Electronic Supplementary Information for:

pH-Responsive supramolecular hydrogel encapsulating CuMnS nanoenzyme catalyst for synergistic photothermal-photodynamic-chemodynamic therapy of tumors

AnQin Dong[a†], Shiwei Huang[b†], Zhiyi Qian[b], Sicheng Xu[b], Weizhong Yuan[a,b*], Bing Wang[a*]

[a]*Department of Vascular Surgery, The Fifth Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, People's Republic of China. E-mail: hnxgwk@163.com (B. Wang)*

[b]*School of Materials Science and Engineering, Tongji University, Shanghai 201804, People's Republic of China. E-mail: yuanwz@tongji.edu.cn (W. Yuan)*

†These authors contributed equally to this work.

Photothermal effect of PCMS NPs

To measure the photothermal conversion effect of PCMS nanoparticles, the PCMS NPs solution (500 μg/mL) was irradiated for 5 min using an 808 nm laser (1 W/cm^2). Meanwhile, the temperature changes were recorded using an infrared thermal imaging camera every 30 s. The photothermal conversion efficiency of the PCMS was calculated by the eq(1).

$$\eta = \frac{hS(T_{max} - T_{surr}) - Q_s}{I(1 - 10^{-A_{808}})}$$

eq(1)

where h was the heat transfer coefficient. S was the surface area of the container. T_{max} was the equilibrium temperature. T_{surr} was the ambient temperature. Q_s was heat loss from light absorbed by the container, and it was calculated to be approximately equal to 0 mW. I was the laser power density. A_{808} was the absorbance of the samples at 808 nm. Where hS can be calculated by eq(2).

$$\tau_s = \frac{m_D C_D}{hS} \quad \text{eq(2)}$$

m_D and C_D were the mass (1 g) and heat capacity (4.2 J·g-1·℃-1) of the solvent (water). Where τ_s was the sample system time constant, calculated by eq(3) and eq(4).

$$t = -\tau_s \ln \theta \quad \text{eq(3)}$$

$$\theta = \frac{T_{surr} - T}{T_{surr} - T_{max}}$$

eq(4)

where t was the cooling time, T was the temperature at cooling time, and θ was a dimensionless dynamic temperature introduced to calculate τ_s ((τ_s was the slope of bule line in Fig. S5).

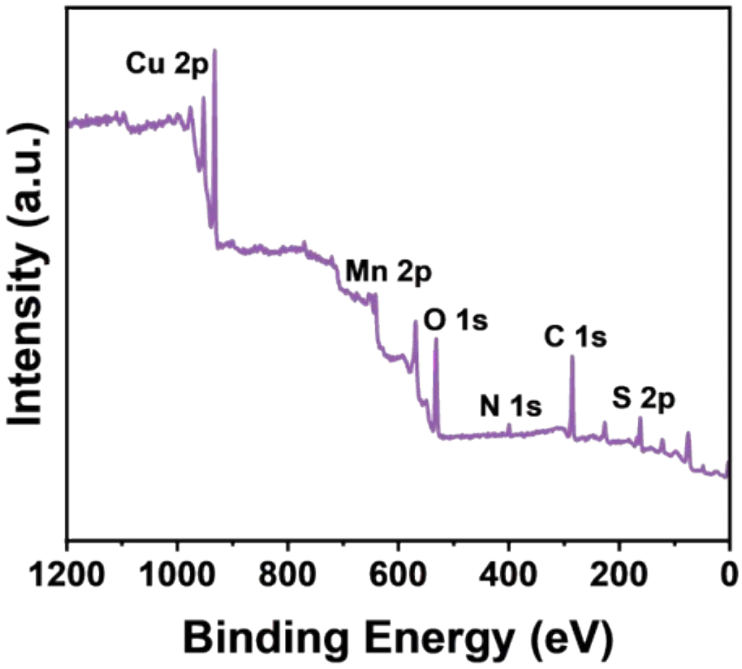

Fig. S1. XPS full spectrum patterns of PCMS NPs.

