Coordination-responsive Selenium-containing Polymer Micelles for Controlled Drug Release

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Supporting information

Calculated MALDI-TOF spectrum

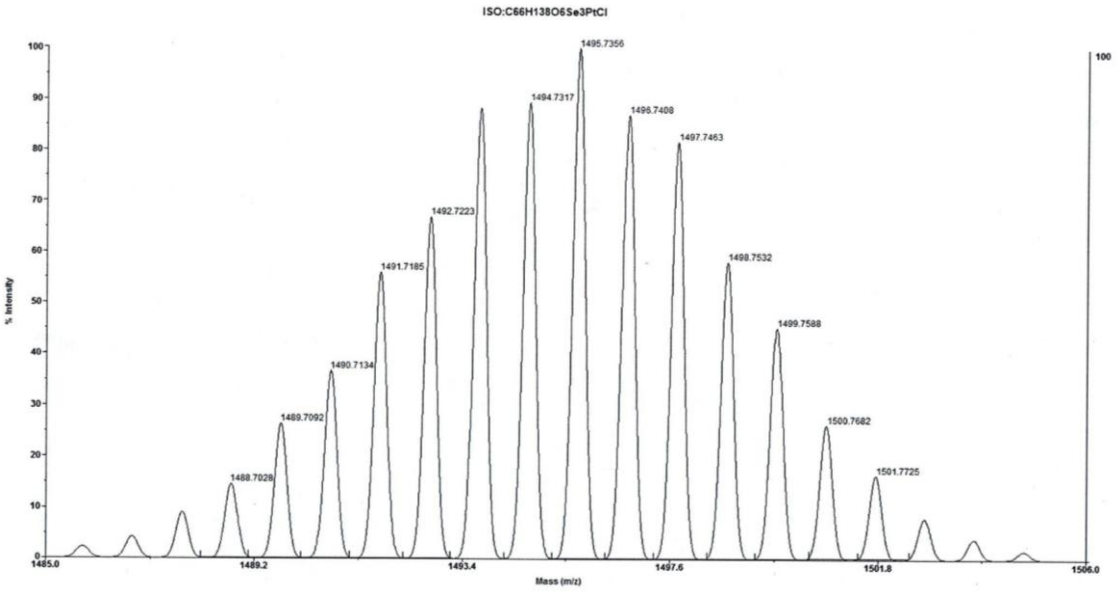

Figure S 1 Calculated MALDI-TOF spectrum of the a coordination fragment of M-SeOH-$PtCl_2$, $[Pt(M\text{-}SeOH)_3Cl]^+$

Synthesis

The selenide-containing polyurethane (PUSe) blocks were terminated by PEG monomethyl ether of different molecular weight, including 1900g/mol and 5000 g/mol. The molecular weight of PEG-PUSe-PEG1900 and PEG-PUSe-PEG5000 was determined by ^{1}H NMR to be 3.8×10^4 g/mol and 2.9×10^4 g/mol, respectively. For PEG-PUSe-PEG1900, n=58. While for PEG-PUSe-PEG5000, n= 31.

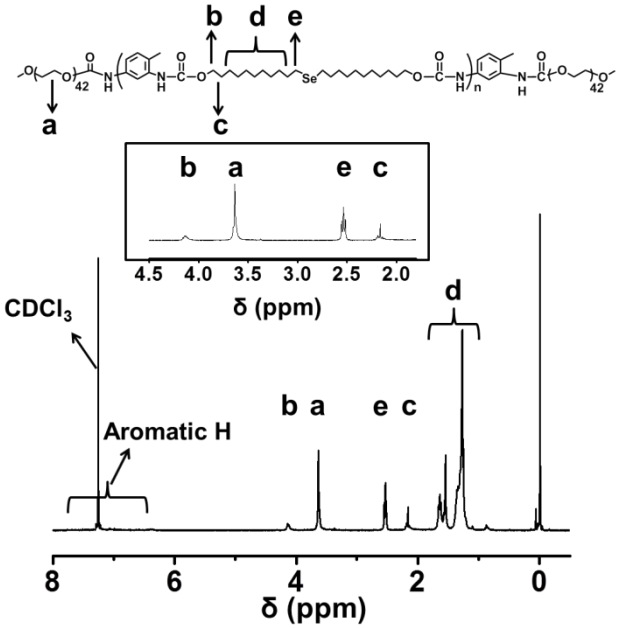

Figure S 2 ^{1}H NMR spectrum of PEG-PUSe-PEG1900, 600MHz, solvent: $CDCl_3$.

