-A and CD-POX-D are different from that of the CD-I. In the DSC thermogram of  $\beta$ -CD endothermic peaks at 80-120 °C and 310 °C are assigned to the evaporation of the water molecules inside the cavity of cyclodextrin and its melting point, respectively. In the DSC thermogram of CD-I, endothermic peaks of the evaporation of water molecules and also the melting point of  $\beta$ -CD are disappeared and a new exothermic peak at 230 °C corresponding to the decomposition of CD-I is appeared. In the DSC thermogram of CD-POX-A, the endothermic peaks appeared at 80-112 °C and 204 °C are attributed to the release of water molecules and decomposition of CD-POX-A, respectively. The endothermic peaks corresponding to the evaporation of the water molecules and decomposition of CD-POX-D can be seen at the 90-105 °C and 240 °C in related DSC thermogram, respectively. It is interesting to note that the exothermic peak at 230 °C corresponding to the decomposition of CD-I completely disappears from the DSC thermograms of CD-POX-A and CD-POX-D, indicating the replacement of iodine groups of CD-I by the oxazoline monomers.

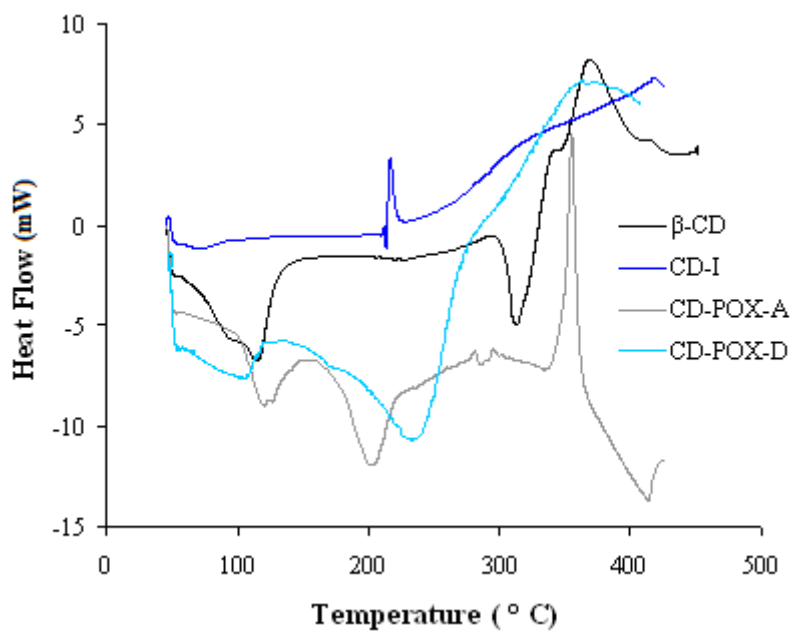
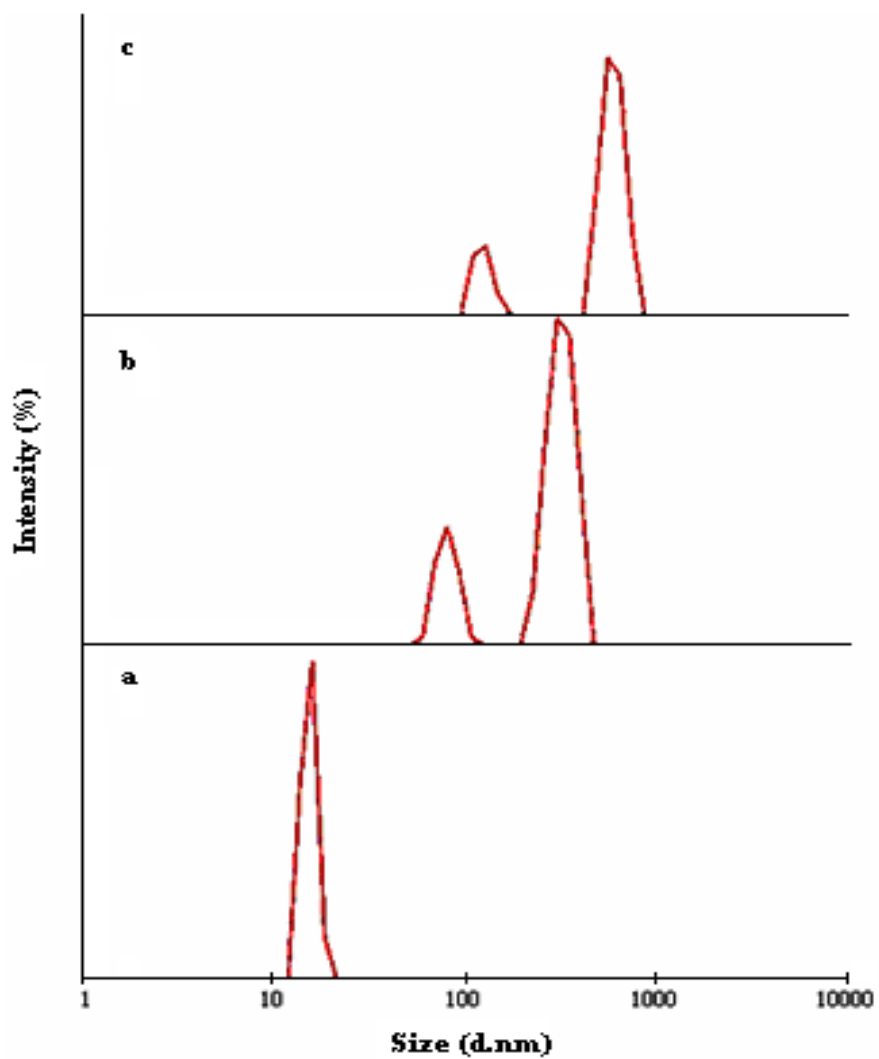
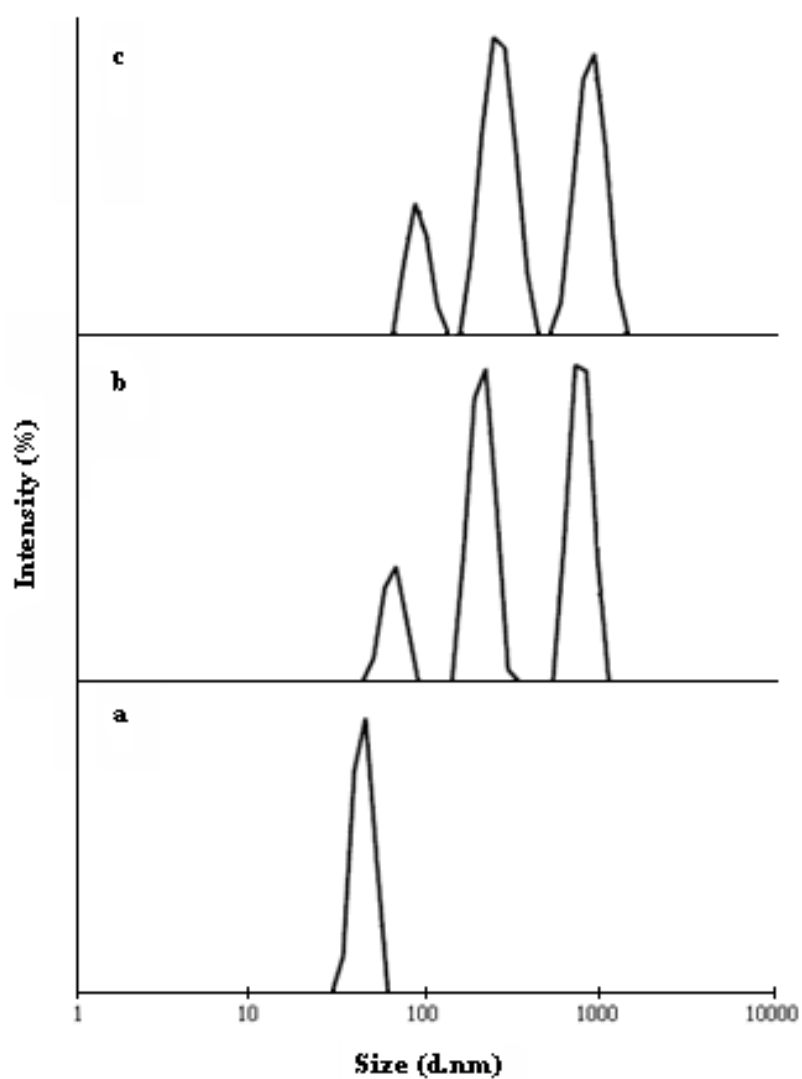


