Supporting Information

Biocompatible Cobaltporphyrin-Based Complex Micelle via Supramolecular Assembly for Oxygen Transfer

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Materials

5, 10, 15, 20-Tetrakis(4-sulfonatophenyl)porphyrin (TPPS) was purchased from Dojindo Laboratories and used without further purification . Cobalt(III)-tetra(4-sulfonatophenyl)porphyrin (Co(III)TPPS) was synthesized according to literatures. $Na_2S_2O_4$ was purchased and used as received. Poly(ethylene glycol) monomethyl ether (CH_3OPEG_{114}-OH) (PDI = 1.05) was purchased from Aladdin. β-benzyl-L-aspartate NCA (BLA-NCA) was synthesized following literature procedures.[1] N, N-dimethylformamide (DMF) and dichloromethane (CH_2Cl_2) were dried with CaH_2 and distilled by a general method before use. Histidine hepatapeptide was purchased from Sigma. TM-β-CD was obtained from TCI used as received.

Instruments

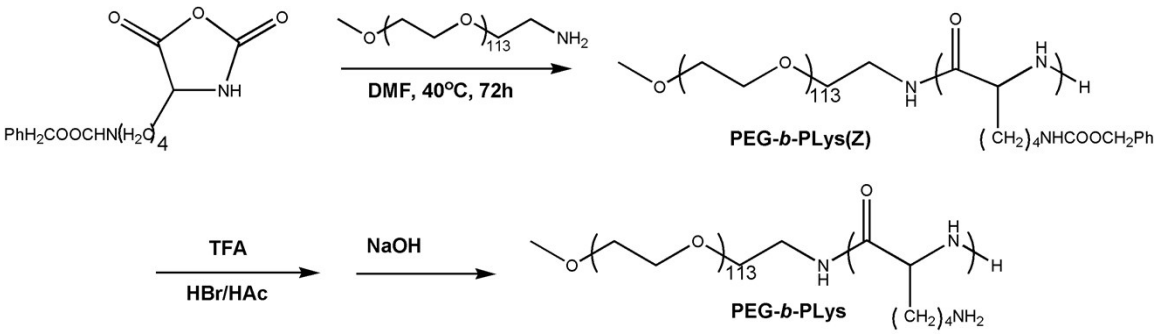
NMR. ^{1}H-NMR spectra were obtained on a Varian UNITY-plus 400M nuclear magnetic resonance spectrometer using $CDCl_3$, D_2O and NaOD as solvents.

UV-vis UV-vis absorption spectra were measured on a TU-1810 UV-vis spectrophotometer (Purkinje General, China).

Light Scattering Measurements. The sizes of the micelles were determined by Dynamic light scattering (DLS). During this investigation, DLS measurements were performed at 636 nm by using a laser light scattering spectrometer (BI-200SM) equipped with a digital correlator (BI-9000AT). Solution A and B were determined after being diluted to some degree. The samples were obtained by Filtering sublayer micelle solutions (about 1.5 mL) through a 0.45 μm Millipore filter into a clean scintillation vial. Characterizations were operated at ambient temperature.

Transmission electron microscopy (TEM). TEM was performed using a Philips T20ST electron microscope at an acceleration voltage of 120 kV. Samples were firstly prepared by depositing 10 μL micelle solution onto a preheated carbon-coated copper EM grid and dried at the same temperature under atmospheric pressure. Then Samples were stained by depositing of a drop of 2 wt% uranyl acetate onto the surface of the sample-loaded grid, and dried at the same temperature.

