

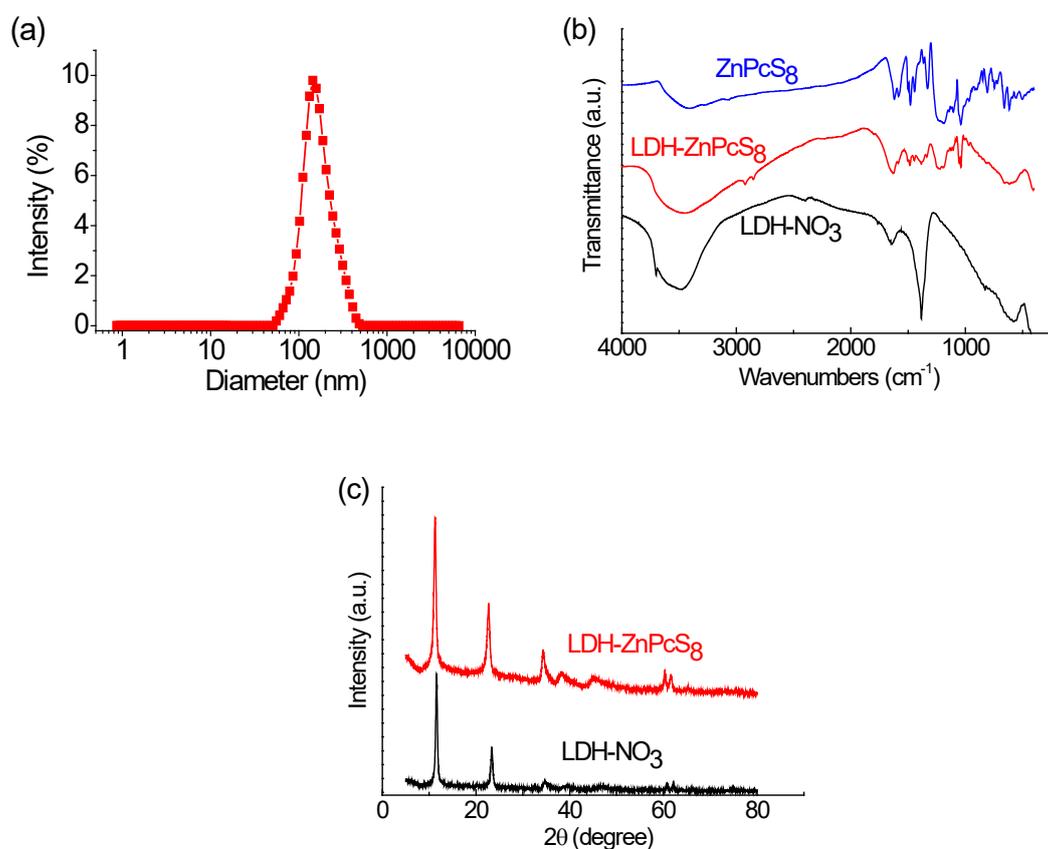
# Supporting Information

## A Tumor-pH-Responsive Supramolecular Photosensitizer for Activatable Photodynamic Therapy with Minimal *In Vivo* Skin Phototoxicity

