Supporting Information

Synthesis, Characterization, and Anticancer Properties of An Asymmetric Binuclear Zinc(II) Complex with Mixed Iminodiacetate and Phenanthroline Ligands

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Table S1. Crystallographic data and structural refinements for **$[Zn_2(ida)(phen)_3(NO_3)]\cdot NO_3\cdot 5H_2O$ (1)**.

empirical formula	$C_{40}H_{39}Zn_2N_9O_{15}$
Formulaweight	1016.54
crystal color	colorless
crystal system	monoclinic
Unit cell dimensions	
a (Å)	12.5947(2)
b (Å)	15.1874(3)
c (Å)	21.5308(4)
α (°)	
β (°)	92.498(2)
γ (°)	
V (Å^3)	4114.51(13)
space group	*P* $2_1/C$
formula units	4
D_{calc} (g ·cm^{-3})	1.641
μ(mm^{-1})	1.251
F_{000}	2088
Diffractometer/radiation	Oxford CCD/Mo Kα
temperature (K)	173(2)
reflections/collected/unique/R_{int}	30755/13581/ 0.0441
crystal size (mm)	0.42 x 0.40 x 0.18
data/restraints/parameters	13581/15/625
θ range (°)	2.544 to 26.373
GOF on F^2	0.946
R_1, wR_2 [$I > 2\sigma(I)$]	0.0320, 0.060
R_1, wR_2 (all data)	0.0538,0.0631
largest diff. peak and hole (e Å^{-3})	0.538, -0.400

[a] $R_1 = \sum(Fo - Fc)/\sum Fo$; [b] $wR_2 = \{\sum w(Fo^2 - Fc^2)^2/\sum w(Fo^2)^2\}^1$

Table S2. Selected bond lengths (Å) and angles (º) for (**1**).

$[Zn_2(ida)(phen)_3(NO_3)]\cdot NO_3\cdot 5H_2O$ (**1**)			
Zn(1)–O(3)	2.3138(14)	Zn(2)–O(1)	2.0401(15)
Zn(1)–O(4)	2.2102(15)	Zn(2)–O(3)	2.1667(15)
Zn(1)–N(2)	2.0855(18)	Zn(2)–O(6)	2.2060(15)
Zn(1)–N(6)	2.0897(18)	Zn(2)–N(4)	2.1126(18)
Zn(1)–N(3)	2.1219(18)	Zn(2)–N(1)	2.1276(17)
Zn(1)–N(7)	2.1344(18)	Zn(2)–N(5)	2.1362(18)
O(4)-Zn(1)-O(3)	57.85(5)	O(1)–Zn(2)–O(3)	91.50(6)
N(3)-Zn(1)-O(3)	95.97(6)	O(1)–Zn(2)–O(6)	90.69(6)
N(2)-Zn(1)-O(3)	91.78(6)	O(1)–Zn(2)–N(1)	82.44(6)
N(7)-Zn(1)-O(3)	86.23(6)	O(1)–Zn(2)–N(4)	92.35(6)
N(6)-Zn(1)-O(3)	152.05(6)	O(1)-Zn(2)-N(5)	170.27(6)
N(3)-Zn(1)-O(4)	87.60(6)	O(3)-Zn(2)-O(6)	177.78(6)
N(2)-Zn(1)-O(4)	145.56(6)	N(1)-Zn(2)-O(3)	79.78(6)
N(7)-Zn(1)-O(4)	93.01(6)	N(4)-Zn(2)-O(3)	96.79(6)
N(6)-Zn(1)-O(4)	98.89(6)	N(5)-Zn(2)-O(3)	85.51(6)
N(4)-Zn(2)-N(5)	78.84(7)	N(1)-Zn(2)-O(6)	100.11(6)
N(3)-Zn(1)-N(7)	177.69(7)	N(4)-Zn(2)-O(6)	83.52(6)
N(6)-Zn(1)-N(3)	98.41(7)	N(5)-Zn(2)-O(6)	92.40(7)
N(2)-Zn(1)-N(7)	101.38(7)	N(4)-Zn(2)-N(1)	173.65(7)
N(2)-Zn(1)-N(6)	114.36(7)	N(1)-Zn(2)-N(5)	106.07(7)
N(2)-Zn(1)-N(3)	79.28(7)	N(4)-Zn(2)-N(5)	78.84(7)

Table S3. Comparisons of Zn–O and Zn–N bond distances (Å) in iminodiacetato zinc complexes (adenine = Hade, imidazole = im).

