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Supplementary Information

One-pot synthesis of biodegradable polydopamine-doped mesoporous silica nanocomposites (PMSNs) as pH-sensitive targeting drug nanocarriers for synergistic chemo-photothermal therapy

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Experimental

Materials

Hexadecyl Trimethyl Ammonium Chloride (CTAC, 99.0%) was purchased from Energy Chemical. Triethanolamine (TEA, 99.0%), dopamine hydrochloride (DA·HCl, 98%), ammonium nitrate (NH_4NO_3, AR), cyclohexane, sulfuric acid (H_2SO_4, 98%), sodium nitrate ($NaNO_3$, 99.0%), potassium permanganate ($KMnO_4$, AR), H_2O_2 (AR, 30%), ammonia solution ($NH_3{\cdot}H_2O$, 25~28%), hexadecyl trimethyl ammonium bromide (CTAB, 99.0%), ascorbic acid (99.99%) and methanol were all obtained from Aladdin Industrial Corporation, Shanghai. Tetraethyl orthosilicate (TEOS, 99%), (3-Aminopropyl) triethoxysilane (APTES, AR), IGEPAL (CO-520), silver nitrate ($AgNO_3$, 99%), sudium borohydride ($NaBH_4$, 99.0%), Gold(III) chloride trihydrate ($HAuCl_4.3H_2O$, 99.0%) and doxorubicin (DOX) were purchased from Sigma. Folic acid (FA, AR) was obtained from Xiya reagent. Graphite power (99.9995%) was purchased from Alfa Aesar. Reagents for biological experiments including DMEM, CCK-8, 4',6-diamidino-2-

phenylindole (DAPI), Fetal bovine serum (FBS) and Trypsin. The ultrapure water with a resistivity of 18.2 MΩ·cm obtained from Milli-Q Gradient System (Millipore, Bedford, MA, USA) was used for the whole experiments.

Synthesis of SiO_2@PMSNs, GO@PMSNs and GNRs@PMSNs

SiO_2 nanoparticles was synthesized by reverse microemulsion method as follows: 6 ml of cyclohexane and 0.6 ml of CO-520 were added to 25 ml round bottom flask, stirred 15 min, then 100 μl ethanol was added, after 30 min, and then 100 μl $NH_3 \cdot H_2O$ was added to the above solution, keeping stirred 30 min. Finally, 200 μl of TEOS was added to the reaction system, stirred 24 h. After centrifugation, the precipitate was washed with ethanol several times, and then the obtained SiO_2 were dispersed in ethanol.

GO was synthesized from graphite power via a modified Hummers method [a]. In detail, 1.0 g of graphite was mixed with 23 mL of 98% H_2SO_4 in a 250 mL round-bottom flask under an ice-water bath, with continuous stirring. After a period more than 15 min, 0.5 g of $NaNO_3$ and 3 g of $KMnO_4$ were added very slowly into the mixture. The solution kept stirring in the ice-water bath for 2 h, and then the temperature rose to 35 °C and kept stirring for 1 h. Afterwards, 46 mL of water was added to the flask and kept the mixture at 98 °C for 15 min in an oil bath before 140 mL of water was added. After another 15 min, the solution was removed from the oil bath and 10 mL of 30% H_2O_2 were slowly added to end the reaction. This suspension was stirred at room temperature for 5 min, then repeatedly centrifuged and washed twice with 5% HCl solution and the power was dried at 60 °C overnight in vacuum drying oven.

GNRs were synthesized by seed growth method [b]. Briefly, the gold seed was firstly synthesized, 0.364 g of CTAB was dissolved in 9.15 mL of deionized water and then 0.25 mL of 10 mM HAuCl4 was mixed with CTAB solution. 0.6 mL of 0.01 M NaBH4 was quickly injected into the $HAuCl_4$-CTAB solution under vigorous stirring for 2 min. Then, the seed solution was aged at room temperature for 1 h before use. Secondly, preparing the growth solution, 3.64 g of CTAB was dissolved in 100 mL of warm water at 60 °C in a 500 mL round bottom flask. The solution was natural cooling to 30 °C, and then 5mL of 10 mM HAuCl4 solution added. The mixture was kept undisturbed at 30 °C for 10 min, subsequently 1 mL of 10 mM AgNO3 solution was added. After 5 min of slow stirring, 2 mL of 0.5 M H_2SO_4 was added into reaction system and stirring for 5 min. After, 0.8 mL of 0.1 M ascorbic acid was added, and the solution was vigorously stirred until it became colorless. Finally, 0.24 mL of seed solution was injected into the growth solution. The resultant mixture was stirred for another 30 s and left undisturbed at 30 °C for 12h for GNRs growth. The reaction products were isolated by centrifugation at 8000 rpm/min for 30 min followed by removal of the supernatant twice. The precipitates were re-dispersed in 40 mL of water.

