Supporting information

Intracellular Self-disassemble Polysaccharide Nanosssembly for Multi-factors Tumor Drug Resistance Modulation of Doxorubicin

Hui Xiong[a], Jiang Ni[a,b], Zhijie Jiang[a], Fengchun Tian[a], Jianping Zhou[a], Jing Yao[a,*]

[a]State Key Laboratory of Natural Medicines and Jiangsu Key Laboratory of Druggability of Biopharmaceuticals, Department of Pharmaceutics, China Pharmaceutical University, 24 Tongjiaxiang, Nanjing 210009, China
[b]Department of Pharmacy, Wuxi Third People's Hospital，Number 585, Xingyuan North Road, Wuxi, Chin
[*]Corresponding to : Jing Yao (E-mail: yaojing@cpu.edu.cn).

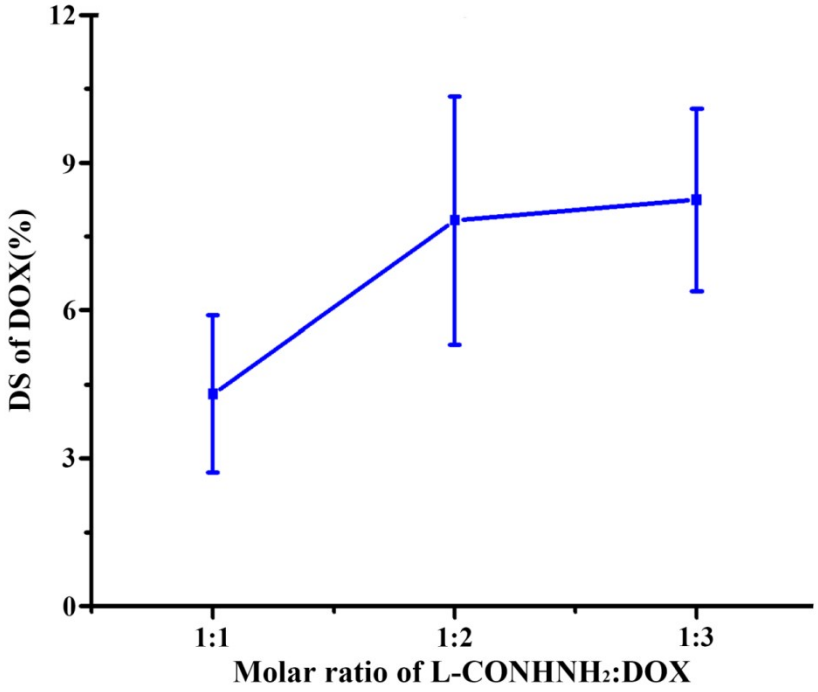

Fig. S1 The degree of substitution (DS) of DOX in L-DOX with diverse molar ratio of L-CONHNH2：DOX in DMSO / PBS (pH6.5) (v:v, 1:1) (n=3).

