Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

for

pH-triggered degradation and release of doxorubicin from zeolitic imidazolate framework-8 (ZIF8) decorated with Polyacrylic Acid

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Methods of Characterization

***Scanning electron microscopy (SEM)*:** Hitachi S-4700 FE-SEM (Japan) was used to measure surface morphology of as-prepared samples at 15 kV accelerating voltage. Samples were dripped on the cover glass (22 x 22 mm). After drying, the cover glass pieces were attached to the polished aluminum stubs substrate through carbon tape. Before SEM analysis, these samples were not coated with gold or palladium for more accurate size measurements. All sample solutions were treated in an ultrasonic (40 seconds) bath and vortex mixer (10 seconds) before deposition on the glass in order to minimize particle aggregations.

***Transmission electron microscopy (TEM)*:** TEM specimens were prepared by placing one drop (6 μL) of the nanoparticle solution onto a carbon-coated copper grid and drying at room temperature. As with other techniques, all sample solutions were treated in an ultrasonic (30 seconds) bath and vortex mixer (5 seconds) before deposition to reduce aggregation. TEM was performed with a Hitachi H-7600 (Japan) microscope operated at 80 kV and a Tecnai G2 F30 (Germany) microscope operated at 300 kV.

Fourier Transform Infrared Spectra (FTIR): After powder samples were dried by a freeze-dryer, then put a small amount of these powder directly on between two support plates without hygroscopic material (such as NaCl or KBr). The FTIR spectra were recorded using a FTIR spectrometer (Vertex 70, Bruker, USA).

UV-visible absorption: With the in-vitro release tests, to determine the amounts of released drugs, standard calibration curves were obtained from the ultraviolet-visible absorption peaks of the drug. Immediately after Dox-ZIF8 and Dox-ZIF8@PAA were added to the PBS solution, an aliquot was periodically sampled from the solution to monitor the released drug amounts by UV-vis spectroscopy (NanoDrop; NanoDrop Technologies, Wilmington, Delaware, USA).

X-ray diffraction*:* XRD patterns of particles were obtained by an X-ray Automatic Diffractometer (Rigaku Rint 2200 Series, Rigaku, Tokyo, Japan) using monochromatized Cu Kα1

radiation of wavelength λ = 1.5406 Å, at 40 kV voltage and 30 mA current with the continuous-scanning 2ϴ mode.

Thermogravimetry and Difference Thermal Analysis: TG and DTA measurements were performed simultaneously on a SDT Q600 Thermoanalyzer. Samples were filled into alumina crucibles and heated in a flow of nitrogen with a ramp of 5^{o}C x min^{-1} from room temperature up to 700^{o}C.

Nitrogen physisorption isotherms: were measured at -196^{o}C on a volumetric instrument. Samples were outgassed in vacuum at room temperature for at least 24 h before the sorption measurements. Surface areas were estimated by applying the Brunauer_Emmett_Teller (BET) equation. The Barrett_Joyner_Halenda (BJH) method was applied to determine mesopore size distributions.

Statistical analysis methods

The data were expressed as the means ± the standard deviations (SD). The kinetic release data was an average value which was periodically sampled more than three times at a predetermined time during the release process. The mean value (μ_x) and standard deviation (SD) of release data were calculated by the following formula (1), (2).

$$\mu_x = \frac{\sum_{i=1}^{n} x_i}{n} \quad (1)$$

$$SD = \sqrt{\frac{\sum_{i=1}^{n} (x_i - \mu_x)^2}{n-1}} \quad (2)$$

The Dox release profiles from ZIF8-Dox at pH 7.4 can also be fitted by a power-law equation, based on the Korsmeyer–Peppas (K-P) model, which is usually applied to predict the diffusion mechanism in anomalous drug release kinetics:

$$\frac{Q_t}{Q_\infty} = k_R t^n \quad (1)$$

where Q_t/Q_∞ is the normalized fraction of the drug release, k_R is the relaxation rate constant, and n is the release exponent. In the K-P model, the value of n characterizes the release mechanism.

