

Supramolecular Solubilization of Cyclodextrin-Modified Carbon Nano-Onions by Host–Guest Interactions

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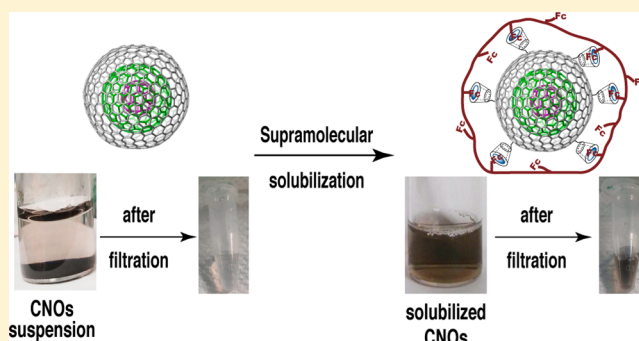
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Supporting Information

ABSTRACT: Small carbon nano-onions (CNOs, 6–12 shells) were prepared in high yields and functionalized with carboxylic groups by chemical oxidation and reacted with β CD-NH₂ to yield CNOs decorated with β CDs. A biocompatible dextran polymer with grafted ferrocene groups was employed for the supramolecular self-assembly on the β CD-CNO surfaces. The β CDs act as hosts and the polymer ferrocene groups as guests (Fc-Dex) by the formation of inclusion complexes. After their assembly these nanostructures were soluble in aqueous solutions. The resulting product was characterized by transmission electron microscopy (TEM), thermogravimetric analysis (TGA), and FT-IR and Raman spectroscopies. Moreover, the deposition of successive layers on the surface of the particles was monitored using DLS measurements and zeta potentials. Through-space interactions between the Fc moieties and the CNO cores and the influence of an additional dextran- β CD outer layer were measured electrochemically.



INTRODUCTION

Since the revolutionary discovery of fullerenes, the field of carbon nanoscience has expanded considerably and gained considerable interest from a number of research groups.¹ The unique all-carbon structures of closed-cage molecules (fullerenes) exhibit many uses in areas ranging from material science to medicinal chemistry because of their electronic properties and nanometer dimensions.² During the initial stages of fullerene research two very important discoveries were made: the formation of carbon nanotubes (CNTs) and of carbon nano-onions (CNOs).³ CNOs, also known as multilayer fullerenes, are built from concentric graphitic shells forming quasi-spherical structures. CNOs can be considered as spherical analogues of multiwalled carbon nanotubes.⁴ However, although CNOs were discovered almost at the same time as CNTs, they have received much less attention to date.

In 1992, Ugarte clearly observed CNOs for the first time upon strong electron beam irradiation of CNTs.⁵ The large scale preparation of CNOs was not realized for many years, but 13 years ago an effective method for CNOs preparation was reported.⁶ Since then, research with CNOs began to attract more interest from different scientific groups as they could be prepared more efficiently and in higher yields.

Some preparation methods of CNOs include high temperature annealing of nanodiamond particles,⁷ implantation of carbon atoms on silver particles⁸ and laser vaporization of composite carbon–metal targets under low helium pressures and in the presence of C₆₀ as a nucleating center.⁹ The last technique is claimed to be very efficient for the production of very small CNOs such as the double-shelled C₆₀@C₂₄₀ and the triple-shelled C₆₀@C₂₄₀@C₅₄₀.^{10,11} Producing CNOs with few layers is highly desirable in order to increase the ability to modify them by chemical reactions, since small-radius particles have greater surface curvature and strain energy and, thus, higher chemical reactivity.³ Chemical functionalization of CNOs plays a crucial role in their potential applications as they exhibit very low solubility or dispersity in most organic and/or inorganic solvents in their pristine state. Surface modification of CNOs increases their solubilities in a variety of solvents.¹² Several methods have been reported for covalent functionalization of CNOs, for instance, esterification, amidation,^{3,4} oxidation reactions at defects with nitric acid or a mixture of sulfuric and nitric acids,¹² 1,3-dipolar cycloaddition

