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Materials and reagents

All of the solvents and chemical reagents were used as received from the commercial sources without further purification. N, N-diisopropylethylamine (DIPEA), O-benzotriazole-N,N,N',N'-tetramethyluronium-hexafluorophosphate (HBTU), N,N'-diisopropylcarbodiimide (DIC), N-hydroxysuccinimide (NHS), and taurine were purchased from ACROS Organics USA. All other amino acid derivatives were purchased from GL Biochem (Shanghai) Ltd.

Instruments

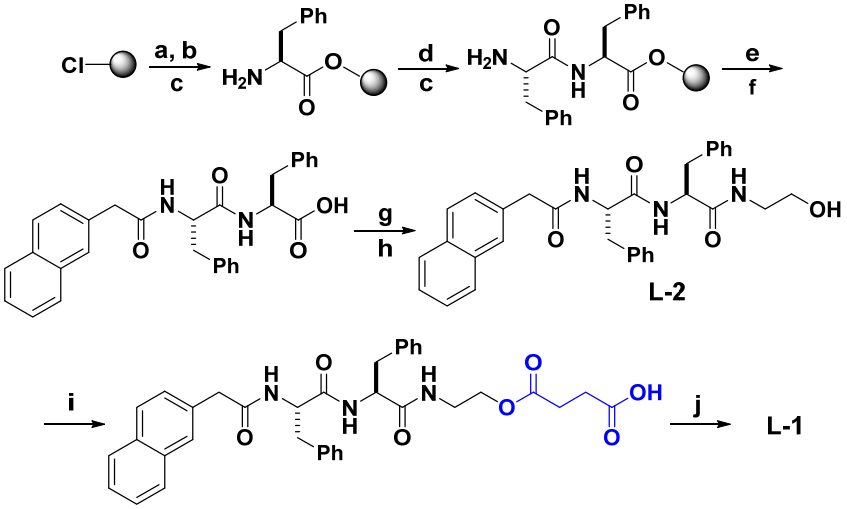
LC-MS was performed on a Waters Acquity Ultra Performance LC with Waters MICRO-MASS detector. Products were purified with Waters Delta600 HPLC system, which equipped with an XTerra C18 RP column and an in-line diode array UV detector. Hydrogen nuclear magnetic resonance (NMR) spectra were recorded on a Varian Unity Inova 400 with DMSO as solvent. Transmission electron microscope (TEM) images were taken on Morgagni 268 transmission electron microscope. Confocal images were taken on a Leica TCS SP2 Spectral Confocal Microscope. MTT assay for cell cytotoxicity was test on DTX880 Multimode Detector.

MTT and WST assays

MTT assay. We seeded SKOV3 cells in exponential growth phase in a 96 well plate at a concentration of 1×10^4 cell/well with 100 μL of McCoy's 5A medium modified supplemented with 10% fetal bovine serum (FBS), 100 U/mL penicillin and 100 μg/ml streptomycin. The cells were allowed to attach to the wells for 24 h at 37 ºC, 5% CO_2. The culture medium was removed and 100 μL culture medium containing compounds (immediately diluted from fresh prepared stock solution of 10 mM) at gradient concentrations (0 μM as the control) was placed into each well. McCoy's 5A medium modified was regarded as blank. After culturing at 37 ºC, 5% CO_2 for 24h, 48h and 72h, 10 μL of 5 mg/mL MTT ((3-(4,5-DimethylthiazoL-2-yl)-2,5-diphenyltetrazolium bromide) was added to each well, and the plated cells were incubate in dark place for 4 h. 100 μL 10% SDS with 0.01 M HCl was added to each well to stop the reduction reaction and to dissolve the purple formazan. After incubation of the cells at 37 ºC for overnight, the OD at 595 nm of the solution was measured in a microplate reader.

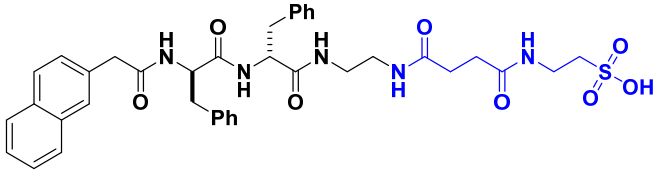
WST assay. Cells in exponential growth phase were seeded in a 96 well plate at a concentration of 1×10^4 cell/well. The cells were allowed to attach to the wells for 24 h at 37 ºC. The culture medium was removed and 100 μL culture medium containing compounds (immediately diluted from fresh prepared stock solution of 10 mM) at gradient concentrations (0 μM as the control) was placed into each well. After the incubation of 72 hours, 10 μL of Cell Proliferation Reagent WST-1 was then added to each well and incubated for 2 hours at 37 ºC, 5% CO_2. The plate was shaken thoroughly for 1 min on a shaker to ensure homogeneous distribution of color. Subsequently, absorbance was measured at 450 nm in a microplate reader from which data points were collected.

Scheme S1. General synthetic route of the precursor (L-**1** as an example).



a) Fmoc-L-Phe-(OH), DIEA, DMF, rt, 40 mins; b) CH_2Cl_2: MeOH:DIEA=16:3:1 solution, rt, 10 mins for twice; c) 20% piperidine in DMF, rt, 20 mins; d) Fmoc-L-Phe-(OH), HBTU, DIEA, DMF, rt, 40 mins; e) 2-naphthaleneacetic acid, HBTU, DIEA, DMF, rt, 40 mins;f) 95% TFA in H_2O, rt, 2h; g) NHS, DIC, THF, rt, 3h; h) ethanolamine, DIEA, THF, rt, 1h; i) succinic anhydride, DIEA, DMF, rt, overnight; j) taurine, HBTU, DIEA, DMF, rt, overnight

Scheme S2. Structure of the control compound **3**.



