Supplementary Data For

Facile fabrication of hypericin-entrapped glyconanoparticles for targeted photodynamic therapy

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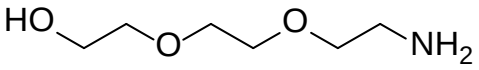

Figure S1. The chemical structure of amino-modified TEG **2**.

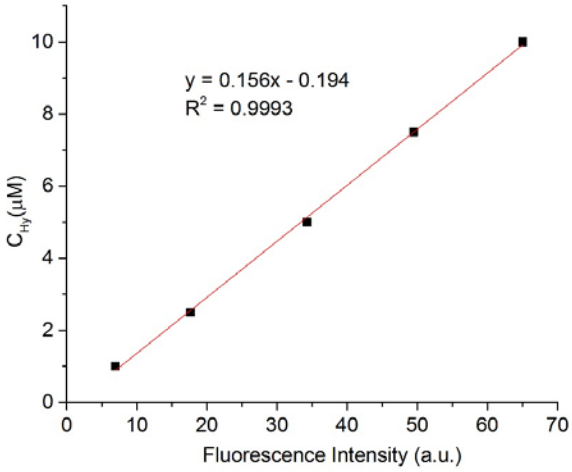

Figure S2 The standard curve for the quantification of cellular uptake of free Hy.

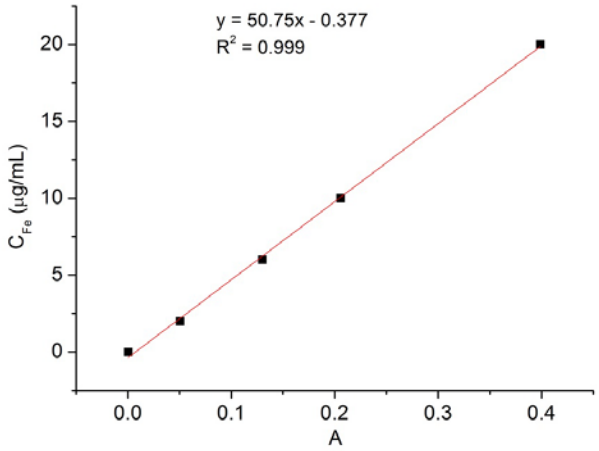

Fig. S3 The standard curve of iron element for the quantification of cellular uptake of Lac-PHMs and TEG-PHMs via atomic absorption spectrometer.

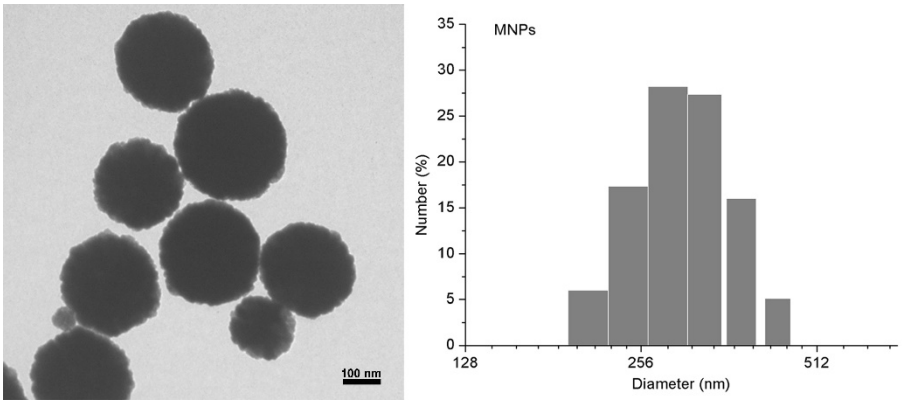

Figure S4. TEM image and DLS analysis result of MNPs.

