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Electronic Supplementary Information

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

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Experimental Details:

Calculation of the photothermal conversion efficiency[1]

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

$$\sum_i m_i C_i \frac{dT}{dt} = Q_{NP} + Q_{sys} - Q_{out} \quad (1)$$

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:

$$Q_{NP} = I(1 - 10^{-A_{808}})\eta \quad (2)$$

Where *I* is incident laser power in W, η 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:

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

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

When the system reaches a steady state temperature (T_{max}), the heat input and output are balanced:

$$Q_{NP}+Q_{sys} = Q_{out} = hS(T_{\max} - T_{surr}) \tag{4}$$

After the laser is removed, the $Q_{NP} + Q_{sys} = 0$, reducing the Eq. (1)

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

Rearranging the Eq. (5) would give

$$dt = -\frac{\sum_i m_i C_i}{hS} \frac{dT}{(T - T_{surr})} \tag{6}$$

And integrating, give the expression

$$t = -\frac{\sum_i m_i C_i}{hS} \ln \frac{T - T_{surr}}{(T_{\max} - T_{surr})} \tag{7}$$

A system time constant τ_s is defined as:

$$\tau_s = -\frac{\sum_i m_i C_i}{hS} \tag{8}$$

And ϑ is introduced using the maximum system temperature, T_{max}

$$\theta = \frac{T - T_{surr}}{(T_{\max} - T_{surr})} \tag{9}$$

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

$$t = -\tau_s \ln \theta \tag{10}$$

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

Since Q_{sys} can be obtained directly as

$$Q_{sys} = hS(T_{\max,H_2O} - T_{surr}) \tag{11}$$

Eq. (4) can be given as:

$$Q_{NP} = I(1 - 10^{-A_{808}})\eta = hS(T_{\max} - T_{\max,H_2O}) \tag{12}$$

Also

$$hS = -\frac{\sum_i m_i C_i}{\tau_s} \quad (13)$$

With τ_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/^{o}C. Substituting I = 2.0 W, A_{808} = 0.3910, T_{max} - T_{surr} = 20.8 ^{o}C into Eq. (12), the photothermal conversion efficiency can be determined to be 36.7%.

References

1. D. K. Roper, W. Ahn and M. Hoepfner, *J Phys Chem C Nanomater Interfaces*, 2007, **111**, 3636-3641.

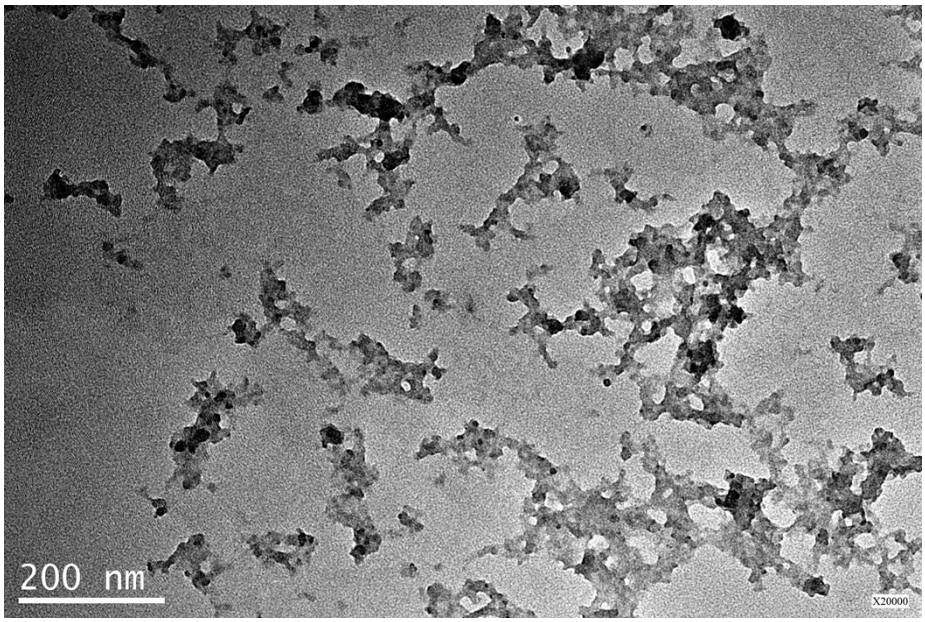

Fig. S1 TEM image of prepared insoluble PB NPs solid.

