Supporting information

Multifunctional SN38-Conjugated Nanosystem for Defeating Myelosuppression and Diarrhea Induced by Irinotecan On Esophageal Cancer

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	Initial (C_I)	Supernatant (C_s)	Loaded (C_l)	Actual FA/Zr ratio ($C_l/4C_{NP}$)	Zeta-Potential(mV)
1：8	10	1.09	8.91	2.78%	-14.6
1：4	20	2.08	17.92	5.60%	-10.8
1：2	40	10.69	29.31	9.16%	-20.8

Table S1. Quantification of actual folate loadings on PDA@PZM sample (80 μM).

	Absorbance of SN38-supernatant (a.u.)	Concentration of SN38-supernatant (μg/mL)	Loading efficiency (%)
1	0.719	7.18	35.32%
2	0.269	1.84	34.16%
3	0.572	5.42	34.11%
4	0.492	4.48	34.13%

Table S2. Quantification of loading efficiency of SN38.

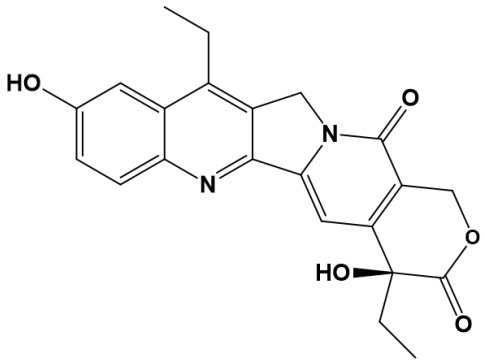


Fig S1. Chemical structure of SN38.

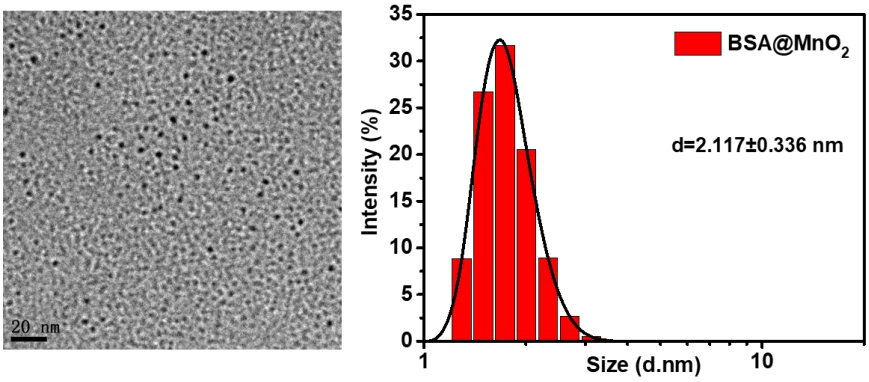
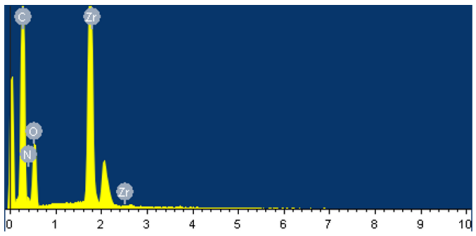


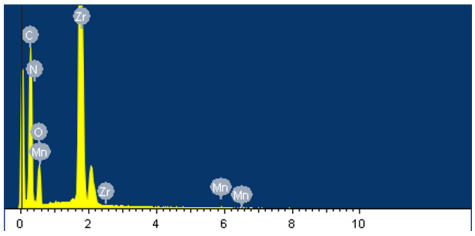
Fig S2. TEM image and size distribution of BSA-MnO_2.

(a)



Element	Wt (%)	At (%)
C	22.33	29.35
N	2.02	2.28
O	67.96	67.05
Zr	7.68	1.33

(b)



Element	Wt (%)	At(%)
C	53.43	25.71
N	7.94	3.21
O	16.47	67.19
Zr	21.09	2.90
Mn	1.08	0.31

Fig S3. EDS and corresponding element weight or atom ratio of (a) PDA@PZM and (b) FA-PPSM.

