**Supporting Information**

# Carbon Nanodots@Zeolitic Imidazolate Framework-8 Nanoparticles for Simultaneous pH-Responsive Drug Delivery and Fluorescence Imaging

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## EXPERIMENTAL SECTION

**Materials.** Citric acid and urea were obtained from Beijing Beihua Jingxi Chemical Reagent Company. 2-methylimidazole (Hmim) was purchased from Chengdu Kelong Chemical Reagent Company. $Zn(NO_3)_2$ was purchased from Tianjin Fengchun Chemical Reagent Technologies Co., Ltd. Methanol was purchased from Beijing Chemical Works. All other reagents and solvents for the synthesis were purchased from commercial sources and used as received. Deionized water (DI-water) was used in all experiments.

**Characterization**. Electron transmission microscopy (TEM) was performed on a JEOL-2100F transmission electron microscope under 200 kV accelerating voltage. Field-emission scanning electron microscope (FE-SEM) images were obtained by using an XL 30 ESEM-FEG field-emission scanning electron microscope (FEI Co.). The UV-vis absorption spectra were obtained on U-3010 spectrophotometer (Hitachi, Japan). Powder X-ray diffraction (PXRD) patterns were recorded on a Siemens D5005 diffractometer with Cu KR ($\lambda$=1.5418 Å) radiation in the range of 3–90°. The fourier transform infrared (FTIR) spectrum was obtained on a Magna 560 FTIR spectrometer (Nicolet, USA). Photoluminescence (PL) spectra were performed with FL-4600 fluorescence spectrophotometer (5J2-0004). Confocal laser scanning microscopy (CLSM) was operated on Olympus Fluo-view FV1000. The $N_2$ sorption measurements were measured on an Autosorb-iQ analyzer (Quantachrome). Before gas adsorption measurements, the sample was activated by drying under a dynamic vacuum at 150 °C overnight to remove methanol. Particle size distribution was

measured on a Mastersizer 2000 laser particle size analyzer.

**Synthesis of C-dots.** First, citric acid (3g) and urea (3g) were mixed, then 10 mL DI-water was poured into the mixture to form a transparent solution. Subsequently the solution was heated in a 700 W microwave oven for 5 min. During the reaction process, the colorless solution changed from brown and finally into dark-brown solid, indicating the formation of C-dots. Afterwards, the product was heated for 1 h at 60 °C in a vacuum oven to remove the residual small molecules. To further purify the aqueous solution of the C-dots, the large or agglomerated particles were removed by centrifugation at 3000 rpm for 20 min. Then the as-prepared C-dots were diluted 10-folds for further use.

**Synthesis of C-dots@ZIF-8 NPs.** Typically, a methanol solution of $Zn(NO_3)_2 \cdot 6H_2O$ (0.06 M) in 25 mL, 2.5 mL of diluted solution C-dots were mixed and then Hmim (0.25 M) in 25 mL of methanol was added. The mixture was allowed to react at room temperature for 24 h without stirring, during which the solution changed from being a clear solution to a milky colloidal dispersion. The product C-dots@ZIF-8 (C-dots@ZIF-8-6) was collected by centrifugation at 9000 rpm for 10 min, washed three times with methanol to remove the remaining reactant and then dried under vacuum for 10 h at 50 °C in an oven to get the powder. The other C-dots@ZIF-8 NPs were synthesized by the same procedure. The obtained samples were designated as C-dots@ZIF-8-1, C-dots@ZIF-8-2, C-dots@ZIF-8-3, C-dots@ZIF-8-4, C-dots@ZIF-8-5 and C-dots@ZIF-8-7 based on the volume ratios

of C-dots to $Zn^{2+}$ ions with 0.75 : 100, 1.75 : 100, 2.50 : 100, 5.00 : 100, 7.50 : 100, 12.5 : 100, respectively. While the C-dots@ZIF-8-8 and C-dots@ZIF-8-9 were prepared in the presence of the concentrations of $Zn^{2+}$ ions with 0.03 M and 0.18 M, respectively, and the molar ratio of Hmim to $Zn^{2+}$ ions of 25: 6.

