# Supplementary Information

## Phosphorylcholine-based zwitterionic copolymer coated ZIF-8 nanodrug with long circulation and charged conversion for enhanced chemotherapy

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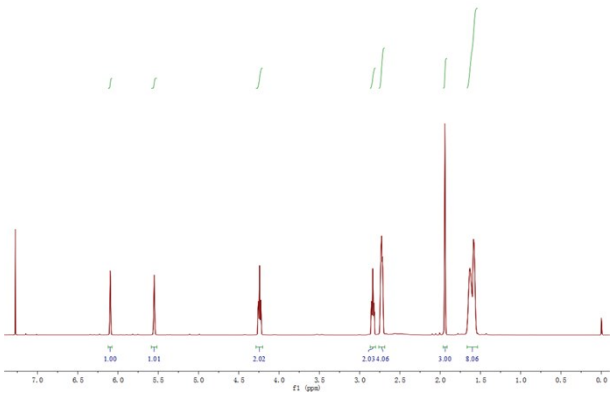

**Figure S1.** The $^{1}$H-NMR spectra of C7A monomer. **1H NMR** (TMS, $CDCl_3$, ppm): 6.09 (br, 1H, C*H*H=C($CH_3$)-),5.55 (br, 1H, CH*H*=C($CH_3$)-), 4.24 (t, *J* = 6.5 Hz, 2H, -OC$H_2$$CH_2$N-), 2.84 (t, *J* = 6.5 Hz, 2H, -O$CH_2$C$H_2$N-), 2.72 (m, 4H, -N(C$H_2$$CH_2$$CH_2$)$_2$), 1.94 (s, 3H, $CH_2$=C(C$H_3$)-), 1.63-1.58 (m, 8H,-N($CH_2$C$H_2$C$H_2$)$_2$).

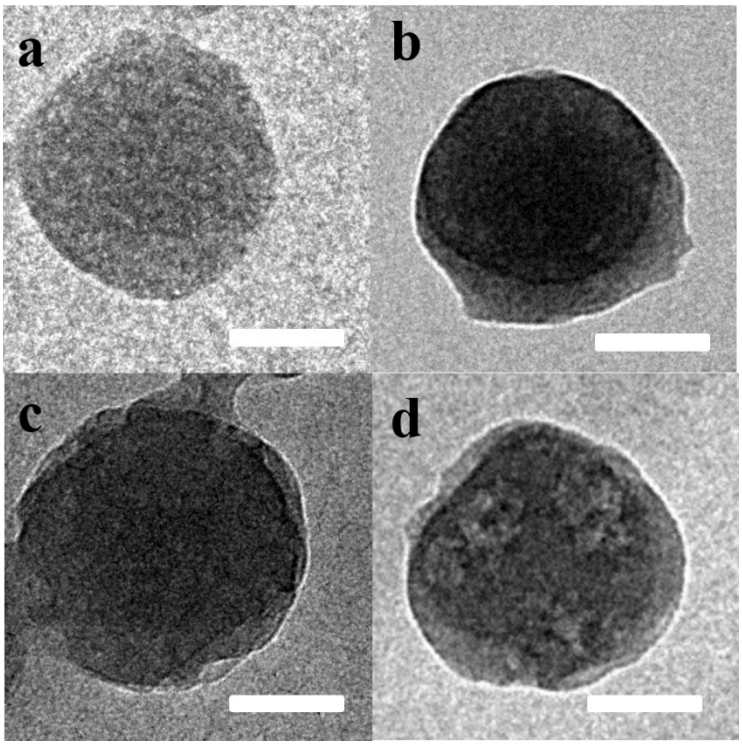


**Figure S2.** The higher magnification TEM images of the DOX@ZIF-8 (a), DOX@ZIF-8@PMPC (b), DOX@ZIF-8@P(MPC-*co*-C7A) (c) and ZIF-8@PMPC-DOX (d). Scale bars were 50 nm.

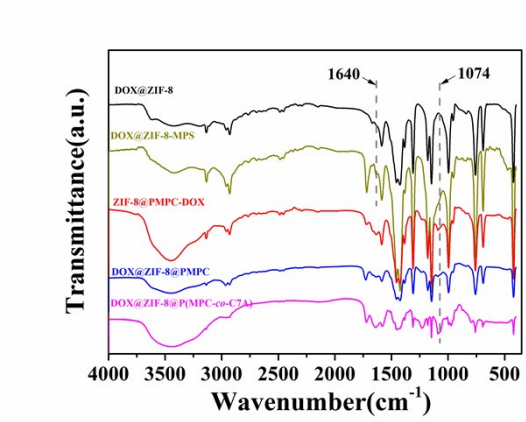


**Figure S3.** The Fourier transform infrared spectra of the DOX@ZIF-8, DOX@ZIF-8-MPS, ZIF-8@PMPC-DOX, DOX@ZIF-8@PMPC and DOX@ZIF-8@P(MPC-*co*-C7A). The peak at 1640 $cm^{-1}$ belongs to carbon-carbon double bonds. The peak at 1074 $cm^{-1}$ belongs to P-O bond.