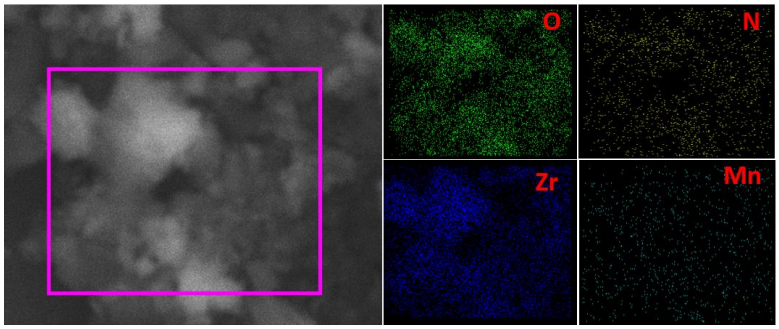


Fig S4. Elemental mappings (O, N, Zr and Mn) of FA-PPSM.

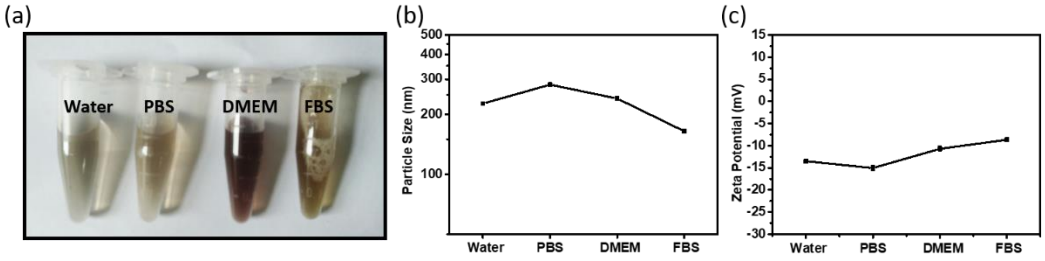


Fig S5. (a) Digital photos, (b) corresponding particle size distribution and (c) zeta potential of FA-PPSM NPs dispersed in water, PBS, DMEM and FBS.

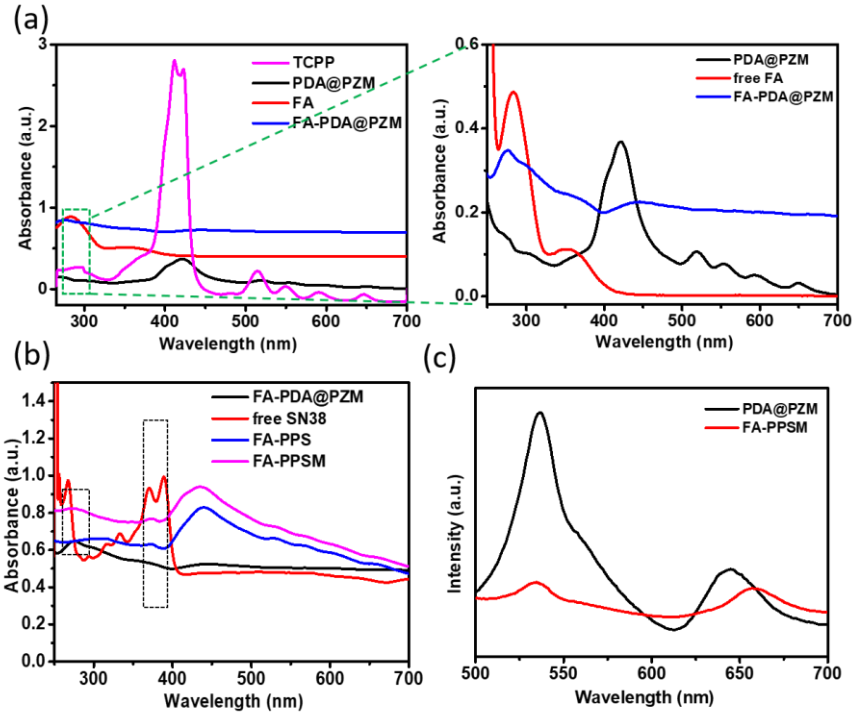


Fig S6. UV-vis adsorption spectra of (a) TCPP, PDA@PZM, free FA and FA-PDA@PZM, (b) FA-PDA@PZM, free SN38, FA-PPS and FA-PPSM in aqueous solution. (c) The fluorescence emission of PDA@PZM and FA-PPSM NPs.