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of azomethine ylides,^{13,14} [2 + 1] Bingel–Hirsch cyclopropanation,¹⁵ polymerization,¹⁶ treatment with diazonium-compounds,¹⁷ and fluorination.^{15,18}

Noncovalent functionalization of carbon nanomaterials has also been described in the literature. Harada et al. reported the modification of single-walled carbon nanotubes (SWNTs) by physical absorption of cyclodextrins with guest molecules, and the formation of host–guest inclusion complexes significantly improved the water solubility of the SWNTs.¹⁹ Although the majority of studies of noncovalent or polymeric modifications have been focused on CNTs, CNOs are considered to be better candidates for these types of functionalization not only because of their higher surface area but also because of their biocompatibility and very low toxicity, making them excellent candidates for many biomedical applications.^{20,21}

β -Cyclodextrins (β -CDs) are well-known molecular hosts because of their ability to form inclusion complexes with many different guests. Because of their low toxicity, excellent biocompatibility, and good complexation capacity with a variety of lipophilic drugs, CDs are widely used for the drugs formulation in the pharmaceutical industries, making them good candidates for drug delivery applications.^{22–26} There are several reports up describing the modification of non-carbon particles with cyclodextrins. For example, Kaifer et al. demonstrated that functionalization of gold and palladium nanoparticles with CDs can be used to control particle aggregation as well as their catalytic activity via simple host–guest interactions. Furthermore, they showed that the binding properties could then be exploited to control in a predictable manner the properties of the colloidal particles.^{27,28}

However, the number of articles involving CNOs with polymer functionalization is still very limited.^{29,30} Poly(4-vinylpyridine-*co*-styrene)^{31,32} (PVPS) and poly(ethylene glycol)^{33–36} (PEG) have been frequently used for solubilization of carbon nanostructures in nonpolar or polar media. Echegoyen et al.²⁰ recently reported the modification of CNOs with biocompatible polymers for flavonoid incorporation, which can be very promising for biosensing and drug targeting applications. They attached hydrophilic or hydrophobic chains to synthesize soluble derivatives of CNOs.²⁰ Earlier reports also demonstrated an impressive amount of research done toward different polymer functionalization of CNOs mainly for their solubilization by constructing CNO-based supramolecular systems, for example, by using complexation with metal ligands. Such structures may have potential applications in the field of catalysis and hydrogen storage.^{3,4}

In this work, we present the functionalization of the CNOs with β -cyclodextrin (β CDs) and ferrocene grafted dextran polymers (Fc-Dex) through host–guest interactions for the formation of highly soluble CNO-based supramolecular nanoarchitectures.

EXPERIMENTAL SECTION

Materials. All chemicals and solvents used were commercially available and used without further purification. Water was purified using a Milli-Q water purification system (Millipore) to a resistivity of 18.2 M Ω -cm. Commercially available nanodiamond was purchased from Carboneon with a crystal size distribution between 4 and 7 nm. The copper grids for TEM were bought from TED PELLA, Inc. (Prod. No. 01830, 200 mesh, silicon monoxide/formvar). β CD-NH₂ was prepared as previously reported.³⁷

Preparation of Fc-Dextran Polymer (Fc-Dex). Lithium chloride (0.125 g) was dissolved in 10 mL of anhydrous DMF, under a nitrogen atmosphere at 70 °C with magnetic stirring. Previously dried dextran

(0.5 g, MW 5 kDa, Pharmacosmos A/S, dried at 115 °C under vacuum overnight) was added to the above solution and stirred until complete dissolution. Subsequently, DMAP (0.8 mmol) and ferrocenecarboxylic acid *N*-hydroxysuccinimide ester³⁸ (0.2 mmol) were added, the temperature was increased to 90 °C, and the reaction continued for 2 h with continuous stirring. The temperature was then switched off, and the reaction was left stirring overnight at room temperature. The product was precipitated with EtOH, dialyzed against water, and freeze-dried. The ferrocene content in the polymer (0.09 mol/mol glucose units) was estimated by UV–vis spectrophotometry at 254 nm using ferrocenecarboxylic acid as standard. ¹H NMR (DMSO-*d*₆): δ (ppm) 3.0–4.4 (m, H_{2,3,4,5}, Fc protons), 4.5–5.0 (m, H_{1dextran} and OH).

