Electronic Supplementary Material (ESI) for Nanoscale.
This journal is © The Royal Society of Chemistry 2015

Supplementary Materials

Co-delivery of doxorubicin and arsenite with reduction and pH dual-sensitive vesicle for synergistic cancer therapy

Lu Zhang,[a†] Hong Xiao,[a†] Jingguo Li,[a] Du Cheng,[*a] Xintao Shuai[*a,b]

[a] PCFM Lab of Ministry of Education School of Chemistry and Chemical Engineering, Sun Yat-sen University, Guangzhou 510275, China

[b] Center of Biomedical Engineering, Zhongshan School of Medicine, Sun Yat-Sen University, Guangzhou 510080, China

†These authors contributed equally to this work.

* Correspondence should be addressed to:

Xintao Shuai

The 135th of Xingang West Road, Guangzhou 510080, China

Tel.: +86-20-84110365

Fax: +86-20-84112245;

E-mail: shuaixt@mail.sysu.edu.cn

Du Cheng

The 135th of Xingang West Road, Guangzhou 510080, China

Tel.: +86-20-84112105

Fax: +86-20-84112245;

E-mail: chengdu@mail.sysu.edu.cn

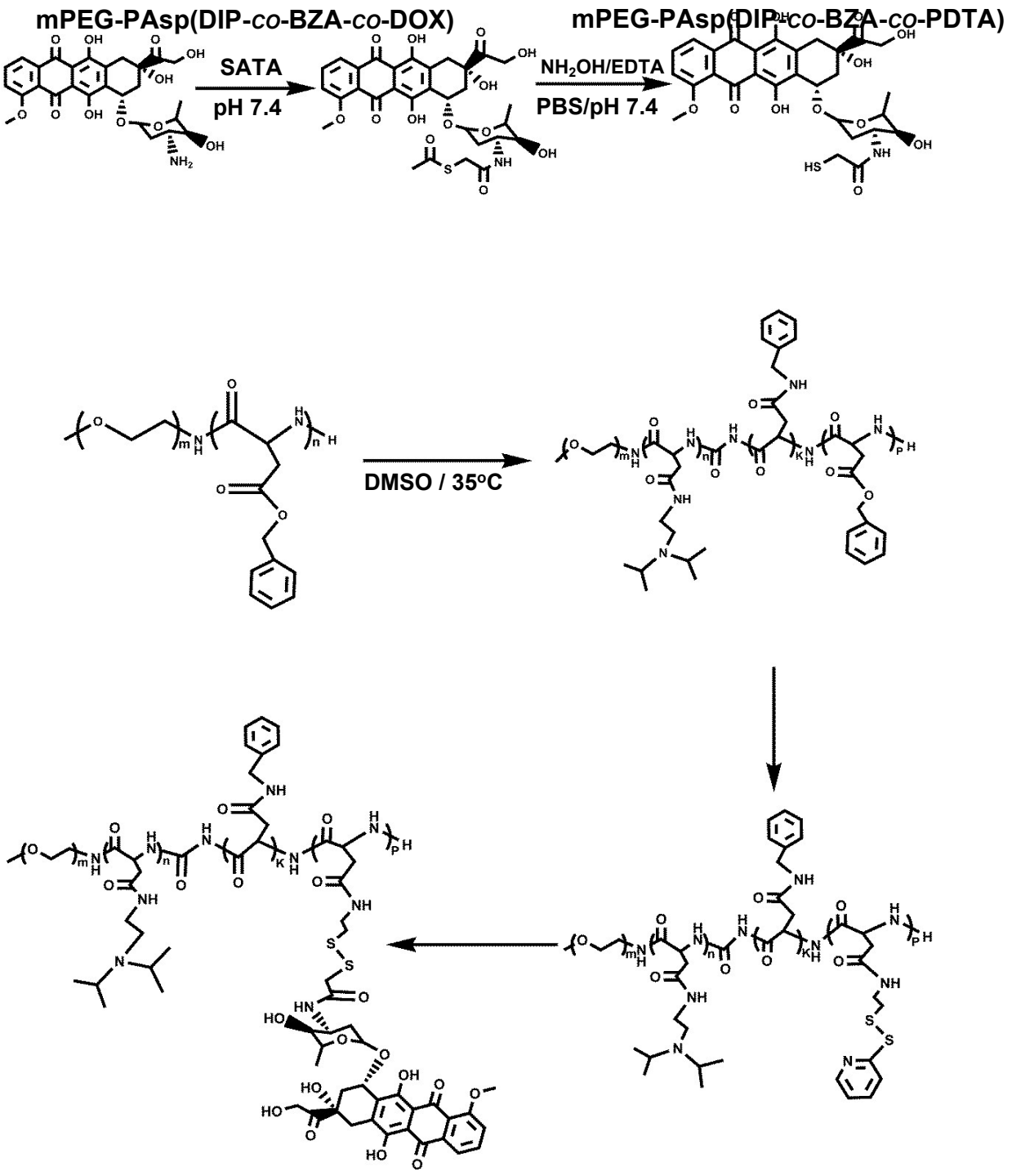

Fig. S1. Synthetic approach for the reduction and pH dual-sensitive diblock copolymer mPEG-PAsp(DIP-*co*-BZA-*co*-DOX).

