Supramolecular Grafting of Doped Polyaniline Leads to an Unprecedented Solubility Enhancement, Radical Cation Stabilization, and Morphology Transformation

Nabasmita Maity,†a Arnab Dawn,†a,b,* Atanu Kuila a and Arun K. Nandi a,*

aPolymer Science Unit, Indian Association for the Cultivation of Science, Jadavpur, Kolkata- 700032, India
bPresent address: James L. Winkle College of Pharmacy, University of Cincinnati, 231 Albert Sabin Way, Cincinnati, OH 45267-0004, USA
Materials
Propargyl bromide, sodium azide, p-toluenesulfonyl chloride (PTSC), N,N,N′,N′′,N′′-pentamethyldiethylenetriamine (PMDETA), calf thymus DNA (type 1 sodium salt) (Sigma-Aldrich), ammonium persulphate (APS), pet ether (Merck, Mumbai, synthetic grade), poly(ethylene glycol) (PEG, \( M_w = 4000 \)) (SRL Chemicals, Mumbai) were used as received. Dimethyl formamide (DMF) (Rankem, New Delhi, analytical grade) and toluene (Merck, Mumbai, 99%) were dried over calcium hydride and distilled before use. \( \beta \)-Cyclodextrin (\( \beta \)CD) (Sigma-Aldrich) was recrystallized from water. CuBr (Sigma-Aldrich) was taken in a Schlenk tube under nitrogen atmosphere and was washed by 10% aqueous HBr solution followed by methanol. Aniline monomer was purchased from Merck, Mumbai and purified under reduced pressure prior to use. Double distilled water was used throughout the work.

Characterization
The \(^1\)H NMR spectra of the samples were recorded using a Bruker 500 MHz NMR spectrometer in DMSO-d6, CDCl\(_3\) and D\(_2\)O as per requirement. Polymerization reactions were performed in D\(_2\)O containing 0.05 wt. % 3-(trimethylsilyl) propionic-2,2,3,3-\( d_4 \) acid, sodium salt as the internal standard. The ultraviolet-visible (UV-Vis) absorption spectra were taken using UV-Vis spectrophotometer (Hewlett-Packard, Model 8453) in a quartz cell of 0.1 cm thickness in the wavelength range of 190–1100 nm. FT-IR spectroscopy was recorded in a Shimadzu FT-IR instrument (model 8400S) using KBr pellets of powder samples (\( \beta \)CD-azide and \( \beta \)CD-PEG) and taking thin film of dried samples casted over silicon wafer. The DLS studies were carried out in a Malvern instrument at a scattering angle of 173°. For the surface morphological investigation, the atomic force microscopy (AFM) was conducted using atomic force microscope (Veeco, model AP 0100) in non-contact mode at a resonance frequency of the tip end ~250 KHz. Field-emission scanning electron microscopy (FESEM) (Jeol GSM-5800) was conducted on the sample drop casted on glass cover slip and coated with platinum prior to observation except control PANI powder, which was directly moulded on carbon tape and studied after platinum coating. The morphology of \( \beta \)CD-PEG-PANI was also monitored using a transmission electron microscope (TEM JEOL, 2010EX) operated at an acceleration voltage of 200 kV. Cyclic voltammetry (CV) experiments were performed using a three-electrode electrochemical station (CH Instrument, CHI600E), where modified glassy carbon electrode (GCE) was used as the working electrode, saturated Ag/AgCl as the reference electrode, Pt wire as the counter electrode, and 0.5 M H\(_2\)SO\(_4\) was used as an electrolyte.
Synthesis of βCD-PEG

**Synthesis of mono-6-deoxy-6-(p-tolylsulfonyl)-β-cyclodextrin (βCD-OTs).**
β-Cyclodextrin (βCD) (15 g, 13.48 mmol) was taken in a round-bottom flask and was suspended in 100 mL of water. The flask was cooled to 0 °C. To this suspension, 5 mL of aqueous NaOH solution (1.65 g, 41 mmol) was added dropwise followed by slow addition of p-toluenesulfonyl chloride (2.52 g, 13.23 mmol in 8 mL acetonitrile). The reaction mixture was stirred for 4 h at 0 °C. Trace of white precipitate appeared during the reaction process was removed by filtration, and the pH of the filtrate was adjusted to 8.0 by adding 1 N HCl solution. At this pH the crude product was precipitated out and was recovered by filtration. To remove any unreacted p-toluenesulfonyl chloride and β-CD, the product was recrystallized from water. Finally, the product in form of white solid was obtained after drying under vacuum at 40 °C for 4 days. (2.85 g, yield: 19 %) (1H NMR, Fig. S1).

**Synthesis of mono-6-deoxy-6-azido-β-cyclodextrin (βCD-N₃).**
βCD-OTs (0.51 g, 0.4 mmol) was taken in a round-bottom flask and 3 mL of DMF was added. The mixture was heated at 70 °C. NaN₃ (0.13 g, 2 mmol) and KI (0.016 g, 0.097 mmol) were added under nitrogen atmosphere. The reaction mixture was maintained at 70 °C for 48 h. The reaction mixture was then cooled to 30 °C and precipitated in acetone. This process was repeated twice. The final product was obtained as white powder after drying under vacuum for 2 days. (0.39 g, yield: 76 %). ¹H NMR (500 MHz, DMSO-d₆): δ 5.64-5.75 (m, 14H), 4.82-4.87 (m, 7H), 4.43-4.49 (m, 6H), 3.56-3.74 (m, 28H), 3.21-3.2d (m, 14H), 2.88 (br, 1H), 2.73 (br, 1H). (Fig. S2). (FTIR spectra, Fig. S3)