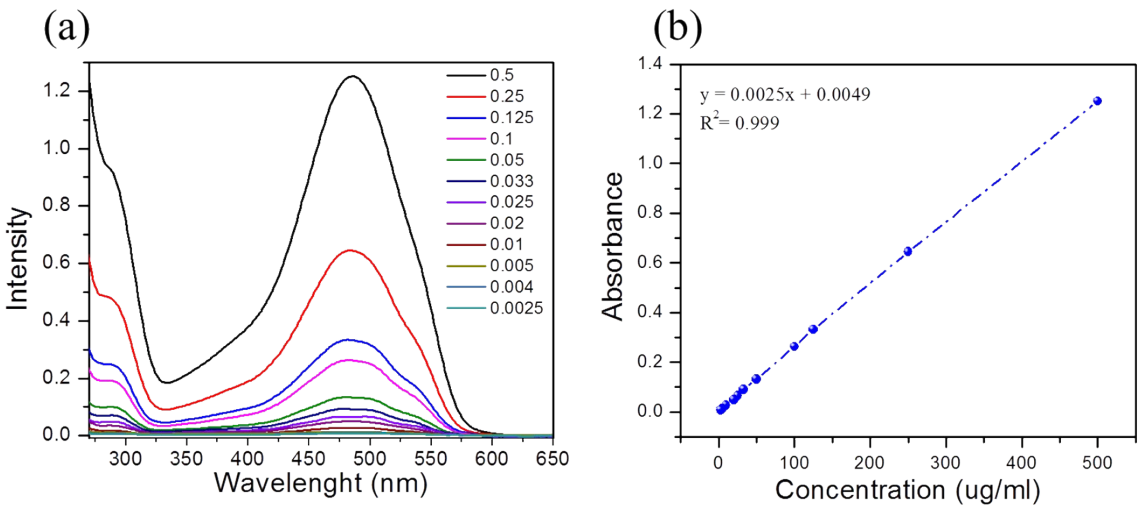

Fig. S1. **(a)** UV-vis absorbance of doxorubicin from 500 ug/ml to 2.5 ug/ml concentration in PBS at pH 7.4; **(b)** the linear part of standard curve for the determination of doxorubicin concentration at 485 nm.

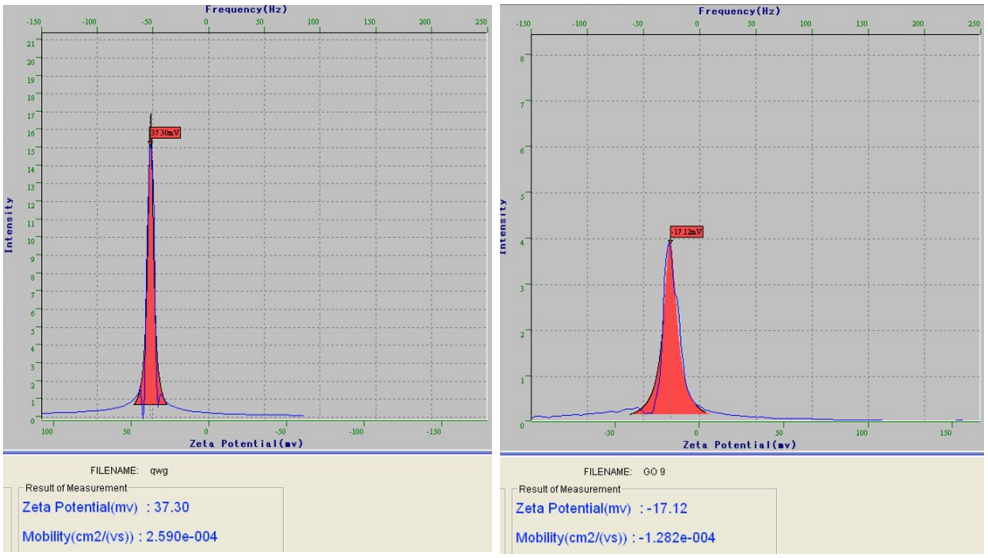

Fig. S2. Zeta potential of ZIF8 and ZIF-8@PAA in PBS at neutral pH.

