Supporting information

Development of carrier-free nanodrugs based on low molecular heparin-doxorubicin conjugate assembly with smart pH-triggered drug release characteristics for combinatorial antitumor therapy

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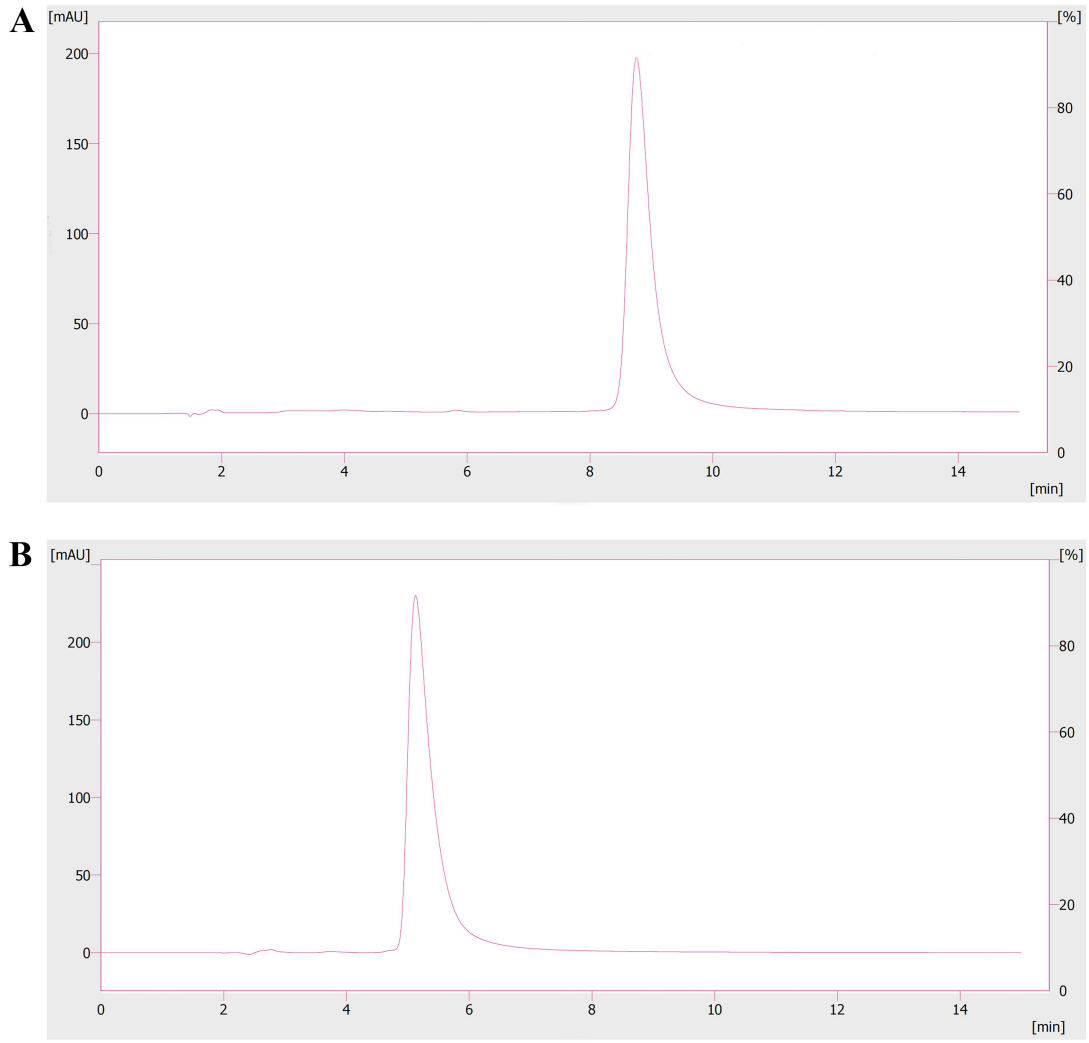

Fig. S1 Chromatogram of DOX (A) and LMWH-DOX conjugate (B) with reversed-phase HPLC analysis. The determination was performed on Diamonsil C_{18} column (250 mm×4.6 mm, 5 μm) with a mobile phase of water/methanol (30:70, v/v) at a flow rate of 1.0 mL/min, column temperature of 25 ℃ and detection wavelength of 233 nm.