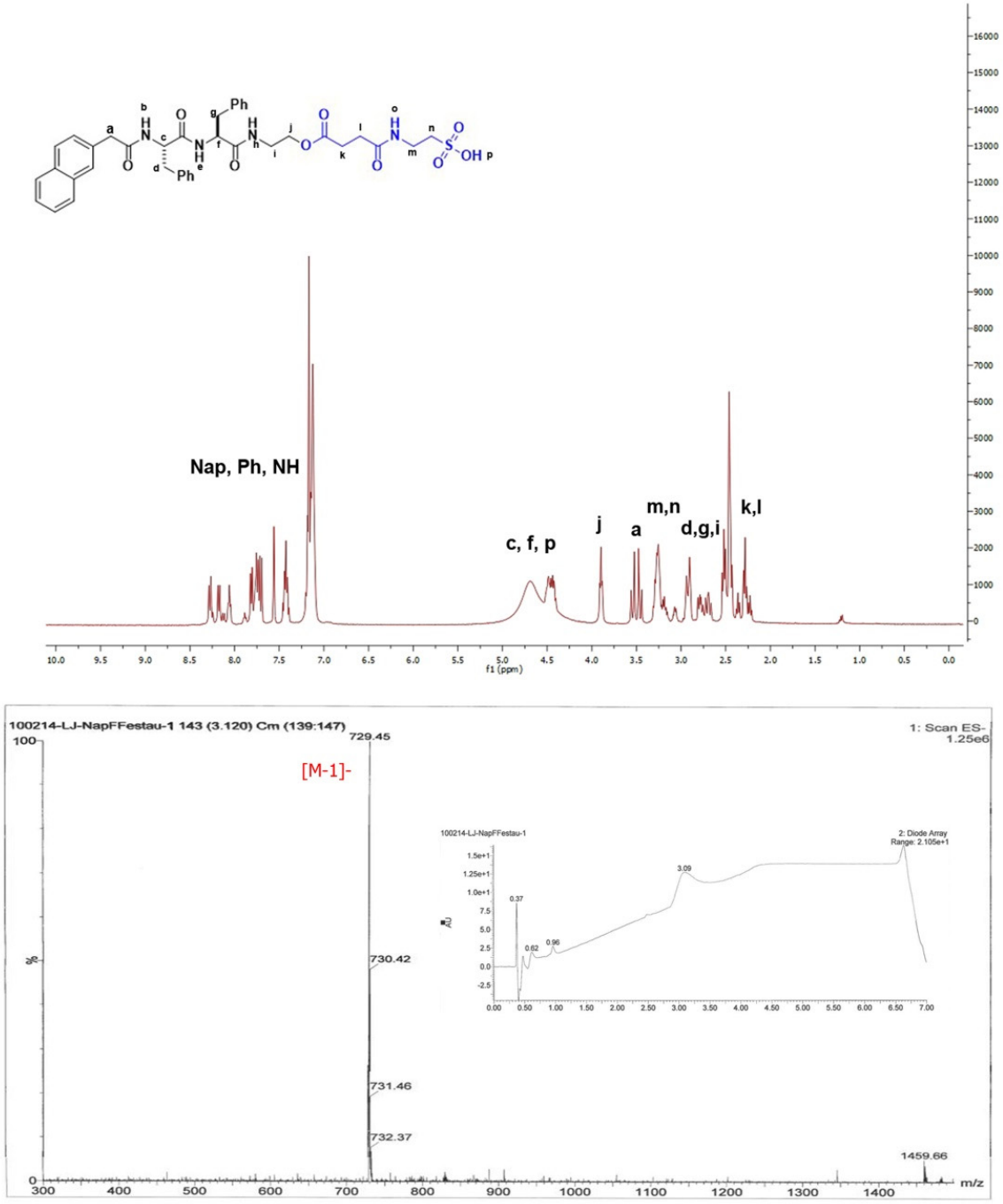


Figure S1. The ^{1}H NMR spectra of L-**1** in DMSO and its LC-MS spectra.

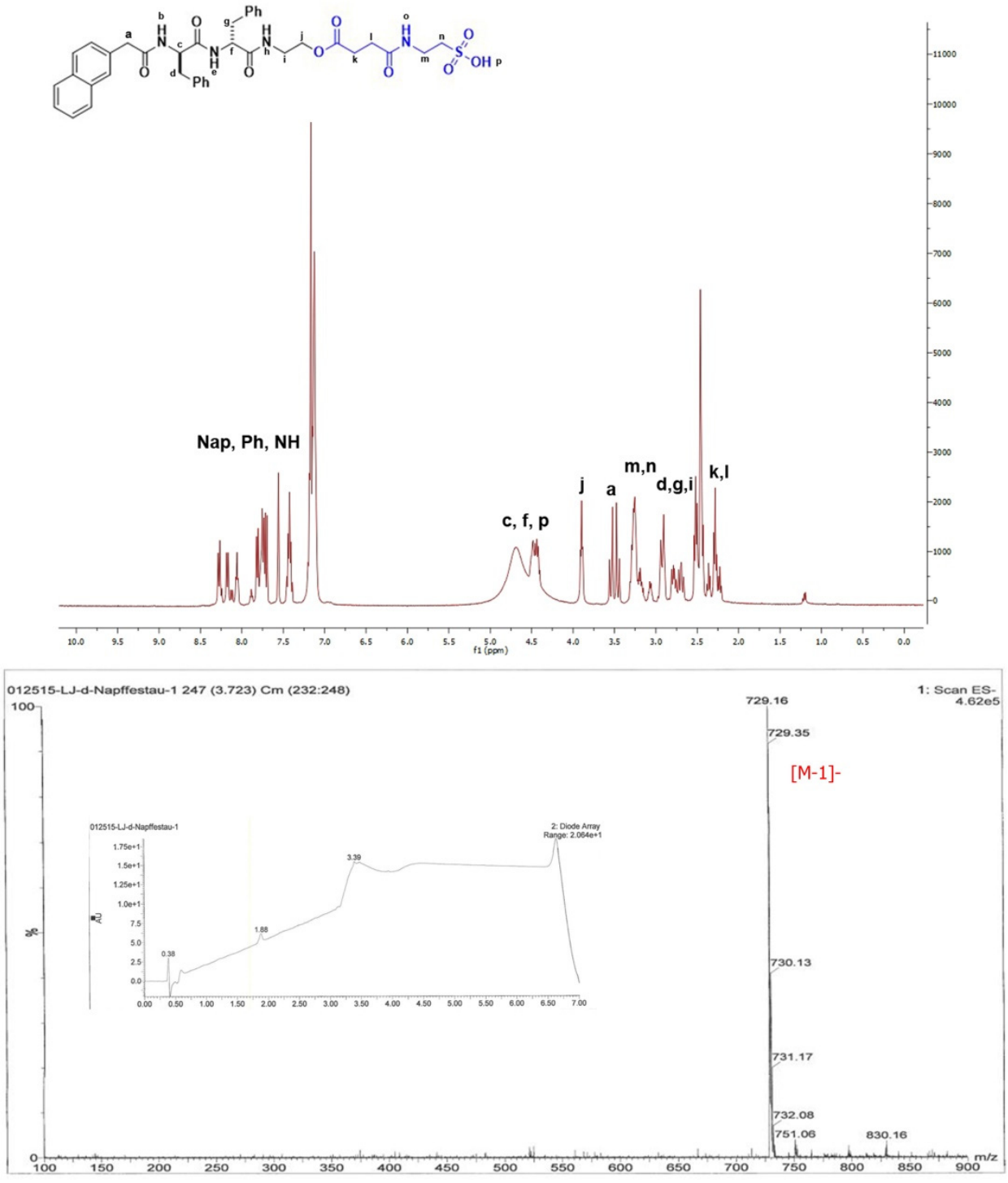


Figure S2. The ^{1}H NMR spectra of D-**1** in DMSO and its LC-MS spectra.

