# Supporting Information

# Duet of (–)-Epigallocatechin-3-Gallate and Doxorubicin Loaded by Polydopamine Coating ZIF-8 in Regulation of Autophagy for Chemo-Photothermal Synergistic Therapy

*Xuerui Chen,[1,3] Rongliang Tong,[2] Bingbing Liu,[1]Hua Liu,[2] Xiaode Feng,[2] Shiping Ding,[4] Qunfang Lei,[1] Guping Tang,[1] Jian Wu*[*,2] Wenjun Fang*[*,1]*

*1. Department of Chemistry, Zhejiang University, Hangzhou 310027, China*

*2. Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310003, China.*

*3. Medical School of Shanghai University (in preparation), Shanghai University, Shanghai 200444, China.*

*4. The National Education Base for Basic Medical Sciences, Zhejiang University School of Medicine, Zhejiang University, Hangzhou 310058, China.*

# Table of Contents

# Experimental Details

### Synthesis of ZIF-8

0.20 g (0.66 mmol) of $Zn(NO_3)_2 \cdot 6H_2O$ was dissolved in 0.8 mL of methanol. Then, 10.00 mL of 2-methylimidazole (24.36 mmol) solution was added dropwise. They were stirred for 15 min. The product was collected by centrifugal separation and washed at least three times with mixture of alcohol and pure water. The powder products (ZIF-8 NPs) were dried at 51 $^{o}$C under vacuum.

### Synthesis of EGCG@ZIF-8

0.2 g (0.66 mmol) of $Zn(NO_3)_2 \cdot 6H_2O$ was dissolved in 0.8 mL methanol. 4 mL of EGCG stock solution (10 $mg \cdot mL^{-1}$) was added into the $Zn(NO_3)_2$ solution under nitrogen atmosphere. After stirred for 5 min, 10 mL of 2-methylimidazole (24.36 mmol) solution was added dropwise. They were stirred for 15 min. The product was collected by centrifugal separation and washed at least three times with mixture of alcohol and pure water. The powder products (EGCG@ZIF-8 NPs) were dried at 51 $^{o}$C under vacuum.

### Synthesis of EZP

The synthesized EGCG@ZIF-8 was dispersed in a mixture solution of ethanol and the deionized water, then tetradecanol ethanol solution was put in the solution and stirred for 3 min. The EGCG@ZIF-8 was completely mixed in the solution of tetradecanol, and then EGCG@ZIF-8/ tetradecanol was synthesized. Because the

tetradecanol has a hydrophilic head and a hydrophobic tail chain, which allows it to act as a surfactant and readily compatible with both hydrophilic and hydrophobic chemicals. In this case, $NH_3 \cdot H_2O$ was added to make it into an alkaline conditions, continued to add dopamine in the solution to form a shell for the EGCG@ZIF/PDA. Then followed by washing with deionized water several times, the precipitates were the product EGCG@ZIF/PDA nanocomposites which were denoted as EZP.

**Intracellular ROS Quantification by flow cytometer and fluorescence microscope**

Dichlorofluorescein-diacetate (DCFH-DA) was used as the fluorescent probe to detect the level of intracellular ROS. $1 \times 10^6$ Hela cells were cultured in a six-well plate and were treated with EGCG, EGCG@ZIF-8 for 24 h, respectively. Cells were trypsinized and collected by centrifugal separation, then incubated with 10 $mmol \cdot L^{-1}$ DCFH-DA for 15 min at 37 °C. Subsequently, cells were washed twice with PBS and analyzed by a flow cytometer. Meanwhile, the levels of intracellular ROS were also determined by a fluorescence microscope (Nikon, Japan).

