Supporting Information

Facile-Synthesized Ultrasmall CuS Nanocrystals as Drug Nanocarries for Highly Effective Chemo-photothermal Combination Therapy

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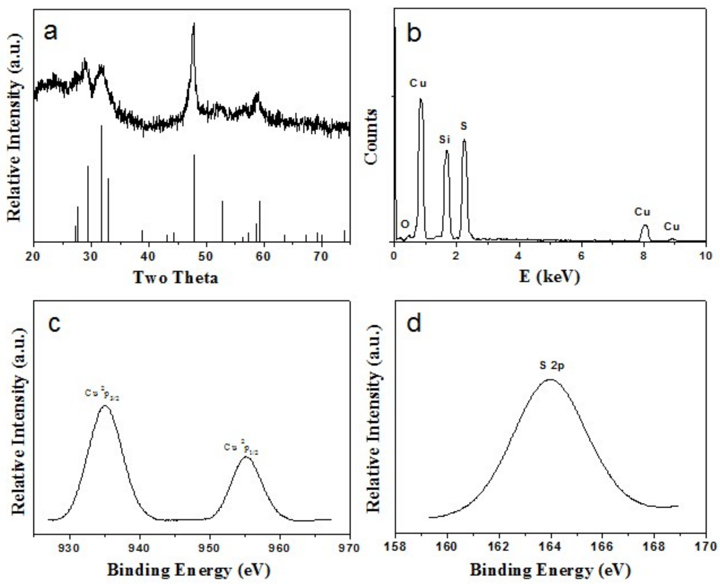

Figure S1. (a) XRD pattern of CuS NCs; (b) EDS of CuS NCs; (c)(d) Cu 2p and S 2p signal in XPS spectrum of CuS NCs.

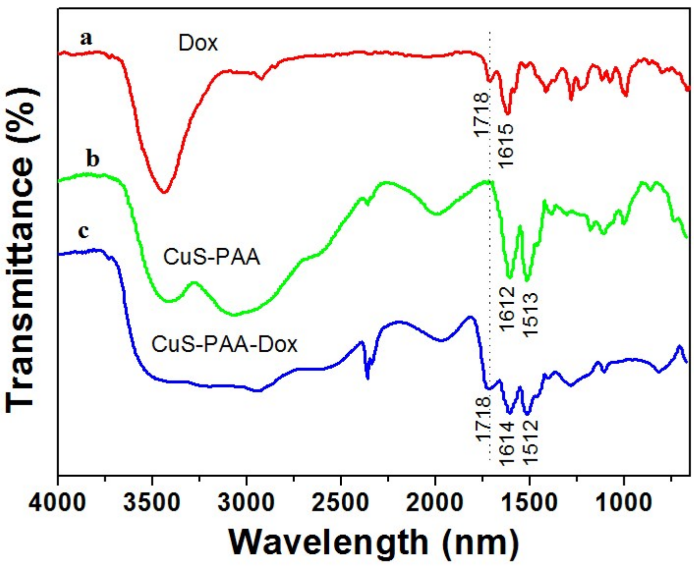

Figure S2. FTIR spectra of Dox(a), CuS-PAA (b), and CuS-PAA-Dox (c).

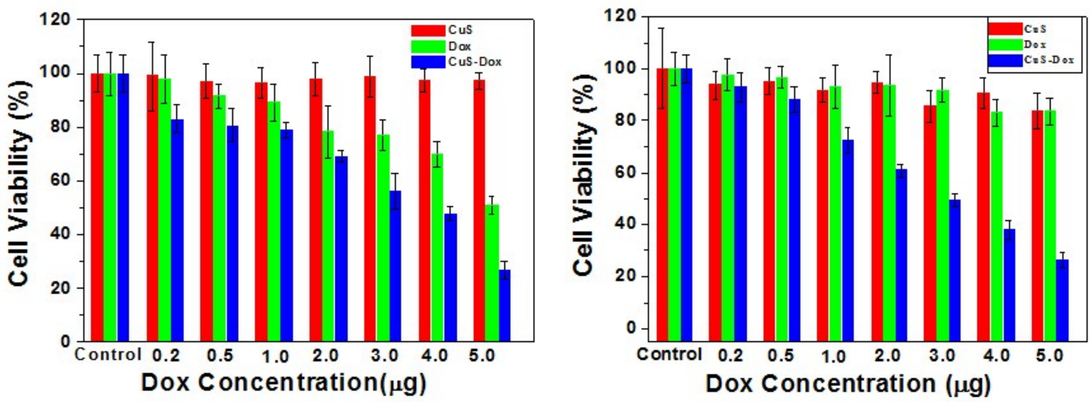

Figure S3. Growth inhibition results for 4T1 and MCF-7 cells treated with CuS NCS, free Dox, and CuS-Dox with concentration of 0-5.0 μg/mL after 24 h incubation.

