Supporting Information

Semiconductor Quantum Dots Photosensitizing Release of Anticancer Drug

Zhenzhen Liu, Qiuning Lin, Qi Huang, Hui Liu, Chunyan Bao, Wenjin Zhang,*

*Xinhua Zhong, and Linyong Zhu**

Key Laboratory for Advanced Materials, Institute of Fine Chemicals, East China

University of Science and Technology, Shanghai, 200237, China

1. **Experiments section**

2. **Stern-Volmer analysis between the NAP Ester 1 and QDs.**

3. **Fluorescence spectra of the used water-soluble PTMP-PAA capped QDs.**

1. Experimental Section

Materials: Deionized water was used in all the experiments. Orange core/shell CdSe/ZnS and Mn:ZnSe quantum dots in chloroform (λ_{em}= 602 nm, and 625 nm) were donated from Prof. Xinhua Zhong's group, and NaOH solution was used to adjust the pH value of the solutions. PTMP-PAA (Pentaerythritol tetra (3-mercaptopropionate)-polyacrylic acid) was prepared as the reference reported,[1] and the molecular weight for the obtained polymer is confirmed by GPC (THF) data: Mn= 1144 g/mol, Mw = 1532 g/mol, PDI = 1.33. All other reagents were purchased from Sigma-Aldrich Inc.

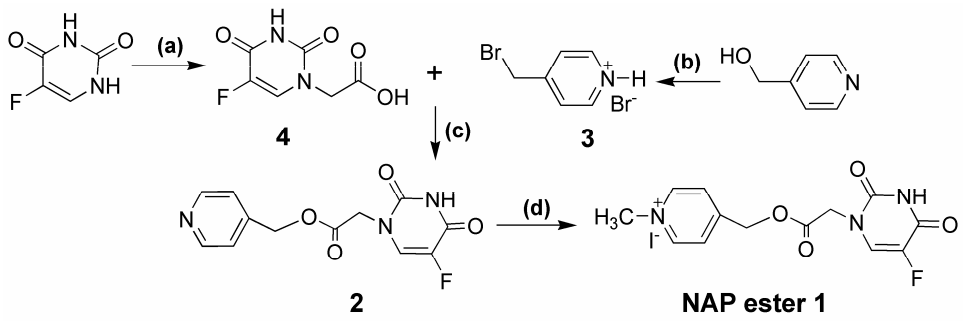
General procedures: All ^{1}H and ^{13}C NMR were obtained using a recorded on a Bruker Avance 500 (400 MHz) spectrometer. Chemical shifts were reported in parts per million (ppm) downfield from the Me_4Si resonance which was used as the internal standard when recording ^{1}H NMR spectra. Mass spectra were recorded on a Micromass GCTTM and a Micromass LCTTM. The steady-state fluorescence experiments were performed on a Varian Cary Eclipses fluorescence spectrometer. Fluorescence lifetime measurements were recorded using an Easylife LS (PTI) using a 490 nm pulsed LED and the appropriate filters for each case. In all cased the experimental error was less than 5%. Cyclic voltammetry (CV) experiments were done on a voltammetry analyzer with $[Bu_4N][ClO_4]$ as the supporting electrolyte. The electrodes used were a carbon working, platinum auxiliary, and an Ag/AgCl reference. Ferrocene was used as the internal standard. The CV data were taken in spectroscopic

grade dry MeCN after N_2 purging the samples for 10 min. The ferrocene/ferrocenium couple was found around 440 mV and the typical scan speed was 100 mV/s.

