1. Experimental Materials

1.1 Reagents and Chemicals

All chemicals and reagents were of analytical grade and used without further purification unless specified. 4-((4-(Pyridin-3-yl) pyrimidin-2-ylamino) methyl) benzoic acid (MGC), $CoCl_2 \cdot 6H_2O$, $NiCl_2 \cdot 6H_2O$, and N,N-dimethylformamide (DMF) were purchased from Sinochem Pharmaceuticals. Human pancreatic cancer cells (BxPC-3) were obtained from Procell Life Science & Technology Co., Ltd. (Wuhan, China). FITC and propidium iodide (PI) were sourced from BD Biosciences. Plasmid pBR322 DNA and calf thymus DNA (CT-DNA) were acquired from Sigma-Aldrich. Staining buffer, RNase A, and PI were supplied by Biosharp.

1.2 Cell Culture

Incubate BxPC-3, Panc-1, L929 cells in a humidified incubator at 37°C with 5% CO_2. cells were cultured in RPMI 1640 or DMEM medium, supplemented with fetal bovine serum (FBS), streptomycin, and penicillin.

1.3 ROS Scavenging Assay

BxPC-3 cells were stained with 2,7-dichlorodihydrofluorescein diacetate (DCFH-DA, Sigma-Aldrich). Cells (5×10^3) from culture dishes were treated with 10 mM N-acetyl-L-cysteine (NAC), followed by co-treatment with 50 μM Co-MGC or 50 μM Ni-MGC for 24 h. Subsequently, the culture medium was aspirated, and the cells were washed with ice-cold phosphate-buffered saline (PBS, 1X). The cells were then detached using EDTA-free trypsin and centrifuged at 1500 rpm for 4 minutes. After two washes with PBS, the cell pellet was resuspended in 100 μL of binding buffer. Next, 5 μL of Annexin V-FITC and 5 μL of propidium iodide (PI) were added, followed by incubation in the dark for 15 minutes. Finally, 400 μL of binding buffer was added, and the samples were filtered and analyzed using an Accuri C6 flow cytometer.

2. Crystallographic Data

Tab. S1 Crystallographic data for Co-MGC and Ni-MGC.

Empirical formula	**$C_{37}H_{37}CoN_9O_7$**
Formula weight	778.68
Temperature/K	300.15
Crystal system	monoclinic
Space group	Pc
a/Å	14.0516(5)
b/Å	6.7554(2)
c/Å	20.0211(7)
α/°	90
β/°	108.084(4)
γ/°	90
Volume/Å^3	1806.61(11)
Z	2
ρ_{calc}g/cm^3	1.431
μ/mm^{-1}	4.255
F(000)	810.0
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	9.294 to 159.652
Index ranges	-16 ≤ h ≤ 15, -7 ≤ k ≤ 5, -24 ≤ l ≤ 24
Reflections collected	8820
Independent reflections	4391 [R_{int} = 0.0274, R_{sigma} = 0.0355]
Data/restraints/parameters	4391/14/469
Goodness-of-fit on F^2	1.137
Final R indexes [I>=2σ (I)]	R_1 = 0.0476, wR_2 = 0.1197
Final R indexes [all data]	R_1 = 0.0612, wR_2 = 0.1593
Largest diff. peak/hole / e Å^{-3}	0.70/-0.83
Flack parameter	0.384(10)

Empirical formula	**$C_{34}H_{32}N_8NiO_6$**
Formula weight	707.38
Temperature/K	299.15
Crystal system	monoclinic
Space group	Pc
a/Å	13.93393(16)
b/Å	6.73940(6)
c/Å	20.0825(2)
α/°	90

β/°	107.9299(13)
γ/°	90
Volume/Å^3	1794.29(4)
Z	2
ρ_{calc}g/cm^3	1.309
μ/mm^{-1}	1.231
F(000)	736.0
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	6.668 to 136.384
Index ranges	-16 ≤ h ≤ 16, -7 ≤ k ≤ 8, -23 ≤ l ≤ 23
Reflections collected	8660
Independent reflections	8660 [R_{int} = ?, R_{sigma} = 0.0375]
Data/restraints/parameters	8660/11/460
Goodness-of-fit on F^2	1.057
Final R indexes [I>=2σ (I)]	R_1 = 0.0439, wR_2 = 0.1228
Final R indexes [all data]	R_1 = 0.0445, wR_2 = 0.1236
Largest diff. peak/hole / e Å^{-3}	0.42/-0.47
Flack parameter	0.62(3)

Tab. S2 The fractional bonding length of Co-MGC and Ni-MGC.

