Supporting Information

Zeolitic Imidzolate Framework-8 as Efficient pH-Sensitive Drug Delivery Vehicle

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Materials and Methods

All reagents and solvents for the syntheses were purchased from commercial sources and used as received. The fourier transformed infrared spectroscopy (FTIR) spectras were recorded from KBr pellets in the range of 4000–400 cm^{-1} on a Mattson Alpha-Centauri spectrometer. PXRD patterns were recorded on a Siemens D5005 diffractometer with Cu KR (λ = 1.5418 Å) radiation in the range of 3–50°. UV–Vis absorption spectroscopy was obtained on U-3010 spectrophotometer (Hitachi, Japan). Fluorescence spectra were performed with Eclipse fluorescence spectrophotometer (Varian, USA). Thermogravimetric analyses (TGA) experiments were performed on a Perkin-Elmer TGA 7 analyzer heated from 50 to 800 °C under nitrogen gas atmosphere with a heating rate of 10 °C min^{-1}.

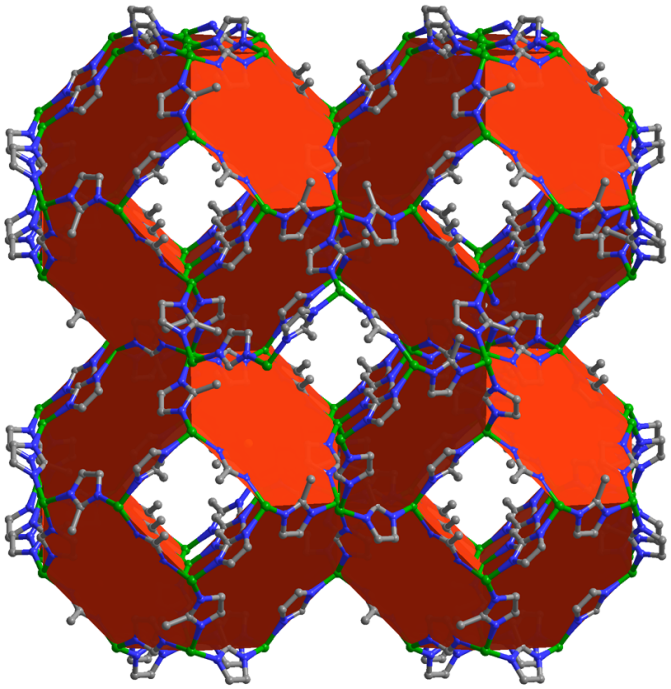

Fig. S1 Polyhedral presentation of ZIF-8, which possesses large pores of 11.6 Å in diameter connected through apertures of 3.4 Å.

Thermogravimetric Analyses

The thermogravimetric analysis under the nitrogen atmosphere performed on ZIF-8, showed a gradual weight loss of 14 wt % between 50 and 350 °C, and the decomposition was observed after 400 °C. When it was heated at 160 °C for 24 h, a long plateau was observed at temperatures up to 400 °C. This indicates that the guest molecule in the sod cages could be removed at the temperature of 160 °C. And the framework collapsed in the temperature range of 400–530 °C