HR-TEM Microscopy. For HR-TEM measurements, samples were deposited on Cu grid holey carbon supports and the solvent was evaporated. Transmission electron microscopy images were recorded using an FEI TecnaiTM transmission electron microscope. The accelerating voltage of the electron beam was 200 keV.

Raman, FT-IR, and Absorption Spectroscopy. Raman measurements were performed using a SmartRaman spectrometer equipped with a 180° sampling holder from Thermo Scientific using an excitation wavelength of 532 nm. FT-IR spectra were recorded using a PerkinElmer 100 spectrometer with neat samples. Absorption studies were performed using a Cary 5000 UV-NIR 15 spectrometer from Varian using fused Quartz glass cuvettes with a 1 cm optical path.

Thermogravimetric Analysis. For TGA analysis a TGA/DSC analyzer from Mettler Toledo was used. A heating rate of 10 °C/min was employed until 1000 °C. All samples were measured in Alumina crucibles with a volume of 0.7 μ L.

Synthesis of CNOs. Small CNOs were obtained by annealing nanodiamond powder (Molto, 5 nm average particle size) under a positive pressure of helium at 1650 °C for 1 h. After separation and purification, CNOs were heated at 200 °C under a CO₂ atmosphere to remove the amorphous carbon residue from the CNO surface.¹⁵

Oxidation of CNOs (Ox-CNOs). 20 mg of crude 6–12 shell CNOs was dispersed by ultrasonication for 30 min and then treated with a sulfuric acid/nitric acid solvent mixture (3:1, v/v) for 3 h. During this process some of the defective sites on their surface were transformed into carboxyl groups by oxidation. The mixture was then centrifuged for 20 min, and the black powder collected at the bottom of the test tube and washed several times with 0.1 M NaOH and Milli-Q water until a neutral pH was reached. After that, the product was dried overnight in a vacuum oven ($T = 100$ °C).

Functionalization of Ox-CNOs with Aminated β -CDs. 5 mg of the ox-CNOs was sonicated in aqueous solution for 30 min, and 0.2 mmol of EDC, 0.1 mmol of NHS, 1 μ mol of β CD-NH₂, and 0.2 mmol of DMAP were added to the reaction mixture and stirred for 24 h at 4 °C. The unreacted cyclodextrins were removed by centrifugation at 4000 rpm for 45 min and washed three times with Milli-Q water. The purified product was dried overnight in a vacuum oven ($T = 45$ °C).

Supramolecular Solubilization of CNOs. 4 mL of the aqueous solution of CNOs- β CD was added dropwise to a 1 mL solution of 0.45 mmol aqueous solution of Fc-Dex and stirred overnight at room temperature. The unreacted substrates were removed by centrifugation at 4000 rpm for 45 min and washed three times with Milli-Q water.

Electrochemical Measurements. Electrochemical measurements were conducted on a CHI-660 electrochemical workstation using a three-electrode cell. A glassy carbon disk (diameter 2 mm) was used as the working electrode in combination with a Ag/Ag⁺ pseudoreference electrode and a Pt wire, which served as the counter electrode. The working electrodes were polished with a diamond slurry, sonicated in water, and checked with a 1 mM potassium ferricyanide standard in 0.1 M KCl.

