Supporting Information

Morphology tunable and acid-sensitive dextran-doxorubicin conjugating nanoparticles for targeted cancer therapy

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Synthesis of amino modified folic acid (FA-NH_2)

Folic acid (FA) (200 mg), DCC (467.1 mg) and NHS (260.7 mg) were dissolved in dried DMSO (10 mL) and stirred at room temperature for 60 min. Then, ethylenediamine (1 mL) was added dropwise. After stirred for 24 h, FA-NH_2 was obtained followed by precipitating in cold ethyl ether.

DOX content evaluation

DD-M (1 mg) and DDF-V (1 mg) was dissolved in DMSO (3 mL), the grafting content of DOX was determined via UV−vis spectrometer based on a calibration curve of DOX in DMSO. Drug loading content (DLC) and drug loading efficiency (DLE) were calculated according to the equations as below:

DLC (%) = [DOX weight in nanoparticles/total weight of nanoparticles] × 100%

DLE (%) = [DOX weight in nanoparticles/initial feeding amount of DOX] × 100%

Cell culture

HeLa cells (human cervical carcinoma cell line) and Skov3 cells (human ovarian cancer cell line) were provided from Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences, Shanghai, China. HeLa cells were cultured in DMEM (10% fetal bovine serum, 5% CO_2 at 37 °C) and Skov3 cells were cultured in RPMI-1640 (10% fetal bovine serum, 5% CO_2 at 37 °C).

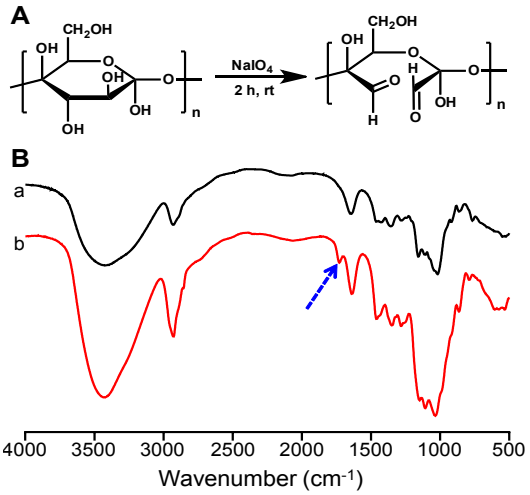
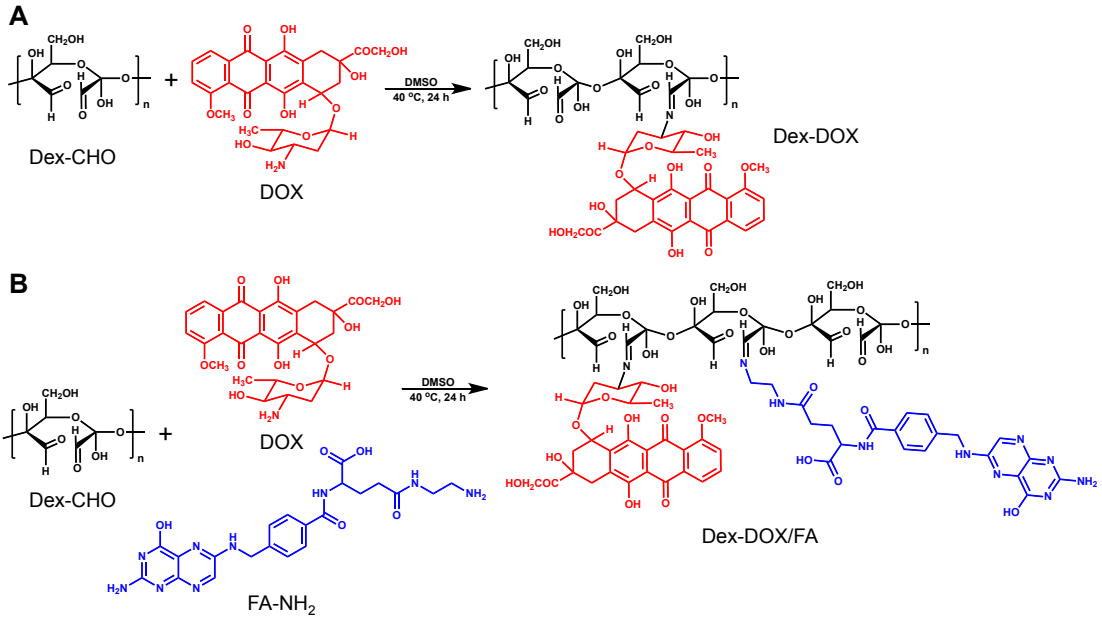


Fig. S1. (A) Synthesis process of Dex-CHO. (B) FT-IR spectra of Dex and Dex-CHO.



