Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.

Supporting Information

Photo-triggered Release of Doxorubicin from Liposomes Formulated by Amphiphilic Phthalocyanines for Combination Therapy to Enhance Antitumor Efficacy

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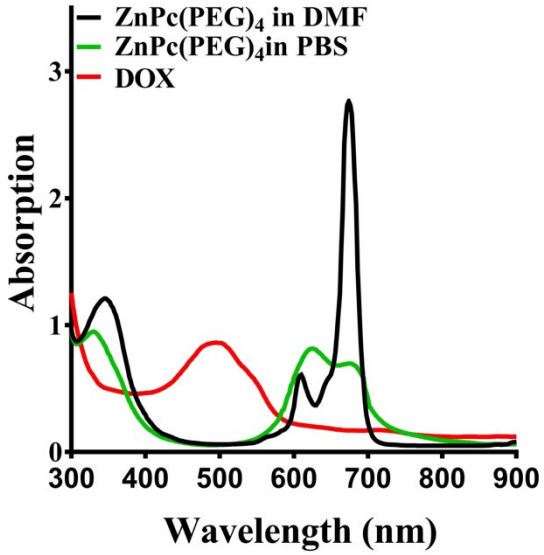

Figure S1. Ultraviolet-visible spectra of DOX and ZnPc(PEG)$_4$ in PBS or DMF.

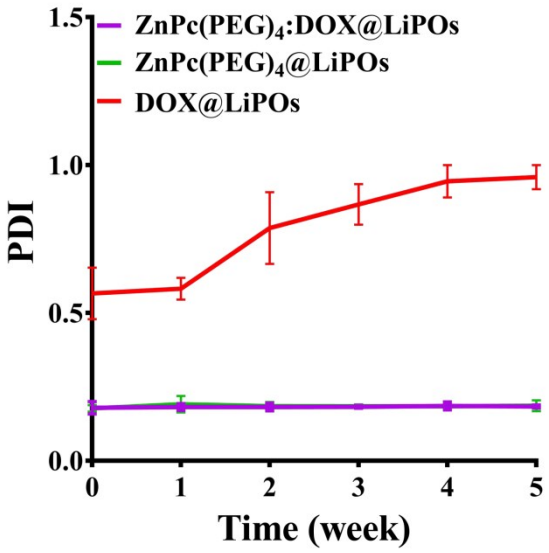

Figure S2. The PDI variation curve of DOX@LiPOs, ZnPc(PEG)$_4$@LiPOs and ZnPc(PEG)$_4$:DOX@LiPOs in PBS during five weeks.

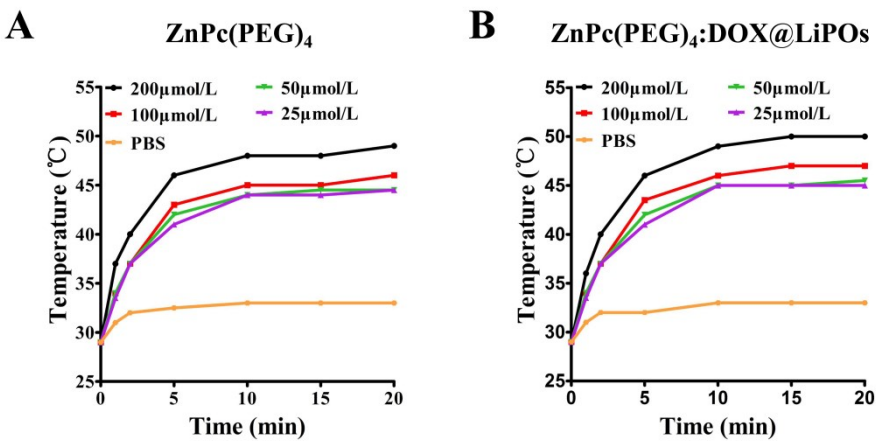

Figure S3. The temperature variation curve of $ZnPc(PEG)_4$ (A) and $ZnPc(PEG)_4$:DOX@LiPOs (B) with different concentrations (25μM, 50μM, 100μM, 200μM) in PBS solutions of 200μl under the laser (680 nm) irradiation of 100mW/cm^2 for 20min.

