Electronic Supplementary Material

for

Transdermal delivery of multifunctional CaO_2@Mn-PDA nanoformulations by microneedles for NIR-induced synergistic therapy against skin melanoma

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Calculation of the photothermal conversion efficiency: The photothermal conversion efficiency of CaO_2@Mn-PDA NPs was calculated according to previous reports [1-4]. Detailed calculation was given as following:

The total energy balance of this system as following equation:

$$\sum_i m_i C_{p,i} \frac{dT}{dt} = Q_{NPs} + Q_s - Q_{loss} \quad (1)$$

where *m* and *Cp* are the mass and heat capacity, respectively. The suffix "*i*" of *m* and *Cp* refers to solvent(water) or dispersed matter (nanoparticles). *T* is the solution temperature.

Q_{NPs} is the photothermal energy input by CaO_2@Mn-PDA NPs.

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

where *I* is incident laser power, A_{808} is the absorbance of CaO_2@Mn-PDA NPs at the wavelength of 808 nm in aqueous solution, and η is the conversion efficiency from the absorbed light energy to thermal energy.

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

$$Q_{loss} = hA\Delta T \quad (3)$$

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

Q_s is the heat associated with the light absorbed by solvent per second. In the situation of heating pure water, the heat input is equal to the heat output at the maximum steady-statue temperature, so the equation can be:

$$Q_s = Q_{loss} = hA\Delta T_{max,H_2O} \quad (4)$$

Where is the temperature change of water at the maximum steady-state temperature.

As it to the experiment of CaO_2@Mn-PDA NPs dispersion, the heat input is equal to the heat output at the maximum steady-state temperature, that is:

$$Q_{NPs} + Q_s = Q_{loss} = hA\Delta T_{max,min} \qquad (5)$$

Where $\Delta T_{max,mix}$ is the temperature change of the CaO_2@Mn-PDA NPs dispersion at the maximum steady-state temperature. According to the equation 2, 4, and 5, the photothermal conversion efficiency (η) can be determined:

$$\eta = \frac{hA\Delta T_{max,min} - hA\Delta T_{max,H_2O}}{I(1-10^{-A_{808}})} = \frac{hA(\Delta T_{max,min} - \Delta T_{max,H_2O})}{I(1-10^{-A_{808}})} \qquad (6)$$

In this equation, only *hA* is unknown for calculation. In order to get the *hA*, here θ is introduced, which is defined as the ratio of ΔT to ΔT_{max}:

$$\theta = \frac{\Delta T}{\Delta T_{max}} \qquad (7)$$

Substituting equation7 into equation1:

$$\frac{d\theta}{dt} = \frac{hA}{\sum_i m_i C_{p,i}} \left[\frac{Q_{NPs} + Q_S}{hA\Delta T_{max}} - \theta \right] \qquad (8)$$

When the laser was shut off, the $Q_{NPs} + Q_s = 0$, equation8 could be expressed to:

$$dt = -\frac{\sum_i m_i C_{p,i}}{hA} \frac{d\theta}{\theta} \qquad (9)$$

Equation 9 changes the expression:

$$t = -\frac{\sum_i m_i C_{p,i}}{hA} \ln \theta \qquad (10)$$

Thus, *hA* can be determined by applying the linear time data from the cooling period vs–lnθ (Figure 1i). Substituting *hA* value into equation 6, the photothermal conversion efficiency (η) of Cu-PDA can be calculated.

The data involved in the calculation of the photothermal conversion efficiency are shown in

Table S1. Compared with solvents, the mass of NPs is too small. And the specific heat of water is higher than that of other materials. Therefore, the m_{NPs} and $C_{p,NPs}$ can be ignored. m_{H_2O} is 1×10^{-3} Kg. C_{p,H_2O} is 4.2×10^{3} J/(kg•°C). I is incident laser power (1.0 W/cm^2).

Table S1. Parameters of photothermal conversion efficiency

NPs	ΔTmax,mix (°C)	ΔTmax,H_2O (°C)	A808	hA (W/°C)	η (%)
CaO_2@Mn-PDA	26.5	2.6	0.5817	0.0186	37.50
CaO_2@PDA	21.4	2.6	0.5715	0.0170	27.20
PDA	30.3	2.6	0.5826	0.0176	41.11

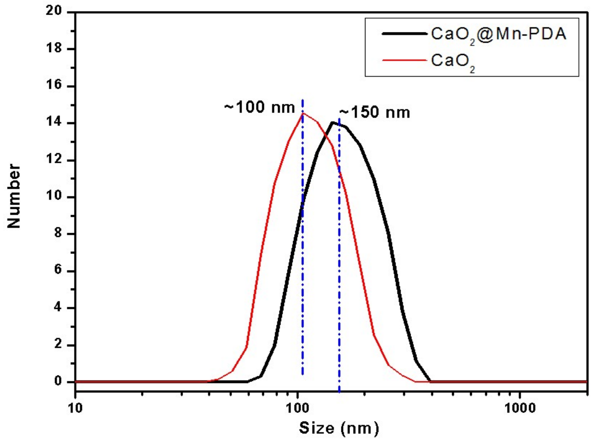

Fig. S1. Particle size distribution of CaO_2 and CaO_2@Mn-PDA measured by DLS.

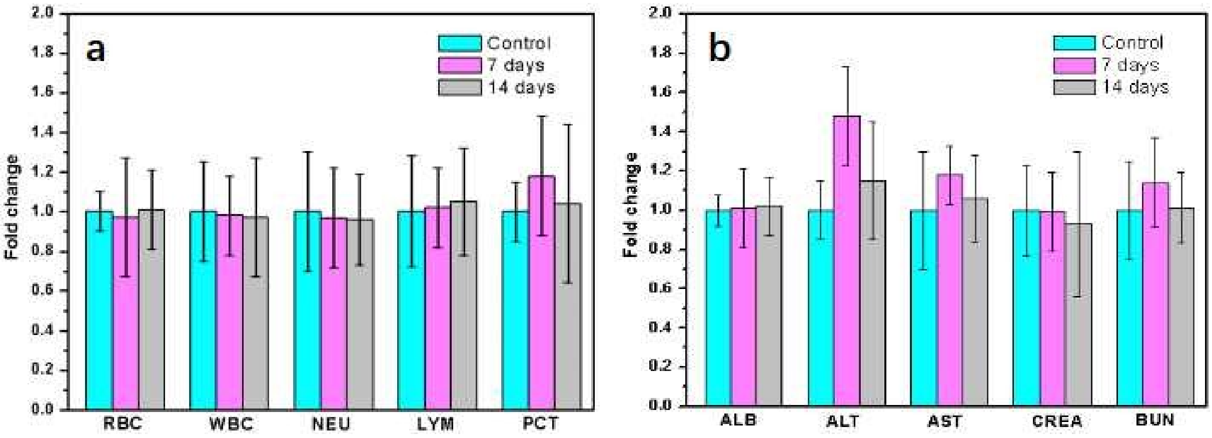

Fig. S2. The blood routine examination indexes (a) and blood biochemistry indexes (b) after application of Cu-PDA loaded MNs at 7th and 14th day, respectively.

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