CN	Complexes	Zn–N	$Zn–O_{carboxy}$	Ref.
6	$[Zn_2(ida)(phen)_3(NO_3)]\cdot NO_3\cdot 5H_2O$.(**1**)	2.0863(15)–2.1371(15)	2.0406(13)–2.3139(12)	**This work**
	$[Zn(ida)(phen)(H_2O)].2H_2O$	2.132(2), 2.091(2), 2.153(2)	2.187(2), 2.070(2)	[15]
	$[Zn(ida)(H_2O)_2]_n$	2.114(2)	2.010(2), 2.092(2), 2.251(2)	[15]
	$La[Zn(Hida)(ida)_2]\cdot ½H_2O$	2.137(3)	2.092(3), 2.126(3)	[21a]
	$[Zn(ida)(Hade)(H_2O)_2]$	2.167(2)	2.112(2), 2.125(2)	[21b]
	$[Zn(ida)(CH_2im_2)]\cdot H_2O$	2.080(3)–2.177(3)	2.106(2)–2.209(3)	[21c]
4	$(NH_4)_n[Zn(Hida)Cl_2]_n$	–	1.989(1), 1.966(1)	[15]
	$[Zn(Hida)]_n.4H_2O$	–	1.963(2), 1.973(2)	[15]

Table S4. Hydrogen bonds (Å and ^{o}) in (**1**).

D–H···A	D–H	H···A	D···A	∠ DHA
O(1w)–H(1w1)···O(2w)	0.871	1.858	2.679(3)	156
O(1w)–H(2w1)···O(4)	0.856	1.959	2.803(2)	170
O(2w)–H(2w2)··· O(1wa)	0.854	2.122	2.928(3)	157
O(2w)–H(2w1)···O(4wb)	0.862	1.876	2.737(2)	177
O(3w)–H(3w1)···O(8d)	0.845	2.057	2.849(3)	156
O(4w)–H(4w2)···O(3wc)	0.840	2.014	2.852(2)	176
O(4w)–H(4w1)···O(2)	0.835	1.971	2.802(2)	173
O(5w)–H(5w2)···O(1wa)	0.868	1.963	2.796(3)	161
N(1)–H(1C)···O(5w)	1.00	2.06	2.934(3)	144.4
C(38)–H(38A)···O(1)	0.95	2.71	3.547(3)	147.0
C(21)–H(21A)···O(4e)	0.95	2.35	3.232(2)	153.9

Symmetry codes : *a, 1-x , 1-y, 1-z; b, -x, 1-y, 1-z; c, -x, -1/2+y, 1/2-z; d, x, 1+y, z; e, x, 1/2-y, -1/2+z*