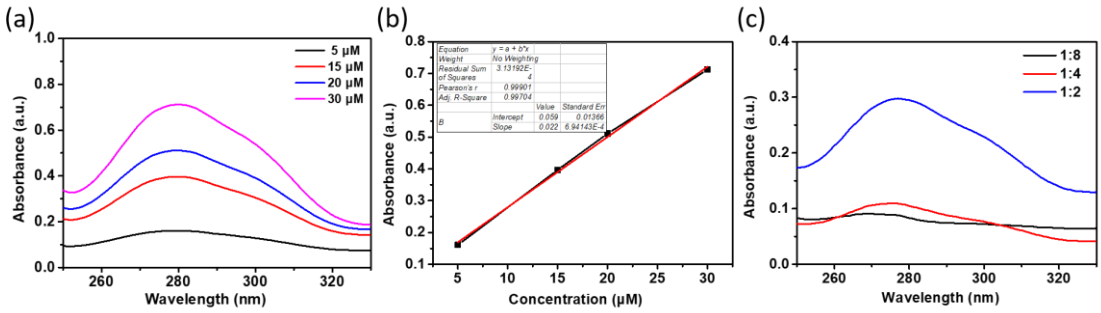


Fig S7. (a) UV-Vis spectra of folic acid in DMSO/Water (v/v, 1/99) solution at various concentrations. (b) Calibration curve of folic acid at 280 nm. (c) UV-Vis spectra of supernatant-folate modified PDA@PZM samples with varying loading ratios.

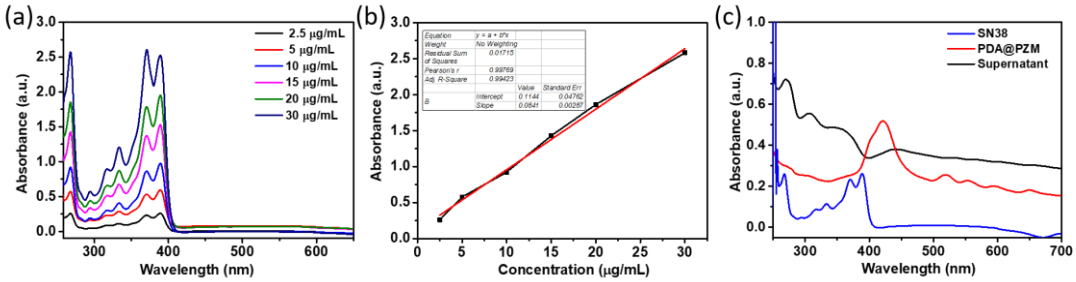


Fig S8. (a) UV-Vis spectra of SN38 at various concentrations. (b) Calibration curve of SN38 at 268nm. (c) UV-vis spectra of supernatant after loading SN38 into FA-PDA@PZM.

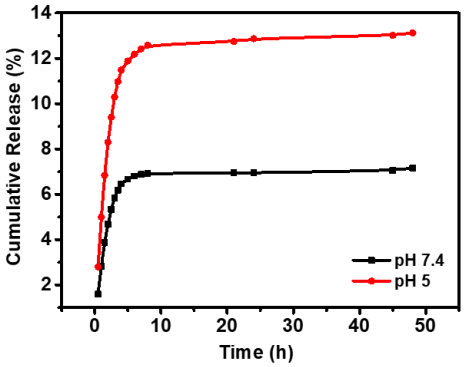


Fig S9. Release profiles of SN38 from FA-PPSM under different release medium.

