Electronic Supplementary Information

Microcapsules: Incorporation of CdTe Quantum Dots, Fe_3O_4 Superparamagnetic Nanoparticles, and Tamoxifen Anticancer Drugs

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S1. Synthesis of Fe_3O_4 nanoparticles (NPs)

Superparamagnetic magnetite Fe_3O_4 NPs were prepared *via* a modified literature method.[R1a] Twenty-three mmol of $Fe(acac)_3$ (Fe(III)-acetylacetonate) was mixed in 10 mL phenyl ether containing 20 mmol of 1,2-hexadecanediol, 6 mmol of oleic acid, and 10 mmol of oleylamine under argon and was then heated to reflux for 30 min. After having been cooled to room temperature, the dark-brown mixture was treated with ethanol under air, and a dark-brown material was precipitated from the solution.

S2. Synthesis of CdTe quantum dots (QDs)

CdTe QDs were prepared *via* a modified literature method.[R1b] Cadmium precursors were prepared by adding 26 mg of cadmium oxide, 1.2 mL of oleic acid, and 20 mL of 1-octadecence to a three-neck flask clamped in a heating mantle. The mixture was heated to about 280°C under argon flow, resulting in a colorless clear solution which was then cooled to 200°C for reaction. At this temperature, 1 mL of the tellurium injection precursors, which were made by dissolving 42.2 mg of tellurium in 0.8 mL trioctylphosphine and diluted with 5 mL of 1-octadecence, was taken and quickly injected into this hot solution for 30 min. All steps in the reactions were carried out under an argon atmosphere.

S3. Fabrication of a polydimethylsiloxane (PDMS) Microfluidic Platform

The proposed concave mold of a microfluidic chip was laid out on a conventional polymethyl methacrylate (PMMA) substrate (length/width/depth: 88.0 mm/44.0 mm/1.5 mm) using a CO_2 laser machine (M300, Universal Laser System, USA). Fabricating a microchannel on a PMMA substrate by means of a laser machine is similar to using a laser printer to print a document. The epoxy was then injected into the PMMA concave mold. After 80 min at 100°C in an oven (OPO-45, CHENG SANG, Taiwan), the PMMA concave mold was turned over, creating an epoxy convex mold. This epoxy convex mold was then turned over and used as a PDMS concave mold. We then injected PDMS into the epoxy convex mold. After 40 min at 70°C the epoxy convex mold was turned over, and a concave mold of PDMS was obtained. The PDMS convex mold was the top layer of the proposed microfluidic chip. A flat PDMS structure was employed as the bottom layer of the proposed microfluidic chip. We coated a thin PDMS gel between the two layers followed by thermal bonding at 80 ± 5°C for 45 min. After natural annealing at room temperature, a PDMS microfluidic platform was created. The microchannel cross-junction in the vertical channel measured 1.5 mm and in the horizontal channel it measured 200 μm.

S4. Encapsulation of Tamoxifen, QDs and Magnetic NPs in PCL Microcapsules

A dispersed phase composed of polycaprolactone (PCL) (100 mg/mL), tamoxifen (30 mg/mL), CdTe QDs (3 mg/mL) and Fe_3O_4 NPs (20 mg/mL) in chloroform was prepared. A continuous phase composed of poly(vinyl alcohol) (PVA) (1% wt/v) in aqueous solution was also prepared. The dispersed phase and the continuous phase were connected to the microfluidic device using Teflon tubing (I.D. 0.76 mm, O.D. 1.22 mm, and 400 mm long) attached to syringes operated by two digital controlled syringe pumps (Kdscientific KDS230, USA) and were simultaneously introduced to the microfluidic chip. We can alter the composition of each PCL microcapsule by adjusting the concentration of Fe_3O_4 NPs, CdTe QDs, and tamoxifen in the dispersed phase because these materials can easily be dissolved in chloroform.

S5. *In Vitro* Drug Release Studies

Tamoxifen is an important anti-breast cancer drug in clinical use and has the potential to be used as a chemo-preventive breast cancer agent.[R2] The tamoxifen loaded PCL microcapsules were dispersed in a transport buffer at pH 7.4, which was used to simulate a physiological fluid. The buffer solution was kept in an orbital shaker (BT-350 PID, Yih Der Instruments, Taiwan) at constant gentle shaking of 100 rpm at 37 ± 0.5°C. At pre-determined time intervals, the suspensions were centrifuged at 3000 rpm for 3 min. The precipitated particles were re-suspended in fresh buffer and placed back into the shaker. The supernatant containing released tamoxifen was then analyzed by reverse-phase high-

performance liquid chromatography (RP-HPLC) to determine the percentage release of the tamoxifen from the PCL microcapsules. All samples were analyzed in triplicate. RP-HPLC was conducted with a LiChrosphere 100 RP-18 column (125×4 mm, Merck, Germany) and a Hitachi HPLC system (L7200, Hitachi, Japan). The mobile phase consisted of a mixture of methanol and triethylamine in a 95:5 ratio. The mobile phase was filtered and pumped at a flow rate of 1 mL/min. Elutions of tamoxifen were monitored by continuous measurement of absorbance at 265 nm. The retention times of tamoxifen were 4 ± 0.1 min, respectively. A standard curve was constructed for tamoxifen in the concentration range of 0.01-0.5 mg/mL with a good linear relationship (R^2= 0.9998).

S6. Characterization

A fluorescence microscope was used to collect data regarding the emission intensity from PCL microcapsules. The image and detection system consisted of an optical microscope (TE2000U, Nikon, USA) and a digital camera (Evolution color VF, Nikon, USA). The nanocrystal solutions were dropped onto copper grids with carbon support by slowly evaporating the solvent in the air at room temperature. The ultra-structure of the nanocrystals was examined using a transmission electron microscope (TEM, Philips, and Tecnai G2 20 S-TWIN) with LaB_6 type filament at an operating voltage of 200 kV. The sizes of the PCL microcapsules were measured from the optical microscope images using image analysis software (Scion). A total

of 100 particles were counted to ensure statistical representation of the PCL microcapsules size.

References:

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[R2] a) M. W. DeGregorio and V. J. Wiebe, in *Tamoxifen and Breast Cancer*, 2nd ed.; Yale University Press: New Haven, CT, 1999; b) A. S. Levenson and V. C. Jordan, *Eur. J. Cancer*, **1999**, *35*, 1628-1639.