Glutathione Triggers Depolymerization of Polydopamine to Facilitate Controlled Drug Release

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Chemicals.

Dopamine hydrochloride, folic acid, N-[3-(dimethylamino)propyl]-N'-ethylcarbodiimide hydrochloride (EDC), N-hydroxysuccinimide (NHS), glutathione is purchased from Aladdin Reagent (Shanghai, China). NH_2-PEG-NH_2 (Mw 3400) is obtained from Xing Jia Feng Science and Technology Development Co. Ltd. (Shenzhen, China). Dulbecco's modification of Eagle's medium (DMEM, high glucose), penicillin/streptomycin, trypsin and fetal bovine serum are received from Thermo Scientific (Logan, Utah, USA). 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) is achieved from Nanjing KeyGEN Biotech (Nanjing, China). Other chemicals used in this study are the products of Sinopharm Chemical Reagent (Shenyang, China). Deionized (DI) water of 18 MΩ cm is used throughout the experiments.

Characterizations.

Transmission electron microscopy (TEM) images are acquired using a JEM-2100 transmission electron microscope (JEOL, Japan). X-ray diffraction (XRD) patterns are obtained on a D8 Advance diffractometer (Bruker, Germany). Solid-state ^{13}C CP-MAS spectra are recorded at 100.5 MHz on a Bruker Avance II 400 spectrometer, equipped with a 4 mm MAS probe at room temperature. The copper content is measured with inductively coupled plasma mass spectrometry (ICP-MS, Agilent 7500a, USA). An Agilent 6540 UHD Accurate-Mass Q-TOF LC/MS (Agilent Technologies, USA) equipped with an orthogonal ESI source is applied in the positive ionization mode for monitoring difference of PDA's relative molecular mass. The zeta potential of the nanoparticles is measured by a Zeta sizer Nano ZS/ZEN3690

instrument (Malvern, England). UV-vis absorption spectra are recorded on a U-3900 spectrophotometer (Hitachi High Technologies, Japan). Thermo gravimetric analysis of the nanospheres is performed on a 290C analyzer (TGA, Netzsch Company, Germany). FT-IR spectra is acquired on a Nicolet 6700 spectrophotometer (Thermo Electron, USA). Photothermal effect of the materials is determined by irradiating with a diode infrared laser (MDL-III-808 nm-2.5 W-14100192, Changchun New Industries Optoelectronics Tech. Co. Ltd, China).

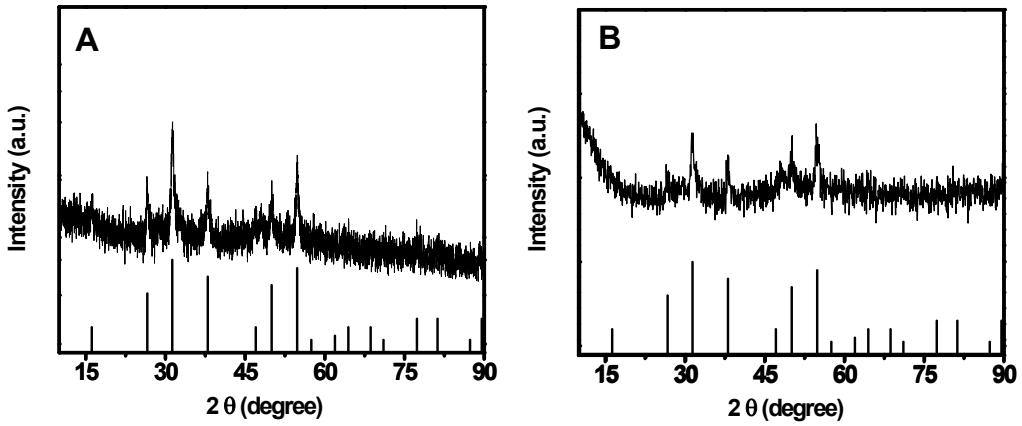

Figure S1. (A) XRD pattern of $CuCo_2S_4$. (B) XRD pattern of $CuCo_2S_4$ after treated with 10 mmol L^{-1} GSH for 72 h.

