Supplementary Material

MnO_2-gated Nanoplatforms with Targeted Controlled Drug Release and Contrast-Enhanced MRI Properties: from 2D Cell Culture to 3D Biomimetic Hydrogels

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Full protocol for the preparation of HMSNs@MnO_2/apt

Synthesis of HMSNs: Bare HMSNs were prepared using previously reported methods [1]. The whole synthesis process of hollow mesoporous silica nanoparticles consists of three steps. Firstly, solid SiO_2 nanoparticles ($sSiO_2$) were prepared using a modified Stöber method. Typically, 74 mL of ethanol, 3.15 mL of ammonium aqueous solution (30%) and 10 mL of ultra-pure water were mixed and further stirred for 1 h. The mixture was then heated up to 50 ° C and 6 mL of TEOS was added. After the reaction with stirring for 3 h, $sSiO_2$ were obtained by centrifugation and washed with ethanol. Secondly, 50 mg of $sSiO_2$ were re-dispersed in 30 mL of ethanol/water mixture 1:2 (v/v), and then 7.5 mL of ethanol/ water mixture 1:2 (v/v) containing 75 mg of CTAB was added. After 30 min of stirring, 125 μL of TEOS and 300 μL of ammonium aqueous solution were added to the above mixture. The mixture was allowed to react for 12 h at room temperature. The $sSiO_2$ @CTAB/SiO_2 spheres were collected by centrifugation, and re-dispersed in 10 mL of water for subsequent use. Thirdly, to transform $sSiO_2$ @CTAB/SiO_2 spheres to HMSS spheres, 10 mL of the above solution containing 50 mg of $sSiO_2$ @CTAB/SiO_2 spheres was mixed with 232 mg of Na_2CO_3. The reaction was stirred at 50 °C for 11 h, the HMSS spheres were harvested by centrifugation. To remove surfactant template, the products were dispersed in 60 mL of NH_4NO_3 ethanol solution (20 mg/mL). The mixture was heated to 45 °C under stirring for 6 h, and then the products were collected by centrifugation, washed with ethanol several times. The procedures were repeated three times.

Synthesis of HMSNs-NH_2: To functionalize the particle surface with amine groups, as-synthesized HMSNs were first dispersed in 20 mL of toluene, followed by addition of 1 mL of APTES. The system was sealed and refluxed at 120 °C in oil bath for 12 h. Afterward, the mixture was centrifuged and washed with ethanol for several times to remove the residual APTES.

Synthesis of HMSNs@MnO_2: 20 mg of HMSNs-NH_2 was dispersed in 4.2 mL MES buffer (0.1M, pH 6.0) and then 0.8 mL of 5 mM $KMnO_4$ in water was added to the mixture under ultrasonic condition. The resulting mixture was sonicated for another one hour during which brown-black colloids were observed. Subsequently, the raw product was collected by centrifugation, washed several times with deionized water and alcohol to remove any possible residual reactants, and redispersed in 2 mL PBS solution (pH 7.4).

Synthesis of HMSNs@MnO_2/apt: The physical adsorption of aptamer on HMSNs@MnO_2 was carried out by mixing 0.8 mL of HMSNs@MnO_2 (20 $mg.mL^{-1}$) in PBS and 200 μL of AS1411 (1 μM). After 3 h of incubation, the solution was centrifuged at 6000 rpm, washed several times, and then dispersed in PBS (pH 7.4) for further application. The preparation of fluorescently-labeled hollow mesoporous silica nanoparticles was performed by adding FITC to the starting solution used for bare HSMNs preparation.

Reference

[1] Chen F, Hong H, Shi S, Goel S, Valdovinos H, Hernandez R, et al. Engineering of hollow mesoporous silica nanoparticles for remarkably enhanced tumor active targeting efficacy. Sci Rep. 2014; 4: 5080.

