Figure S1. Molecular structure of PLGA-PEG-PLGA copolymer. a, the CH_2 of PEG; b, the CH_2 of GA; c, the CH of D,L-LA; d, the CH_3 of D,L-LA; e, the CH_2 of PEG near the PLGA.

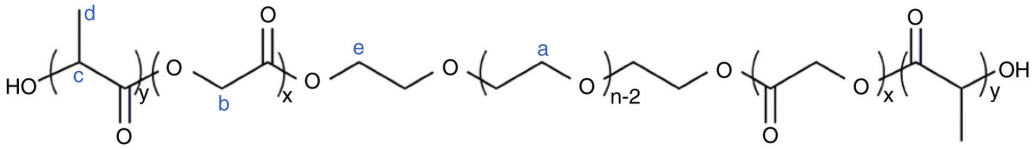

Figure S2. Proton nuclear magnetic resonance spectrum of PLGA-PEG-PLGA copolymer in CD_3Cl. a, CH_2 of PEG; b, CH_2 of GA; c, CH of D,L-LA; d, CH_3 of D,L-LA; e, CH_2 of ester bond.

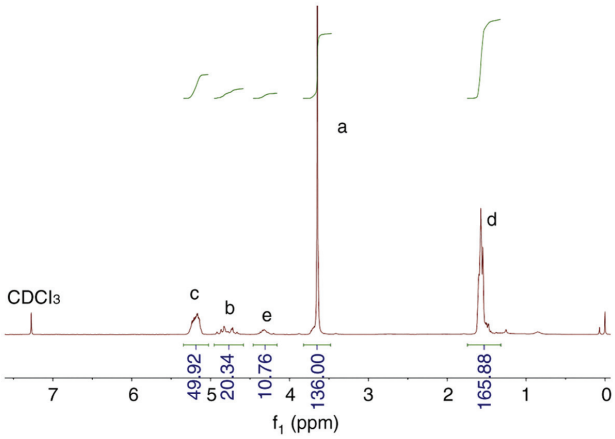

Figure S3. Scanning electron microscopy image of CD-CUR inclusion complex, native CUR and β-CD. CD-CUR, β-cyclodextrin curcumin.

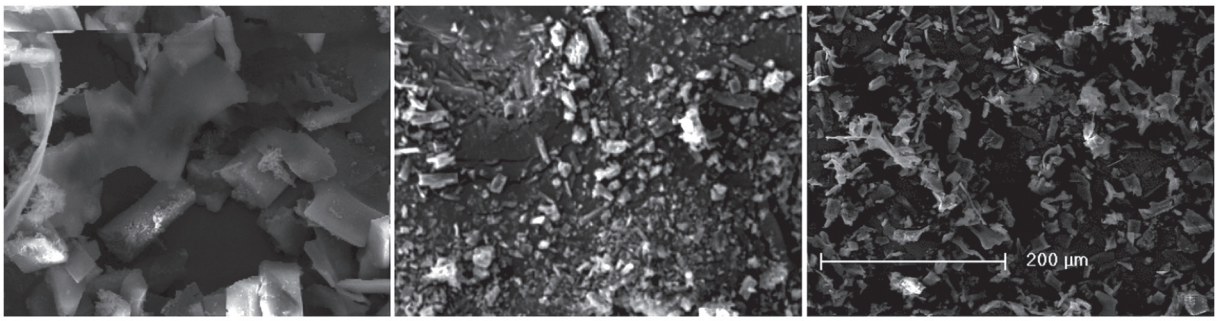

Figure S4. Stability of CD-CUR and native CUR in neutral medium (PBS pH 7.4). CD-CUR, β-cyclodextrin curcumin.