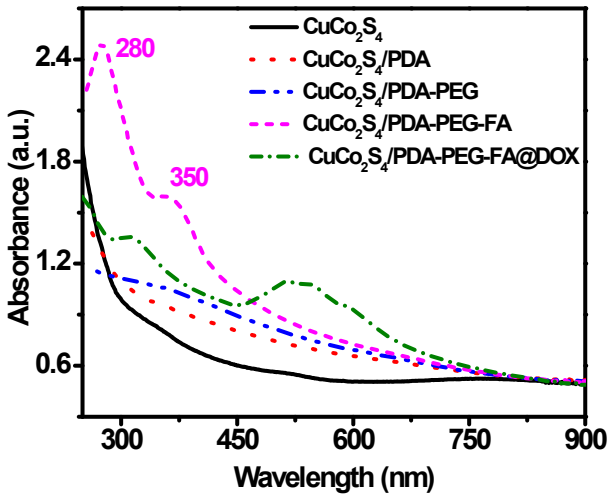

Figure S2. UV-vis-NIR absorption spectra of $CuCo_2S_4$, $CuCo_2S_4$/PDA, $CuCo_2S_4$/PDA-PEG, $CuCo_2S_4$/PDA-PEG-FA and $CuCo_2S_4$/PDA-PEG-FA@DOX (150 μg mL^{-1} for $CuCo_2S_4$, 20 μg mL^{-1} for the loaded DOX).

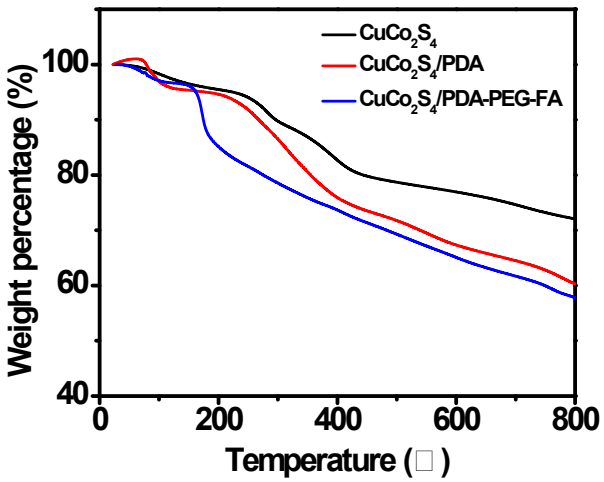

Figure S3. TGA analysis results for $CuCo_2S_4$, $CuCo_2S_4$/PDA and $CuCo_2S_4$/PDA-PEG-FA.

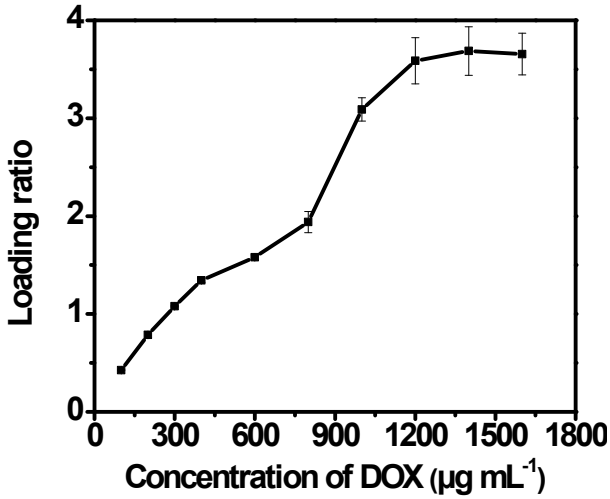

Figure S4. The dependence of DOX loading ratio on DOX concentration.