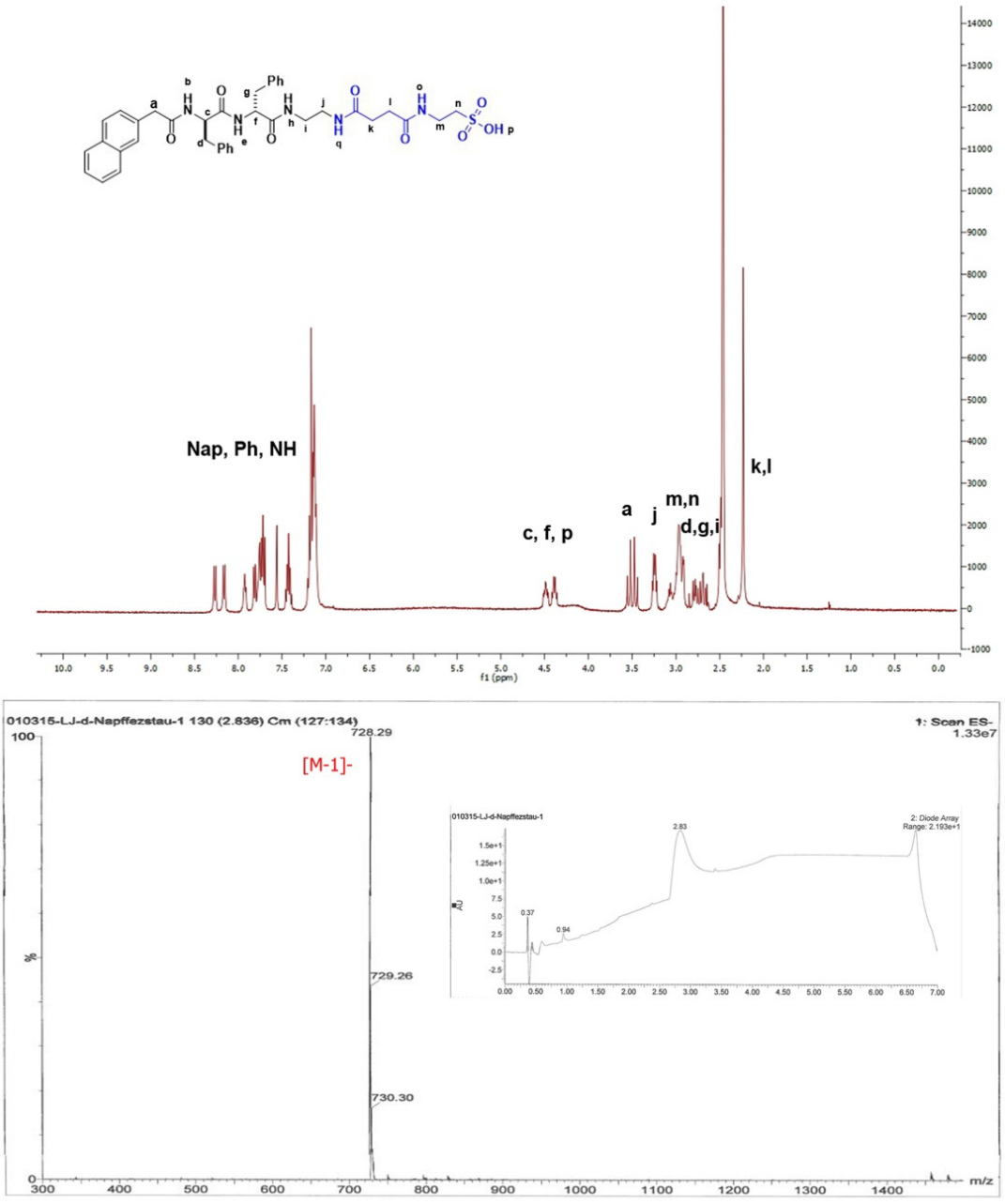


Figure S3. The ^{1}H NMR spectra of **3** in DMSO and its LC-MS spectra.

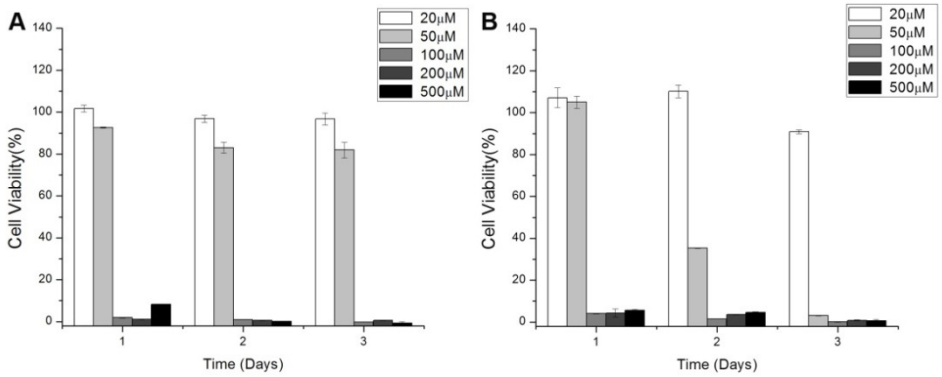


Figure S4. Cell viability of SKOV3 cells incubated with the precursors for 3 days. A) Cell viability of SKOV3 cells incubated with L-**1**. B) Cell viability of SKOV3 cells incubated with D-**1**.

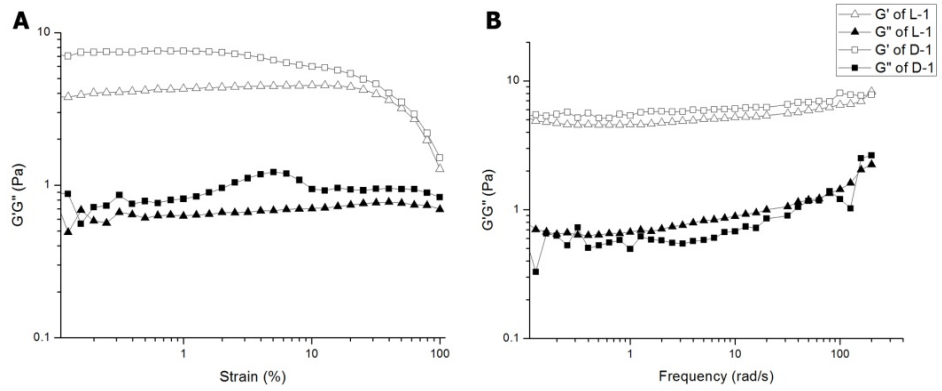


Figure S5. The (A) strain and (B) frequency dependence of dynamic storage modulus G' and loss modulus G'' of the gels formed by L-**1** and D-**1** at 0.4 wt% upon the treatment of 2 U/mL of CES at pH 7.4 in PBS buffer.

