

## Supporting Information

# Tellurium-Containing Nanoparticles for Controlled Delivery of Cisplatin Based on Coordination Interaction

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## 1 EXPERIMENTAL SECTION.

### 1.1 Materials.

N,N'-Carbonyldiimidazole (CDI), 8-bromooctanoic acid was the products of TCI. Tellurium powder was obtained from Aladdin chemical company. Sodium borohydride was purchased from Alfa-aesar. Cisplatin and triethylene glycol monomethyl ether were from Sigma-Aldrich. All the other chemicals and solvents were used as received unless otherwise stated.

### 1.2 Methods.

The  $^1\text{H}$  NMR spectra and  $^{13}\text{C}$  NMR spectra were measured on a Bruker AVANCE III HD 400 (400 MHz). While  $^{125}\text{Te}$  NMR spectra were recorded on a JEOL JNM-ECA 600 (600 MHz) spectrometer.

The TEM images were obtained by a JEM-2010 Microscope with an accelerating voltage of 80 kV. Samples were prepared by drop-coating the aqueous solution on the carbon-coated copper grid for 10 min and then observed without staining. DLS measurements were performed by a Malvern ZEN3690 Zetasizer at 25 °C. ESI-mass was carried out on a LTQ LC/MS apparatus.

**Synthesis of TeCOOEG.** The telluride containing compound was synthesized according to the synthetic procedure in Figure S 1. Briefly, 8-bromooctanoic acid was dissolved in anhydrous DCM and stirred with 1.2 equiv CDI for 30 min. Then triethylene glycol monomethyl ether of 1.3 equiv was added via a syringe and stirred for 3 h under room temperature. Then the reaction was concentrated under reduced pressure and then washed in sequence with 3 M HCl, 1 M  $\text{NaHCO}_3$ , and 0.5 M NaCl aqueous solutions. Colorless viscous liquid was obtained as Compound 1 after rotary evaporation. Yield: 60%.

Disodium telluride was prepared by the reaction of Te powder and excess amount of sodium borohydride in water under the protection of nitrogen at 50 °C. Compound 1 in THF was added under  $\text{N}_2$  flow at 50 °C for 6 h. Products were purified by filtration and extraction. Light yellow liquid was generated at a yield

of 55%.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , 298 K)  $\delta$  (ppm): 4.25(4H, t,  $\text{CH}_2\text{OCO}$ ), 3.72-3.58(20H, m,  $\text{CH}_3\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCO}$ ), 3.41(4H, s,  $\text{OCH}_3$ ), 2.64(4H, t,  $\text{TeCH}_2$ ), 2.35(4H, t,  $\text{CH}_2\text{COOH}$ ), 1.75-1.25(20H, m,  $\text{OOCCH}_2(\text{CH}_2)_5\text{CH}_2\text{Te}$ ).  $^{13}\text{C}$  NMR (400MHz,  $\text{CDCl}_3$ , 298 K),  $\delta$  (ppm): 173.8 (1C, s,  $\text{COOCH}_2$ ), 71.9-63.4(6C, m,  $\text{CH}_3\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCO}$ ), 59.1(1C, s,  $\text{OCH}_3$ ), 34.2-24.8 (6C, m,  $\text{OOC}(\text{CH}_2)_6\text{CH}_2\text{Te}$ ), 2.7 (1C, s,  $\text{TeCH}_2$ ).

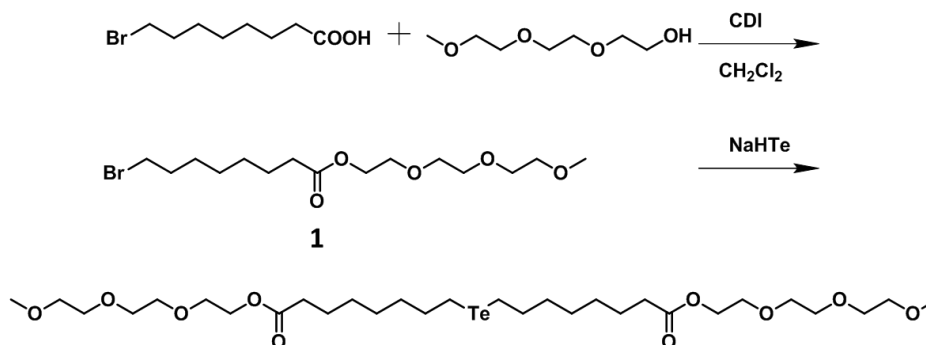


Figure S 1 . The synthetic routes of the TeCOOEG.