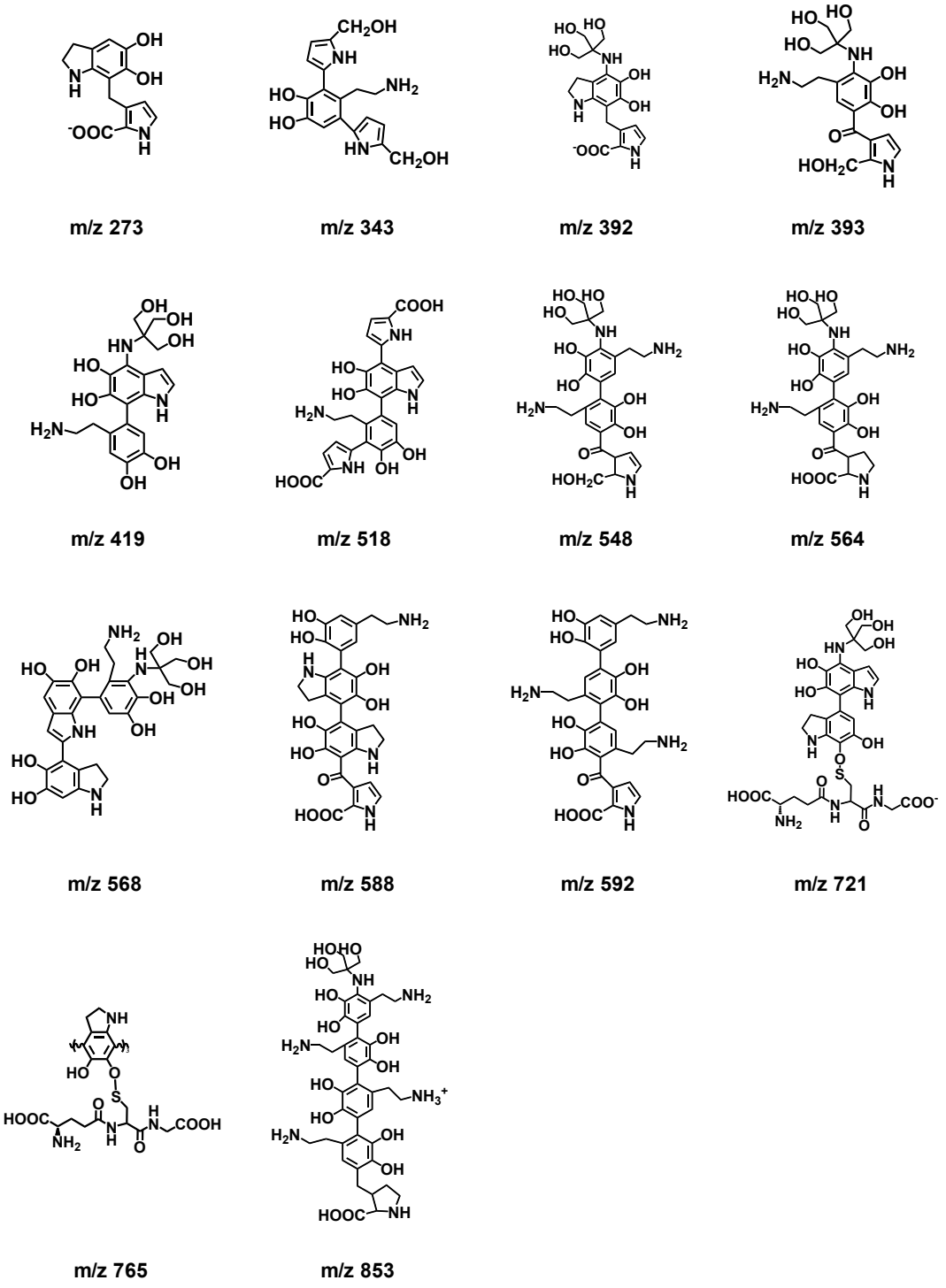

Figure S5. The tentative configurations of some major peaks identified in the mass spectra of native PDA and that after treated with 10 mmol L^{-1} GSH for 72 h. The configurations of a few fragments, i.e., those at m/z of 273, 393 and 518, are identical with those reported in a previous study.[1]

