

## Supporting Information

# Facile Synthesis of Ternary CdMnS QDs-Based Hollow Nanospheres as Fluorescent /Magnetic Probes for Bioimaging

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### Experimental Section

#### *Chemicals:*

Tellurium powder (99.9%), NaBH<sub>4</sub> (96%), CdCl<sub>2</sub>, MnCl<sub>2</sub>•4H<sub>2</sub>O, NaOH were purchased from Sinopharm Chemical Reagent Co., Ltd., China, L-Glutathione reduced (GSH) was purchased from Sigma Aldrich.

#### *Preparation of Precursor Solution:*

Hydrogen telluride (NaHTe) was prepared as described previously.<sup>[1]</sup> Sodium borohydride was loaded to a small flask, then 3ml deionized water was added, after which telluride powder (Te:NaBH<sub>4</sub>=1:2) was added to the flask. The flask was sealed quickly with only a small pinhole exposed to atmosphere and placed in the oven at 30°C. After the black telluride powder dissolved completely, the resulting clear aqueous solution contained NaHTe.

The GSH stabilizing reagent was prepared by dissolving CdCl<sub>2</sub>, MnCl<sub>2</sub>, and GSH in deionized water. The pH of the mixed solution was adjusted by dropwise addition of 1 M NaOH solution with stirring. The solution was then degassed using N<sub>2</sub>.

All precursor solutions were prepared freshly.

#### *Synthesis of CdMnS hollow spheres:*

The freshly prepared NaHTe solution was injected into the GSH stabilizing reagent solution under vigorous stirring. The precursor solution was transferred into a Teflon-lined stainless autoclave and maintained at 200°C under vigorous stirring for a certain time, and then cooled to room temperature by a hydro cooling process.

#### *Characterization:*

Fluorescence data were obtained using an RF-5301PC Shimadzu spectrofluorophotometer at room temperature. Aliquots were measured without any size sorting. Power X-ray diffraction (XRD) patterns were collected using a Bruker diffractometer with Cu K $\alpha$  radiation (Germany). Transmission electron micrographs (TEM) were obtained on a JEOL-JEM 2100 electron microscope operated at an accelerating voltage of 200 kV (Japan). High-resolution TEM (HRTEM) images were obtained on a JEM-2100F (Japan). Electron Paramagnetic Resonance (EPR) spectra was measured on a Bruker BioSpin Corp., EMX-8 (Germany). (VSM) spectra were measured on Quantum Design PPMS-9T (ET-II) (USA).

#### *In vitro MR imaging:*

The MRI relaxation times were obtained using a Siemens 3.0 T scanner (Magnetom Trio, Siemens, Munich, Germany) with a wrist coil. Phantom MRI analysis was carried out at various concentrations of Mn in agarose gel. The experimental conditions were as follows: The samples were tested using T<sub>1</sub>-weighted and T<sub>2</sub>-weighted pulse sequences, respectively. T<sub>1</sub>-weighted pulse sequences held the time of echo (T<sub>E</sub>) constant at 11ms while varying the time of repetition (T<sub>R</sub>) to T<sub>R</sub>=24, 100, 200, 400, 600, 900, 1200, 2000, 3000, 5000ms, respectively. T<sub>2</sub>-weighted pulse sequences held T<sub>R</sub> constant at 3000 ms, and varied the T<sub>E</sub>=13.2, 26.4, 39.6, 52.8, 66, 79.2, 92.4, 105.6, 118.8, 132, 145.2 ms. The signal intensity of the samples was measured for image, and T<sub>1</sub> and T<sub>2</sub> were calculated for each concentration of the different contrast agents, respectively.