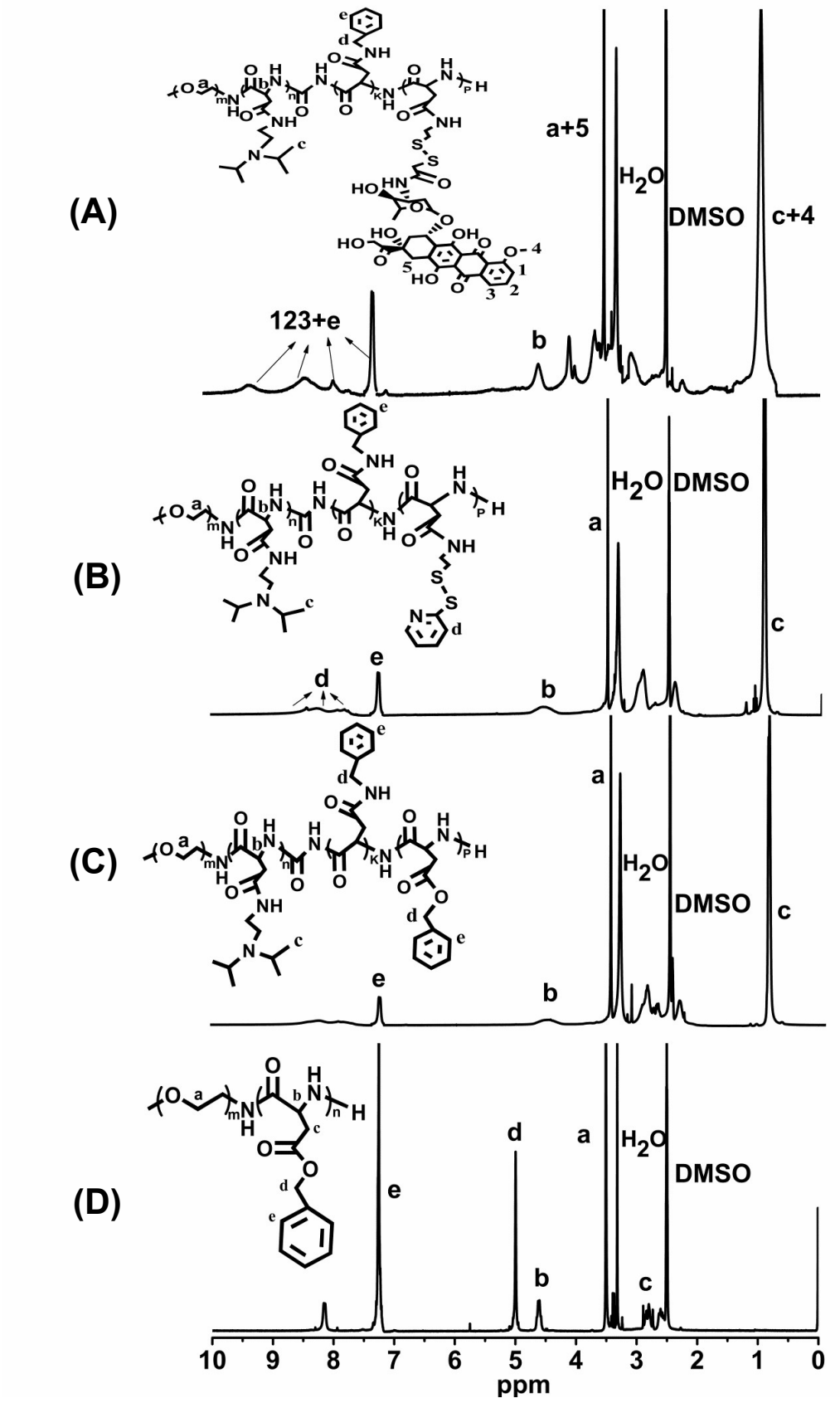

Fig. S2. ^{1}H NMR spectra of mPEG-PAsp(DIP-*co*-BZA-*co*-DOX) (A), mPEG-PAsp(DIP-*co*-BZA-*co*-PDTA) (B), mPEG-PAsp(DIP-*co*-BZA) (C) and mPEG-PBLA

(D) in DMSO-d_6. As shown in Fig. S2C, the DP of the PAsp(DIP) was calculated to be 45 by calculating the peak intensity ratio of the terminal CH_3 group of diisopropyl (DIP) group at 0.95 ppm and the CH_2 group of PEG at 3.62 ppm. After excess MEA reacted with mPEG-PAsp(DIP-*co*-BZA), the all signals of the C_6H_5 at 7.25 ppm were from the C_6H_5 group of PAsp(BZA). Compared the peak intensity ratio of the C_6H_5 at 7.25 ppm with the CH_2 group of PEG at 3.62 ppm, the DP of the PAsp(BZA) was calculated to be 5 (Fig. S2B). In Fig. S2A, the integral values at 0.9-1.1 ppm enlarged compared with that of the terminal CH_3 group of diisopropyl (DIP), so the number of conjugated DOX was 8 by calculating integral ratio.