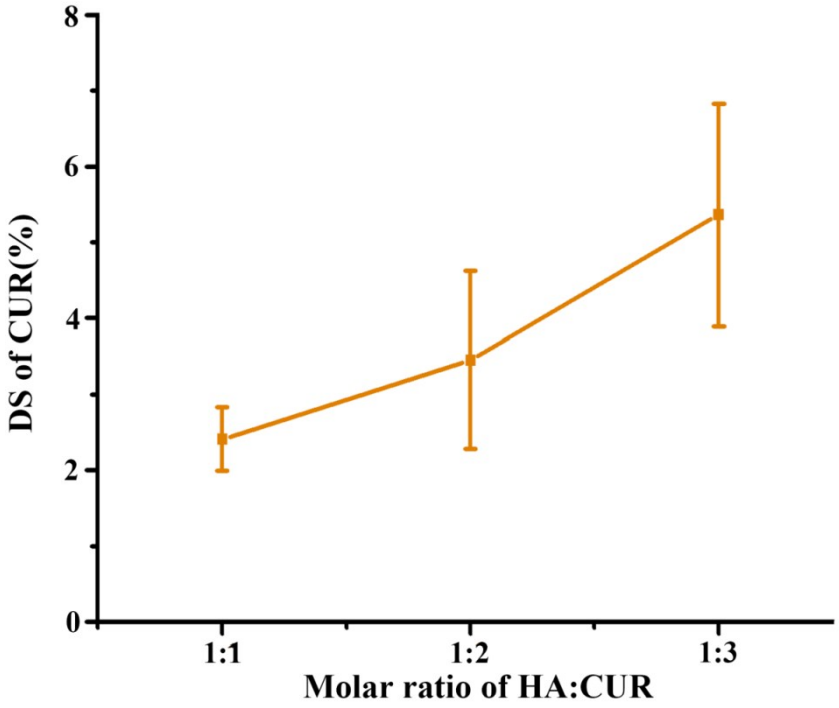

Fig. S2 The degree of substitution (DS) of CUR in HA-CUR with some kinds of molar ratio of HA:CUR in formamide (n=3).