Preparation of water-soluble PTMP-PAA capped QDs: QDs (CdSe/ZnS and Mn: ZnSe QDs) were precipitated twice from the chloroform solution (4 mL) by addition of acetone (10 mL) and subsequent centrifugation for 10 min at 3000 rpm. The resulting precipitate was dissolved in 2 mL chloroform again, and a 200 μL PTMP-PAA solution (containing 100 mg PTMP-PAA and 100 mg KOH in 5 mL methanol) was added, and the mixture was then shaken for 3 min. After addition of 2 mL of 1 mM NaOH solution in water, all the particles were transferred to the water phase and the chloroform became clear. The water phase with QDs solution was separated from the chloroform, and the excess of the PTMP-PAA ligand was removed by two successive precipitation steps of QDs with acetone and subsequent centrifugation. The obtained QDs were dissolved in 2 mL water, and kept in dark.

General methods of the PET-induced drug release: Photolysis solutions containing NAP ester **1**, QDs and donor (L-cysteine) were prepared in phosphate-buffered saline (PBS solution) (pH= 7.4, 0.01 M). A duplicated mixture was created to use as a dark control. The solutions were purged with nitrogen for 10 min and irradiated with a CHF-XM-500w lamp (UV-cut filter) for a predetermined amount of time. Between certain time intervals, a small aliquot (10 μL) of the suspension was taken out and filtered by a Millipore Microcon YM-50, the obtained transparent solution was analyzed by reversed-phase HPLC using a BetaBasic-18 column eluted with a gradient mixture of Methanol/HOAC buffer solution (0.1 M, pH= 4.5) from 3% to

10% at a flow rate of 0.2 mL/min. The chromatogram was plotted by using absorbance detection at 254 nm. Yields were calculated relative to the amount of NAP ester **1** kept in dark condition.



Scheme S1 The synthesis route for the NAP ester **1**. (a): $BrCH_2COOH$, KOH, rt ; (b): HBr, refluxed, 4h; PBr_3, refluxed, 4.5h; (c): triethylamine/DMF, 90 ^oC, 4h; (d): acetonitrile, 75 ^oC, 3h.

The synthesis of NAP ester 1:

The synthesis of 5-Fluorouracil-1-acetic Acid (Compound **4)**[2]: Into a solution of 5-fluorouracil (5-FU, 1.3 g, 10 mmol) and potassium hydroxide (1.12 g, 20 mmol) in water (7.5 mL), a solution of bromoacetic acid (1.39 mg, 10 mmol) in water (4 mL) was then added and stirred at room temperature, the pH of the reaction mixture was adjusted to pH=10 by the addition of a potassium hydroxide aqueous solution dropwise. The mixture was then refluxed for 2h, cooled and acidified to pH=2 by the addition of concentrated hydrochloric acid. The obtained crystals were filtered and washed with a little cold water to give compound **4** (1.24 g) in a 66% yield. The crude was purified by dissolving the solid in a saturated aqueous potassium bicarbonate and reprecipitating with concentrated hydrochloric acid to give colorless needles.

Mp:276-277 ^{o}C; ^{1}H NMR (400MHz, d-DMSO) δppm:11.9 (s,1H), 8.0 (d, J (H,H) = 6.8, 1H), 4.3 (s, 1H).

The synthesis of compound **3**[3]: 4-(hydroxymethyl) pyridine (3.64 g, 33.40 mmol) was dissolved in 32 mL of 48% HBr and refluxed for 4 h. The water was removed under vacuum to give a thick gum which was treated with 20 mL of absolute ethanol at 5 ℃ and then filtered. The obtained white crystals were washed with 5mL of cold absolute ethanol to yield 6.00 g of 4-(Hydroxymethyl) pyridinium bromide (94.5%). ^{1}H NMR(400MHz, D_2O) δppm: 4.6 (2H, s, CH_2OH), 8.1 (2H, d, aryl H), 8.5 (2H, d, aryl H). Neat PBr_3 (0.87 mL, 9.22 mmol) was added to a suspension of 4-(Hydroxymethyl) pyridinium bromide (3.5 g, 18.42 mmol) in chloroform (50 mL). The mixture refluxed for 4.5 h was then allowed to cool to room temperature. The white precipitate was filtered off and washed with 10 mL of cold chloroform to give 3.62 g (78%) of the desired compound **3**. ^{1}H NMR (400MHz, $CDCl_3$) δppm: 4.4 (2H, s, CH_2Br), 7.2 (2H, d, aryl H), 8.5(2H, d, aryl H).