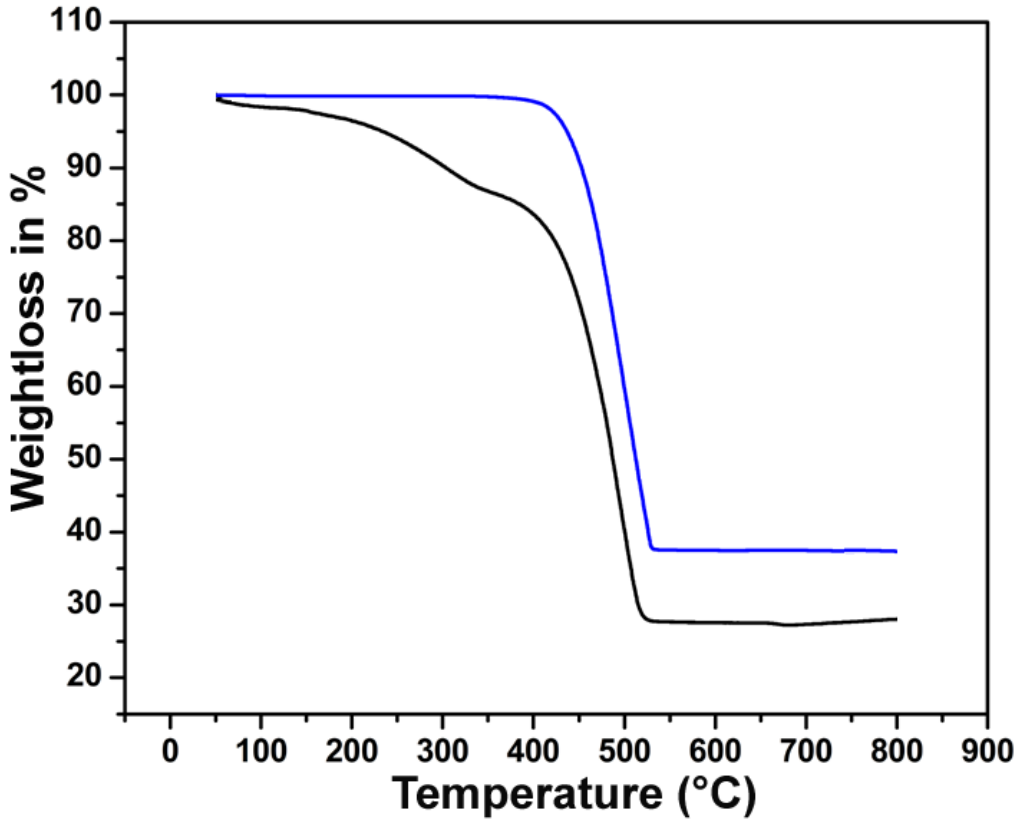

Fig. S2 The TG curves of as-synthesized (black) and activated samples (blue) (dried at 160 °C) of ZIF-8.

pH-mediated Dissolution Property Examination

The test was performed at 37 °C and by immerging dehydrate ZIF-8 (20 mg) in phosphate-buffer saline (pH 7.4, 5ml) and acetate buffer (pH 5.0, 5ml), respectively. When immersing dehydrate ZIF-8 in acetate buffer, it lost its crystallinity quickly and followed by gradual solution. After 30 minutes, the material was thoroughly soluble in acetate buffer. Whereas immersed in PBS at 37 °C, the solid sample was stable and maintained their full crystallinity after 7 days which was monitored by aliquoting portions of the samples for PXRD analysis after every 24 h period.

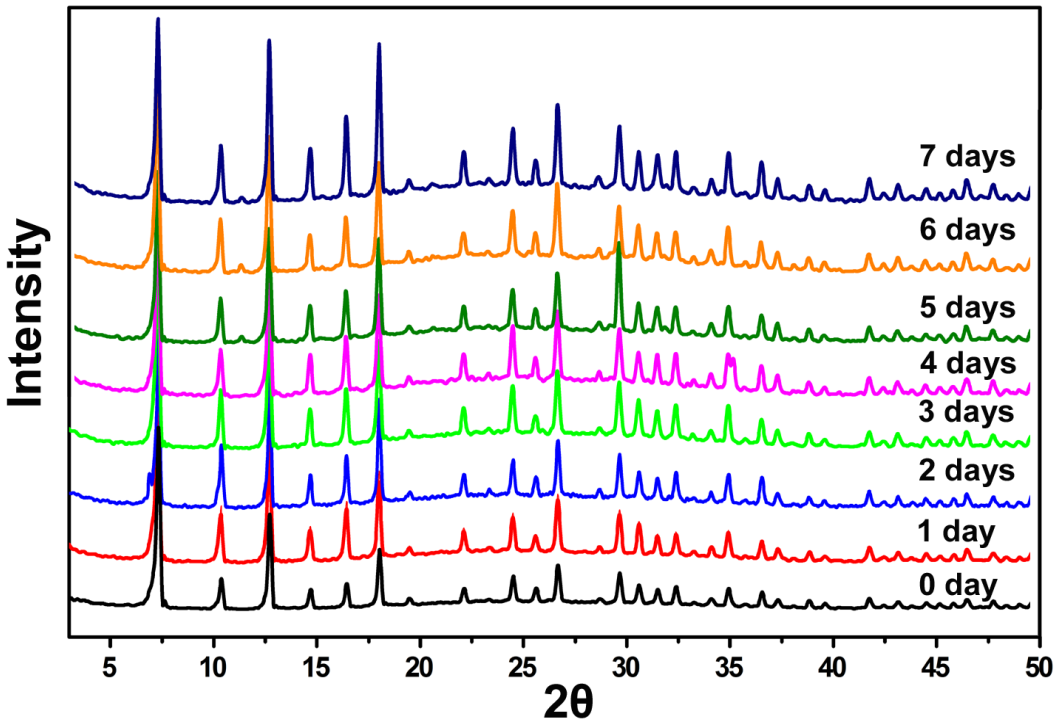

Fig. S3 The PXRD patterns for ZIF-8 suspending in phosphate-buffer saline (pH 7.4).