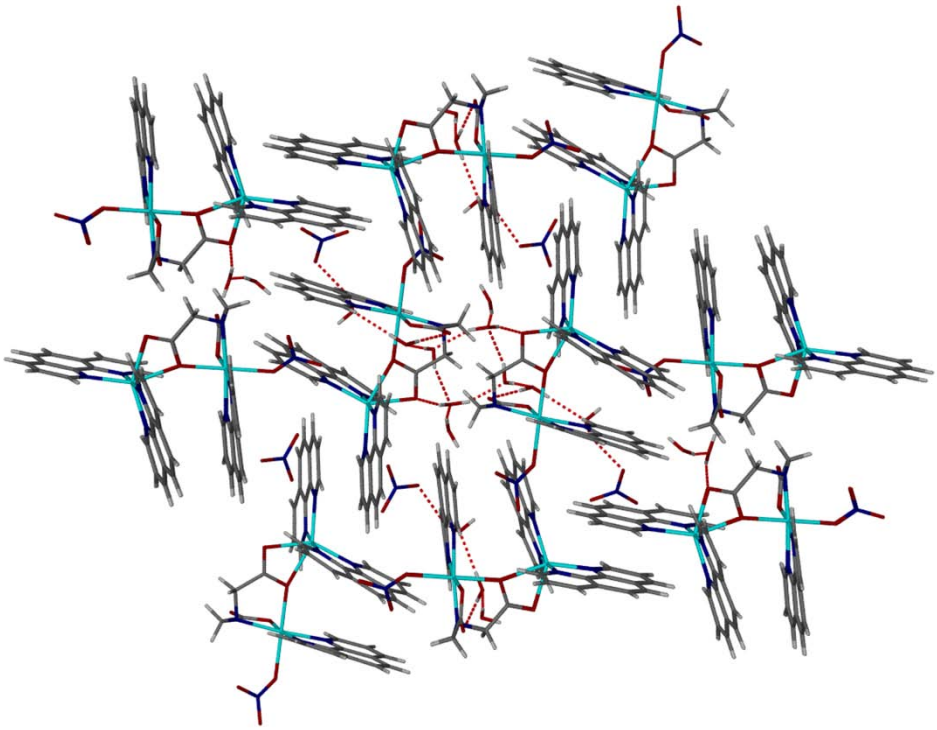

Figure S1. Crystal packing of complex (**1**) by hydrogrn-bond and π-πinteraction.

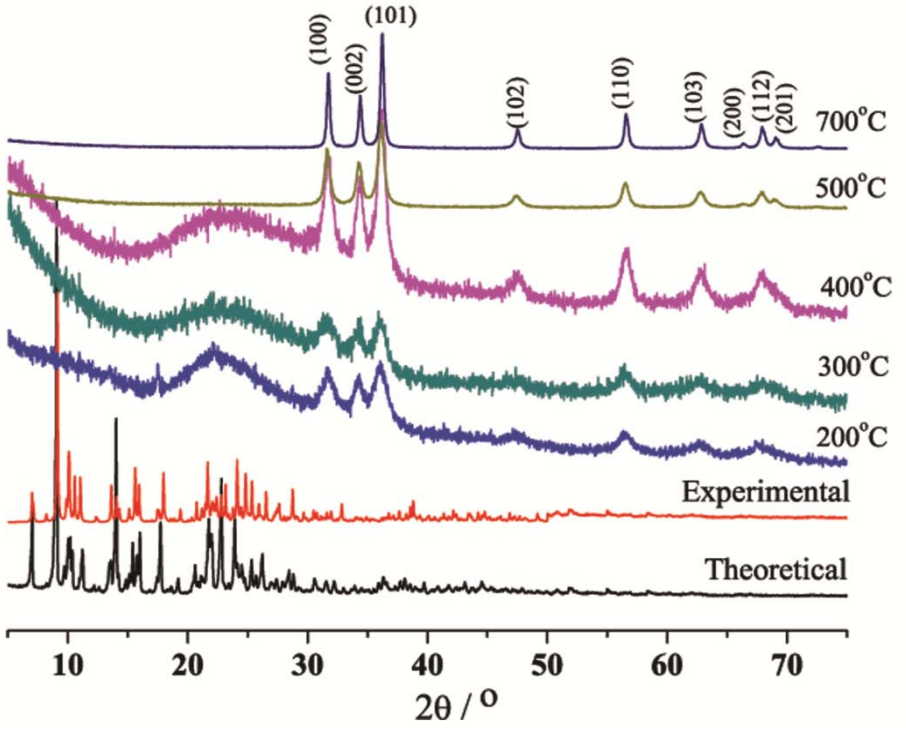

Figure S2. X-ray powder diffraction patterns of bulk (**1**) and the sample calcined at different temperatures, and the calculated pattern of (**1**).

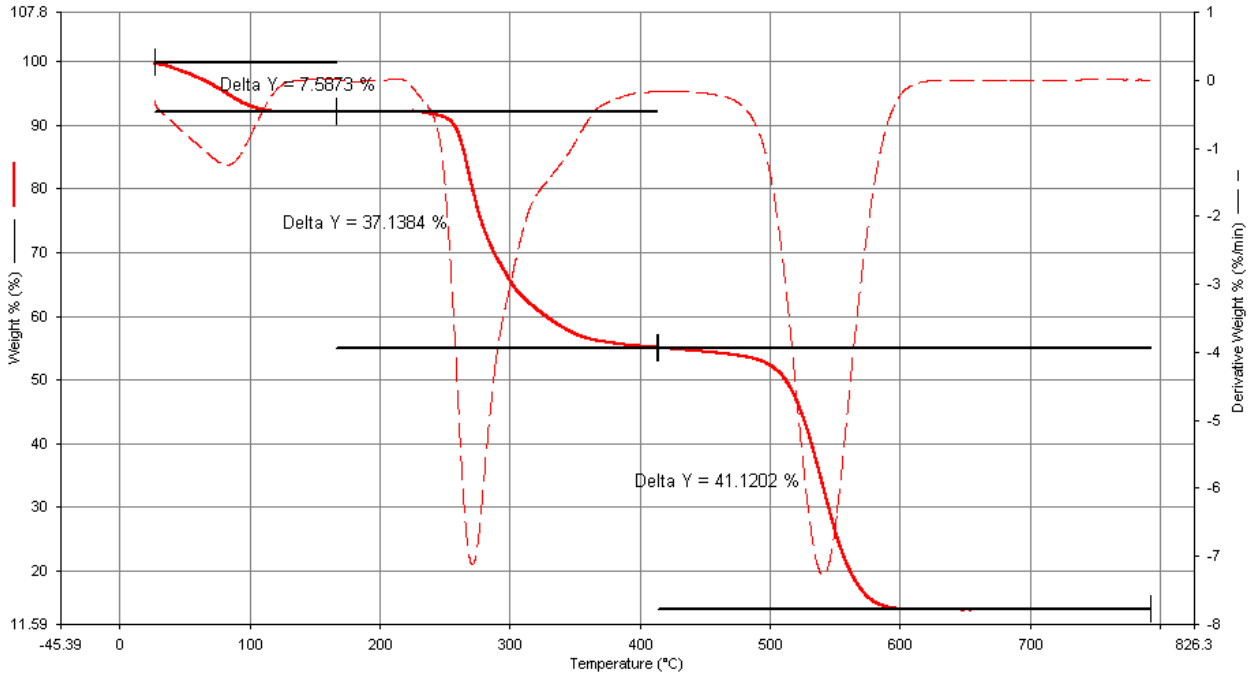

Figure S3. Thermogravimetric curves of complex (**1**) in flowing air atmosphere with a purge rate of 20°C/minute.