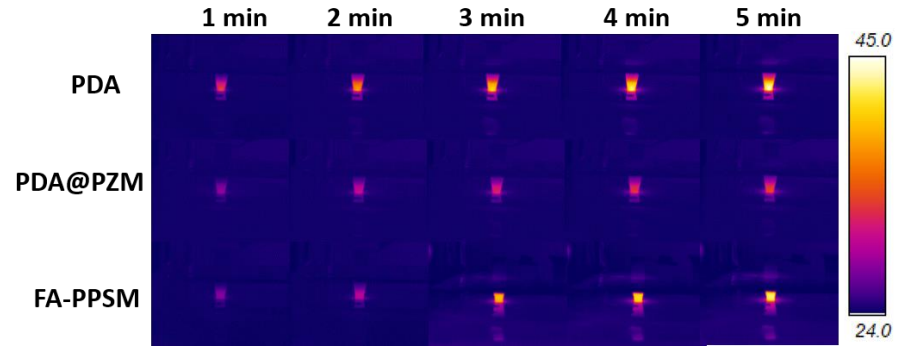


Fig S10. Infrared thermal images of PDA, PDA@PZM and FA-PPSM solution (100 μg/mL) versus different irradiation times.

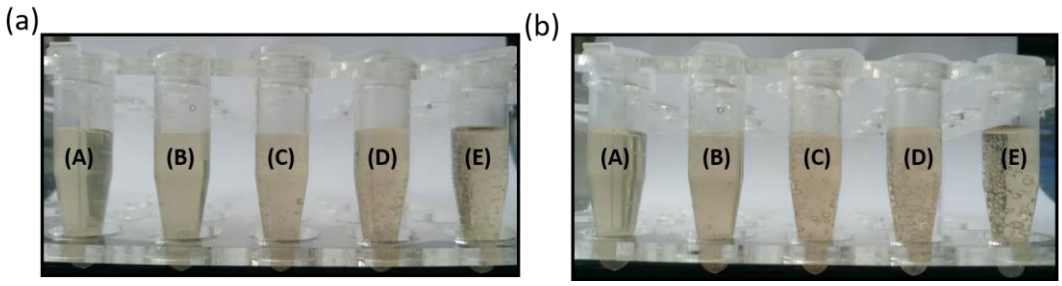


Fig S11. The photograph of FA-PPSM after reaction with increased concentrations of H_2O_2: A) 0, B) 1×10^{-2}M, C) 1×10^{-1}M, D) 5×10^{-1}M and E) 1M after 30 min (a) and 1 h (b). The bubbles indicate the generation of oxygen.

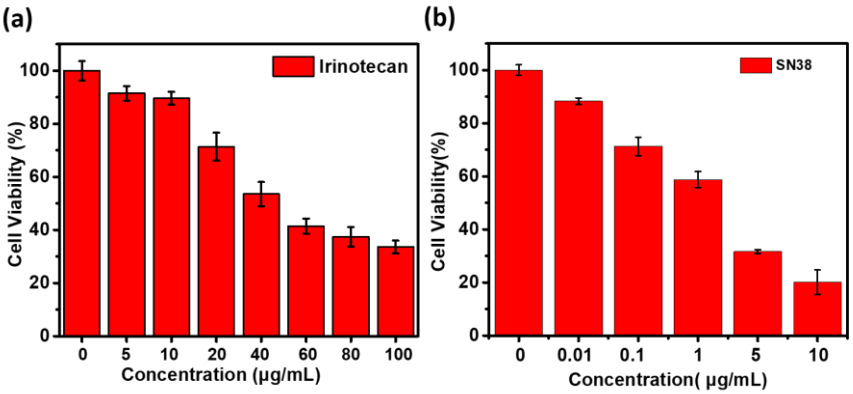


Fig S12. Viability of Eca-109 cells treated with free Irinotecan and SN38 under gradient concentrations without laser irradiation. The error bars are based on the SD of three wells.

