Supplementary Material

Poly[platinum(IV)-*alt*-PEI]/Akt1 shRNA complexes for enhanced anticancer Therapy

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Materials and Methods

FTIR spectrum measurement

The FTIR spectrum of DHP was carried out using the KBr disk method in the wavelength region of 4000-400 cm^{-1} by FTIR spectrophotometer. (Bruker, TENSOR 27)

Energy Dispersive X-Ray Spectroscopy (EDX) measurement

The EDX measurement was carried out using JEOL JEM-2100 equipped with an IN-CA x-sight at 200 kV. The area of DP/shAkt1 nanoparticles was analysed by EDX to reveal atomic components.

Endosomal buffering capacity of DP

The buffering capacity of DP was measured by acid-base titration over the pH range of 10.0 to 3.0. Briefly, 2 mg of DP and PEI 25K were dissolved in 10 mL of 0.15 M NaCl solution, respectively. The solution was brought to pH of 10.0 using 0.1 M NaOH and then titrated with 0.1 M HCl solution until the pH value decreased to 3.0. The pH of solutions was measured by a pH meter (Satorious, German). Meanwhile, 0.15 M NaCl solution, PEI 25K solution were titrated in the same way as controls, respectively.

Released Pt(II) species by MALDI-TOF-MS

DP (10 mg) was dissolved in distill water (2 mL), and then dialyzed against distill water (molecular weight cut-off = 1000 Da) in the presence of 5 mM sodium ascorbate. After dialysis for 48 h, the solution out of the dialysis bag was collected in a vial, to which 2′-deoxyguanosine 5′-monophosphate sodium salt hydrate (GG, Sigma Aldrich) was added to a final concentration of 50 μM. The vial was kept in the dark and shaken for 24 h at 37 ^{o}C, and then aliquots were collected for MALDI-TOF-MS study (AB SCIEX TOF/TOF 5800).

Release profile of platinum from DP *in vitro*

The *in vitro* release of platinum from DP was evaluated as previously reported.[1] DP (50 mg) was dissolved in 2 mL PBS (pH 7.4, 100 mM), then transferred into a pre-swelled dialysis bag (molecular weight cut-off = 1500 Da), and immersed into 100 mL PBS (pH 7.4, 100 mM). The drug release experiment was carried out at 37 ^{o}C with stirring at 120 rpm. At indicated time points (1 h, 4 h, 12 h, 24 h, 48 h, 72 h), 1.0 mL sample solution was withdrawn and its platinum concentration was measured by ICP-MS (Agilent 7700e). Equal volume of fresh PBS was immediately replenished.

^{195} NMR spectroscopy

For ^{195}Pt NMR measurement, DP was dissolved in D_2O at a concentration of 30 mg mL^{-1}. ^{195}Pt NMR spectra were recorded on a Bruker AVANCE-400 NMR spectrometer. Chemical shifts were externally referenced to K_2PtCl_6 in D_2O (δ = 0 ppm).

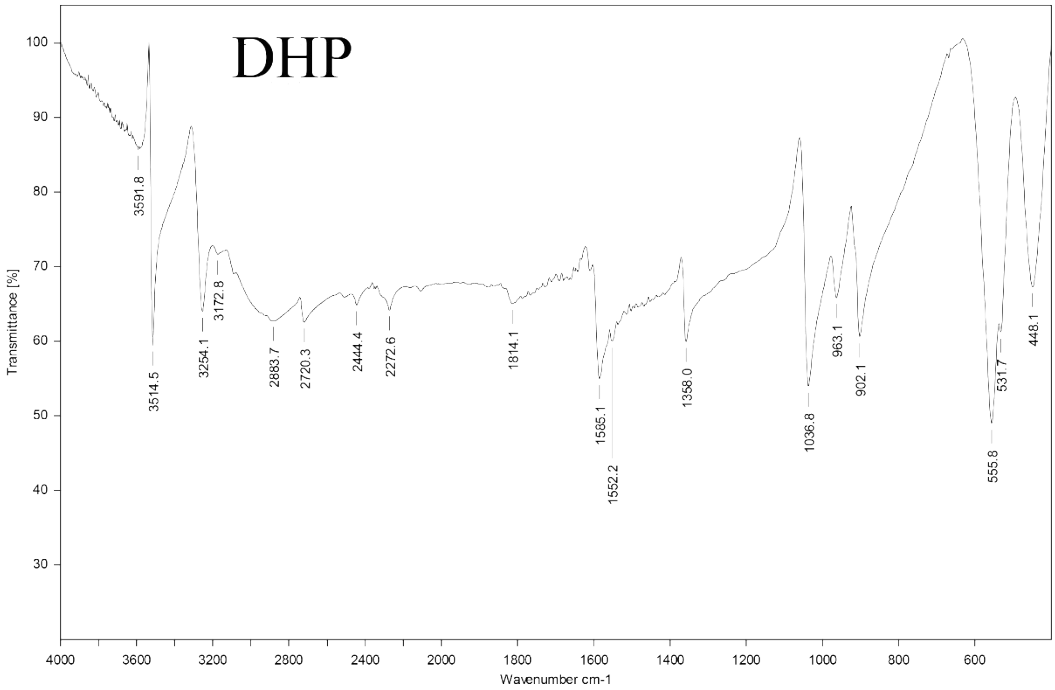

Figure S1. FTIR spectrum of DHP.

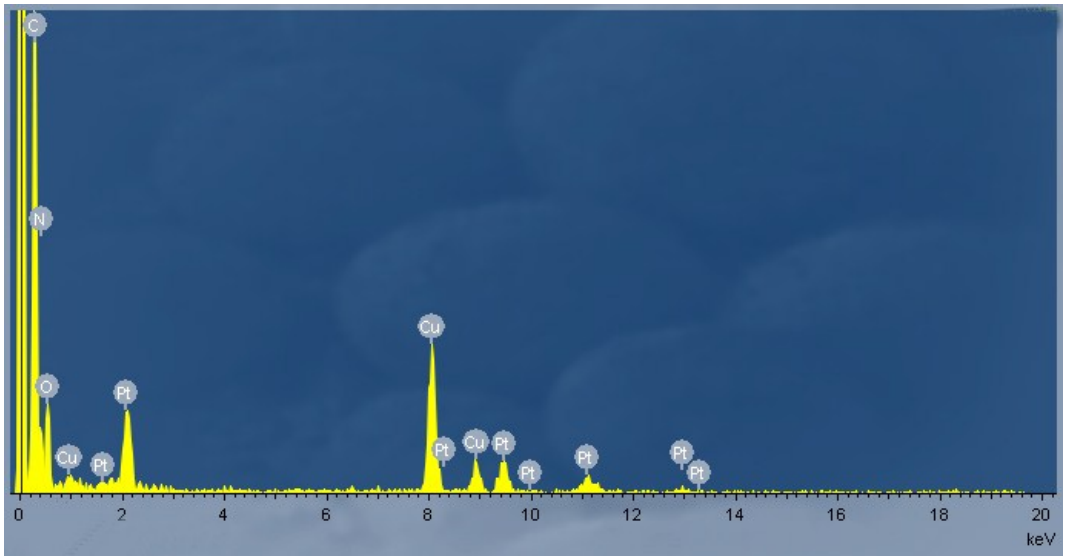

Figure S2. EDX spectrum of DP/shAkt1 complexes.

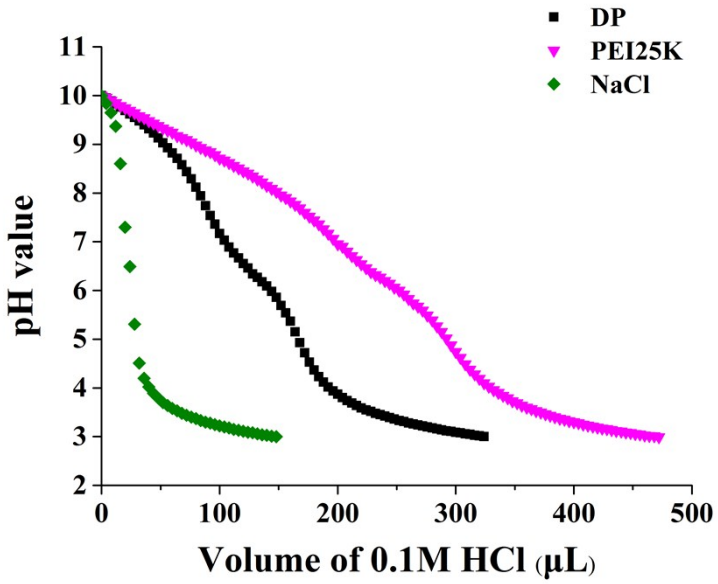

Figure S3. Acid-base titration curves of NaCl, DP and PEI 25K obtained by titrating 0.2 mg mL^{-1} aqueous solutions (starting pH 10.0, adjusted by 0.1M NaOH) of the samples in 0.15 M NaCl solution to pH 3.0 with 0.1M HCl.

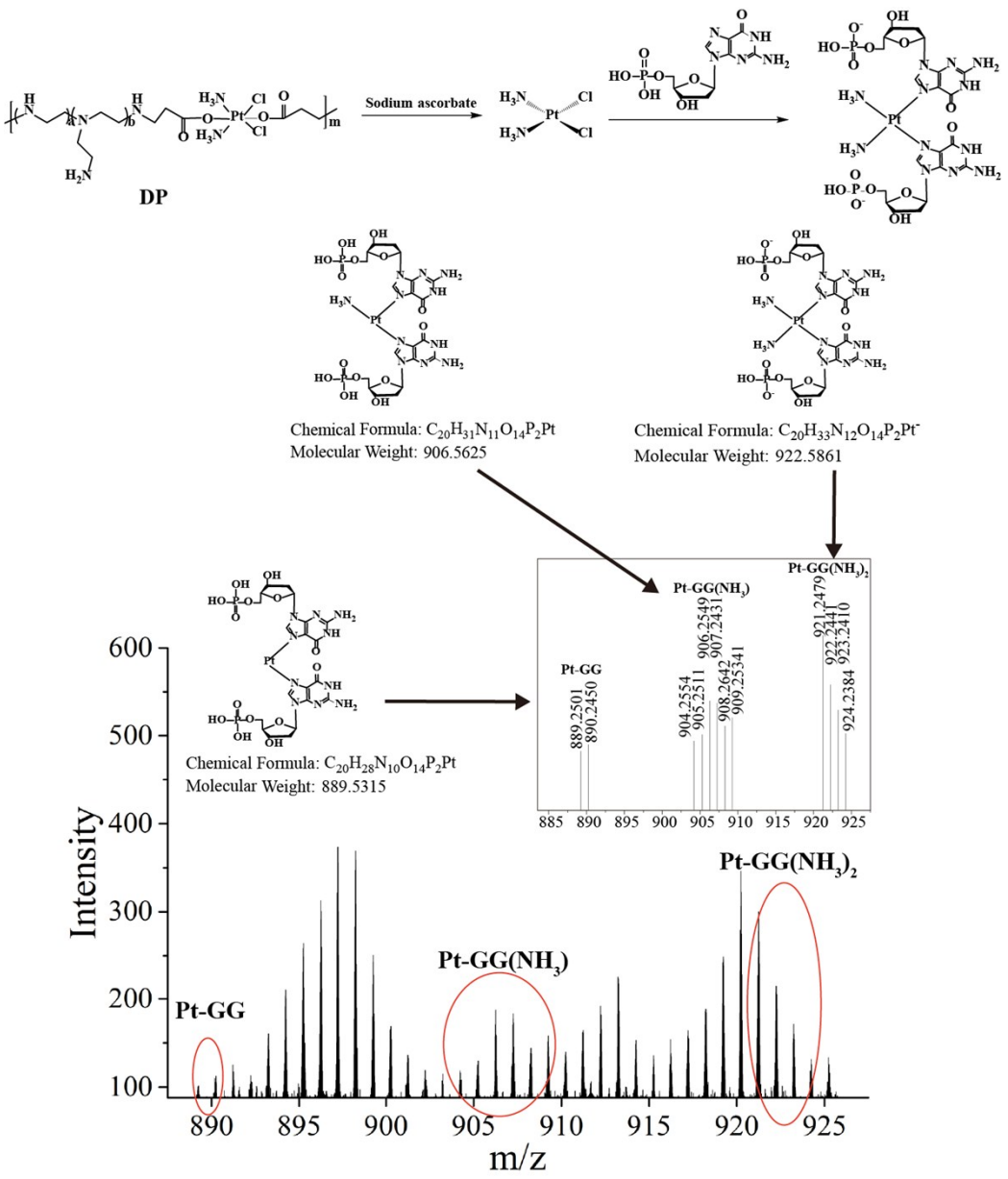

Figure S4. MALDI-TOF-MS chromatogram of Pt-GG adducts obtained by the reaction of DP and 5′-GMP in the presence of sodium ascorbate. Exhibited isotopic peak pattern confirms the presence of Pt species in Pt-GG adduct.

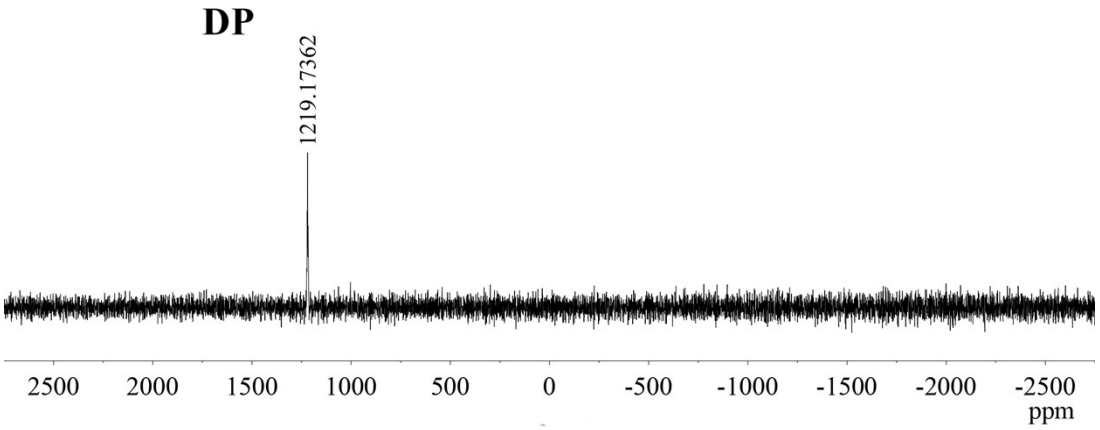

Figure S5. ^{195}Pt NMR of DP in D_2O

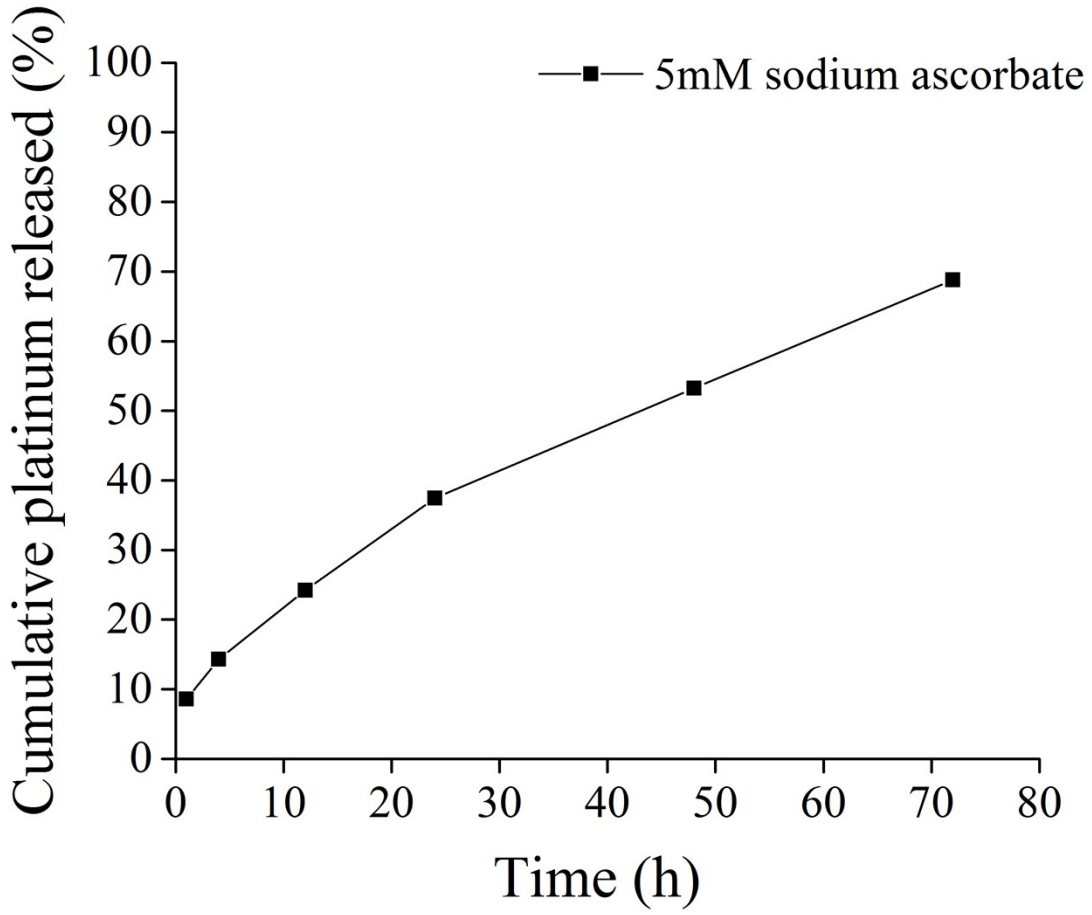

Figure S6. Platinum release profiles of DP.

Table S1. The molecular weight and polydispersity index of DP.

	Mw	Mn	PDI
DP	**2654**	**1935**	**1.37**

Table S2. The theoretical and actual platinum(IV) prodrug content in the polymer synthesized by DHPAA and PEI 800 with different molar ratios. (means ± SD, n=3).

Molar ratios of DHPAA/PEI 800	Theoretical platium (Ⅳ) prodrug content (wt%)	Actual platium (Ⅳ) prodrug content (wt%)
1:1	35.9	35.946 ± 0.1243
0.5:1	17.95	18.0546 ± 0.0248

1. H. Song, H. Xiao, Y. Zhang, H. Cai, R. Wang, Y. Zheng, Y. Huang, Y. Li, Z. Xie and T. Liu, *Journal of Materials Chemistry B*, 2013, **1**, 762-772.