Electronic Supplementary Information

Facile synthesis of layered double hydroxide nanosheets assembled porous structures for efficient drug delivery

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Experimental section

Materials synthesis

Synthesis of ZIF-8 nanocrystals

In a typical synthetic procedure, 1,2-dimethylimidazole (2.052 g) and cobalt(II) nitrate hexahydrate ($Co(NO_3)_2 \cdot 6H_2O$, 7.438 g) were firstly dispersed into methanol (1 L), respectively, and were stirred for 30 min. The methanolic solution of 1,2-dimethylimidazole was quickly poured into a beaker containing the methanolic solution of cobalt nitrate ($Co(NO_3)_2$). The resulting mixture was sealed well and left the reaction at room temperature for 24 h. After that, the final products were collected by centrifugation, washed with ethanol thrice, and dried in vacuum at 40 ^oC for 8 h.

Synthesis of ZIF-8@LDHs core-shell structures

In a typical synthetic procedure, $Co(NO_3)_2 \cdot 6H_2O$ (79.8 mg) dissolved in 50mL methanol was transferred to a 100-mL Teflon-lined autoclave, and then ZIF-8 (21 mg) was added to the aforementioned solution with gently stirring for 1 h. The resulting mixture was sealed and kept at 90 °C for 12 h. After the reaction, the final product was collected by centrifugation at 8000 rpm, washed thrice with ethanol, and dried in vacuum at 40 °C for 8 h.

Synthesis of porous cages of LDHs (PC-LDHs)

The synthetic process is the same as that of ZIF-8@LDHs core-shell structures, except that the reaction temperature was increased from 90 ^oC to 110 ^oC.

Drug loading on ZIF-8@LDHs core-shell structures and PC-LDHs

LDHs-based nanocarriers (40 mg) was dispersed a 20-mL vial containing small molecular drugs (doxorubicin hydrochloride (DOX) and 5-fluorouracil (5-FU)) that were dissolved in phosphate buffer solution (PBS, 10 mL) with pH 7.4 to form an aqueous solution (1 mg/mL). The resulting mixture was gently stirred for 24 hours at room temperature in dark. Afterwards, the solid nano-drugs were collected by centrifugation at 11000 rpm for 30 min, washed with de-ionized water (10 × 2 mL), and dried in vacuum at 40 ^oC for 12 h. The Ultraviolet-visible (UV-vis) absorption

spectra of all supernatants were collected by a HITACHI U-4100 spectrometer to estimate the concentration of drugs in supernatants according to Lambert-Beer's Law. The UV-vis absorbance at 500 nm and 266 nm was used to calculate the DOX concentration and the 5-FU concentration in supernatants, respectively.

The drug loading capacity (LC) and the entrapment efficiency (EE) were respectively calculated using Eq. (1) and (2):

$$\text{LC(wt.\%)} = \frac{weight\ of\ loaded\ drug}{weight\ of\ loaded\ drug + weight\ of\ loaded\ nanocarriers} \times 100\% \quad \text{Eq. (1)}$$

$$\text{EE(wt.\%)} = \frac{weight\ of\ loaded\ drug}{Total\ amount\ of\ drug\ added} \times 100\% \quad \text{Eq. (2)}$$

Drug release

Typically, DOX loaded ZIF-8@LDHs core-shell structures (ZIF-8@LDHs/DOX, 10 mg) was dispersed in 2 mL of PBS with pH 7.4 by sonication and then sealed in a 3500 Da molecular weight cut-off dialysis bag, which was immersed in 48 mL of PBS (pH 7.4). The drug delivery system was placed in a shaking bath at 37 °C for 48 h. At the specified time intervals, 3 mL of buffer solution was extracted, and an equal amount of fresh buffer solution was added. The release amount of DOX was measured using a UV-vis spectrophotometer at λ_{max} = 500 nm. In the experiments of drug release, the temperature and the pH value were adjusted to 25 ^{o}C and 5, respectively.

DOX loaded PC-LDHs (PC-LDHs/DOX) and 5-FU loaded PC-LDHs (PC-LDHs/5-FU) were used for drug release under otherwise identical conditions.