Scheme S1. Synthesis processes of (A) Dex-DOX and (B) Dex-DOX/FA.

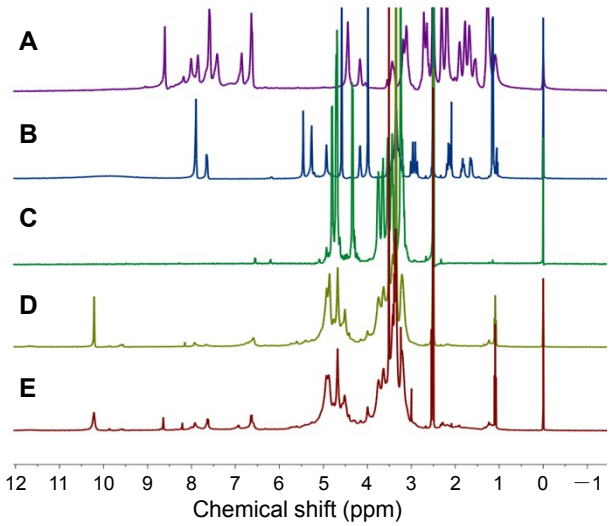


Fig. S2. ^{1}H NMR spectra of (A) FA-NH_2, (B) DOX, (C) Dex, (D) Dex-DOX, (E) Dex-DOX/FA in DMSO-d_6.

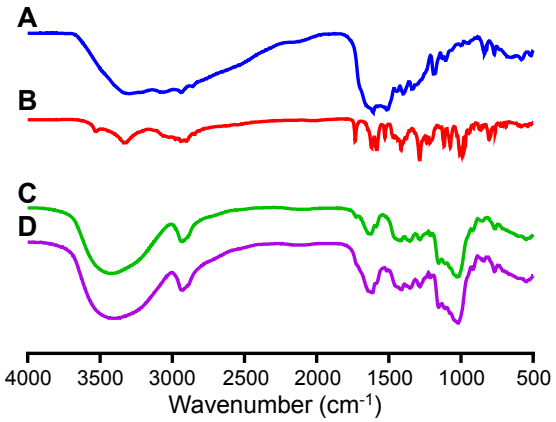


Fig. S3. FT-IR spectra of (A) FA-NH2, (B) DOX, (C) Dex-DOX and (D) Dex-DOX/FA.

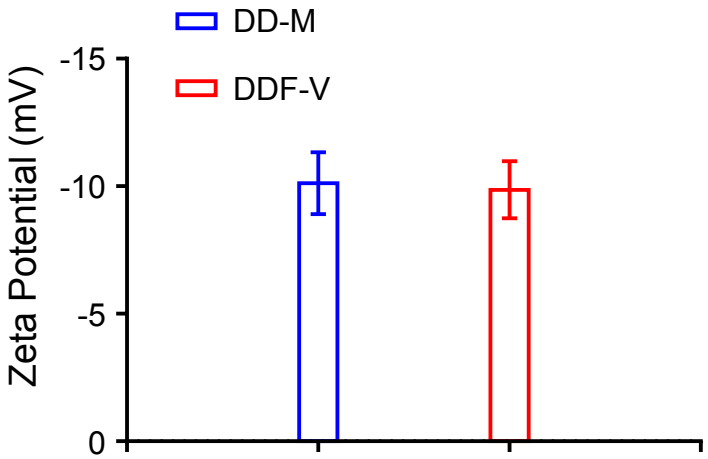


Fig. S4. Zeta potentials of DD-M and DDF-V.