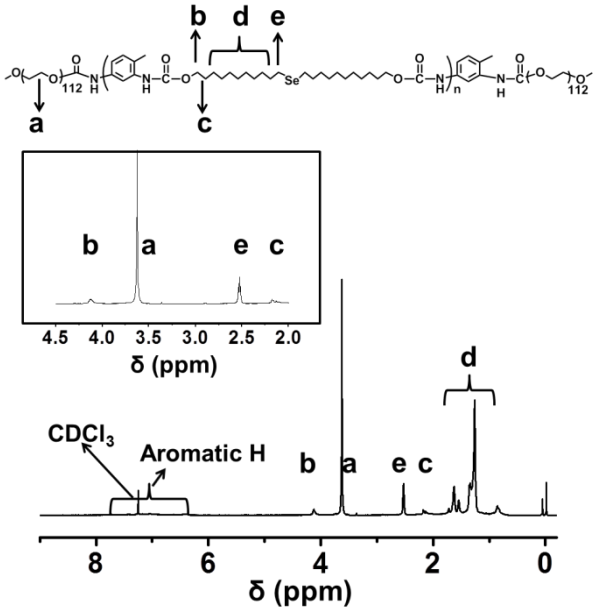

Figure S 3 ^{1}H NMR spectrum of PEG-PUSe-PEG5000, 600MHz, solvent: $CDCl_3$.

Self-assembly behaviors of PEG-PUSe-PEG

PEG-PUSe-PEG copolymer can self-assemble to aggregates in an aqueous environment because of its amphiphilic nature. The critical aggregate concentration (CAC) of PEG-PUSe-PEG1900 was determined by the fluorescent probe method using pyrene as the probe[1] to be 3.2×10^{-3} mg/mL. The size of the aggregates was ~65 nm average diameter, measured by dynamic light scattering (DLS) measurements. Transmission electron microscopy (TEM) was employed to observe the morphology of the aggregates. The results show (Figure S 4) that the aggregates are micellar structure with solid cores. Similarly, the CAC of PEG-PUSe-PEG5000 was determined to be 6.3×10^{-3} mg/mL, as shown in Figure S 5. In addition, it was found that PEG-PUSe-PEG5000 forms micellar aggregates with a hydrodynamic diameter of about 55 nm.