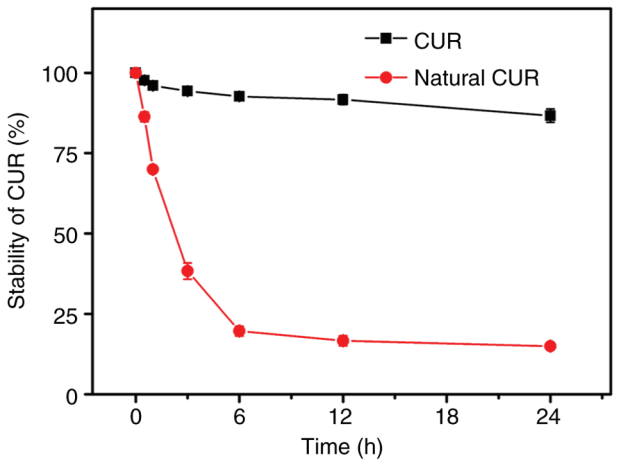

Figure S5. *In vitro* antitumor efficiencies of different strategies in (A) K-7 and (B) Saos-2 cells at 48 h. The CD-CUR inclusion complex was dissolved in PBS, and native CUR was dispersed in PBS and DMSO. The final concentration of DMSO was 0.5% (v/v). *P<0.05; **P<0 .01; n=3. CD-CUR, β-cyclodextrin curcumin.

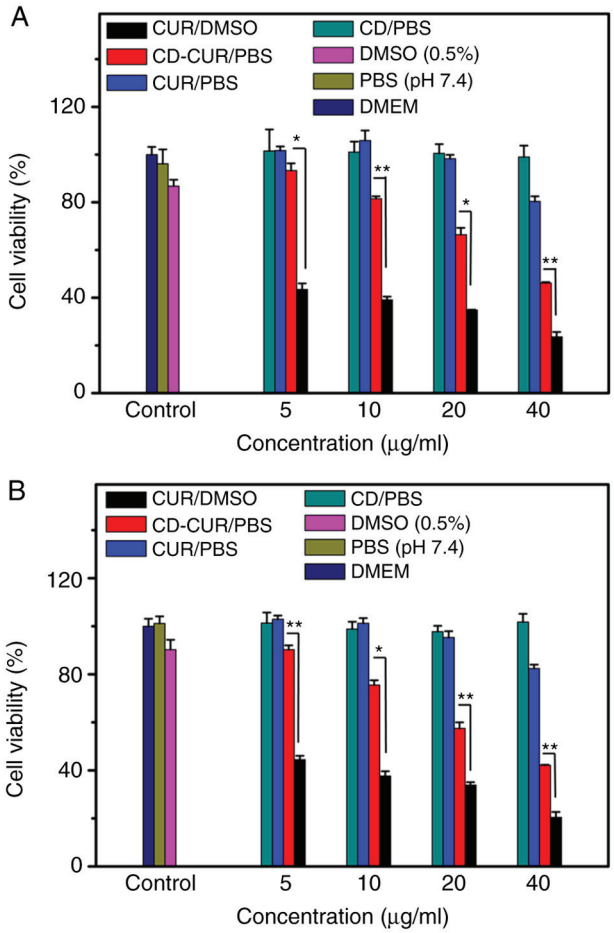

Figure S6. Phase transition diagrams and storage moduli of different drug-loaded hydrogels. (A) Phase transition diagrams of DOX, CD-CUR, or DOX+CD-CUR loaded hydrogels (i.e. Gel+DOX, Gel+CUR, Gel+DOX+CD-CUR). (B) Phase transition diagrams of CD, CUR loaded hydrogels or free Gel (i.e. Gel+CD, Gel+CUR, Gel). (C) Storage moduli of different drug-loaded hydrogels, including Gel, Gel+CD, Gel+CUR, Gel+DOX, Gel+CUR, Gel+DOX+CD-CUR. The concentration of hydrogel selected for rheology analysis was 20% wt. CD-CUR, β-cyclodextrin curcumin; DOX, doxorubicin.

