

## **A facile route to core-shell nanoparticulate formation of arsenic trioxide for effective solid tumor treatment**

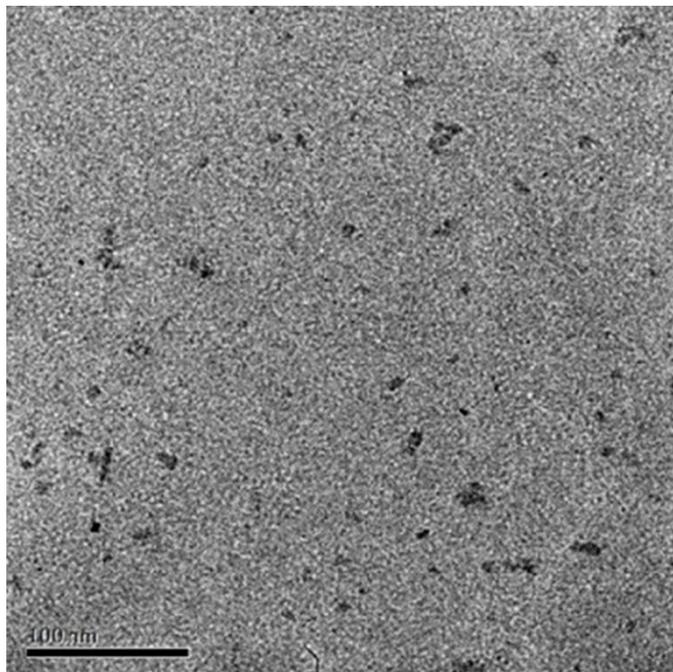
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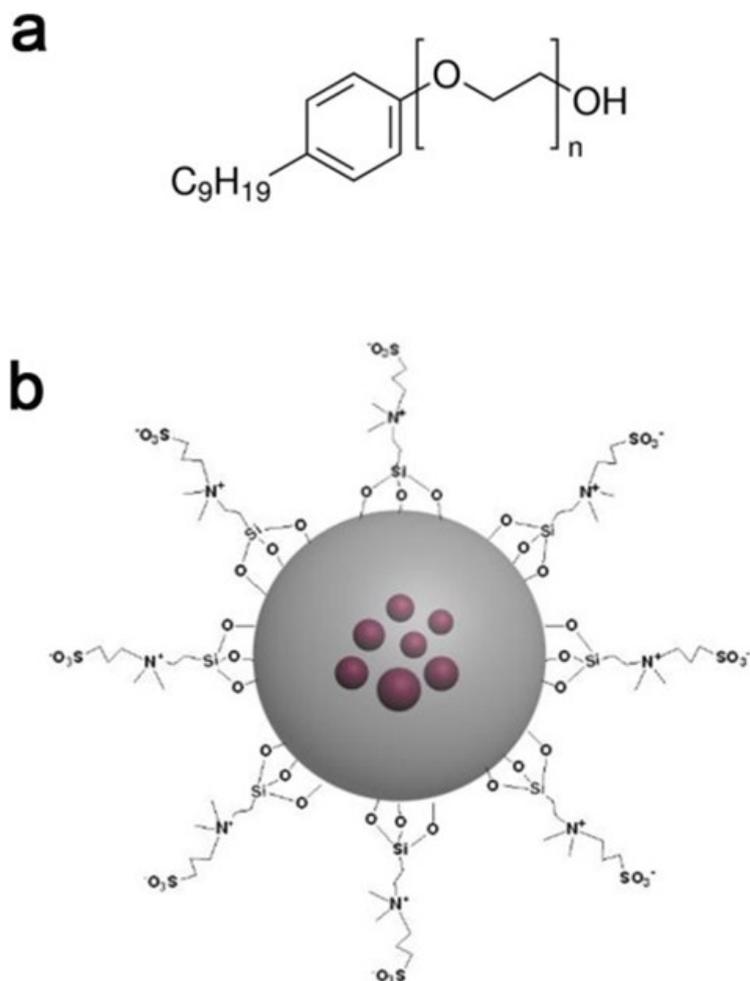