**Synthesis of C-dots+ZIF-8.** The as-synthesized ZIF-8 was physically mixed with the C-dots for 24 h to form ZIF-8+C-dots composites. The contents of all the reactants were set at the same level as the preparation of C-dots@ZIF-8. Subsequently, the C-dots+ZIF-8 composites were obtained by centrifugation at 9000 rpm for 10 min, washed three times with methanol to remove the remaining C-dots and then also dried well under vacuum for 10 h at 50 °C in an oven to get the powder.

**Drug Loading Experiment:** The incorporation of 5-fluorouracil (5-FU) into C-dots@ZIF-8 was performed by vertical mixing for two days. A 1 mL of initial 5-FU (3 mg $mL^{-1}$) solution was mixed with 2 mg C-dots@ZIF-8 powder that was dried for 24 h at 50 °C in an oven. Then the obtained product was centrifuged at 9000 rpm for 20 min to get the supernatant. To evaluate the 5-FU-loading efficiency, the concentration of 5-FU was determined by UV-vis absorption spectrum at 265 nm. The 5-FU loading efficiency (LE%) of C-dots@ZIF-8 was calculated by Equation (1):

$$LE\% = [(Abs_{(original\ 5\text{-}FU)} - Abs_{(residual\ 5\text{-}FU)}) / Abs_{(original\ 5\text{-}FU)}] \times 100\%. \quad (1)$$

**Drug Release Experiment:** The semi-permeable dialysis bag diffusion technique was used to evaluate the cumulative drug release of 5-FU from 5-FU loaded C-dots@ZIF-8 at 37 °C. The as-obtained 5-FU loaded C-dots@ZIF-8 was dispersed in 1 mL phosphate-buffer saline (PBS) with different pH values (pH = 7.4 and 5.5) and then transferred into two semi-permeable dialysis bag respectively. Afterwards, the release mediums were immersed into 3 mL corresponding PBS solution at 37 °C to simulate the normal blood temperature environment. During the release process, 5-FU entered into outer solution by diffusion from the semi-permeable dialysis dag. Then the release amount of 5-FU was measured by fluorescence emission spectra at 426 nm with 390 excitation at certain time intervals.

**Cell culture.** Hela, as a human cervical cancer cell line, was grown as a monolayer in a humidified incubator at 37 °C in a 95 % air/5 % $CO_2$ in DMEM supplemented with 10% fetal bovine serum.

**Fluorescence imaging of cancer cells.** The Hela cells ($1\times10^5$/mL) were seeded onto glass cover slips in a 24-well plate in a humidified incubator at 37 °C with a 95 % air/5 % $CO_2$ in DMEM medium containing 10 % fetal bovine serum for 24 h to allow the cells to attach. Afterwards, the medium was removed and the adherent cells were washed twice with PBS buffer to remove the remaining particles and dead cells. The medium was then replaced with 1 mL culture serum-free medium containing

5-FU loaded C-dots@ZIF-8 (30 μg $mL^{-1}$). After incubation for 24 h, the cell monolayer on the cover slip was repeatedly washed with PBS to remove the remaining particles and dead cells and then the cells sealed with a microscope glass slide and observations were performed by using CLSM.

**In vitro cytotoxicity against Hela cells.** The in vitro cell cytotoxicities of empty C-dots@ZIF-8 and 5-FU loaded C-dots@ZIF-8 were evaluated by 3-(4,5-dimethyl-2-thiazole)-2,5-diphenyl-2-tetrazolium bromide (MTT) assay using Hela cells. Cells were seeded in a 96-well plate at the density of $1\times10^{5}$/mL per well and incubated at 37 °C in a humidified atmosphere with 5% $CO_2$ in RMPI 1640 medium containing 10% fetal bovine serum for 24 h. Then different concentrations of empty C-dots@ZIF-8 NPs, 5-FU loaded C-dots@ZIF-8, and free 5-FU in serum-free medium with 100 μL replaced the original medium followed by incubated for 24 h. One row of a 96-well plate was used as control with 100 μL culture medium only. After incubation, 20 μL MTT (5 mg $mL^{-1}$) solution was added to each well and the mixture was incubated for another 4 h, allowing the live cells to reduce the yellow MTT into dark-blue formazan crystals. The medium was then replaced with DMSO (150 μL) and the absorbance was monitored with a microplate reader at a wavelength of 490 nm. Cell viability was determined by