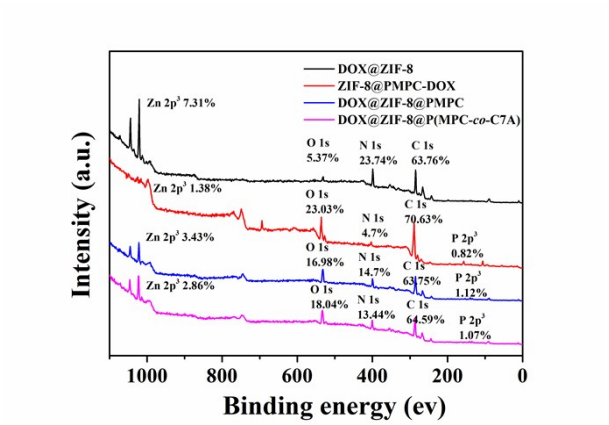


**Figure S4.** The X-ray photoelectron spectroscopy (XPS) spectra of the DOX@ZIF-8, ZIF-8@PMPC-DOX, DOX@ZIF-8@PMPC and DOX@ZIF-8@P(MPC-*co*-C7A).

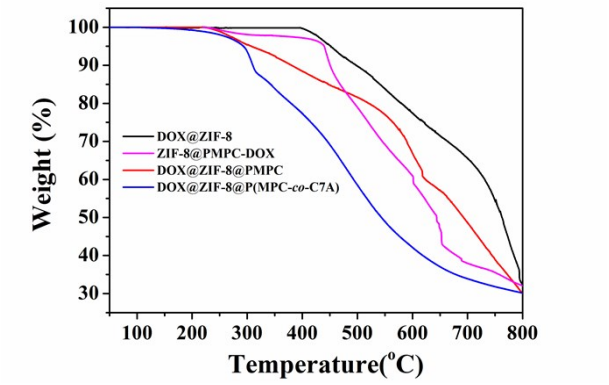


**Figure S5.** Thermogravimetric analysis curve of DOX@ZIF-8, ZIF-8@PMPC-DOX, DOX@ZIF-8@PMPC and DOX@ZIF-8@P(MPC-*co*-C7A) in the atmosphere of $N_2$.

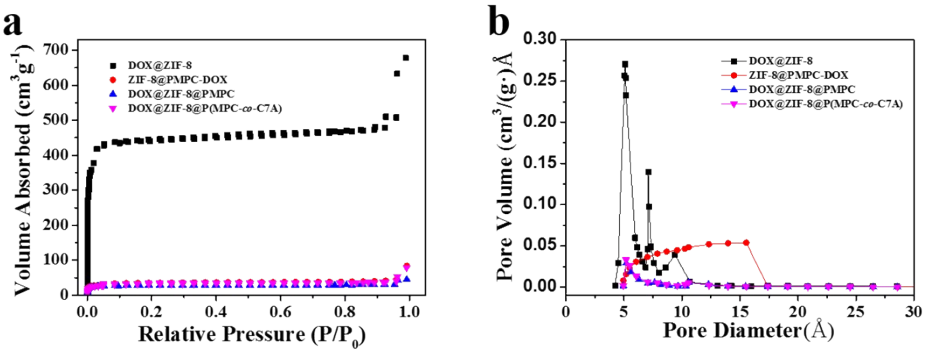


**Figure S6.** Nitrogen adsorption-desorption isotherms (a) and pore size distribution curves (b) for DOX@ZIF-8, ZIF-8@PMPC-DOX, DOX@ZIF-8@PMPC and DOX@ZIF-8@P(MPC-*co*-C7A).

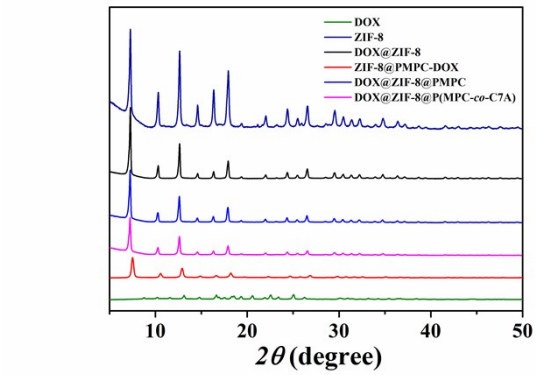


**Figure S7.** Powder X-ray diffraction patterns of DOX, ZIF-8, DOX@ZIF-8, ZIF-8@PMPC-DOX, DOX@ZIF-8@PMPC and DOX@ZIF-8@P(MPC-*co*-C7A).