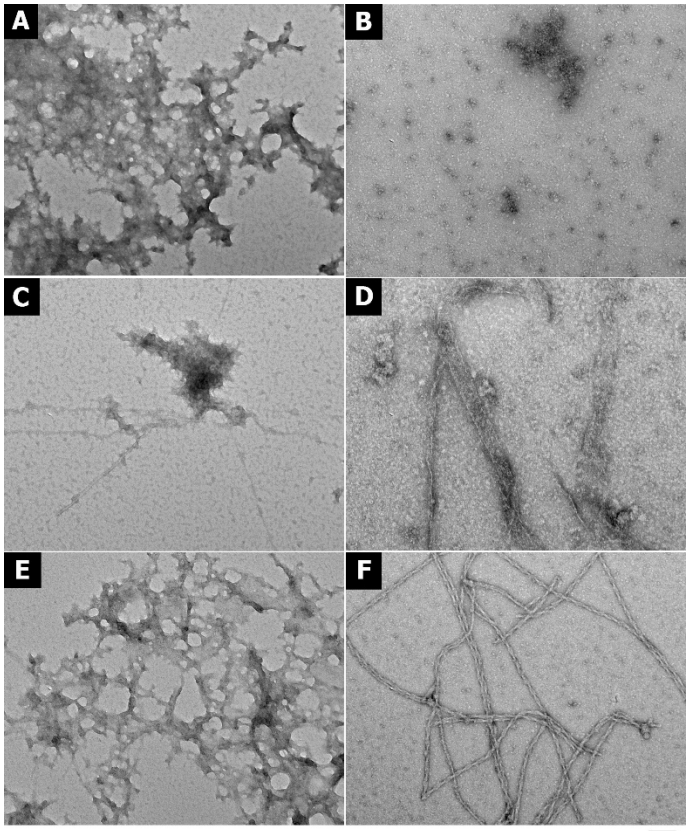


Figure S6. TEM images of the solutions of L-**1** or D-**1** at concentrations from 20 to 100 μM after being treated with CES (2 U/mL). (A) solution of L-**1** at concentration of 20 μM, (B) solution of D-**1** at concentration of 20 μM, (C) solution of L-**1** at concentration of 50 μM, (D) solution of D-**1** at concentration of 50 μM, (E) solution of L-**1** at concentration of 100 μM, (F) solution of D-**1** at concentration of 100 μM, after being treated with CES (Scale bar = 100 nm).

Table S1. Composition and concentrations of the culture medium after being incubated with SKOV3 cells and A2780cis cells.

Compd.	Precursor (**1**) (μM)	Hydrogelator (**2**) (μM)	ratio[a]
L-**1**[b]	39	9	0.23
D-**1**[b]	16	3	0.18
D-**1**[c]	75	12	0.16

[a]The ratio of hydrogelator to precursor after 4 h. [b]The culture medium incubated with SKOV3 cells is collected after 4 h incubation with 20 μM (15 μg/mL) of D-**1** or with 50 μM (37 μg/mL) of L-**1** at 37 ˚C. [c]The culture medium incubated with A2780cis cells is collected after 4 h incubation with 100 μM (73 μg/mL) of D-**1** at 37 ˚C.

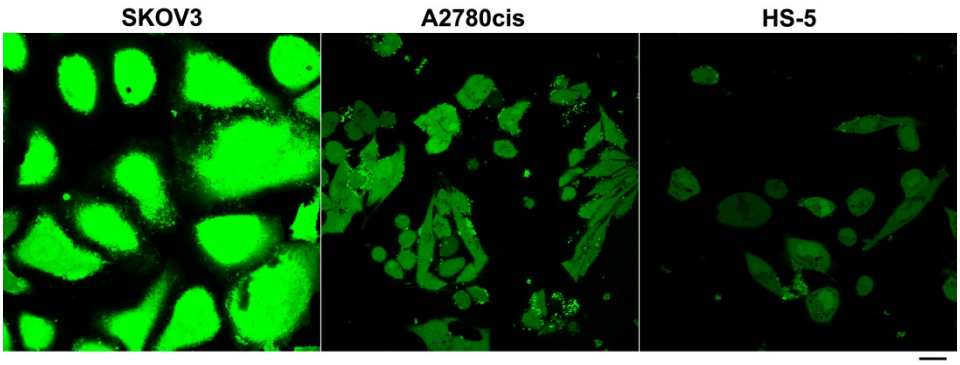


Figure S7. The fluorescence images of SKOV3, A2780cis and HS-5 cells stained by 6-CFDA (25 μM in PBS buffer) for 20 minutes (PMT = 500 V, Pinhole = 0.000114 m). Scale bar = 20 μm.

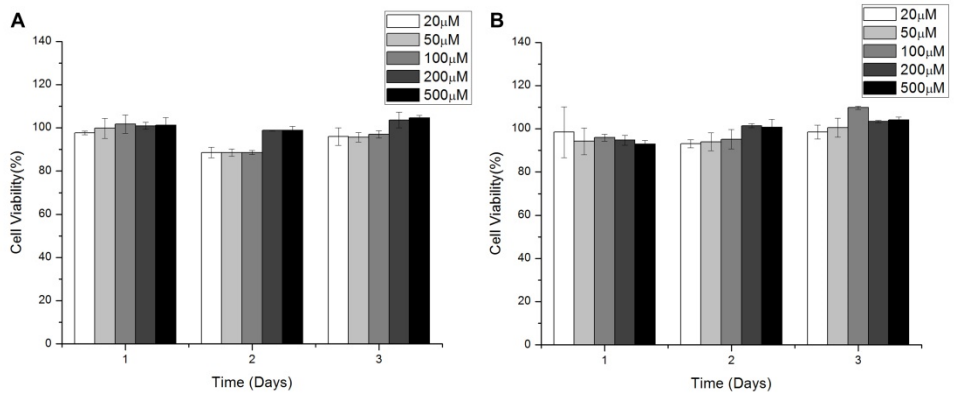


Figure S8. (A) Cell viability of SKOV3 cells incubated with the control **3** for 3 days. (B) Cell viability of A2780cis cells incubated with the control **3** for 3 days.

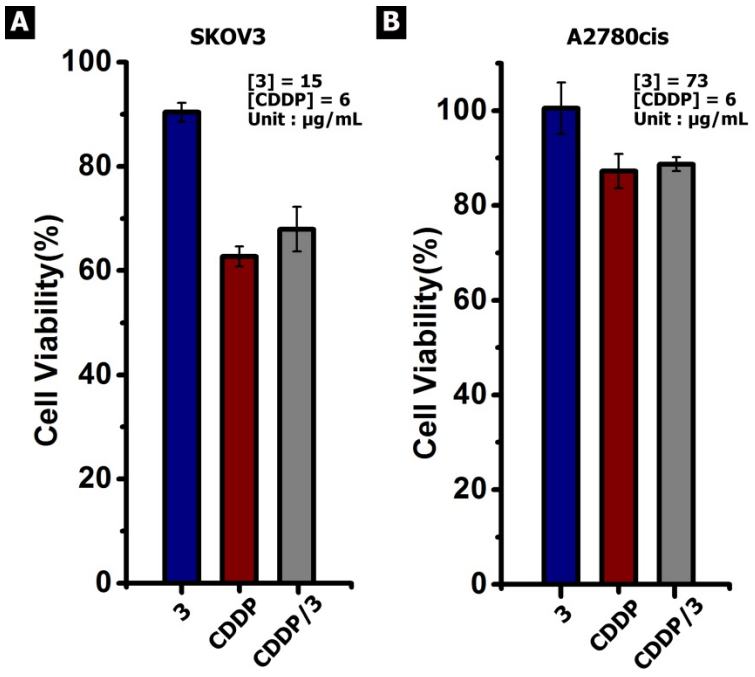


Figure S9. (A) Cell viability of SKOV3 cells incubated with the control **3** alone or in combination with cisplatin (CDDP) for 72 h. (B) Cell viability of A2780cis cells incubated with the control **3** alone or in combination with cisplatin (CDDP) for 72 h.