In addition, PC-LDHs/5-FU were treated prior to drug release. The treatment procedure involved dispersing PC-LDHs/5-FU in deionized water and gently stirring for half an hour, followed by collection via centrifugation and final drying in vacuum at 40 °C for 8 h.

Characterization

The microstructure and morphology of samples were observed using a Tecnai F30 transmission electron microscope (TEM) at 300 kV, a HITACHI UHR FE-SEM SU8220 scanning electron microscope (SEM), and a JEOL JEM-ARM200F microscope with spherical aberration (Cs) correction at 200 kV. The samples were dispersed ultrasonically in ethanol before being deposited on a carbon-coated copper grid and air dried. For SEM measurement, the samples were directly deposited on a silicon wafer.

X-ray diffraction (XRD) was conducted in a Rigaku D/Max 2400 automatic powder X-ray diffractometer with Cu-*K*α radiation (λ = 1.5418 Å) to analyze the crystalline structure of samples. The samples were scanned with a scanning speed of 5 degree/min from 5 degree to 80 degree.

FT-IR spectra were recorded on a Nicolet-iS10 spectrometer (Thermo Fisher Scientific, USA) to identify the chemical functional groups of the samples. The materials were finely grounded, dispersed into KBr powder, and pressed pellets to test.

An ASAP 2460 fully automatic adsorption apparatus (micromeritics, USA) was used to conduct N_2 sorption isotherms. The samples were loaded onto the equipment for nitrogen adsorption testing at 77 K after being pretreated in vacuum for 8 h at 150 ^{o}C. The Barrett-Joyner-Halenda (BJH) model was used to determine the distribution of pore sizes. The Brunauer-Emmett-Teller (BET) method was used to calculate the specific surface areas.

Zeta potential was performed on ZS-90 (Malvern, UK). The samples were dispersed in water to test after sonication.

UV-Vis absorption spectroscopy was measured on a HITACHI U-4100 spectrometer.

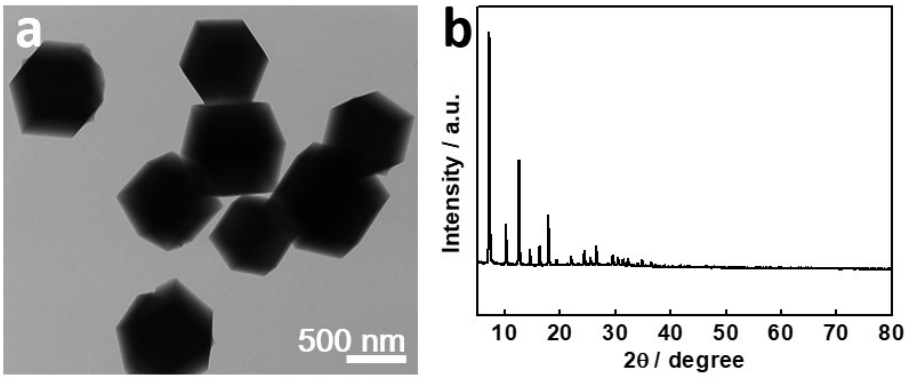

Figure S1. (a) TEM image and (b) XRD pattern of ZIF-8 nanocrystals.

