Doxorubicin-conjugated CuS nanoparticles for efficient synergistic therapy triggered by near-infrared light

Huiting Bi, Yunlu Dai*, Ruichan Lv, Chongna Zhong, Fei He, Shili Gai, Arif Gulzar, Guixin Yang, and Piaoping Yang*

The rough calculations process of the number of DOX molecules released from per CuS-DOX.

The number of DOX molecules released from per CuS-DOX in the sample was determined according to previous method.\(^1\) We obtained the standard curve of DOX, \(y = 18.327x + 0.001\). In order to determine the density and content, according to the standard curve, the release amount of DOX from nanoparticles can be calculate:

The initial concentration of DOX is 0.5 mg/mL, and the absorbance of supernatant after loading is 8.065. The Cu\(^{2+}\)-concentration of CuS-DOX NPs is about 2.8 \(\mu\)g/mL obtained by ICP-MS.

Loaded concentration \(\Delta X = 0.5 \text{mg/mL} - (8.065-0.001)/18.327 = 0.44 \text{mg/mL}\).

The number of DOX can be calculate:

\[
\text{n}_{\text{DOX}} = \frac{0.44 \text{mg/mL}}{1000 \times 577.99 \text{g/mol}} \times 6.02 \times 10^{23}/\text{mol} = 4.58 \times 10^{17}/\text{mL}
\]

The quality of CuS: \(m_{\text{CuS}} - \rho V = 4.6 \text{g/cm}^3 \times \frac{4}{3}\pi(5\text{nm} \times 10^{-7})^3 = 7.67 \times 10^{-19} \text{g}\)

\[
\text{n}_{\text{CuS}} = \frac{2.8 \mu\text{g/mL}}{7.67 \times 10^{-19} g} = 3.65 \times 10^{12}/\text{mL}
\]

\[
R_{\text{DOX}} = \frac{4.58 \times 10^{17}/\text{mL}}{3.65 \times 10^{12}/\text{mL}} = 1.25 \times 10^5
\]

About \(1.25 \times 10^5\) of DOX molecules were released from per particle after 24 hour.
The calculation of the photothermal conversion efficiency.

The photothermal conversion efficiency of CuS was determined according to previous method. Detailed calculation was given as following:

Based on the total energy balance for this system:

\[ \sum_i m_i C_p, i \frac{dT}{dt} = Q_{NPs} + Q_s - Q_{loss} \]  \hspace{1cm} (1)

where \( m \) and \( C_p \) are the mass and heat capacity of solvent (water). \( T \) is the solution temperature.

\( Q_{NPs} \) is the photothermal energy input by CuS:

\[ Q_{NPs} = I (1 - 10^{-A_\lambda}) \eta \]  \hspace{1cm} (2)

\( I \) is the laser power, \( A_\lambda \) is the absorbance of CuS at the wavelength of 808 nm, and \( \eta \) is the conversion efficiency from the absorbed light energy to thermal energy. \( A_\lambda = \varepsilon \lambda L c \), where \( \varepsilon \lambda \) is the wavelength-dependent molar absorptivity, \( L \) is path length, and \( c \) is molar concentration.

\( Q_s \) is the heat associated with the light absorbance of the solvent, which is measured independently to be \( Q_s = (5.4 \times 10^{-4}) I J s^{-1} \) using pure water without CuS.

\( Q_{loss} \) is thermal energy lost to the surroundings:

\[ Q_{loss} = hA\Delta T \]  \hspace{1cm} (3)

\( h \) is the heat transfer coefficient, \( A \) is the surface area of the container, and \( \Delta T \) is the temperature change, which is defined as \( T - T_{surr} \) (\( T \) and \( T_{surr} \) are the solution temperature and ambient temperature of the surroundings, respectively).

At the maximum steady-state temperature, the heat input is equal to the heat output, that is:

\[ Q_{NPs} + Q_s = Q_{loss} = hA\Delta T_{max} \]  \hspace{1cm} (4)

\( \Delta T_{max} \) is the temperature change at the maximum steady-state temperature. According
to the Eq.2 and Eq.4, the photothermal conversion efficiency ($\eta$) can be determined:

$$\eta = \frac{hA \Delta T_{\text{max}} - Q_s}{I(1 - 10^{-A_I})} \quad (5)$$

In this equation, only $hA$ is unknown for calculation. In order to get the $hA$, we herein introduce $\theta$, which is defined as the ratio of $\Delta T$ to $\Delta T_{\text{max}}$:

$$\theta = \frac{\Delta T}{\Delta T_{\text{max}}} \quad (6)$$

Substituting Eq.6 into Eq.1 and rearranging Eq.1:

$$\frac{d\theta}{dt} = \sum_i m_i C_{p,i} \left[ \frac{Q_{\text{NPs}} + Q_s}{hA \Delta T_{\text{max}}} - \theta \right] \quad (7)$$

When the laser was shut off, the $Q_{\text{NPs}} + Q_s = 0$, Eq.7 changed to:

$$\frac{dt}{d\theta} = -\frac{\sum_i m_i C_{p,i}}{hA \theta} \quad (8)$$

Integrating Eq.8 gives the expression:

$$t = -\frac{\sum_i m_i C_{p,i}}{hA} \ln \theta \quad (9)$$

Thus, $hA$ can be determined by applying the linear time data from the cooling period vs $\ln \theta$ (Fig. S2). Substituting $hA$ value into Eq.5, the photothermal conversion efficiency ($\eta$) of CuS solution can be calculated.
Fig. S1 CuS-DOX NPs dispersed in water before and after 24 h.
Fig. S2 Linear time data versus $-\ln \theta$ obtained from the cooling period of Fig. 2b.
Fig. S3 Zeta potentials of CuS NPs, CuS-CONNH₂ NPs and CuS-DOX NPs.

Notes and references