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Size-Dependent Ag_2S Nanodots for Second Near-Infrared Fluorescence/Photoacoustics Imaging and Simultaneous Photothermal Therapy

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Introduction:

- Semiconductor metal sulfide nanoparticles such as CuS and Ag_2S nanocrystals have been extensively explored for photo thermal therapy (PTT) or fluorescence imaging because of their good near-infrared (NIR) absorbance, enhanced resistance to photobleaching, effective photoconversion efficiency, ultrasmall size etc.

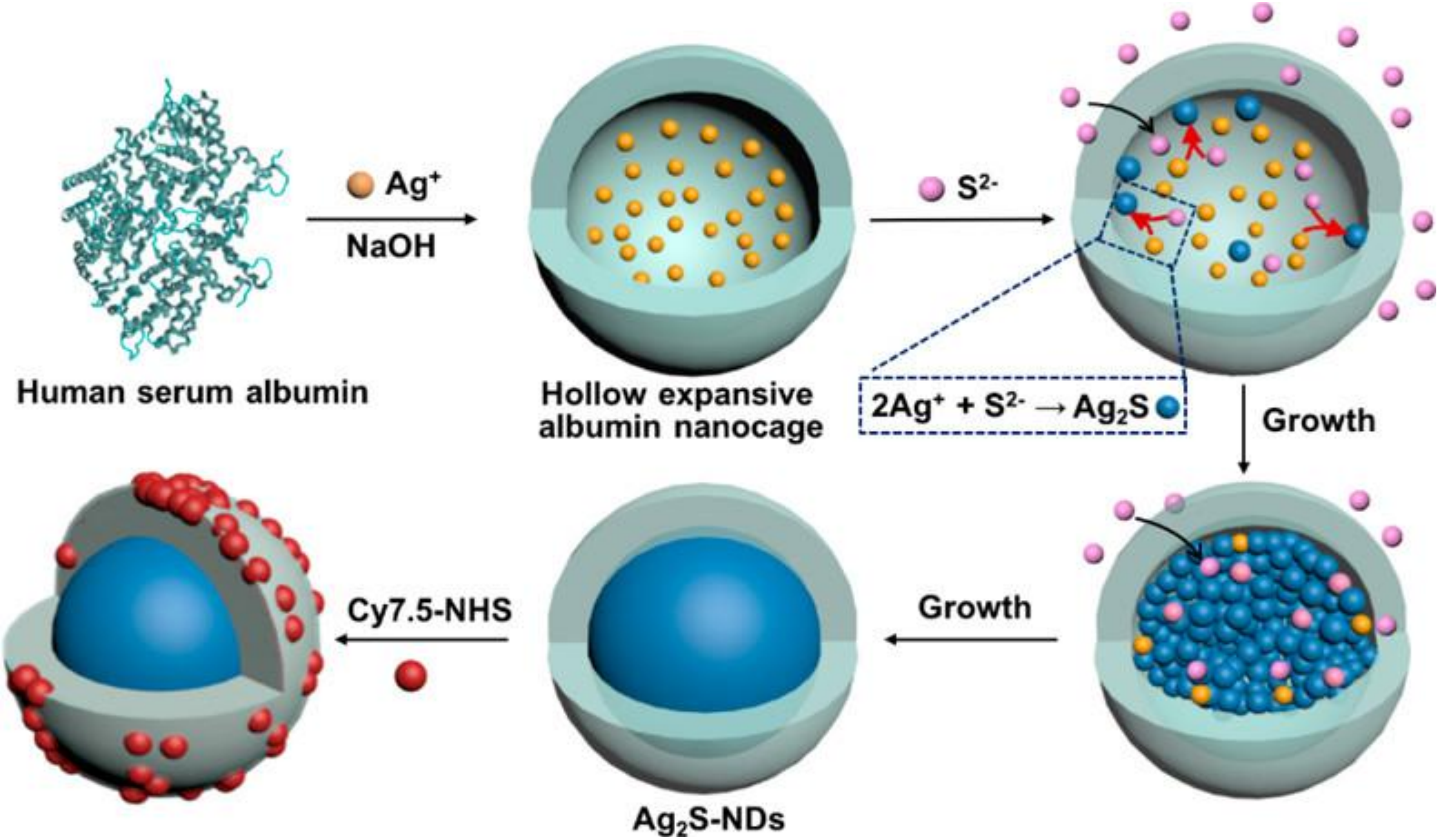
- Unlike single-component theranostic agents, this class of semiconductor nanocrystals only possess either fluorescence or a photothermal effect instead of theranosticcharacteristics.