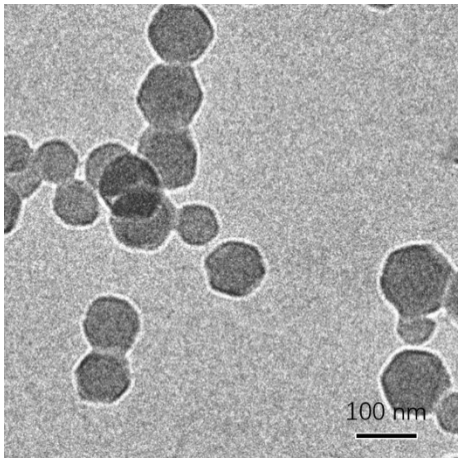


**Figure S8.** TEM images of ZIF-8.

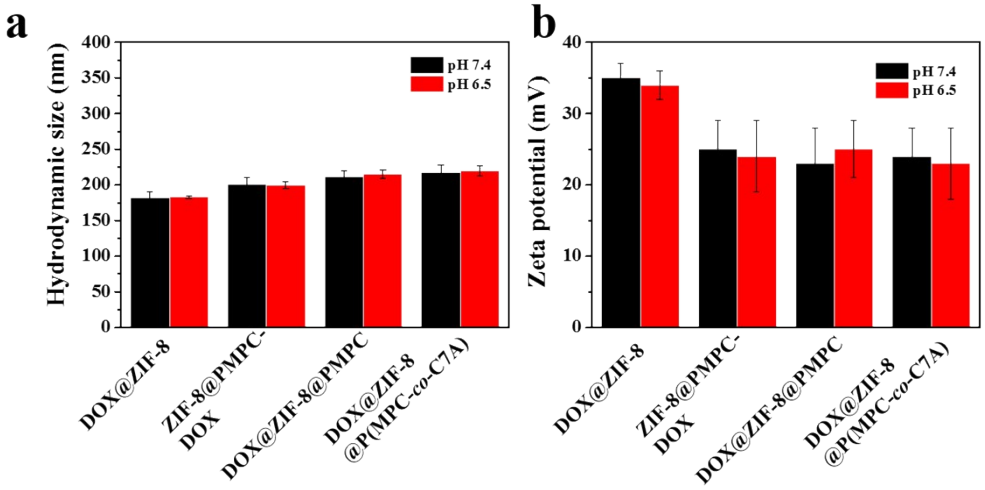


**Figure S9.** The hydrodynamic size (a) and zeta potential (b) change of DOX@ZIF-8, ZIF-8@PMPC-DOX, DOX@ZIF-8@PMPC and DOX@ZIF-8@P(MPC-*co*-C7A) after incubation in 10 mM GSH at pH 7.4 or pH 6.5 for 2 h.

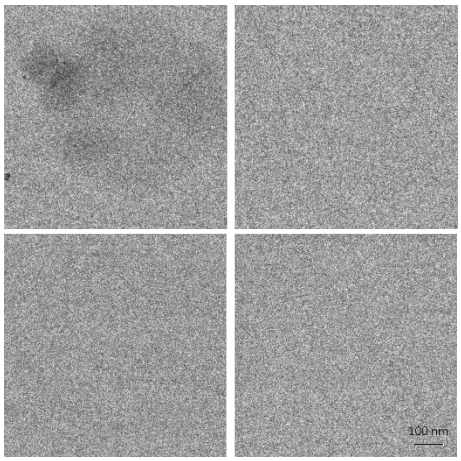


**Figure S10.** The TEM images of DOX@ZIF-8, ZIF-8@PMPC-DOX, DOX@ZIF-8@PMPC and DOX@ZIF-8@P(MPC-*co*-C7A) after incubation at pH 5.0 for 24 h.

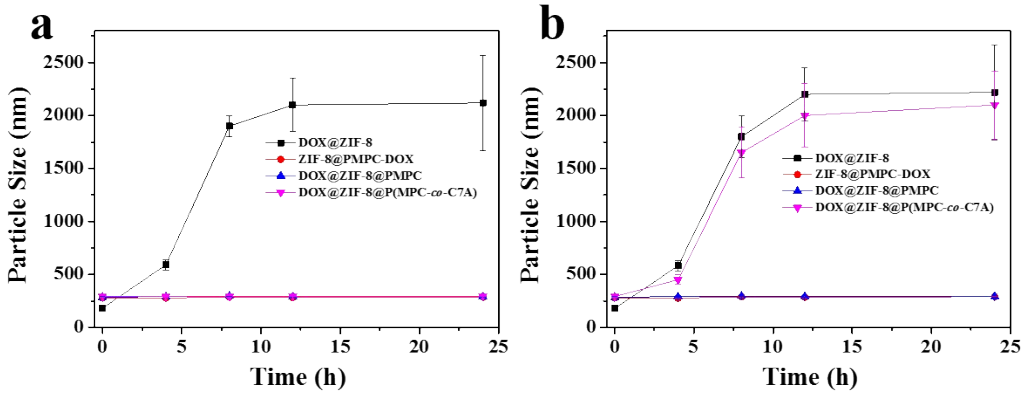


**Figure S11.** The variation of particle size of the DOX@ZIF-8, ZIF-8@PMPC-DOX, DOX@ZIF-8@PMPC and DOX@ZIF-8@P(MPC-*co*-C7A) at pH 7.4 (a) or 6.5 (b).