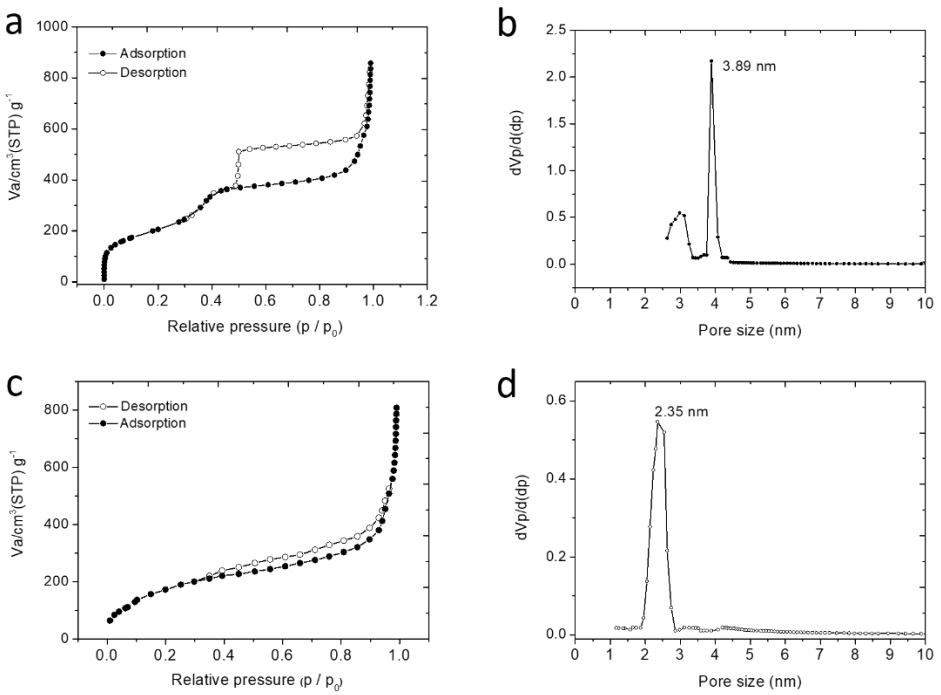

Figure S1. N_2 adsorption-desorption isotherms at 77 K of a) HMSNs and c) HMSNs@MnO_2 with the corresponding pore diameter distribution obtained by the BJH method on the adsorption branch of b) HMSNs and d) HMSNs@MnO_2.

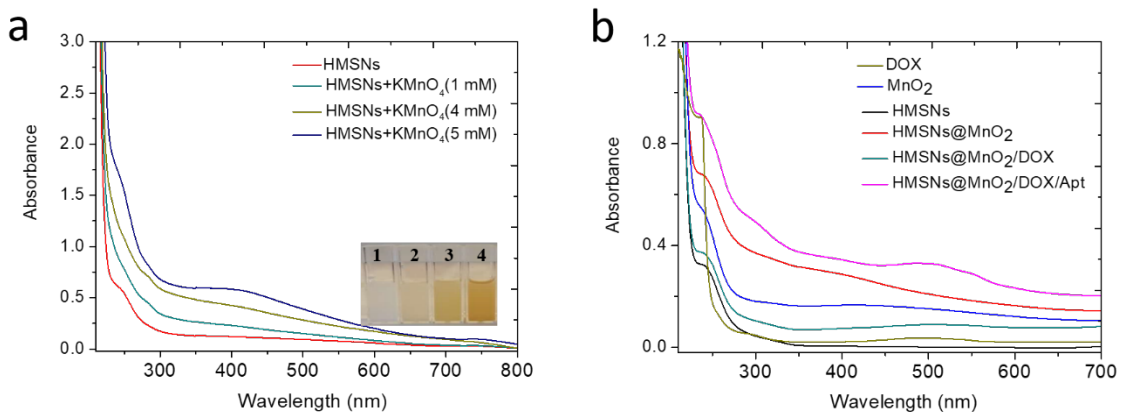

Figure S2. (a) Absorbance spectra of the HMSNs after addition of $KMnO_4$ with different concentrations （1 mM, 4 mM and 5 mM）and the corresponding insert digital pictures with the solution color change from white to brown. (b) Absorbance spectra of the DOX, MnO_2, HMSNs, HMSNs@MnO_2, HMSNs@MnO_2(DOX) and HMSNs@MnO_2(DOX)/apt.