### ***In vitro* cell cytotoxicity experiments.**

HepG2 cells were cultured in Dulbecco's modified Eagle's medium (DMEM) (SH30022.01B; Thermo Inc., Bremen, Germany), supplemented with 10 % fetal bovine serum at 37 °C in a humidified atmosphere containing 5%  $\text{CO}_2$ . Cells were seeded into 96-well plates at a density of 5000 cells per well. 12 h after seeding, the cells were treated with various drug formulations for up to a further 24 h. Cell viability was evaluated using a CCK-8 assay according to the manufacturer's instructions (Dojindo, Japan).

**Imaging of Tumor Cells *in Vitro*.** HepG2 cells were seeded onto a 35 mm borosilicate chambered cover glasses (Nunc, USA.) at a density of  $2 \times 10^5$  cells/well and grown at 37 °C for 12 h. After treatment with cisplatin or cisplatin-loaded nanoparticles for 3 h, the HepG2 cells were washed three times with PBS and incubated with DCFH-DA (10 mm; Sigma, USA) at 37 °C for 20 min. The fluorescence intensities were measured by using a LSM 710 confocal microscope (Carl Zeiss, USA) at 40 $\times$  magnification.

### ***In vivo* antitumor activity assay.**

Tumor xenografts were formed in female BALB/C nude mice by injecting  $5 \times 10^6$  HepG2 cells into the right flank (4 mice/group). When the tumor volume reached 60-70  $\text{mm}^3$ , various drug formulations (Saline, cisplatin, cisplatin-loaded nanoparticles) were injected intravenously every three or four days. The



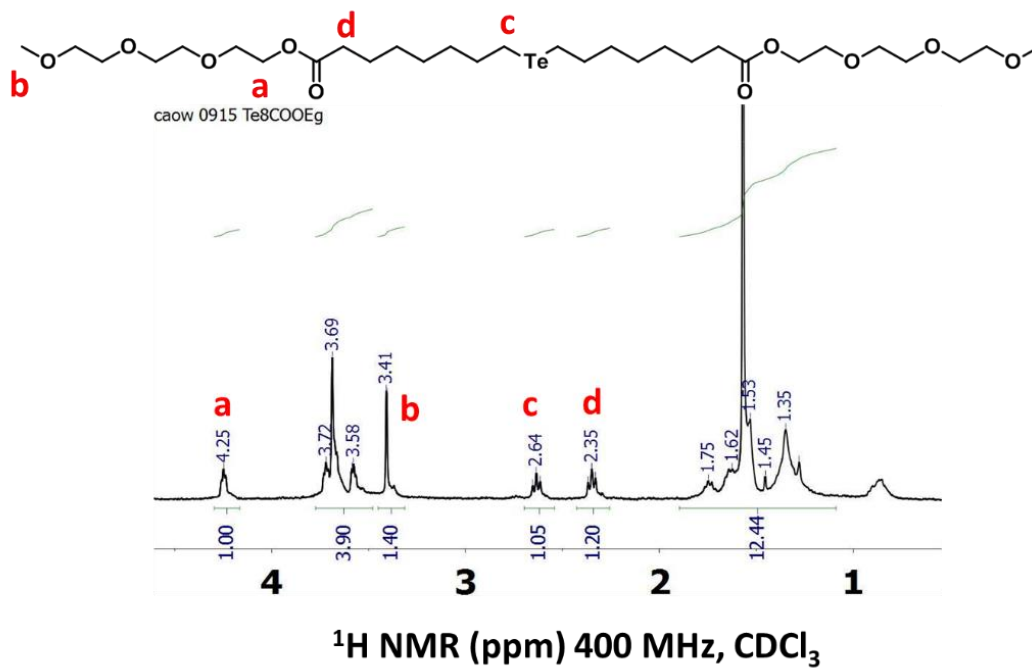


Figure S 3 <sup>1</sup>H NMR spectrum of TeCOOEG. Solvent: CDCl<sub>3</sub>.