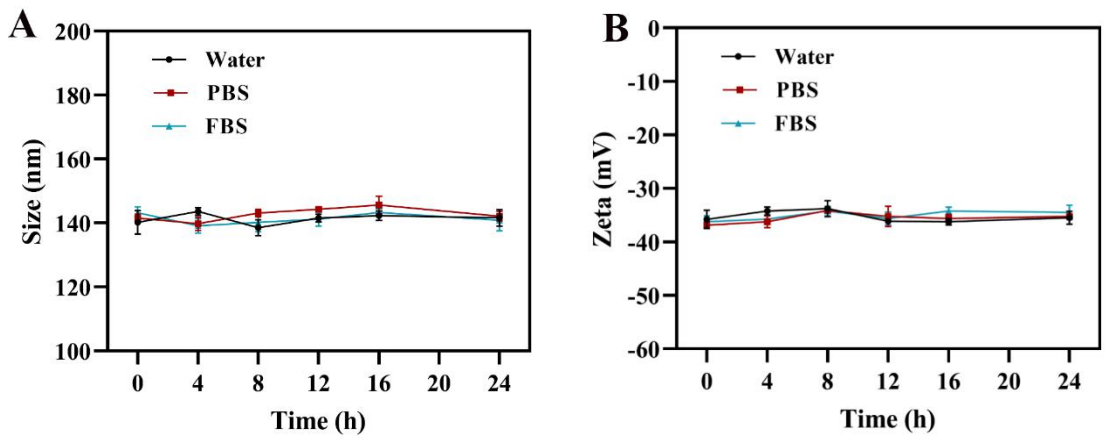

Fig. S2. Stability study on size (A) and zeta potential (B) of LD NDs in water, PBS and FBS over 24 hours.

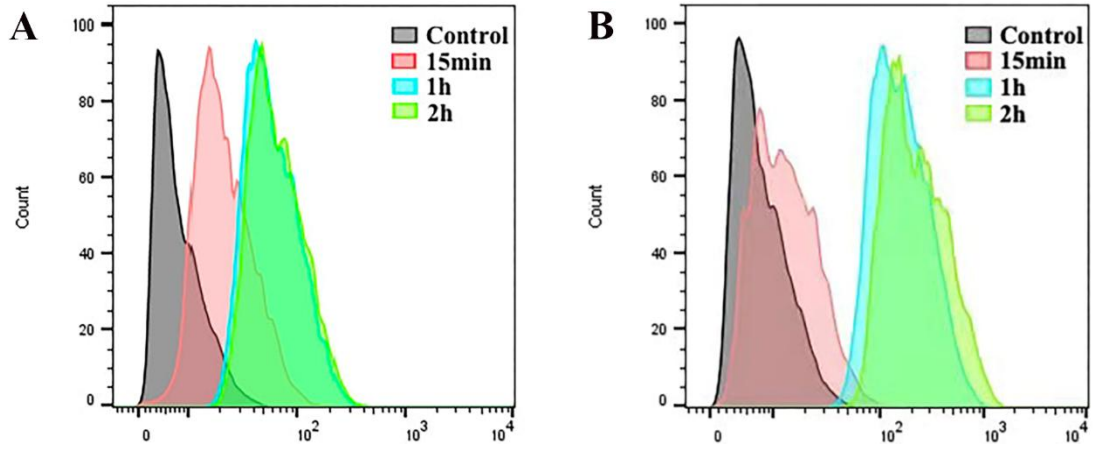

Fig. S3 Flow cytometry analysis for free DOX (A) and LD NDs (B) on 4T1 cells after 15min, 1 h and 2 h incubation.