#### Cell Viability Assay:

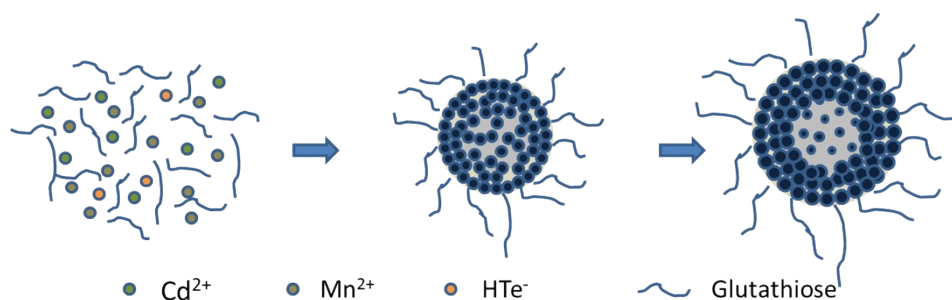
Colorimetric 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide (MTT) assays were performed to assess the metabolic activity of cells in the presence of hollow spheres. The assay was conducted in triplicate in the following manner. For MTT assay, 4T1 cells were seeded into 96-well plates at a density of 3000~10000 cells per well in 200  $\mu\text{L}$  of media and grown overnight. The cells were then incubated with various concentrations of the hollow spheres for 24h at 37°C under a humidified atmosphere (5%  $\text{CO}_2$ ) in the dark. The media containing hollow spheres was then replaced by fresh culture media. The cells were incubated for another 24h, after which they were incubated in media containing 0.5 mg/mL MTT for 4 h at 37 °C. The media was removed and 150  $\mu\text{L}$  DMSO was added to each well. The cells were then incubated for 0.5 h at 37 °C. Absorbance was measured at 570 nm by POLARstar OPTIMA Multidetector Microplate Reader (BMG LABTECH).

**Cell Labeling and Fluorescent Imaging:** HepG2 cells were propagated in Roswell Park Memorial Institute's medium (RPMI1640, DMEM) supplemented with FBS (10%) and penicillin/streptomycin (2%). Then the cultured cells were trypsinized and resuspended in the RPMI1640 medium at a concentration of about  $2 \times 10^4$  /well. The cell suspension (200  $\mu\text{L}$ ) was transferred to each Petri dish (35 mm). After 24 h of incubation, the cells were carefully rinsed with PBS (0.01 mol/L, pH7.4). For each Petri dish, RPMI1640 medium (without fetal blood serum and FAs, 900  $\mu\text{L}$ ) and the CdMnS hollow nanospheres (100  $\mu\text{L}$ , 1 mg/mL) were added and incubated for 24 h. The labeled cells were carefully rinsed with PBS to remove the unbonded CdMnS hollow nanospheres. After wards the labeled cells in the dish were fixed with 4% paraformaldehyde for fifteen minutes and then the cells were washed three times with PBS. The fluorescent imaging of the HepG2 cells was performed with a Leica TSC SP5 confocal microscope.

#### *In vivo MR imaging*

Animal experiments were conducted on 4-week-old female nude mice. Animal procedures were in agreement with the guidelines provided by the Institutional Animal Care and Use Regulations of Shanghai Jiao Tong University. All animal operations were performed in accord with institutional regulations of animal use and care of Shanghai Jiao Tong University. A suspension of  $2 \times 10^6$  4T1 cancer cells in 60  $\mu\text{L}$  phosphate buffered saline (PBS) were subcutaneously administered into the hind leg of each nude mice. When their tumor size reached about 60  $\text{mm}^3$ , the 4T1 tumor mice were treated. *In vivo* MR imaging was performed on a 7.0 T MR imaging system (Pharmascan, Bruker, Germany) using anesthetized nude mice (body weight *ca.* 20 g). Images were obtained at baseline (prior to injection) and at subsequent intervals following injection of CdMnS hollow spheres solution (2 mg/kg body weight).  $T_1$ -weighted images were acquired using a MSME sequence ( $T_R = 220$  ms,  $T_E = 8.7$  ms. Matrix =  $256 \times 256$ , FOV = 4 cm) with respiratory gating technology. Image post-processing was performed using the TopSpin 5.1 software (Bruker, Germany).

[1] Y. Zheng, Z. Yang, J. Y. Ying, *Adv. Mater.* **2007**, *19*, 1475-1479.



**Scheme S1** The Schematic diagram of the formation of the hollow structure

Table S1 ICP-MS results for the hollow spheres with different Cd/Mn ratio.