RESULTS AND DISCUSSION

Figure 1 shows the overall procedure for the preparation of supramolecularly engineered soluble CNOs. The initial step involves an oxidation reaction to create carboxyl groups on the graphitic shell of the CNOs. The amidation reaction between

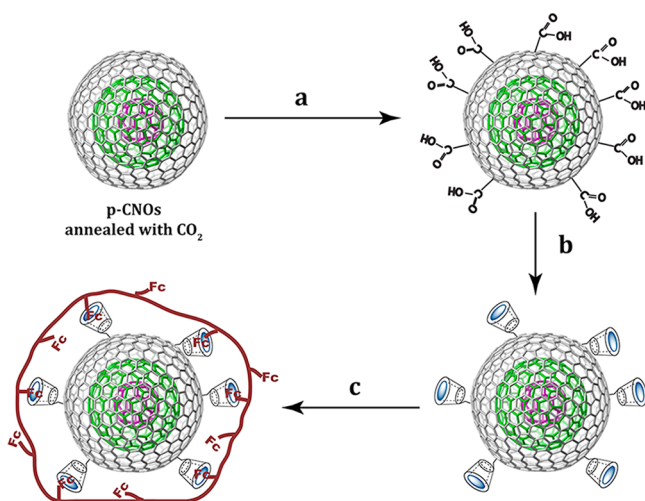


Figure 1. Schematic representation of the synthesis of ox-CNOs modified with host (β CD) and guest polymer (Fc-Dex) via supramolecular interactions: (a) $\text{H}_2\text{SO}_4\text{:HNO}_3$ (3:1), 3 h, ultrasound bath; (b) amidation reaction with $\beta\text{CD-NH}_2$, EDC, NHS, and DMAP; (c) addition of Fc-Dex polymer in water.

ox-CNOs and aminated β -cyclodextrins ($\beta\text{CD-NH}_2$) resulted in water-soluble carbon nanostructures (CNOs- βCD). Next, the Fc-Dex polymer layer was self-assembled through supramolecular interactions by wrapping around the CNO nanoparticles by the formation of inclusion complexes between Fc and βCD molecules. This dramatically increased the solubility of the modified CNOs even more due to well-known solubilizing properties of cyclodextrins and their complexes.¹⁹

The first evidence for the functionalization of CNOs was provided by thermogravimetric analysis measurements (TGA). In order to determine the degree of functionalization of CNOs/ βCD /Fc-Dex, TGA studies were conducted under an inert atmosphere from 30 °C until 1000 °C, using a heating rate of 10 °C min^{-1} . Pristine CNOs were used as reference under the same conditions (Figure 2).

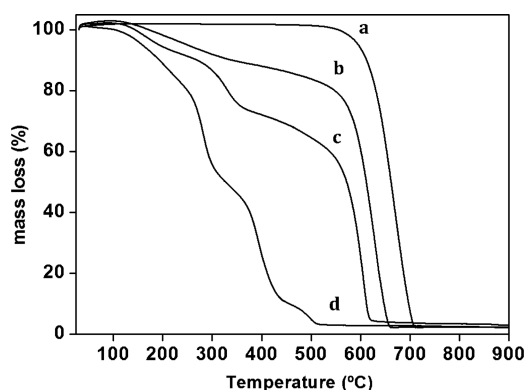


Figure 2. TGA analysis of (a) pristine CNO, (b) oxidized CNOs, (c) CNOs- βCD , and (d) CNOs- βCD /Fc-Dex.

The TGA curves indicate the following:

Oxidized CNOs (ox-CNOs) exhibit two different thermal stages for a total mass loss of 15%, at 175 °C, corresponding to the loss of the carboxylic groups from the surface of the CNOs and final decomposition of the CNOs at 575 °C.

βCD -modified CNOs (CNOs/ βCD) show three different thermal stages for a total mass loss of 40%: (−25%) at 245 °C

corresponding to the removal of the βCD s, (−15%) at 150 °C corresponding to the loss of the carboxylic groups, and the final decomposition of the CNOs at 545 °C. According to the TEM images, the prepared CNOs contain ~ 6 shells. The outer sixth shell contains $60 \times 6^2 = 2160$ carbon atoms, and the total number of carbon atoms in the CNOs is 5460 with an average molecular weight of $5460 \times 12 = 65\,520 \text{ g mol}^{-1}$.¹⁴ Thus, the loss of weight of about 15% at 175 °C after oxidation indicates that there are ~ 257 COOH groups per CNO (~ 1 per every 8 carbons of the outer shell). For βCD -CNOs, the −25% loss of weight indicates there are ≈ 19 βCD molecules attached to the carboxyl groups on the CNO surface or 1 βCD molecule per every 14 COOH groups. This means that the efficiency of the immobilization procedure is about 7%.