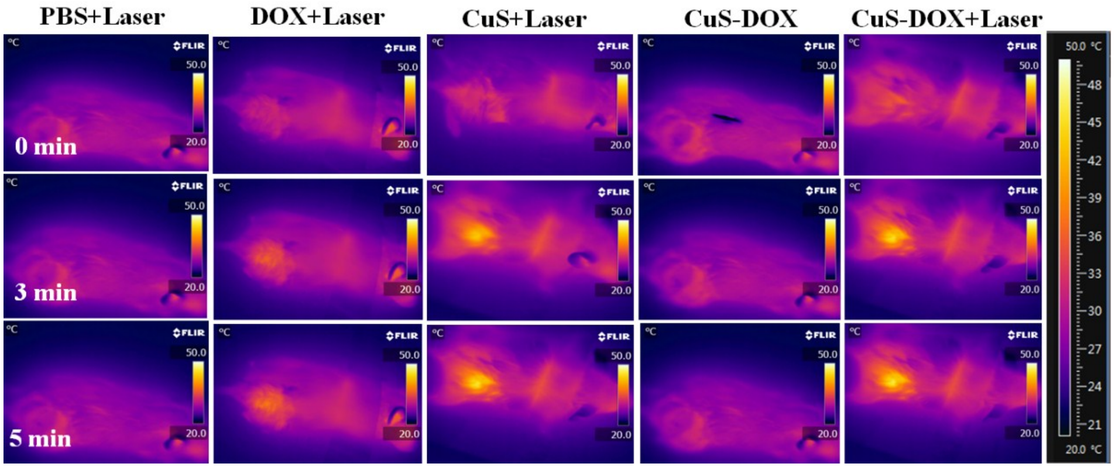

Figure S4. Infrared thermo images of 4T1-tumor-bear mice with intratumoral injection of PBS, free Dox, CuS, and CuS-Dox under the 808 nm laser irradiation and CuS-Dox without laser irradiation taken at different time intervals. The laser power density was 1.0 W/cm2.

Calculation of the photothermal conversion efficiency

According to Roper's reports, the total energy balance for the system can be expressed by Eq (1):[1]

$$\sum_i m_i C_{P,i} \frac{dT}{dt} = Q_{NC} + Q_{Dis} - Q_{Surr} \qquad (1)$$

where m and C_p are the mass and heat capacity of water, respectively, T is the solution temperature, Q_{NC} is the energy inputted by NCs, Q_{Dis} is the baseline energy inputted by the sample cell, and Q_{surr} is het conduction away from the system surface by air.

The laser-induced source term of Q_{NC} represents heat dissipated by electron-phonon relaxation of the plasmons on the CuS NCs surface under an 808 nm irradiation:

$$Q_{NC} = I\left(1 - 10^{-A_{808}}\right)\eta \qquad (2)$$

where I is incident laser power, η is the conversion efficiency from incident laser energy to thermal energy, and A_{808} is the absorbance of the CuS NCs at the wavelength of 808 nm. In addition, source term, Q_{Dis}, expresses heat dissipated from light absorbed by the quartz sample cell itself, and it was measured using adquartz cuvette cell containing pure water without CuS NCs. Furthermore, Q_{surr} is linear with temperature for the outgoing thermal energy, as given by Eq 3:

$$Q_{Surr} = hS(T - T_{Surr}) \quad (3)$$

where h is heat transfer coefficient, S is the surface area of the container, and T_{Surr} is ambient temperature of the surroundings.

Once the laser power is defined, the heat input $(Q_{NC}+Q_{Dis})$ will be finite. Since the Q_{Surr} is increased with the increase of the temperature according to the Eq 3, the system temperature will rise to a maximum when the heat input is equal to heat output:

$$Q_{NC} + Q_{Dis} = Q_{Surr-Max} = hS(T_{Max} - T_{Surr}) \quad (4)$$

As the sample cell reaches the equilibrium temperature, the $Q_{Surr\text{-}Max}$ is heat condition away from the system surface by air, and T_{Max} is the equilibrium temperature. The 808 nm laser heat conversion efficiency (η) can be determined by substituting Eq2 for QNC into Eq4 and rearranging to get

$$\eta = \frac{hS(T - T_{Surr}) - Q_{Dis}}{I(1 - 10^{-A808})} \quad (5)$$

Where Q_{Dis} was measured to be 57.6 mW, the (TMax-TSurr) was 28.6 ^{o}C according to Figure 1h, I is 1.78 W/cm^2, A_{808} is the absorbance (0.159) of the CuS NCs at 808 nm (Figure 2a). Thus, to calculate η, the hS is needed to be known

In order to get the hS, a dimensionless driving force temperature, θ is introduced using the maximum system temperature, T_{Max}

$$\theta = \frac{T - T_{Surr}}{T_{Max} - T_{Surr}} \quad (6)$$

And the τ_s

$$\tau_s = \frac{\sum_i M_i C_{P,i}}{hS} \qquad (7)$$

Which is substituted into Eq 1 and obtained the Eq8

$$\frac{d\theta}{dt} = \frac{1}{\tau}\left[\frac{Q_{NC} + Q_{Dis}}{hS\left(T_{Max} - T_{Surr}\right)} - \theta\right] \qquad (8)$$

At the cooling stage of the aqueous dispersion of the CuS NCs, the light source was shut off, the $Q_{NC}+Q_{Dis}=0$, yield the Eq. 9

$$\frac{d\theta}{dt} =- \tau_s d_t \qquad (9)$$

And integrating, giving the expression

$$t =- \tau_s ln\theta \qquad (10)$$

Therefore, time constant for heat transfer from the system is determined to be τ_s=213.65s by applying the linear time data from the cooling period *vs* negative natural logarithm of driving force temperature (Figure 1i). In addition, the m is 0.2 g and the C is 4.2 J/g. Thus, according to Eq. 7 the hS is deduced to be 3.93 mJ, substitute to Eq.5, the 808 nm laser heat Conversion efficiency (η) of the CuS NCs can be calculated to be 19.5%.

Reference:

[1] Roper DK, Ahn W, Hoepfner M. Microscale heat transfer transduced by surface plasmon resonant gold nanoparticles. J Phys Chem C. 2007;111:3636-41.