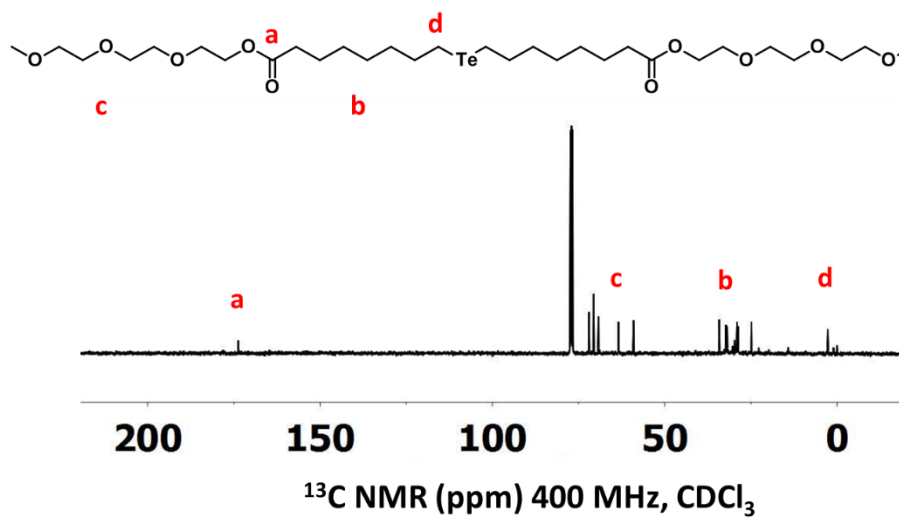


Figure S 4 <sup>13</sup>C NMR spectrum of TeCOOEG. Solvent: CDCl<sub>3</sub>.

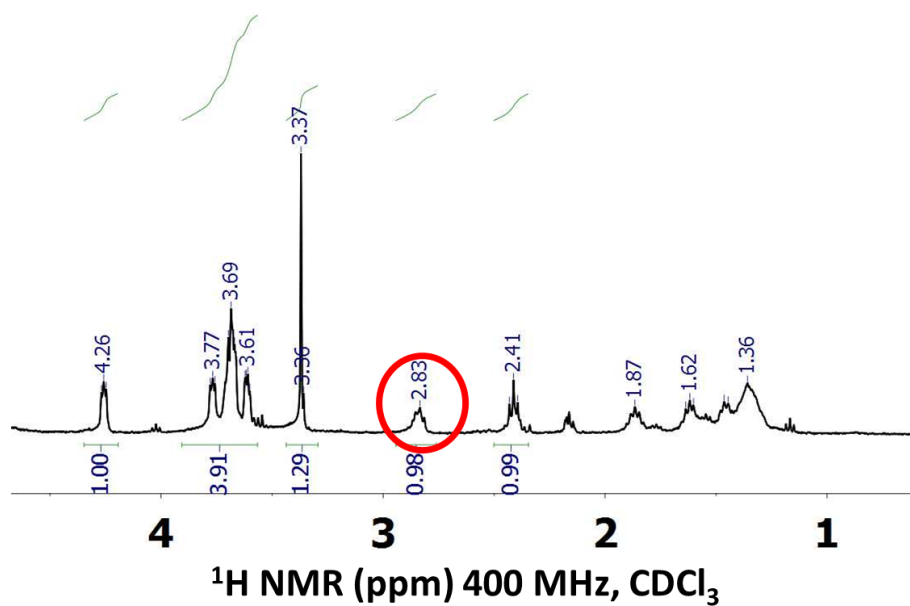


Figure S 5  $^1\text{H}$  NMR spectrum of TeCOOEG after coordination. Solvent:  $\text{CDCl}_3$ . After coordination, the chemical shift of  $\alpha$  proton of tellurium atom in TeCOOEG shifted from 2.64 to 2.83 ppm.