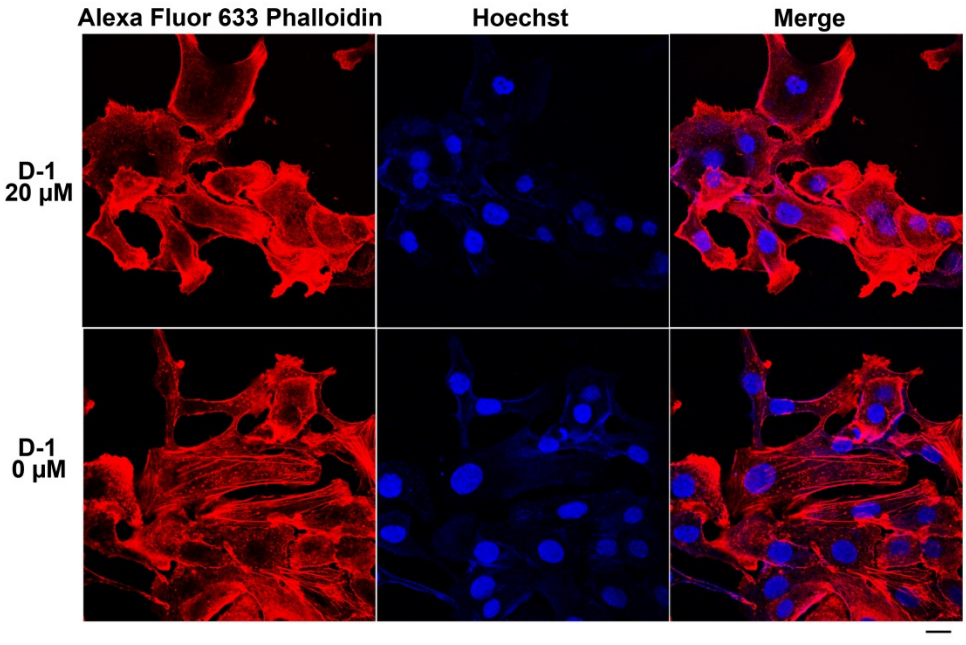


Figure S10. The fluorescence images of SKOV3 cells stained with Alexa Fluor 633 Phalloidin (F-actin) and Hoechst (nuclei) (upper) after treatment of D-**1** at concentration of 20 μM for 20 h or (bottom) without the treatment of D-**1**. Scale bar = 20 μm.

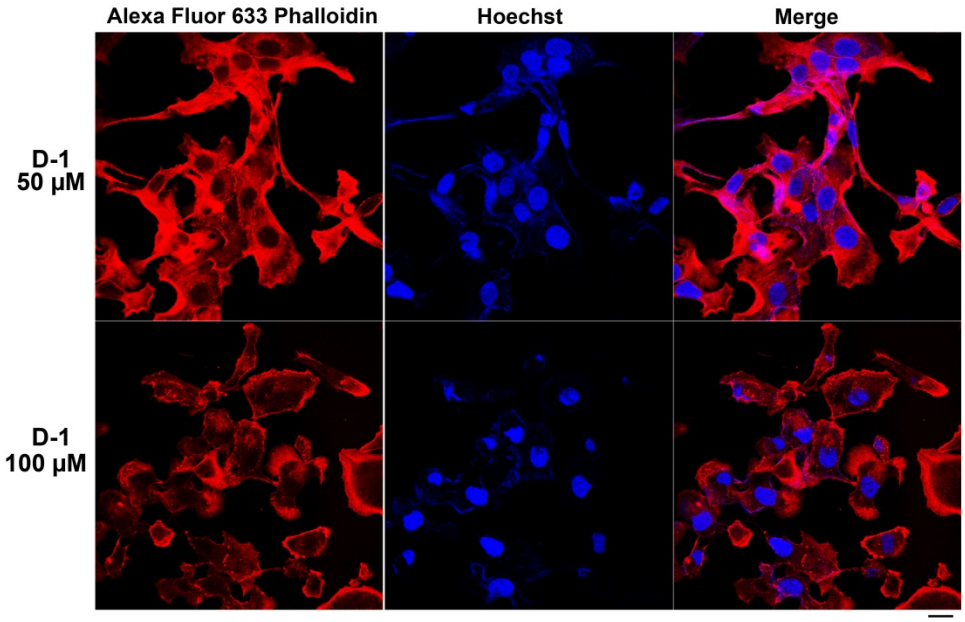


Figure S11. The fluorescence images of SKOV3 cells stained with Alexa Fluor 633 Phalloidin (F-actin) and Hoechst (nuclei) (upper) after treatment of D-**1** at concentration of 50 μM for 20 h or (bottom) after the treatment of D-**1** at concentration of 100 μM for 20 h. Scale bar = 20 μm.