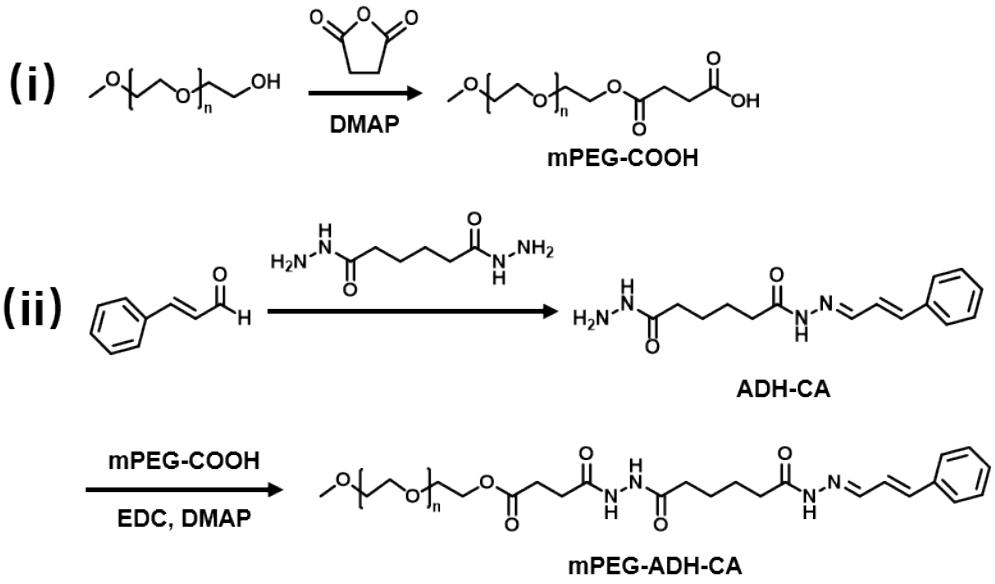

Fig. S2. Synthetic scheme for mPEG-ADH-CA.

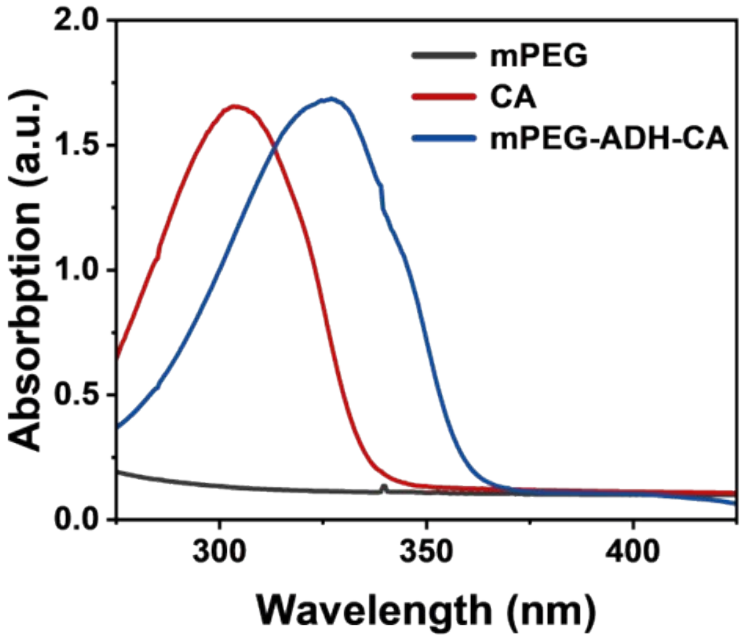

Fig. S3. UV-vis absorption spectra of mPEG, CA and mPEG-ADH-CA.

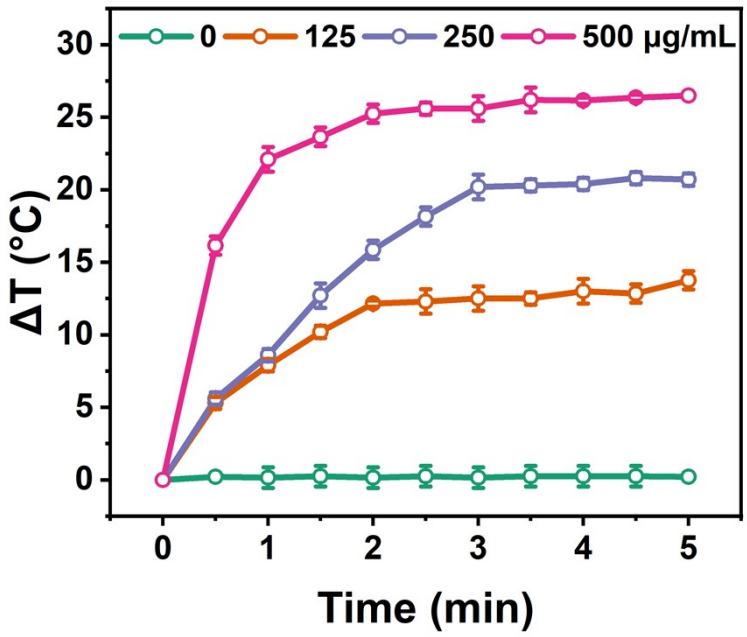

Fig. S4. Time-ΔT curves of aqueous solutions of PCMS NPs (125, 250, 500 μg/mL) with different concentrations under NIR (808 nm, 1 W/cm^2) irradiation.