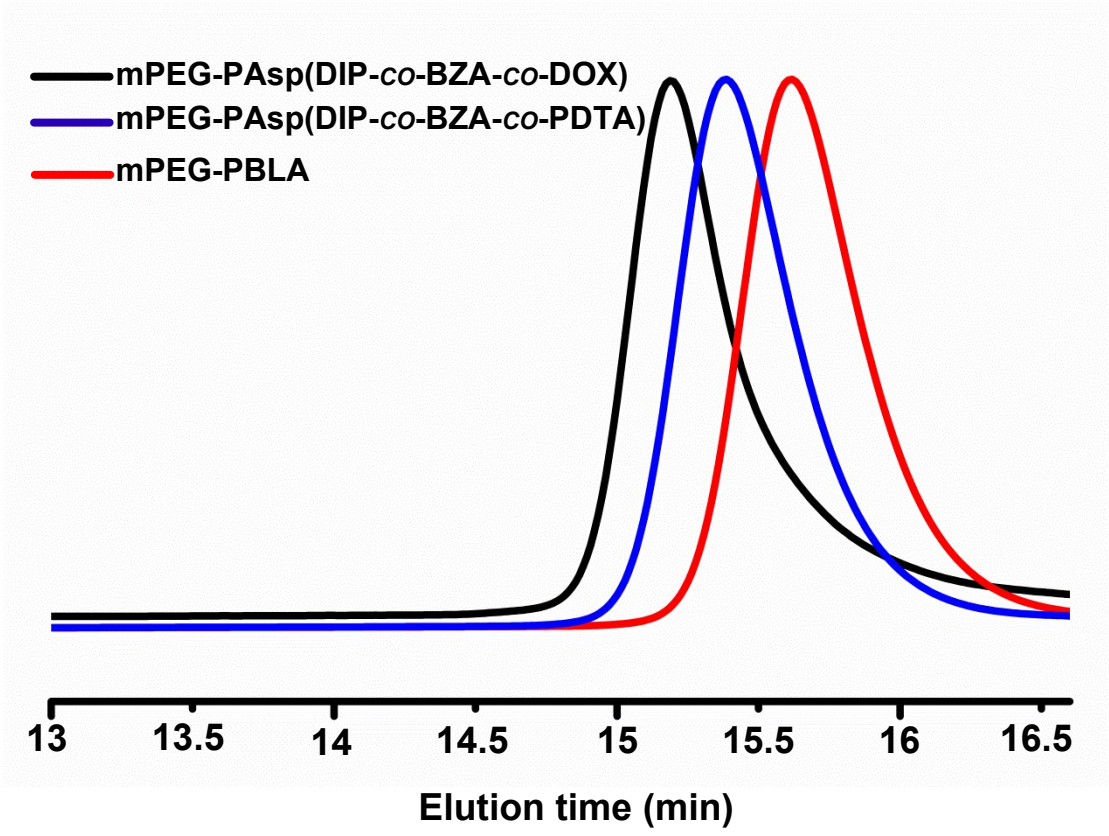

Fig. S3. GPC traces of mPEG-PBLA, mPEG-PAsp(DIP-*co*-BZA-*co*-PDTA) and mPEG-PAsp(DIP-*co*-BZA-*co*-DOX) with DMF as an eluent.

Table S1 Characteristics of the synthesized block copolymers

Sample name	M_n [a] (Da)	M_n [b] (Da)	M_w/M_n [b]
mPEG-PBLA	14300	15110	1.04