Atom	Atom	Length/Å
Co01	O002	2.140(6)
Co01	O003	2.071(8)
Co01	O005	2.175(6)
Co01	N007[1]	2.180(7)
Co01	O00A	2.048(8)
Co01	N00I[2]	2.180(8)

[1]+X,2-Y,-1/2+Z; [2]+X,-Y,1/2+Z

Atom	Atom	Length/Å
Ni1	O24	2.059(4)
Ni1	O47	2.046(4)
Ni1	O48	2.121(4)
Ni1	N8	2.115(4)
Ni1	O49	2.090(4)
Ni1	N31	2.123(4)

[1]+X,2-Y,1/2+Z; [2]+X,-Y,-1/2+Z

Tab. S3 The selected bond angles of Co-MGC and Ni-MGC.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
O002	Co01	O005	173.4(3)	O005	Co01	N007[1]	91.7(3)
O002	Co01	N007[1]	93.9(3)	O005	Co01	N00I[2]	88.8(3)
O002	Co01	N00I[2]	85.6(3)	O00A	Co01	O002	91.9(3)
O003	Co01	O002	90.8(3)	O00A	Co01	O003	177.3(3)
O003	Co01	O005	93.0(3)	O00A	Co01	O005	84.3(3)
O003	Co01	N007[1]	86.8(3)	O00A	Co01	N007[1]	93.0(3)
O003	Co01	N00I[2]	92.2(3)	O00A	Co01	N00I[2]	88.0(3)

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C22	O24	Ni1	127.3(4)	C9	N8	Ni1	120.3(3)
C45	O47	Ni1	126.1(4)	C32	N31	Ni1	121.6(4)
C13	N8	Ni1	121.4(4)	C36	N31	Ni1	120.9(4)

3. Supplementary Experimental Data

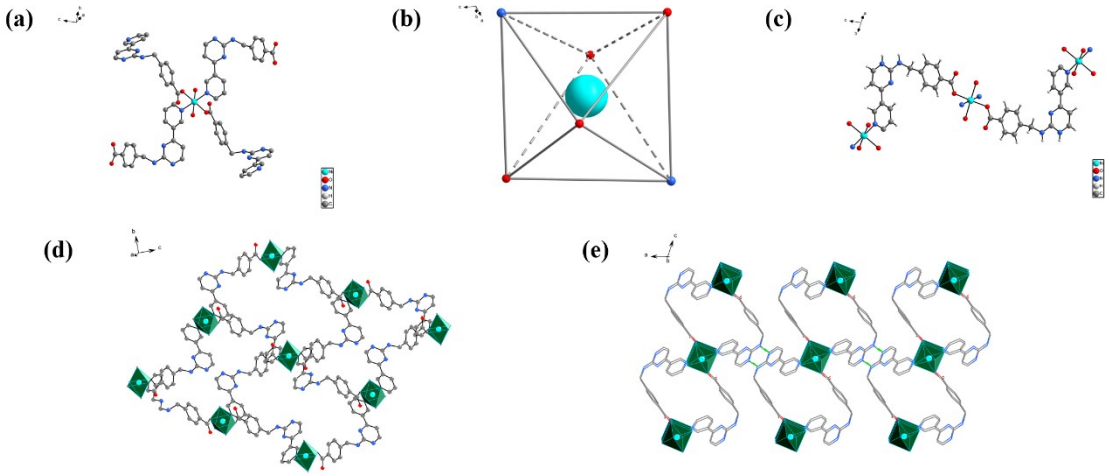

Fig. S1. Single - crystal structure of Ni - MGC (C, gray; O, red; N, deep blue; Ni, sky blue; all hydrogen atoms are omitted for clarity): (a) Coordination environment of Ni; (b) Symmetrical unit of Ni - MGC; (c) Coordination mode of ligand; (d) 2D structure; (e) 3D structure.