$$\text{Cell viability}(100\%) = \text{Abs}_{(\text{test cells})} / \text{Abs}_{(\text{reference cells})} \times 100\ \% \qquad (2)$$

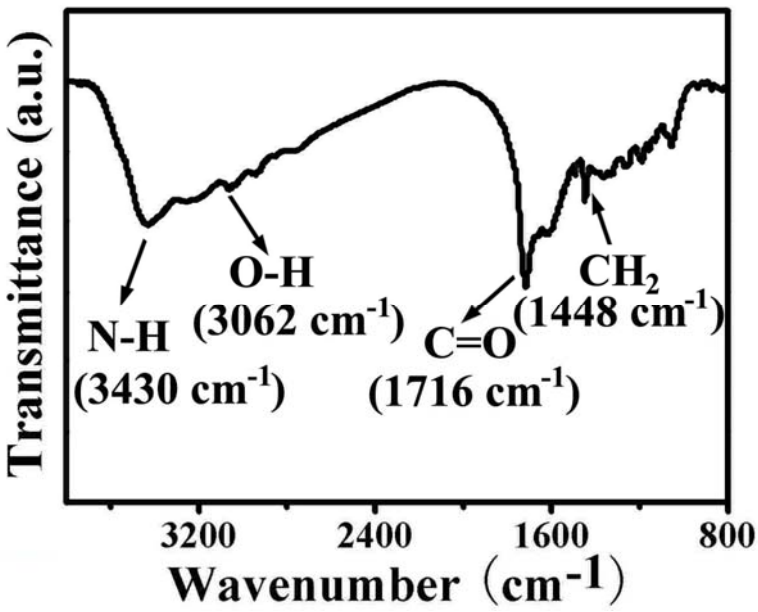


**Fig. S1** FTIR spectrum of C-dots.

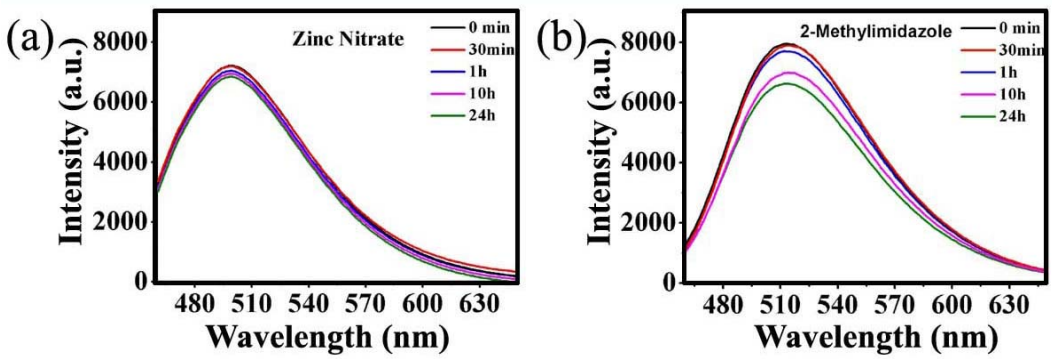


**Fig. S2** PL spectra of the mixture of (a) C-dots and $Zn(NO_3)_2 \cdot 6H_2O$, and (b) C-dots and Hmim in the methanol solution.