mPEG-PAsp(DIP-*co*-BZA-*co*-PDTA)	16670	17900	1.07
mPEG-PAsp(DIP-*co*-BZA-*co*-DOX)	20180	23000	1.08

[a)] Calculated based on ^{1}H NMR spectra, [b)] determined by GPC analyses.

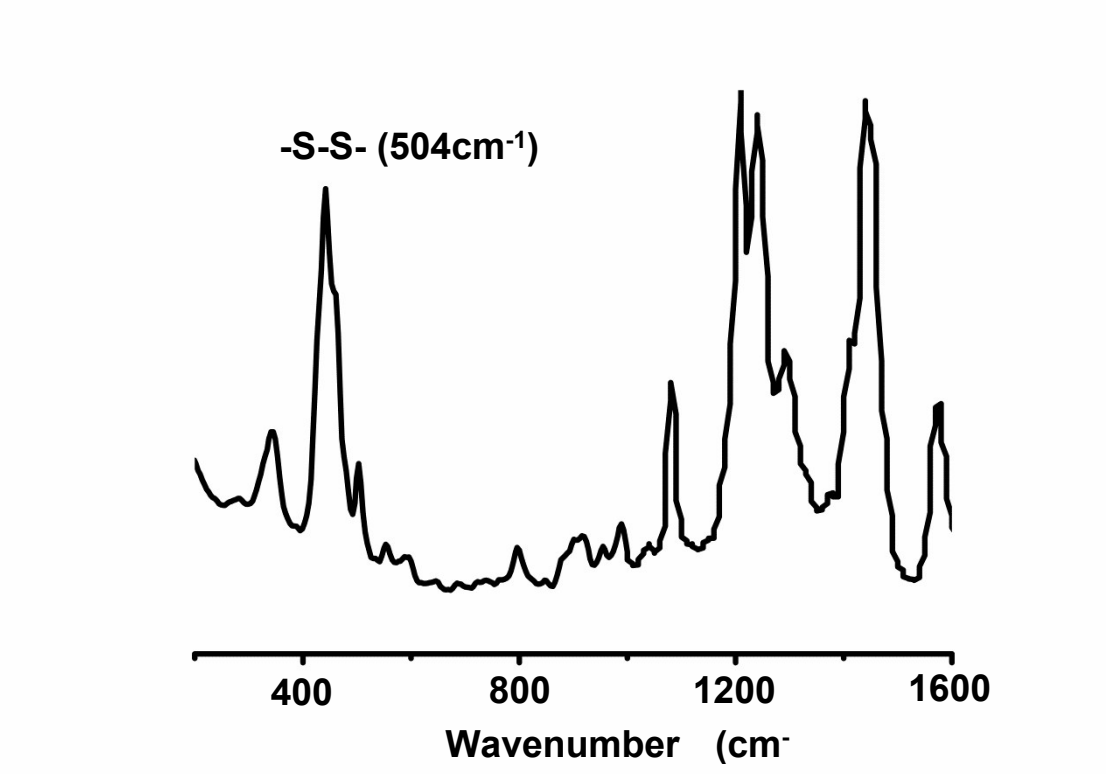

Fig. S4. Raman spectrum of mPEG-PAsp(DIP-*co*-BZA-*co*-DOX).