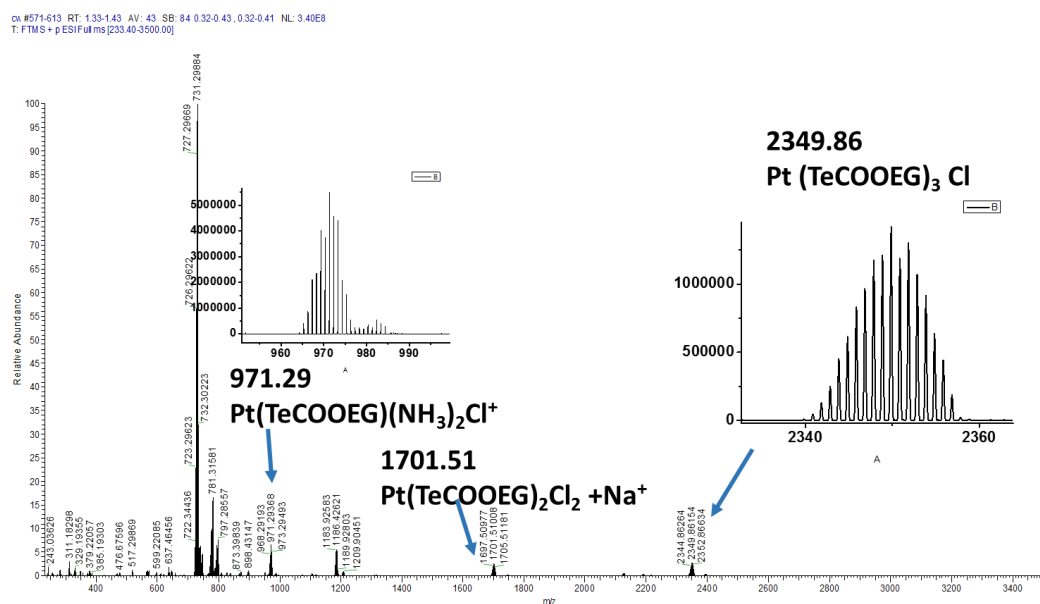


Figure S 6 ESI MS of TeCOOEG/cisplatin coordination complex.

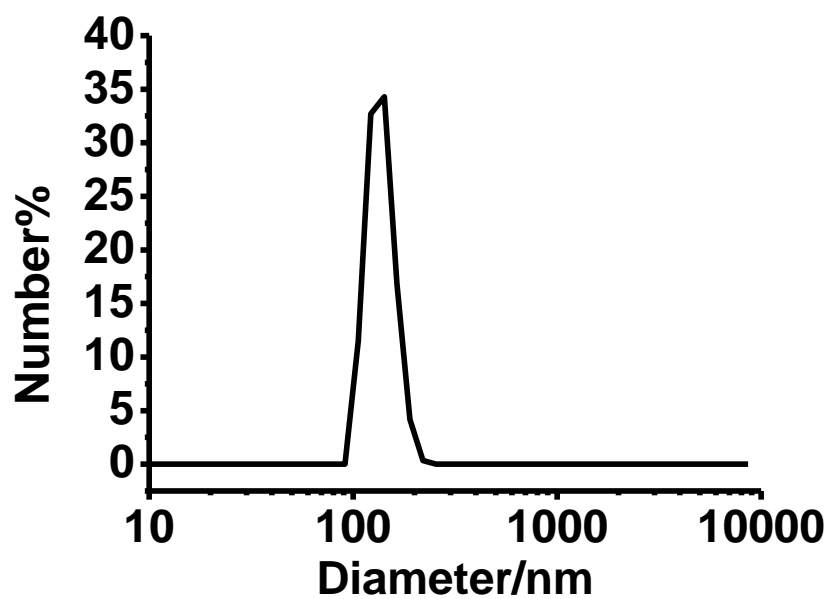


Figure S 7 DLS result of TeCOOEG nanoparticles. The hydrodynamic diameter was about 120 nm.

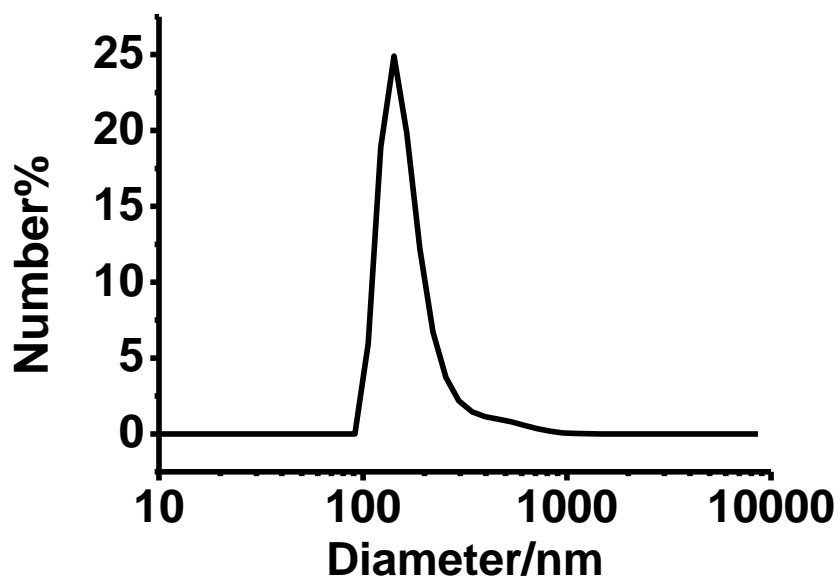


Figure S 8 DLS measurement of cisplatin-loaded nanoparticles showed the hydrodynamic diameter was about 140 nm.