- Various strategies such as thermal decomposition, microemulsion method, biomimetic approach, sol−gel method, hydrothermal method and microwave method have been developed to synthesize various Ag_2S nanocrystals.

- It is highly desired to explore a facile synthetic approach that is accomplished under mild conditions using clinically acceptable ingredients, thereby satisfying fundamental theranostic demands.

- In this paper, they have demonstrated the multifunctional Ag_2S nanodots (Ag_2SNDs) as a theranostic agent. These NDs are synthesized through precisely controlled growth within clinically acceptable human serum albumin (HSA) nanocages.

Synthesis:



Scheme 1. Schematic Illustration of Theranostic Ag_2S Nanodots with Clinical Potential Synthesized through Precisely Controlled Growth in Albumin Nanocages.

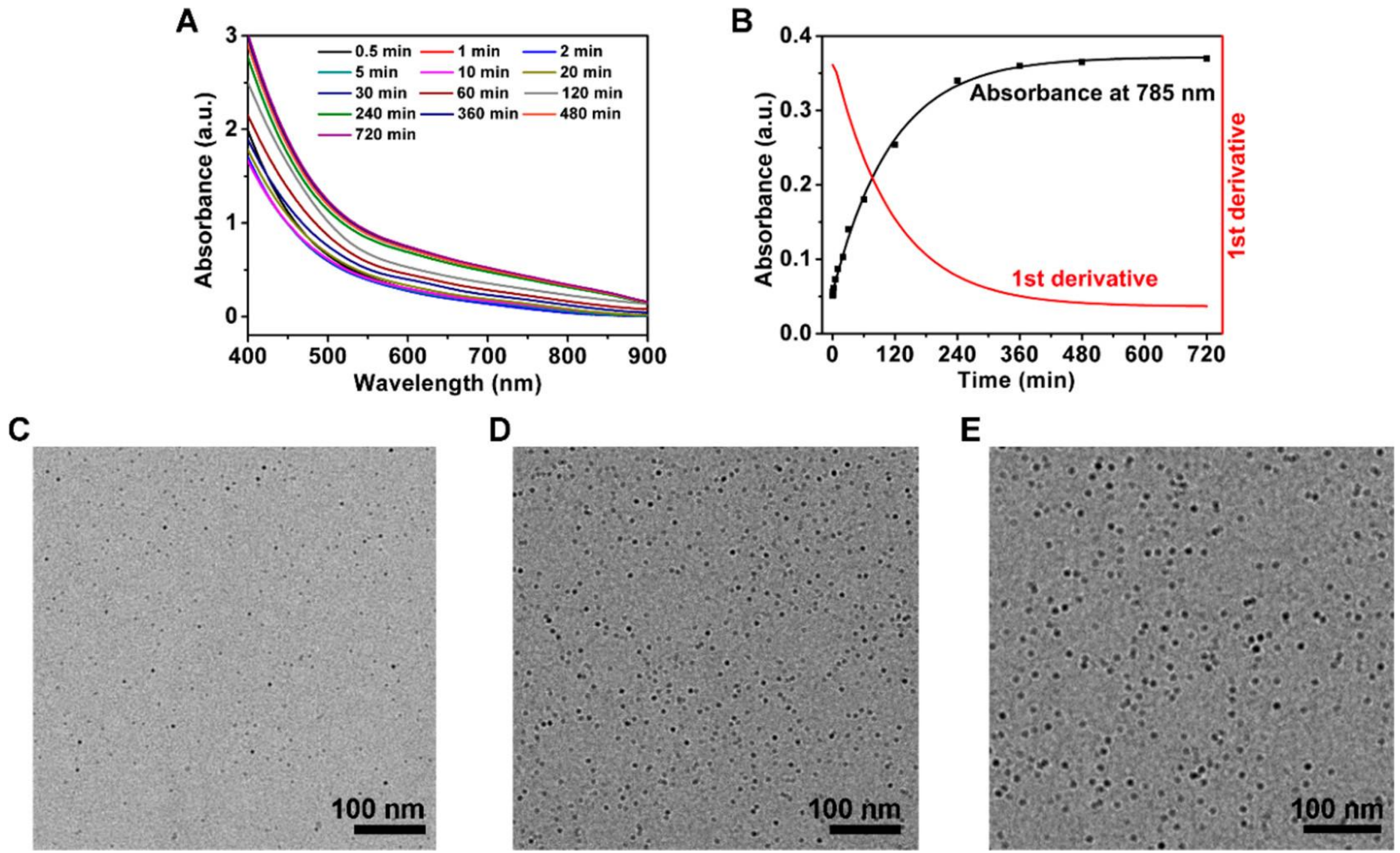


Figure 1. (A) Absorption spectra of Ag_2S-NDs synthesized with the Ag:S ratio of 1:2 at different reaction times. (B) Their absorbance at 785 nm at different reaction times during 720 min and the corresponding first derivative curve. (C−E) TEM images of Ag_2S-NDs synthesized with the Ag:S ratio of 1:2 at various reaction times: (C) 5 min; (D) 60 min; (E) and 240 min.