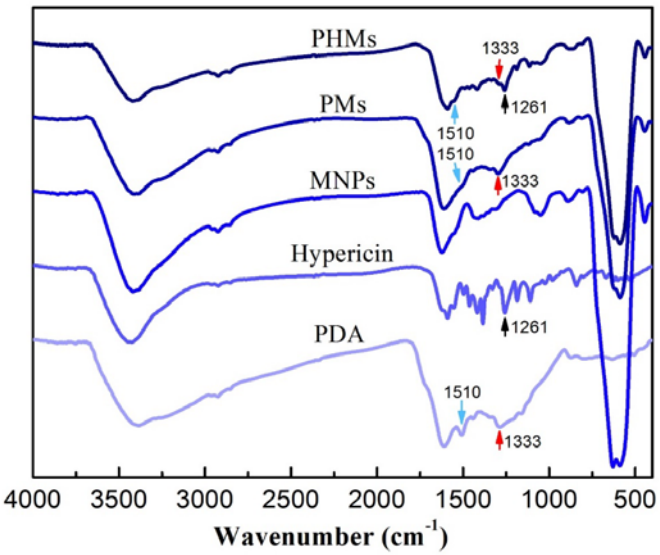

Figure S5. FT-IR spectra of PDA, hypericin, MNPs, PMs and PHMs.

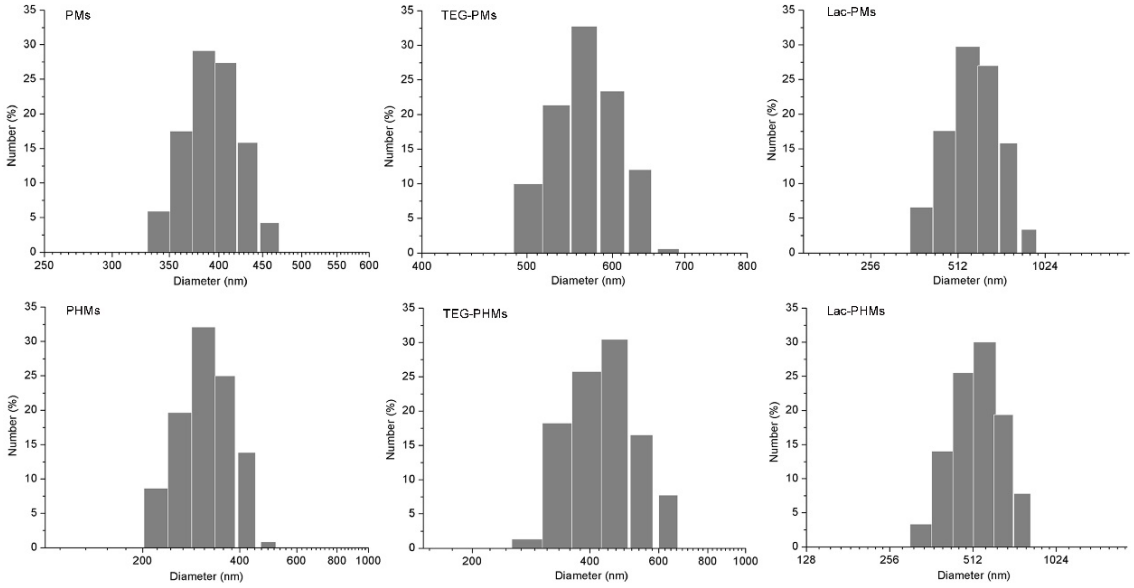

Figure S6. DLS analysis results of PMs, TEG-PMs, Lac-PMs, PHMs, TEG-PHMs and Lac-PHMs.

Determination of hypericin content

We employed the UV-visible absorption spectroscopy to indirectly detect the hypericin content in Lac-PHMs and TEG-PHMs. In experimental group, the PHMs was fabricated according to the fabrication method described in experimental part. The supernatants in the whole fabrication process were collected and the volume of the mixture was fixed by ultrapure water via a volumetric flask (50 mL). Subsequently, 1 mL of the mixture was moved to a 10 mL volumetric flask and the volume was fixed with acetone. In the control group, all the operations were the same as those in experimental group, but no hypericin was added in the PDA coating process. Then we detected the absorbance of the acetone diluted supernatant of experimental group in 595 nm, and the acetone diluted supernatant of control group was employed as the reference. The amount of hypericin can be determined by comparison to the standard curve (Figure S7). The hypericin content in Lac-PHMs and TEG-PHMs can be calculated according to the following equation:

$$N = \frac{M_{Hy} - C \times 504.44 \times 50 \times 10}{504.44 \times M}$$

Where M_{Hy} stands for the mass of hypericin added to the reaction system (mg); C stands for the hypericin concentration of the acetone diluted supernatant of experimental group (μM); M stands for the mass of Lac-PHMs or TEG-PHMs (g); N stands for the content of hypericin in Lac-PHMs or TEG-PHMs (μmol/g NPs).

