Supporting Information

Synergistic platinum (II) prodrug nanoparticle for enhanced breast cancer therapy

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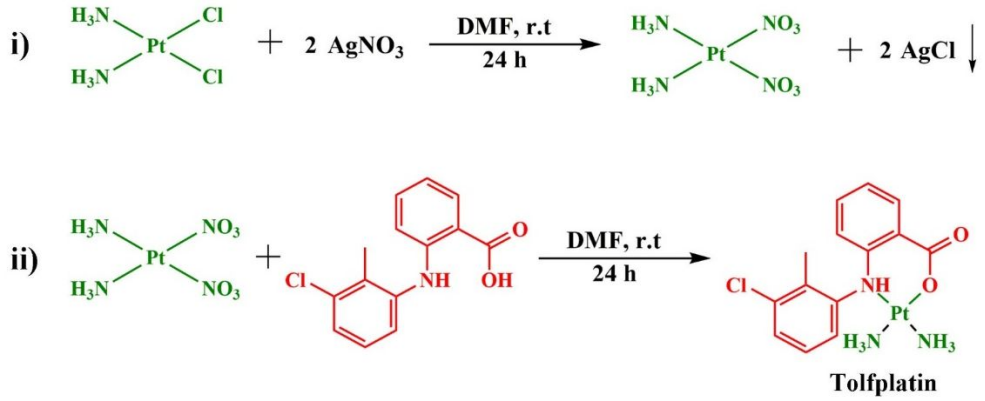

Figure S1. Synthesis process of Tolfplatin. i) cisplatin with two-fold molar ratio silver nitrate was mixed and stirred in DMF solution at room temperature for 24 h. ii) cis-Dinitrodiamine platinum (II) with equal molar ratio Tolf was mixed and stirred in DMF solution at room temperature for 24 h.

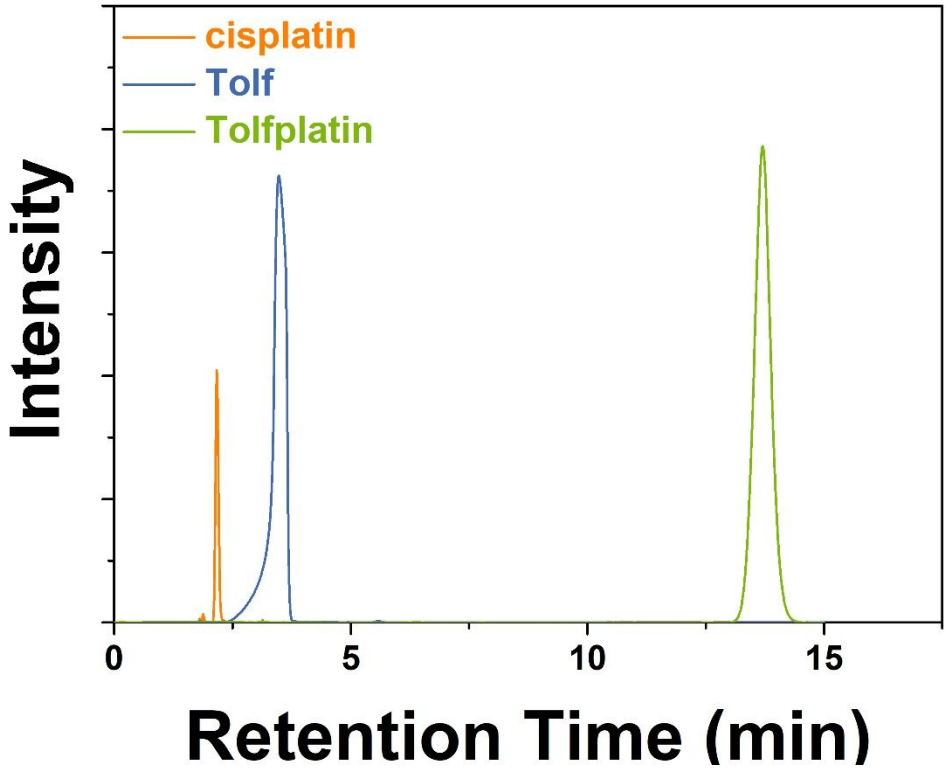

Figure S2. RP-HPLC (290 nm) chromatograms of cisplatin, Tolf and Tolfplatin. 20 % solvent A (H_2O) and 80 % solvent B (ACN) were used for an isocratic elution at a flow rate of 1 mL/min. The injection volume was 20 μL.

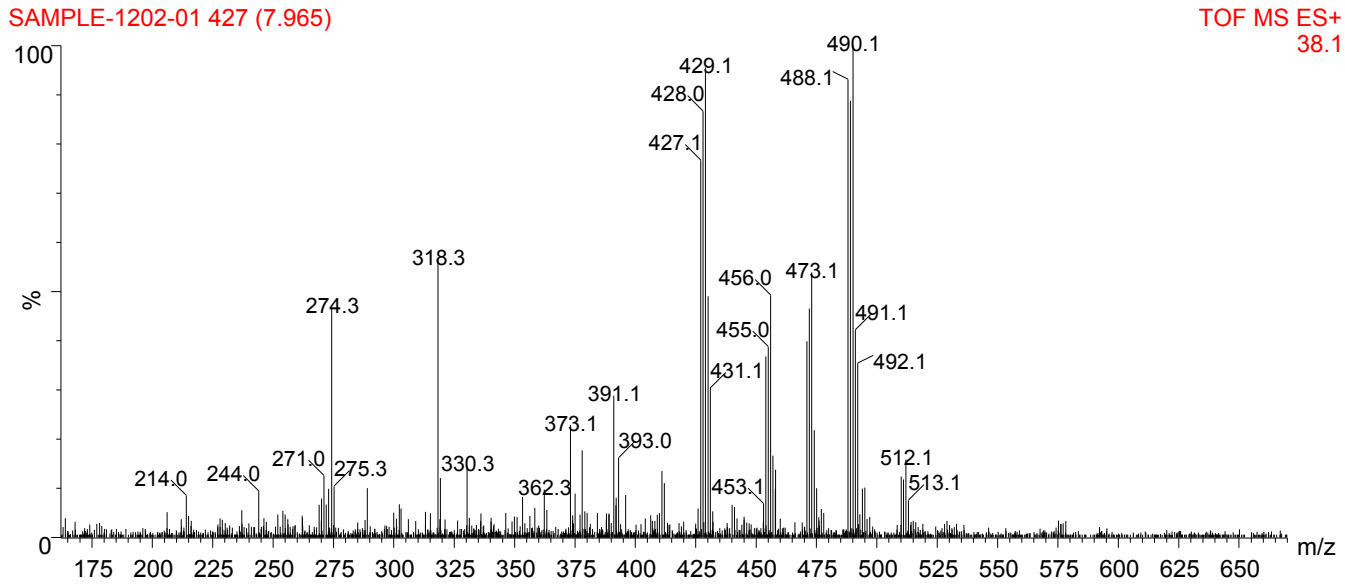

Figure S3. ESI-MS spectrum of Tolfplatin, m/z=490.1 $[M+H]^+$.