Element	Cd <sub>0.57</sub> Mn <sub>0.43</sub> S	Cd <sub>0.29</sub> Mn <sub>0.71</sub> S
Mn	19.93	35.86
Cd	30.77	18.62
S	49.30	45.52

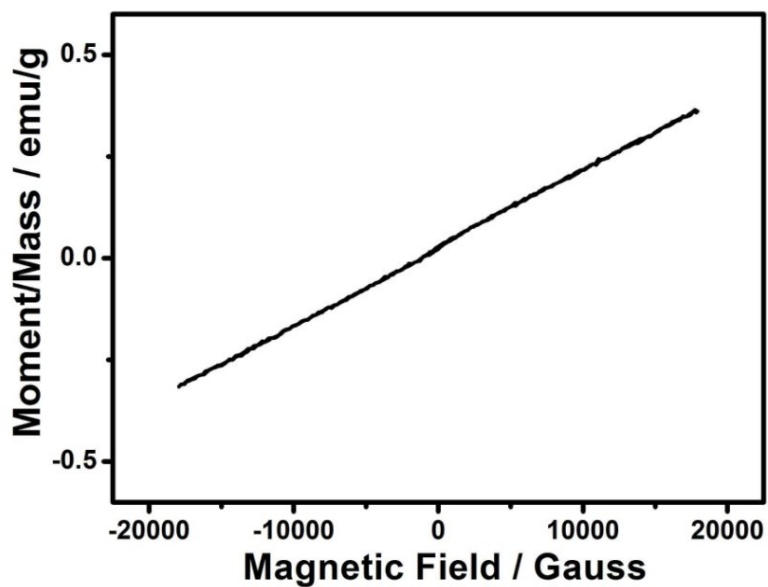


Figure S1. Vibrating sample magnetometer curve of the Cd<sub>0.29</sub>Mn<sub>0.71</sub>S hollow nanospheres.

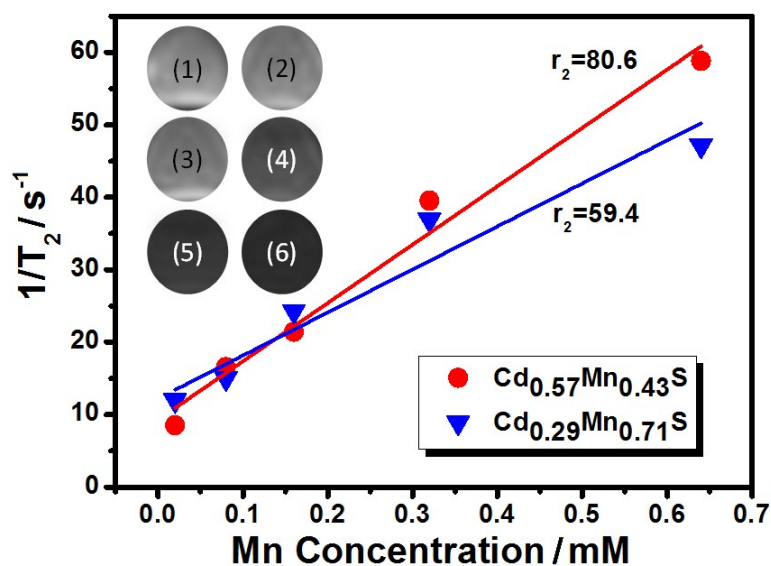
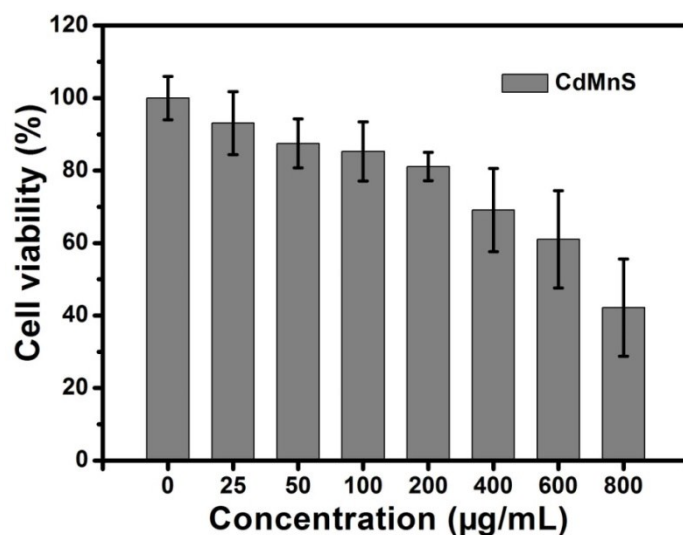
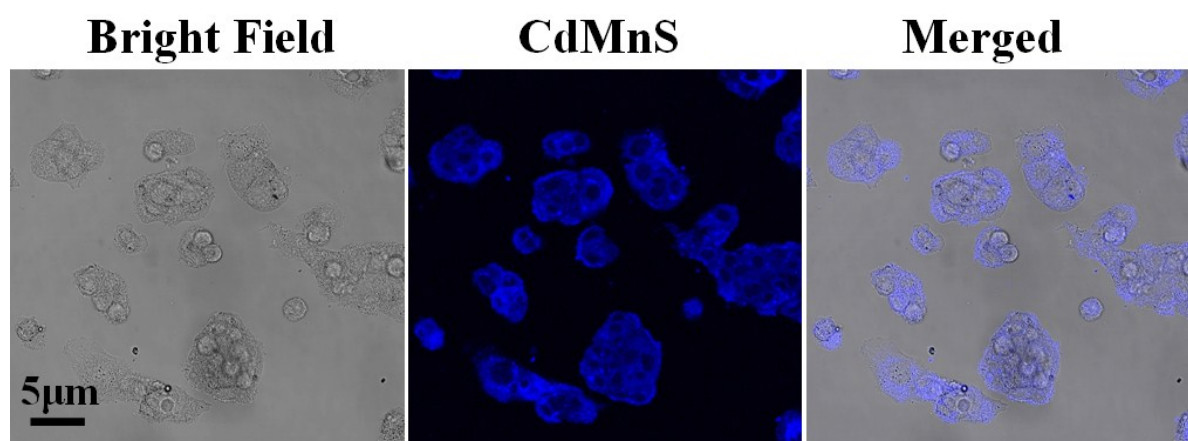