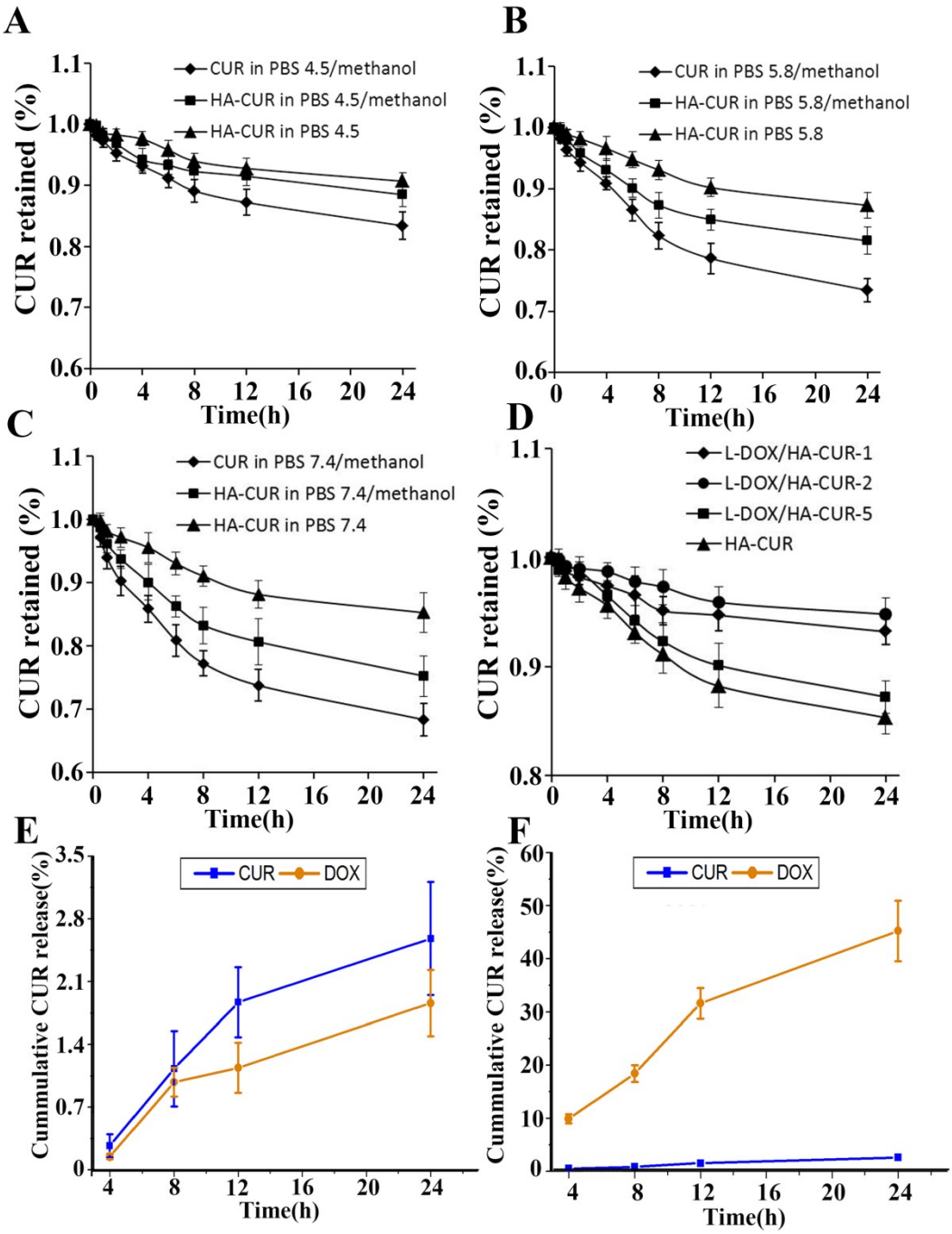

Fig. S3 Stability of CUR and HA-CUR in buffer solutions with diverse pH, such as 4.5(A), 5.8(B), 7.4(C) for 24h (n=3). Stability of HA-CUR and different LH in pH 7.4 PBS (D) for 24h (n=3). CUR and DOX release behavior in plasma(E) and tumor tissue homogenate（F）.