Synthesis of SiO_2@PMSNs, GO@PMSNs and GNRs@PMSNs were based on the method of PMSNs. Briefly, 8 ml of 25% CTAC aqueous solution was added to 12 ml of ultrapure water, and then 48μl of TEA was successively added in 50 ml round bottom flask, keeping rapidly stirred in a water bath at 60 °C for 1 h. Then, suitable concentration of the prepared SiO_2 or GO or GNRs was added to the flask, after stirring 1h, 50 mg of DA·HCl was added to the above solution. Subsequently, 10 ml of 20 % TEOS/cyclohexane solution was slowly added and gently stirred for 12 h. After centrifugation, the precipitate was washed with ethanol and water several times, and then SiO_2@PMSNs, GO@PMSNs and GNRs@PMSNs were obtained. The product was dispersed to 0.6% NH_4NO_3/ethanol solution at 60 °C water bath for 12 h to remove the extra template CTAC. After centrifugation, the precipitate was washed with ethanol and water several times, the final nanocomposites were dispersed in water.

References

a. W.S.H. Jr and R.E. Offeman, J. Am. Chem. Soc, 1958, 80 1339.

b. X. Ye, L. Jin, H. Caglayan, J. Chen, G. Xing, C. Zheng, V. Doannguyen, Y. Kang, N. Engheta and C.R. Kagan, ACS Nano, 2012, 6 2804-2817.

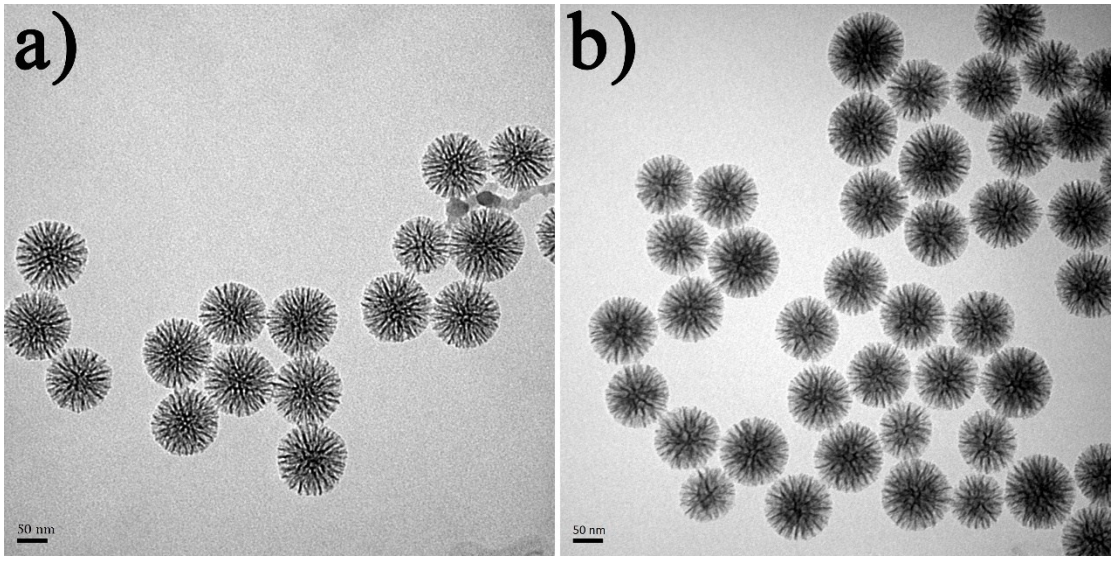

Fig. S1 (a) TEM images of PMSNs dispersed in water and kept for different times of (a) 1 day and (b) 144 days. All scale bars represent 100 nm.