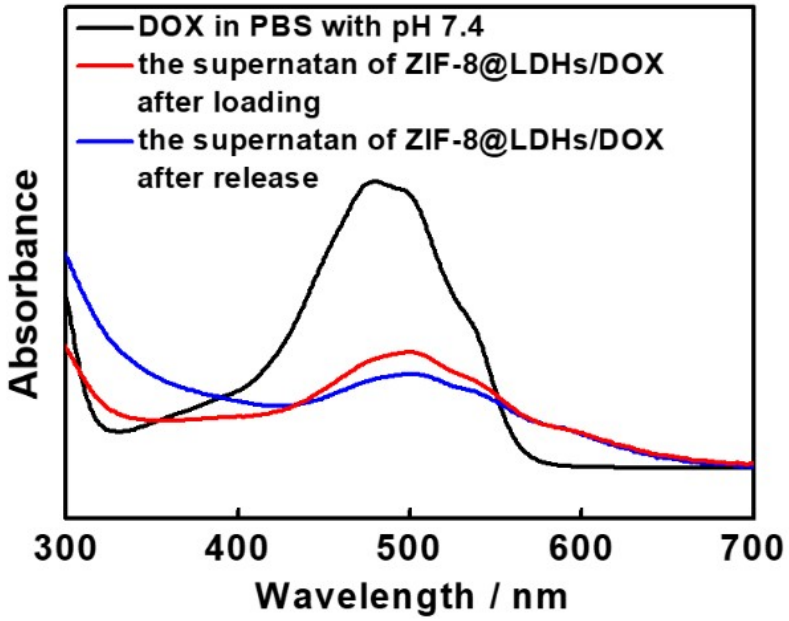

Figure S2. UV-visible absorption spectra of DOX under different conditions.

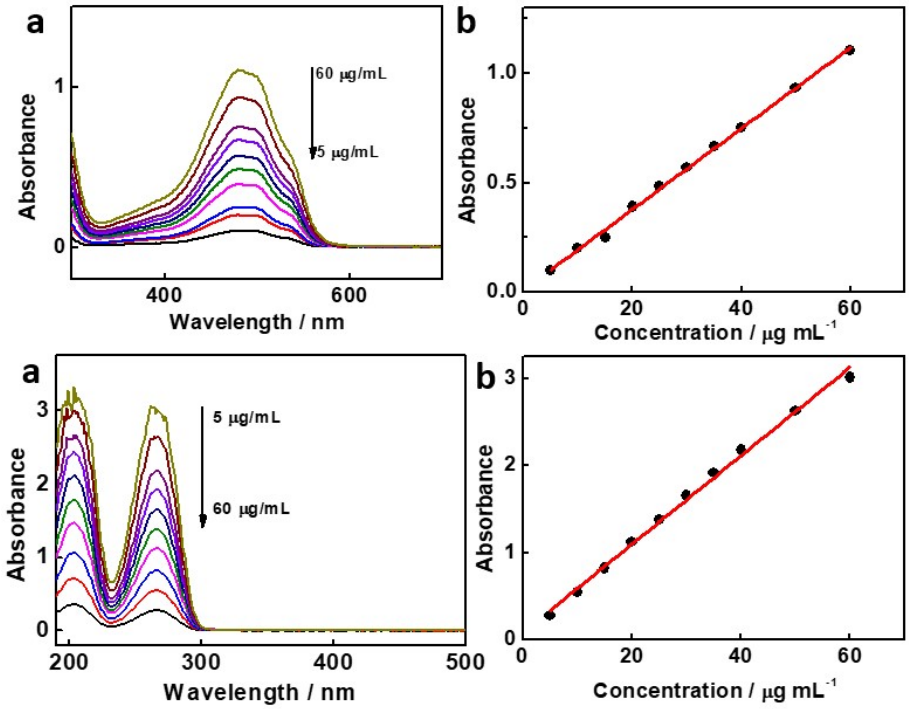

Figure S3. (a) UV-visible absorption spectra of DOX with different concentrations from 5 to 60 μg/mL, and (b) a calibration curve based on the absorbance-concentration relationship from the UV-visible absorption spectra at λ= 500 nm. (c) UV-visible absorption spectra of 5-FU with different concentrations from 5 to 60 μg/mL, and (d) a calibration curve based on the absorbance-concentration relationship from the UV-visible absorption spectra at λ = 266 nm.