The synthesis of compound **2**: A solution of **3** (0.26 g, 1.06 mmol), **4** (0.2 g, 1.06 mmol) and triethylamine (0.22g，2.12 mmol) in DMF (15 mL) was heated at 90 ^{o}C for 4 h. Then the solution was poured into water and extracted with ethyl acetate for three times. The obtained organic phase was dried over Na_2SO_4, and evaporated in vacuum. The crude product was recrystallized from methanol to give compound **2**. (0.12 g, 40% yield). ^{1}H NMR(400MHz, d-DMSO) δppm: 12.01 (d, J(H,H)=4.4, 1H), 8.6 (d, J(H,H)=5.6,2H), 8.1 (d,J(H,H)=6.4, 1H), 7.4 (d,J(H,H)=5.6,2H), 5.3 (s,2H), 4.6 (s,2H); ^{13}C NMR (d-DMSO): δppm =167.749, 157.528, 157,721, 149,658,

144,558, 140.542, 138.262, 130.397, 130.057, 121.675, 64.667, 48.684; MS(ESI): m/z : 280.1$[M+H]^+$.

The synthesis of NAP ester **1**: Into a Compound **2** (0.1 g, 0.36 mmol) solution in absolute Acetonitrile (5 mL), methyl iodide (0.3 g, 2.16 mmol) was added slowly. The reaction mixture was refluxed at 80 ^oC for 3 h, the solvent was removed under reduced pressure to give 0.15 g pure products without further purification. ^1H NMR (400 MHz, MeOD) δppm: 8.9 (d, J(H,H)=6.4, 2H), 8.0 (d, J(H,H)=6.4, 2H), 7.8 (d, J(H,H)=6, 1H), 5.5 (s, 2H), 4.7 (s, 2H), 4.4 (s, 3H); ^{13}C NMR (D_2O): δppm=168.576, 159.898, 159.642, 154.792, 150.761, 145.050, 141.616, 139.299, 131.015, 130.678, 125.138, 64.720, 49.808, 47.825; MS(ESI): 294.1$[M-I]^+$.

2. Stern-Volmer analysis between the NAP Ester 1 and QDs.

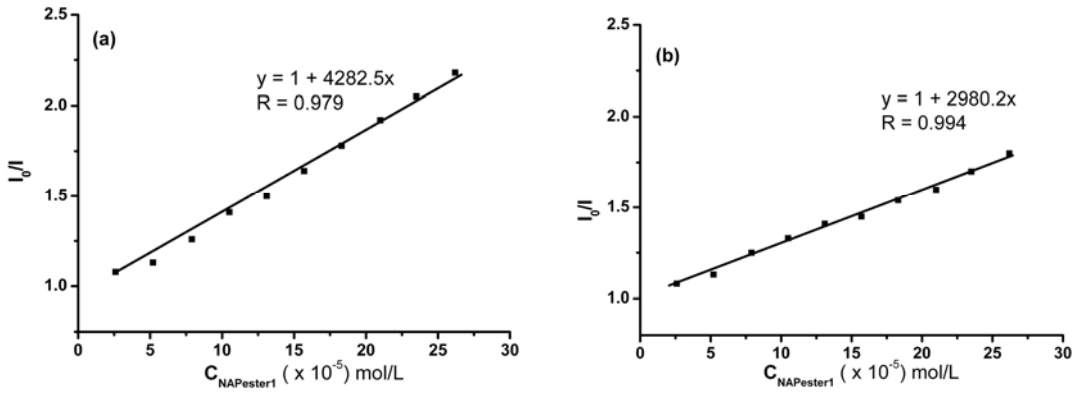


Figure S1 The Stern-Volmer plots of a CdSe/ZnS QDs_{602} (0.1 μM) PBS solution (left) and a CdSe/ZnS QDs_{625} (0.1 μM) PBS solution (right) based on fluorescence change with different amounts of NAP ester **1**.