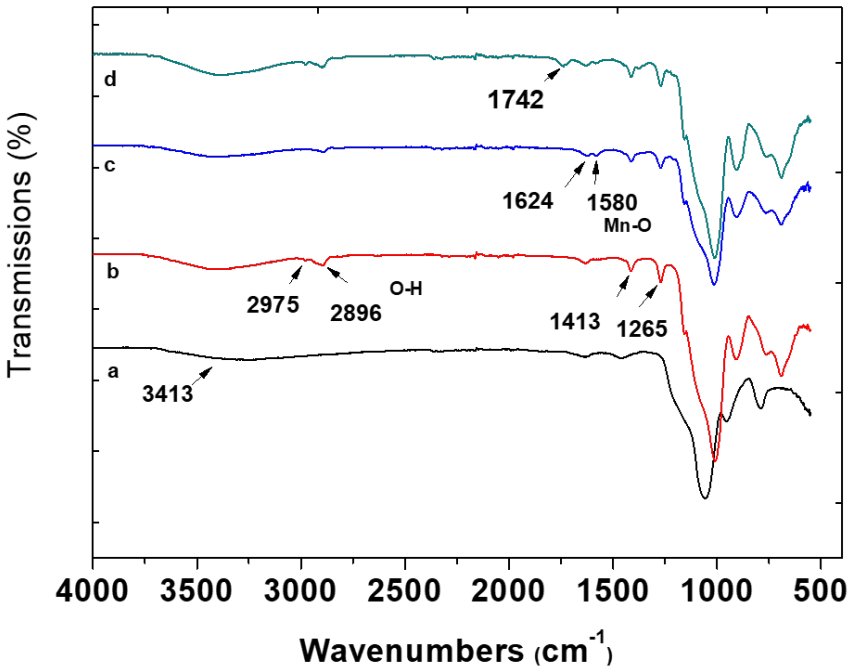

Figure S3. FTIR spectra of (a) HMSNs, (b) HMSNs@MnO_2, (c) HMSNs@MnO_2(DOX), (d) HMSNs@MnO_2(DOX)/apt.

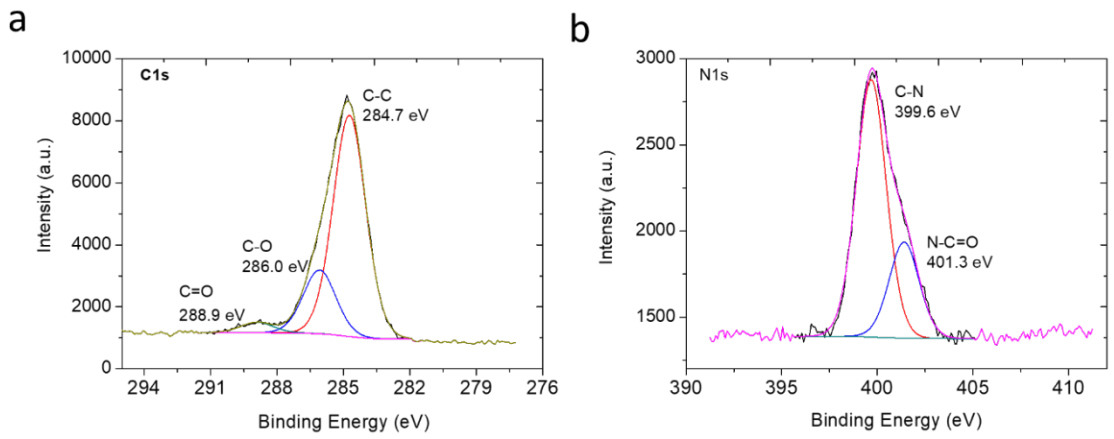

Figure S4. Deconvoluted XPS spectra of (a) C1s, (b) N1s for HMSNs@MnO_2(DOX)/apt.

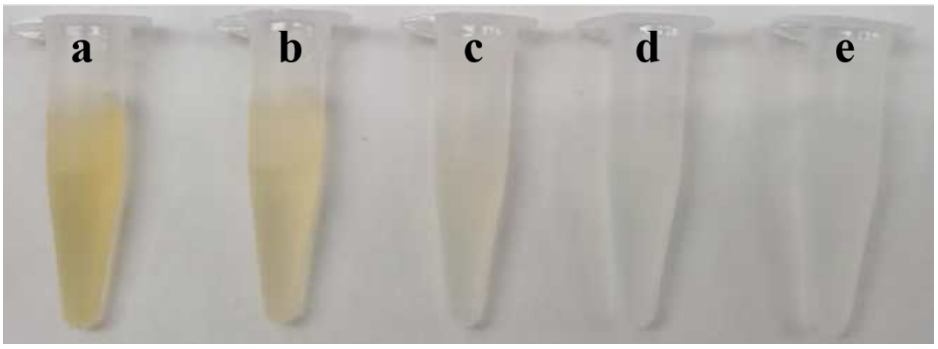

Figure S5. Images of HMSNs@MnO_2/apt suspensions in different conditions, (a) pH 7.4; (b) pH 5.5; (c) pH 7.4, 5mM GSH; (d) pH 7.4, 10mM GSH; (e) pH 5.5, 5mM GSH.

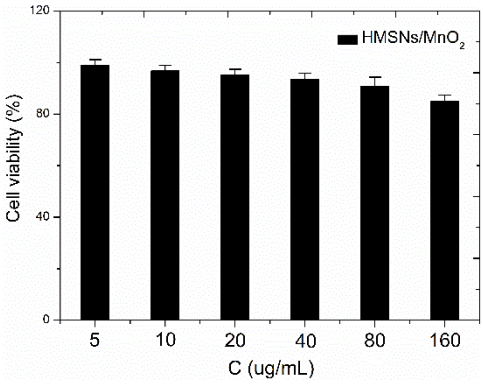

Figure S6. HeLa cell viability after incubation with drug-free HMSNs@MnO_2 nanoparticles for 24 h as a function of particle concentration.