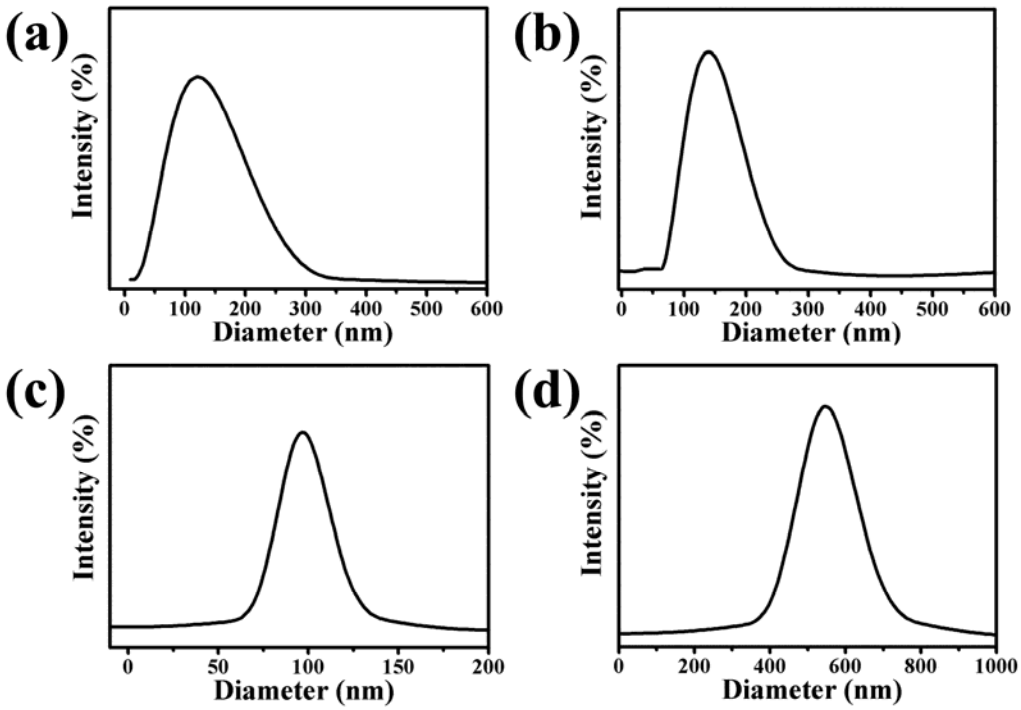


**Fig. S3** The size distribution of C-dots@ZIF-8-6 (a), as-synthesized ZIF-8 (b), C-dots@ZIF-8-8 (c) and C-dots@ZIF-8-9 (d) measured by DLS.