# Figures and Tables

**Table S1** In vivo cytotoxicities and combination index (CI)[a] of different treatment formulations against HeLa cells for 24 h incubation.

| Formulations | $IC_{50}$DOX/($\mu g \cdot mL^{-1}$) | $IC_{50}$EGCG/($\mu g \cdot mL^{-1}$) | $CI_{50}$ |
|---|---|---|---|
| Free DOX | 57.677 | | |
| Free EGCG | | 19.543 | |
| EZPPD+NIR | 3.5466 | 10.115 | 0.43977 |

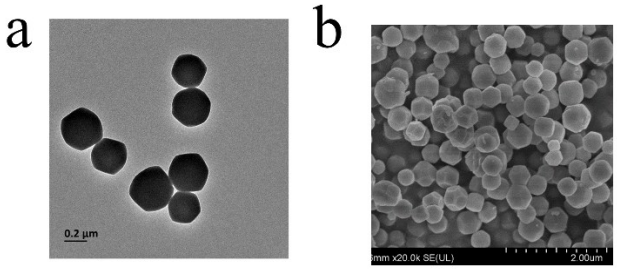


**Figure S1** (a) TEM image of ZIF-8 NPs; (b) SEM image of ZIF-8 NPs.

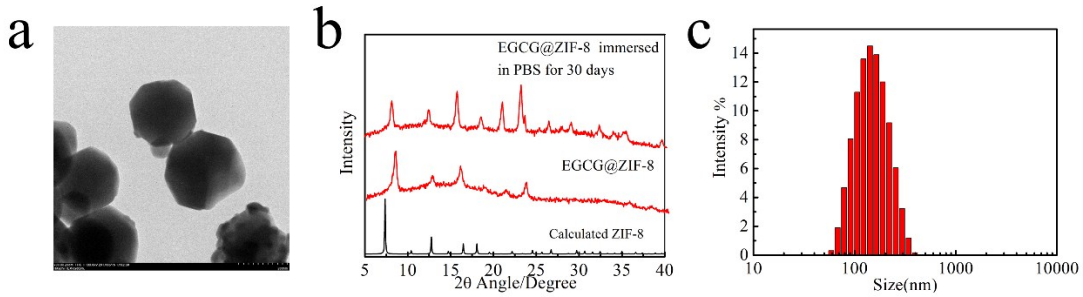


**Figure S2** (a) TEM image of EGCG@ZIF-8 immersed in PBS (pH =7.4) for one month; (b) PXRD patterns of EGCG@ZIF-8 NPs and EGCG@ZIF-8 NPs immersed in PBS of pH 7.4 for 30 days; (c) Representative particle size distribution of EGCG@ZIF-8 NPs immersed in PBS of pH 7.4 for 30 days determined by DLS.

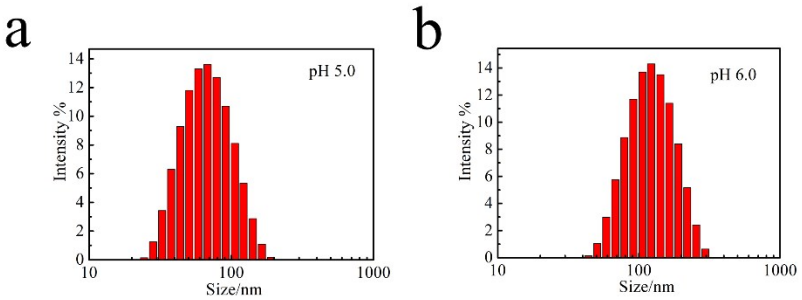


**Figure S3** Representative particle size distribution of EGCG@ZIF-8 NPs in the PBS of pH 5.0 (a) and pH 6.0 (b) for 12 h determined by DLS.

