Supporting Information

Engineering Multifunctional Coatings on Nanoparticles Based on Oxidative Coupling Assembly of Polyphenols for Stimuli-Responsive Drug Delivery

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Experimental

1. Materials

Zein (Z0001) was purchased from Tokyo Chemistry Industry, Co., Ltd. (Tokyo, Japan). Tannin acid (TA) was purchased from Aladdin Chemistry Co., Ltd. (-)-epigallocatechin-3-gallate (EGCG) was purchased from Xi'an Natural Field Bio-Technique Co., Ltd. (Xi'an China). Persimmon tannin (PT, 98.7% purity) was kindly provided by Shanghai Ocean University composed of polymers ranging from 7 to 20 kDa. 3-(N-morpholino)-propanesulfonic acid (MOPS) was obtained from the Sinopharm Chemical Reagents Co., Ltd. (Shanghai, China).

2. Preparation and characterization of polyphenol-coated zein NPs

All solutions were freshly prepared for immediate use. The standard preparation process was described as follows: zein was dissolved in aqueous ethanol solutions (75% v/v) to obtain a stock solution with final concentration of 10 mg/mL. Then 0.5 mL zein solution was added to 9.5 mL of MOPS buffer (10 mM, pH 7.8). Next, different volume (40 μL, 60 μL, 80 μL or 100 μL) of TA solution (24 mM) was added and the dispersion was under vigorous stirring for 1 h at room temperature. The product was then purified by successive dialysis (MWCO 3500) against deionized water for 48 h to remove the free TA. Then 200 μL of $HAuCl_4$ aqueous solutions (10 mM) was added in the zein-TA solution to observe the metallization of gold.

UV-vis spectroscopy: The UV-vis absorption spectra of polyphenol-coated zein NPs solutions were measured on a spectrophotometer (UV-1100, MAPADA).

Table S1. Characterization of NPs (pH 7.4), the results were displayed as the mean ± standard deviation (n=3).

Samples	size, nm	PDI	zeta potential, (mV)
zein	89.2±1.2	0.15±0.04	-25.2±1.6
zein/TA_1	66.9±0.6	0.21±0.01	-35.1±0.5
zein/TA_2	76.0±1.5	0.22±0.02	-37.9±0.7
zein/TA_3	85.4±1.4	0.25±0.01	-38.6±0.3
zein/TA_4	85.2±1.8	0.24±0.02	-40.4±1.6

zein represented zein nanoparticles; zein/TA_1, zein/TA_2, zein/TA_3 and zein/TA_4 represented TA-coated zein nanoparticles with TA volume of 40, 60,80 and 100 μL respectively.

Table S2. IC_{50} Values for DOX or DOX-loaded NPs against HeLa cells.

Samples	Cell	IC_{50} (μg/mL)
DOX	HeLa	0.918±0.05
DOX-zein	HeLa	0.939±0.04
DOX-zein/TA	HeLa	1.087±0.02**
DOX- zein/EGCG	HeLa	0.941±0.02
DOX-zein/PT	HeLa	1.192±0.03**

DOX represented free doxorubicin; DOX-zein represented DOX loaded zein nanoparticles; DOX-zein/TA, DOX-zein/EGCG and DOX-zein/PT represented DOX-loaded TA/EGCG/PT-coated zein nanoparticles with TA/EGCG/PT volume of 60 μL. Data displayed as mean±SD (n=3). *$p < 0.05$; **$p < 0.01$; versus DOX group.

Table S3. Characterization of NPs or DOX-loaded NPs (pH 7.4), the results were displayed as the mean ± standard deviation (n=3).

Samples	size, nm	PDI	zeta potential, (mV)	encapsulation efficiency (%)
zein/EGCG	67.9±1.1	0.25±0.02	-37.5±1.6	-
zein/PT	96.4±1.0	0.27±0.01	-38.3±0.9	-
DOX- zein/EGCG	95.3±1.6	0.12±0.03	-32.9±0.7	85.3±0.4
DOX-zein/PT	120.1±3.1	0.18±0.01	-32.3±1.2	95.7±0.6

zein/EGCG and zein/PT represented EGCG/PT-coated zein nanoparticles with EGCG/PT volume of 60 μL. DOX-zein/EGCG and DOX-zein/PT represented DOX-loaded EGCG/PT-coated zein nanoparticles with EGCG/PT volume of 60 μL.