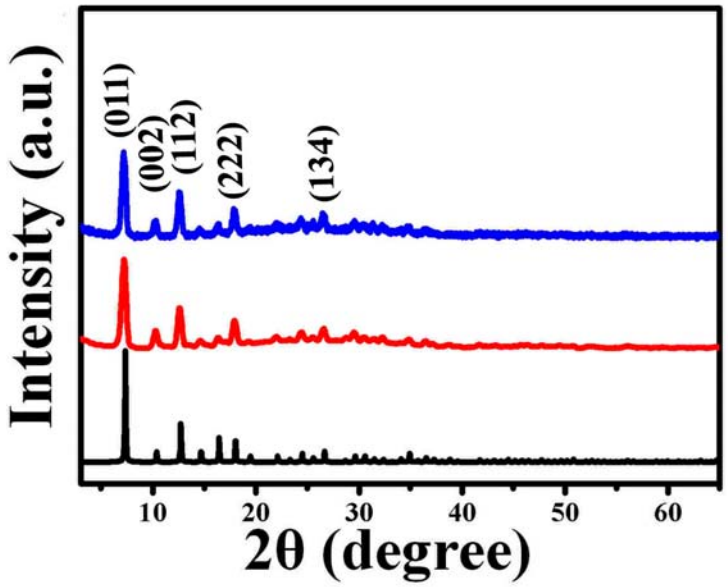


**Fig. S4** PXRD patterns of simulated ZIF-8 (black), as-synthesized ZIF-8 (red), C-dots@ZIF-8 (blue).

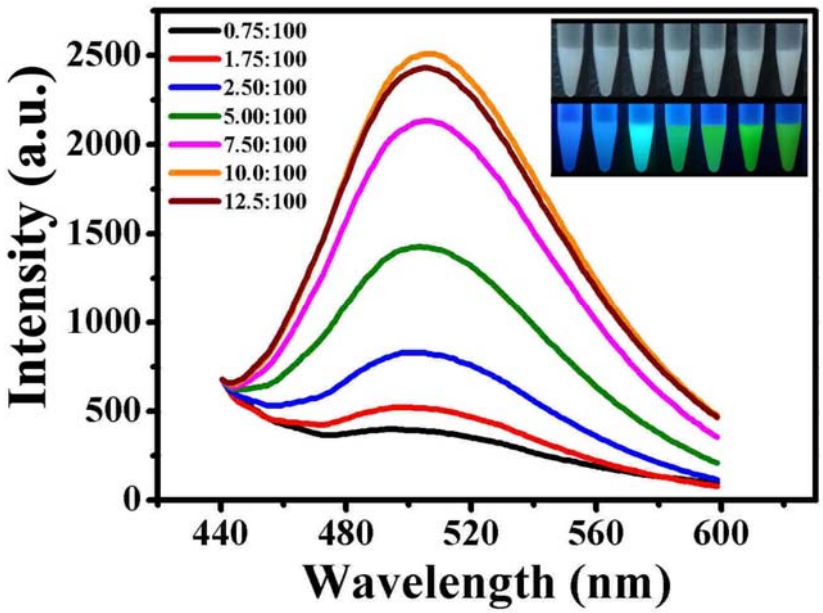


**Fig. S5** PL spectra of C-dots@ZIF-8 NPs solution in methanol with different volume ratios of C-dots to $Zn^{2+}$ ions with 0.75 : 100 (C-dots@ZIF-8-1), 1.75 : 100 (C-dots@ZIF-8-2), 2.50 : 100 (C-dots@ZIF-8-3), 5.00 : 100 (C-dots@ZIF-8-4), 7.50 : 100 (C-dots@ZIF-8-5), 10.0 : 100 (C-dots@ZIF-8-6), 12.5 : 100 (C-dots@ZIF-8-7) during the synthesis process [insets: digital photos of the corresponding C-dots@ZIF-8 NPs under natural light (top) and under 365 nm laboratory UV light (bottom)].