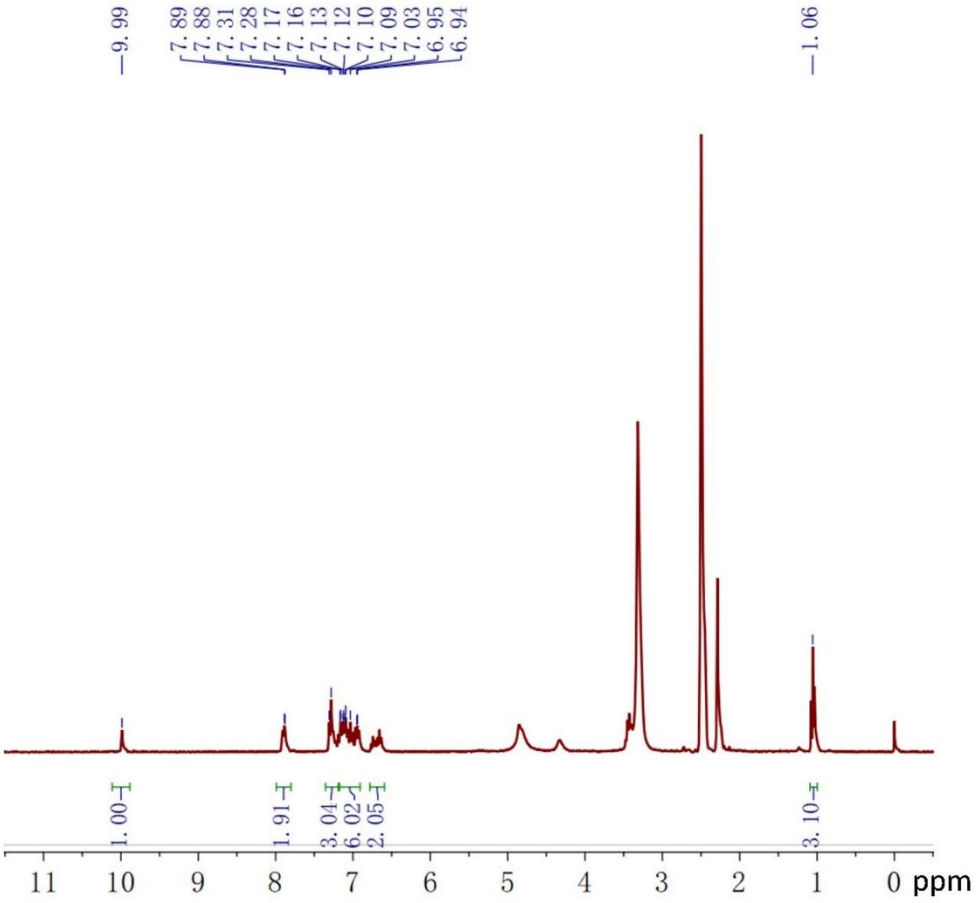

Figure S4. ^{1}H-NMR spectrum of Tolfplatin in DMSO-d_6. δppm, 9.99 (s, 1H), 7.89 (s, 2H), 7.31-7.29 (d, 3H, *J*=9 Hz), 7.16-6.94 (m, 6H), 6.78-6.59 (t, 2H, *J*=6 Hz), 1.06 (s, 3H).

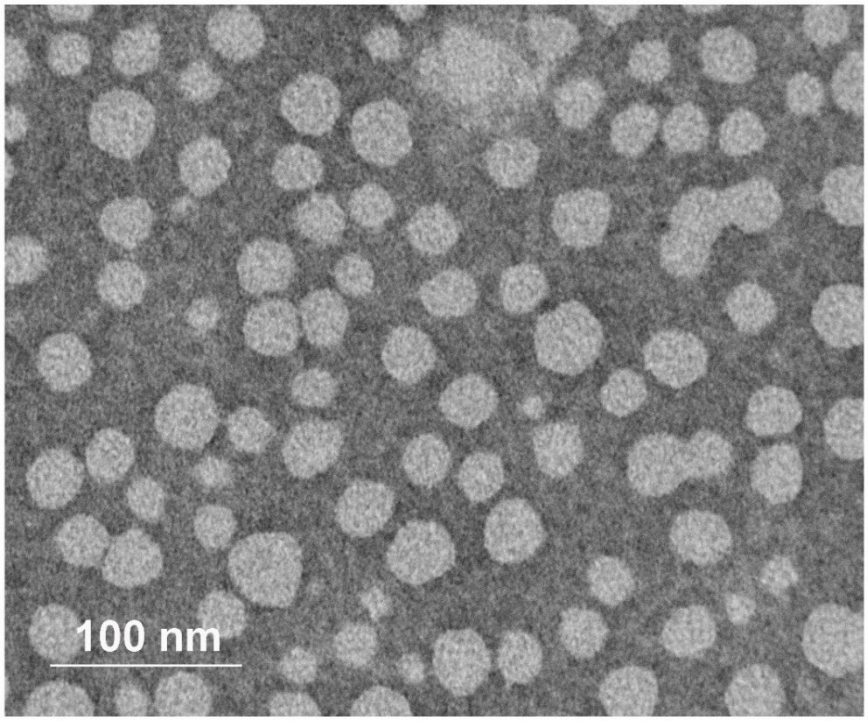

Figure S5. TEM morphological characterization of LP NPs.

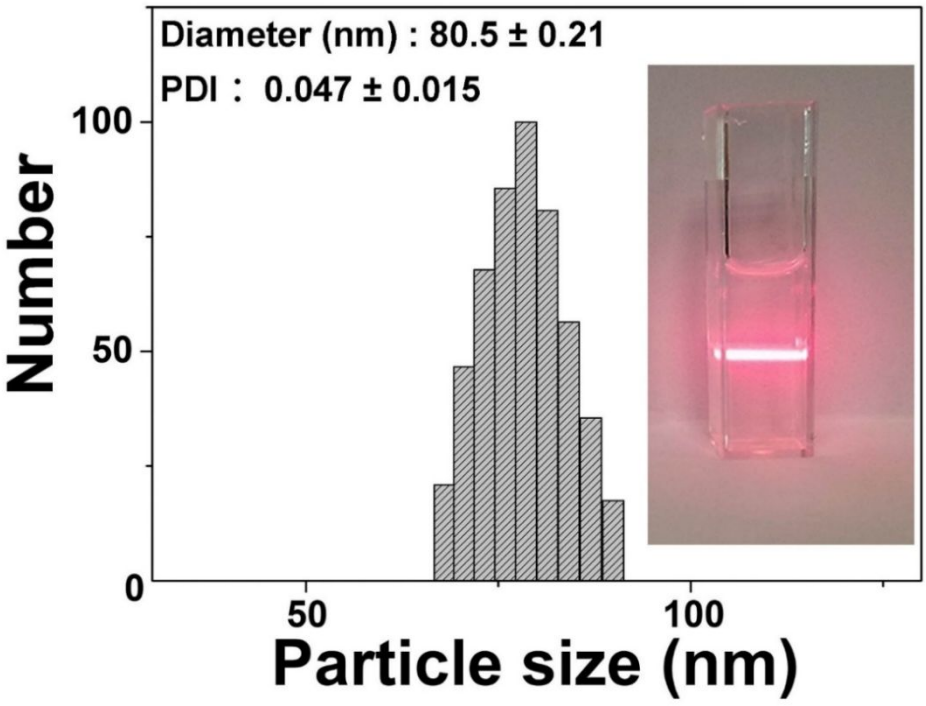

Figure S6. Diameter distribution of LP NPs measured by DLS and appearance of LP NPs under laser beam, the zeta potential is -37.81 ± 2.76 mv.

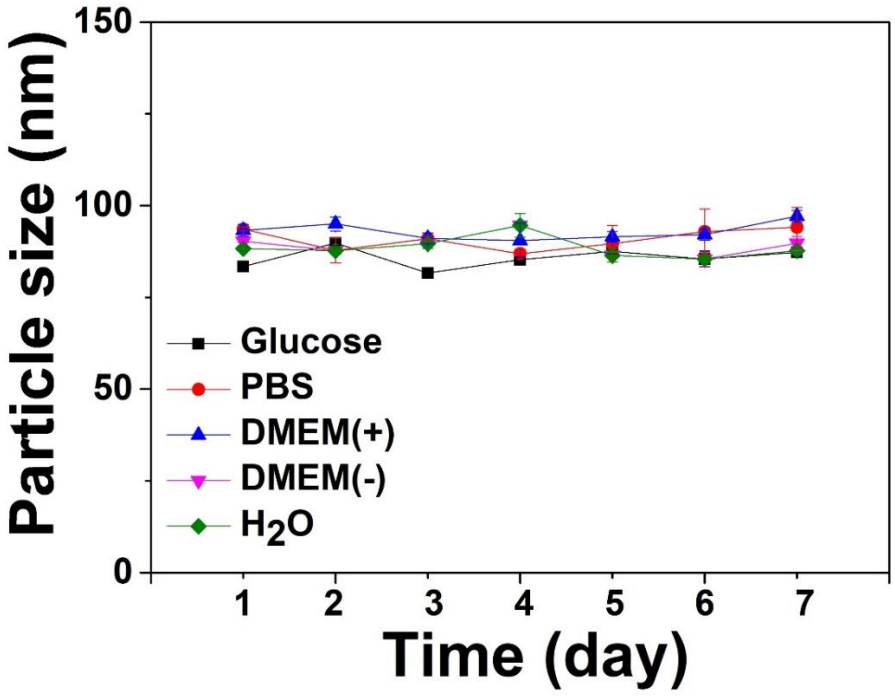

Figure S7. Stability of LPTP NPs dispersed in different solutions at 4 ^{o}C.

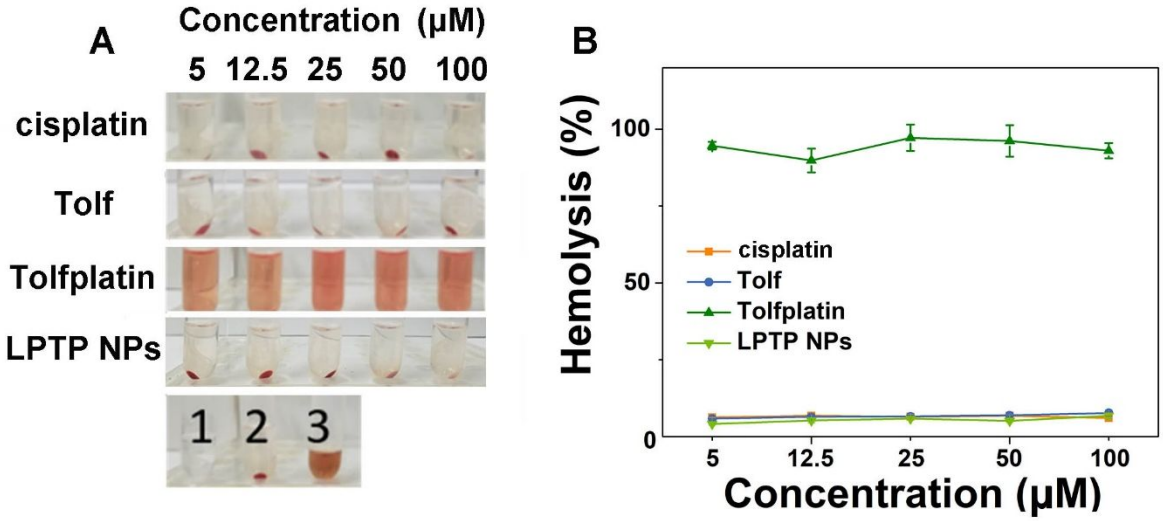

Figure S8. A) The appearance of red blood cells suspension after incubation with different concentrations of drugs. 1, 2, 3 represent glucose solution, glucose and red blood cells suspension, Triton X-100 and red cell suspension, respectively. B) The hemolysis rate of different concentrations of drugs was measured by UV-vis at 540 nm.

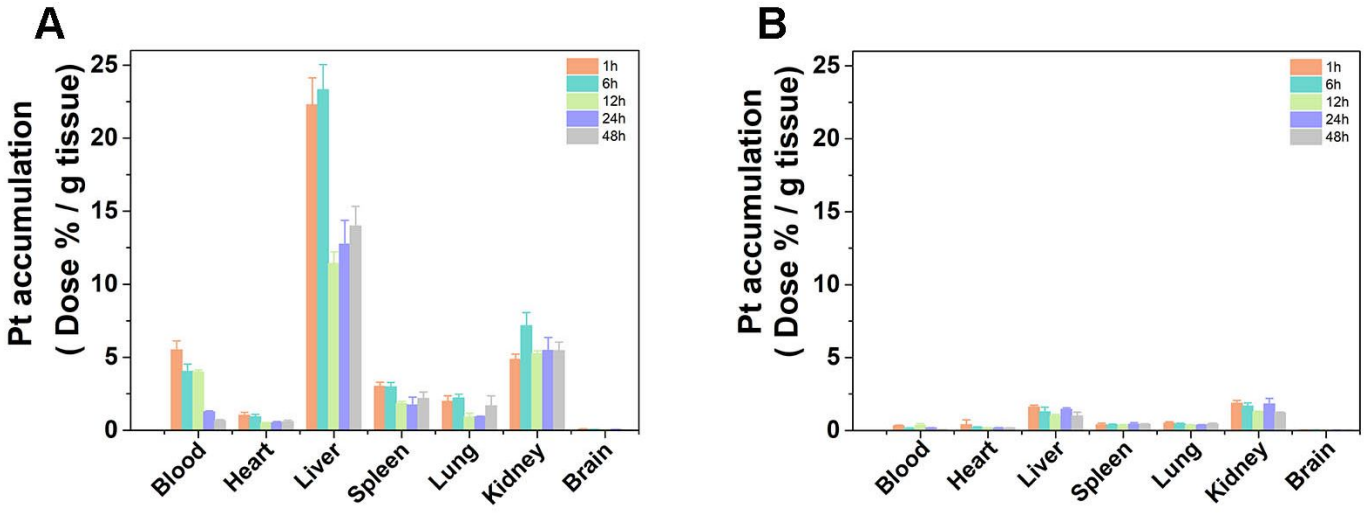

Figure S9. A) Pt accumulation in different tissues at different time points (1 h, 6 h, 12 h, 24 h, 48 h) after intravenous injection of LPTP NPs (n=15). B) Pt accumulation in different tissues at different time points (1 h, 6 h, 12 h, 24 h, 48 h) after intravenous injection of cisplatin (n=15).

