## **Supporting information**



Fig. S1. TEM images of DOX@Ps 80-SPIONs after 72h of incubation with 10% FBS-containing pH7.4PBS or 10% FBS-containing DMEM culture medium at **37** °C.



Fig. S2. Cell apoptotic analysis of C6 cell after treatment of blank Ps 80 SPIONs with different centration (A) and different DOX-containing formulation (B) by flow cytometry. C6 cells were seeded at a density of  $10^5$  cells/well into 12-well plates. After incubation for 24 h, different DOX formulations were added into the plates with DOX concentration 6 µg/ml in each well, blank Ps 80-SPIONs with different concentration of Fe (25 µg/ml, 50 µg/ml and 100 µg/ml) in each well, untreated cells were served as control. 24 h later, cells were treated according to Annexin V-FITC apoptosis detection kit and the percent of early apoptosis, late apoptosis and necrosis cells were analyzed by flow cytometry (BD, USA).



Fig. S3. T2-weighted MRI of DOX@Ps 80-SPIONs alone (A) and C6 cells (B) incubated with the different concentration of DOX@Ps 80-SPIONs. T2-weighted turbo spin echo MRI was performed on a 3T scanner (Trio with Tim, Siemens, Erlangen, Germany) and sequence was acquired using the following image parameters: pulse repetition time (TR)/echo time (TE) = 2300/110 ms; matrix size= $256 \times 256$ ; FOV= 56 mm×70 mm; slice thickness = 2.4 mm.



Fig. S4. The frozen sections of OCT-embedded brain of rat were stained with Prussian blue after administration of PBS. The bar represented 100 µm.