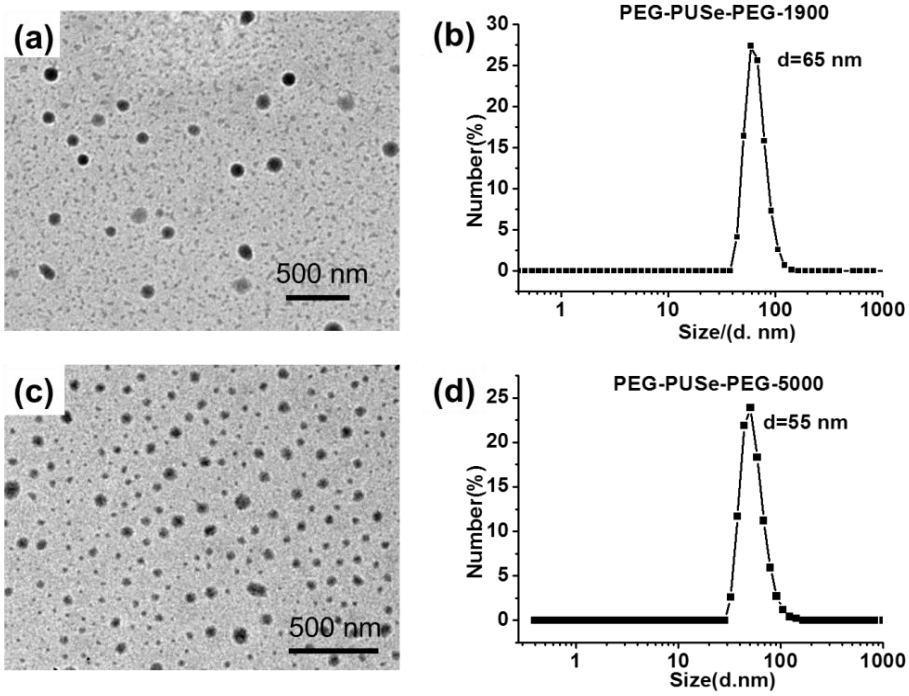

Figure S 4 Self-assembly behaviours of PEG-PUSe-PEG. TEM images of aggregates, PEG-PUSe-PEG1900 (a), PEG-PUSe-PEG5000 (c), stained by 1.5% uranium acetate. DLS determination of PEG-PUSe-PEG1900 (b), PEG-PUSe-PEG5000 (d).

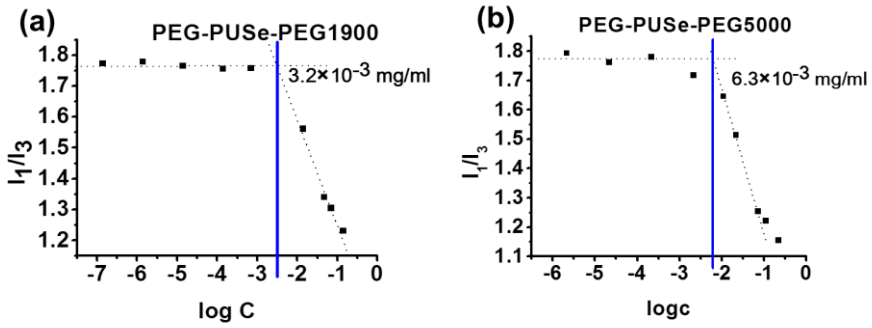

Figure S 5 Determination of CAC of PEG-PUSe-PEG using the fluorescent method with pyrene as a probe. I_1/I_3 refers to the fluorescence intensity ratio of the emission intensity of the first and third bands in the fluorescence spectrum of pyrene. (a) PEG-PUSe-PEG1900 (b) PEG-PUSe-PEG5000.

DLS study for the Pt-coordinating micelles of PEG-PUSe-PEG1900

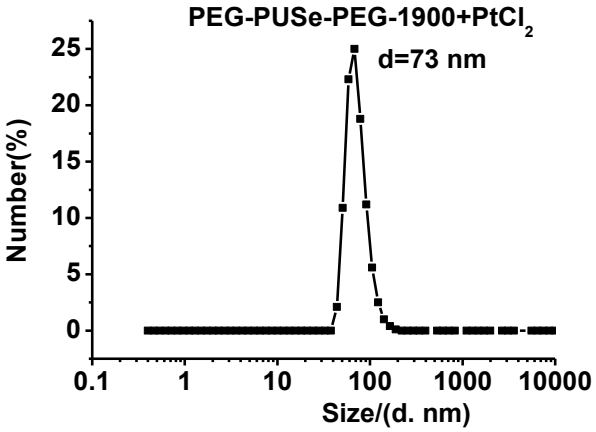

Figure S 6 DLS result for the Pt-coordinating aggregates of PEG-PUSe-PEG1900.