For both Lac-PHMs and TEG-PHMs, the hypericin content was averaged from three independent measurements. Lac-PHMs and TEG-PHMs were fabricated directly from all the obtained PHMs in each measurement.

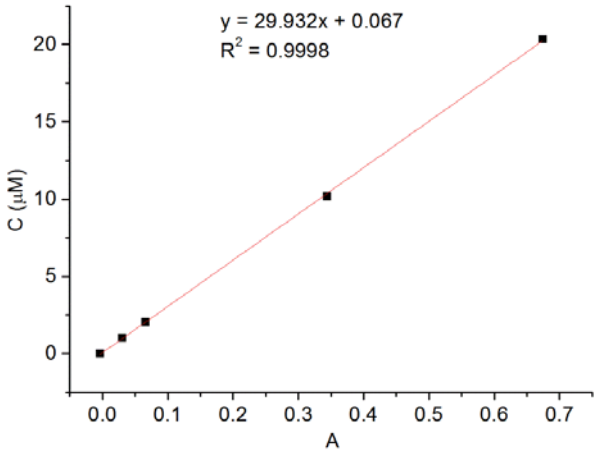

Fig. S7 The standard curve of hypericin for the determination of hypericin content in Lac-PHMs and TEG-PHMs by UV-visible absorption spectroscopy.

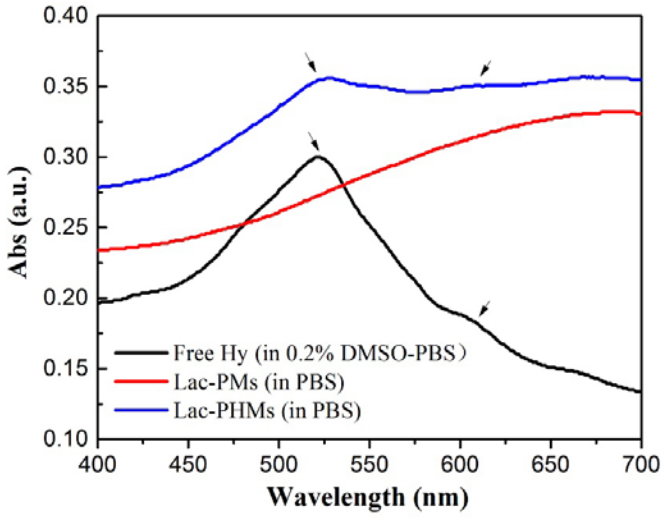

Figure S8. The absorption spectra of free hypericin (in 0.2% DMSO-PBS), Lac-PMs and Lac-PHMs (in PBS).

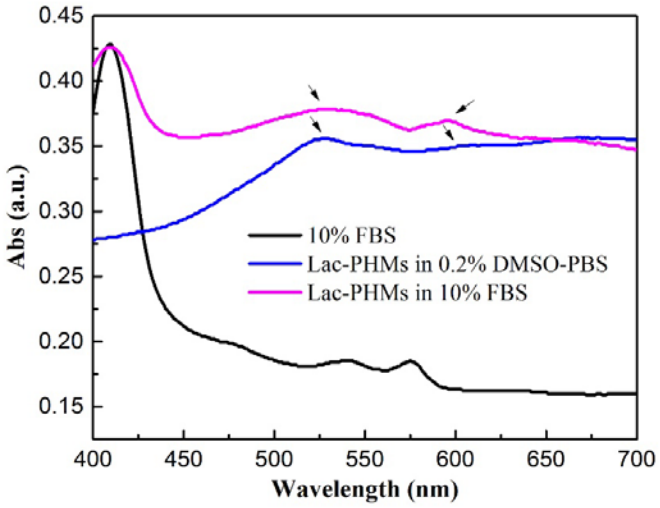

Figure S9. The absorption spectra of 10 % FBS and Lac-PHMs (in 0.2% DMSO-PBS and in 10% FBS).