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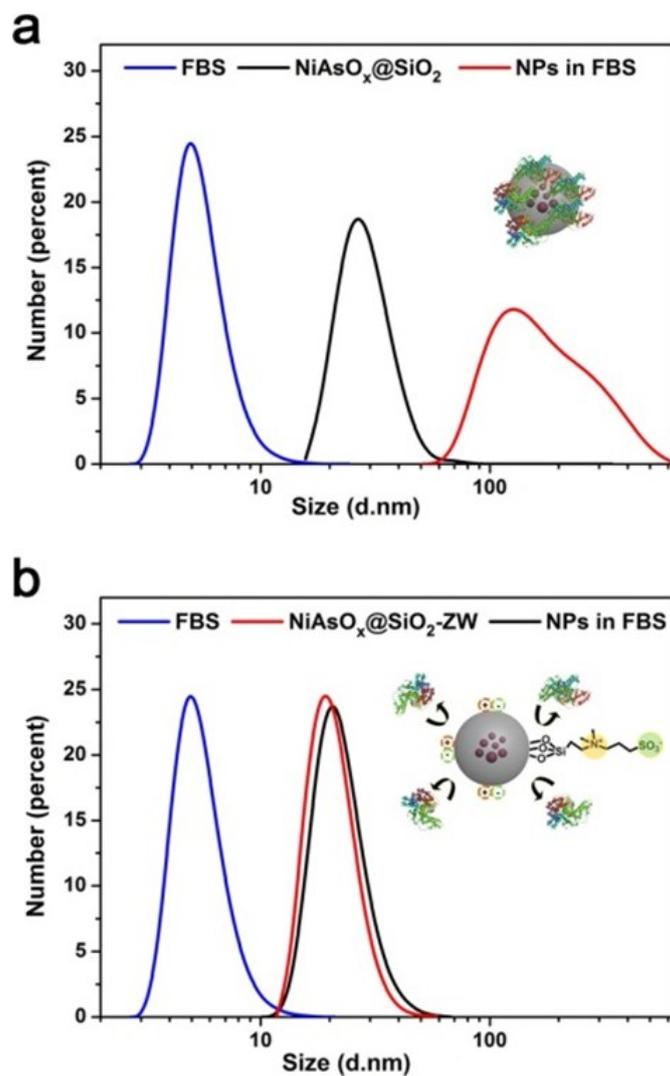
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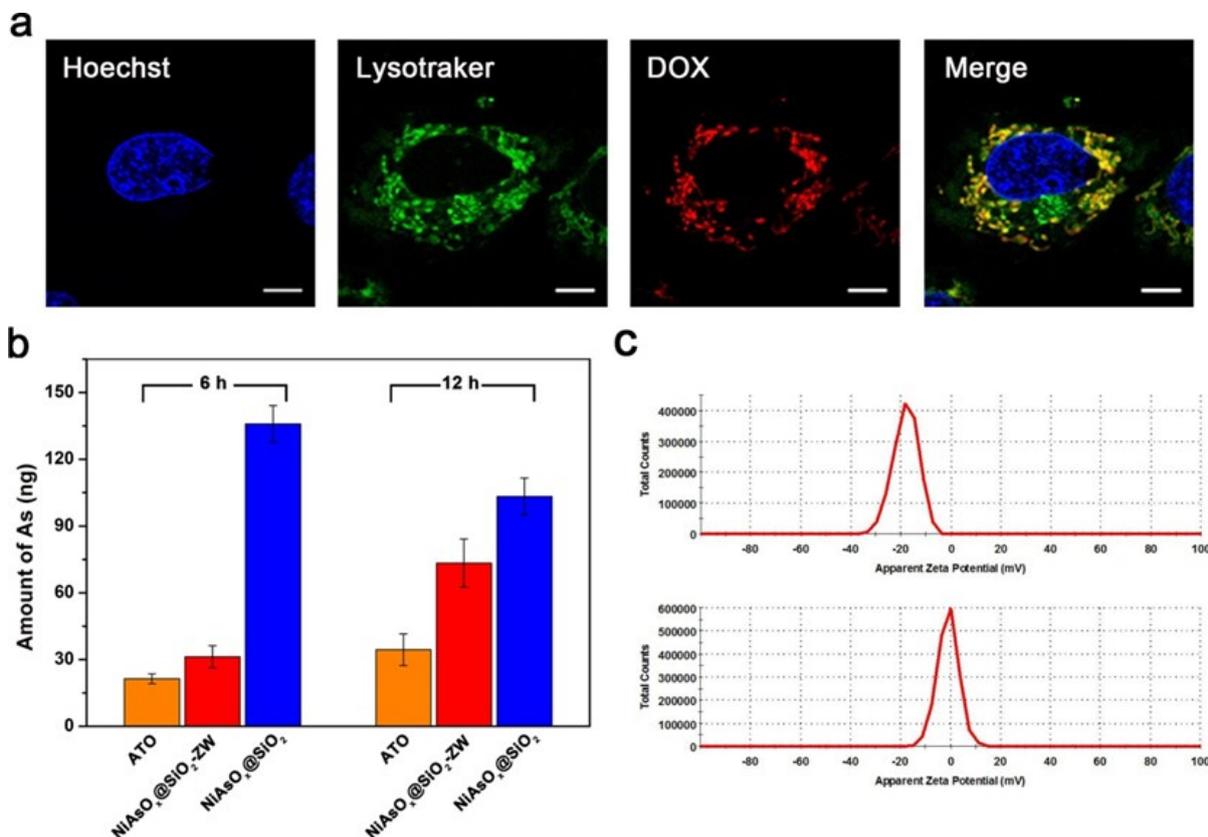
**Fig. S1** TEM image of NiAsO<sub>x</sub> nanoparticles. Scale bar, 100 nm.