The determination of singlet oxygen quantum yield and photothermal conversion efficiency for ZnPc(PEG)$_4$:DOX@LiPOs

Singlet oxygen quantum yield (Φ_Δ) of ZnPc(PEG)$_4$:DOX@LiPOs was determined using 1,3-diphenylisobenzofuran as chemical quencher and methylene blue as the standard. Equation (1) was used to measure the Φ_Δ.

$$\phi_\Delta = \phi_\Delta^{Std} \frac{R \cdot I_{abs}^{Std}}{R^{Std} \cdot I_{abs}} \qquad (1)$$

Φ_Δ^{std} was singlet oxygen quantum yield of methylene blue in D_2O (Φ_Δ^{std}=0.52). Where R and R^{std} was the photobleaching rate of the quencher in the presence of ZnPc(PEG)$_4$:DOX@LiPOs and methylene blue, respectively. I_{abs} and I_{abs}^{std} was the rate of light absorption by ZnPc(PEG)$_4$:DOX@LiPOs and methylene blue, respectively.

Photothermal conversion efficiency of ZnPc(PEG)$_4$:DOX@LiPOs was determined according to the following equation (2).

$$\eta = \frac{hS(T_{MAX} - T_{surr}) - Q_{dis}}{I(1-10^{-A680})} \qquad (2)$$

Where η represented the photothermal conversion efficiency, I was the laser power (100 mW/cm^2), A680 was the absorbance of ZnPc (PEG)$_4$:DOX@LiPOs at 680nm, T_{surr} was ambient temperature, and T_{MAX} was the maximum temperature of ZnPc(PEG)$_4$:DOX@LiPOs solution during the illumination, h was heat transfer coefficient, and S was the surface area of the container. The value of hS can be calculated by equation (3) and (4).

$$hS = \frac{mC_{water}}{\tau_S} \qquad (3)$$

$$t = -\tau_S \ln\theta = -\tau_S \ln\left(\frac{T - T_{surr}}{T_{MAX} - T_{surr}}\right) \qquad (4)$$

Where m was the mass of ZnPc(PEG)$_4$:DOX@LiPOs solution, C_{water} was the heat capacity of solvent (4.2 J/g•°C). τ_s was the system time constant, which was defined as the expression in equation (4). τ_s was obtained from the linear correlation of cooling time versus -lnθ (Fig. S4).

Q_{dis}, the energy consumption by the container, was measured according to equation (5) using container containing pure water under the same irradiation conditions.

$$Q_{dis} = \frac{mC_{water}(T_{MAX(water)} - T_{surr})}{\tau_{water}} \qquad (5)$$