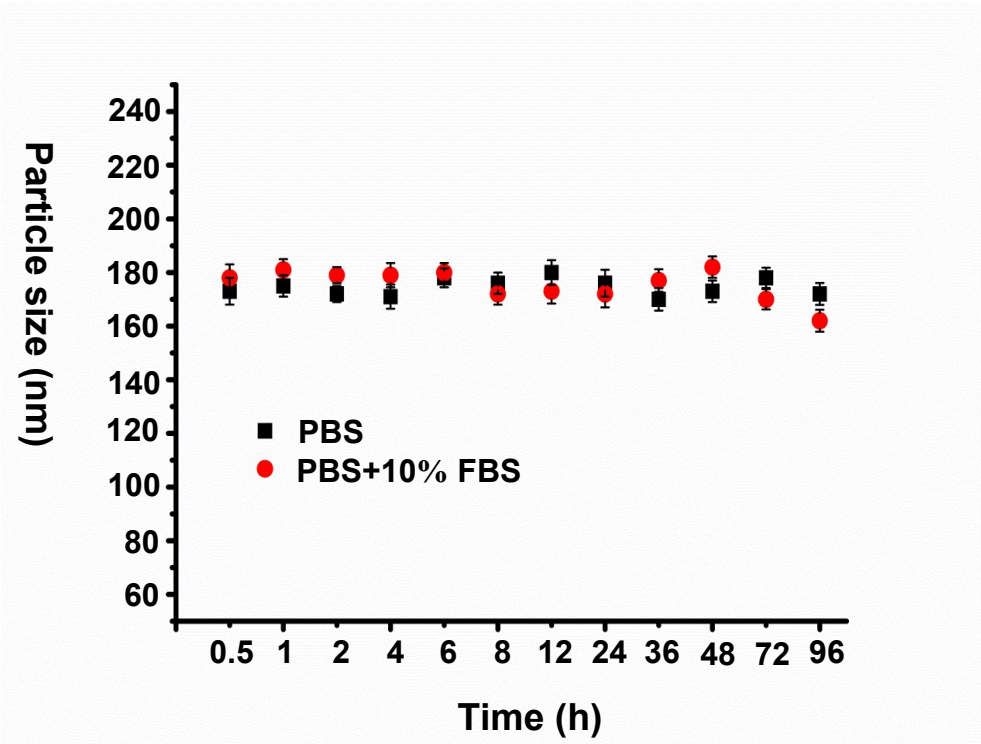

Fig. S5. Serum stability of D-As-PDBD vesicle in the PBS solution with/without 10% FBS. Incubation temperature: 37 °C; Data are mean ± SD (n = 3).