Fully modified CNOs (CNOs/ βCD /Fc-Dex) exhibit four different thermal stages for a total mass loss 60%: (−45%) at 250 °C corresponding to the removal of βCD s/Fc-Dex polymer, (−15%) at 150 °C corresponding to the removal of the carboxylic groups, and the final decomposition of the CNOs at 385 °C.

Pristine CNOs remain stable at high temperatures (up until 600 °C), so the lower thermal stability of the functionalized CNOs is the result of the insertion of “structural defects” upon functionalization, as observed for carbon nanotubes.³⁹ TGA first-derivative plots showing minima at the inflection points are shown in the Supporting Information (Figure S1).

Raman spectroscopy is one of the most powerful methods for the characterization of CNOs, providing unambiguous information about the size and the degree of functionalization of the CNOs by comparison of the relative intensities of the defective bands. The D band is related to defects in the CNOs lattice (sp^3 -hybridized carbon), and the G band is due to the vibrations of the sp^2 -hybridized framework. The Raman spectrum of the pristine CNOs exhibits a varying ratio of $I_{\text{D}}/I_{\text{G}}$, depending on the size of the CNOs. For CNOs prepared by arc discharge of graphite under water (20–30 shells) the $I_{\text{D}}/I_{\text{G}} = 0.8$, but CNOs obtained by annealing of nanodiamond particles (1650 °C) under an inert atmosphere lead to the formation of small CNOs (6–12 shells) with an $I_{\text{D}}/I_{\text{G}}$ ratio of 1.4, depending on the crystal size of the carbon nanodiamond precursor.¹²

Aqueous solutions of pristine CNOs and modified CNOs at each step of their functionalization were deposited onto silicon wafers. The Raman spectrum of the small pristine CNOs after excitation at 532 nm (Figure 3) shows the typical peaks, namely, the D band at 1335 cm^{-1} and the G band at 1577 cm^{-1} .^{40,41} The D and G bands for the oxidized and modified CNOs are shifted and noticeably broadened. In particular, the shift in both peaks after oxidation (Figure 3b) can be attributed to the presence of disordered carbon structures and loss of symmetry due to incorporation of the carboxylic groups to unsaturated carbon–carbon bonds. In addition to the G band, another at about 1618 cm^{-1} is observed.²⁰ This band has been described as a shoulder of the G band.⁴² It is assigned as a D' peak and is also due to a disorder induced peak⁴³ and thus not observed in highly oriented pyrolytic graphite (HOPG), but often observed in highly defective graphite.³ Furthermore, the $I_{\text{D}}/I_{\text{G}}$ ratio increased for the oxidized CNOs, indicating an increase in the number of defects (sp^3 -hybridized).¹² After the deposition of the supramolecular polymer layer (Fc-Dex) the $I_{\text{D}}/I_{\text{G}}$ ratio gradually decreased, but the reason for this behavior is not presently understood.

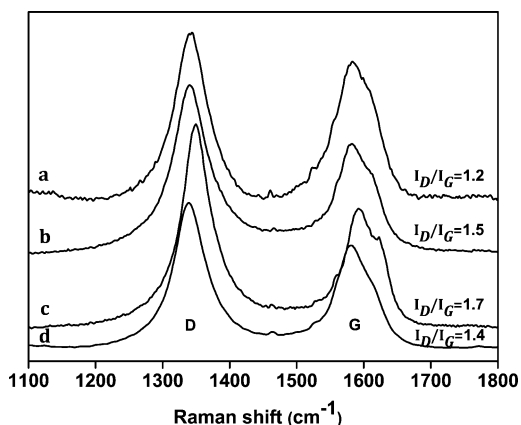


Figure 3. (a) Raman spectra ($\lambda = 532$ nm) of CNOs- β CD/Fc-Dex, (b) CNOs- β CD, (c) ox-CNOs, and (d) pristine CNOs.