Colloidal studies based on DLS

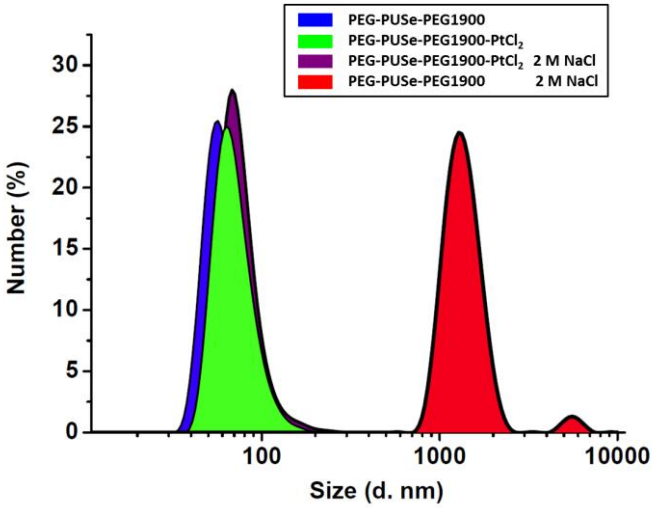

Figure S 7 Colloidal studies based on DLS of PEG-PUSe-PEG1900 micelles and Pt-coordinating micelles in water and at high salt concentration (2 M NaCl)

Self-assembly behaviors of PEG-PUSe-PEG5000 / $PtCl_2$ complex

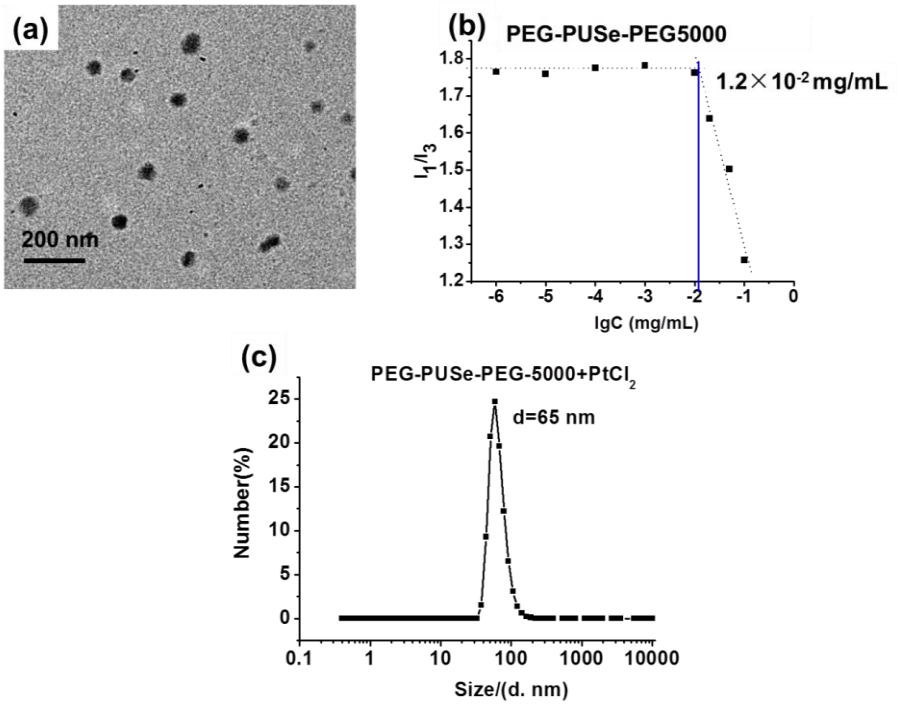

Figure S 8 Self-assembly behaviours of PEG-PUSe-PEG5000 / $PtCl_2$ complex. (a) TEM images of aggregates, without staining, (b) the CAC determination of PEG-PUSe-PEG5000/Pt complexs. (c) DLS result for the Pt-coordinating aggregates of PEG-PUSe-PEG5000.