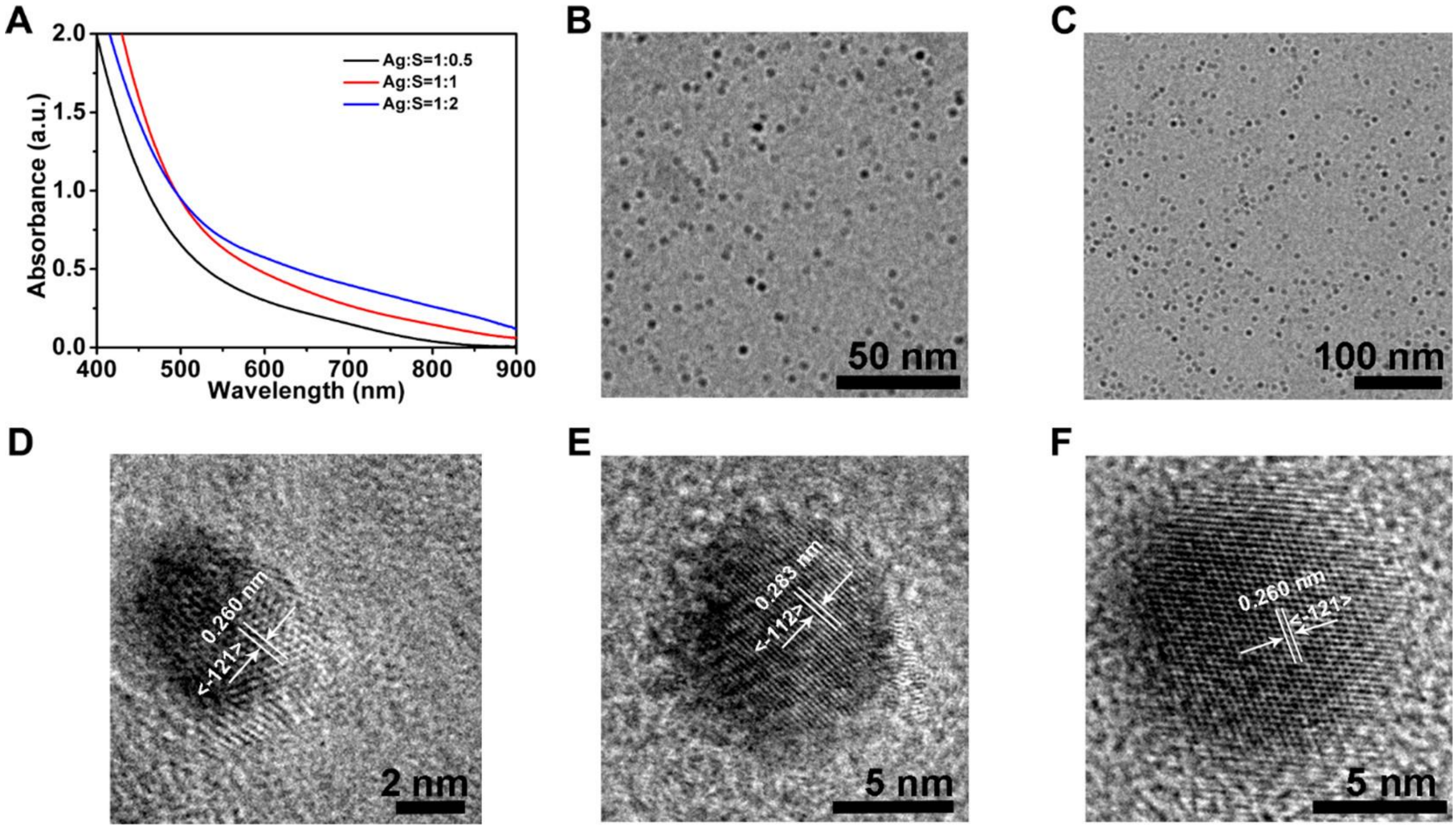


Figure 2. (A) Absorption spectra of Ag_2S-NDs synthesized with Ag:S ratios of 1:0.5, 1:1, and 1:2 at 240 min, respectively. (B, C) TEM images of Ag_2S-NDs synthesized with Ag:S ratios of (B) 1:0.5 and (C) 1:1 at 240 min, respectively, HR-TEM images of Ag_2S-NDs synthesized with Ag:S ratios of (D) 1:0.5, (E) 1:1, and (F) 1:2 at 240 min.