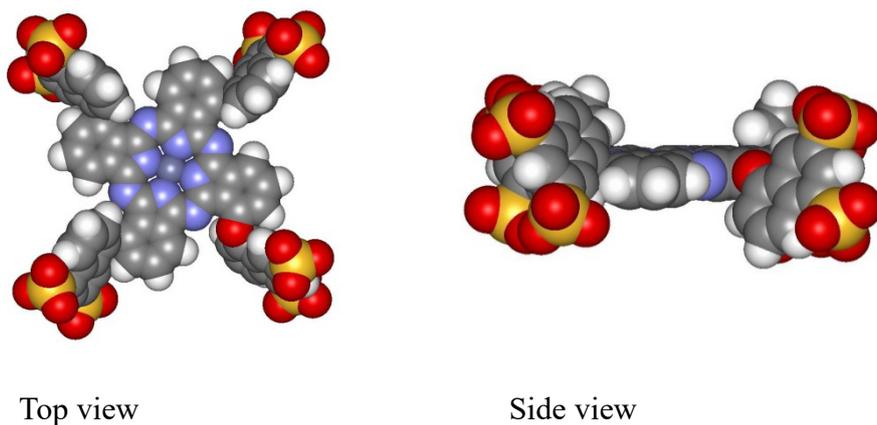
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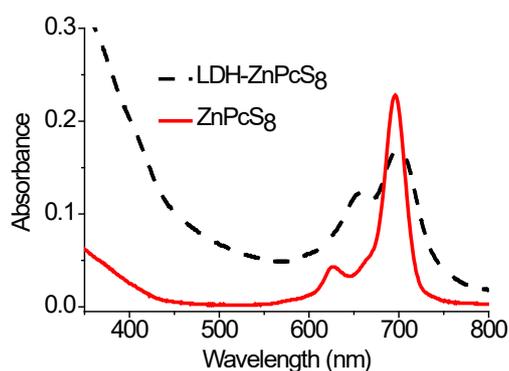
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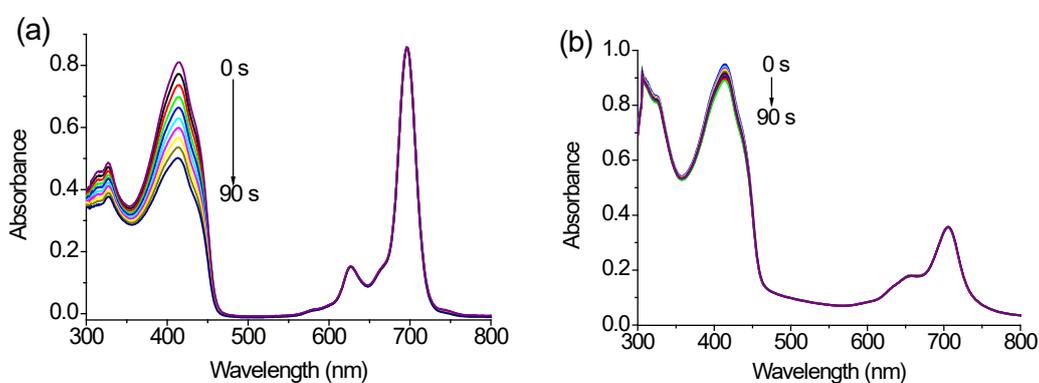
**Figure S1.** Characterization of LDH-ZnPcS<sub>8</sub>. (a) DLS of LDH-ZnPcS<sub>8</sub>. (b) FTIR spectra of ZnPcS<sub>8</sub>, LDH-ZnPcS<sub>8</sub>, and LDH-NO<sub>3</sub>. (c) XRD patterns of LDH-ZnPcS<sub>8</sub> and LDH-NO<sub>3</sub>.



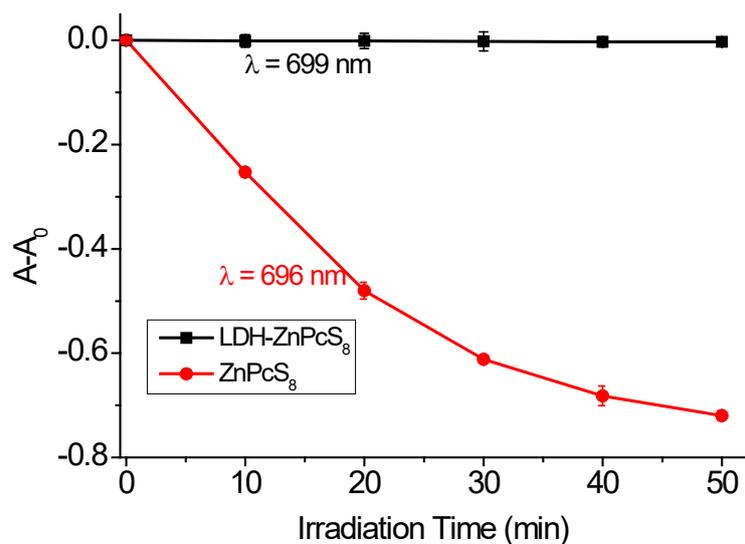
**Figure S2.** Top view and side view of ZnPcS<sub>8</sub> structure. The three-dimension of ZnPcS<sub>8</sub> was calculated to be  $2.00 \times 2.00 \times 0.85$  nm by a PM3 method.