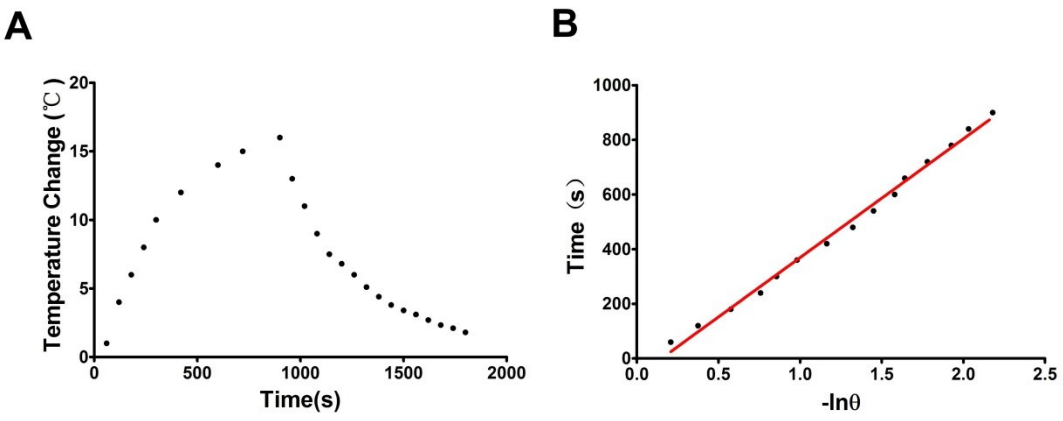

Figure S4. A. Photothermal properties of ZnPc(PEG)$_4$:DOX@LiPOs in aqueous solution with 680nm light source at 100mW/cm^2. The irradiation lasted for 900s and then was shut off. B. linear correlation of cooling time versus negative natural logarithm of driving force temperature.

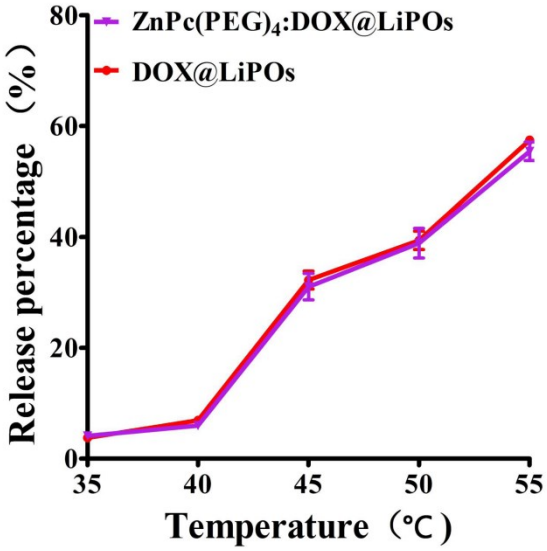

Figure S5. The release percentage of DOX from DOX@LiPOs and ZnPc(PEG)$_4$:DOX@LiPOs after heating to different temperature (35°C, 40°C, 45°C, 50°C, 55°C) for 30 minutes.

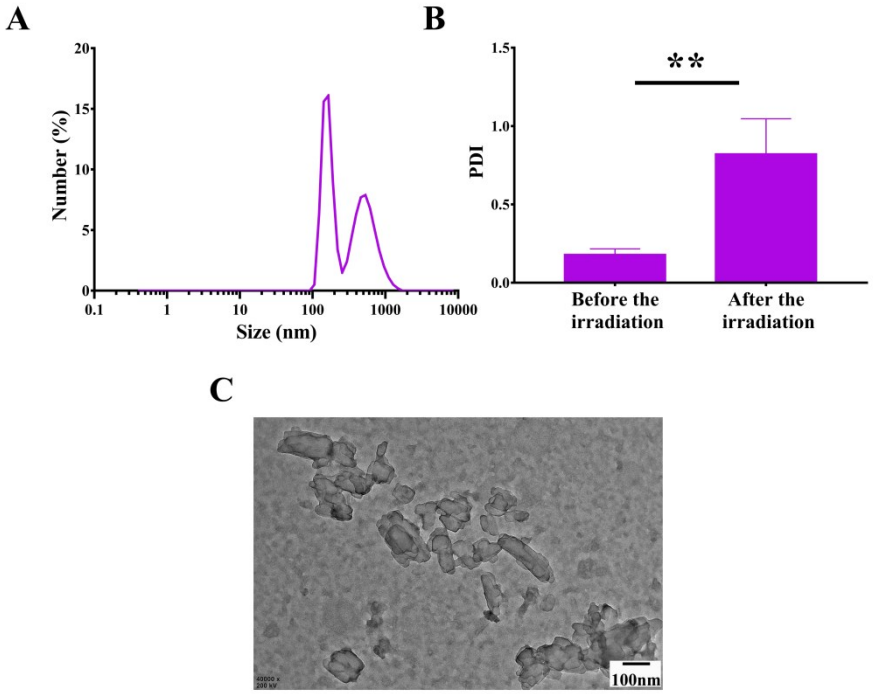

Figure S6. (A) Diameter distribution of ZnPc(PEG)$_4$:DOX@LiPOs after the irradiation (680 nm) for 20min at light dosage 100mW/cm^2. (B) There was significant difference in PDI of ZnPc(PEG)$_4$:DOX@LiPOs before and after the irradiation. (C) The morphology of ZnPc(PEG)$_4$:DOX@LiPOs observed by TEM after the illumination for 20min at light dosage 100mW/cm^2.