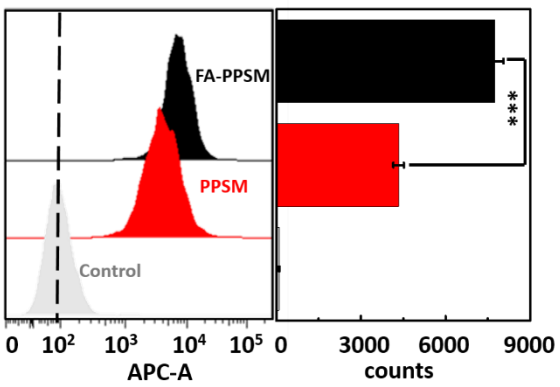


Fig S13. Flow cytometric assay of Eca-109 cells incubated with PPSM and FA-PPSM for 6 h. P values were calculated by Student's t test (***$p < 0.001$).

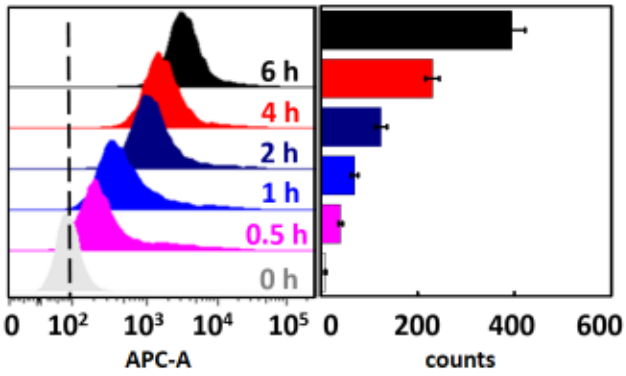


Fig S14. Flow cytometric assay of Eca-109 cells incubated with FA-PPSM for different time periods. (n = 3).

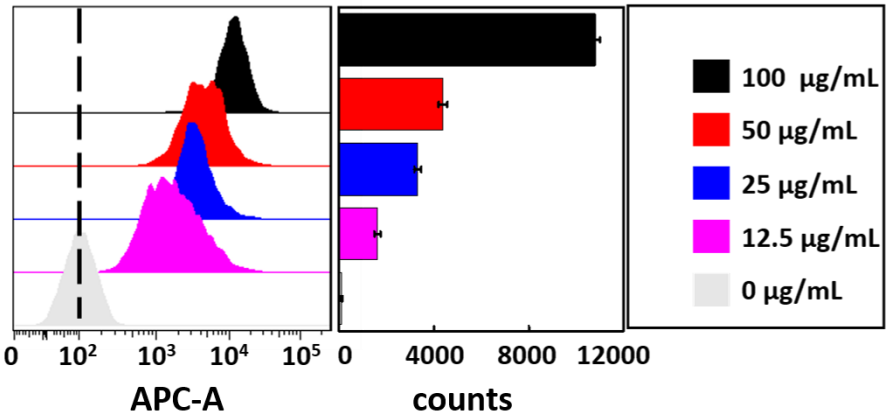


Fig S15. Flow cytometric assay of Eca-109 cells incubated with various concentrations FA-PPSM. The error bars are based on the SD of three wells.

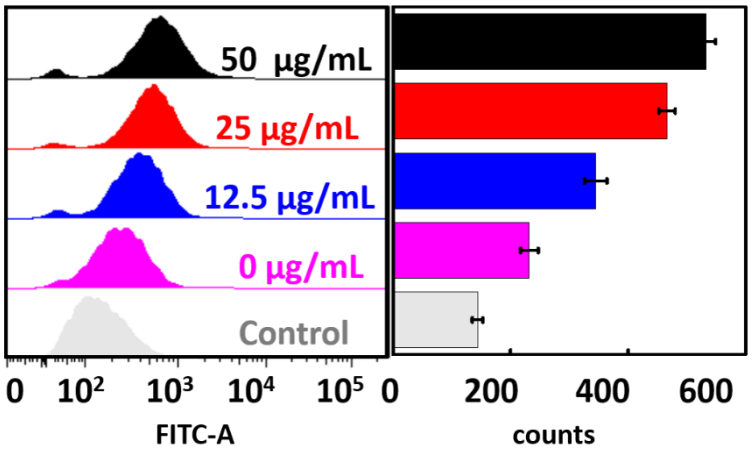


Fig S16. intracellular ROS detection in Eca-109 cells incubated with various concentrations of FA-PPSM under 650 nm irradiation.

