Electronic Supplementary Information

Facile synthesis of prussian blue nanoparticles as pH-responsive drug carriers for combined photothermal-chemo treatment of cancer

Huajian Chen†, Yan Ma†, Xianwen Wang*, Xiaoyi Wu* and Zhengbao Zha*

aSchool of Biological and Medical Engineering, Hefei University of Technology, Hefei, Anhui 230009, P. R. China.
bDepartment of Aerospace and Mechanical Engineering, Biomedical Engineering IDP and Bio5 Institute, University of Arizona, Tucson, Arizona 85721, USA

†These authors had equal contributions for this work.
* Corresponding author. Email: zbzha@hfut.edu.cn; xwu@email.arizona.edu

Experimental Details:

Calculation of the photothermal conversion efficiency

According to Roper’s report, the total energy balance between input and dissipation for the system can be given as:

\[
\sum_i m_i C_i \frac{dT}{dt} = Q_{NP} + Q_{sys} - Q_{out}
\]  

(1)

Where \( m \) and \( C \) are the mass and heat capacity of water, respectively, \( T \) is the solution temperature, \( Q_{NP} \) is the energy absorbed by NPs, \( Q_{sys} \) is the energy imputed by the pure water system, and \( Q_{out} \) is heat dissipation of the system.

The heat absorbed (\( Q_{NP} \)) by PEGylated PB NPs can be shown as:

\[
Q_{NP} = I(1 - 10^{-A_{808}})\eta
\]  

(2)

Where \( I \) is incident laser power in W, \( \eta \) is the photothermal conversion efficiency, and \( A_{808} \) indicates the absorbance of the PEGylated PB NPs at 808 nm.

\( Q_{out} \) is linear with system temperature, as expressed as:

\[
Q_{out} = hS(T - T_{surr})
\]  

(3)

Where \( h \) is heat transfer coefficient, \( S \) is the surface area of the container, and \( T_{surr} \) is ambient temperature of the surroundings.
When the system reaches a steady state temperature \( T_{\text{max}} \), the heat input and output are balanced:

\[
Q_{\text{np}} + Q_{\text{sys}} = Q_{\text{out}} = hS(T_{\text{max}} - T_{\text{surr}})
\]  
(4)

After the laser is removed, the \( Q_{\text{np}} + Q_{\text{sys}} = 0 \), reducing the Eq. (1)

\[
\sum_i m_i C_i \frac{dT}{dt} = -Q_{\text{out}} = -hS(T - T_{\text{surr}})
\]  
(5)

Rearranging the Eq. (5) would give

\[
dt = - \frac{\sum_i m_i C_i}{hS} \frac{dT}{(T - T_{\text{surr}})}
\]  
(6)

And integrating, give the expression

\[
t = - \frac{\sum_i m_i C_i}{hS} \ln \left( \frac{T - T_{\text{surr}}}{(T_{\text{max}} - T_{\text{surr}})} \right)
\]  
(7)

A system time constant \( \tau_s \) is defined as:

\[
\tau_s = - \frac{\sum_i m_i C_i}{hS}
\]  
(8)

And \( \theta \) is introduced using the maximum system temperature, \( T_{\text{max}} \)

\[
\theta = \frac{T - T_{\text{surr}}}{(T_{\text{max}} - T_{\text{surr}})}
\]  
(9)

Substituting Eq. (8) and (9) giving:

\[
t = -\tau_s \ln \theta
\]  
(10)

Therefore, the time constant for heat transfer from the system \( \tau_s \) can be determined by applying the linear time data from the cooling period vs. negative natural logarithm of driving force temperature (\( \theta \))

Since \( Q_{\text{sys}} \) can be obtained directly as

\[
Q_{\text{sys}} = hS(T_{\text{max,II},\theta} - T_{\text{surr}})
\]  
(11)

Eq. (4) can be given as:

\[
Q_{\text{np}} = I(1 - 10^{-\text{hess}})\eta = hS(T_{\text{max}} - T_{\text{max,II},\theta})
\]  
(12)

Also
With $\tau_s$ is equal to 539.59 s, $m$ is 3.0 g and $C$ is 4.2 J/g, $hS$ can be calculated to be 0.02335 W/$^\circ$C. Substituting $I = 2.0$ W, $A_{808} = 0.3910$, $T_{\text{max}} - T_{\text{surr}} = 20.8$ $^\circ$C into Eq. (12), the photothermal conversion efficiency can be determined to be 36.7%.

References
Fig. S2 Characterization of hydrophilic PEGylated PB NPs. a) TEM image; b) DLS diameter distribution.

Fig. S3 The absorbance of PEGylated PB NPs at 808 nm increased as the concentration of PEGylated PB NPs increased.
Fig. S4 TEM image of PEGylated PB NPs after five LASER ON/OFF cycles.

Table S1 Characterization of PEGylated PB-DOX NPs with different mass ratio of DOX and NPs.

<table>
<thead>
<tr>
<th>mass ratio (DOX : DSPE-PEG)</th>
<th>loading efficiency</th>
<th>loading content (DOX : DOX+NPs)</th>
<th>DLS Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:100</td>
<td>100%</td>
<td>1.0%</td>
<td>156.7 ± 36.1nm</td>
</tr>
<tr>
<td>1:50</td>
<td>100%</td>
<td>2.0%</td>
<td>140.5 ± 2.1nm</td>
</tr>
<tr>
<td>1:20</td>
<td>100%</td>
<td>4.8%</td>
<td>93.1 ± 37.0 nm</td>
</tr>
<tr>
<td>1:10</td>
<td>98%</td>
<td>9.2%</td>
<td>119.0 ± 30.5nm</td>
</tr>
<tr>
<td>1:5</td>
<td>95.5%</td>
<td>16.3%</td>
<td>116.1 ± 58.7nm</td>
</tr>
<tr>
<td>1:1</td>
<td>93.6%</td>
<td>48.8%</td>
<td>168.1 ± 70.9nm</td>
</tr>
</tbody>
</table>
Table S2 Model parameters for PEGylated PB-DOX NPs drug release simulation.

<table>
<thead>
<tr>
<th>Sample</th>
<th>( \Delta G/k_BT )</th>
<th>ks (1/h)</th>
<th>koff (1/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH 4.0 free DOX in 1 mL DMSO</td>
<td>1.36</td>
<td>0.847</td>
<td>0.018</td>
</tr>
<tr>
<td>pH 7.4 free DOX in 1 mL DMSO</td>
<td>-1.12</td>
<td>1.137</td>
<td>0.003</td>
</tr>
<tr>
<td>NPs in pH 4.0 buffer + 15 min irradiation</td>
<td>-0.73</td>
<td>1.457</td>
<td>0.004</td>
</tr>
<tr>
<td>NPs in pH 4.0 buffer</td>
<td>-0.8</td>
<td>1.025</td>
<td>0.004</td>
</tr>
<tr>
<td>NPs in pH 7.4 buffer + 15 min irradiation</td>
<td>-1.58</td>
<td>1.8</td>
<td>0</td>
</tr>
<tr>
<td>NPs in pH 7.4 buffer</td>
<td>-1.64</td>
<td>1.791</td>
<td>0</td>
</tr>
</tbody>
</table>