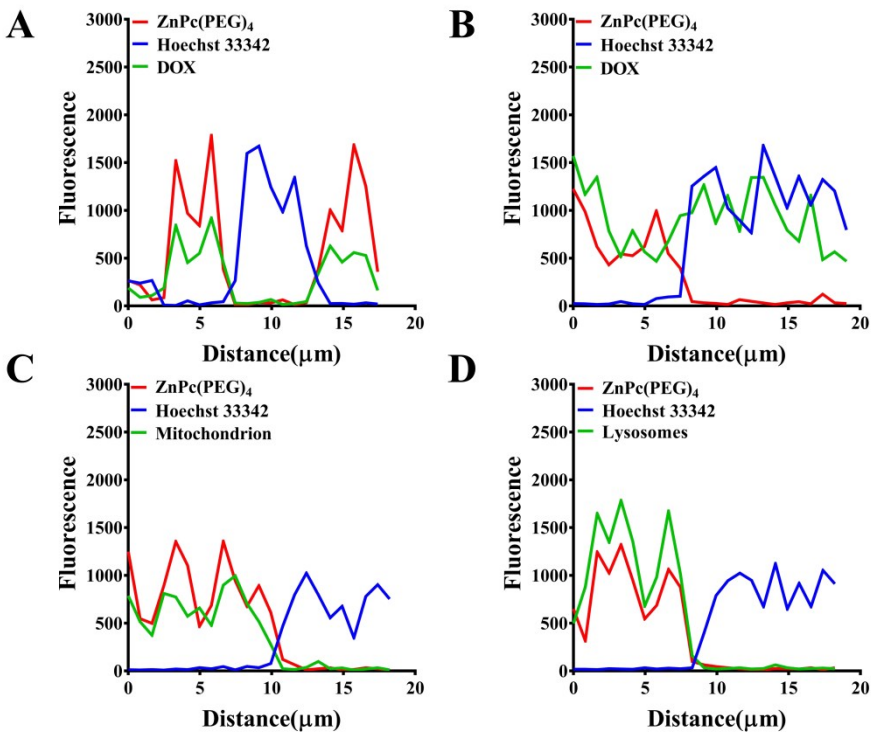

Figure S7. The fluorescence intensity profile in the subcellular localization detection of ZnPc(PEG)$_4$:DOX@LiPOs (Fig. 5). (A) The distribution of DOX was consistent with that of ZnPc(PEG)$_4$, and both of them did not enter the cell nucleus. (B) Through the illumination by LED light source (680nm), some DOX was separated from ZnPc(PEG)$_4$ and entered the nucleus. In addition, after the incubation with ZnPc(PEG)$_4$:DOX@LiPOs for 24 hours, ZnPc(PEG)$_4$ could distributed in both mitochondria (C) and lysosomes (D) of cells.