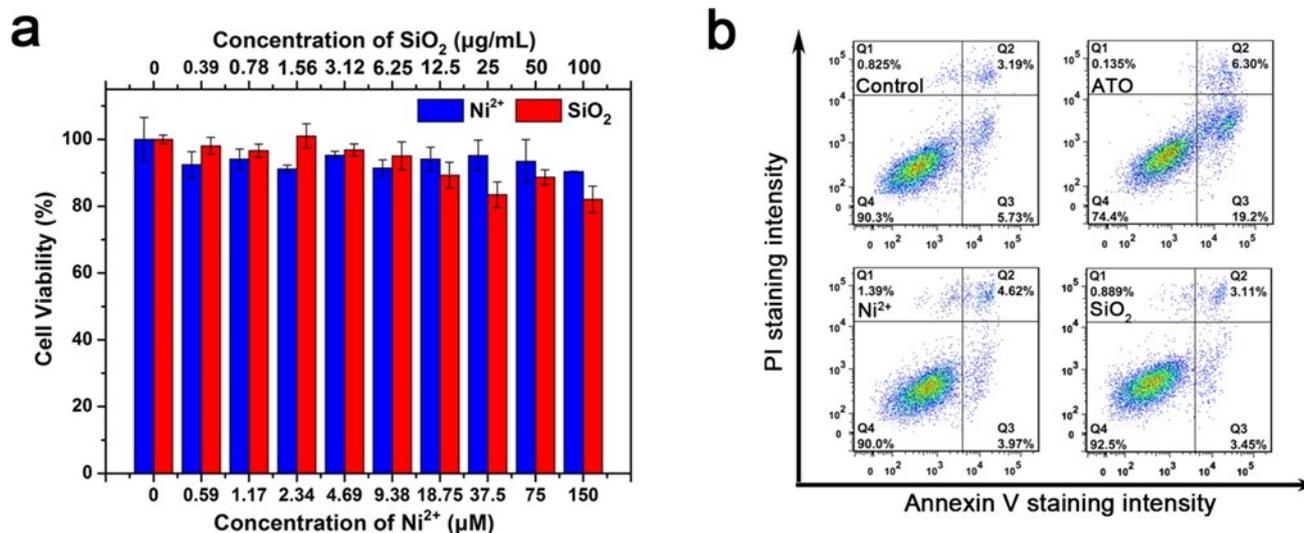
**Fig. S2** (a) Molecular structure of Igepal Co-520; (b) Scheme of NiAsO<sub>x</sub>@SiO<sub>2</sub>-ZW nanocomposites with the sulfobetaine siloxane zwitterion molecules on surface.