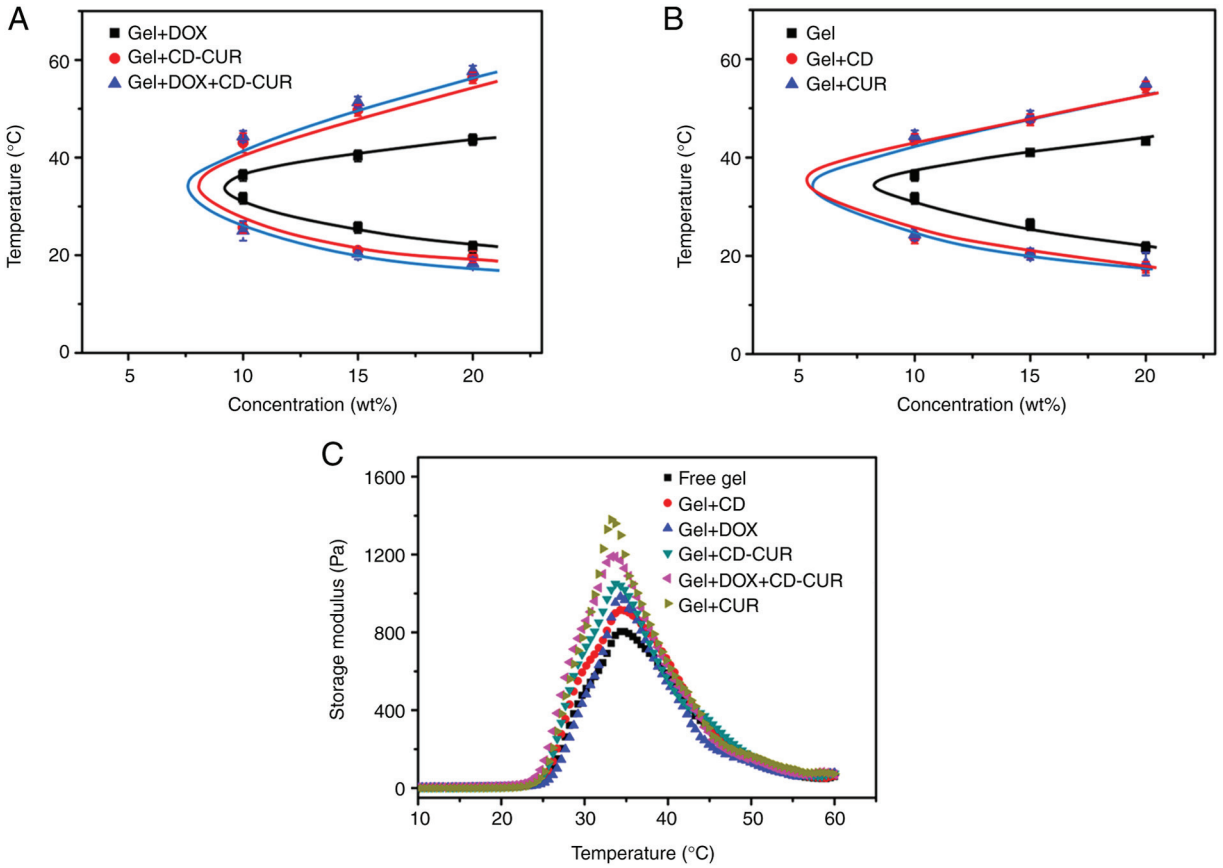

Figure S7. Histological analysis of major organs in different treated groups, including PBS, free gel, CD-CUR loaded gel, free DOX, DOX loaded gel, free DOX+CD-CUR and DOX+CD-CUR co-loaded gel. Magnification, x100. NC, negative control.

