

Supplementary information

Cancer cell membrane fused liposomal platinum (IV) prodrugs overcome cisplatin resistance in esophageal squamous cell carcinoma chemotherapy

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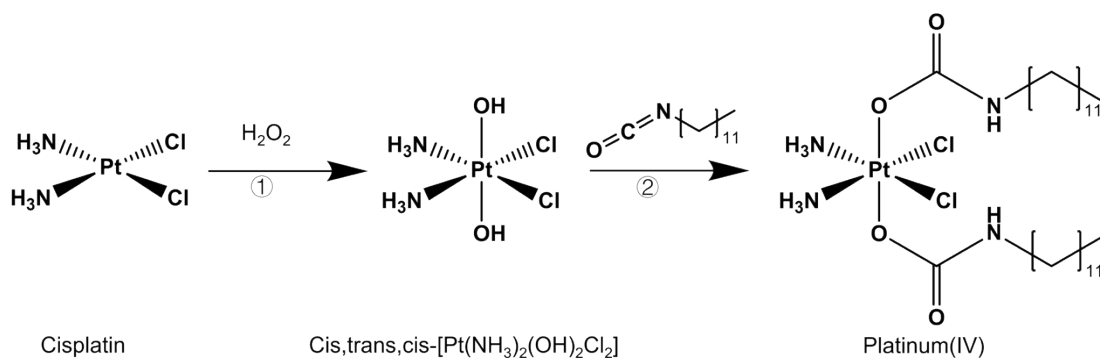


Fig. S1 Schematic illustration of synthesis of Pt(IV). Step 1: Cisplatin (300 mg) was dispersed in H₂O₂ (30% w/v, 10 mL), stirred overnight at 50 °C in the dark, then boiled at 100 °C for 30 min, cooled to room temperature, and recrystallized for 12 h at 4 °C. After washing three times each with water, ethanol, ether and acetone, yellow product (Cis,trans,cis-[Pt(NH₃)₂(OH)₂Cl₂]) was obtained after drying; Step 2: Cis,trans,cis-[Pt(NH₃)₂(OH)₂Cl₂] (200 mg) was added to 40 mL DMF and stirred and dispersed. After the temperature reached 65 °C, 397 mg of 12-alkyl isocyanate was added and reacted until the solution became clear and transparent orange liquid. The crude product was obtained by removing DMF by vacuum rotary steaming at 65 °C. This was followed by dissolution using hot methanol and precipitation of the product using large amounts of diethyl ether. The supernatant was removed by centrifugation and dried in a vacuum drying oven.