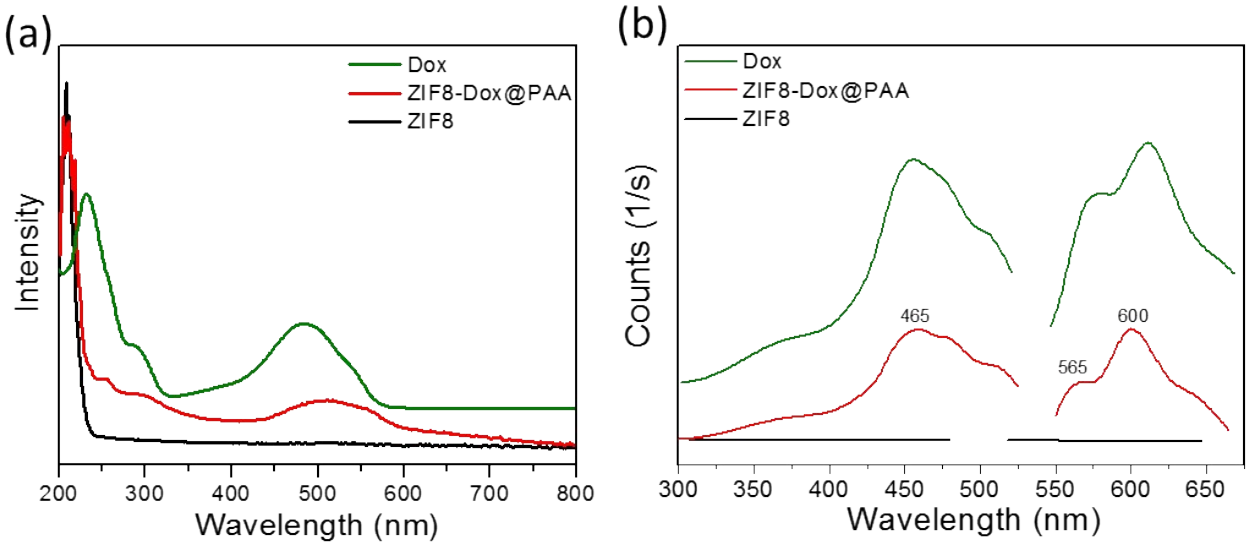

Fig. S3. UV-vis spectra and PL spectra of ZIF8, Dox and ZIF8-Dox@PAA.

Table S1. The summary of fitted parameter values of kinetic models used for the release data of Dox from ZIF8-Dox and ZIF8-Dox@PAA at pH 7.4

As-prepared NPs	Diffusion models	Formula	Released parameters
ZIF8-Dox@PAA (pH 7.4)	Sigmoid behavior (S-shaped behavior)	$Q_t/Q_\infty = (Q_{max}\, t^\gamma)/(Q_{1/2} + t^\gamma)$	$\gamma = 5.20$
ZIF8-Dox (pH 7.4)	1st stage: K-P model#	$Q_t/Q_\infty = k_R\, t^n$	$k_R = 5.24$ $n = 0.33$
	2nd stage: Weibull model	$Q_t/Q_\infty = A(1-e^{-k_w (t-T)})$	$T = 3.0$ $k_w = 2.2$

K-P model indicate the Korsmeyer-Peppas model.

Table S2. Kinetic models used for the release data of Dox release from ZIF8-Dox and ZIF8-Dox@PAA at pH 4.0

Diffusion models	Formula	Released parameters	ZIF8-Dox (pH 4)	ZIF8-Dox@PAA (pH 4)
BiDoseResp Model release	$\frac{Q_t}{Q_\infty} = \frac{Q_1}{Q_\infty} + \left(\frac{Q_2}{Q_\infty} - \frac{Q_1}{Q_\infty}\right)\left[\frac{A}{1+10^{\log\left((t_1-t)^{0.5}\right)h_1}} + \frac{1-A}{1+10^{\log\left((t_2-t)^{0.5}\right)h_2}}\right]$	Q_1/Q_∞	0	0
		Q_2/Q_∞	85.50	81.69
		h_1	2.50	3.20
		h_2	3.20	2.00
		A	0.49	0.41