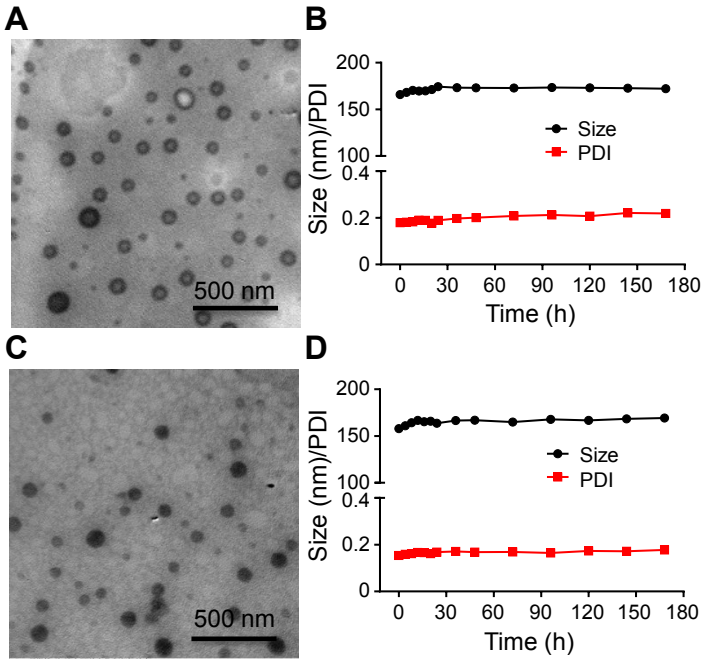


Fig. S5. Stability of DDF-V and DD-M. TEM morphologies of DDF-V (A) or DD-M (C) after incubation in PBS 7.4 for one week. Size distribution and PDI of DDF-V (B) or DD-M (D) after incubation in PBS 7.4 for one week.

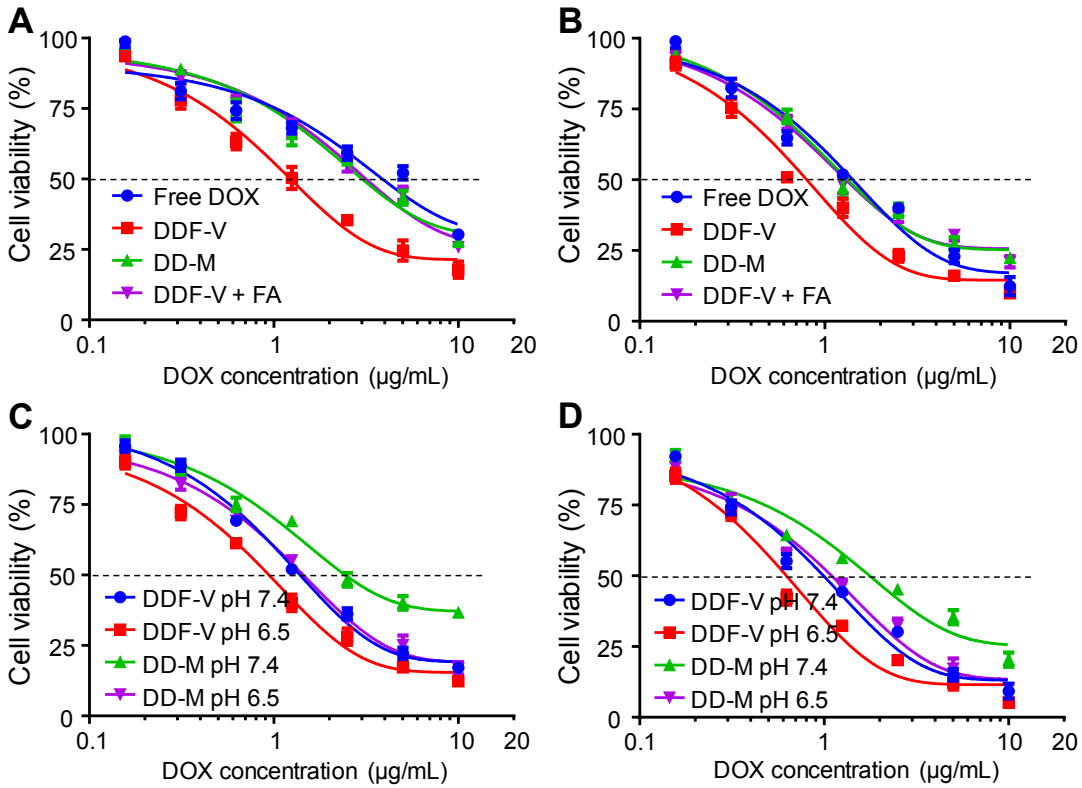


Fig. S6. *In vitro* anti-cancer efficacy of DDF-V and DD-M against Skov3 cells. Cell viability curves of Hela cellls after incubation with different drugs for 48 h (A) or 72 h (B). Cell viability curves of Hela cellls after incubation with different drugs at pH 7.4 or 6.5 for 4 h and further incubated for (C) 48 h and (D) 72 h.