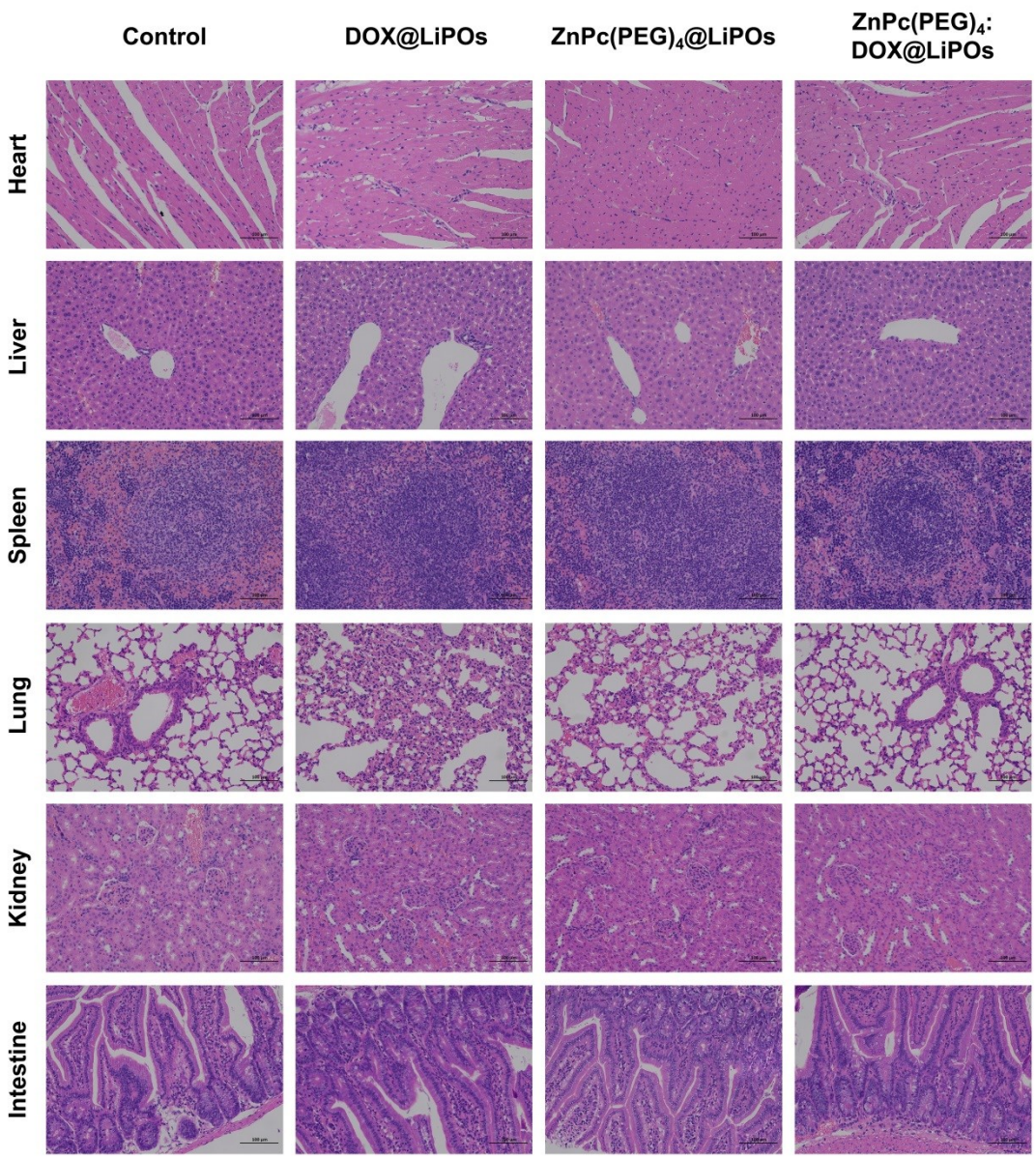

Figure S8. After the mice were injected with $ZnPc(PEG)_4$:DOX@LiPOs, $ZnPc(PEG)_4$@LiPOs or DOX@LiPOs at the equal dosage of $ZnPc(PEG)_4$ (0.2 μmol/kg) or DOX (1.04 μmol/kg), PDT was administered for seven days with a 680nm light source at a light dose of 1 W/cm^2 for 3 min daily. After then, different tissues (heart, liver, spleen, kidney, lung and intestine) were harvested for H&E staining. Representative histopathological images (H&E, 200×) showed no significant pathological changes, demonstrating the safety of these liposomes *in vivo*.