Supporting Information

A self-assembled albumin based multiple drug delivery nanosystem to overcome multidrug resistance

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Study on the interaction between BSA and drugs by fluorescence spectroscopy

After the co-incubation of the drug (DOX or VER) with BSA, drug molecules bind to BSA act as quenchers. The quenching reaction between the drug (quencher, Q) and BSA (protein, B) is shown as follows:

$$nQ + B \rightleftharpoons Q_nB \quad (1)$$

where n is the number of drug molecules bound to the residue with intrinsic fluorescence in BSA. Q_nB is the non fluorescent fluorophore–quencher complex.

The association constant, K_A, can be calculated as:

$$K_A = [Q_nB]/([Q]^n[B]) \quad (2)$$

$$[Q_nB] = [B_0] - [B] \quad (3)$$

where $[B_0]$ is total protein concentration.

$$K_A = ([B_0]-[B])/[Q]^n[B] \quad (4)$$

$$[B]/[B_0] = F/F_0 \quad (5)$$

where F_0 is initial fluorescence intensity and F is fluorescence intensity in the presence of the quenching agent.

From Equations 4 and 5, we can obtain

$$\log[(F_0 - F)/F] = \log K_A + n \log[Q] \quad (6)$$

By plotting $\log[(F_0 - F)/F]$ vs $\log[Q]$, n can be determined. For both DOX and VER, n values are approximately equal to 1.