Fluorescent spectra of Dox-loaded Pt-coordinating micelles of PEG-PUSe-PEG1900

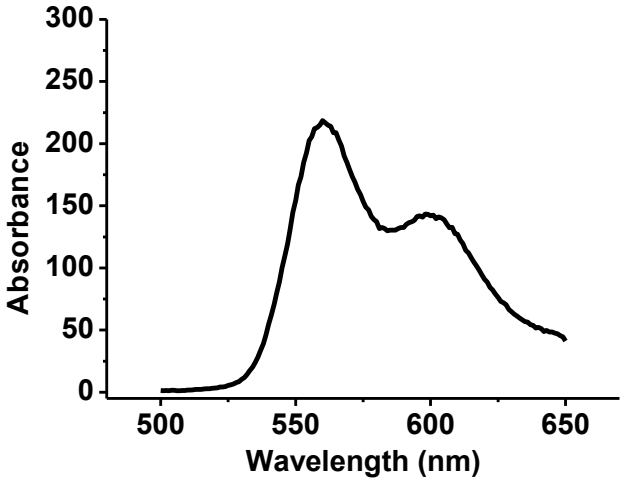

Figure S 9 Fluorescent spectra of Dox-loaded Pt-coordinating micelles of PEG-PUSe-PEG1900 desolved in 4 times its volume of DMF.

Morphology of the Dox-loaded Pt-coordinating micelles of PEG-PUSe-PEG5000

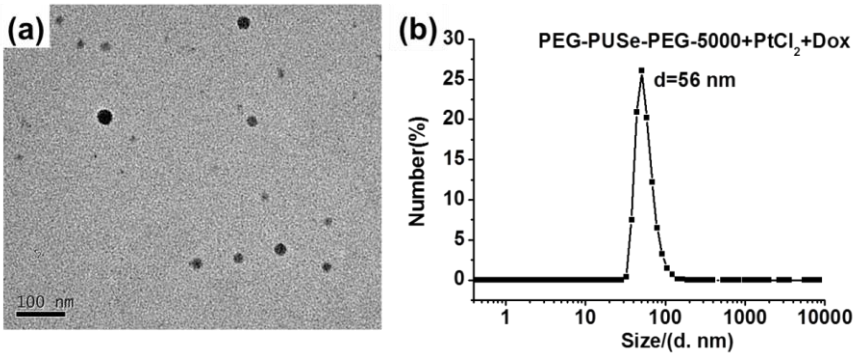

Figure S 10 Morphology of the Dox-loaded Pt-coordinating micelles of PEG-PUSe-PEG5000. (a) TEM images of coordination micelles without staining, (b) DLS result for the micelles.

Mass spectra for competitive coordination

$PtCl_2$ was added into the aqueous solution of GSH under sonication, the resulting solution was tested by ESI-MS (Figure S 11).

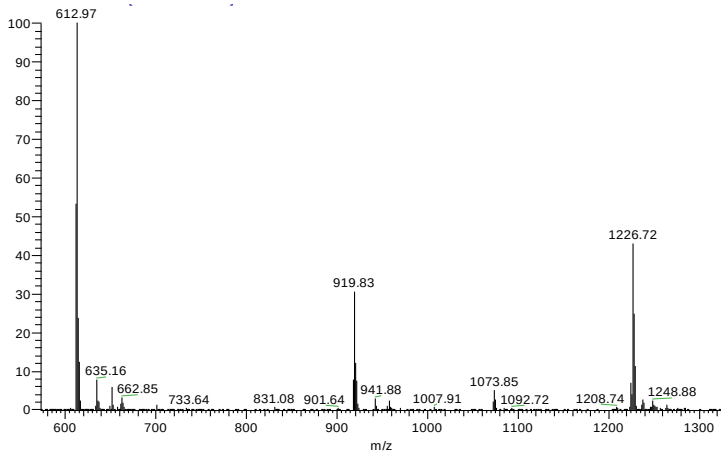

Figure S 11 ESI-MS spectrum of the complex formed by GSH and $PtCl_2$.

0.1mmol GSH was mixed with 1 mL 0.01 mM aqueous solution of M-SeOH+$PtCl_2$, the solution was then measured by ESI-MS. As shown in Figure S 12, a peak at m/z 1226.68 , in agreement with $[Pt(GSH)_3Cl]^-$ (+Br), was observe, while the peak for the complex of M-SeOH and Pt disappeared. The results indicate that GSH coordinate better with platinum and can replace the selenium-containing ligand.