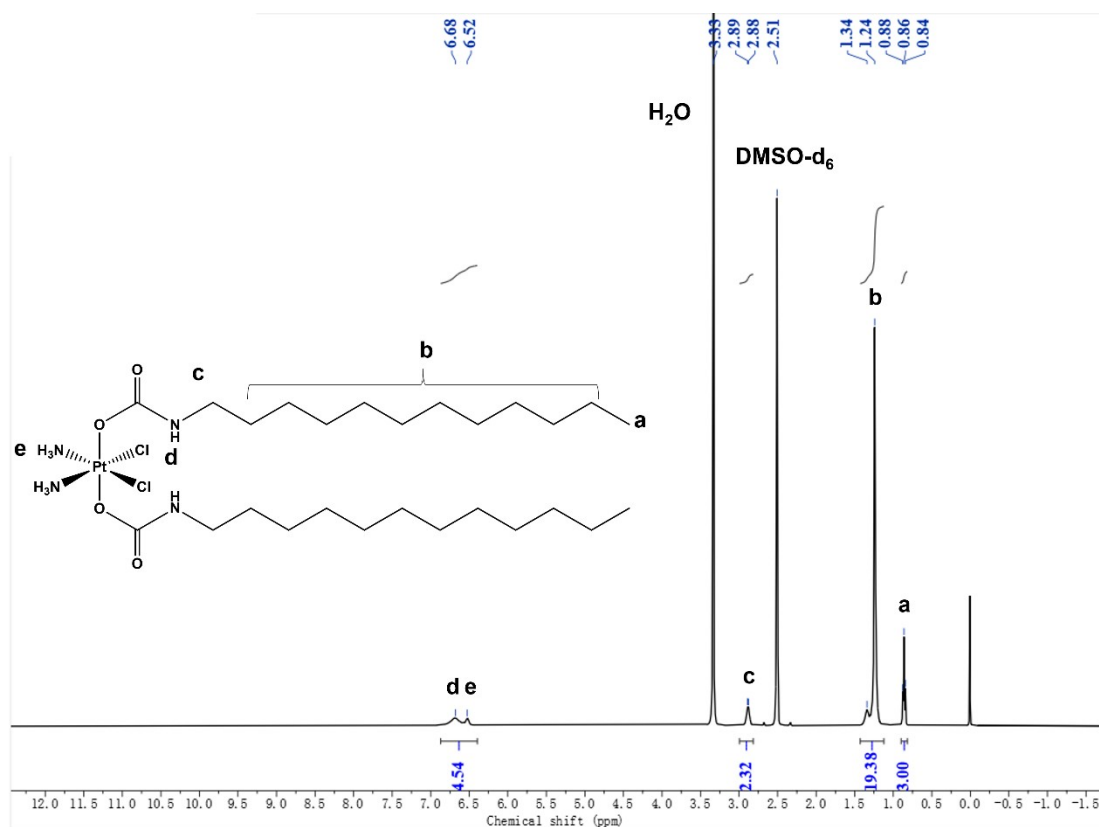


Fig. S2 Characterization of Pt(IV) by ¹H NMR 400 MHz in DMSO-d₆.

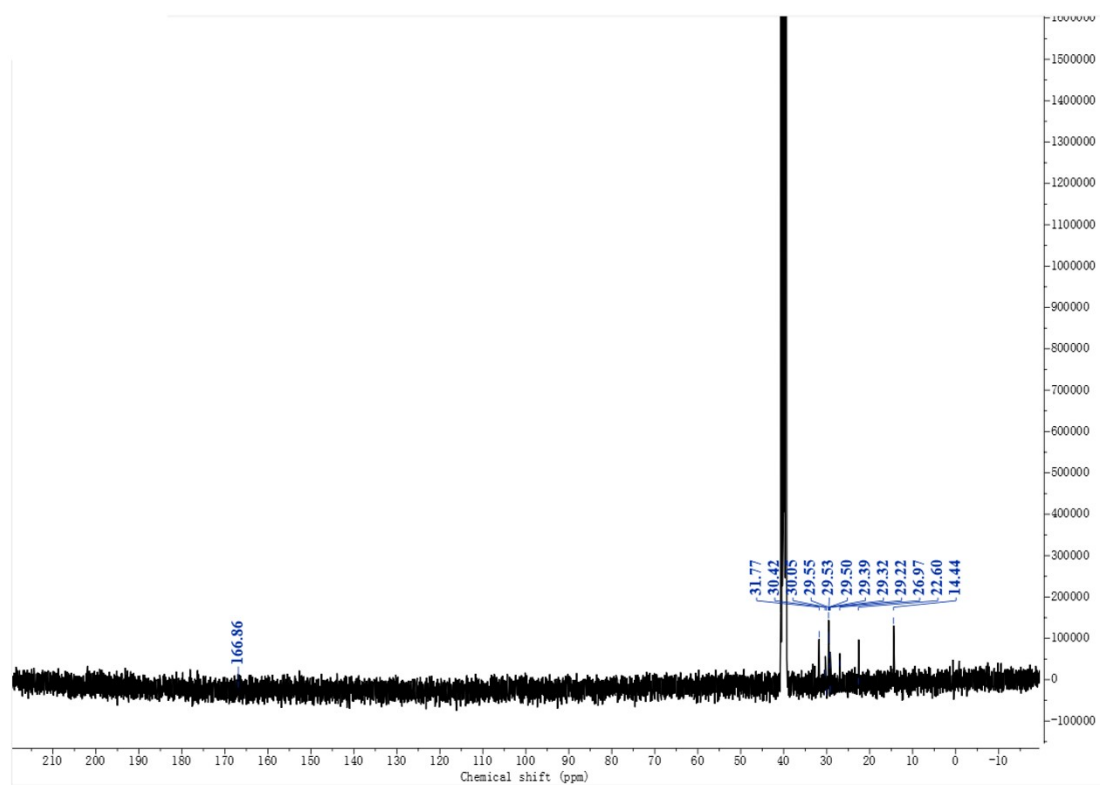


Fig. S3 Characterization of Pt(IV) by ^{13}C NMR 100 MHz in $\text{DMSO-}d_6$.

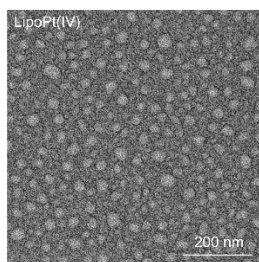


Fig. S4 Transmission electron microscopy (TEM) image of LipoPt(IV). Scale bar = 200 nm.

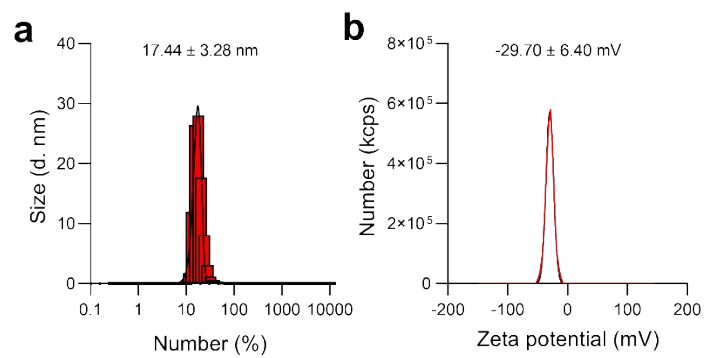


Fig. S5 (a) Size distribution and (b) Zeta potential of LipoPt(IV) measured by DLS.

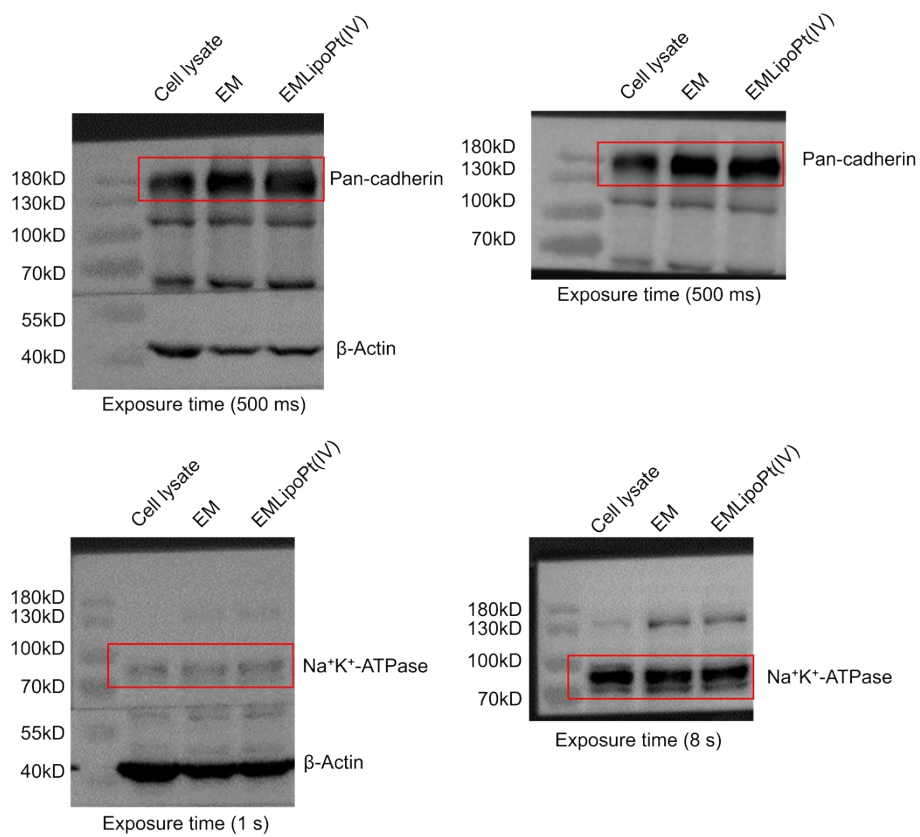


Fig. S6 Raw western blot data for Fig. 1e

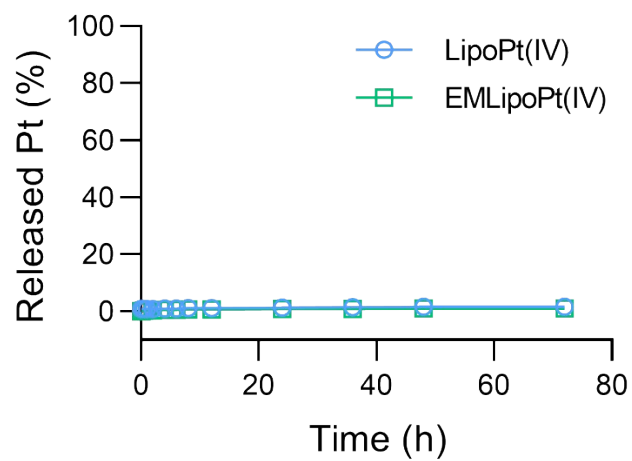


Fig. S7 Pt release of LipoPt(IV) and EMLipoPt(IV) *in vitro*

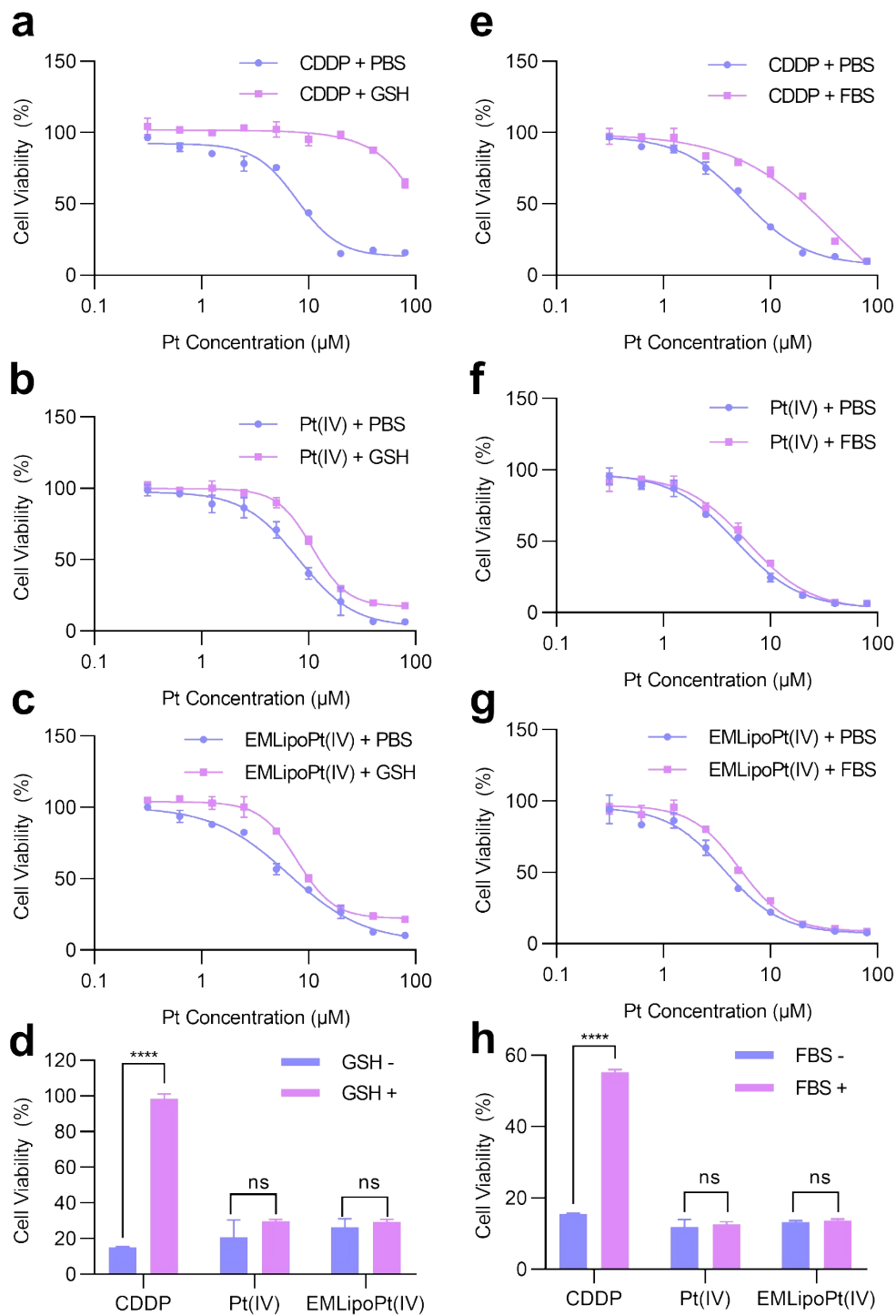


Fig. S8 (a-d) Cell viability of EC109 cells treated with CDDP, Pt(IV) or EMLipoPt(IV) (Pt equivalent, pre-incubated with GSH or PBS) for 48 h. (e-g) Cell viability of EC109 cells treated with CDDP, Pt(IV) or EMLipoPt(IV) (Pt equivalent, pre-incubated with FBS or PBS) for 48 h. The Pt concentrations in (d and h) were 20 μM . Data are presented as mean \pm SD ($n = 3$).

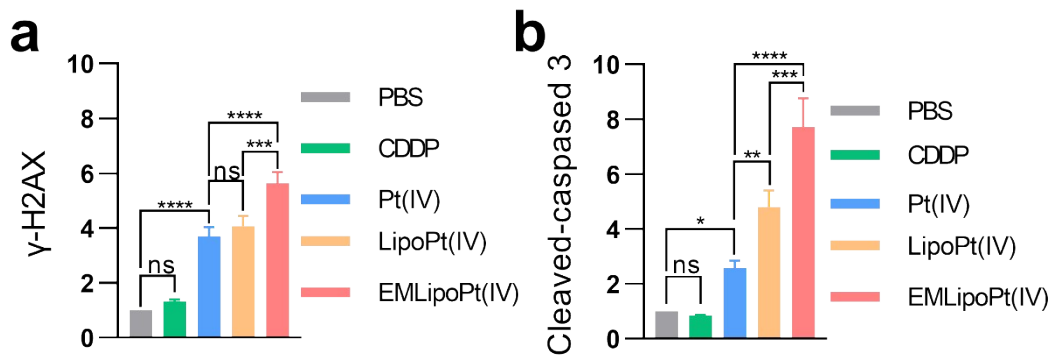


Fig. S9 Quantitative analysis of western blotting of (a) γ -H2AX and (b) Cleaved-caspase 3 in EC109DDP cells treated with PBS, CDDP, Pt(IV), LipoPt(IV), or EMLipoPt(IV) (10 μ M Pt equivalent) for 24 h. Data are presented as mean \pm SD (n = 3). ns: no statistical significance; * p < 0.05; ** p < 0.01; *** p < 0.001; **** p < 0.0001.