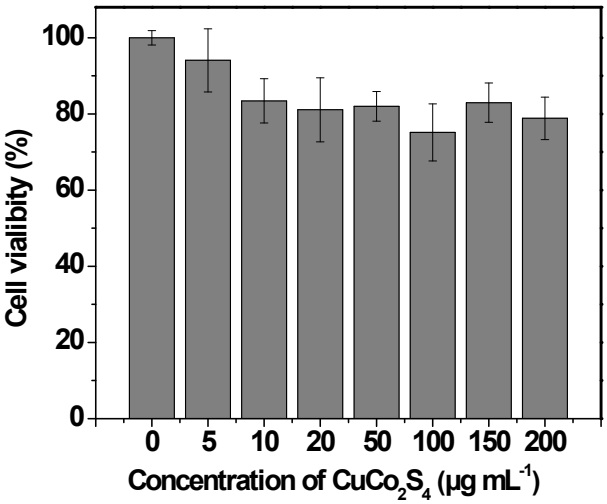

Figure S6. The cytotoxicity test for $CuCo_2S_4$/PDA-PEG-FA.

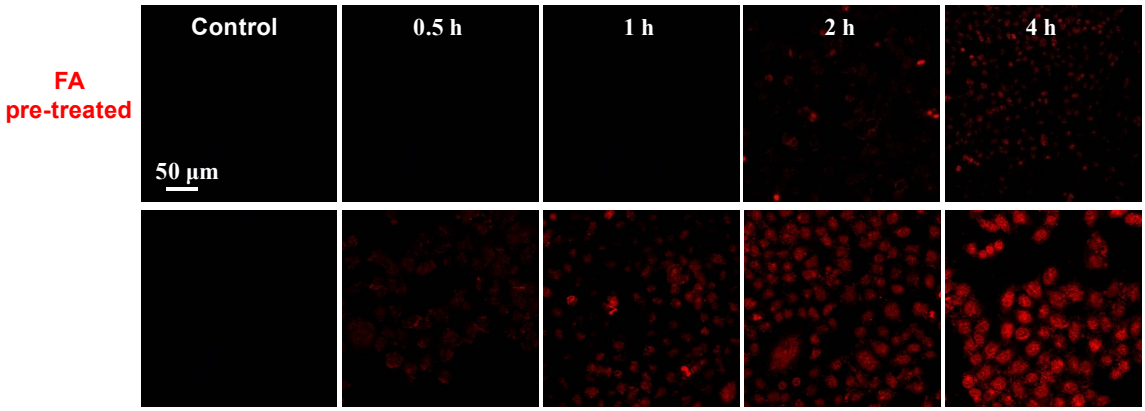

Figure S7. Fluorescence images of HeLa cells after incubating with $CuCo_2S_4$/PDA-PEG-FA@DOX (upper) and FA (bottom) for different times. (The amount of the materials corresponds to a concentration of 50 μg mL^{-1} DOX in all the cases).

Table S1. Comparisons on performances of LR values for some recently reported drug-delivery vehicles.

Materials	LR ($g\ g^{-1}$)	Ref.
Polydopamine nanoparticles	0.7	[2]
Polydopamine/mesoporous calcium phosphate hollow Janus nanoparticles	0.73	[3]
CuS nanoparticles	1.7	[4]
Hydroxyethyl starch stabilized polydopamine nanoparticles	2.0	[5]
Hyaluronic acid-methotrexate conjugates coated magnetic polydopamine nanoparticles	1.5	[6]
$CuCo_2S_4$/PDA-PEG-FA	3.7	This work

Table S2. Cur release from $CuCo_2S_4$/PDA-PEG-FA@Cur at a single stimulus of pH 4.7, 6.3 and 7.4.

pH	Cumulative Cur release (%)
4.7	7.3
6.3	7.1
7.4	6.9

Reference

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