Further FTIR studies were conducted to corroborate the covalent attachment of the β CDs on the outer sphere of the CNOs and additional deposition of the Fc-Dex polymer. Peaks in the range from 950 to 1150 cm^{-1} can be assigned to the $\nu_{\text{C-O}}$ stretching (Figure S3). Bands at 1650 and 1510 cm^{-1} were assigned to the $\nu_{\text{C=O}}$ mode and defined as the “amide I” band and to the N–H bending vibration $\delta_{\text{N-H}}$, defined as the “amide II” band. The intensity of the N–H bending absorption is considerably weaker than that of the carbonyl absorption. It can be concluded that β CD is covalently linked to ox-CNOs through amide bonds. FTIR studies also reveal the appearance of three bands at 2919 and 2876 cm^{-1} corresponding to C–H stretching and one at 3322 cm^{-1} corresponding to an O–H stretching (Figure S4).^{44,45}

The solubility was determined by filtering CNOs solutions, following the procedure reported in the literature in aqueous solutions.¹² The functionalized CNOs were dissolved in water (no sonication was needed for the CNOs- β CD/Fc-Dex) and filtered through PVDF filters of 0.2 μm porosity. This resulted in a more homogeneous distribution of CNOs with smaller average size domains (Figure 4).

The average size of the modified CNOs before and after filtration through PVDF filters of 0.45 and 0.22 μm porosity was studied by dynamic light scattering (DLS) (Figure S5). The filtered solutions appear to contain more homogeneously sized CNOs possessing smaller sizes than the pristine CNOs. Modified CNOs- β CD/Fc-Dex possess hydrodynamic diameters of approximately 280 nm after filtration through PVDF 0.45 μm filter and approximately 160 nm after filtration through PVDF 0.22 μm filter, while p-CNOs do not pass through the PVDF filters. Therefore, it is likely that the filtered dispersions contain small sized aggregates if compared with the TEM image of individual CNOs showed in Figure 4d, which may be the result of interparticle interactions mediated by Fc-Dex.

UV spectroscopy also shows a red-shift in the characteristic peaks for CNOs¹² that gradually grows with the size increase of the particles after β CD functionalization and deposition of the Fc-Dex polymer, filtered through 0.45 and 0.22 μm PVDF filters (Figure S6).

Moreover, zeta potential measurements revealed changes in potentials before and after functionalization of the CNOs, from -40 mV for the ox-CNOs, to -30 mV for CNOs- β CD and -25 mV for the CNOs- β CD/Fc-Dex. This increase toward more positive potentials can be explained as resulting from