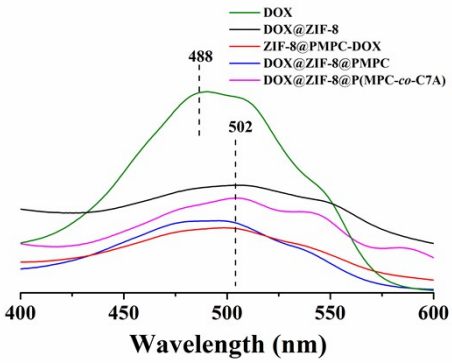


**Figure S12.** UV-Vis spectra of DOX, DOX@ZIF-8, ZIF-8@PMPC-DOX, DOX@ZIF-8@PMPC and DOX@ZIF-8@P(MPC-*co*-C7A) at pH 7.4 PBS solution.

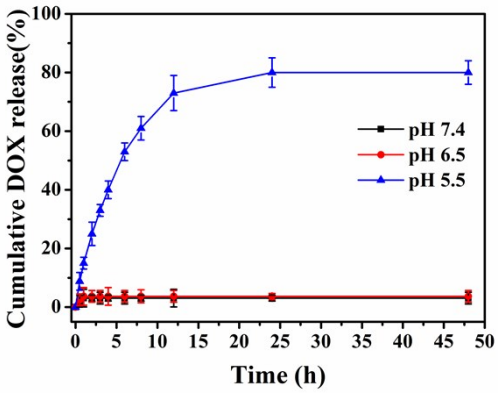


**Figure S13.** The DOX release of DOX@ZIF-8 at different pH values.

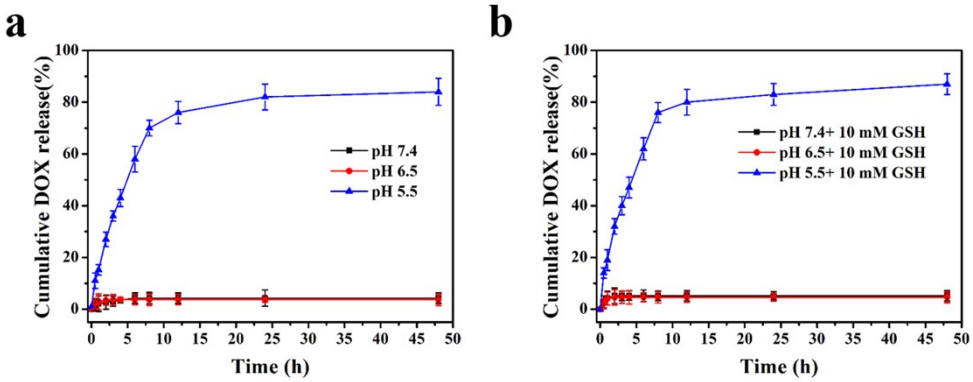


**Figure S14.** The DOX release of DOX@ZIF-8@n-P(MPC-*co*-C7A) at different pH without (a) or with (b)10 mM of GSH.

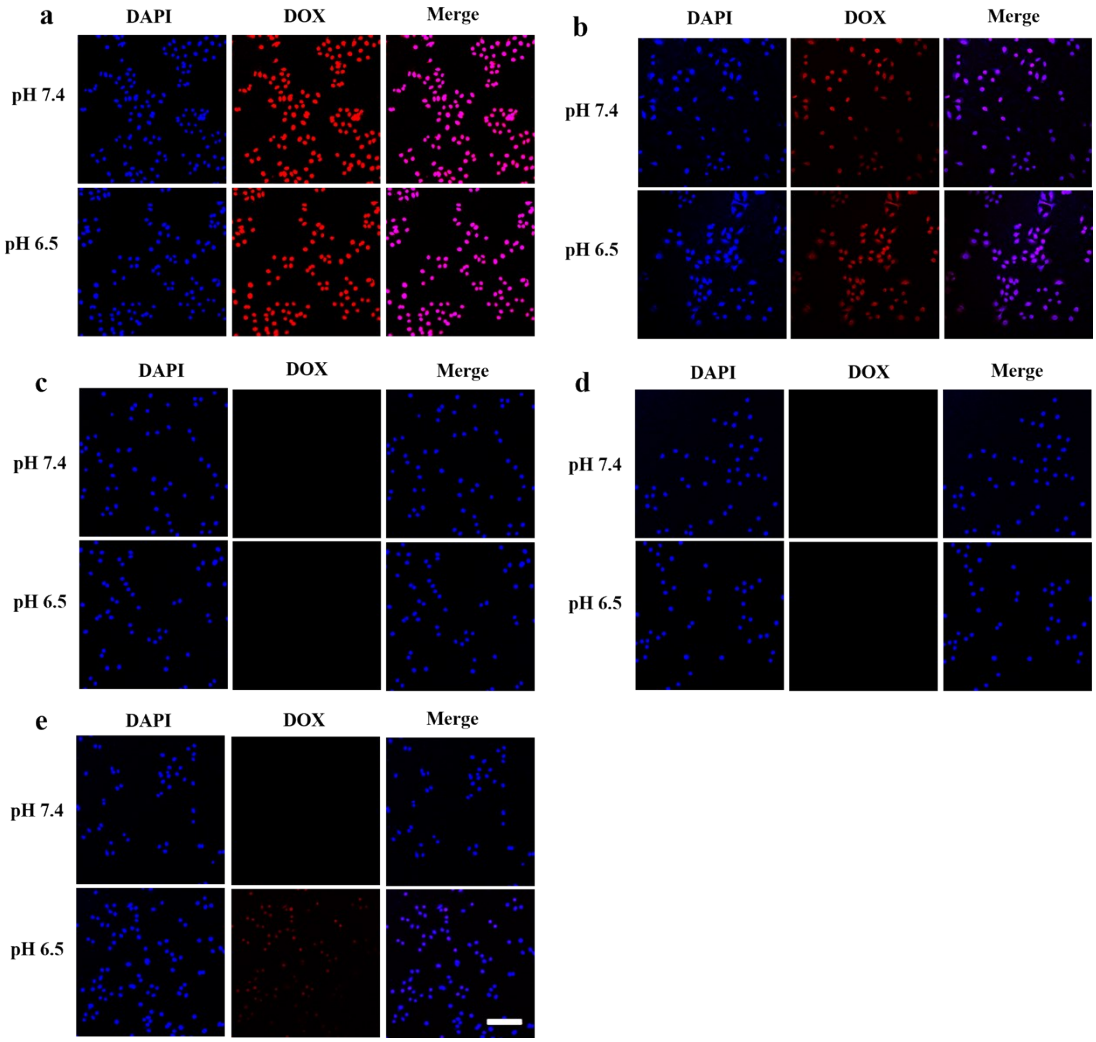