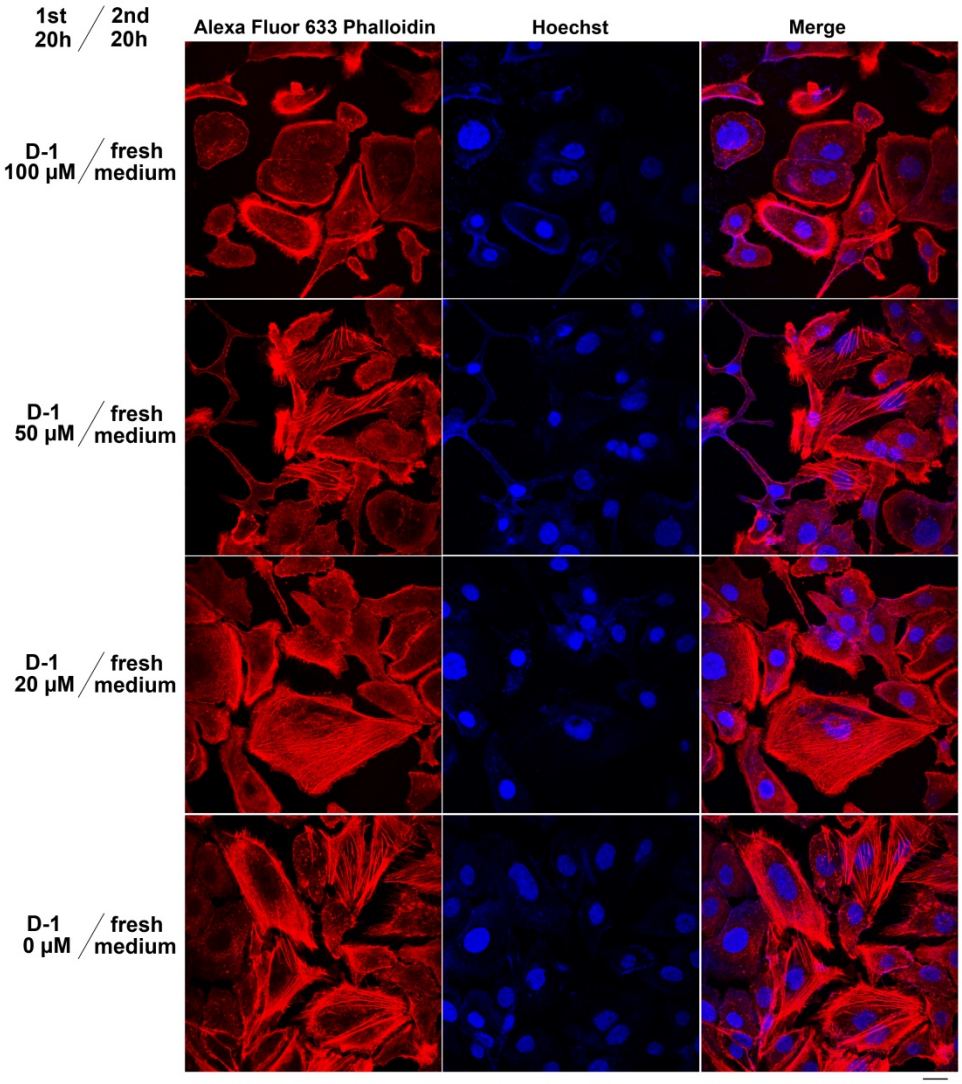


Figure S12. The fluorescence images of SKOV3 cells stained with Alexa Fluor 633 Phalloidin (F-actin) and Hoechst (nuclei) after treatment of D-**1** at concentrations of 100 μM, 50 μM, 20 μM and 0 μM (control) for 20 h and then replace the medium contains D-**1** with fresh medium and incubate for another 20 h. Scale bar = 20 μm.

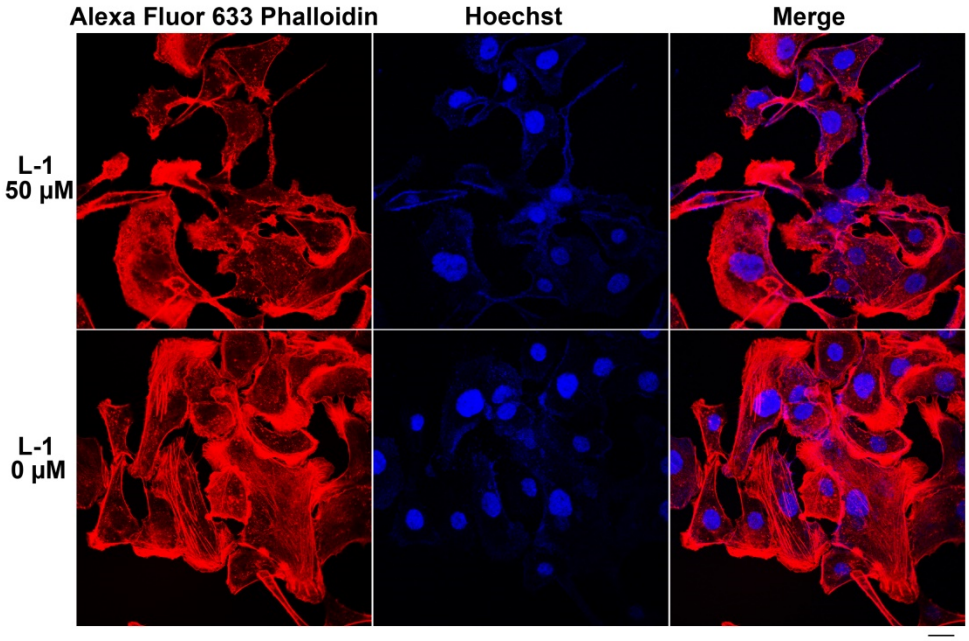


Figure S13. The fluorescence images of SKOV3 cells stained with Alexa Fluor 633 Phalloidin (F-actin) and Hoechst (nuclei) (upper) after treatment of L-**1** at concentration of 50 μM for 20 h or (bottom) without the treatment of L-**1**. Scale bar = 20 μm.

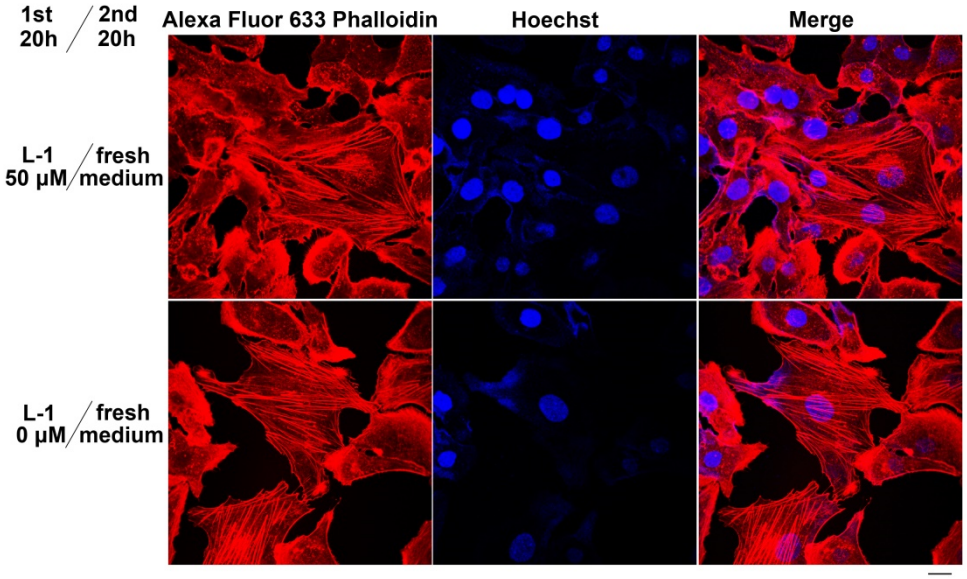


Figure S14. The fluorescence images of SKOV3 cells stained with Alexa Fluor 633 Phalloidin (F-actin) and Hoechst (nuclei) after treatment of L-**1** at concentrations of 50 μM and 0 μM (control) for 20 h and then replace the medium contains L-**1** with fresh medium and incubate for another 20 h. Scale bar = 20 μm.

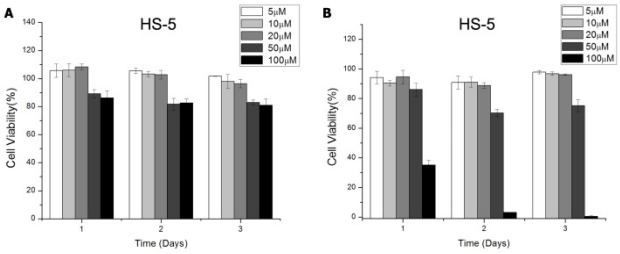


Figure S15. Cell viability of HS-5 cells incubated with the precursors for 3 days. A) L-**1**. B) D-**1**.

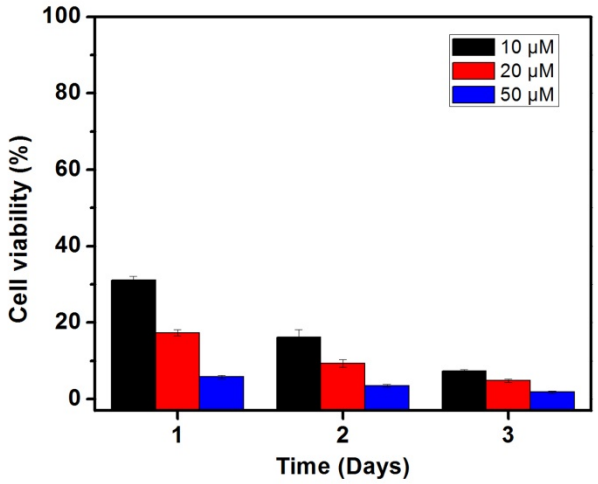


Figure S16. Cell viability of HS-5 cells incubated with cisplatin for 3 days.