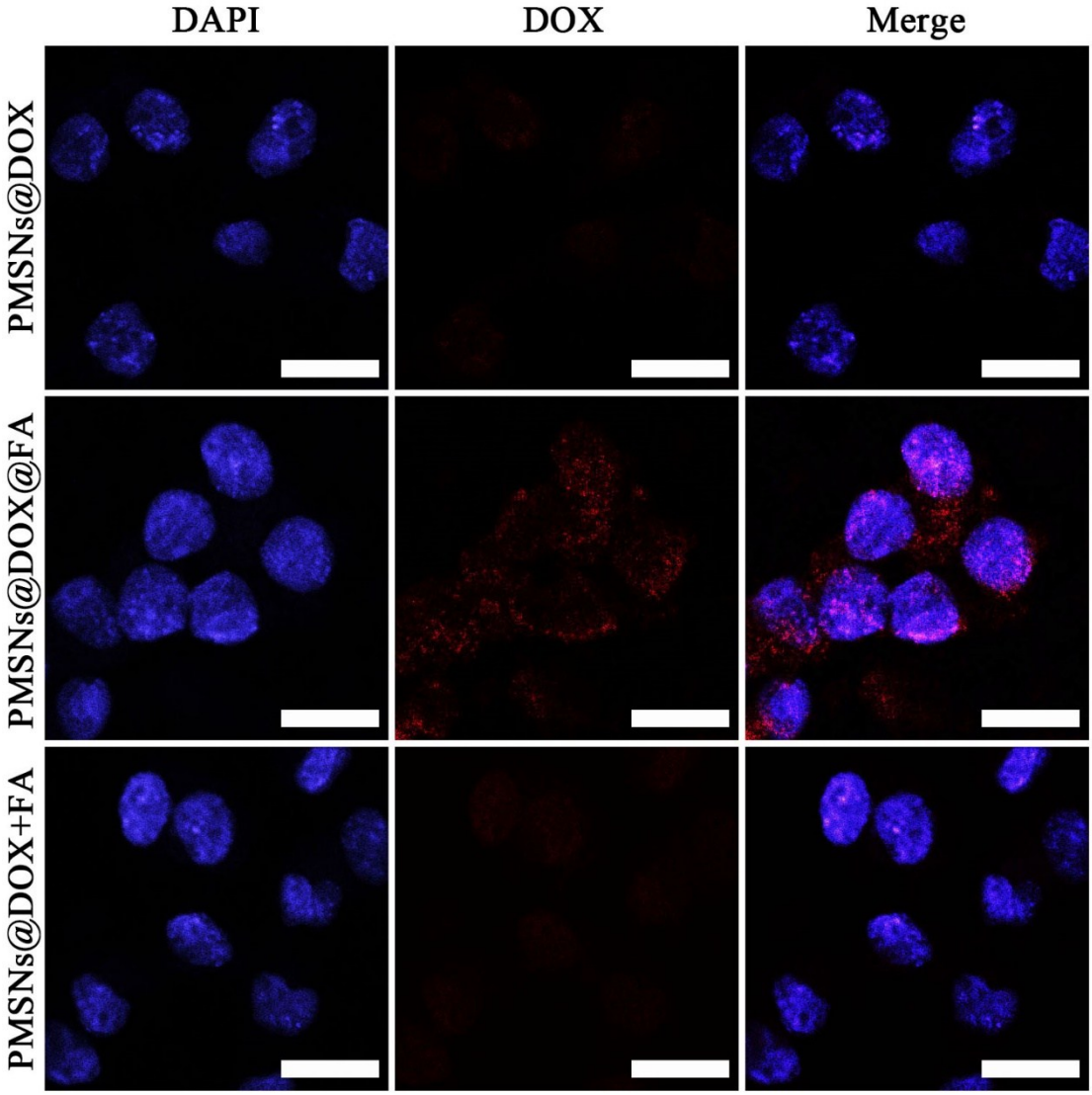

Fig. S2 (a) CLSM-images of HepG2 cells incubated with PMSNs@DOX, PMSNs@DOX@FA and PMSNs@DOX + free FA, for each series, images from left to right can be classified to the cells in the nuclei of cells (blue, being stained by DAPI), DOX fluorescence in cells (red), and the merged images of DAPI (blue) and DOX (red), respectively. Scale bars, 20 μm.