**Figure S3.** UV-vis spectra of ZnPcS<sub>8</sub> and LDH-ZnPcS<sub>8</sub> in water (both [ZnPcS<sub>8</sub>] = 1.5 μM).

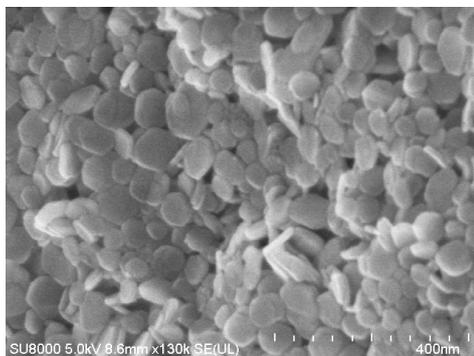


**Figure S4.** The UV-vis spectra of (a) ZnPcS<sub>8</sub> or (b) LDH-ZnPcS<sub>8</sub> (both [ZnPcS<sub>8</sub>] = 3.5 μM) in the presence of DPBF (60 μM) in water (containing 0.12% DMF and 0.06% Cremophor EL) at different irradiation time.

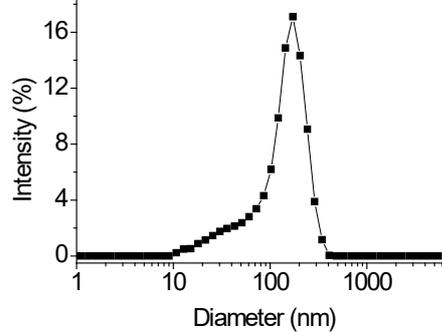


**Figure S5.** Comparison of the rates of photodegradation of ZnPcS<sub>8</sub> and LDH-ZnPcS<sub>8</sub> in water (both [ZnPcS<sub>8</sub>] = 4 μM) with irradiation time. Data are expressed as mean values ± standard deviation of three separate experiments.

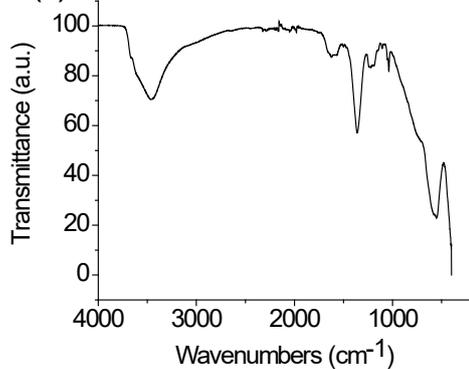
(a)



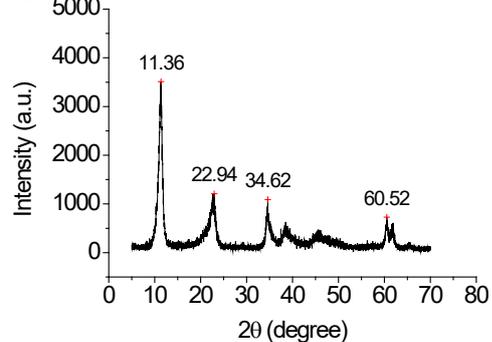
(b)



(c)