Synthesis



Scheme S1. Synthesis of diblock copolymer PEG_{113}-*b*-$PLys_{40}$

Synthesis of PEG-*b*-PLys

First, poly(ethylene glycol)-*b*-poly(ε -(benzyloxycarbonyl)-L-lysine) (PEG-*b*-PLys(Z)) block copolymer was prepared by the polymerization of Lys(Z)-NCA initiated by the terminal amino group of PEG-NH_2. Briefly, a total of 1.35 g (4.4 mmol) of Lys(Z)-NCA was dispersed in 20 mL of DMF followed by the addition of 0.5 g (0.1 mmol) of PEG_{113}-NH_2. The reaction mixture was stirred for 72 h at 40 °C under a dry argon atmosphere. Then the solution was diluted with $CHCl_3$. Subsequently, the mixture was precipitated into excess cold diethyl ether to obtain 1.35 g (yield 81.5%) PEG-*b*-PLys(Z). (Mn = 15 k, Mw/Mn = 1.13). To obtain PEG-*b*-PLys, 1.3 g PEG-b-PLys(Z) was dissolved in 20 mL of trifluoroacetic acid and stirred for 0.5 h. Then, 2 mL hydrogen bromide (HBr) (45% in acetic acid) was added into the solution and stirred for further 24 h at room temperature. The reaction mixture was diluted with 30 mL of distilled water and vigorously shaken with 200 mL of diethyl ether. The water phase was neutralized by sodium hydroxide and dialyzed against distilled water using a dialysis membrane (molecular weight cutoff = 3.5 k). The aqueous solution of purified product was lyophilized.

Preparation of the inclusion of Co(III)TPPS and TM-β-CD

The inclusion solution was prepared by dissolving Co(III)TPPS and TM-β-CD（cal.mol/mol =1:3）in the pH7.4 PBS and the concentration of Co(III)TPPS solution was determined by UV-Vis spectrum.

Preparation of the Co(III)TPPS-based complex micelle

A certain amount of PEG-*b*-PLys and Histidine hepatapeptide were dissolved in pH=7.4 PBS. Afterwards, the inclusion solution of Co(III)TPPS and TM-β-CD was added while stirring and simultaneously the micellization occurred mediated by both electrostatic interaction and coordination interaction.

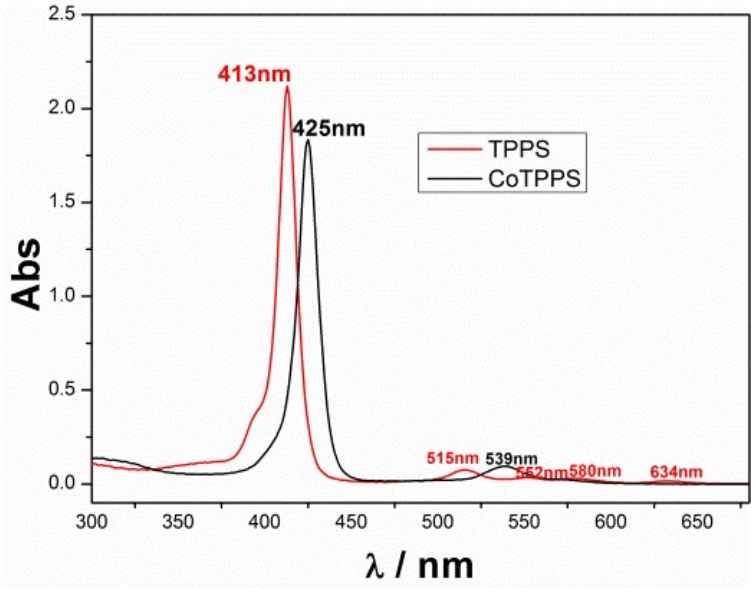
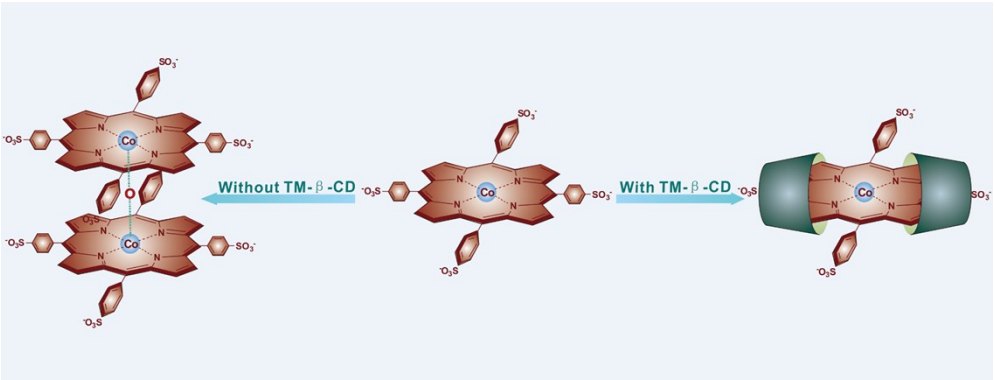