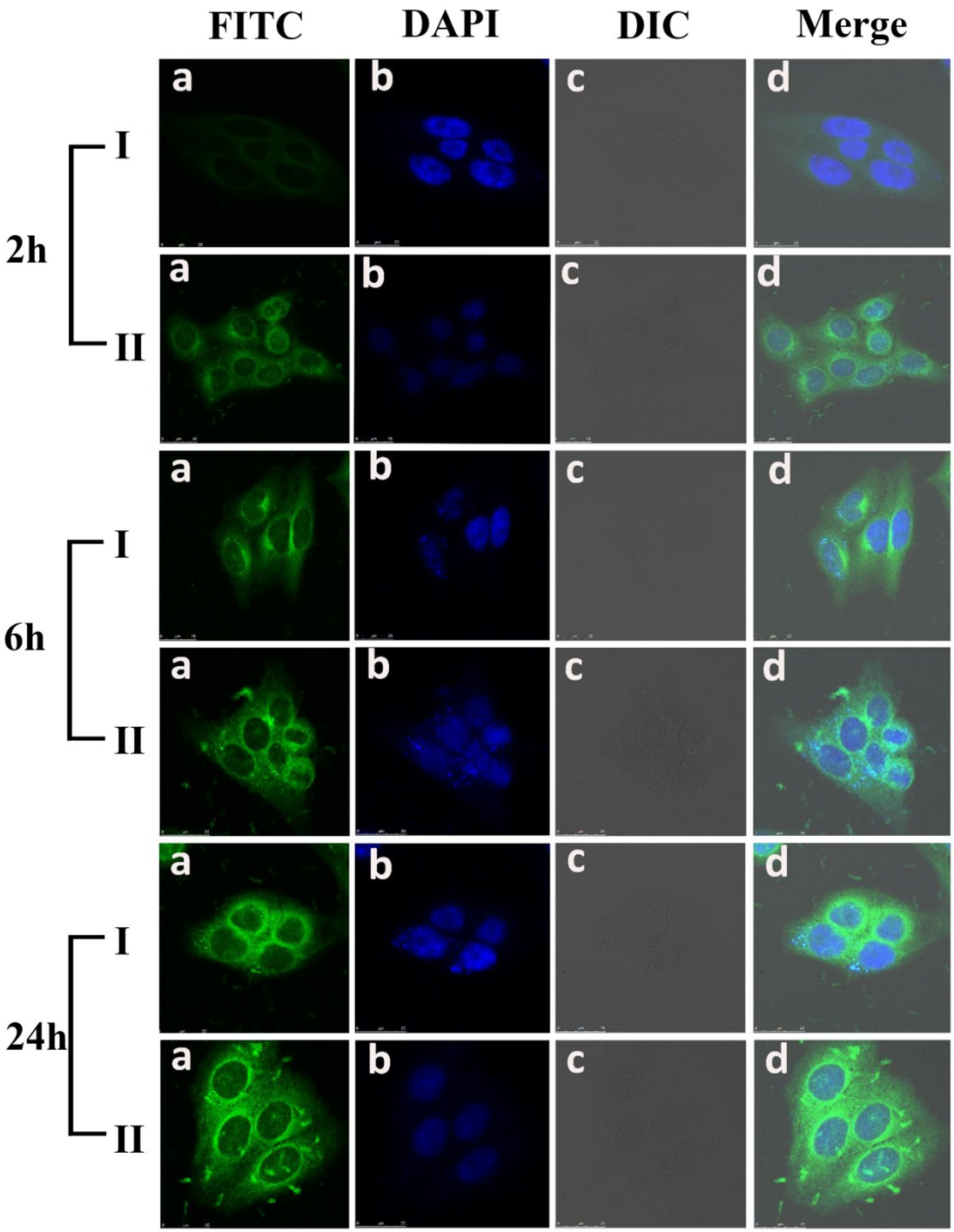

Fig. S4 Intracellular delivery of nanodrug in HepG2 cells at different time observed by CLSM. Cells were incubated with free coumarin-6 (I), coumarin-6 loaded HA-CUR (II). Nuclei stained by DAPI (Blue) while coumarin-6 showed green fluorescence. For each panel, 1: Coumarin-6 (green); 2: Nuclei stained by DAPI (Blue); 3: cells under light field; Merged: overlay of 1, 2 and 3.