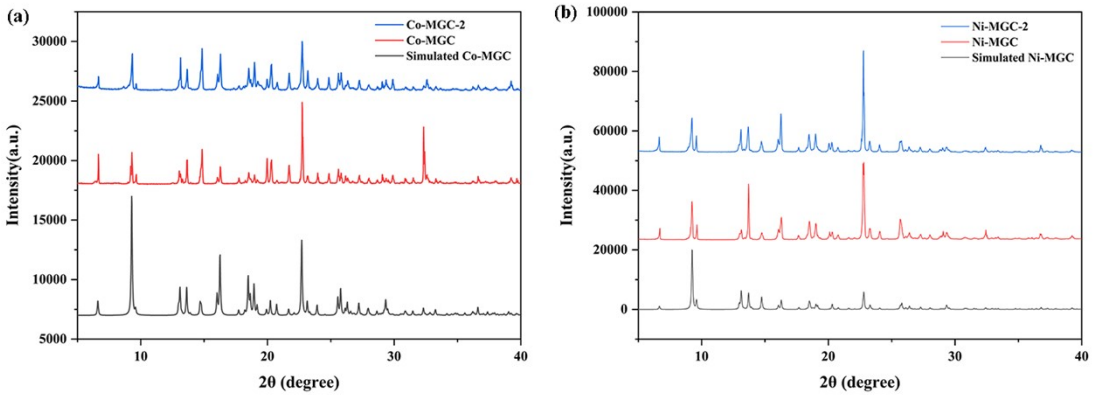

Fig. S2. XRD patterns of different batches of Co-MGC and Ni-MGC

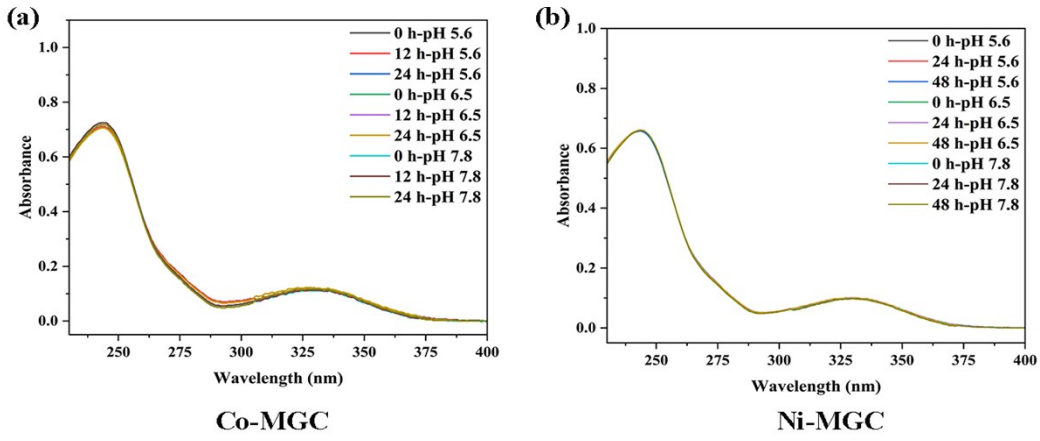

Fig. S3. (a) and (b) Stability of Co-MGC and Ni-MGC in buffer solutions at pH 7.4, pH 6.5, and pH 5.6 at different time points (0h, 24h and 48h)