Figure S1. UV/Vis spectral changes of TPPS and Co(III)TPPS in ultrapure water.



Scheme S2. Schematic diagram of the role of the TM-β-CD to prevent the μ-oxo dimer of Co(III)TPPS.

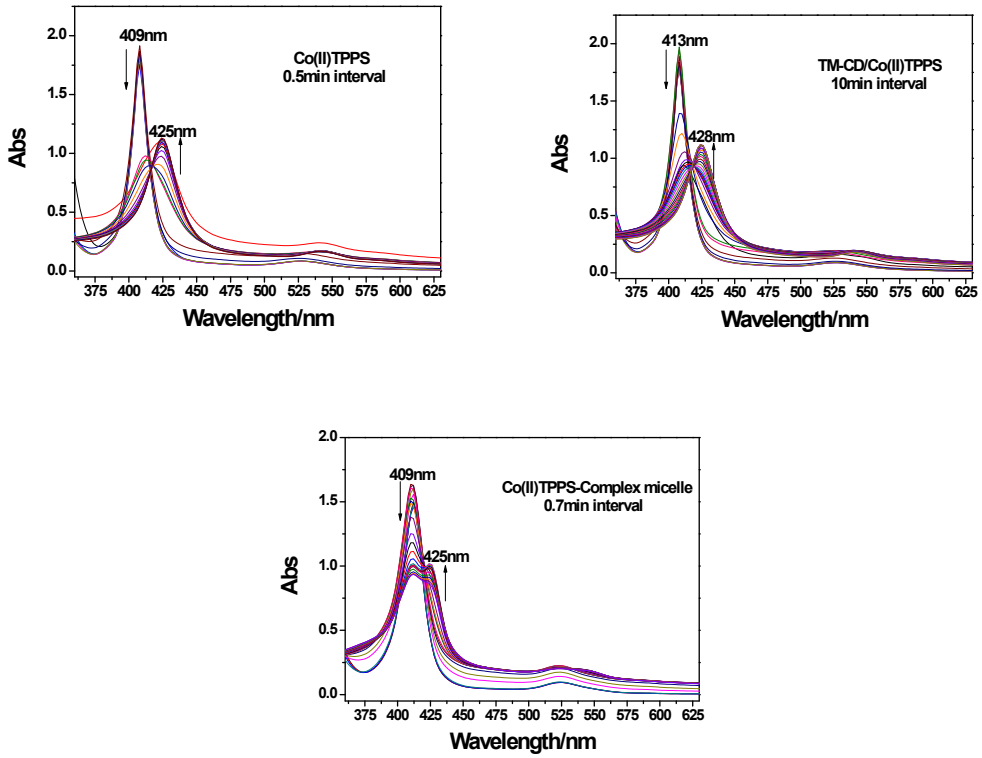


Figure S2. Stability of Co(II)TPPS in three different samples when the samples were exposed to aerobic conditions: Sample I）Co(II)TPPS aqueous solution at pH7.4 PBS；Sample II）Co(II)TPPS/TM-β-CD inclusion at pH7.4 PBS；Sample III）Co(II)TPPS based complex micelle pH7.4 PBS;

References:

1. H. Gao, J. Xiong, T. Cheng, J. Liu, L. Chu, J. Liu, R. Ma, and L. Shi*, *Biomolecules*, 2013, **14**, 460-467.