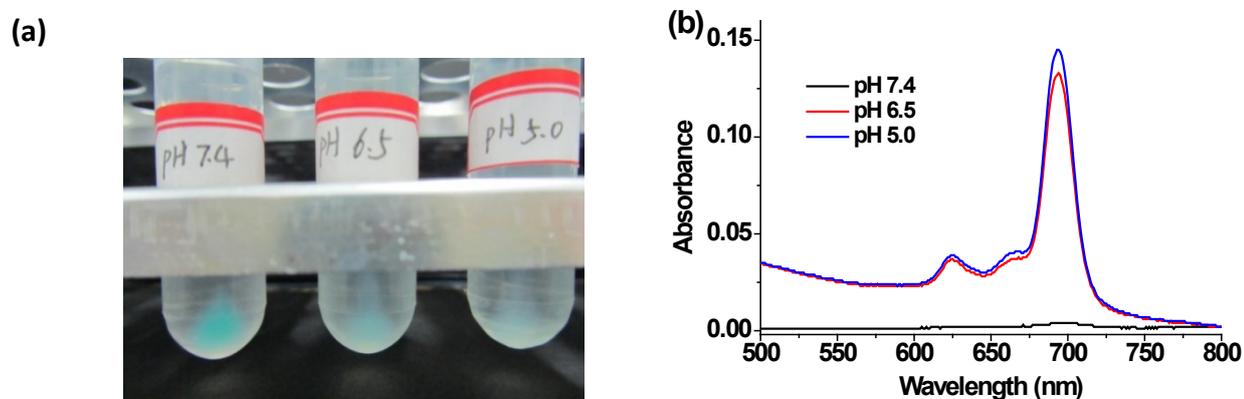


(d)

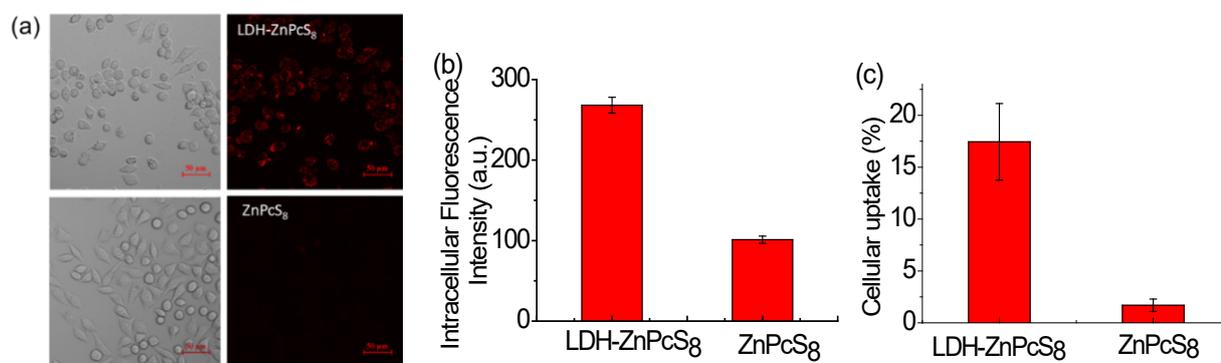


**Figure S6.** Characterization of LDH-S<sub>2</sub>. (a) SEM image, (b) DLS measurement, (c) FTIR spectra, and (d)

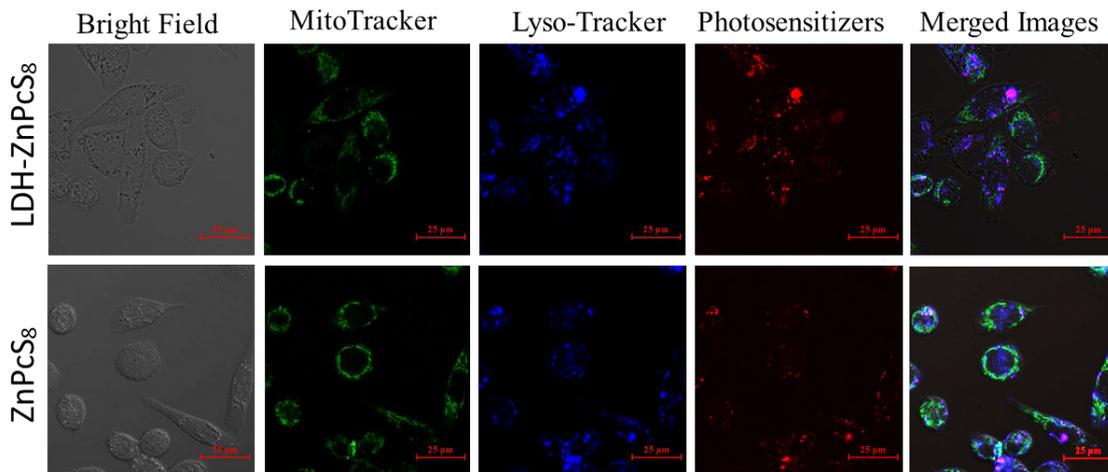
XRD patterns of LDH-S<sub>2</sub>.