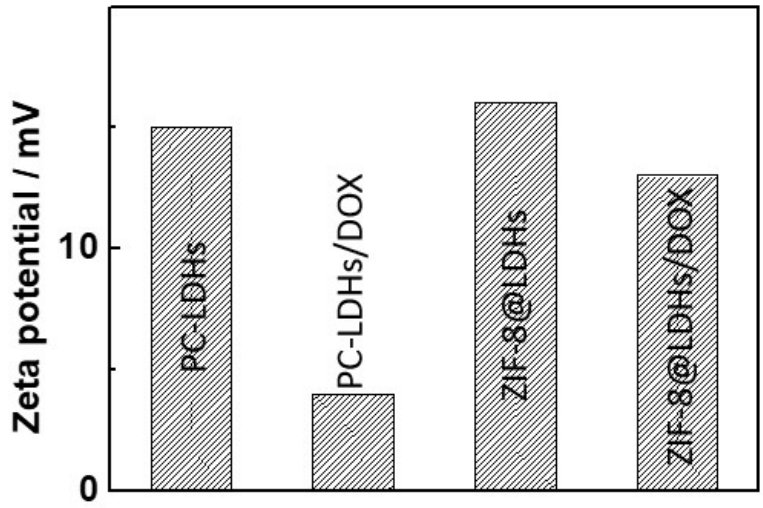

Figure S4. The bar charts of zeta potential of different materials.

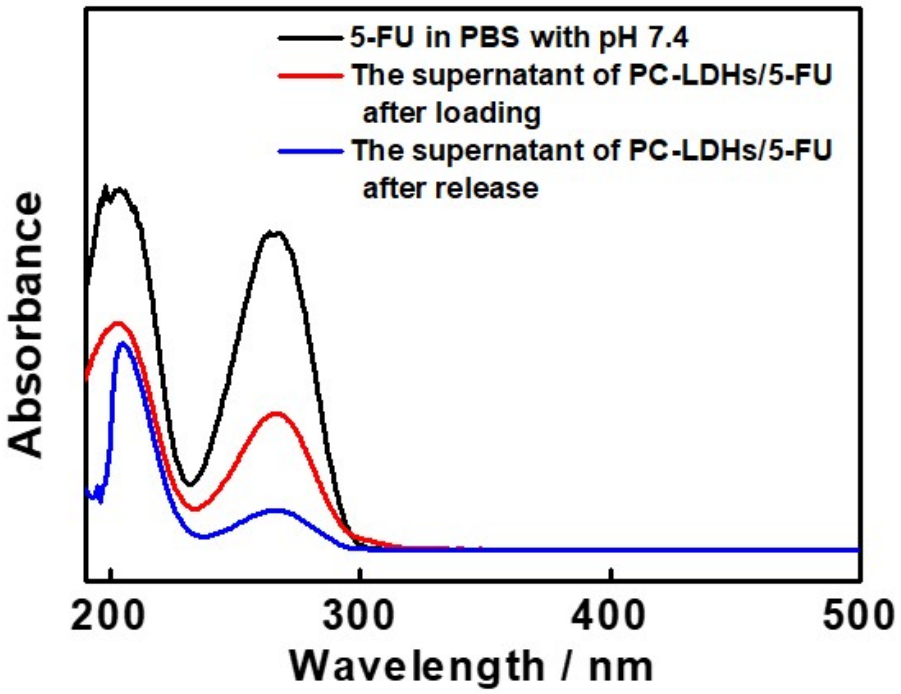

Figure S5. UV-visible absorption spectra of 5-FU under different conditions.

