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Supporting information

pH-responsive Nanocatalyst for Enhancing Cancer Therapy via H_2O_2 Homeostasis Disruption and Disulfiram Sensitization

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Contents

Materials

All of the chemicals were used without further purification. Anhydrous calcium chloride ($CaCl_2$), hydrogen peroxide (H_2O_2), zinc nitrate hexahydrate (Zn $(NO_3)_2 \cdot 6H_2O$, 99%), copper nitrate trihydrate (Cu $(NO_3)_2 \cdot 3H_2O$, 99%), disulfiram (DSF), and 2',7'-dichlorodihydrofluorescein diacetate (DCFH-DA) were purchased from China Aladdin Reagent Co., Ltd. Hyaluronic acid (HA), methanol, $NH_3 \cdot H_2O$, 2-methylimidazole (99%) and 3-aminotriazole (3-AT) were purchased from Tianjin Heowns Reagent Co.Ltd. Fetal bovine serum (FBS) was purchased from thermofisher Scientific (Waltham, USA). Methylene blue (MB), DTNB, rhodamine B (RB) and Titanic sulfate ($Ti(SO_4)_2$) were obtained from Macklin(Chian). Fluorescein diacetate (FDA) and propidium iodide (PI) probes were obtained from Dojindo (Shanghai, China). Thiazolyl blue tetrazolium bromide (MTT) was purchased from Merck. Annexin V-FITC apoptosis detection kit, DAPI staining solution, JC-1 and acridine orange (AO) were purchased from Beyotime (China). Trypsin-EDTA (0.05%) with phenol red, FBS and Gibco Dulbecco's Modified Eagle Medium (DMEM) cell culture medium were purchased from Merck. All other reagents were of analytical grade and used as received.

Cell lines

Murine breast cancer 4 T1 cells and mouse fibroblasts L929 cells were purchased from the Pricella (Wuhan, China) and cultured in DMEM containing 10% FBS and 1% penicillin-streptomycin solution at 37°C in a humidified atmosphere of 5% CO_2.

Animals

BALB/c female mice (8~9 weeks, 18~22 g) were provided by Provincial Center for Disease Control and Prevention (WuHan, China). All experimental procedures were carried out based on the protocols approved by the regulations on the management of animal rooms in the scientific experiment center.

Characterization

The size and zeta potential of different materials were measured using dynamic lig ht scattering (DLS, NanoZS90,MalvernLtd).The morphologies of samples were chara cterized by TEM (HT7700, Hitachi, Japan) and SEM (JSM6390LV).The elemental m apping images of nanoparticles were acquired using a JEM 2100 (JEOL) transmission electron microscope. UV–vis spectrophotometer (TU-1900) and fluorescence spectrophotometer (Hitachi F-7000) were used to obtain absorption and photoluminescence (PL) spectra, respectively. X-ray photoelectron spectrometry (XPS) assay was performed using a PHI 5000 VersaProbe (UIVAC-PHI, Japan) spectrometer. The Fourier transform infrared (FTIR) spectra of the samples through KBr pellet method were recorded using a Thermo Scientific Nicolet iS10 in the range of 4000-400 cm^{-1}. Nitrogen adsorption/desorption analysis was measured by Brunner-Emmet-Teller (BET) measurements (Micromeritics ASAP 2020, USA). The drug loading of DSF was investigated using an analytical high performance liquid chromatograph (HPLC, Shimadzu LC-20AD). Fluorescence microscopy images of the cells were obtained using an inverted fluorescence microscopy (IX73, Olympus, Japan). The in vivo imaging experiments were performed using an IVIS imaging system (PerkinElmer).

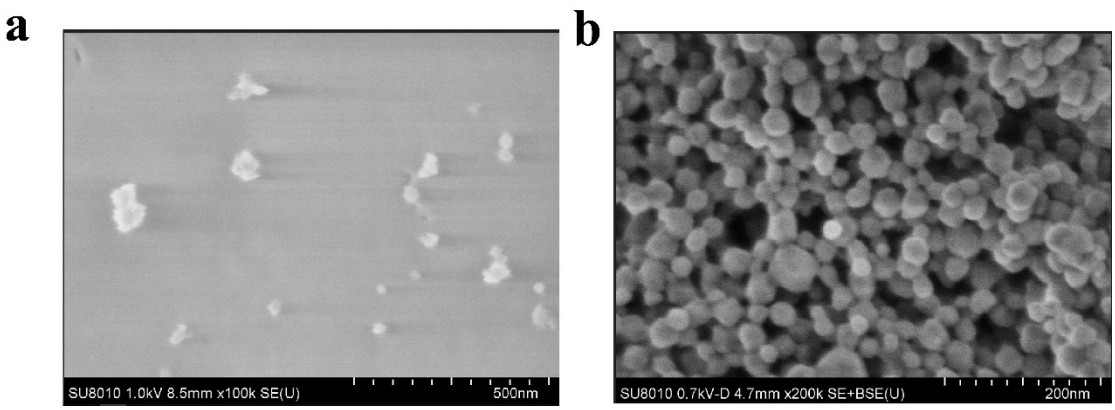

Fig. S1 SEM images of CaO_2 (a) and CaO_2@MAF(b).