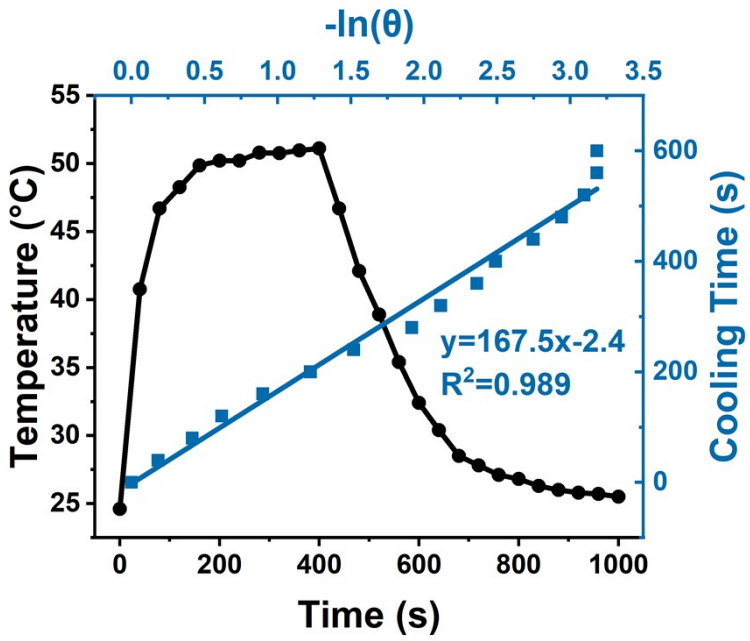

Fig. S5. Calculation of the photothermal conversion efficiency.

Table S1. Photothermal performance of recently reported photothermal agents

Photothermal agents	C	Laser (nm)	Laser power (W/cm^2)	ΔT (°C)	η (%)
PCMS NPs	500 μg/ml	808	1	26.5	67.8
CuCoS NPs[1]	100 μg/ml	808	1	40.3	29.4
Black phosphorus quantum dots (BPQDs)[2]	50 ppm	808	1	31.5	28.4
Au@MOF[3]	50 ppm	808 1064	0.8	35.1 43.5	30.2 48.5
$MoSe_2$ nanosheets[4]	100 μg/ml	808	2.5	29.3	57.9
CMC-rGO/CHO-PEG hydrogel[5]	-	808	1	39	86.7
MSN-SS-PDA[6]	200 μg/ml	808	2	50.4	40.21

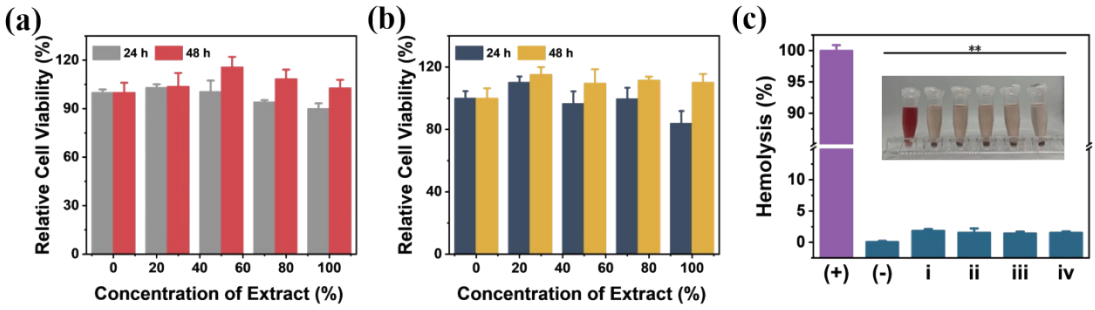

Fig. S6. Relative cell viability of NIH 3T3 cells after incubation with different extracts of (a) PAC/α-CD hydrogel, and (b) PCMS@PAC/α-CD composite hydrogel for 24 h and 48 h.(c) Hemolytic activity evaluation of different solutions and hydrogels and the digital photos of the hemolysis test (n = 3, mean ± SD, **p < 0.01).