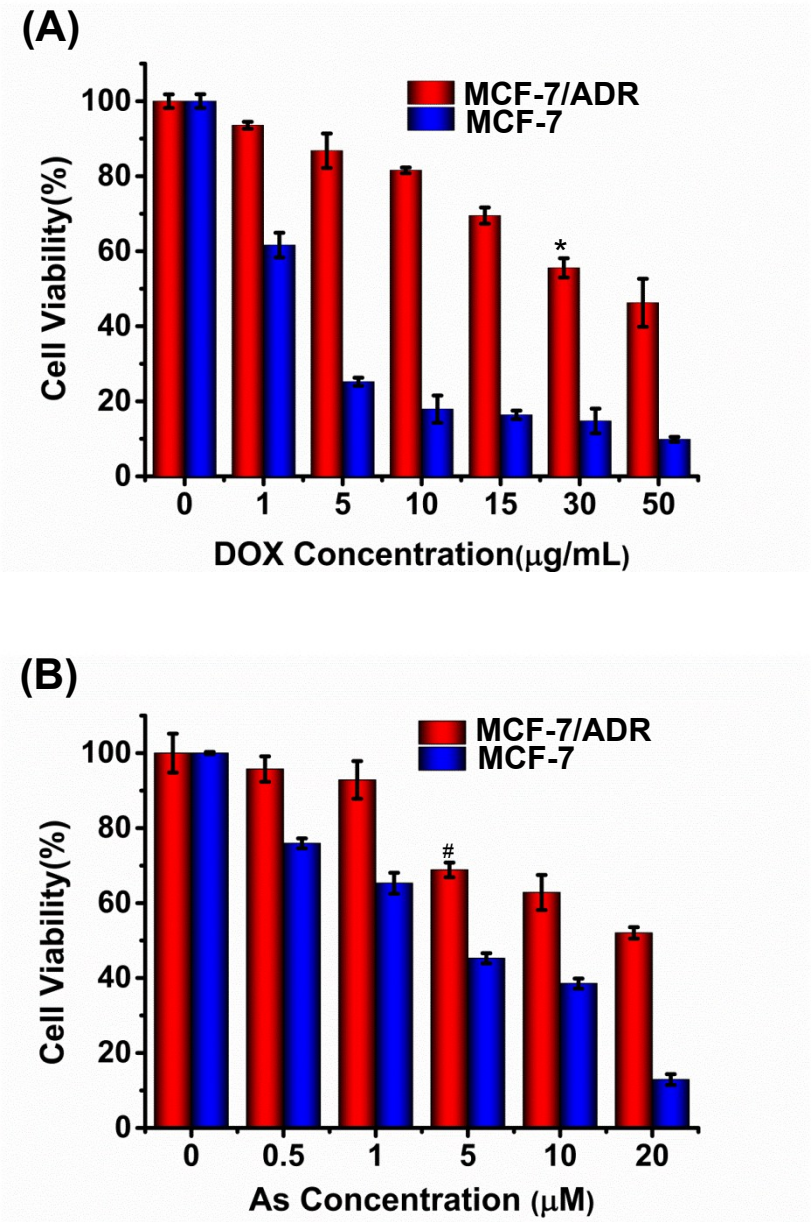

Fig. S6. Cytotoxicities of free DOX (A) and free As (B) in the MCF-7/ADR cells and MCF-7 cells. Cell viabilities were detected by MTT assay (mean ± SE; n =3). $^{*}P < 0.05$ *vs* treatment group without DOX; $^{\#}P < 0.05$ *vs* treatment group without As.

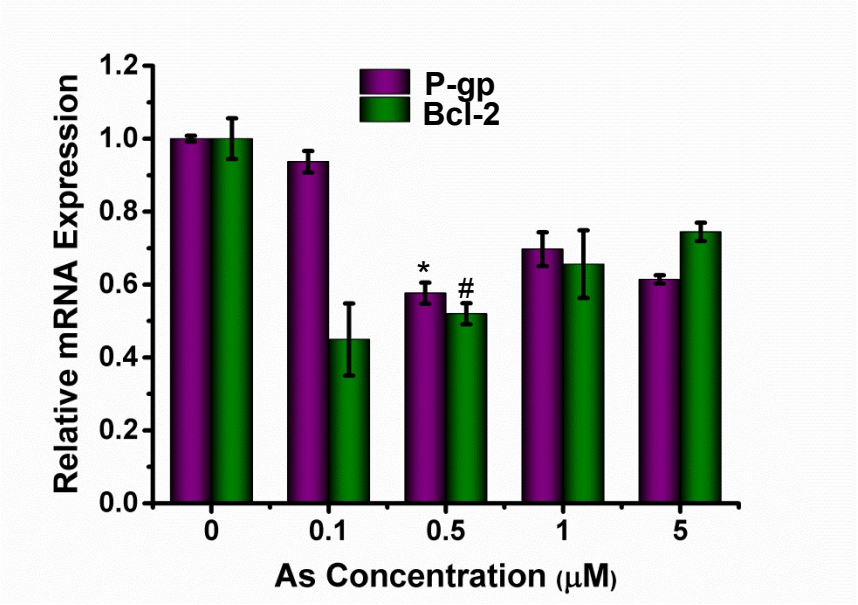

Fig. S7. The suppression of P-gp and Bcl-2 gene with different concentrations of free As in MCF-7/ADR cells at mRNA level evaluated by quantitative RT-PCR. (Mean ± SE; n =3). $^{*}P < 0.05$ *vs* treatment group without As; $^{\#}P < 0.05$ *vs* treatment group without As.