Figure S1

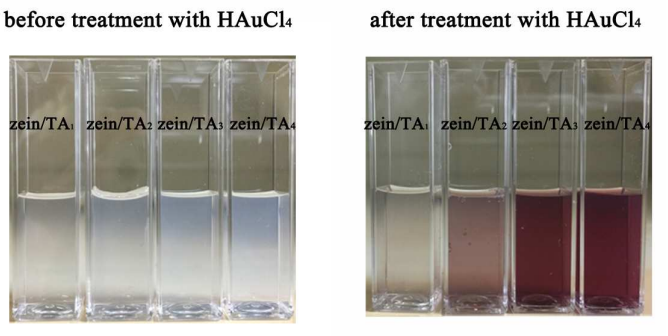

Figure S1. Photographs of zein/TA_1, zein/TA_2, zein/TA_3 and zein/TA_4 NPs before (left) and after (right) treatment with aqueous $HAuCl_4$.

Figure S2

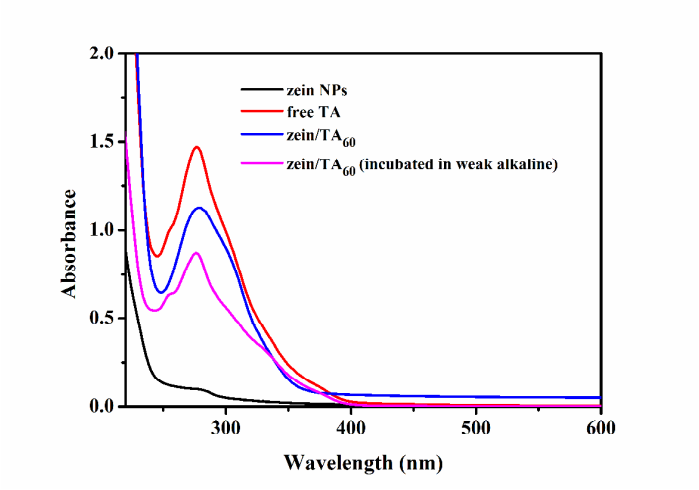

Figure S2. UV-vis spectra of zein NPs, free TA, zein/TA_1 NPs without incubation, zein/TA_1 NPs incubated in weak alkaline.

Figure S3

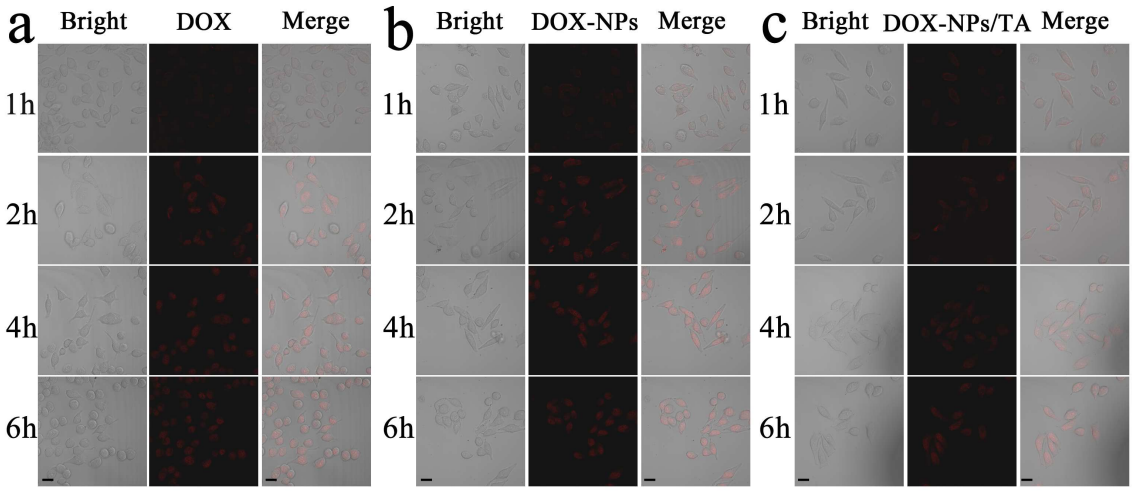

Figure S3. CLSM images of intracellular uptake of free DOX (a), DOX-loaded zein NPs (b) and DOX-loaded zein/TA NPs (c) by HeLa cells with DOX concentration of 1.0 μg/mL. The scale bars represented 20 μm.