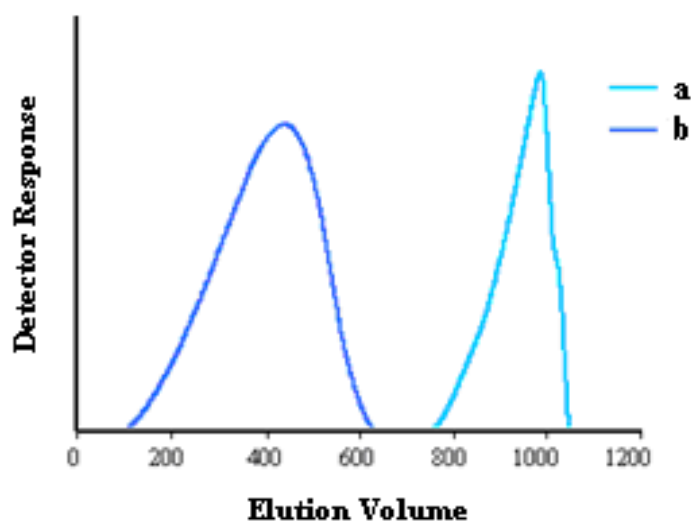
Fig. ESI4 DSC curves of  $\beta$ -CD, CD-I, CD-POX-A and CD-POX-D.



**Fig. ESI5** DLS diagrams of aqueous solution of CD-POX-A in the concentration of (a) 0.5 mg·mL<sup>-1</sup>, (b) 1 mg·mL<sup>-1</sup> and (c) 2 mg·mL<sup>-1</sup>.



**Fig. ESI6** DLS diagrams of aqueous solution of CD-POX-D in the concentration of (a)  $0.5 \text{ mg}\cdot\text{mL}^{-1}$ , (b)  $1 \text{ mg}\cdot\text{mL}^{-1}$  and (c)  $2 \text{ mg}\cdot\text{mL}^{-1}$ .