**Figure S15.** Confocal microscopic images of free DOX (a), DOX@ZIF-8 (b), ZIF-8@PMPC-DOX (c), DOX@ZIF-8@PMPC (d) and DOX@ZIF-8@P(MPC-*co*-C7A) (e) at pH 7.4 or 6.5 (scale bar:100 μm).

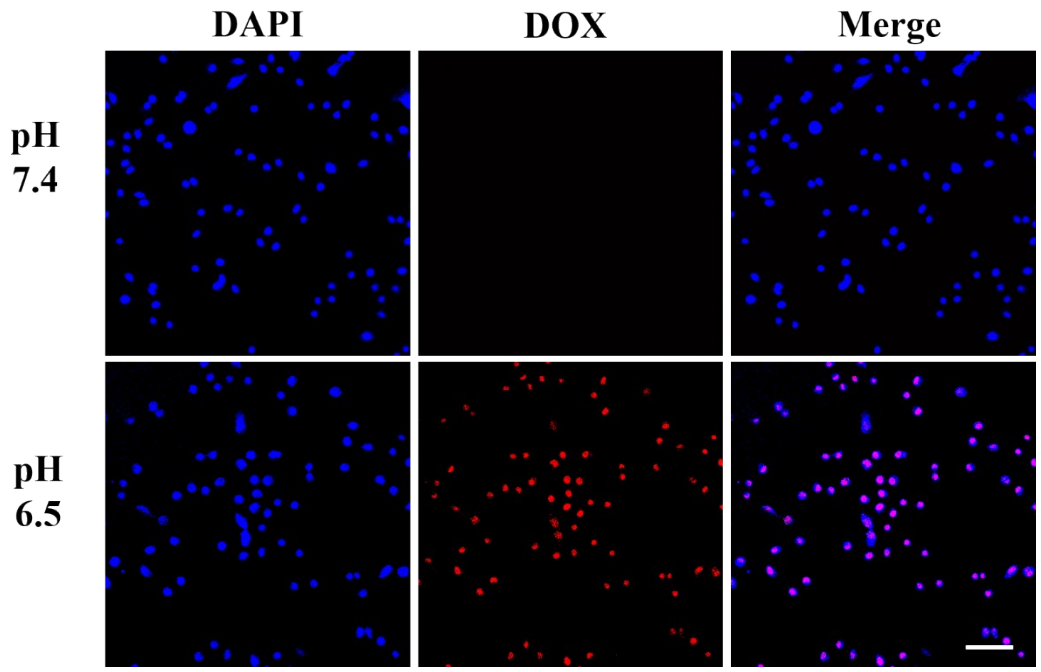


**Figure S16.** The confocal microscopic images of A549 cells treated with DOX@ZIF-8@n-P(MPC-*co*-C7A) at pH 7.4 or 6.5, respectively. Scale bar was 100 μm.

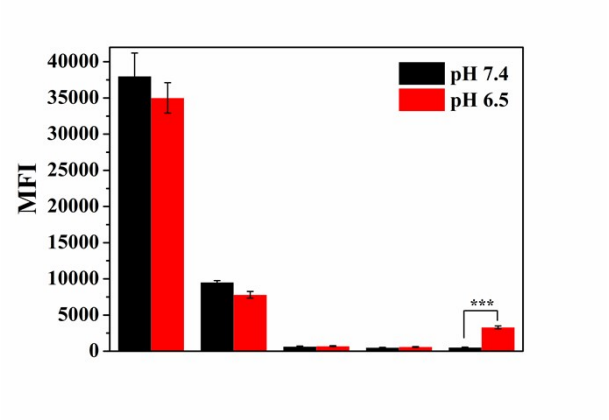


**Figure S17.** Mean fluorescence intensity of A549 cells incubation with DOX, DOX@ZIF-8, ZIF-8@PMPC-DOX, DOX@ZIF-8@PMPC and DOX@ZIF-8@P(MPC-*co*-C7A) at pH 7.4 or 6.5. The tests repeated for three times.