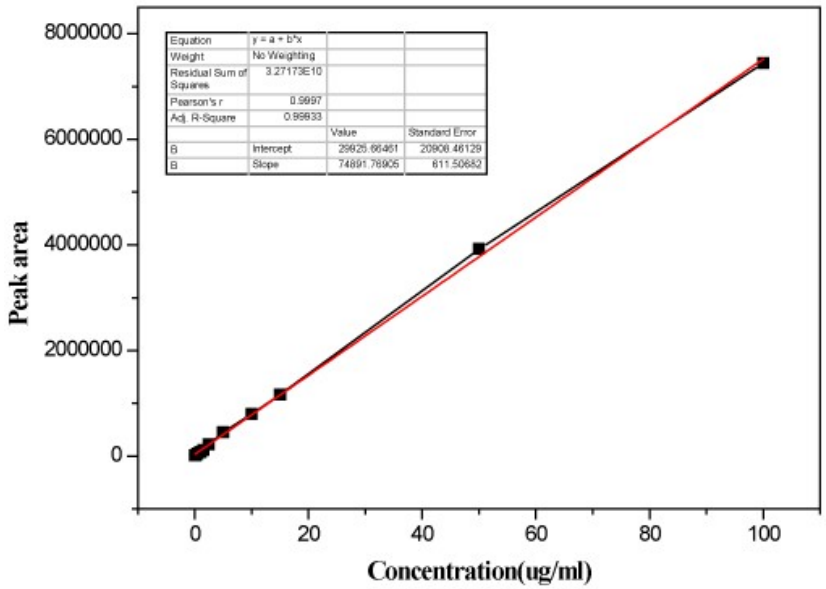

Fig. S2 Standard curve of DSF.

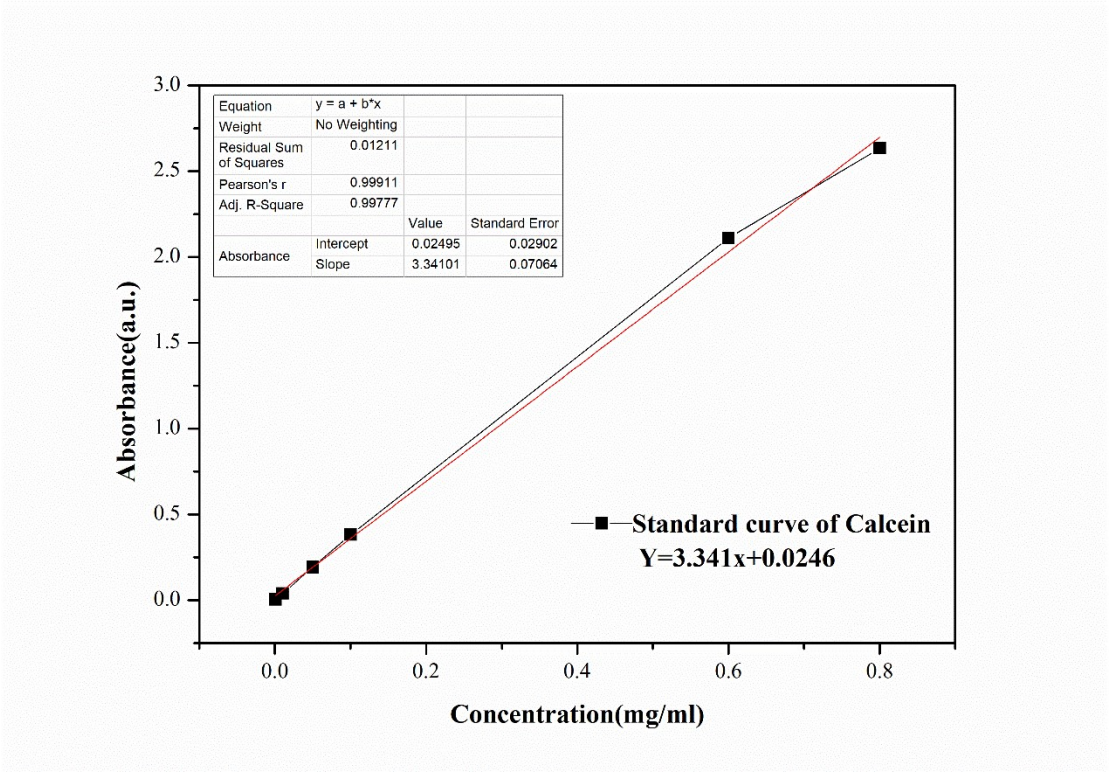

Fig. S3 Standard curve of calcein.

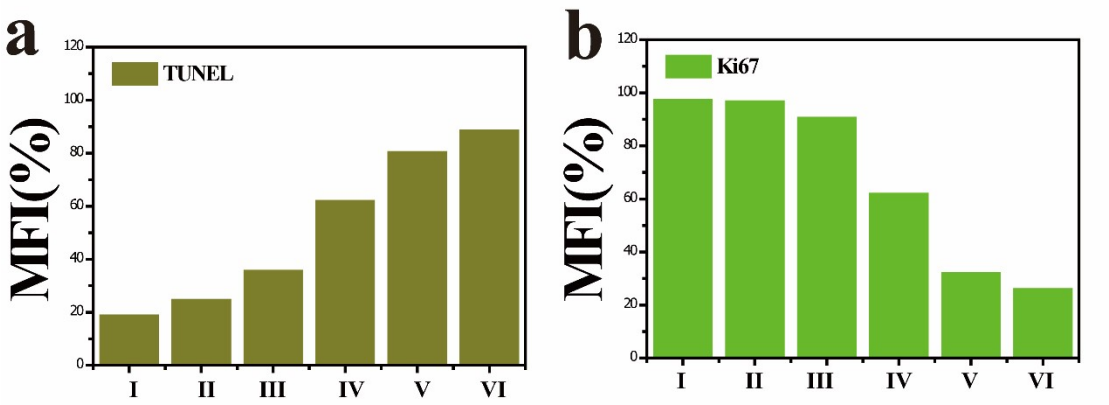

Fig. S4 Quantitative histogram of TUNEL (a) and Ki67 (b) staining results. (I: Control; II: DSF; III: CaO_2@ZIF-8@HA; IV: CaO_2@Cu/ZIF-8@HA; V: CMH; VI: CMDH)