Drug Loading Experiment

The 5-fluorouracil (5-FU) loading was performed by introducing, under stirring during 2 days, 20 mg of the dehydrated powder material (dried 24 hours at 160°C in an oven) in a 5 ml solution of methanol containing 30 mg of 5-Fu . After the insertion of drug, the sample was dried at 50ºC overnight. The adsorbed amount of 5-Fu into the porous solids was estimated by UV–Vis absorption spectroscopy, thermogravimetric analysis (TGA), and FTIR.

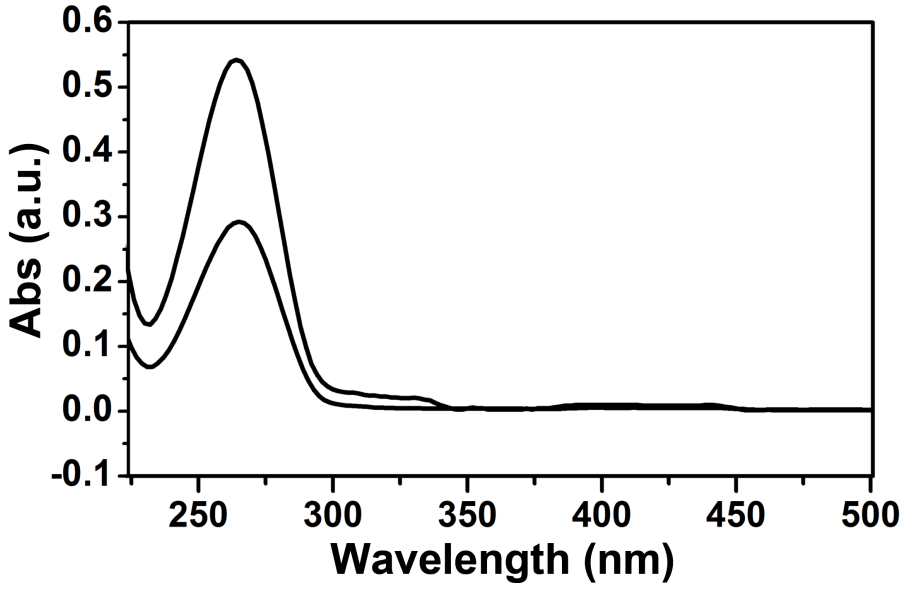

Fig. S4 The UV–Vis absorption spectra of 5-FU methanol solution before and after the interaction with ZIF-8.

Thermogravimetric Analyses

In Figure S4, the initial weight loss, range of 50 to 190 °C, corresponding to the departure of the methanol molecules, which were adsorbed by ZIF-8. Two weight loss of 5-Fu-containing sample were observed between 190 to 380 °C and 400 to 530 °C corresponding to the departure of 5-Fu. and decomposition of the framework.