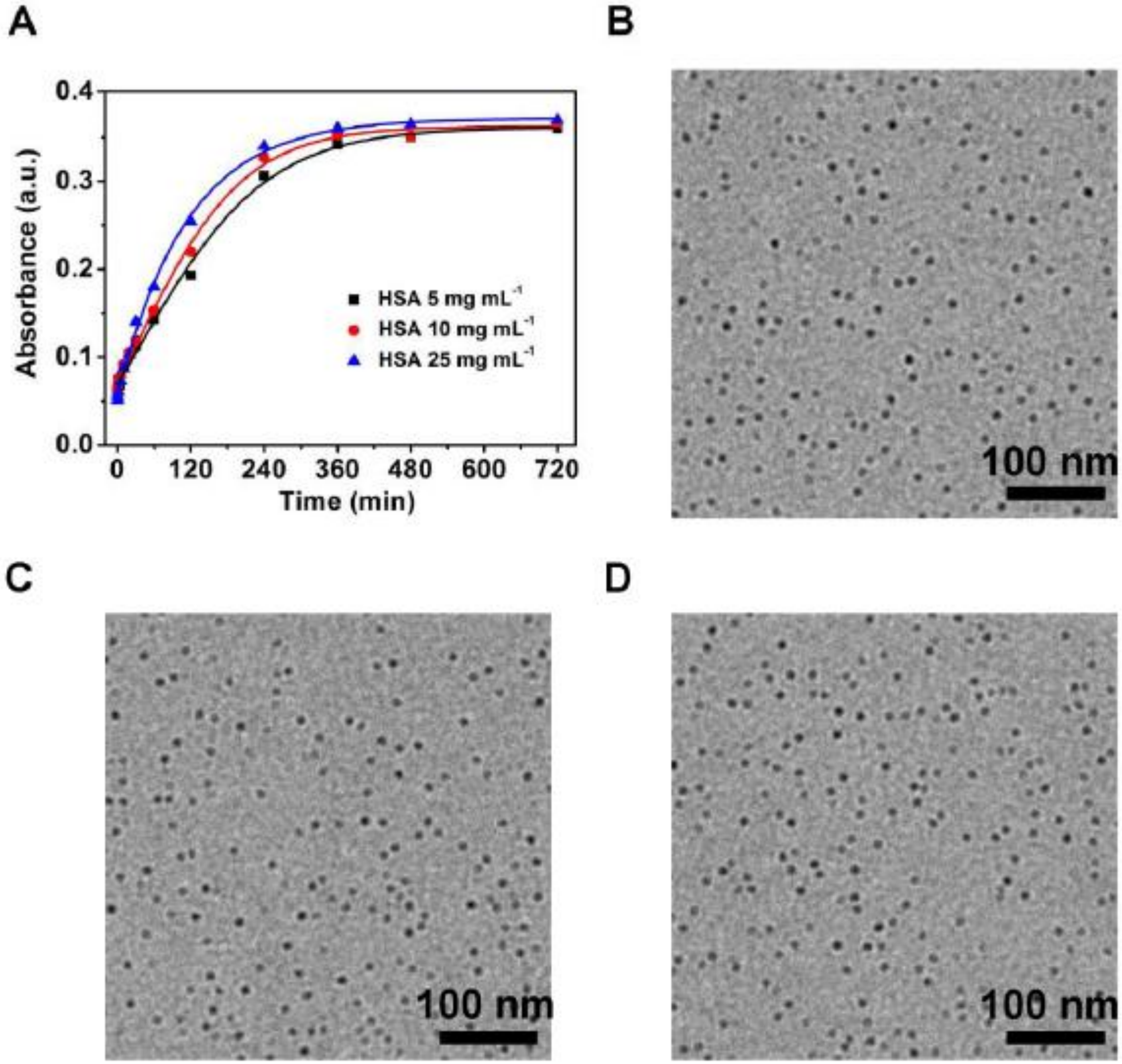


Figure 3. A) Absorbance at 785 nm of Ag_2S-NDs synthesized with HSA concentrations of 5, 10, and 25 mg mL-1 at different time, respectively. TEM images of Ag_2S-NDs synthesized with HSA concentrations of 5.0 mg mL-1 B), 10.0 mg mL-1 C), and 25.0 mg mL-1 D) after 240 min reaction, respectively. The average diameters of Ag_2S-NDs synthesized with HSA concentrations of 5 mg mL-1, 10 mg mL-1, and 25.0 mg mL-1 are 9.3 ± 0.6 nm, 9.4 ± 0.4 nm, and 9.8 ± 0.4 nm, respectively.

