Supporting information

Magnetically Triggered Drug Release from Biocompatible Microcapsules for Potential Cancer Therapeutics

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Materials

Doxorubicin (Dox), 3-Aminopropyltriethoxysilane (APTES), Triton X-100, ferric chloride, ferrous chloride and chloroform were purchased from Sigma (China). 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC) and 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC) were purchased from Avanti Polar Lipids (USA). Texas red-labeled 1,2-dihexadecanoyl-sn-glycero-3-phosphoethanolamine, triethylammonium salt (TR-DHPE), fluorescence-labeled 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine-N-(7-nitro-2-1,3-benzoxadiazol-4-yl)(NBD PE), 5-(6)-carboxyfluorescein (CF), calcein-AM and Propidium Iodide (PI) were all obtained from Invitrogen (China). Indium tin oxide (ITO, sheet resistance $\approx 8$ to 12 $\Omega/\Box$, thickness $\approx 160$ nm) electrodes were purchased from Hangzhou Yuhong technology co. Ltd. (China). D (+)-Sucrose and D (+)-Glucose were purchased from Xilong Chemicals (China). Ethanol, ammonium hydroxide, trisodium citrate and acetic acid were purchased from FuYu Chemicals (China). Millipore Milli-Q water with a resistivity of 18.0 M$\Omega$ cm was used for solution preparation in all experiments.

Synthesis and Modification of Magnetic Nanoparticles

A well-known method of coprecipitation of FeCl$_3$ and FeCl$_2$ in alkaline condition was described elsewhere.\textsuperscript{1} Briefly, 1.0 g of FeCl$_3$•6H$_2$O and 0.5 g of FeCl$_2$•4H$_2$O were dissolved in 35.0 mL pure water and stirred for 5 min at 80°C in a water bath. 5.0 mL 14.7 M NH$_3$•H$_2$O was then added at once into the solution and stirred for 30 min at 80°C. The citrate-coated or amino-coated MNPs were prepared by following steps respectively. In terms of citrate stabilized MNPs, 5.0 mL 0.2 g/mL trisodium citrate was added to above solution, and vigorously stirred at 95 °C for 90 min, followed by washing with pure water for three times.\textsuperscript{2} As for amino coated MNPs, the slurry of coprecipitation from the first step was added into 40.0 mL 10% (v/v) APTES solution, and stirred for 3h at 60°C at pH 4.0, followed by washing three times with pure water.\textsuperscript{3} Zeta potential measurements of these nanoparticles was finished using Malvern Zetasizer Nano ZSP (UK).

Figure S1
Fig. S1. Schematic illustration of the LMs electroformation setup. (a) Two ITO electrodes were separated by a PTFE spacer. (b) Side view of the LMs electroformation setup. Not to scale.

Figure S2

Fig. S2. (a) TEM images of citrate-coated (left) and APTES-coated (right) magnetic nanoparticles. The mean diameter of citrate-coated nanoparticles is about 10.2±2.1 nm, while it is about 12.0±2.3 nm of APTES-coated nanoparticles. (b) FTIR spectrum of citrate and APTES-coated Fe₃O₄ nanoparticles. The peaks in the red curve are attributed as below. The peak of 572 cm⁻¹ is the stretching vibration of Fe-O bonding, which is the characteristic absorption peak of Fe₃O₄; the peak of 1048 cm⁻¹ is the stretching vibration of Si-O-Si; the peaks of 2925 cm⁻¹ and 2852 cm⁻¹ are the asymmetric and symmetric stretching vibration of CH₂ respectively; the peak of 3432 cm⁻¹ is the stretching vibration of N-H. These absorption peaks indicate that the Fe₃O₄ surface was modified by silanization of APTES. The strong peaks of 1624 cm⁻¹ and 1390 cm⁻¹ in black curve are the asymmetric and symmetric stretching vibration of carbonyl, which indicates that the Fe₃O₄ surface was carboxyl. (c) X-ray powder diffraction pattern for citrate and APTES-
coated Fe₂O₄ nanoparticles. Peak positions and relative intensities recorded in the literature for bulk Fe₂O₄ samples are indicated by the vertical bars. All diffraction peaks can be exclusively indexed as cubic spinel Fe₂O₄ (JCPDS no. 19-0629) and no other impurities are observed. (d) Hysteresis loop of citrate and APTES-coated Fe₂O₄ nanoparticles at room temperature (300K). According to Fig. S2d, the saturation magnetization values of citrate and APTES-coated Fe₂O₄ nanoparticles are 62.8 and 60.7 emu g⁻¹, respectively. There was no hysteresis in the magnetization with both remanence and coercivity being zero, which proves that these magnetic nanoparticles are superparamagnetic.

**Figure S3**

Fig. S3 The histogram diagrams of carboxyl modified MLMs diameters distribution (a) and amino modified MLMs diameters distribution (b). The sample for the statistics was selected randomly and the sampling size was over 200 for each diagram.

**Figure S4**

Fig. S4. (a) The bright field microscope images of magnetic (carboxyl MNPs) DOPC LMs with (left) and without (right) an external magnetic field. (b) The bright field microscope images of magnetic (amino MNPs) DPPC LMs with (left) and without (right) an external magnetic field. Scale bar is 10 µm.

**Figure S5**
Fig. S5 (a) is the SEM image of DPPC MLMs loaded with Dox and amino MNPs. (b) and (c) are the AFM images of DPPC MLMs loaded with Dox and amino MNPs.

**Figure S6**

![Fluorescence images](image)

Fig. S6 Fluorescence images of DPPC MLMs loaded with Dox and amino MNPs as a function of time (a) without AMF (control) and (b) upon applying AMF (2 kHz, 20mT). These images were obtained by merging the images from FITC channel (for Dox) and rhodamine channel (for TR-DHPE). Scale bars are 10 µm in all images.

**Figure S7**

![TGA curve](image)

Fig. S7. TGA curves of magnetic lipid microcapsules

**Figure S8**

![Magnetic field](image)
Fig. S8. (a) The model of coils in the experiment and (b) magnetic field distribution in vertical direction of the centre area between the coils.

Fig. S8a is the diagram of coils in the experiment. Fig. S8b is the magnetic field intensity distribution in vertical direction of the centre area (diameter of 2 cm) between the coils. From the color change, it is noted that the field intensity is stronger in the centre of the coils than the edge area. The sample was put in the centre region to get uniform magnetic field.

**Figure S9**

![Graph](image)

Fig. S9. MTT assays of cell viability (24 h at 37 °C) with Dox loaded magnetic carriers and pure Dox as a function of Dox concentration. Data show the normalized mean and standard error of three independent experiments. AMF was applied for 5 minutes at 2 kHz and 20 mT.

**Table S1. The Input Parameters in the Simulations.**
<table>
<thead>
<tr>
<th>Material</th>
<th>Solution</th>
<th>$\text{Fe}_3\text{O}_4$</th>
<th>Cu</th>
<th>Air</th>
</tr>
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<tbody>
<tr>
<td>Density (g cm$^{-3}$)</td>
<td>1.0</td>
<td>5.18</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Conductivity (S m$^{-1}$)</td>
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<td>-</td>
<td>$5.998\times 10^7$</td>
<td></td>
</tr>
<tr>
<td>Relative permittivity</td>
<td>81.0</td>
<td>1.0</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Relative permeability</td>
<td>1</td>
<td>2300</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Convective heat transfer coefficient (W/m$^2$·K)</td>
<td>500</td>
<td>-</td>
<td>-</td>
<td>15</td>
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</table>

Reference: