Experimental Supporting Information

Materials and general methods:

Chemicals: Fmoc-amino acids were obtained from GL Biochem (Shanghai, China). Taxol and cis-Dichlorodiamineplatinum(II) (Mw=300.05) were received from Baoman bio. (Shanghai, China). All the other starting materials were obtained from *Alfa*. Chemical reagents and solvents were used as received from commercial sources.

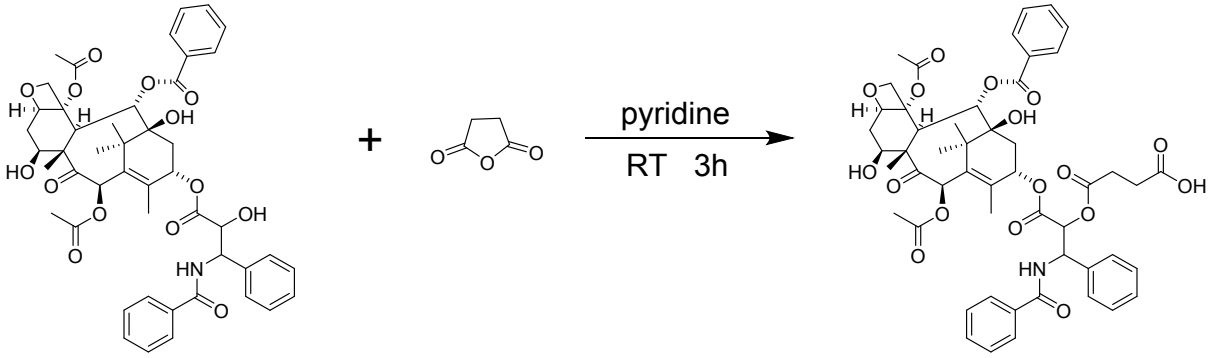
General methods: The synthesized compounds were characterized using ^{1}H NMR (Bruker ARX 400) using DMSO-d_6 as the solvent; HR-MS were received from VG ZAB-HS system (England). HPLC was conducted at LUMTECH HPLC (Germany) system using a C_{18} RP column with MeOH (0.05% of TFA) and water (0.05% of TFA) as the eluents; TEM images were done on a Tecnai G2 F20 system, operating at 200 kV, Rheology was performed on a AR 1500ex (TA instrument) system using a parallel plate (40 mm) at the gap of 500 μm.

Synthesis and characterizations:

Peptide synthesis: The peptide derivative was prepared by solid phase peptide synthesis (SPPS) using 2-chlorotrityl chloride resin and the corresponding N-Fmoc protected amino acids with side chains properly protected. The first amino acid was loaded on the resin at the C-terminal with the loading efficiency about 1.0 mmol/g. 20% piperidine in anhydrous N,N'-dimethylformamide (DMF) was used during de-protection of Fmoc group. Then the next Fmoc-protected amino acid was coupled to the free amino group using O-(Benzotriazol-1-yl)-N,N,N',N'-tetramethyluroniumhexafluorophosphate (HBTU) as the coupling reagent. The growth of the peptide chain was according to the established Fmoc SPPS protocol. After the last coupling step, excessive reagents were removed by a single DMF wash for 5 minutes (5 mL per gram of resin), followed by five steps of washing using DCM for 1 min (5 mL per gram

of resin). The peptide derivative was cleaved using 95% of trifluoroacetic acid with 2.5% of TMS and 2.5% of H_2O for 45 minutes. 20 mL per gram of resin of ice-cold diethylether was then added to cleavage reagent. The resulting precipitate was centrifuged for 10 min at 4 ^{0}C at 10,000 rpm. Afterward the supernatant was decanted and the resulting solid was ready for the next step.

Preparation of Taxol-SA: 0.50 g (0.59 mmol) of paclitaxel was dissolved in 12 mL of pyridine and 0.90g (7.6 mmol) of succinic anhydride was added. After being stirred 3 hrs at room temperature, the mixture was evaporated under reduced pressure, then treated with 20 mL of water, stirred for 20 min, and filtered. The precipitate was dissolved in acetone, water was then slowly added. 0.52 g of fine crystals were collected. (Yield = 92.0%)



Scheme S-1. Synthetic route for Taxol-SA

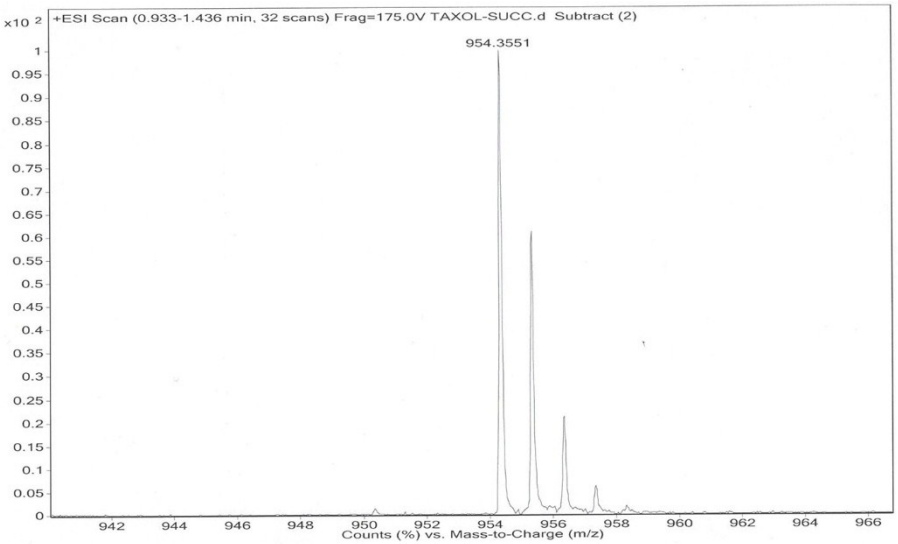
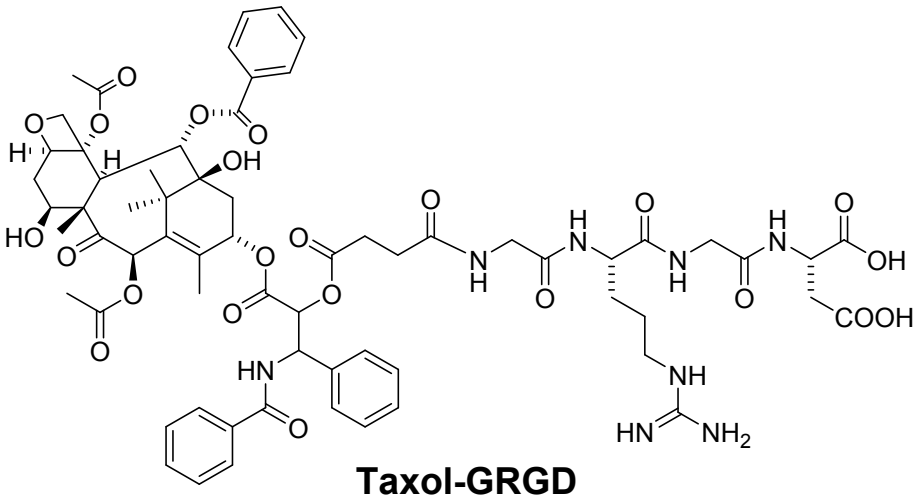


Figure S-1. HR-MS of Taxol-SA

Taxol-GRGD systhesis: 100 mg of Taxol-SA (0.105 mmol) was dissolved in 10 mL of dichloromethane. 1.1 equiv. (13.3 mg, 0.116 mmol) of N-Hydroxysuccinimide and 26 mg (0.126 mmol) of N,N'-dicyclohexylcarbodiimide were added. After being stirred 3hrs at room temperature, the solution was filtered to remove precipitation, dried and evaporated under reduced pressure to yield a white power. The white powder was used for the next step without further purification. The white powder obtained in last step was dissolved in 5 mL N,N-Dimethylformamide, 51 mg (0.126 mmol) of GRGD was then added with 120μL of N-Ethyldiisopropylamine. After being stirred overnight, HPLC was used for purification to yield the title product in a yield of 75%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.21-9.29 (d, J=8.56 Hz, 1H), 8.22-8.29 (m, 2H), 8.06-8.21 (m, 3H), 7.97-8.08 (d, J=7.65 Hz, 2H), 7.84-7.92 (d, J=7.59 Hz, 2H), 7.65-7.78 (m, 3H), 7.43-7.63 (m, 7H), 7.17-7.26 (m, 1H), 6.29 (s, 1H), 5.77-5.86 (m, 1H), 5.50-5.57 (t, 1H), 5.31-5.45 (m, 2H), 4.88-4.99 (m, 2H), 4.66 (s, 1H), 4.51-4.58 (m, 1H), 4.26-4.33 (m, 1H), 3.97-4.15 (m, 3H), 3.65-3.81 (m, 4H), 3.54-3.60 (d, J=7.11 Hz, 1H), 3.03-3.13 (m, 2H), 2.53-2.72 (m, 2H), 2.27-2.36 (m, 2H), 2.24 (s, 3H), 2.11 (s, 3H), 1.77 (s, 3H), 1.58-1.69 (m, 2H), 1.38-1.54 (m, 7H), 0.91-1.05 (d, 6H). HR-MS: calc. M^{+}= 1338.52, obsvd. $(M+1)^{+}$= 1339.5264.



Scheme S-2. Chemical structure of Taxol-GRGD.

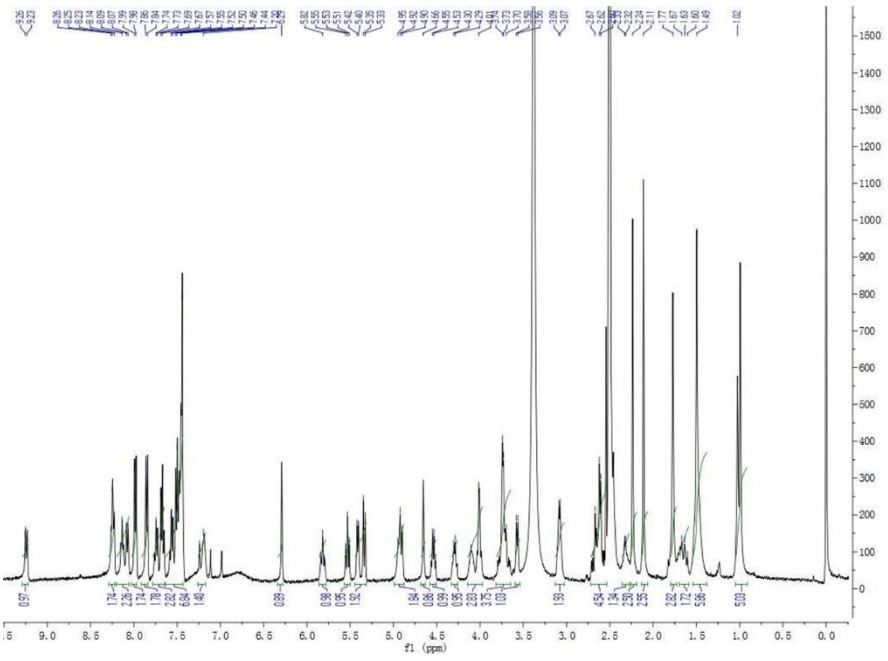


Fig. S-2. ^{1}H NMR of Taxol-GRGD.

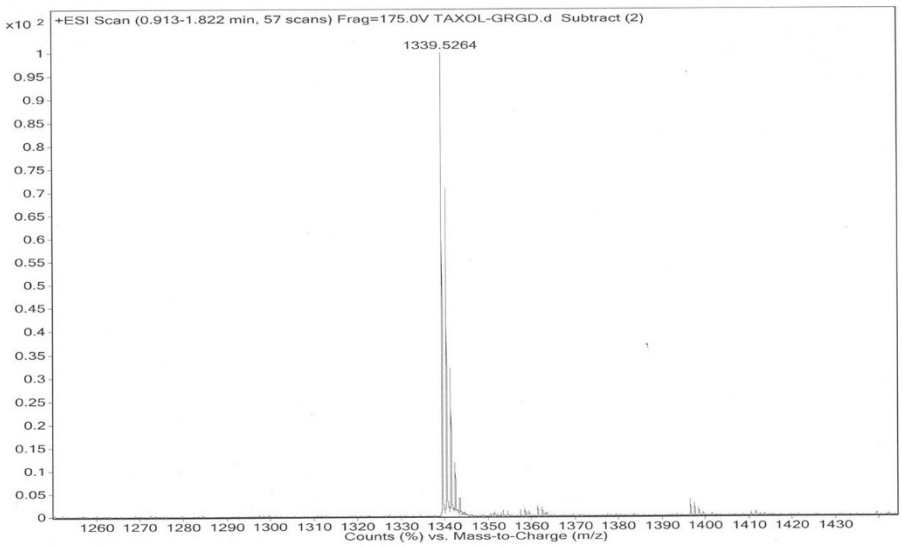


Fig. S-3. HR-MS of Taxol-GRGD.

The separation condition of HPLC to purify Taxol-GRGD was described as following:

Eluant (%) / Time (min)	H_2O	CH_3OH
0	65	35
18	10	90
19	0	100
24	0	100
25	65	35
30	65	35

Table S-1. The separation condition of HPLC for Taxol-GRGD.

Preparation of solution of Taxol-GRGD: 1.4 mg of Taxol-GRGD (1.05 μmol) were dissolved in 1.4 mL of PBS buffer solution containing 0.22 mg (2 equiv. to Taxol-GRGD) of Na_2CO_3 (2 equiv. of Na_2CO_3 were used to neutralize the carboxylic acids on Taxol-GRGD to make the final pH value to 7.4). Then stired the mixture till it turned into a transparent solution for use.

Preparation of hydrogel: To a 0.16 mL of the solution of Taxol-GRGD prepared above in a small vial, 0.04 mL of PBS buffer solution containing 0μg, 1.8μg, 3.6μg, 7.2μg, 18.0μg, 28.8μg, or 43.2μg of cis-Dichlorodiamineplatinum(II) (0 μmol, 0.006 μmol, 0.012 μmol, 0.024 μmol, 0.060 μmol, 0.096 μmol or 0.144 μmol, respectively (0, 0.05, 0.1, 0.2, 0.5, 0.8 or 1.2 equiv.,

respectively) to Taxol-GRGD) was added. Gels would form after being kept at room temperature (22-25℃) for about 30 minutes (the final concentration of Taxol-GRGD was 0.08wt%).

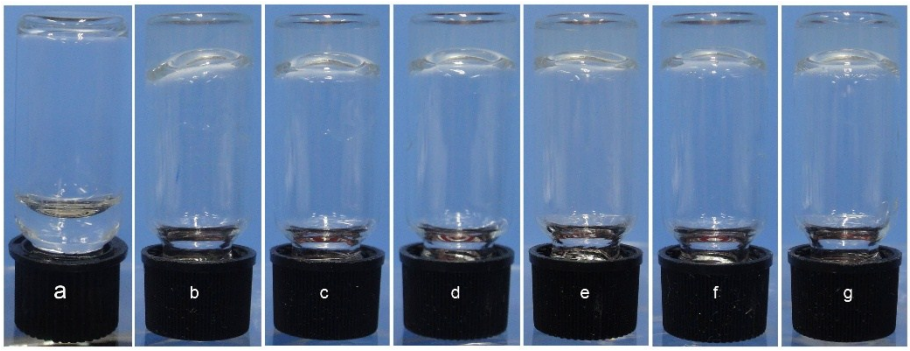


Fig. S-4. Optical images of gel formed by treating the solution containing 0.08 wt% of Taxol-GRGD with different concentrations of cis-Dichlorodiamineplatinum(II): a) 0 equiv. To Taxol-GRGD; b) 0.05 equiv. To Taxol-GRGD; c) 0.1 equiv. To Taxol-GRGD; d) 0.2 equiv. To Taxol-GRGD; e) 0.5 equiv. To Taxol-GRGD; f) 0.8 equiv. To Taxol-GRGD; g) 1.2 equiv. To Taxol-GRGD.

Rheology: Rheology test was done on an AR 1500ex (TA instrument) system, 40 mm parallel plate was used during the experiment at the gap of 500 μm. The dynamic time sweep was conducted at the frequency of 0.5 rad/s and the strain of 0.5%, after waiting for 20min. Dynamic strain sweep was performed and the strain values within the linear range were chosen for the following dynamic frequency sweep. The gels were characterized by the mode of dynamic frequency sweep in the region of 0.1-100 rad/s at the strain of 0.5%.

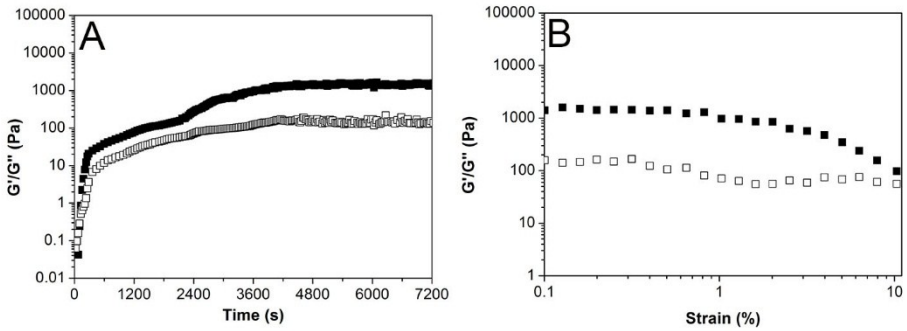


Fig. S-5. Rheological measurements with A) the mode of dynamic time sweep at a frequency of 0.5 rad s^{-1} and strain of 0.5 % for PBS solutions containing 0.08 wt % Taxol-GRGD and cis-Dichlorodiamineplatinum(II) (0.05 equiv. relative to Taxol-GRGD); B)the mode of dynamic Strain sweep at a frequency of 0.5 % for PBS solutions containing 0.08 wt % Taxol-GRGD and cis-Dichlorodiamineplatinum(II) (0.05 equiv. relative to Taxol-GRGD). (closed symbols: G' and open symbols: G'').

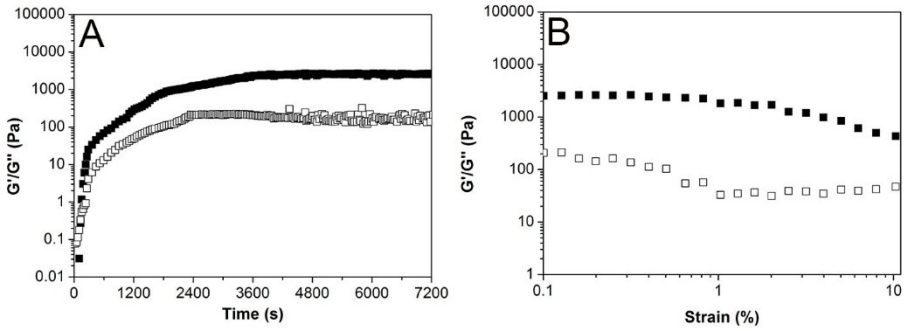


Fig. S-6. Rheological measurements with A) the mode of dynamic time sweep at a frequency of 0.5 rad s^{-1} and strain of 0.5 % for PBS solutions containing 0.08 wt % Taxol-GRGD and cis-Dichlorodiamineplatinum(II) (0.10 equiv. relative to Taxol-GRGD); B)the mode of dynamic Strain sweep at a frequency of 0.5 % for PBS solutions containing 0.08 wt % Taxol-GRGD and cis-Dichlorodiamineplatinum(II) (0.10 equiv. relative to Taxol-GRGD). (closed symbols: G' and open symbols: G'')

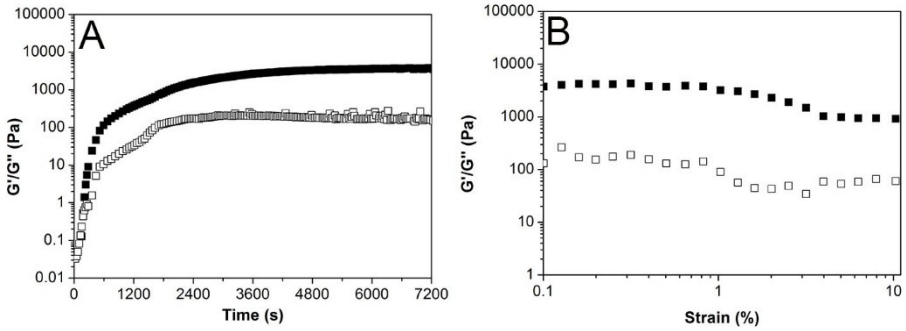


Fig. S-7. Rheological measurements with A) the mode of dynamic time sweep at a frequency of 0.5 rad s^{-1} and strain of 0.5 % for PBS solutions containing 0.08 wt % Taxol-GRGD and cis-Dichlorodiamineplatinum(II) (0.20 equiv. relative to Taxol-GRGD); B)the mode of dynamic Strain sweep at a frequency of 0.5 % for PBS solutions containing 0.08 wt % Taxol-GRGD and cis-Dichlorodiamineplatinum(II) (0.20 equiv. relative to Taxol-GRGD). (closed symbols: G' and open symbols: G'')

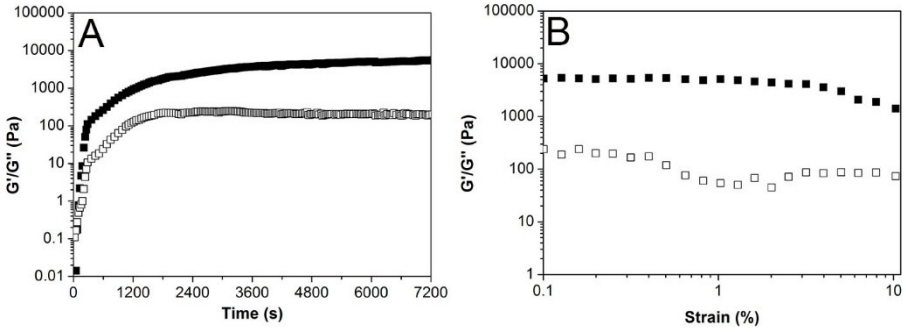


Fig. S-8. Rheological measurements with A) the mode of dynamic time sweep at a frequency of 0.5 rad s^{-1} and strain of 0.5 % for PBS solutions containing 0.08 wt % Taxol-GRGD and cis-Dichlorodiamineplatinum(II) (0.50 equiv. relative to Taxol-GRGD); B)the mode of dynamic Strain sweep at a frequency of 0.5 % for PBS solutions containing 0.08 wt % Taxol-GRGD and cis-Dichlorodiamineplatinum(II) (0.50 equiv. relative to Taxol-GRGD). (closed symbols: G' and open symbols: G'')

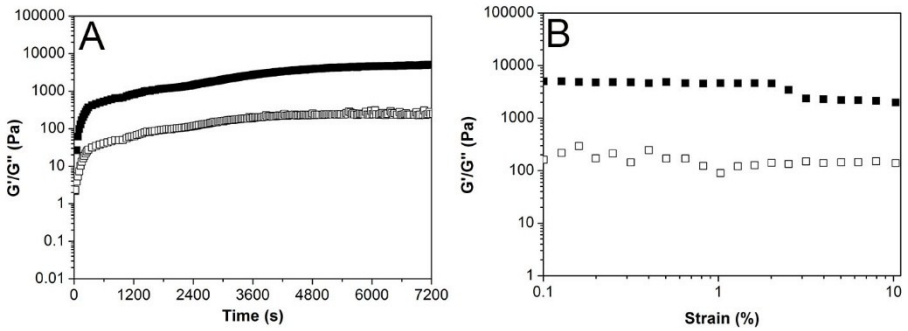


Fig. S-9. Rheological measurements with A) the mode of dynamic time sweep at a frequency of 0.5 rad s^{-1} and strain of 0.5 % for PBS solutions containing 0.08 wt % Taxol-GRGD and cis-Dichlorodiamineplatinum(II) (0.80 equiv. relative to Taxol-GRGD); B)the mode of dynamic Strain sweep at a frequency of 0.5 % for PBS solutions containing 0.08 wt % Taxol-GRGD and cis-Dichlorodiamineplatinum(II) (0.80 equiv. relative to Taxol-GRGD). (closed symbols: G' and open symbols: G'')

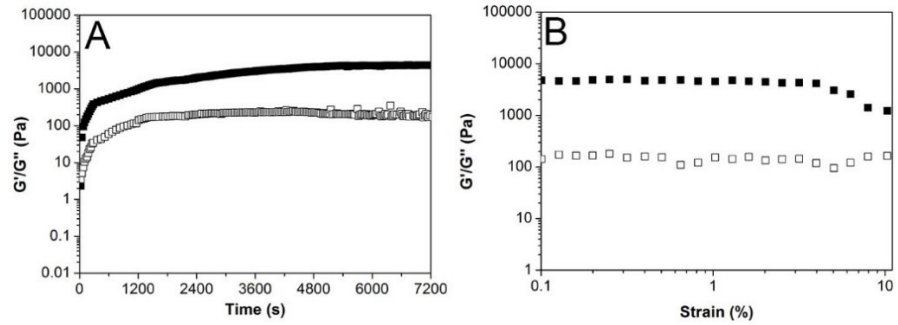


Fig. S-10. Rheological measurements with A) the mode of dynamic time sweep at a frequency of 0.5 rad s^{-1} and strain of 0.5 % for PBS solutions containing 0.08 wt % Taxol-GRGD and cis-Dichlorodiamineplatinum(II) (1.2 equiv. relative to Taxol-GRGD); B)the mode of dynamic Strain sweep at a frequency of 0.5 % for PBS solutions containing 0.08 wt % Taxol-GRGD and cis-Dichlorodiamineplatinum(II) (1.2 equiv. relative to Taxol-GRGD). (closed symbols: G' and open symbols: G'')

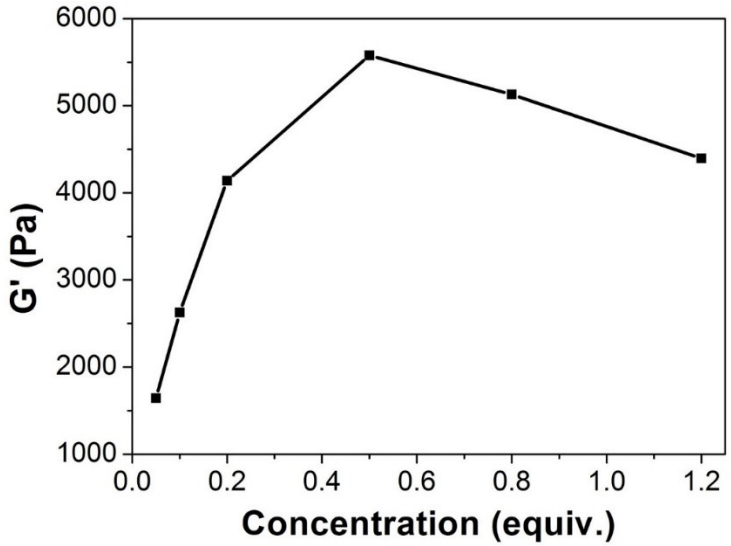


Fig. S-11. The pressure values of different amounts of cis-Dichlorodiamineplatinum(II) at the frequency of 0.5 rad/s.

TEM images:

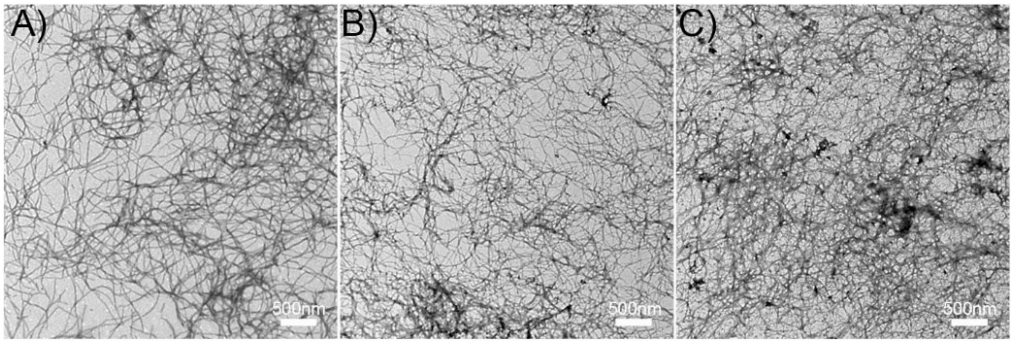


Fig. S-12. TEM images: 0.08 wt % Taxol-GRGD and different concentrations of cis-Dichlorodiamineplatinum(II) A) 0.05 equiv. To Taxol-GRGD; B) 0.8 equiv. To Taxol-GRGD; C) 1.2 equiv. To Taxol-GRGD.

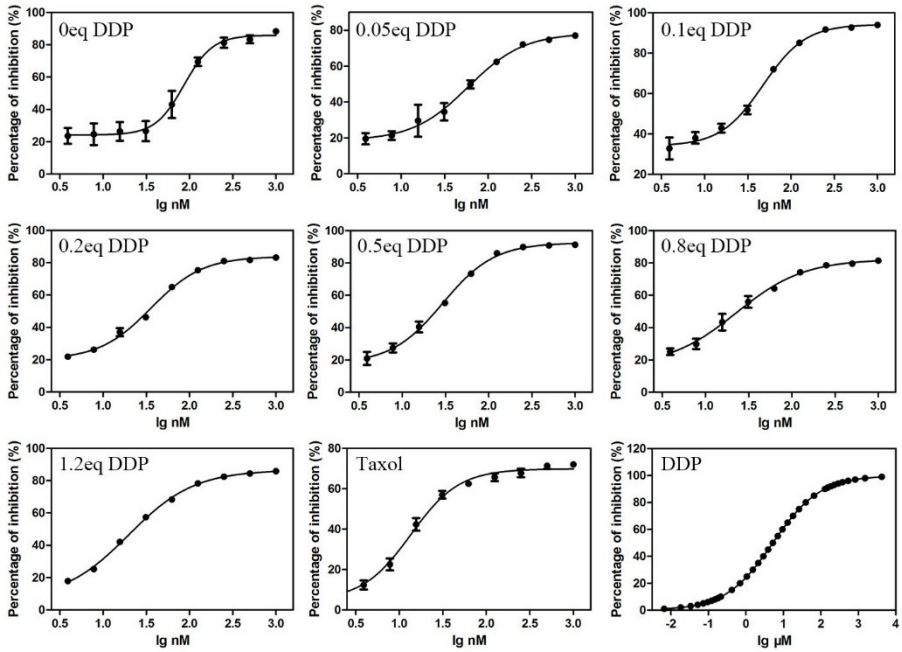


Fig. S-13. Representative congress curve of HepG2 cell inhibition of the gels with different amounts of DDP

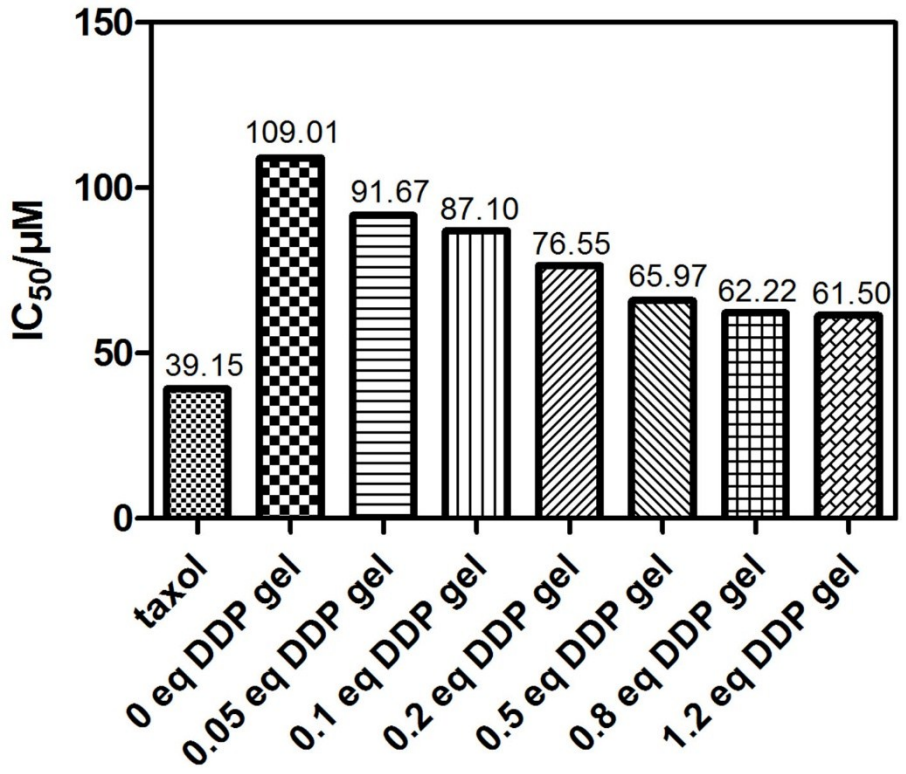


Fig. S-14. Cytotoxicity of Taxol-GRGD with different amounts of DDP against NIH 3T3 cells.