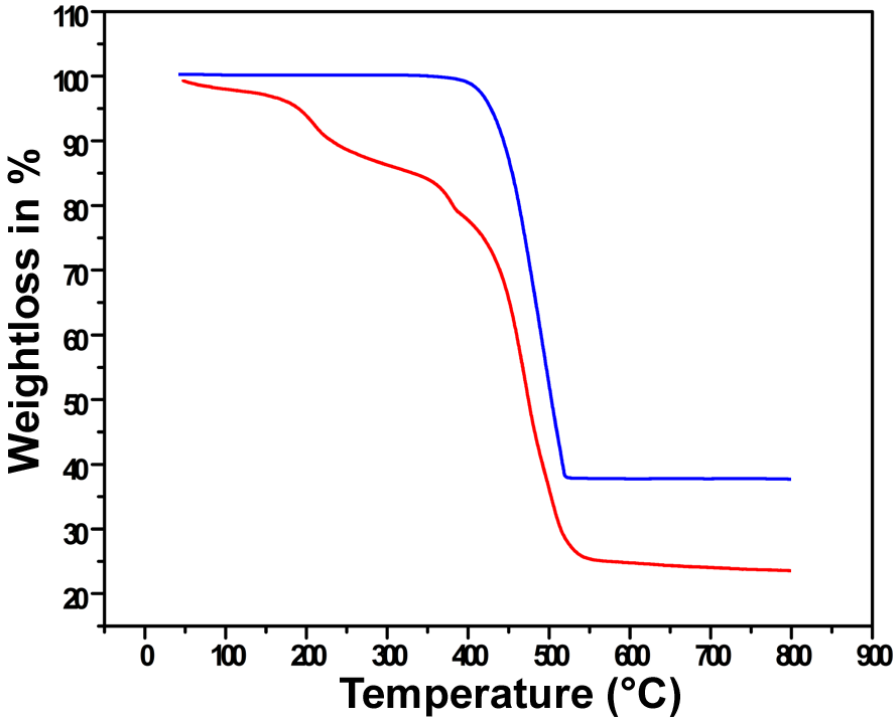

Fig. S5 TGA under nitrogen gas atmosphere of ZIF-8 before (blue) and after (red) the 5-Fu adsorption.

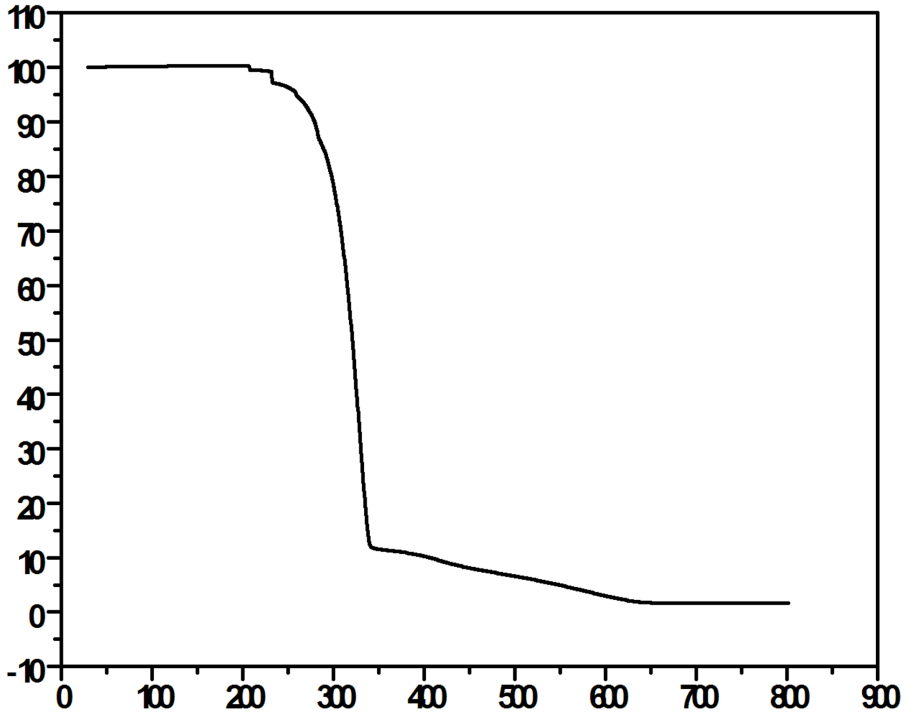

Fig. S6 TGA under nitrogen gas atmosphere of pure 5-FU.

Determination of the 5-Fu Content

Optimisation of 5-Fu adsorption

Table S1. Estimated 5-Fu content = f(several impregnation parameters).

Impregnation parameters		UV-Vis adsorption intensity	g 5-FU/g dehydrated ZIF-8
Solvent	H_2O	0.445	0.285
	CH_3OH	0.300	0.660
5-FU/material weight ratio	1:1	0.202	0.603
	1.5:1	0.300	0.660
	2:1	0.484	0.534
Dehydration	100	0.366	0.502
	150	0.300	0.660
Immersion time (days)	1	0.385	0.450
	2	0.300	0.660
	3	0.360	0.518

Drug Release Experiment

The release of 5-FU from 5-FU-loaded ZIF-8 was evaluated using a semi-permeable dialysis bag diffusion technique right after the 5-FU loading. The as-prepared 5-FU-loaded ZIF-8 was dispersed in 2 mL acetate buffer (pH 5.0) and PBS (pH 7.4), respectively. The release mediums were placed into pretreated semi-permeable dialysis bags and then immersed into 4 ml deionized water at 37 °C with gentle shaking. At certain time intervals, 5-FU concentration moved out of semi-premeable dialysis dag into water was measured by fluorescence spectrophotometer with the fluorescence excitation at 453 nm.