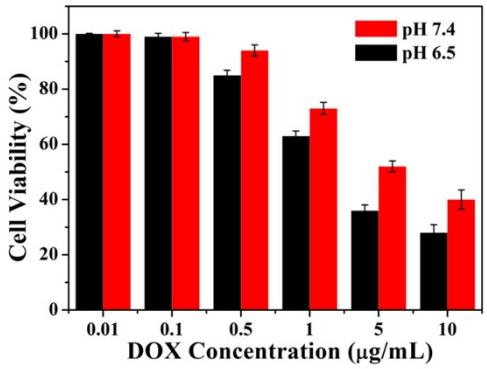


**Figure S18.** The cell viability of A549 cells incubation with DOX@ZIF-8@n-P(MPC-*co*-C7A) at pH 7.4 or 6.5 for 24 h.

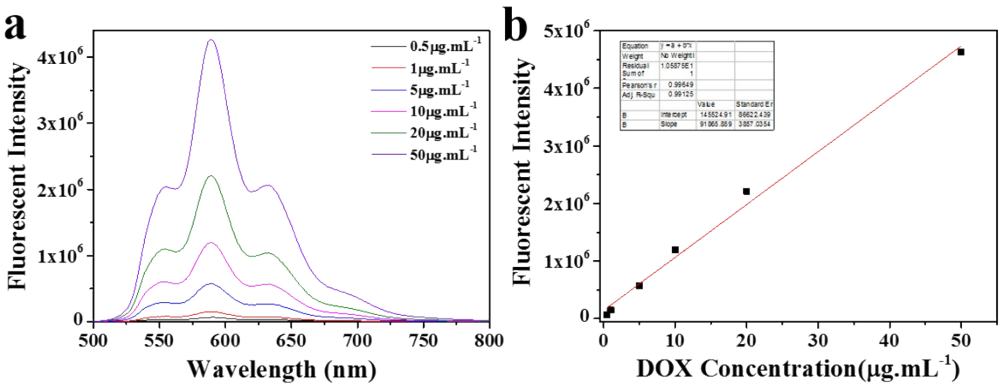


**Figure S19.** (a) Fluorescence emission spectra of free DOX at different concentrations in n-butyl alcohol solution. (b) Linear curve was fitted from the fluorescence intensity of free DOX. (λem = 590 nm)