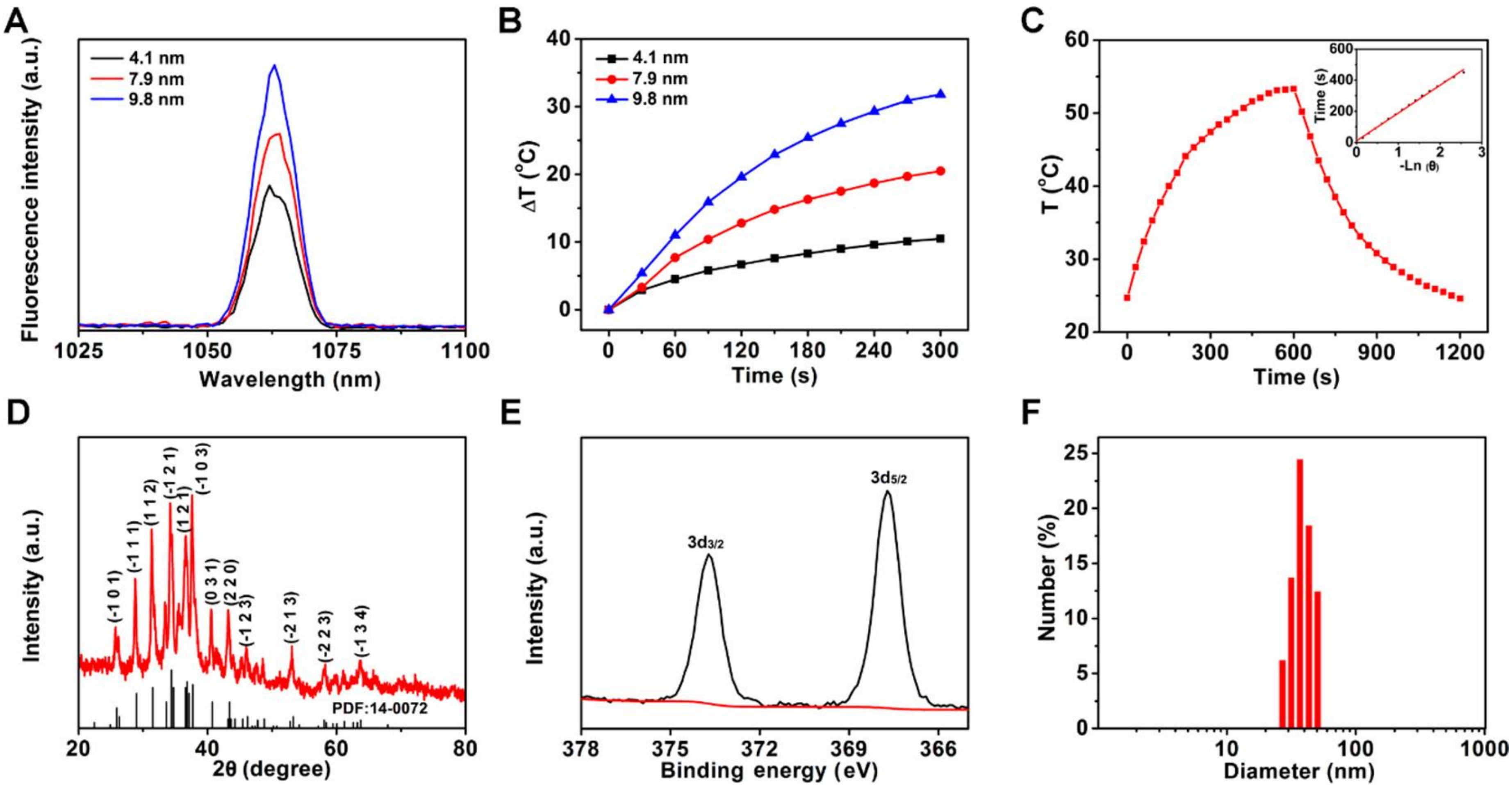


Figure 4. (A) Fluorescence spectra of Ag_2S-NDs with diameters of 4.1, 7.9, and 9.8 nm. (B) Temperature elevations of Ag_2S-NDs with diameters of 4.1, 7.9, and 9.8 nm at a concentration of 1.0 mM Ag under 5 min irradiation at 785 nm. (C) Photothermal conversion efficiency of 9.8 nm Ag_2S-NDs, which was calculated to be 35.0%. (D) XRD pattern of Ag_2S NDs. (E) XPS analysis of Ag_2S-NDs. (F) Size distribution of Ag_2S-NDs using DLS.