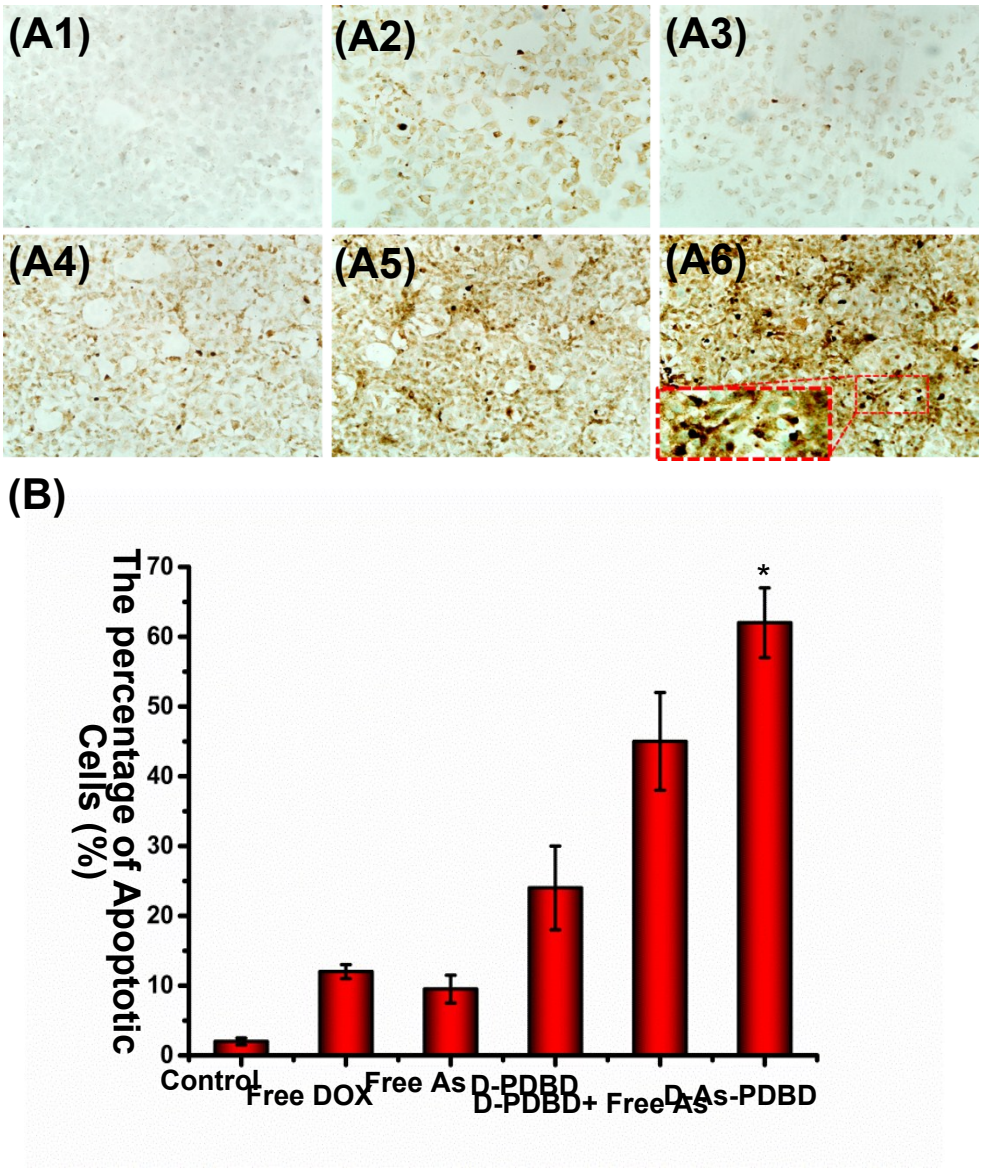

Fig. S8. The apoptosis of MCF-7/ADR cells was evaluated by TUNEL assay. MCF-7/ADR cells were incubated with PBS (A1), free DOX (A2), free As (A3), D-PDBD (A4), D-PDBD + free As (A5) and D-As-PDBD) (A6), respectively. DOX concentrations if applied: 10 μg/mL; As concentrations if applied: 0.5 μM; Scale bars: 50 μm. The nuclei of apoptotic cells were stained brown. The statistical apoptosis rate was shown in (B). $^{*}P < 0.05$ *vs* D-PDBP + Free As treatment group.