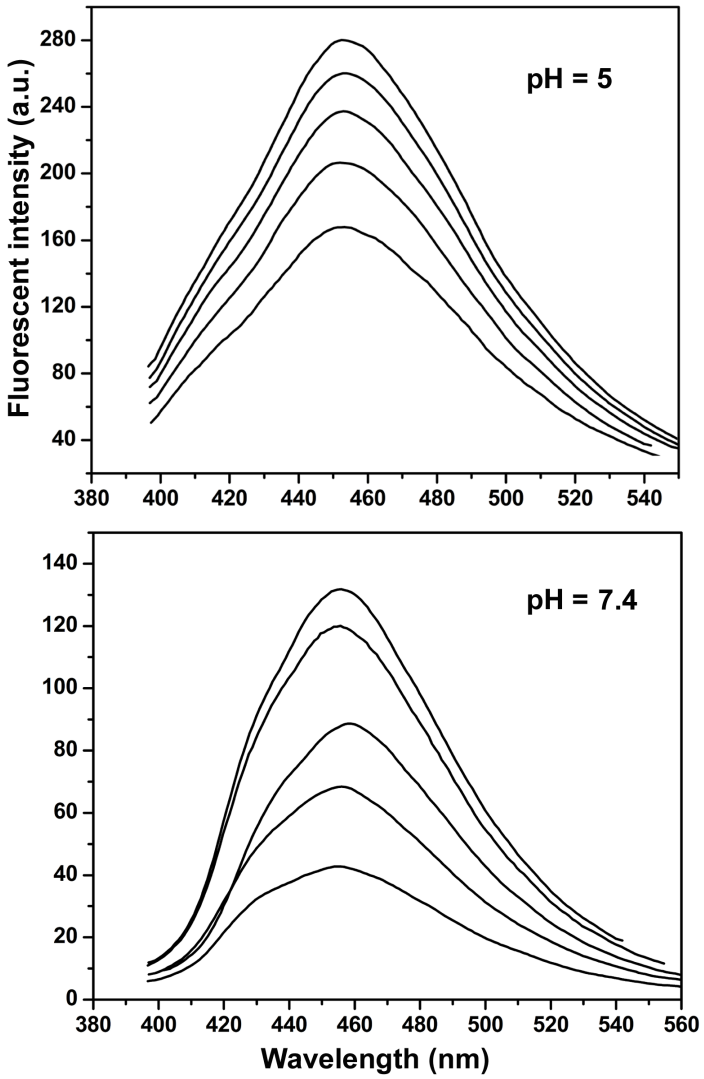

Fig. S7 Photoluminescence spectra of 5-FU relaesing from ZIF-8 in acetate buffer (pH 5.0, top) and PBS (pH 7.4, bottom), respectively.

X-ray Powder Diffraction

Owing to the weak acidity of 5-FU, the degradation of 5-FU-loaded ZIF-8 occured after relaesing experiment, which is confirmed by X-ray powder diffraction.

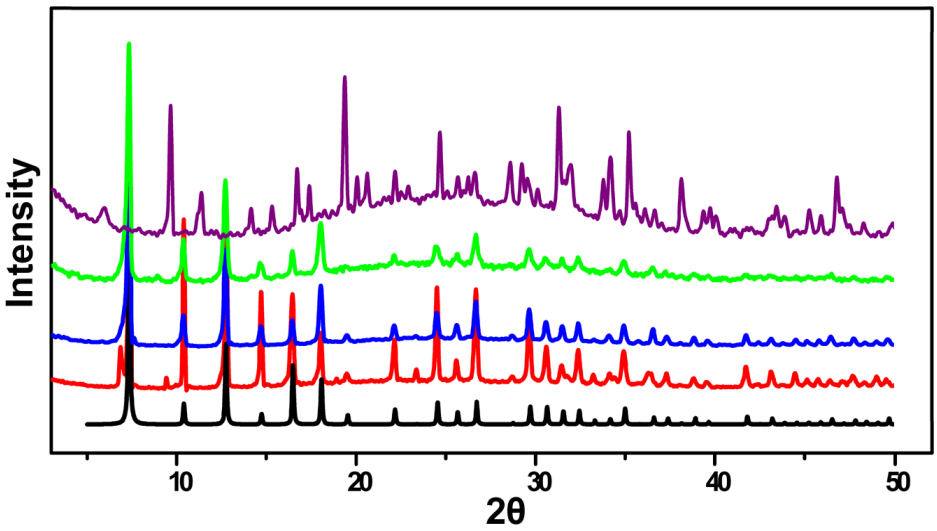

Fig. S8 XRPD patterns for ZIF-8 (black, simulated; red, as-synthesized ZIF-8; blue, dehydrated ZIF-8; green, 5-FU loading ZIF-8; 5-FU-released ZIF-8).