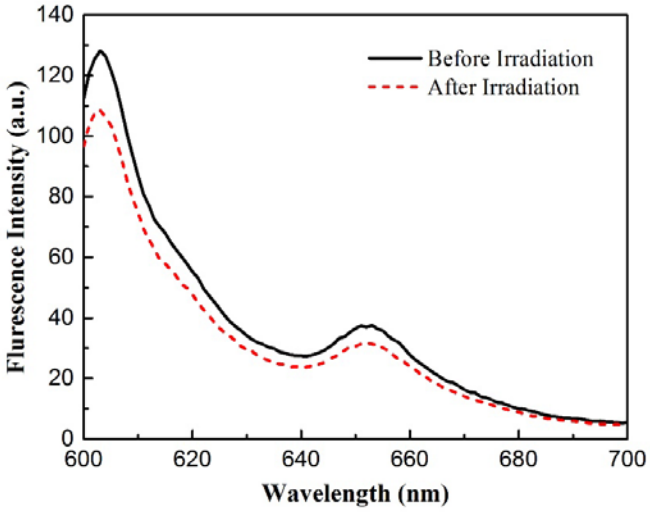

Figure S10. The fluorescence spectra of free hypericin (in DMSO) before and after light irradiation for 30 min (λ = 595-600 nm, 8.6 mW cm^{-2}; the excitation wavelength was 590 nm).

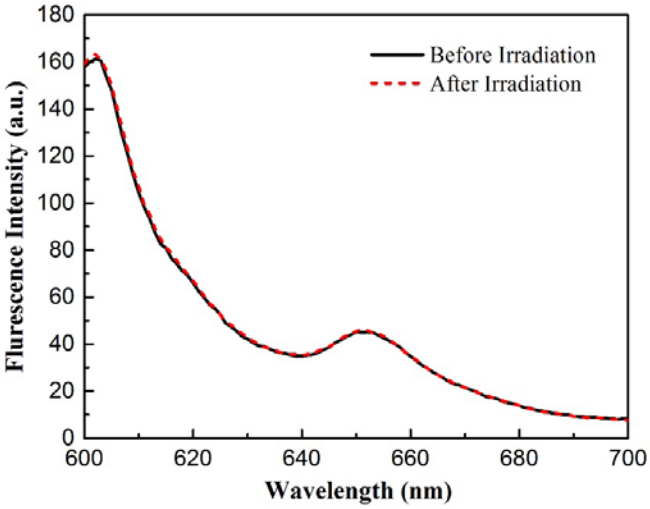

Figure S11. The fluorescence spectra of Lac-PHMs (in DMSO) before and after light irradiation for 30 min (λ = 595-600 nm, 8.6 mW cm^{-2}; the excitation wavelength was 590 nm)

Detection of $^1O_2$ quantum yield (Φ) of free hypericin (in 0.2% DMSO-PBS) and Lac-PHMs (in PBS)

The *p*-nitroso-dimethylaniline (RNO)-bleaching method was employed here. The $^1O_2$ generation efficiency could be reflected by the bleaching of RNO at 440 nm with the trans-annular peroxide intermediate formed as a result of the reaction between singlet oxygen and imidazole. Methylene blue (MB) was used as a standard (Φ_{MB} = 0.52 in aqueous solution). In the experiment, imidazole (8.0 mM) and RNO (12.5 mM) were added to MB aqueous solution (1.0 μM), free hypericin solution (1.0 μM, in 0.2% DMSO-PBS) and Lac-PHMs dispersion (in PBS), and then irradiated with the LED array photosource (λ = 595-600 nm, 8.6 mW cm^{-2}) for 200 s, the absorptions at 440 nm of the three solutions were determined every 20 s.

The $^1O_2$ quantum yield could be calculated via the following equation:

$$\Phi = \Phi_{MB} \frac{k \times I_{MB}}{I \times k_{MB}}$$

Where Φ_{MB} stands for the $^1O_2$ quantum yield of MB (0.52); k and k_{MB} are the rate constants of the photoreaction of RNO with the samples (free hypericin and Lac-PHMs) and MB, respectively; I and I_{MB} are the absorptions of the samples and MB solution at 440 nm.