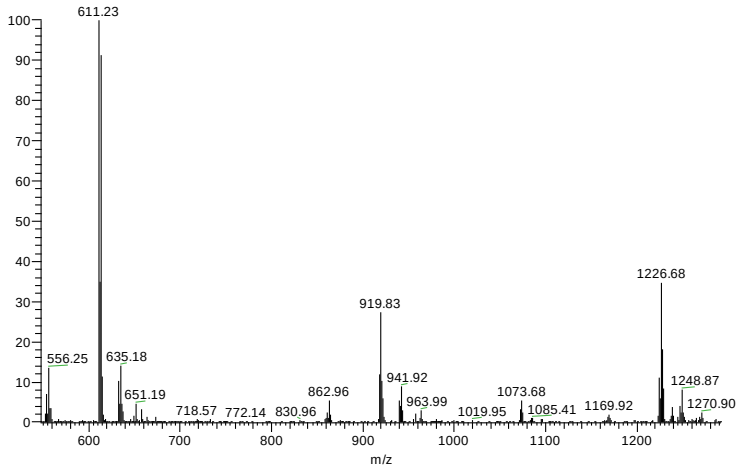

Figure S 12 ESI-MS spectrum of the production of competitive coordination.

In vitro release

Similarly, as shown in Figure S 13, Dox loaded in the coordination micelles of PEG-PUSe-PEG5000 was also released in a GSH-rich environment.

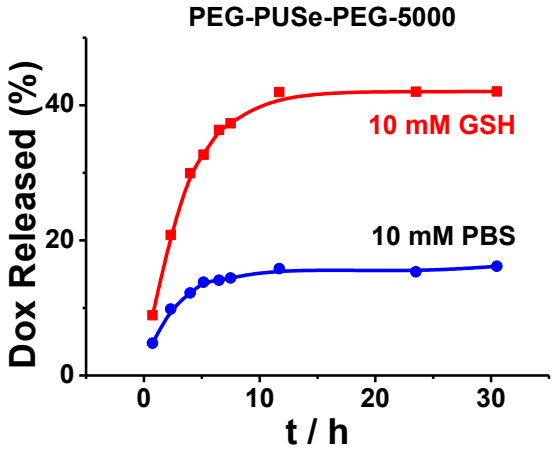

Figure S 13 In vitro release plot of Dox -loaded platinum-coordinating micelles of PEG-PUSe-PEG5000 with and without GSH at pH 7.4 and 37 °C.

MTT assays of cisplatin-containing micelles of PEG-PUSe-PEG5000.

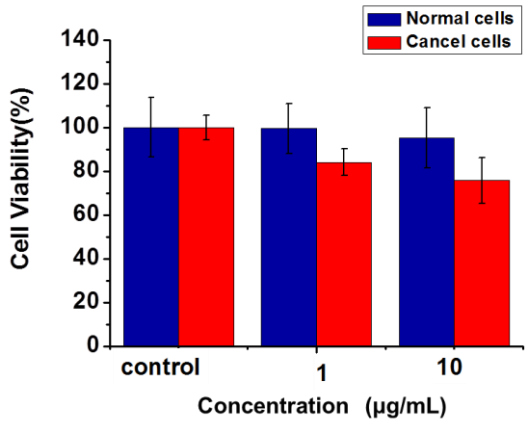

Figure S 14 MTT assays of cisplatin-containing micelles of PEG-PUSe-PEG5000 based on human normal liver L-02 cells and human hepatocellular liver carcinoma cell line (HepG2). The cells were incubated for 24 h with micelles. Data are presented as the average ± standard deviation (n=6).

1. T. Cao, P. Munk, C. Ramireddy, Z. Tuzar and S. E. Webber, *Macromolecules*, 1991, **24**, 6300-6305.