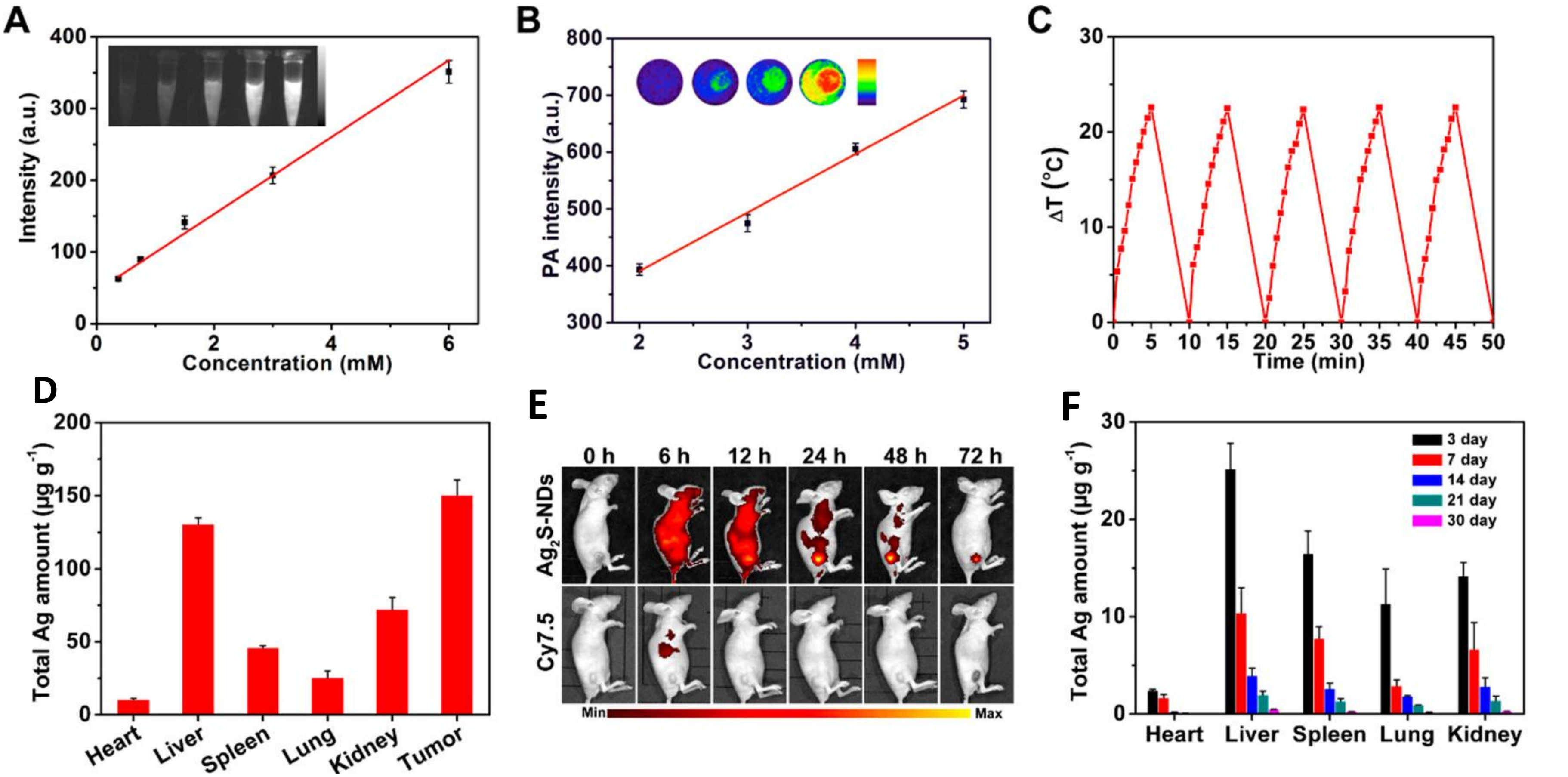


Figure 5. (A) Fluorescence mapping of Ag_2S-NDs at various concentrations in the NIR-II region. (B) PA mapping of Ag_2S-NDs at various concentrations. (C) Temperature elevation of Ag_2S-NDs under five irradiation/cooling cycles. (D) Biodistribution of Ag_2S-NDs at a dose of 50.0 μmol kg−1 Ag at 24 h postinjection. (E) NIR fluorescence imaging of 4T1-tumor-bearing mice treated with Cy7.5-labeled Ag_2S-NDs at a dose of 50.0 μmol kg−1 Ag at 72 h postinjection. (F) Long-term distributions of Ag_2S-NDs in various major tissues at a dose of 50.0 μmol kg−1 Ag during 30 days postinjection.