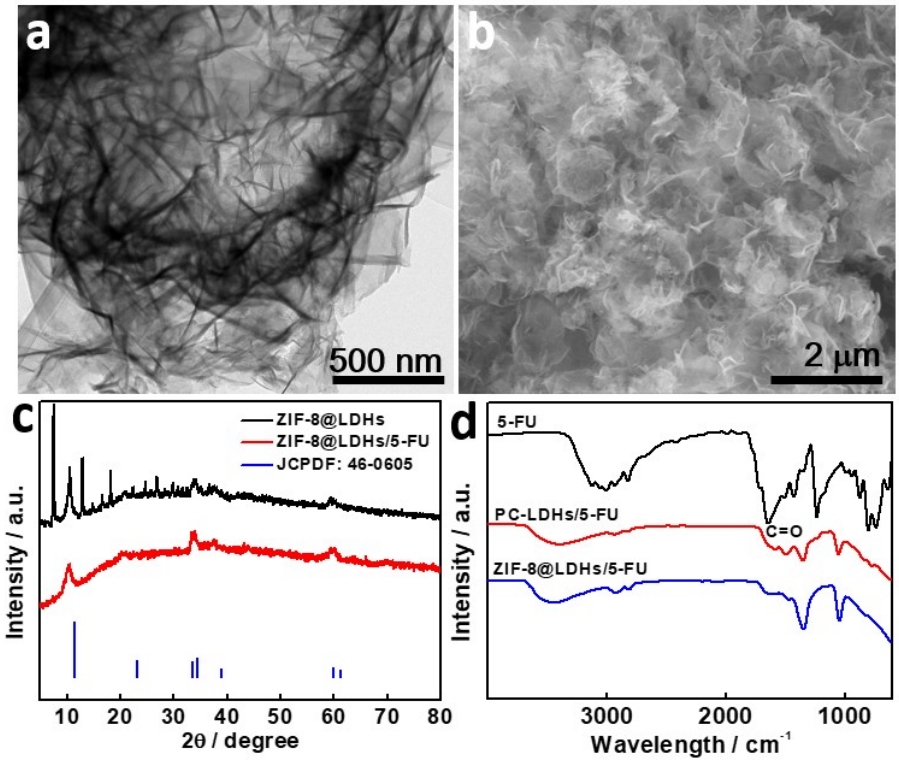

Figure S6. TEM and SEM images, XRD patterns, and FT-IR spectra of ZIF-8@LDHs after 5-FU loading.

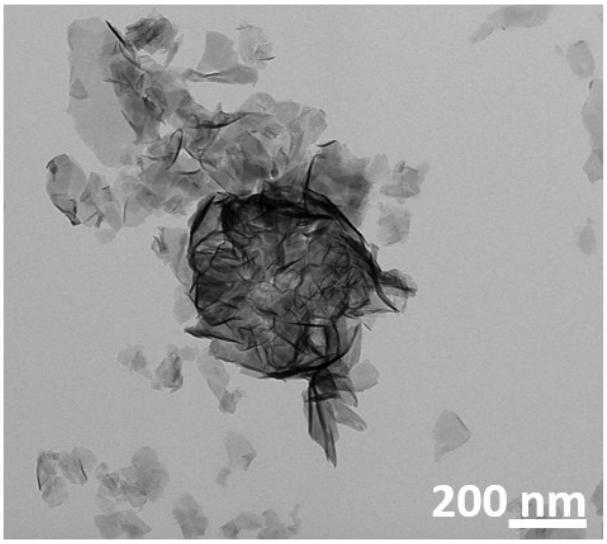

Figure S7. TEM image of PC-LDHs after DOX release for 48 h at 37 °C and pH 7.4.

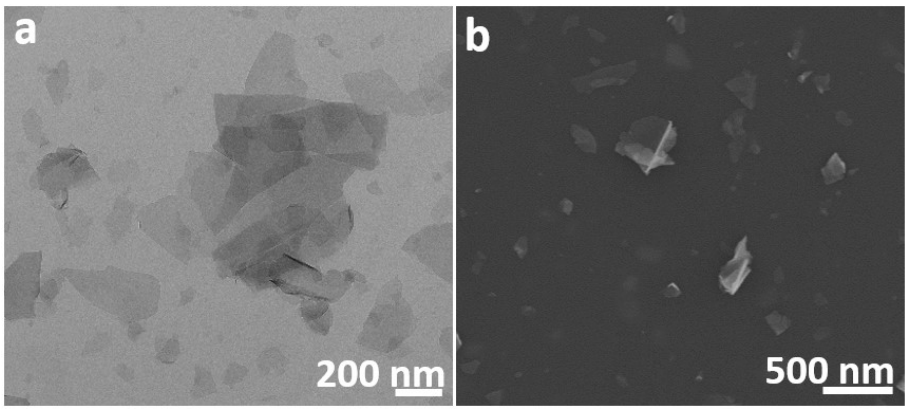

Figure S8. (a) SEM and (b) TEM images of PC-LDHs after being ground and sonicated.