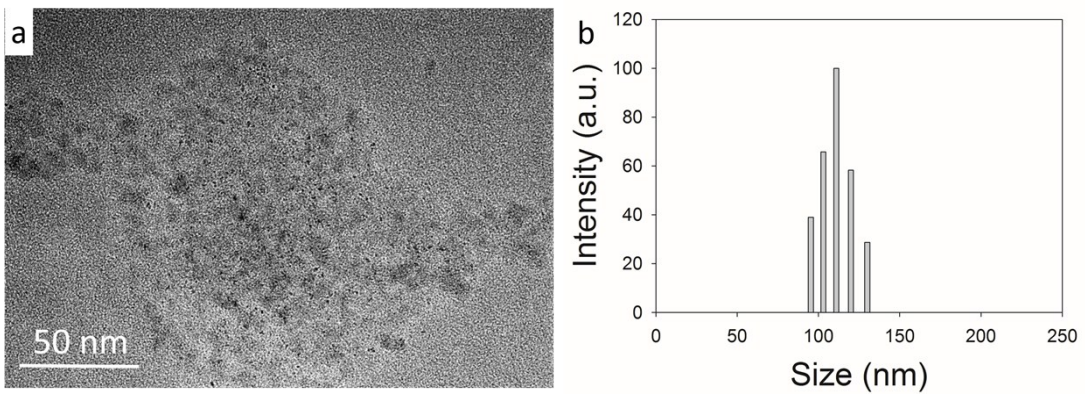

Fig. S2 Characterization of hydrophilic PEGylated PB NPs. a) TEM image; b) DLS diameter distribution.

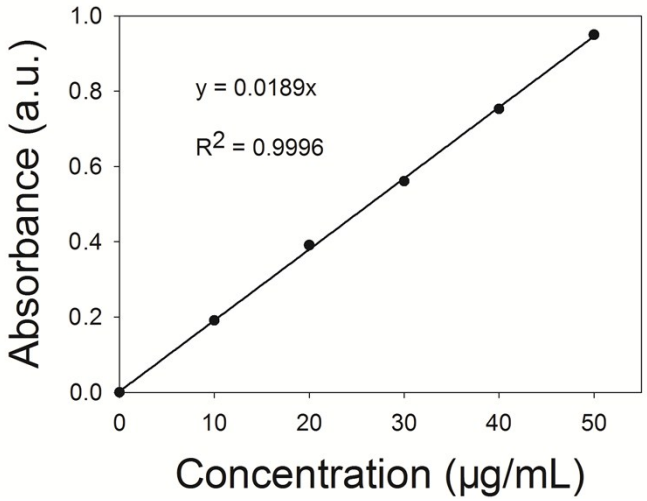

Fig. S3 The absorbance of PEGylated PB NPs at 808 nm increased as the concentration of PEGylated PB NPs increased.

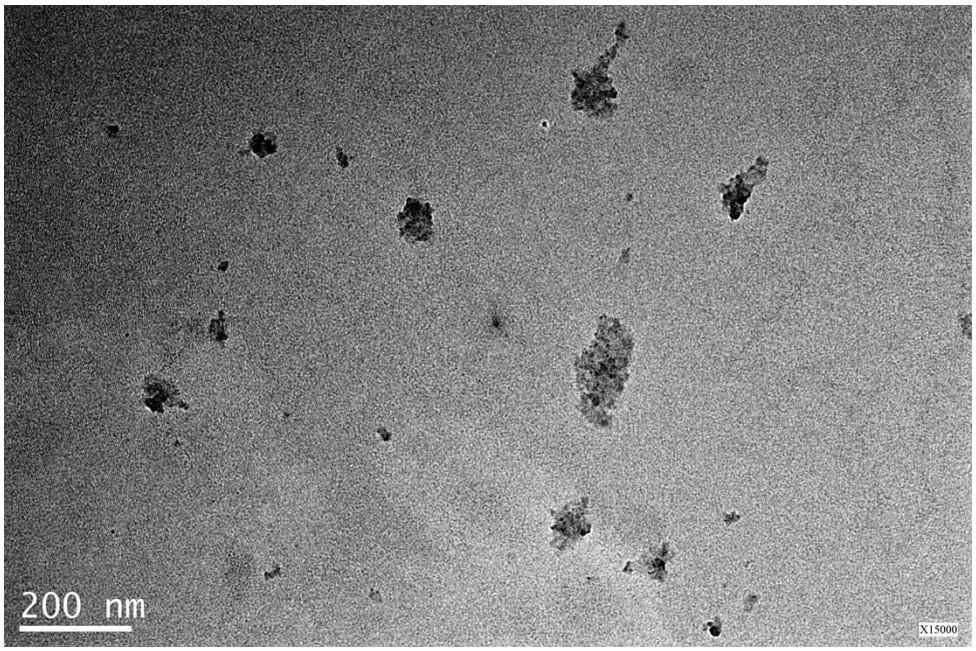

Fig. S4 TEM image of PEGylated PB NPs after five LASER ON/OFF cycles.

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

mass ratio (DOX : DSPE-PEG)	loading efficiency	loading content (DOX : DOX+NPs)	DLS Size
1:100	100%	1.0%	156.7 ± 36.1nm
1:50	100%	2.0%	140.5 ± 2.1nm
1:20	100%	4.8%	93.1 ± 37.0 nm
1:10	98%	9.2%	119.0 ± 30.5nm
1:5	95.5%	16.3%	116.1 ± 58.7nm
1:1	93.6%	48.8%	168.1 ± 70.9nm

Table S2 Model parameters for PEGylated PB-DOX NPs drug release simulation.

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