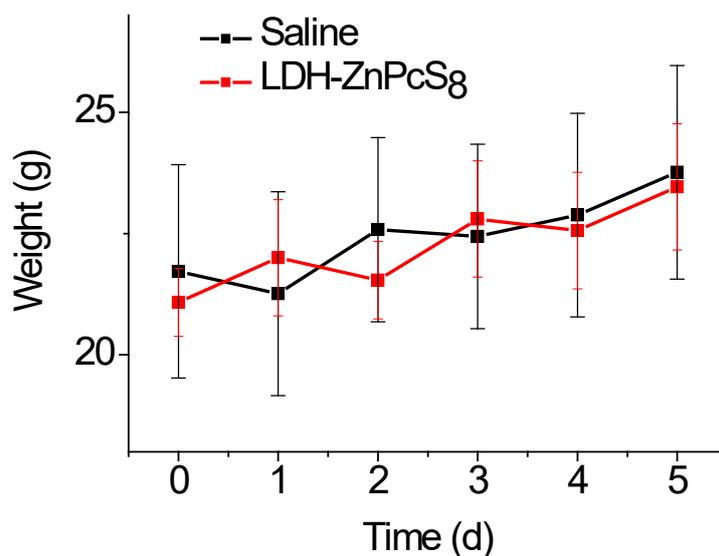
**Figure S7.** pH-controlled release of LDH-ZnPcS<sub>8</sub>. (a) The photo of LDH-ZnPcS<sub>8</sub> suspension precipitated by centrifugation after incubation for 4 h in different pH solutions. (b) The corresponding UV-vis spectra of LDH-ZnPcS<sub>8</sub> in solution phase after 4 h incubation in different pH solutions.



**Figure S8.** Cellular uptake of LDH-ZnPcS<sub>8</sub> and ZnPcS<sub>8</sub> by HepG2 cells. (a) The bright field (left column) and intracellular fluorescence (right column) images of HepG2 cells after incubation with LDH-ZnPcS<sub>8</sub> or ZnPcS<sub>8</sub> (both [ZnPcS<sub>8</sub>] = 0.1 μM) for 2 h. Scale bars = 50 μm. (b) Comparison of the intracellular fluorescence intensities of LDH-ZnPcS<sub>8</sub> and ZnPcS<sub>8</sub>. Data are expressed as the mean ± standard deviation (number of cells = 50). (c) Percentage of cellular uptake of LDH-ZnPcS<sub>8</sub> and ZnPcS<sub>8</sub> determined by an extraction method. Data are expressed as the mean ± standard error of the mean of three independent experiments.



**Figure S9.** Subcellular localization of LDH-ZnPcS<sub>8</sub> and ZnPcS<sub>8</sub> in HepG2 cells. Visualization of the intracellular fluorescence of HepG2 cells by using filter sets specific for LDH-ZnPcS<sub>8</sub> and ZnPcS<sub>8</sub> (both [ZnPcS<sub>8</sub>] = 0.1 µM) (in red, column 4), MitoTracker (in green, column 2), and Lyso-Tracker (in blue, column 3). The bright field images and the corresponding superimposed images are given in column 1 and column 5, respectively. Scale bars = 25 µm.



**Figure S10.** Body weight changing of mice after intravenous injection with saline or LDH-ZnPcS<sub>8</sub> and keeping them under room light.