***In vitro* cytotoxicity of verapamil**

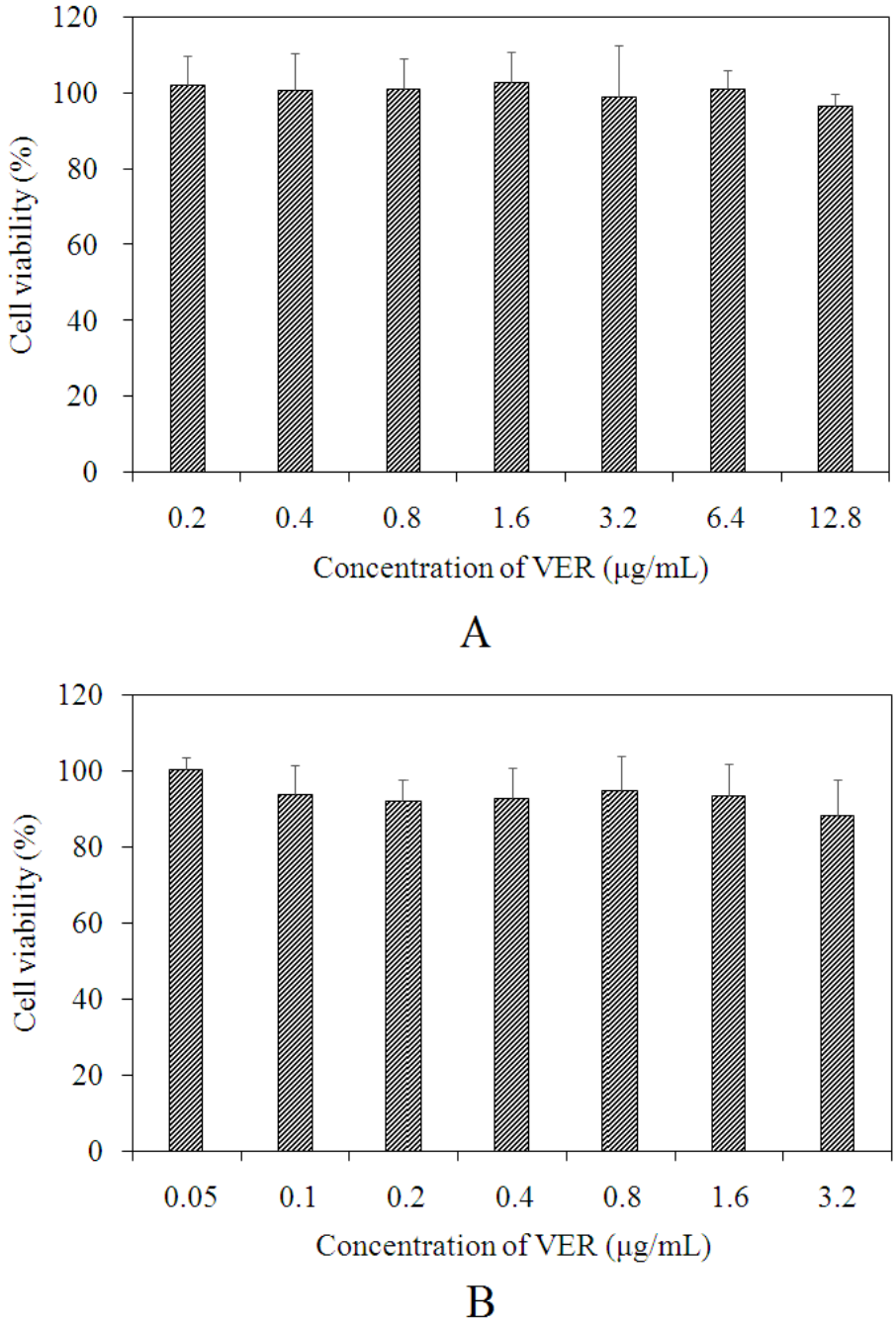

Figure S1. Cell viability of HCT-15 cells (A) and 293T cells (B) after being treated by free verapamil (VER) for 48 h.

Study on cellular internalization by fluorecent microscopy

1 mL of HCT-15 cells were seeded at a density of 1×10^5 cells/mL in a glass-bottomed dish and incubated at 37 °C for 24 h to form a confluent monolayer. Then the culture medium was changed with 1 mL of fresh medium containing a particular agent containing 3.2 μg of DOX (free DOX, DOX/BSA nanoparticles and DOX/VER/BSA nanoparticles, respectively) and incubated at 37 °C for 2 h. Then the cells were washed with PBS three times and the cell nuclei were stained with Hoechst 33342 solution for 20 min. Subsequently, the cells were washed with PBS three times and then incubated with 1 mL of PBS. The cells were visualized on a fluorecent microscope.

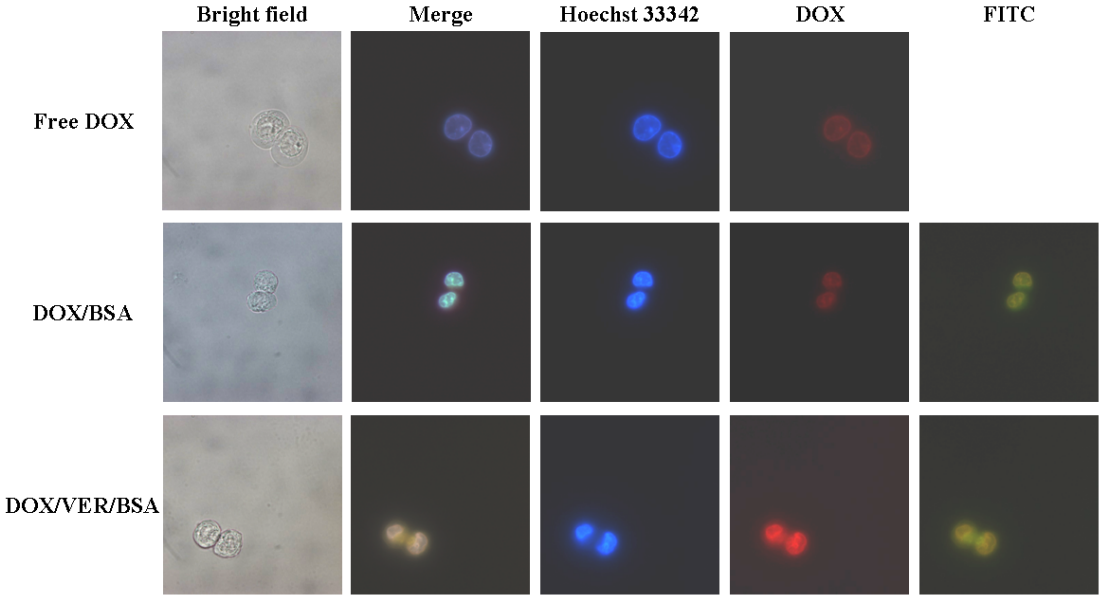

Figure S2. Fluorecent microscopy images of HCT-15 cells after being treated by free DOX, DOX/BSA nanoparticles and DOX/VER/BSA nanoparticles for 2 h. The cell nuclei were stained with Hoechst 33342. BSA was labeled by FITC. The cells were treated by a particular agent with a DOX concentration of 3.2 μg/mL.