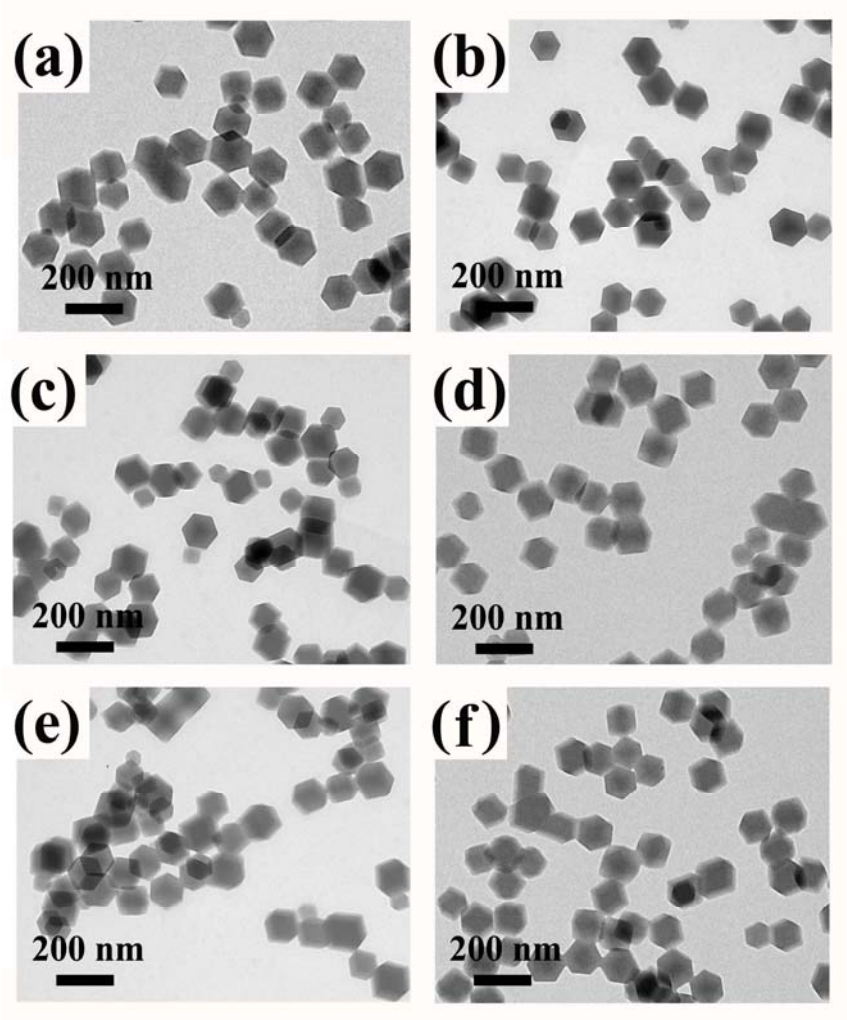


**Fig. S6** TEM images of C-dots@ZIF-8-1 (a), C-dots@ZIF-8-2 (b), C-dots@ZIF-8-3 (c), C-dots@ZIF-8-4 (d), C-dots@ZIF-8-5 (e), C-dots@ZIF-8-7 (f).

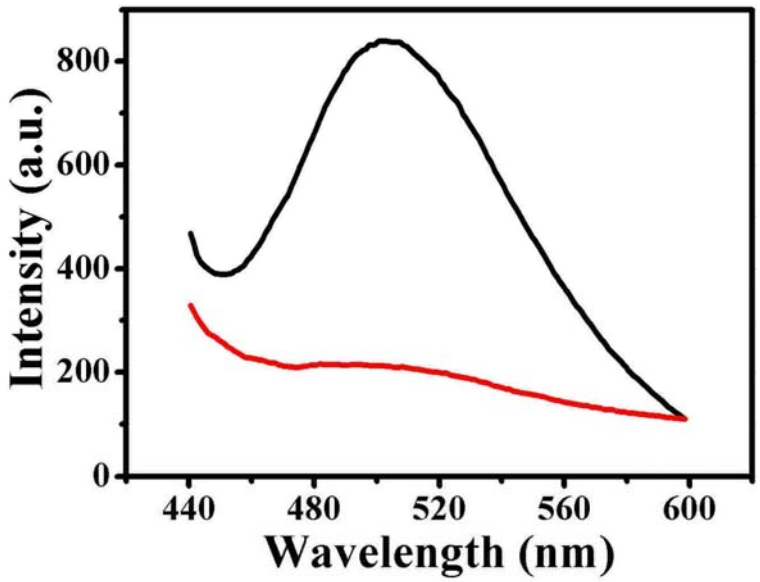

**Fig. S7** PL spectra of the as-prepared C-dots@ZIF-8 (black) and C-dots+ZIF-8 (red) after washed with methanol for ten times.