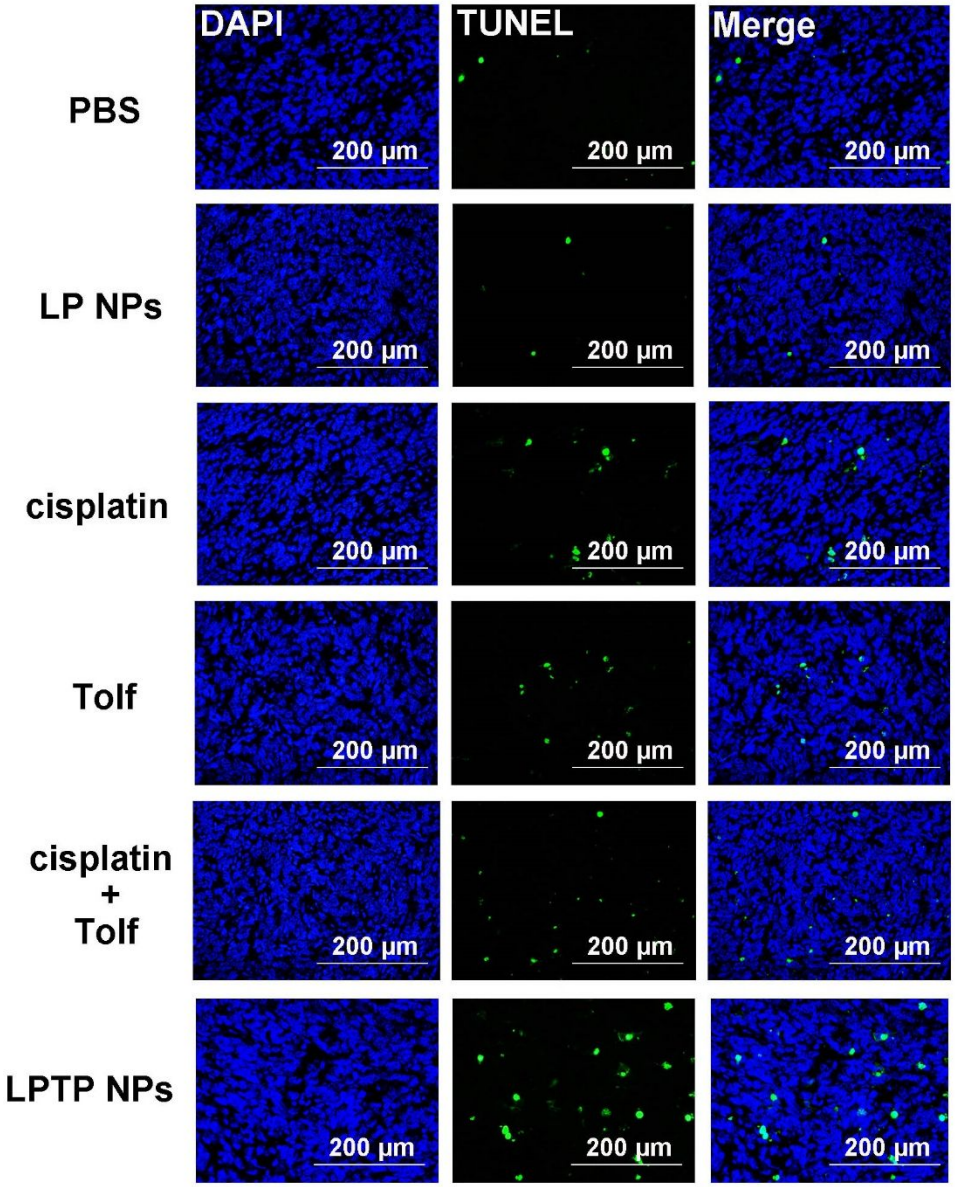

Figure S10. TUNEL staining in tumors of mice treated with different formulations after five treatments.

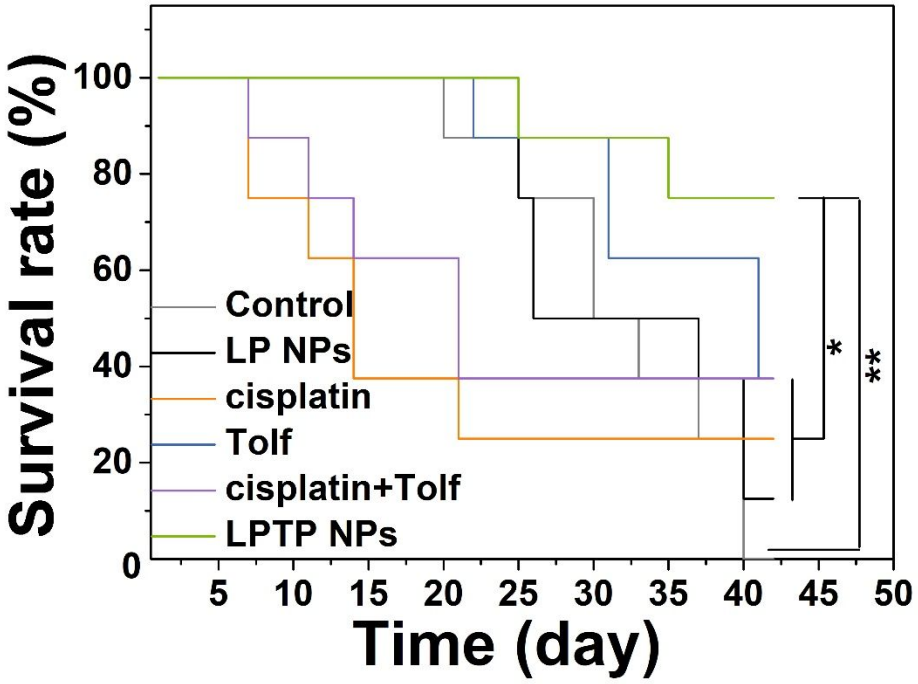

Figure S11. Survival rate of tumor-bearing mice after different formulations treatments (n=8, *P < 0.05, **P < 0.01).