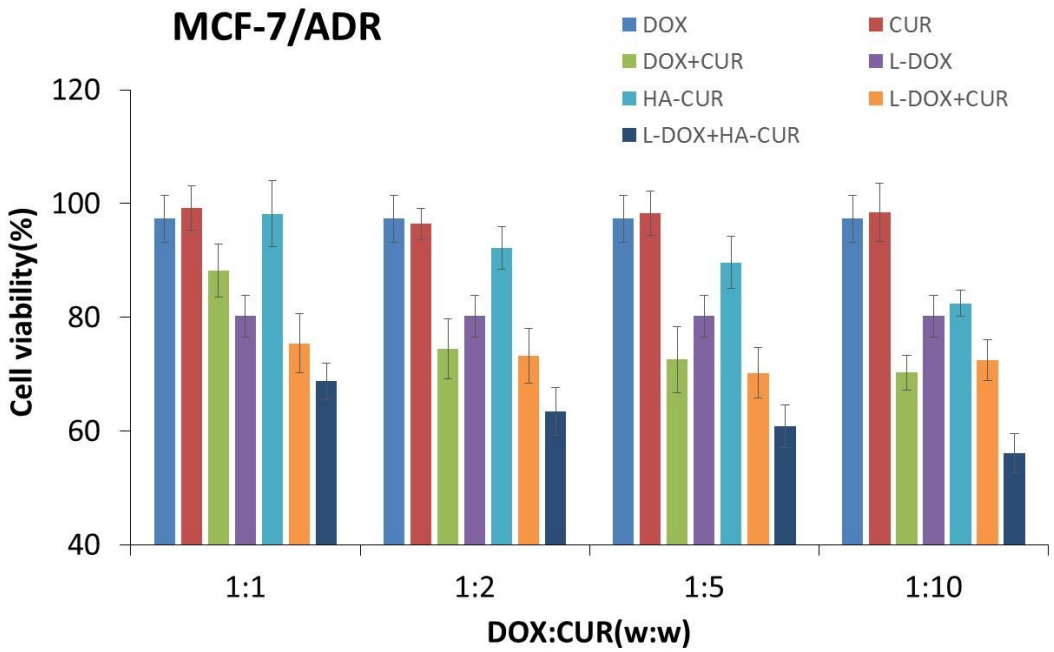

Fig. S5 Viability of MCF-7/ADR cells after incubation of DOX, CUR, DOX+CUR, L-DOX, HA-CUR, L-DOX +CUR, LH for 72 h, the raitos of DOX and CUR were 1:1; 1:2; 1:5; 1:10, the concentration of free DOX is 0.5 μg/mL. The values are represented as mean ± S.D. (n = 5).

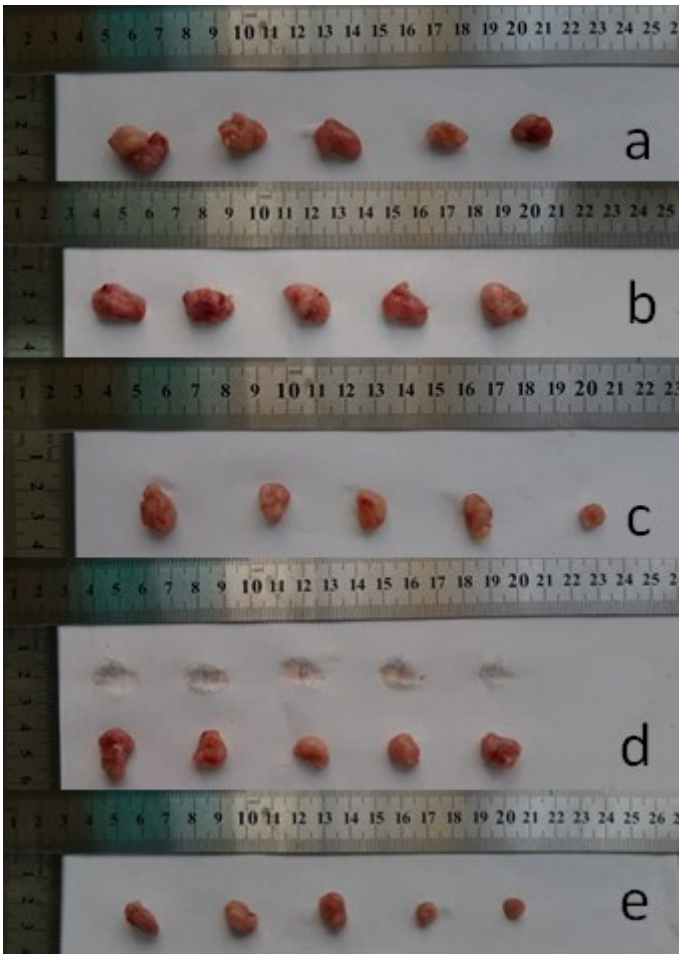

Fig. S6 Tumor images excised from enthanized MCF-7 tumor bearing nude mice treated with saline (a), HA-CUR(b), DOX(c) ,L-DOX (d) and L-DOX/HA-CUR (e).