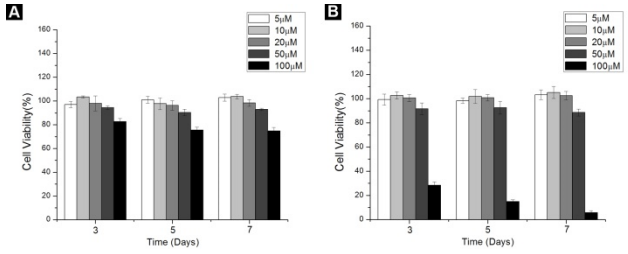


Figure S17. Cell viability of PC12 cells incubated with the precursors for 7 days. A) L-**1**. B) D-**1**.

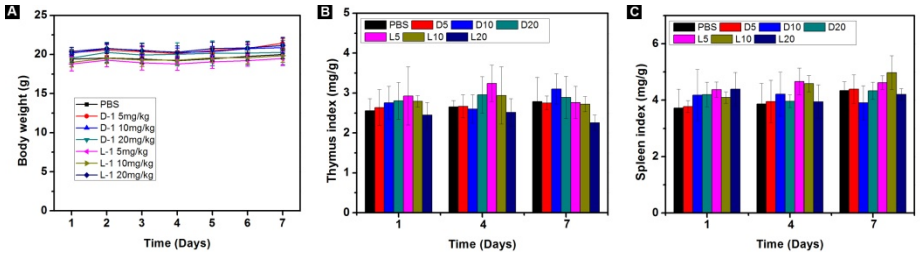


Figure S18. (A) Body weight curves of mice after injection of D-**1** or L-**1** at 5 mg/kg, 10mg/kg and 20 mg/kg or PBS buffer. Data are shown as mean ± SD of body weight (n = 4). (B) Thymus index, (C) spleen index of mice after injection of D-**1** or L-**1** at 5 mg/kg, 10mg/kg and 20 mg/kg or PBS buffer.

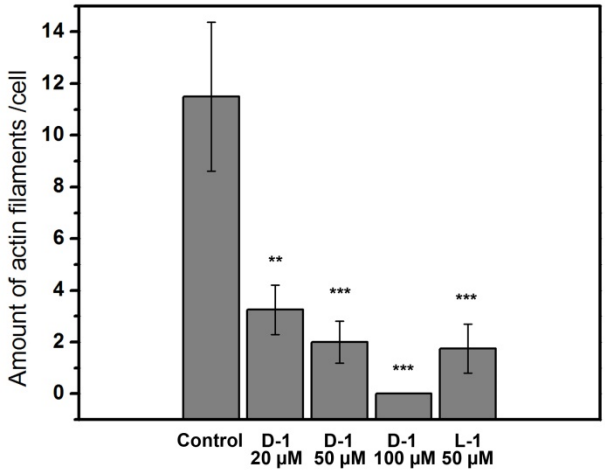


Figure S19. The amount of actin filaments (longer than 5 μm) in SKOV3 cells after been treated by medium contains 0 μM, 20 μM, 50 μM and 100 μM of D-**1** or 50 μM of L-**1** (** = $p \leqslant 0.01$, *** = $p \leqslant 0.001$ versus control).

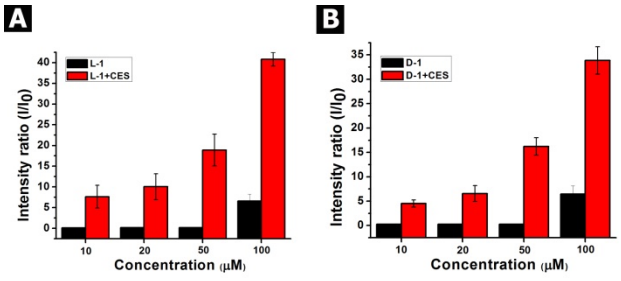


Figure S20. A repeated SLS experiment. The signal intensity ratio of static light scattering (SLS) of the solution of (A) L-**1** or (B) D-**1** at concentrations from 10 to 100 μM before (black bar) and after (red bar) being treated CES (2 U/mL) for three hours.

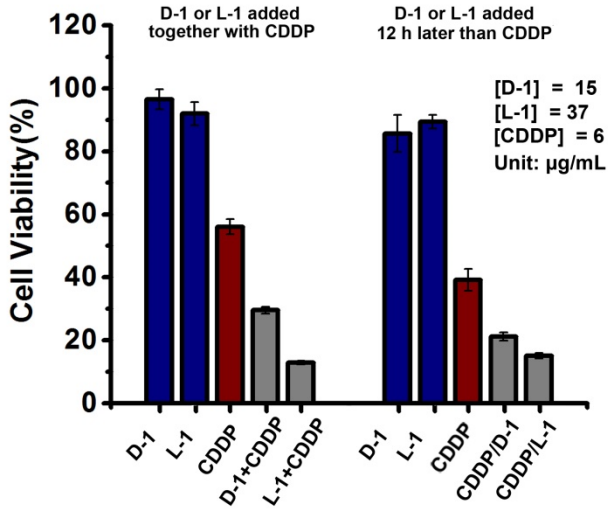


Figure S21. A repeated SKOV3 cytotoxicity experiment. Cell viability of SKOV3 cells incubated with the precursors D-**1** or L-**1** alone, or in combination with CDDP for 72 h.