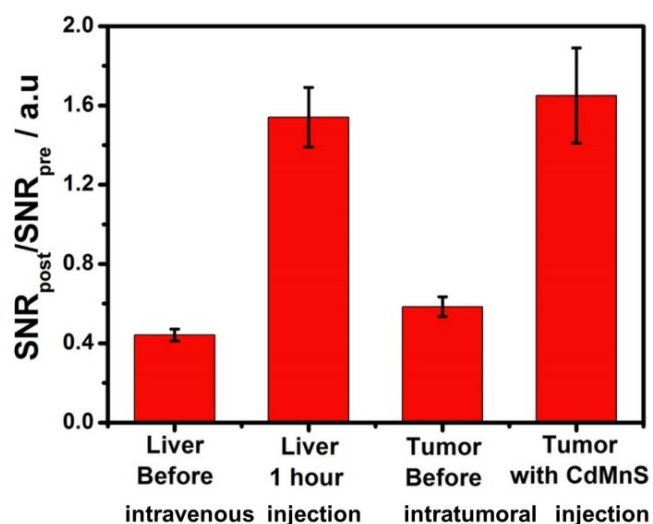
Figure S2. T<sub>2</sub>-weighted images (B<sub>0</sub>=3.0T, T<sub>R</sub>=3000 ms) of the CdMnS hollow spheres as a function of Mn concentrations (mM), (1)-(6) with the increase of the Mn concentration.



**Figure S3.** Cell viability results after incubation of 4T1 cells with various concentrations of the CdMnS hollow spheres



**Figure S4** The confocal laser scanning microscopy (CLSM) images of HepG2 cells labeled with CdMnS hollow nanospheres. The left box corresponds to bright field image, fluorescence image of CdMnS hollow nanospheres is shown in the middle, and the right one shows overlay of the bright field and fluorescence images.



**Figure S5.** Signal change (SNR ratio) in the liver and tumor before and after administration of CdMnS nano hollow spheres (2 mg/kg body weight and 20 µg for intravenous and intratumoral injection respectively). The SNR values were calculated according to  $SNRRIOs = SIRIOS/SIniose$  (SI denotes signal intensity).