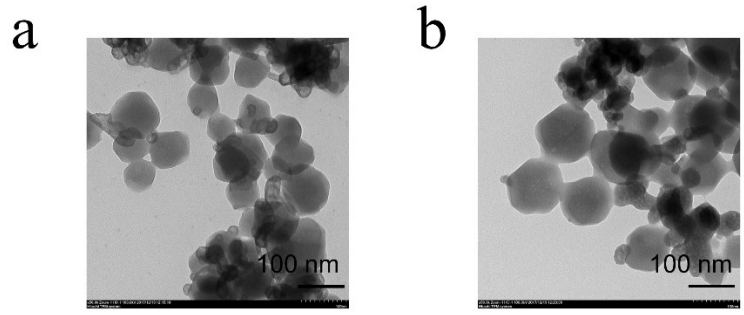


**Figure S4** TEM image of EGCG@ZIF-8 immersed in PBS of pH 5.0 (a) and pH 6.0 (b) for 12 h.

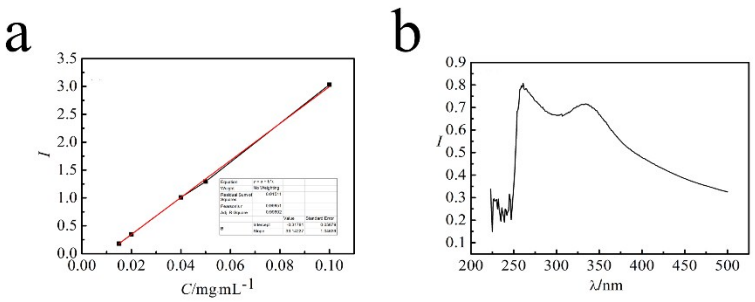


**Figure S5** (a) The relationship between absorbance and EGCG concentration calculated by standard curve; (b) the UV-Vis spectra of EGCG@ZIF-8 NPs dissolved in 1 mol·L$^{-1}$ HCl and diluted by ultrapure water.

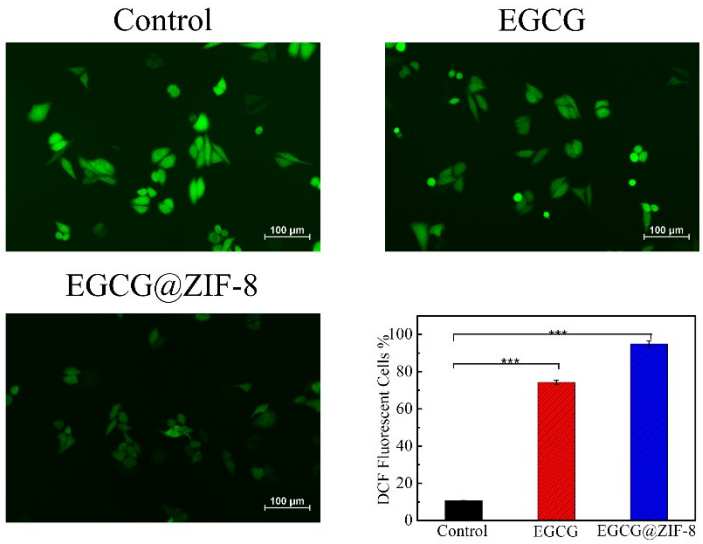

**Figure S6** Intracellular ROS generation of HeLa cells incubated with EGCG@ZIF-8 NPs or EGCG for 12 h detected by flow cytometry and fluorescence microscope.

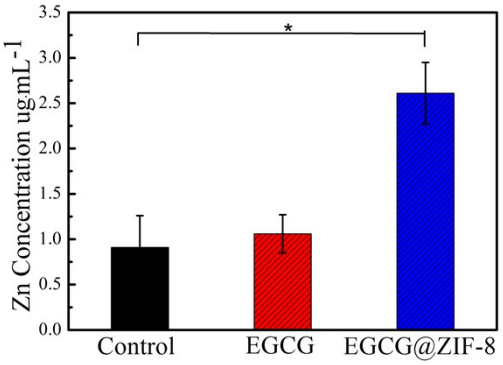


**Figure S7** Cellular uptake of EGCG@ZIF-8 NPs. Zn concentration of cells incubated with EGCG@ZIF-8 NPs (20 μg·mL$^{-1}$) and EGCG (10 μg·mL$^{-1}$) for 24h.

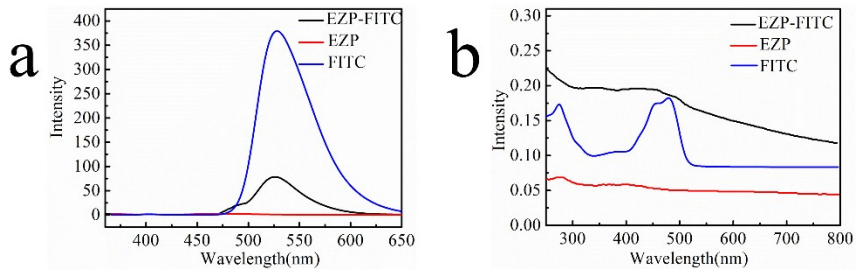


**Figure S8** (a) Fluorescence emission spectra of EZP-FITC, EZP and FITC at λex=350 nm; (b) The UV/Vis spectra of EZP-FITC, EZP and FITC.