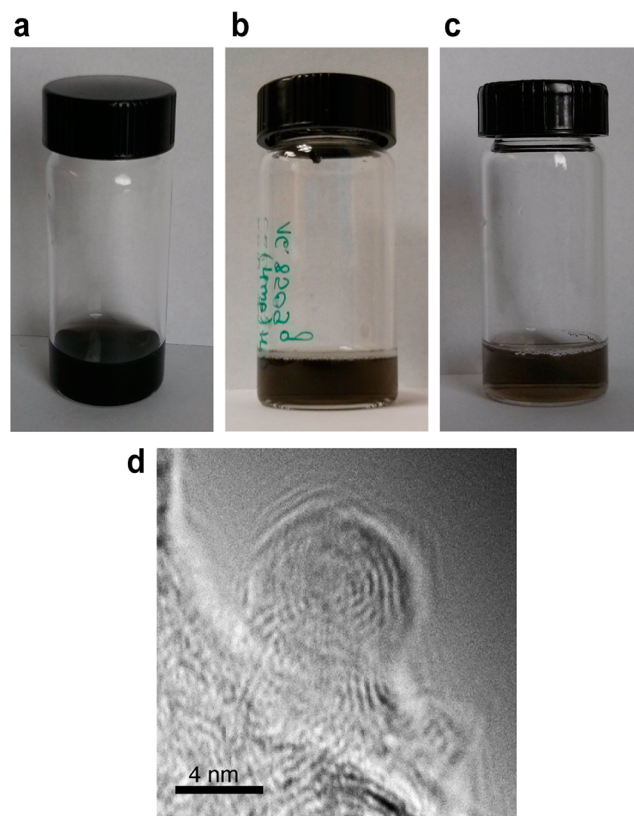


Figure 4. Solubility of modified CNOs: CNOs- β CD/Fc-Dex before filtration (a), CNOs- β CD/Fc-Dex after filtration through PVDF 0.45 μm filter (b), CNOs- β CD/Fc-Dex after filtration through PVDF 0.22 μm filter (c). HRTEM image of filtered CNOs- β CD/Fc-Dex through PVDF 0.22 μm filter (d).

covering the negative particle surfaces (due to carboxyl groups) with β CD and Fc-Dex polymer (Figure 5).

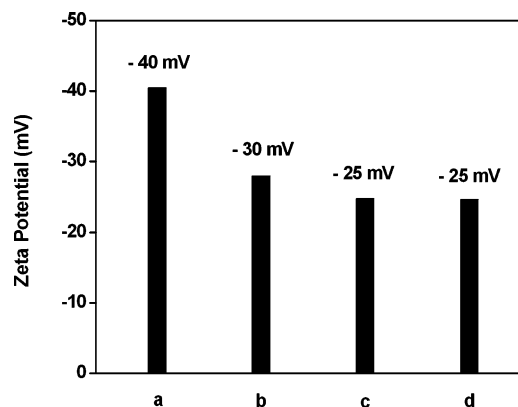


Figure 5. Zeta potential changes for (a) ox-CNOs, (b) CNOs- β CD, (c) CNOs- β CD/Fc-Dex (0.45 μm), and (d) CNOs- β CD/Fc-Dex (0.22 μm).

The soluble CNOs- β CD/Fc-Dex particles were further characterized by electrochemical techniques. In most voltammetric techniques such as cyclic voltammetry and square wave voltammetry, the intensity of the current signal depends on the diffusion coefficients (D) of the diffusing species, among other factors, such as concentration and electrode area. Since ferrocene is electrochemically active and is known to form