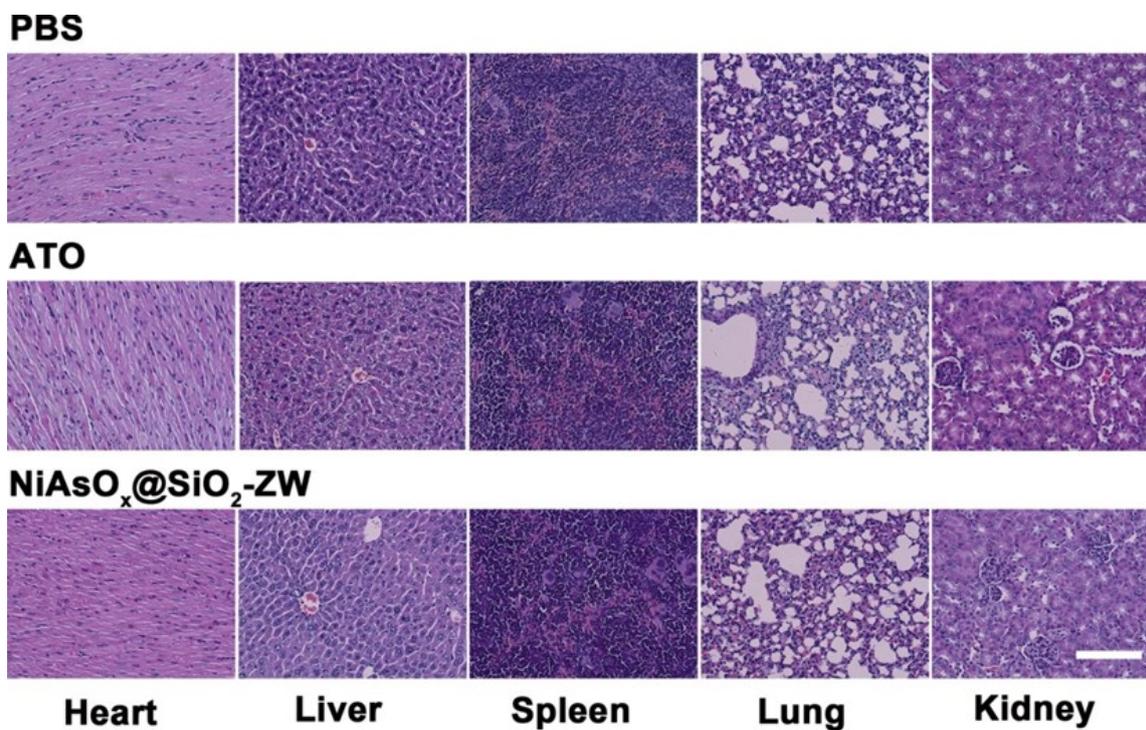
**Fig. S3** Particle size distribution for NiAsO<sub>x</sub>@SiO<sub>2</sub> (a) and NiAsO<sub>x</sub>@SiO<sub>2</sub>-ZW (b) nanocomposites in the presence and absence of 20% (v/v) fetal bovine serum (FBS) after 48 h.



**Fig. S4** (a) Confocal fluorescence imaging of HuH-7 cells treated with NiAsO<sub>x</sub>@SiO<sub>2</sub>-DOX (4 μM DOX) for 6 h, scale bars: 7.5 μm. Hoechst 33342 and LysoTracker green were used to stain cell nuclei (blue) and lysosome (green), respectively. (b) Total amount of As ions in Huh-7 cancer cells incubated with free ATO, NiAsO<sub>x</sub>@SiO<sub>2</sub> and NiAsO<sub>x</sub>@SiO<sub>2</sub>-ZW for 6 h or 12 h. The concentration of As was tested by ICP-MS (*n* = 3/group). (c) The zeta-potential analysis of NiAsO<sub>x</sub>@SiO<sub>2</sub> (upper) and NiAsO<sub>x</sub>@SiO<sub>2</sub>-ZW (below) in PBS buffer.



**Fig. S5** (a) The cytotoxicity of Ni ions and  $\text{SiO}_2$  nanoparticles against Huh-7 cell after incubation for 24 h. (b) Quantitative flow cytometric analysis of Huh-7 cells after treatment with PBS, ATO (10  $\mu\text{M}$ ), Ni ions (150  $\mu\text{M}$ ) and  $\text{SiO}_2$  (100  $\mu\text{g/mL}$ ) for 24 h, respectively. Cells were stained with propidium iodide (PI) and Annexin-V for recognizing the phosphatidylserine presented on apoptosis cells at room temperature.



**Fig. S6** Histopathology of mouse tissues following an intravenous injection of PBS, ATO, NiAsO<sub>x</sub>@SiO<sub>2</sub>-ZW with the dose of 2.0 mg As per kg via tail vein. Representative sections of various organs taken from mice were stained by hematoxylin and eosin (H&E) at 24 h post-injection.

Scale bar: 100  $\mu$ m.