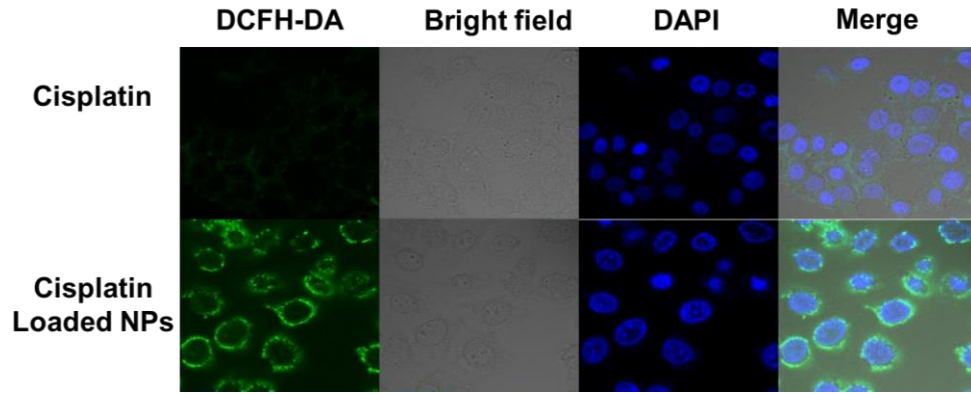


Figure S 9 Fluorescent micrograph study based on dichlorofluorescein diacetate on HepG2 cells.

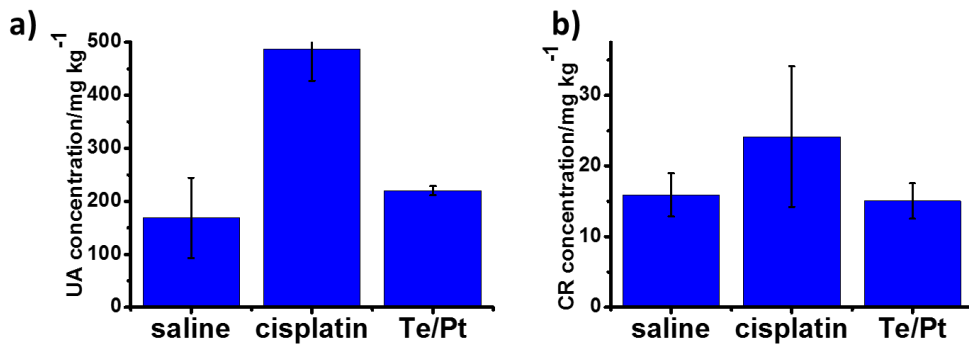


Figure S 10 Serum biochemical parameters of healthy BALB/c mice. UA, Uric Acid. CR, creatinine after i.v. injection of saline, cisplatin and the cisplatin-loaded nanoparticles.

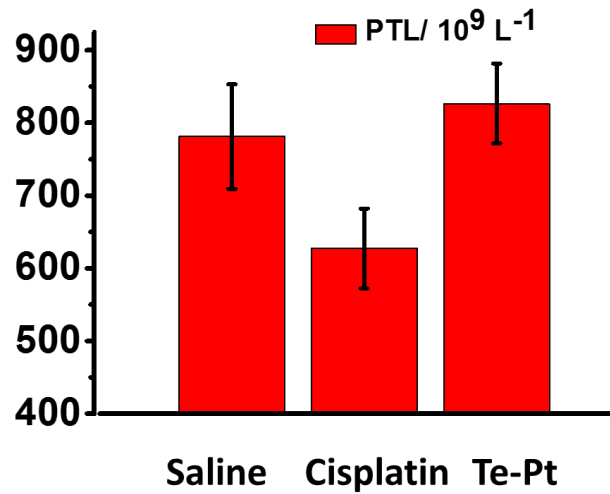


Figure S 11 The side effects of cisplatin and the cisplatin-loaded nanoparticles on PTL.