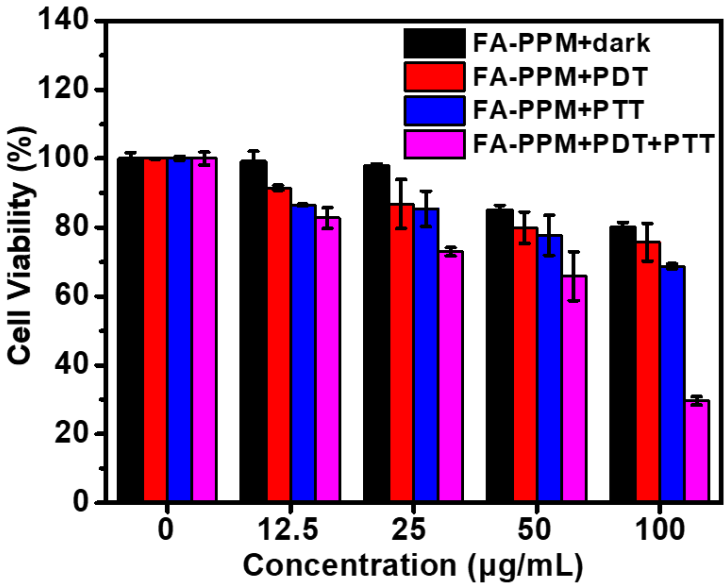


Fig S17. Viabilities of Eca-109 cells treated with FA-PPM under laser irradiation. (n = 3)

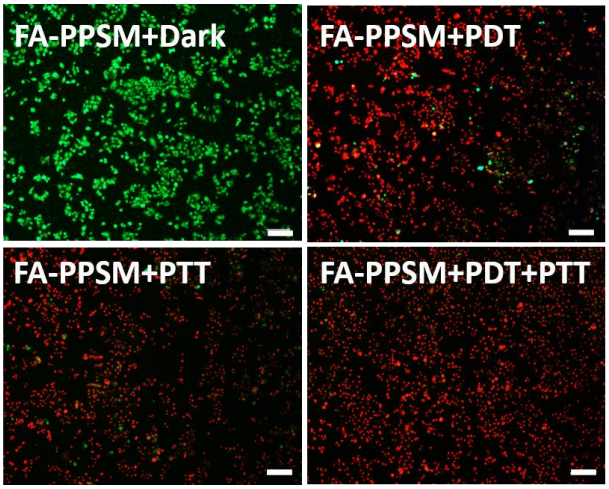


Fig S18. Live/dead staining assay of Eca-109 costained with calcein AM (live cells, green) and propidium iodide (dead cells, red) with various treatments. Scale bar: 100 μm.

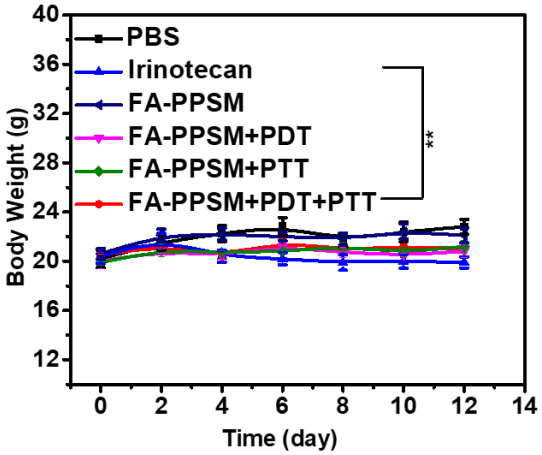


Fig S19. Body weights of mice after different treatments. P values were calculated by Student's t test (**p < 0.01). The error bars are based on the SD of four mice.