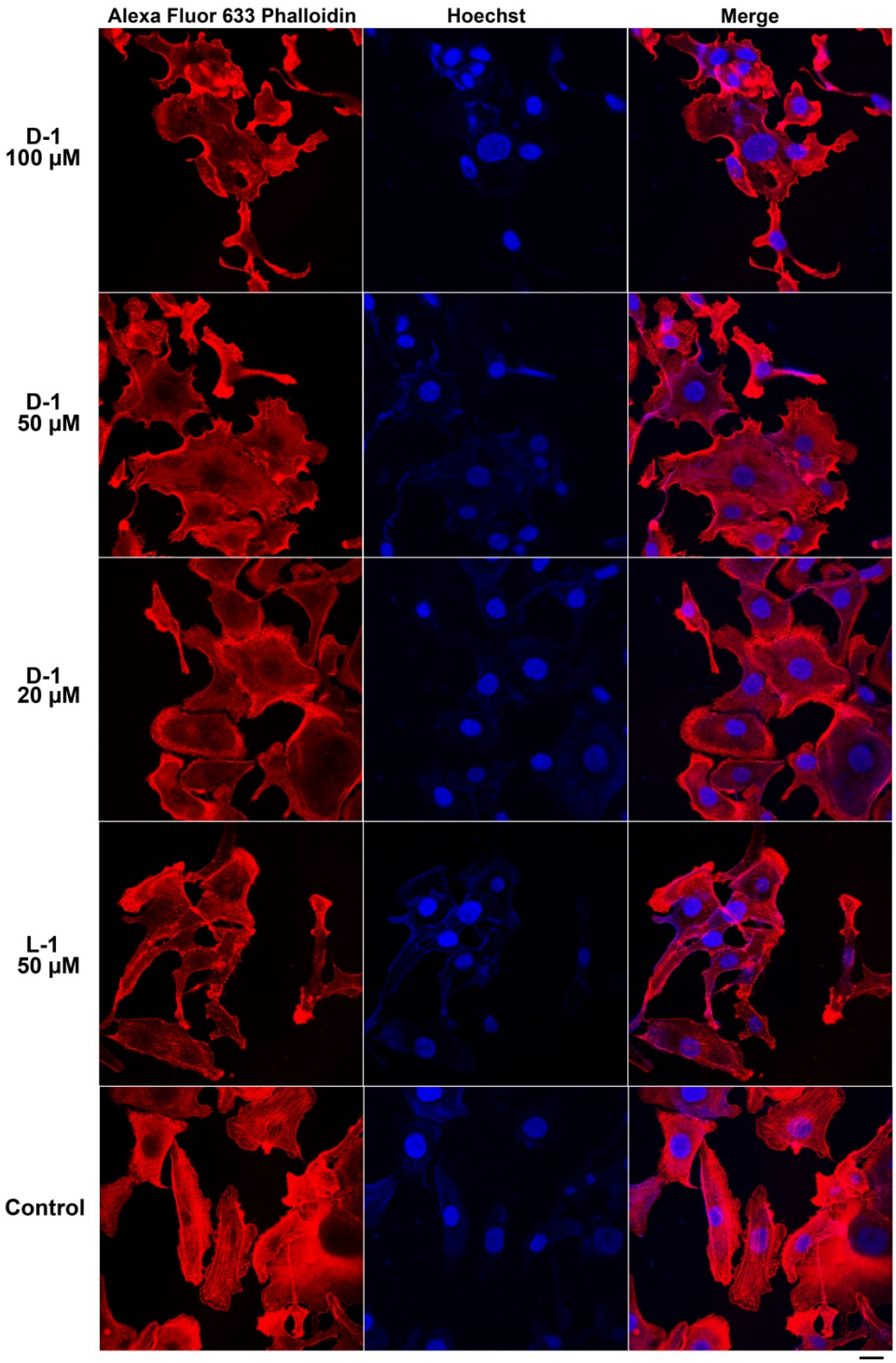


Figure S22. Repeated fluorescence images. The fluorescence images of SKOV3 cells stained with Alexa Fluor 633 Phalloidin (F-actin) and Hoechst (nuclei) after treatment of D-**1** at concentration of 100 μM, 50 μM, 20 μM and 0 μM (control) or L-**1** at concentration of 50 μM for 20 h. Scale bar = 20 μm.

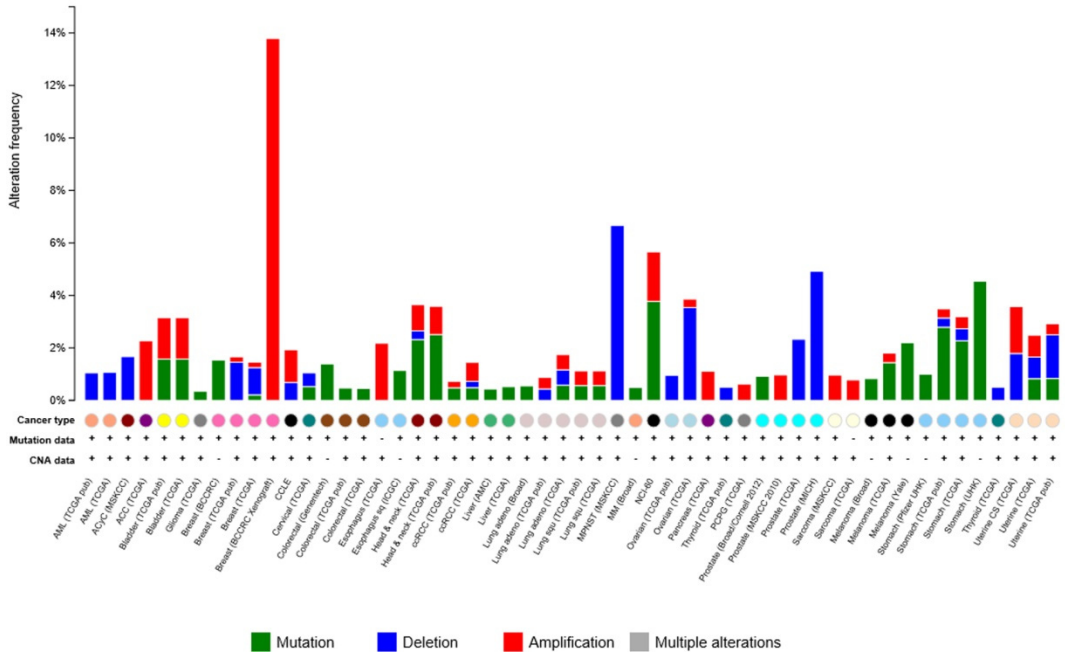


Figure S23. Cross-cancer alteration summary for CES from different databases (TCGA etc.) and cancer types: the alteration frequency profile of CES includes mutation (green), deletion (blue), amplification (red) and multiple alterations (grey). From this figure, CES expressions differ dramatically throughout various cancers and organs.

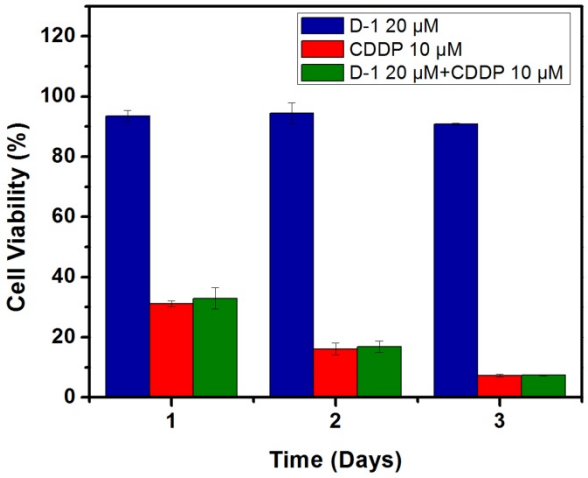


Figure S24. Cell viability of HS-5 cells incubated with D-**1** alone or in combination with cisplatin (CDDP) for 72 h.

Table S2. Summary of IC_{50} and IC_{90} values of the precursors against the ovarian cancer cells for 48 h.

Compd.	SKOV3		A2780cis	
	IC_{50}	IC_{90}	IC_{50}	IC_{90}
L-**1**	62	78	94	98
D-**1**	48	53	69	73

Table S3. Summary of IC_{90} values of the precursors and NapFF against HeLa cells for 48 h.

Compd.	IC_{90} (μM)
L-**1**	500
D-**1**	78
NapFF	400