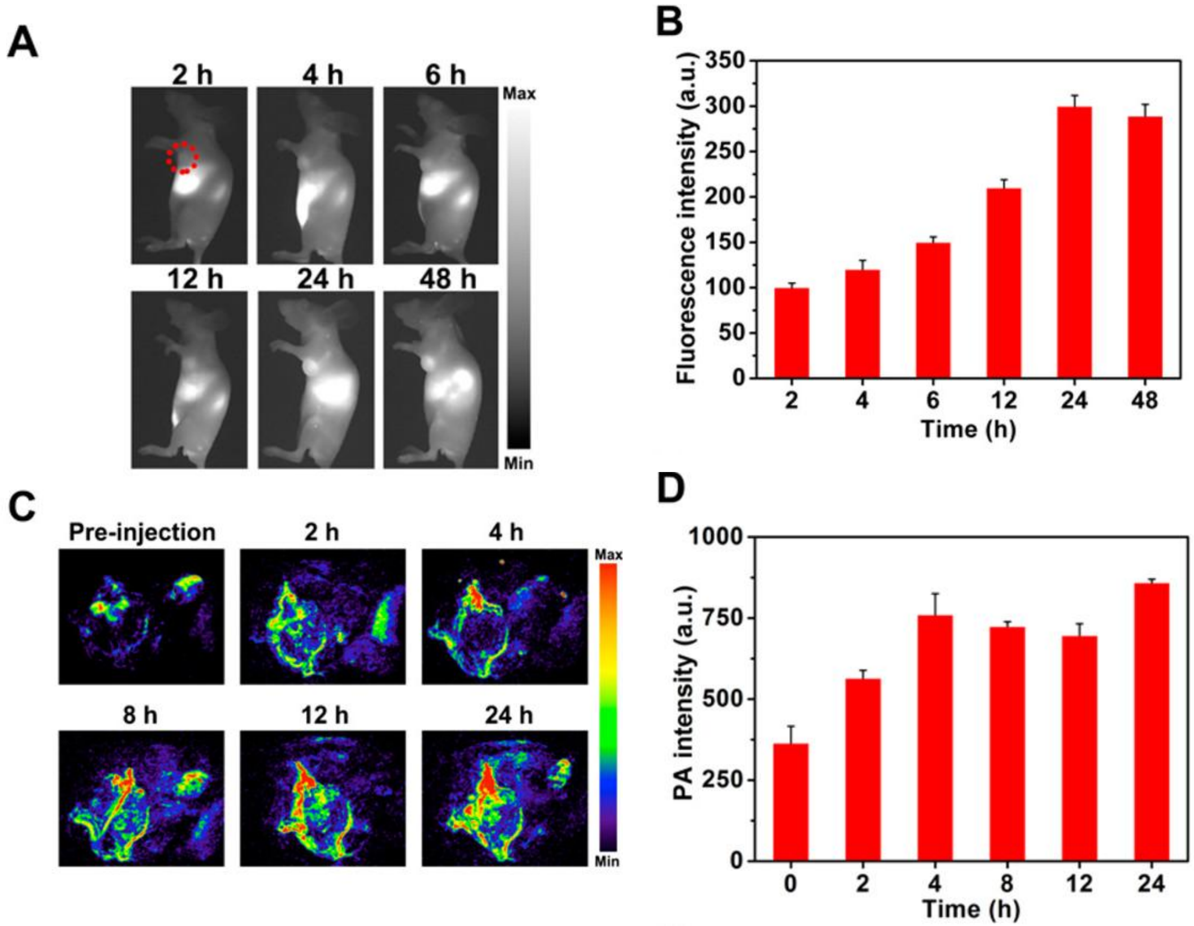


Figure 6. (A) In vivo NIR-II fluorescence imaging and (B) their calculated intensity in 4T1-tumor-bearing mice treated with Ag_2S-NDs at a dose of 50.0 μmol kg−1 Ag during 48 h postinjection. (C) In vivo PA imaging (few PA signals from oxyhemoglobin and deoxyhemoglobin before injection (D) their calculated intensity in the 4T1-tumor-bearing mice treated with Ag_2S-NDs at a dose of 50.0 μmol kg−1 Ag during 24 h postinjection.

Summary

- ❑ Ag_2S-NDs with well-defined nanostructure were synthesized through precisely controlled growth of Ag_2S in albumin nanocages which is used as a theranostic agent for multimodal imaging and simultaneous photothermal therapy.

- ❑ The particle size of Ag_2S-NDs was precisely regulated through control of the reaction time and initial ratio of reactants.

- ❑ Ag_2S-NDs possess size dependent NIR-II fluorescence intensity, photothermal effect.

- ❑ Ag_2S-NDs exhibit the collective characteristics of ideal resistance to photobleaching, good cellular uptake, preferable tumor accumulation, and in vivo elimination, thereby enabling Ag_2S-NDs to generate ultrasensitive fluorescence imaging in the NIR-II region and PA imaging.

Thank you