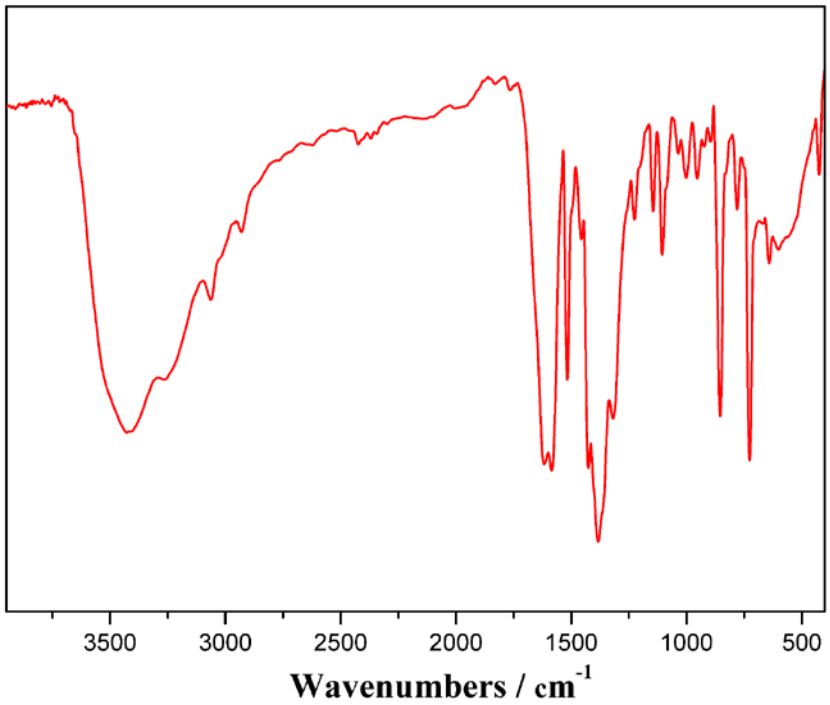

Figure S4. FT-IR spectra of (**1**) (recorded on KBr discs).

Table S5. Absorption data in aqueous solution (molar absorption coefficient) for complex (**1**) and free phen ligand.

Molecules	λ_{max}^{abs} nm (L. mol^{-1}.cm^{-1})		
$[Zn_2(ida)(phen)_3(NO_3)]\cdot NO_3\cdot 5H_2O$ **(1)**	226 (1.59×10^5)	268 (1.33×10^5)	290 (4.1×10^4)
1, 10-phen	225 (7.6×10^4)	262 (5.4×10^4)	—

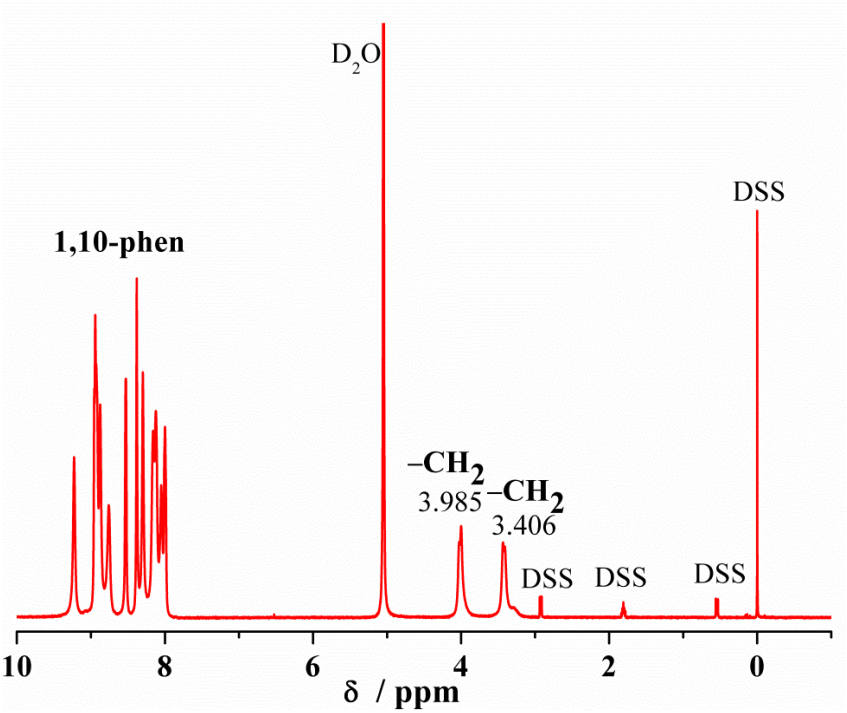

Figure S5. ^{1}H NMR spectrum of complex (**1**) in D_2O solution.

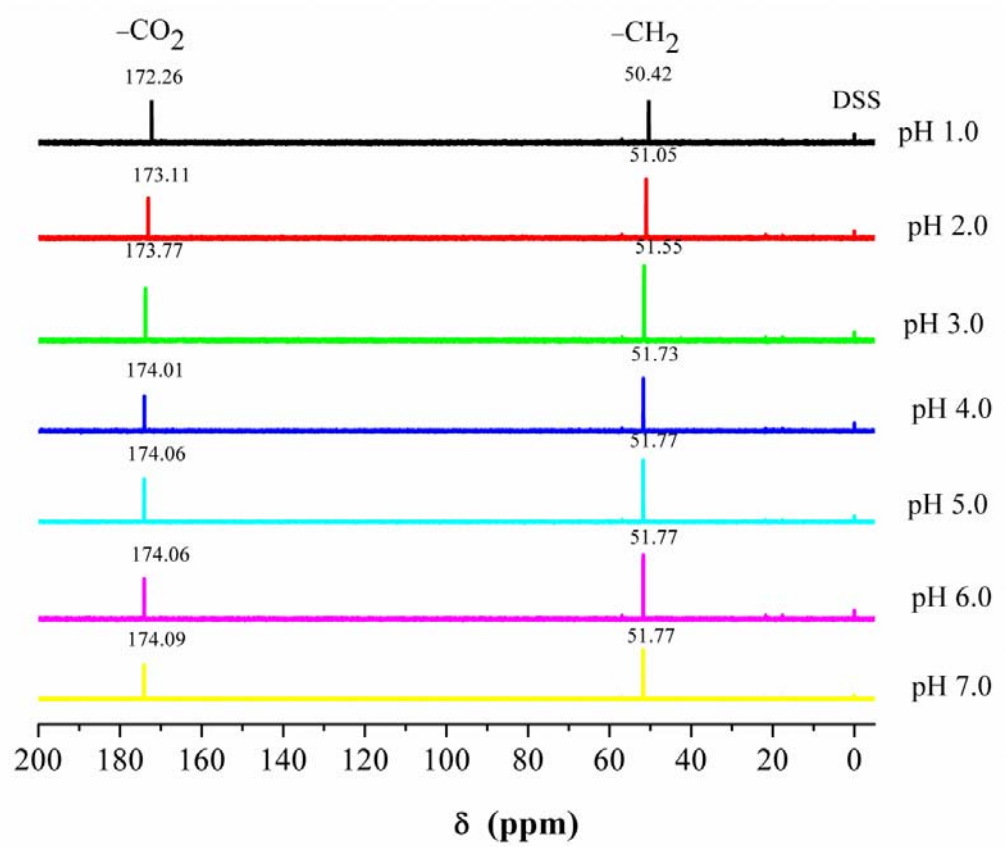

Figure S6. ^{13}C NMR spectra of the solutions of free iminodiacetate ligand at various pH values.

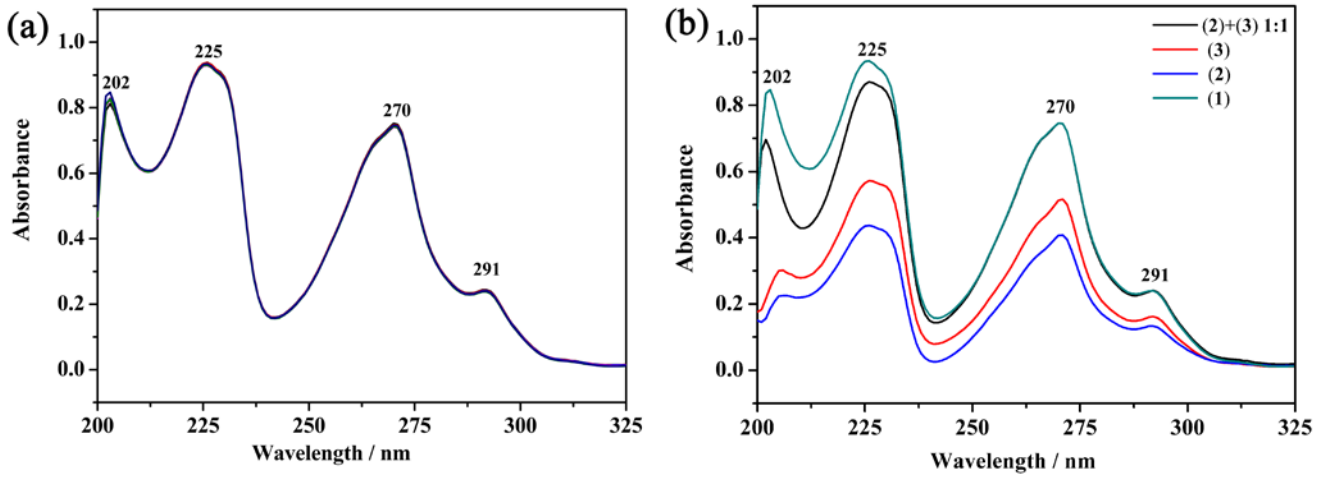

Figure S7. (a) UV-vis spectra of complex (**1)** recorded in PBS buffer at room temperature over 2 h with 2 min intervals. (b) UV-vis spectra of complex (**1)-(3)** (C= 0.01mM), mixed species (**2)** and (**3**) (1:1 molar ratio, *C* = 0.01mM) in PBS buffer at room temperature.

Table S6. Hematological parameters in mice treated with (**1**) at a dose of 474 mg/kg or 632 mg/kg after 14 days.

	Experiment groups		
Male	**Normal（n = 5）**	**(1)（474mg/kg, n = 5）**	**(1)（632mg/kg, n = 3）**
RBC(10^{12}.L^{-1})	11.3±0.45	11.0±0.66	11.0±0.52
Hb (g/L)	159.8±7.19	159.2±7.36**	157.0±6.93*
HCT (%)	68.6±0.82	68.7±3.03	69.6±1.48
MCV (fL)	62.0±0.82	61.7±1.60	59.5±0.79
MCH (Pg)	14.1±0.23	14.1±0.42	13.8±0.00
MCHC (g/L)	228.4±5.86	228.4±1.51	226.5±2.12
RDW (%)	16.8±0.62	17.0±0.79	17.2±0.32
WBC(10^{9}.L^{-1})	6.58±0.96	6.21±1.21**	6.10±1.70**
LY (%)	48.4±4.96	48.7±0.19	50.7±5.54*
NE (%)	34.9±4.07	35.1±3.39	32.1±7.82*
MO (%)	16.0±1.54	15.8±3.48**	15.6±2.73**
EOS (%)	0.45±0.45	0.27±0.41	0.20±0.14
BASO (%)	0.14±0.09	0.12±0.02	0.11±0.01
PL (10^{9}.L^{-1})	1337.8±204.9	1371.4±229.7	1406.0±40.7
MPV (fL)	5.24±0.29	5.26±0.15	5.25±0.07
Female			
RBC(10^{12}.L^{-1})	10.9±0.44	10.5±0.29	10.5±0.10
Hb (g/L)	160.2±8.14**	147.0±4.53*	147.0±1.41
HCT (%)	63.4±4.74	64.4±1.36	64.8±3.42
MCV (fL)	62.4±1.74	62.9±1.40	64.2±0.07
MCH (Pg)	14.4±0.51	14.2±0.51	14.2±0.47
MCHC (g/L)	231.4±3.21	230.4±4.28	228.8±6.60
RDW (%)	16.9±0.71	16.7±0.54	17.0±1.00
WBC(10^{9}.L^{-1})	7.15±1.08	5.36±0.87**	4.59±0.59***
LY (%)	46.7±7.27	49.9±1.21	56.0±4.88*
NE (%)	37.1±4.88	35.5±1.98	28.30±0.88
MO (%)	21.5±3.17	14.8±1.12**	13.2±0.71**
EOS (%)	0.56±0.46	0.56±0.85	0.52±0.45
BASO (%)	0.14±0.02	0.13±0.12	0.09±0.07
PL (10^{9}.L^{-1})	1188.6±232.7	1219.7±166.8	1248.5±316.1
MPV (fL)	5.16±0.15	5.17±0.15	5.20±0.10

Data are expressed as the means ± S.E.M. *p < 0.05, **p < 0.01, ***p < 0.001, compared with the normal group.