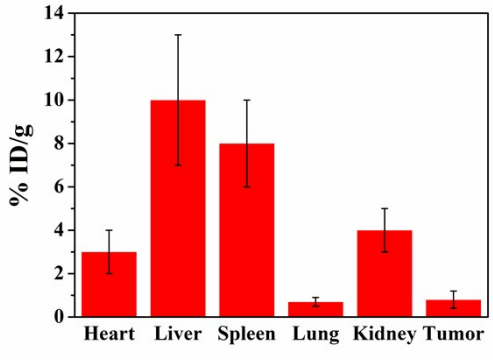


**Figure S20.** The biodistribution of free DOX in tumor-bearing mice at 1 h after intravenous injection.

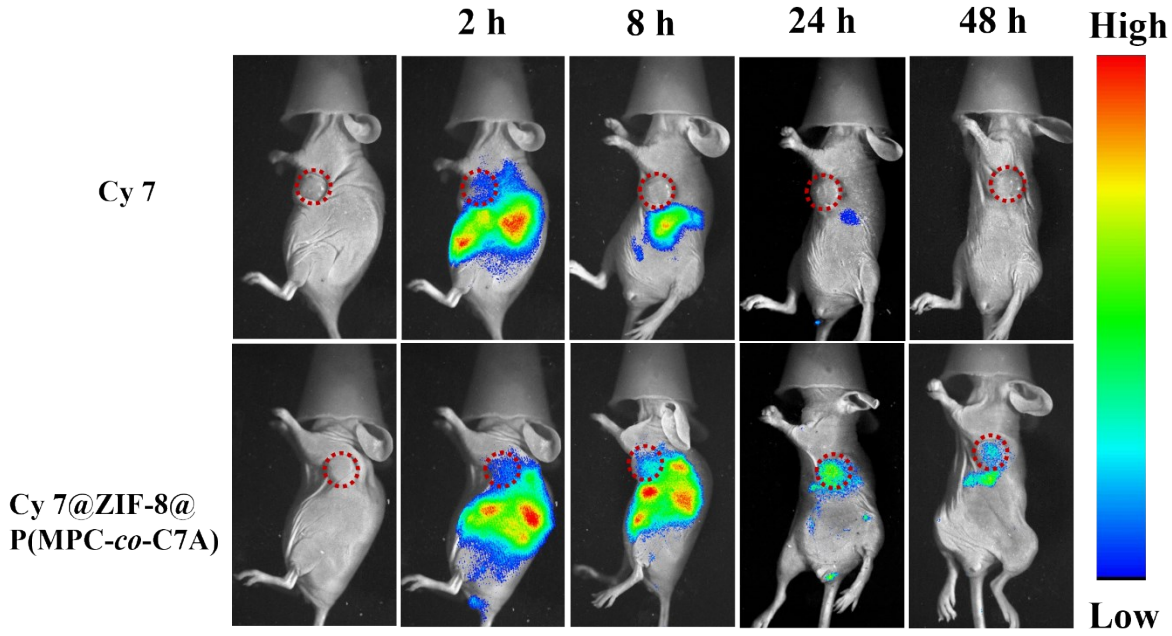


**Figure S21.** The fluorescence images of A549 tumor-bearing mice after injection with free Cy 7 and Cy 7@ZIF-8@P(MPC-*co*-C7A) through the tail vein at different times. Red circles indicate tumor sites.

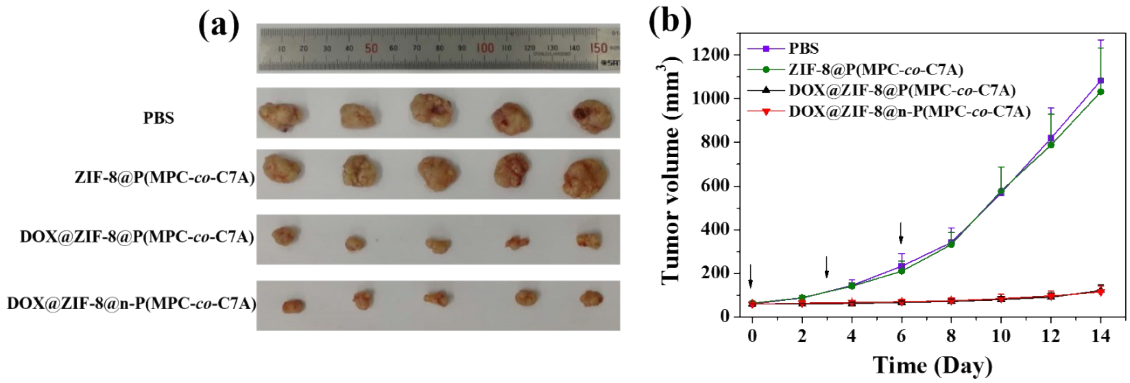


**Figure S22.** (a) Photographs of tumors at the end of the experiment. (b)Tumor growth curves after intravenous administration of PBS, ZIF-8@P(MPC-*co*-C7A), DOX@ZIF-8@P(MPC-*co*-C7A) and DOX@ZIF-8@n-P(MPC-*co*-C7A). Treatments were performed on day 0, 3, 6 (n=5).

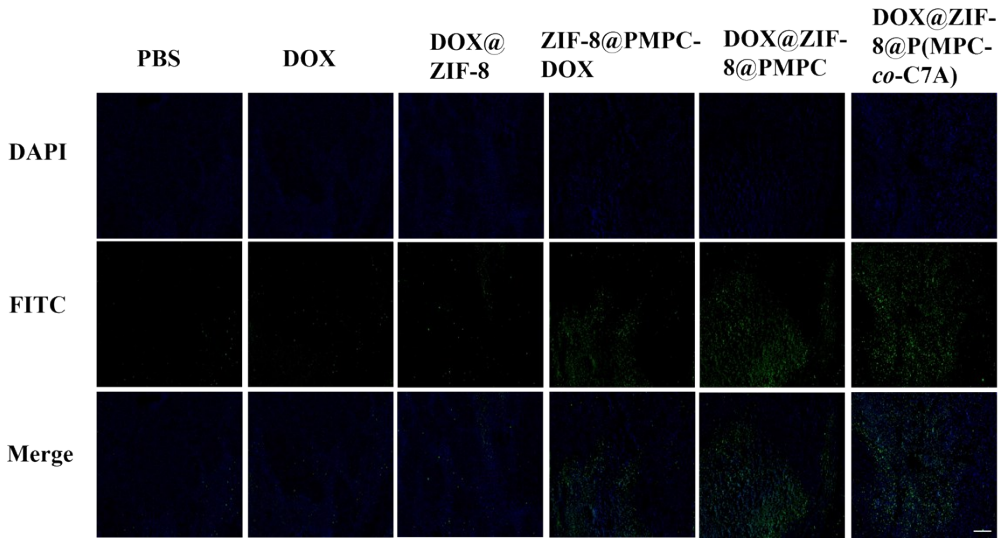


**Figure S23.** TUNEL staining of tumor sections 14 days after treatment. Nuclei and apoptotic cells were stained blue and green, respectively. Scale bar was 200 μm.