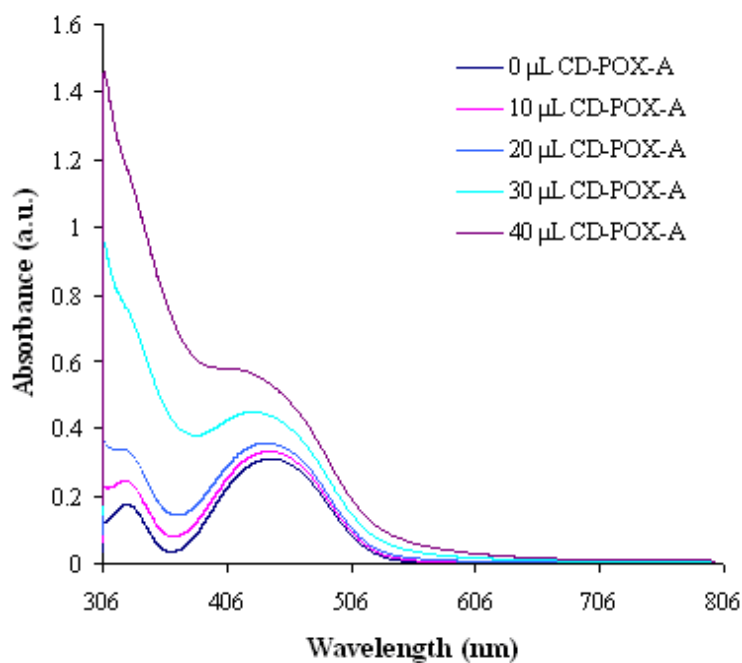


**Fig. ESI7**

aqueous

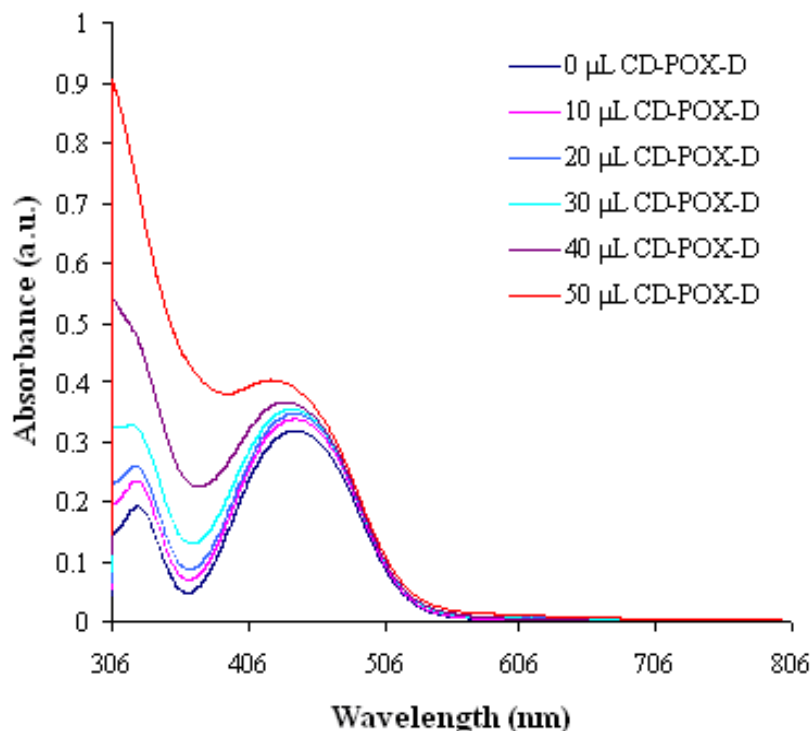
POX-A in the concentration of (a)  $0.04 \text{ mg}\cdot\text{mL}^{-1}$  and (b)  $0.1 \text{ mg}\cdot\text{mL}^{-1}$ .

GPC diagrams of  
solution of CD-



**Fig. ESI8** Absorption spectrum of ferrocene ( $0.02 \text{ M}$ ) in water/ tetrahydrofuran ( $1:1 \text{ (v/v)}$ ) mixture upon addition of 10, 20, 30 and 40  $\mu\text{L}$  of CD-POX-A aqueous solutions ( $0.06 \text{ mg}\cdot\text{mL}^{-1}$ ).

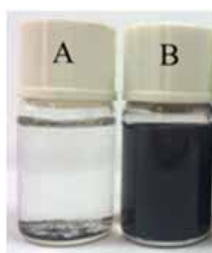




**Fig. ESI9** Absorption spectrum of ferrocene (0.02 M) in water/ tetrahydrofuran (1:1 (v/v)) mixture upon addition of 10, 20, 30, 40 and 50  $\mu\text{L}$  of CD-POX-D aqueous solutions ( $0.06 \text{ mg}\cdot\text{mL}^{-1}$ ).

In a typical experiment, CNTs were added to an aqueous solution of CD-POX-A or CD-POX-D, and then the mixture was sonicated for 30 min at room temperature.

CD-POX-A was not able to soluble CNTs in water and CNTs were immediately precipitate out of aqueous solution of CD-POX-A (a in Fig. ESI10). However, non-covalent interactions between CNTs and CD-POX-D led to stable aqueous solutions of carbon nanotubes (b in Fig. ESI10). This result prove that aniline end groups of CD-POX-A prefer formation of inclusion complexes with  $\beta$ -CD core than  $\pi$ - $\pi$  staking interactions with the surface of CNTs while in the case of CD-POX-D which is not containing groups to form inclusion complexes with  $\beta$ -CD core interactions with the CNTs surface are preferred than weak interactions between individual CD-POX-D polymers.



**Fig. ESI10** Photo images of a mixture of (a) CNT and CD-POX-A and (b) CNT and CD-POX-D in water.

#### **Additional references**

- 1 S-W. Choi, J-H. Jang, Y-G. Kang, C-J. Lee and J-H. Kim, *Colloids and Surfaces A: Physicochem. Eng. Aspects*, 2005, **257–258**, 31-36.
- 2 M. Adeli, E. Mehdipour and M. Bavadi, *J Appl Polym Sci*, 2010, **116(4)**, 2188.