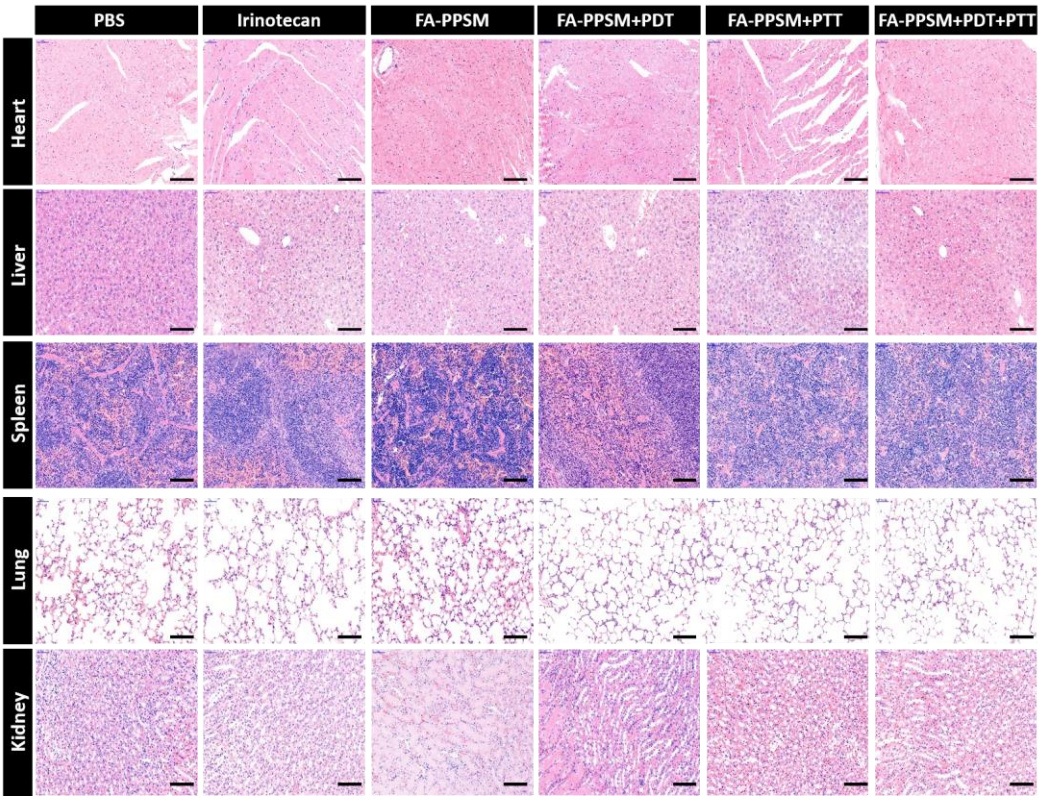


Fig S20. H&E staining of main organs (heart, liver, spleen, lung and kidney) tissue slices after treatment for different groups. Scale bar: 50 μm.

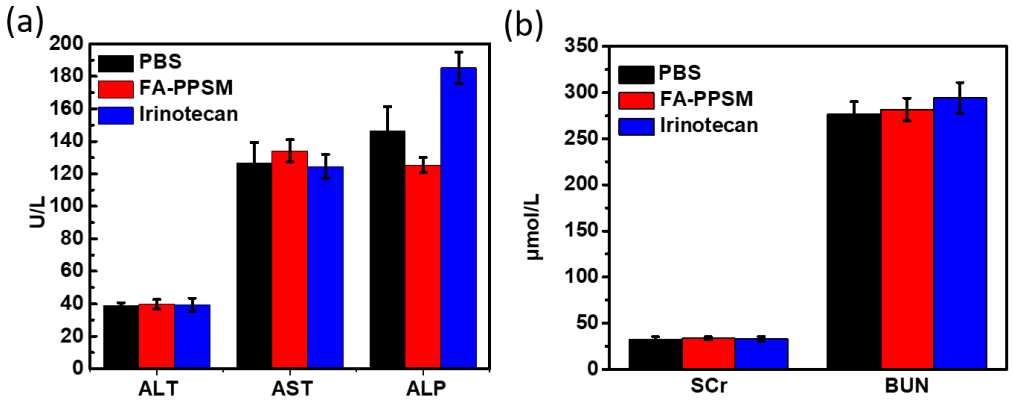


Fig S21. Hematological index and biochemical blood analysis of mice after intravenous injection with FA-PPSM. The error bars are based on the SD of four mice.