As shown in figure S1, the Stern-Volmer plots have marked positive properties and are linear dependence of fluorescence intensity ratio with concentration of NAP ester

1. The electron transfer rate constant (k_{ET}) or bimolecular quenching constant (k_q) between CdSe/ZnS QDs and NAP ester **1** were calculated by Stern-Volmer equation as following.[4]

$$I_0 / I = 1 + \tau_0 k_q [\mathrm{Q}]$$

In the equation, I_0 and I are the fluorescence intensities of QDs in the absence and presence of NAP ester **1**, respectively; τ_0 is the lifetime of QDs in the absence of quencher NAP ester **1**; k_q is the bimolecular quenching constant and [Q] is the concentration of added NAP ester **1**.

From this plots the Stern-Volmer constants ($\tau_0 k_q$) were deduced giving the values of 4282.5 M^{-1} and 2980.2 M^{-1} for CdSe/ZnS QDs_{602} (λ_{em} = 602 nm) and QDs_{625} (λ_{em} = 625 nm), respectively. Taking into account the fluorescence average lifetimes for QDs_{602} and QDs_{625} (17.7 ns and 22 ns respectively), the values of bimolecular quenching constants are 2.4 x 10^{11} $M^{-1}S^{-1}$ and 1.3 x 10^{11} $M^{-1}S^{-1}$, respectively, which is significantly larger than the diffusion controlled kinetics (near 1 x 10^{10} $M^{-1}S^{-1}$). This analysis suggested some type of binding interaction, and NAP ester **1** should be absorbed on the surface of the QDs by electrostatic action in the drug release system, which promotes the process of PET-based release mechanism.

3. Fluorescence spectra of the used water-soluble PTMP-PAA capped QDs.

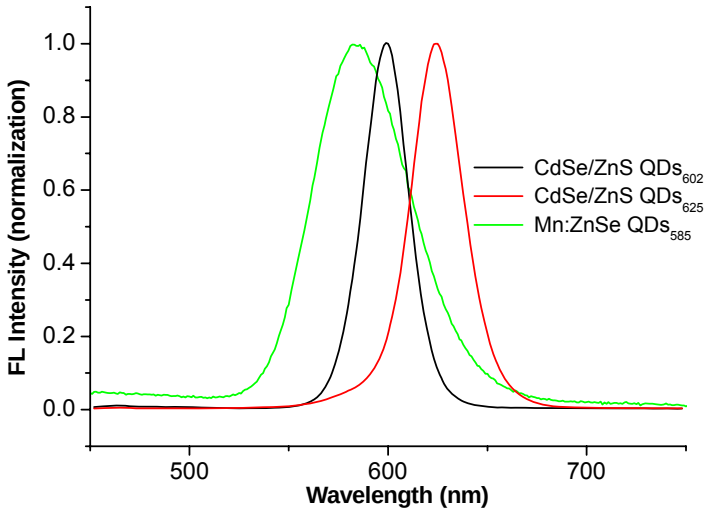


Figure S2 The emission spectra for the used water-soluble PTMP-PAA capped QDs.

Refencences:

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2. M. Tada, *Bull. Chem. Soc. Jap.*, 1975, **48**, 3427-3428.

3. V. Ferri, E. Costa, M. Biancardo, R. Argazzi, C. A. Bignozzi, *Inorganica Chimica Acta.*, 2007, **360**, 1131-1133.

4. J. R. Lakowicz, *Principle of Fluorescence Spectroscopy*, Springer Science & Business Media, LLC, New York, 2006, Charpter **8**, 278-285.