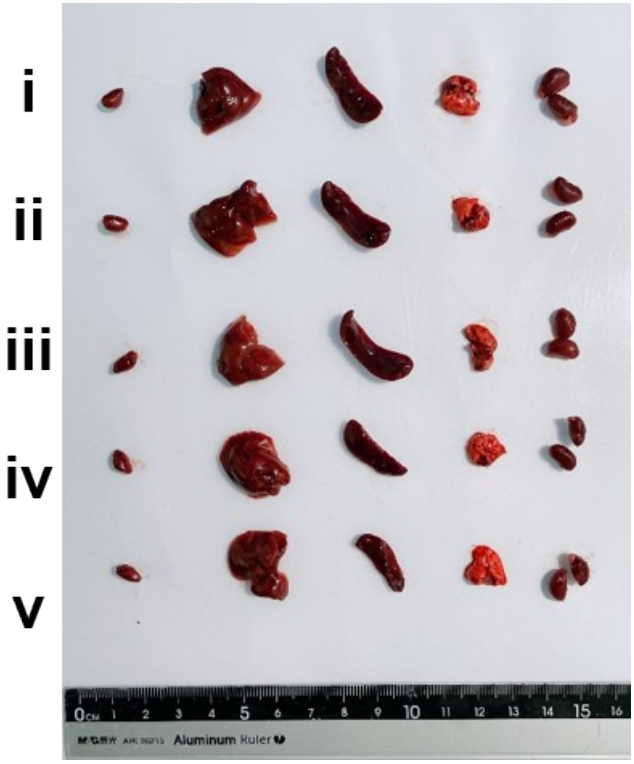

Fig. S7. Digital photos of tumors and major organs of mice under different treatments (i-v: Control, Gel, PCMS+PAC+NIR, Gel@PCMS, Gel@PCMS+NIR).

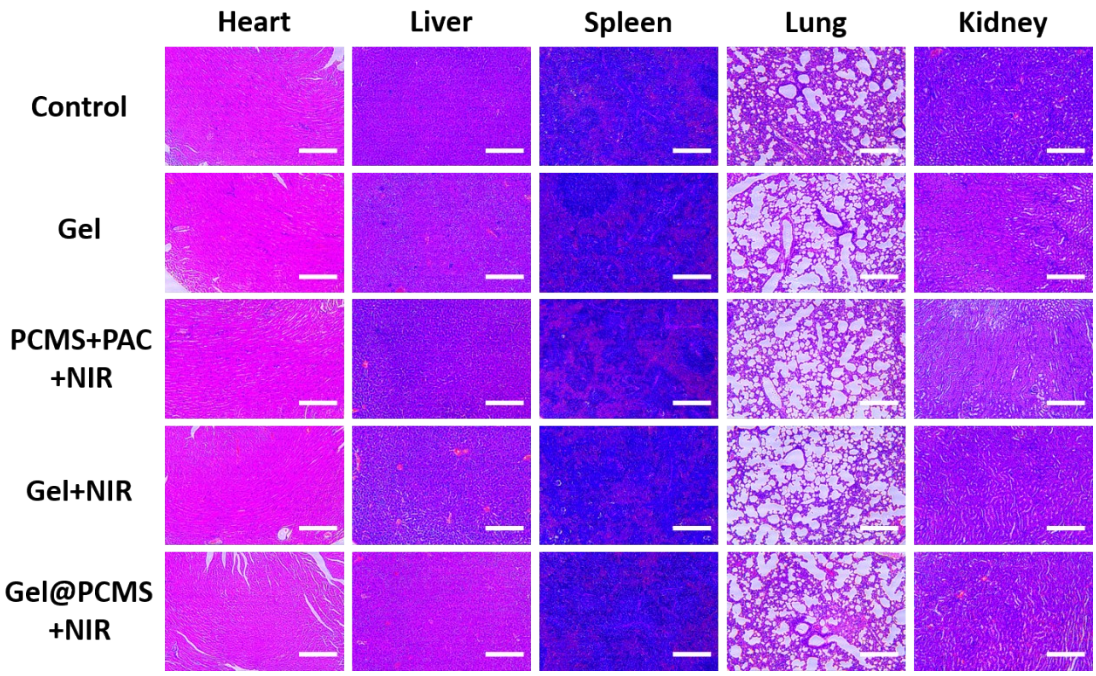

Fig. S8. H&E analysis of the major organs of mice under different treatments (scale bar: 200 μm).

References

[1] G. Zhu, P. Zheng, M. Wang, W. Chen and C. Li, *Inorg. Chem. Front.* 2022, **9**, 1006-1015.

[2] Z. Sun, H. Xie, S. Tang, X. F. Yu, Z. Guo, J. Shao, H. Zhang, H. Huang, H. Wang and P. K. Chu, *Angew. Chem. Int. Ed.* 2015, **54**, 11526-11530.

[3] X. Deng, S. Liang, X. Cai, S. Huang, Z. Cheng, Y. Shi, M. Pang, P. Ma and J. Lin, *Nano Lett.* 2019, **19**, 6772-6780.

[4] Z. Lei, W. Zhu, S. Xu, J. Ding, J. Wan and P. Wu, *ACS Appl. Mater. Interfaces* **2016,** *8*, 20900-20908.

[5] W. Liu, X. Zhang, L. Zhou, L. Shang and Z. Su, *J. Colloid Interface Sci.* 2019, **536**, 160-170.

[6] W. Lei, C. Sun, T. Jiang, Y. Gao, Y. Yang, Q. Zhao and S. Wang, *Mater. Sci. Eng. C Mater. Biol. Appl.* 2019, **105**, 110103.