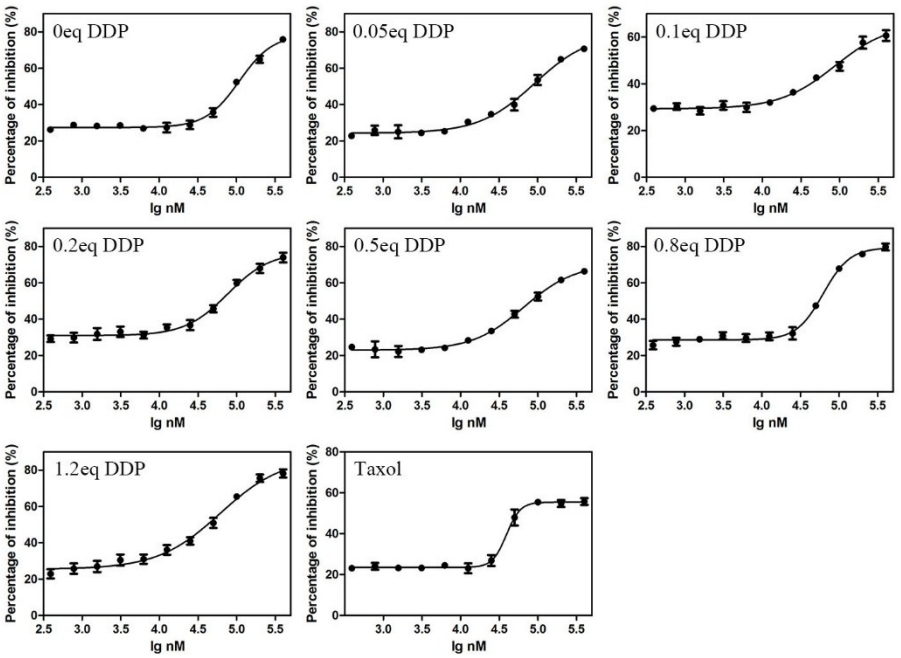


Fig. S-15. Representative congress curve of 3T3 cell inhibition of the gels with different amounts of DDP

Release Profile: 0.2 mL of hydrogel was formed as described above (the final concentrations of the DDP was 0.1, 0.2, and 0.5 equiv. to Taxol-GRGD, respectively. Taxol-GRGD was 0.1 wt%). 10 hours after the formation of gels, each gel was treated with 0.2 mL of fresh PBS buffer

solution (pH 7.4). 0.2 mL of the upper buffer solution was taken out and used to test by LC-MS at the wavelength of 220 nm at designated time intervals. A fresh 0.2 mL of PBS was then added back to the gel. Standard curve of taxol was determined before the test. The experiment was conducted in three parallel experiments.

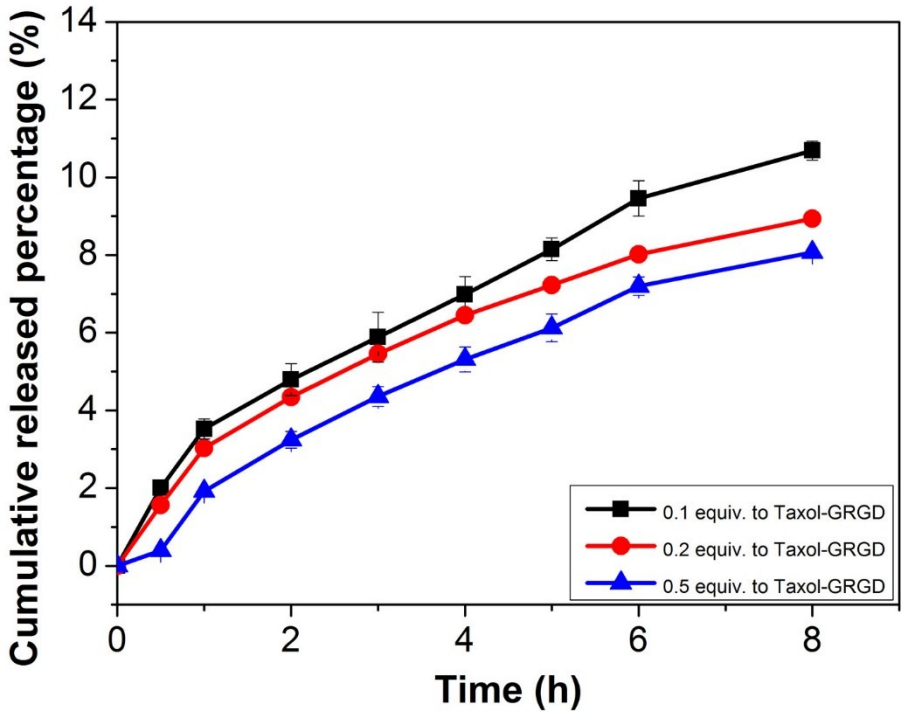


Fig. S-16. Drug release profile of taxol from hydrogels in the presence of different concentrations of DDP (0.1, 0.2 and 0.5 equiv. to Taxol-GRGD)