Qualitative and quantitative detection of intracellular ROS generation with DHE

For the qualitative detection with LSCM, HepG2 and MCF-7 cells were respectively seeded onto 35 mm cell-culture dishes (5 × 10^4 cells) and incubated for 24 h (37 °C, 5% CO_2), then RPMI 1640 or DMEM medium containing free Hy (1.0 μM, in 0.2% DMSO-medium) or the NPs (at Hy equivalent concentration of 1.0 μM for Lac-PHMs and TEG-PHMs, at the concentration of 15 μg mL^{-1} for Lac-PMs and TEG-PMs) was employed to replace the previous mediums, After further incubation at 37 °C for 4 h, the mediums were removed and the cells were washed twice with PBS. Here, the cells without treatment were used as PBS control, the

cells treated with 10.0 mM *N*-Acetylcysteine (NAC) for 12 h were used as negative control, and the cells treated with 2.0 mM H_2O_2 for 2 h were used as positive control. Subsequently, 1.5 mL DHE solution (10 μM) was added to each dish and incubated with cells at 37 °C for 30 min. After removing the unloaded DHE, the cells were washed with PBS for three times and then exposed to an LED array photosource (λ = 595-600 nm, 8.6 mW cm^{-2}) for 30 min. The cell-culture dishes were immediately taken to get the fluorescent images with an LSCM. The fluorescence was excited by 552 nm laser and observed through the red channel. Quantitative analysis of the fluorescence intensity inside cells was carried out using Leica Application Suite X (LAS X) software, and the integrated fluorescence intensities were calculated based on 50 cells, respectively.

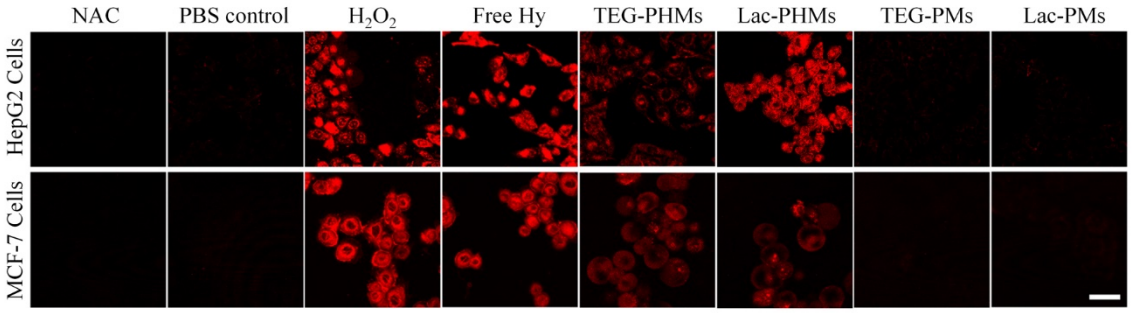

Figure S12 The fluorescence images of the oxyethidium-DNA in HepG2 and MCF-7 cells incubated with Free hypericin, TEG-PHMs, Lac-PHMs, TEG-PMs and Lac-PMs after receiving 595-600 nm light exposure for 30 min (scale bar: 50 nm).

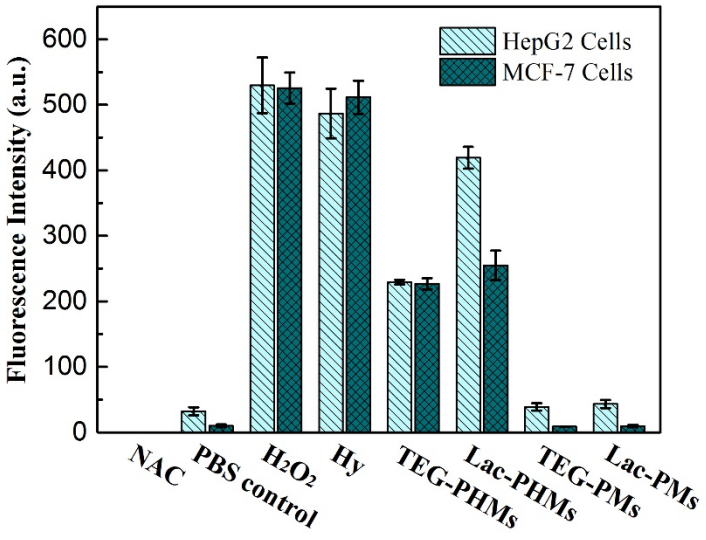

Figure S13 Quantitative analysis of fluorescence intensity analyzed via LAS X software.