Synthesis of alkynyl end-terminated poly(ethylene glycol) (Alkynyl-PEG).
In a round bottom flask, PEG (4 g, 1 mmol) was dissolved in 50 mL of freshly distilled dry toluene, under nitrogen atmosphere. The flask was cooled to 0 °C and NaH (0.24 g, 10 mmol) was added. The reaction mixture was stirred for 1 h at 30 °C. Propargyl bromide (0.6 mL, 7.9 mmol) in 10 mL of dried toluene was added dropwise and the mixture was stirred at 30 °C for 48 h. Insoluble salts produced were removed by filtration. The filtrate was evaporated. The solid obtained was dissolved in 45 mL of CH₂Cl₂ and extracted with brine solution. The organic phase was dried over anhydrous sodium sulphate and was precipitated in cold petroleum ether. This process was repeated for three times. The white solid was obtained as final product after drying under vacuum at 30 °C. (4.18 g, yield: 83 %). ¹H NMR (500 MHz, CDCl₃): δ 4.21 (d, 4H) 3.63 (m, 360H), 2.44 (t, 2H) (Fig. S4).

Synthesis of poly(ethylene glycol)-β-cyclodextrin (PEG-βCD).
Alkynyl-PEG (2 g, 0.5 mmol) and βCD-N₃ (1.4 g, 1.2 mmol) were dissolved in DMF under nitrogen purging. After 30 min of purging, CuBr (215 mg, 1.5 mmol) and PMDETA (173.3 mg, 1.0 mmol) were added sequentially and the reaction mixture was stirred for 48 h at 60 °C. The reaction mixture was then cooled to room temperature and exposed to air. The product obtained after DMF removal was dissolved in chloroform and passed through a basic alumina column to eliminate major amount of copper catalysts. In order to remove trace amount of copper, the residue collected after solvent evaporation was dissolved in 10 mL of 5% ammoniacal water, and was then extracted with CHCl₃. After chloroform evaporation, the process was repeated thrice using water to remove unreacted βCD-N₃, followed by extraction with CHCl₃. The organic part was dried over anhydrous Na₂SO₄ and the desired product was obtained by precipitation in 300 ml cold petroleum ether. After filtration, the product was obtained as faint brown sticky solid after vacuum drying for 3 days at 35 °C (0.78 g, yield: 22.9 %). ¹H NMR (500 MHz, DMSO-d₆): δ 8.04 (2H, s), 5.68-5.87 (28H, m), 4.83 (14H, m), 4.49 (14H, m), 4.29 (2H, br), 3.99 (2H, br), 3.64 (28H, m), 3.5(380 H, m), 3.37 (merged with H₂O peak). (Fig. S5). (FTIR spectra, Fig. S6)
Fig. S1. $^1$H spectra of βCD-OTs in DMSO-d$_6$.

Fig. S2. $^1$H spectra of βCD-N$_3$ in DMSO-d$_6$.  

S5
Fig. S3. FTIR spectra of βCD-N₃. The characteristic signal of azide is indicated with arrow.
Fig. S4. $^1$H spectra of alkynyl PEG in CDCl$_3$. 
Fig. S5. $^1$H spectra of βCD-PEG in DMSO-d$_6$. 
Fig. S6. FTIR spectra of βCD-PEG.

Scheme S1. Possible structures of PANI at doped state during polymerization: Arrows indicating various types of aromatic protons.
Fig. S7. SEM image of (a) βCD-PEG-PANI (ES) from water and (b) PANI powder.

Fig. S8. AFM image of βCD-PEG-PANI (ES) prepared in CDCl$_3$. 
Fig. S9. (a) FESEM and (b) HRTEM images of βCD-PEG-PANI (ES) from CDCl$_3$.

Fig. S10. AFM image of βCD-PEG-PANI (EB) from water (NH$_4$OH).
Fig. S11. Photographs of the solution obtained by stirring a mixture of control PANI (ES) with βCD-PEG, in water: (a) After stirring for 48 h, and then after keeping for (b) 24 h and (c) 48 h.
Case study

A mixture was prepared by adding 200 μL of a 0.01% (w/v) aqueous solution of DNA to 400 μL aqueous solution (2 mg/mL) of βCD-PEG-PANI. Similarly, another mixture with DNA and control PANI was prepared.

![Figure S12](image)

**Figure S12.** UV-Vis spectra of the aqueous mixtures at different time intervals after mixing: (a) βCD-PEG-PANI (ES) and DNA, (b) control PANI (ES) and DNA. The arrows indicate a change (decrease) in intensities of the associated absorption maxima with time, and dotted lines indicate the shift (or no shift) in π-polaron band transition of PANI.

**Discussion:**

The signal at 260 nm corresponds to the characteristic DNA absorption, while other three signals are associated with different transition bands of PANI. With aging time the signals corresponding to DNA as well as those from PANI in βCD-PEG-PANI (ES) spectra (Figure S12a) decrease signifying a complexation and subsequent precipitation from the systems. Also, a red shift of π-polaron band transition of PANI in supramolecularly grafted state implies a conformational rearrangement (chain extension) in presence of DNA. On the other hand, only the PANI signals decrease with time in the mixture of control PANI and DNA, signifying a precipitation of PANI alone without any interaction with DNA (Figure S12b) as there is no shift in the polaron band of PANI. Therefore, it is evident that owing to the high water solubility only the supramolecularly grafted PANI in βCD-PEG-PANI can interact with the DNA making a biocomposite. This clearly supports the indispensability of the supramolecular grafting approach, in utilizing a conducting polymer for biocommunication. The added advantage in this approach is the presence of biocompatible PEG and βCD, which should enhance the overall applicability of the system in a biological environment.