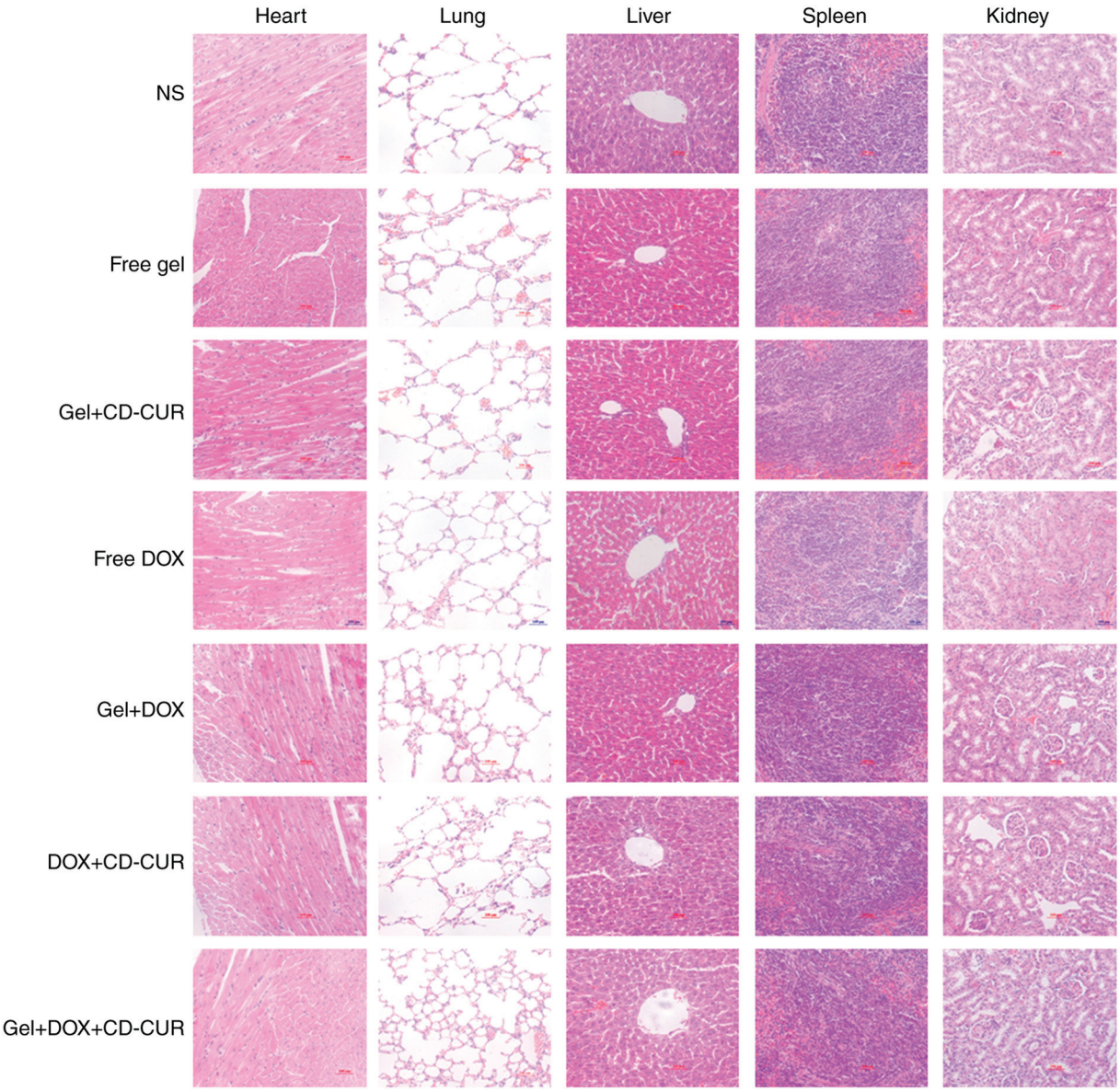

Table SI. IC_{50} of different strategies in K-7 and Saos-2 cells.

Strategies	IC_{50} (μg/ml) in K-7 cells	IC_{50} (μg/ml) in saos-2 cells
Free DOX	0.35±0.12	0.39±0.06
Gel+DOX	0.59±0.25	0.47±0.13
Free DOX+CD-CUR	0.24±0.06	0.29±0.02
Gel+DOX+CD-CUR	0.34±0.14	0.40±0.07

Data presented as the mean ± SD. The concentration of DOX in all strategies was equal, and the concentration of CUR was equivalent in both combination therapies. CD-CUR, β-cyclodextrin curcumin; DOX, doxorubicin.