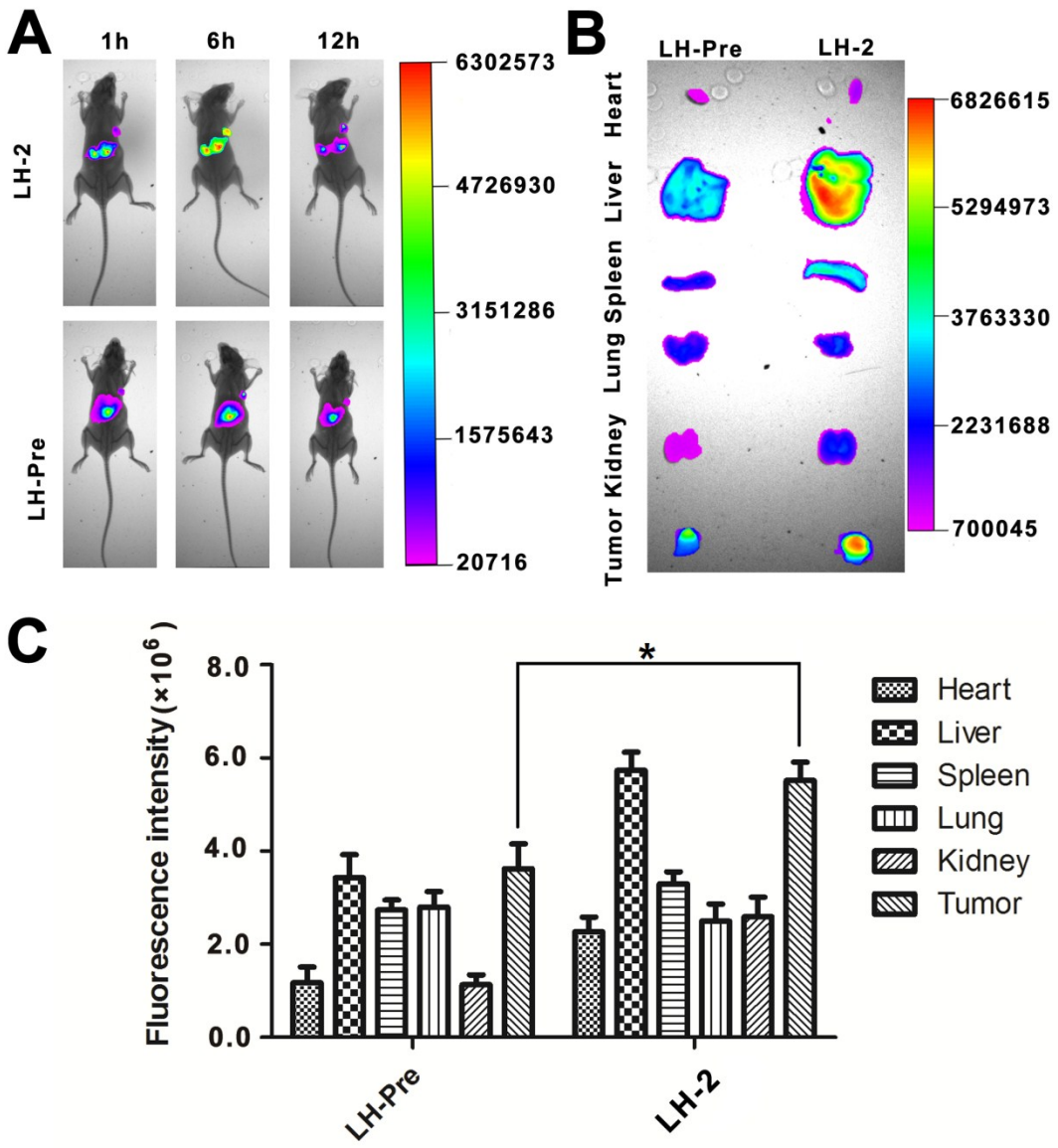

Fig.S7 Tumor targetability of LH nanoparticles. (A) *In vivo* fluorescence imaging of the MCF7/ADR tumor-bearing mice at 1,6 and 12 h after intravenous injection of DiR/LH-2 nanoparticles and DiR/LH-2 nanoparticles with pre-injection of free HA. Arrows indicate the sites of tumors. (B) *Ex vivo* fluorescence imaging of the tumor and normal tissues harvested from the euthanized MCF7/ADR tumor-bearing mice at 12 h post injection. (C) Region-of-interest analysis of fluorescent signals from the tumors and normal tissues. Error bars indicated s.d. (n = 3). $^{*}P < 0.05$.