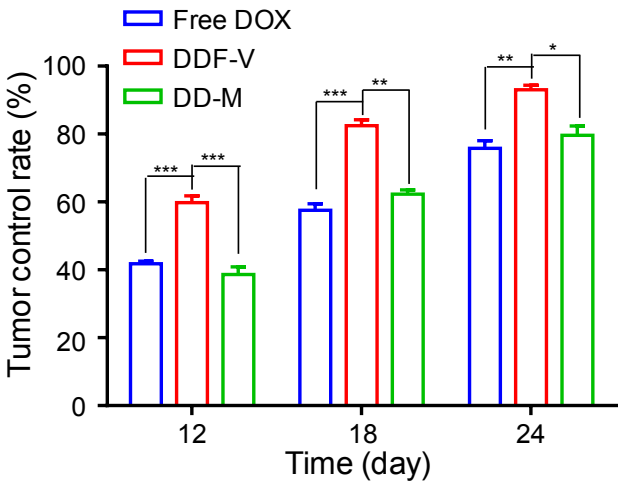


Fig. S7. Tumor control rate of DOX, DDF-V and DD-M treatment groups at day 12, 18 and 24. (Data are expressed as mean ± standard deviation, n = 5. Student's t test was carried out to analyze the statistical significance: *p < 0.05, **p < 0.001, ***p < 0.001.)

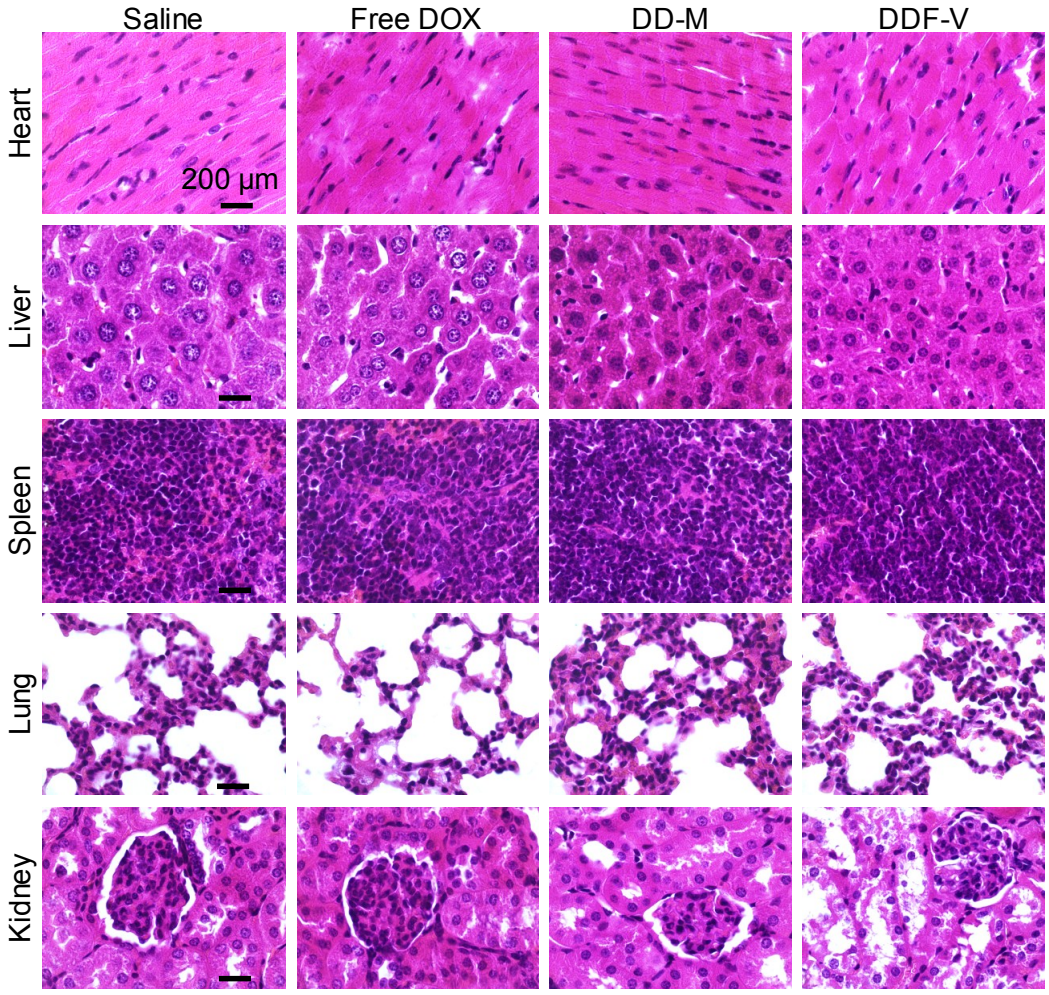


Fig. S8. H&E staining analyses of major tissues at the end of treatment.