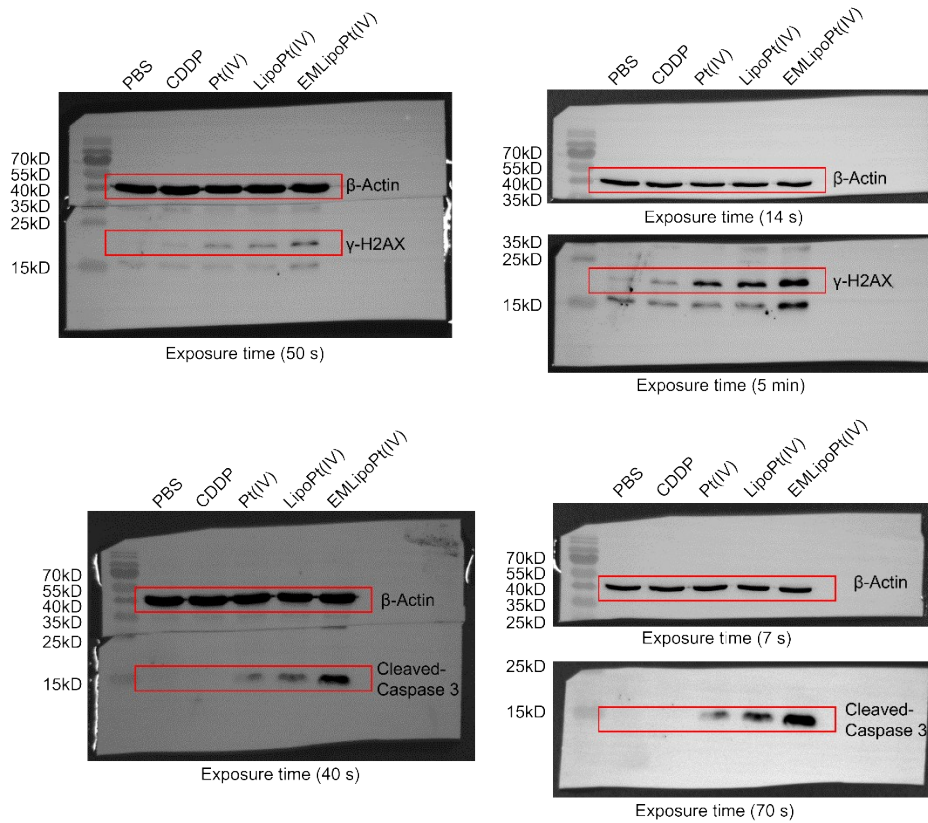


Fig. S10 Raw western blot data for Fig. 2i

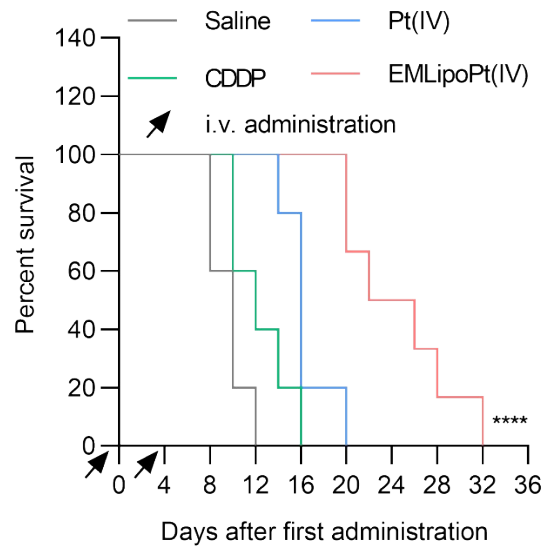


Fig. S11 Survival curves of mice from different treatment groups.

Table S1. Blood routine data of healthy female BALB/c mice after injected with EMLipoPt at 2.5 mg/kg CDDP equivalent for 14 d.

	Saline	CDDP	Pt(IV)	EMLipoPt(IV)	Units	Normal value
WBC	2.63±0.80	2.10±1.30	2.70±0.73	4.87±3.93	10 ⁹ /L	0.8-6.8
Lymph#	1.77±0.61	1.20±0.67	1.90±0.59	3.77±3.70	10 ⁹ /L	0.7-5.7
Mon#	0.10±0.00	0.07±0.09	0.10±0.00	0.13±0.05	10 ⁹ /L	0.0-0.3
Gran#	0.77±0.19	0.83±0.54	0.70±0.14	0.97±0.26	10 ⁹ /L	0.1-1.8
Lymph%	66.40±2.77	58.20±4.78	69.80±3.80	65.50±14.63	%	55.8-90.6
Mon%	4.03±0.24	3.67±0.40	3.43±0.17	3.60±0.93	%	1.8-6.0
Gran%	29.57±2.67	38.13±4.39	26.77±3.81	30.90±13.70	%	8.6-38.9
RBC	7.94±0.38	9.09±0.10	8.66±0.83	8.47±0.12	10 ¹² /L	6.36-9.42
HGB	128.67±4.78	145.67±3.30	135.67±11.90	137.67±3.30	g/L	110-143
HCT	40.97±1.81	46.20±0.79	44.00±3.55	42.53±0.96	%	34.6-44.6
MCV	51.67±1.23	50.87±1.07	50.97±0.88	50.27±1.52	fL	48.2-58.3
MCH	16.17±0.65	16.00±0.36	15.60±0.14	16.17±0.40	pg	15.8-19
MCHC	313.67±5.56	314.67±3.30	308.00±2.45	323.33±15.17	g/L	302-353
RDW	14.70±0.57	15.03±0.29	15.60±0.51	16.03±0.53	%	13-17
PLT	506.00±363.14	805.33±203.12	623.67±138.06	506.33±241.03	10 ⁹ /L	450-1590
MPV	6.97±0.52	6.23±0.12	6.73±0.48	7.23±0.39	fL	3.8-6.0
PDW	17.17±0.33	16.90±0.29	16.73±0.26	17.53±0.26		
PCT	0.34±0.23	0.50±0.12	0.42±0.11	0.37±0.19	%	