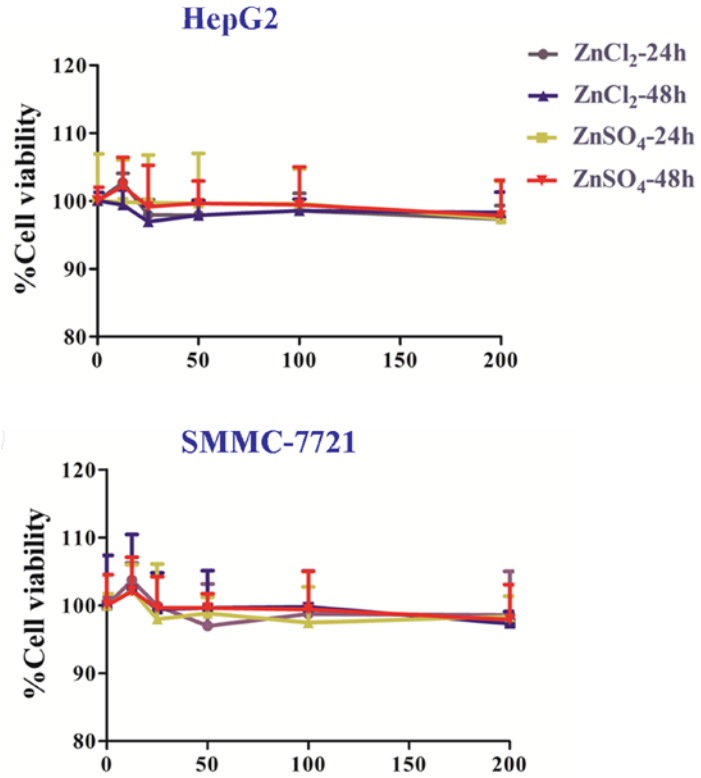

Figure. S8. Zinc ion affects the proliferation of hepatoma cell lines. (a and b) HepG2 and SMMC-7721 cells were incubated with various concentrations of $ZnCl_2$ or $ZnSO_4$ for 24 or 48h, respectively. The results are presented as the means ± S.E.M.

Table S7. The comparison of anti-proliferation activity between complex (**1**) and the marketed platinum-based drugs on hepatoma cells.

		IC50 (μM)			
	Hepatoma cell lines	24h	48h	72h	Refs
Complex (**1**)	HepG2	24.95 ± 1.54	10.01 ± 1.08	ND[a]	-
	SMMC-7721	29.52 ± 0.74	11.75 ± 1.75	ND	-
Cisplatin	HepG2	ND	3.67 ± 0.80	1.06 ± 0.26	[32a]
	Hep3B	ND	4.97 ± 0.86	2.13 ± 0.37	[32a]
	BEL-7404	62.0 ± 11.4	11.1 ± 0.6	9.5 ± 0.5	[32b]
Carboplatin	HepG2	ND	ND	61.30 ± 6.33	[32c]
	BEL-7402	ND	ND	41.69 ± 4.32	[32c]
	BEL-7404	505.6 ± 108.3	190.8 ± 17.8	180.2 ± 18.2	[32b]
Oxaliplatin	HepG2	129.2 ± 1.02	12.10 ± 5.03	8.21 ± 6.12	[32d]
	BEL-7404	92.2 ± 15.9	24.7 ± 3.3	22.4 ± 2.0	[32b]
Dicycloplatin	HepG2	ND	ND	48.01 ± 2.45	[32c]
	BEL-7402	ND	ND	30.27 ±3.18	[32c]

a: ND means not detected

Table S8. The comparison of acute toxicity between complex (1) and the marketed platinum-based drugs on mice.

	Administration methods	Animal	LD50 (mg/kg)	Refs
Complex (**1**)	*i.g.*[a]	ICR mice	736	-
Cisplatin	*i.p.*[b]	CD-I albino mice	17	[38a]
Carboplatin	*i.p.*	ICR mice	150	[38b]
Oxaliplatin	*i.p.*	ICR mice	19.8	[38b]

a: *i.g.* means intragastrically administered; b: *i.p.* means intraperitoneally injection.