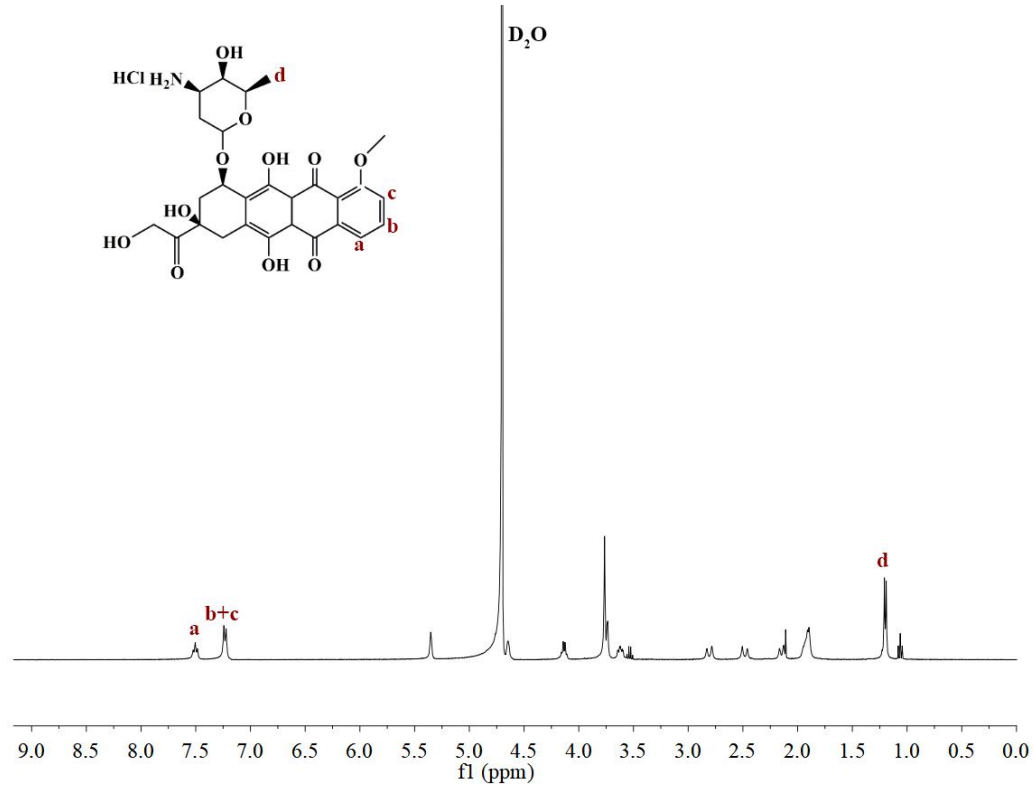

Fig. S4 [1]H NMR spectra of DOX.

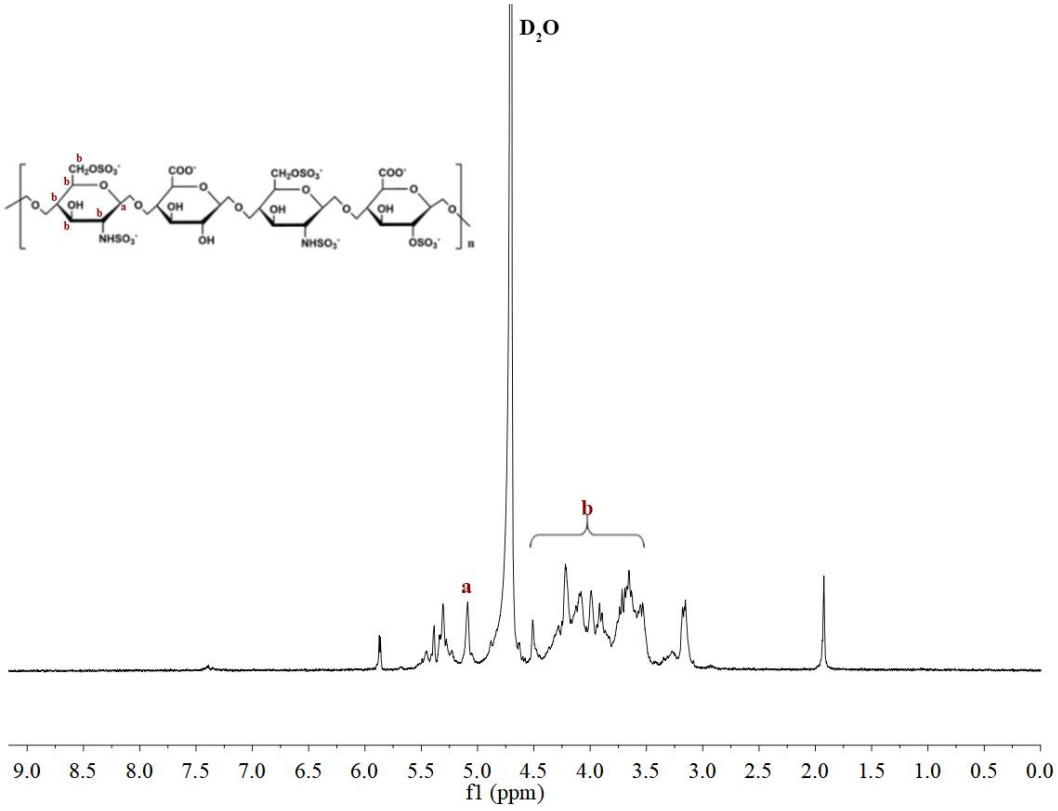

Fig. S5 [1]H NMR spectra of LMWH. (a) LMWH backbone C1 proton; (b) LMWH backbone C2-C6 proton.

Table S1. Combination indexes of DOX with LMWH on 4T1 cells

DOX (μg/ml)	LMWH (μg/ml)	CI [a]
0.57	4.178	0.581
5.7	41.78	0.748
14.14	103.6	0.600

[a] CI means the Combination index and is calculated by CalcuSyn software based on Chou-Talalay method.