Figure S4

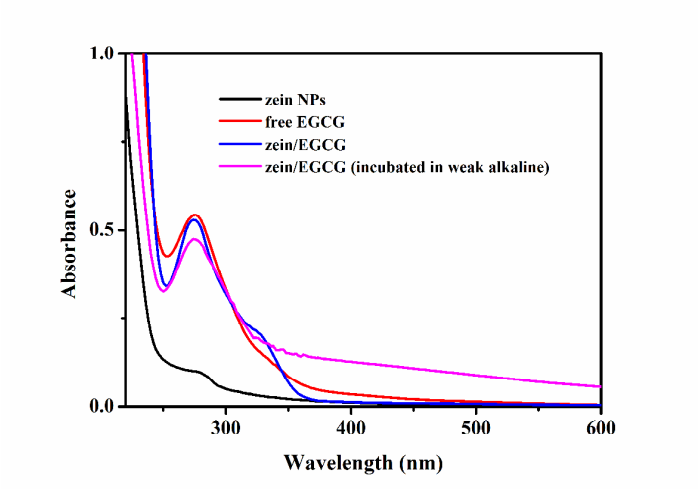

Figure S4. UV-vis spectra of zein NPs, free EGCG, zein/EGCG NPs without incubation, zein/EGCG NPs incubated in weak alkaline.

Figure S5

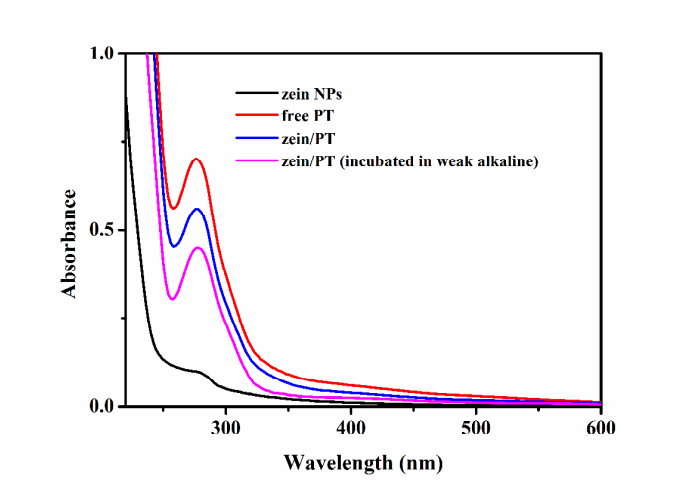

Figure S5. UV-vis spectra of zein NPs, free PT, zein/PT NPs without incubation, zein/PT NPs incubated in weak alkaline.

Figure S6

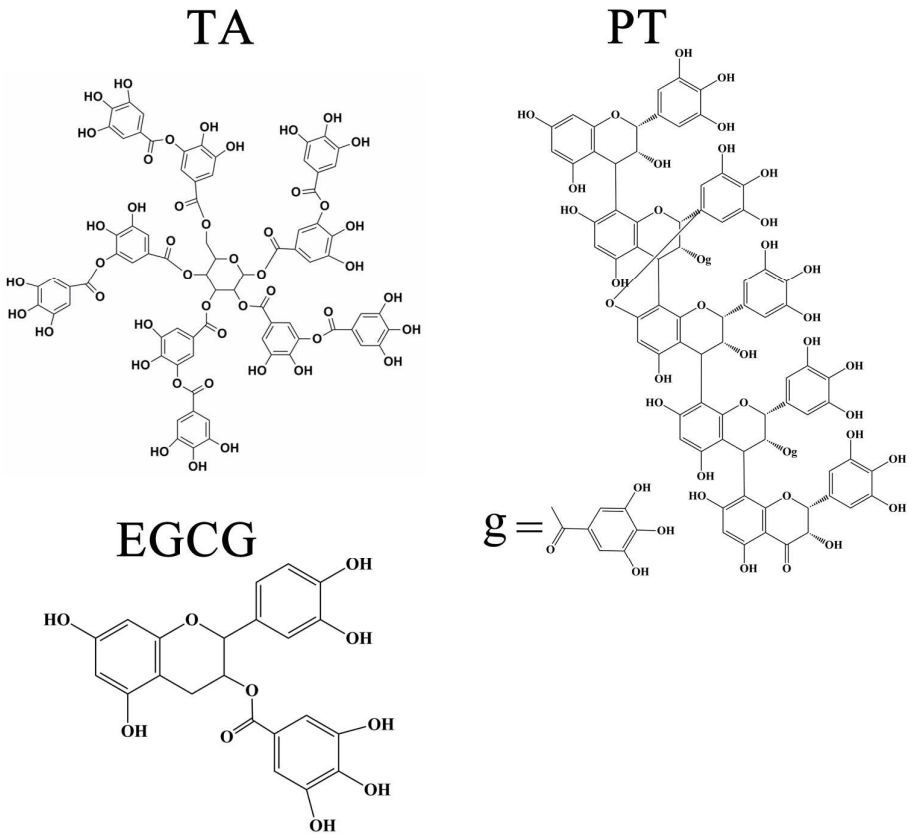

Figure S6. Chemical structure of TA, EGCG and PT.