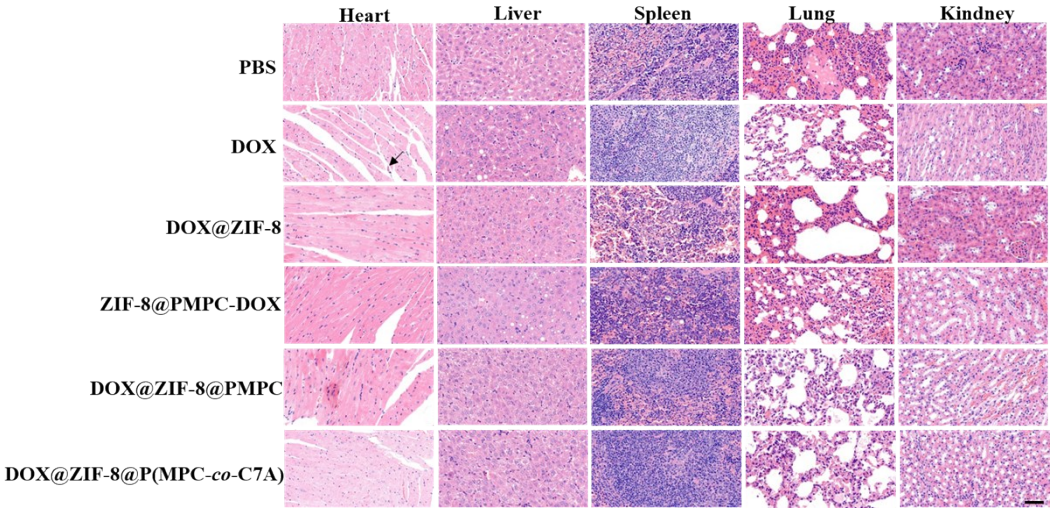


**Figure S24.** H&E-stained slices of major organs including heart, liver, spleen, lungs, and kidneys from each group. Scale bar was 50 μm**.**

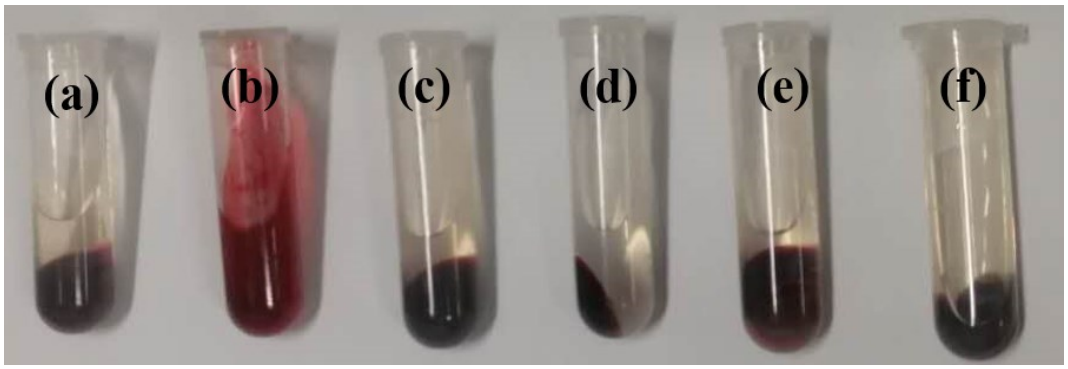


**Figure S25.** Photos of hemocompatibility experiments of the saline (a), distilled water (b) DOX@ZIF-8 (c), ZIF-8@PMPC-DOX (d), DOX@ZIF-8@PMPC (e) and DOX@ZIF-8@P(MPC-*co*-C7A)(f).

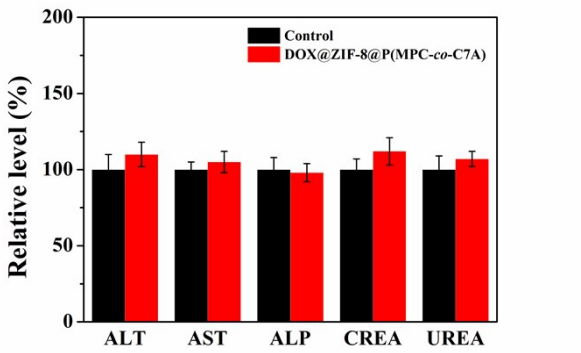


**Figure S26.** Blood biochemistry indices of hepatic and renal function after 24 h injection (aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) creatinine (CREA) and UREA).

**Table S1.** Whole blood panel analysis of nanoparticle-treated mice at 24 h injection. Normal mice without any treatment were used as a negative control.

| | Unit | Control | DOX@ZIF-8@P(MPC-*co*-C7A) |
|---|---|---|---|
| WBC | X $10^9$ cells/L | 6.0±1.0 | 5.1±0.5 |
| RBC | X $10^{12}$ cells/L | 6.4±0.1 | 5.5±1.6 |
| HGB | g/L | 100.3±11.0 | 98±10.1 |
| HCT | % | 43.8±7.9 | 43.7±3.8 |
| MCV | fL | 75.5±4.0 | 77.9±2.8 |
| MCH | pg | 17.4±1.7 | 17.6±1.2 |
| MCHC | g/L | 225.0±10.9 | 224.3±9.9 |
| RDW | % | 16.8±0.4 | 16.7±0.6 |
| PLT | X $10^9$ cells/L | 267.0±70.3 | 277.3±77.4 |

WBC, white blood cell; RBC, red blood cell; HGB, hemoglobin; HCT, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RDW, red blood distribution width; PLT, platelets.