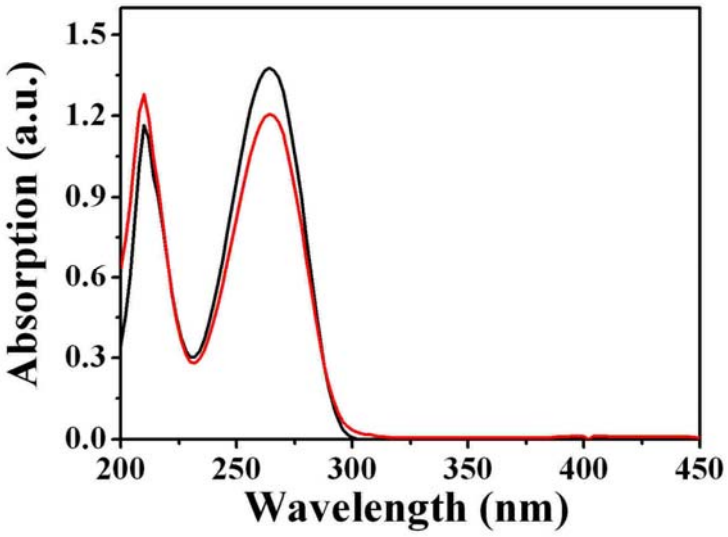


**Fig. S8** The UV-vis absorption spectra of 5-FU methanol supernatant before (black) and after (red) the interaction with C-dots@ZIF-8.

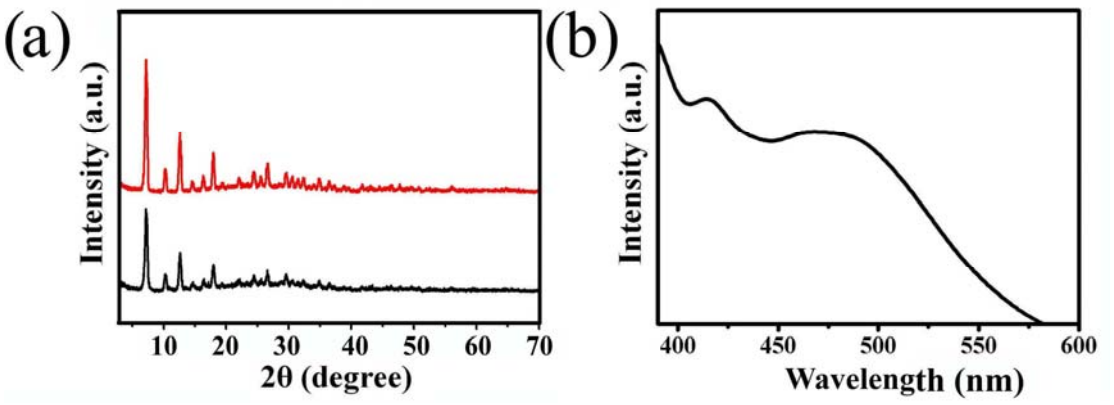


**Fig. S9** (a) PXRD patterns of C-dots@ZIF-8 (black) and 5-FU loaded C-dots@ZIF-8 (red). (b) PL spectrum of 5-FU loaded C-dots@ZIF-8 with excitation wavelength at 370 nm.

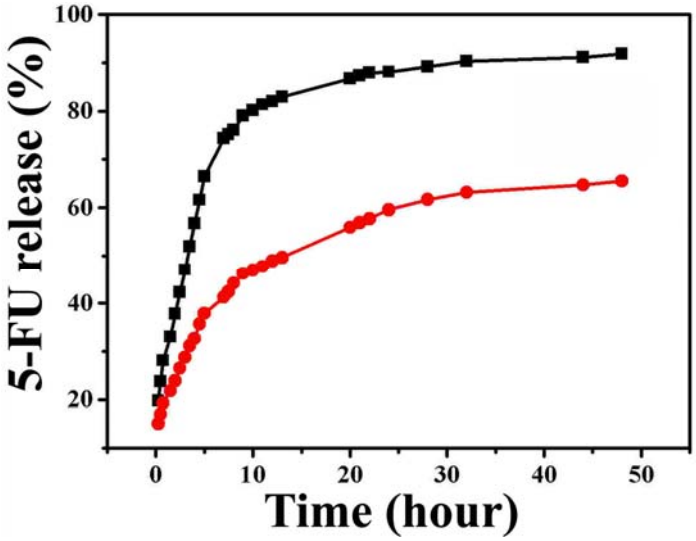


**Fig. S10** Release profiles of 5-FU from 5-FU loaded C-dots@ZIF-8 in PBS buffer solution with pH 5.5 (black) and pH 7.4 (red) at 37 °C for 48 h.