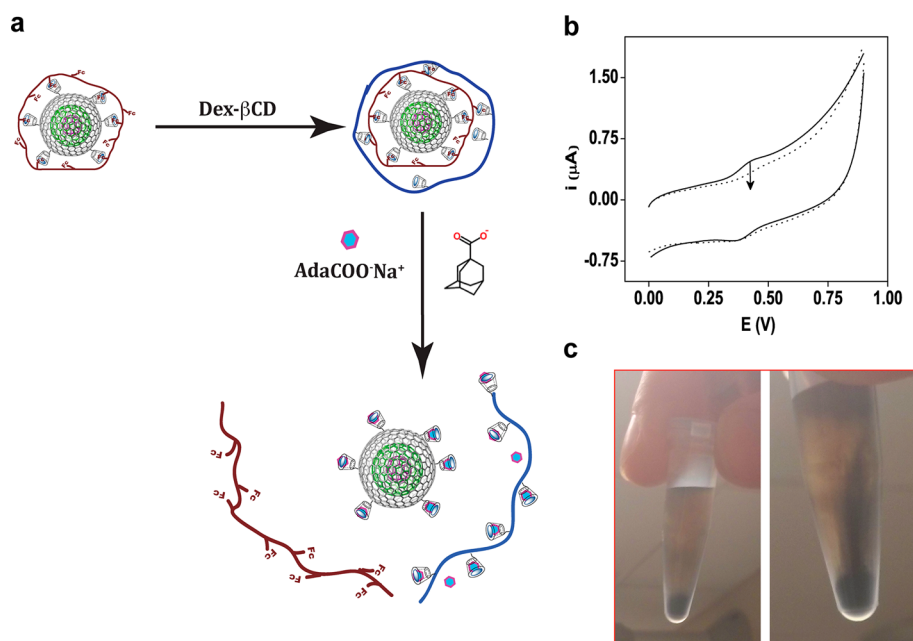


Figure 6. (a) Interaction of CNOs- β CD/Fc-Dex particles with a dextran- β CD polymer and displacement of the ferrocene-guest molecule after the addition of 1 mM adamantane carboxylic acid; (b) cyclic voltammograms (at 0.2 V/s in 0.1 M KCl) for the interaction of CNOs- β CD/Fc-Dex particles with a dextran- β CD polymer; (c) pictures of the sample precipitation after the addition of excess of sodium adamantanecarboxylate (1 mM) as a competitive binding agent.

inclusion complexes with β CD, it is possible to study the interaction of the outer ferrocene units with a β CD polymer. This interaction increases the effective molecular weight of the system and thus reduces its diffusion coefficient and the associated current responses (Figure 6a).

Figure 6b shows the cyclic voltammogram of CNOs- β CD/Fc-Dex particles before and after interaction with a 10 kDa dextran- β CD polymer having 0.2 mol of β CD per mole of glucose units.⁴⁶ The peak-to-peak separation for CNOs- β CD/Fc-Dex is 80 mV, indicating that the attached ferrocene units retain their quasi-reversible electron transfer properties. After interaction of the β CD polymer the signal intensity dramatically decreases, due to the effective molecular mass increase due to the polymer adhering to the surface of the modified CNO particles. This signal decrease was also evident by square-wave voltammetry (Figure S7), in which a gradual signal drop is observed after interaction with increasing concentrations of the β CD-appended polymer.

The Stokes–Einstein model for the diffusion of large spherical particles states that the values of D depend inversely on the radius R of the particles according to the equation

$$D = \frac{kT}{6\pi\eta R}$$

where k is the Boltzmann constant, T is the absolute temperature, and η is the solution viscosity. Assuming a radius of ~ 4 nm for the CNOs- β CD/Fc-Dex particles, based on TEM photograph (Figure 4d), the estimated value of D is 6×10^{-11} m²/s at 298 K in water ($\eta = 8.9 \times 10^{-4}$ Pa·s), which is about the same order of magnitude as values observed for high molecular weight macromolecules.⁴⁷

On the other hand, the Randles–Sevcik equation relates the peak current with D at 298 K:

$$i_p = 268600n^{3/2}Acv^{1/2}D^{1/2}$$

where A is the area of the electrode, c is the concentration, and v is the scan rate. Using the calculated value of D , the estimated peak current is $0.29 \mu\text{A}$ for a $100 \mu\text{M}$ solution at 200 mV/s , which is close to the experimental value observed from the cyclic voltammogram.

Upon addition of a large excess of adamantane carboxylate (which is known to have higher affinity for the β CD cavity), precipitation of the CNOs and the polymers was observed (Figure 6c), which results from the displacement of ferrocene molecules from the β CD cavities by the adamantane molecules.

CONCLUSIONS

In summary, the oxidation and modification of CNOs with β CDs resulted in increased solubilization. CNO-based supramolecular nanosystems formed by further complexation with a Fc-Dex polymer significantly increased their solubility even more. This solubility increase is the result of the formation of the inclusion complexes between Fc and β CD and moieties. Additionally, after filtration of the CNOs through 0.45 or 0.22 μm PVDF filters resulted in smaller and more homogeneous nanoparticles. The oxidation, covalent amidation, and final supramolecular functionalization sequence presented here for CNOs solubilization open many possibilities for a wide range of potential applications, such as in photovoltaics, molecular electronics, or biosensors.

ASSOCIATED CONTENT

Supporting Information

TGA analysis, FTIR spectra, DLS measurements, UV spectra, and square-wave voltammograms of modified CNOs. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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