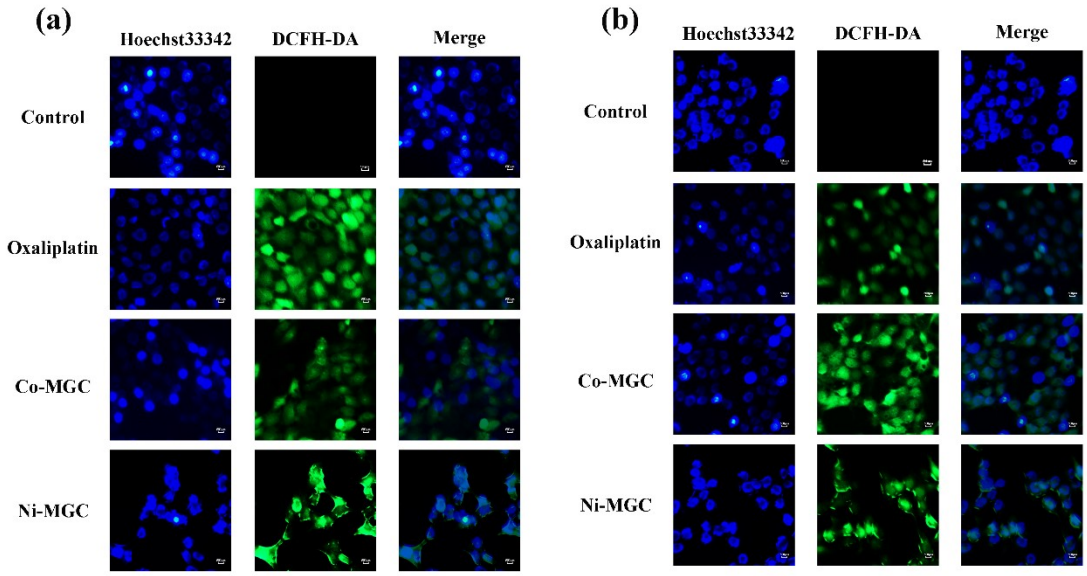

Fig. S4. Fluorescence imaging of ROS in BxPC - 3 cells (scale bar: 500 μm): (a) Cycle 2; (b) Cycle 3.

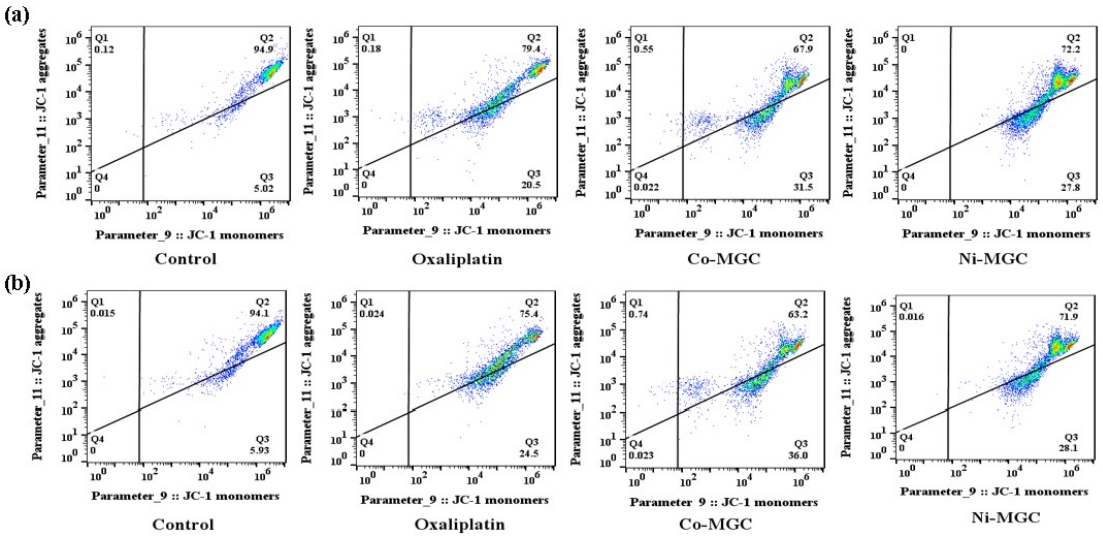

Fig. S5. JC-1 flow cytometry analysis of mitochondrial membrane potential (ΔΨm). Membrane potential detection in untreated cells, cells treated with oxaliplatin (50 μM), Co-MGC (50 μM), or Ni-MGC (50 μM) for 24 hours: (a) Cycle 2; (b) Cycle 3.

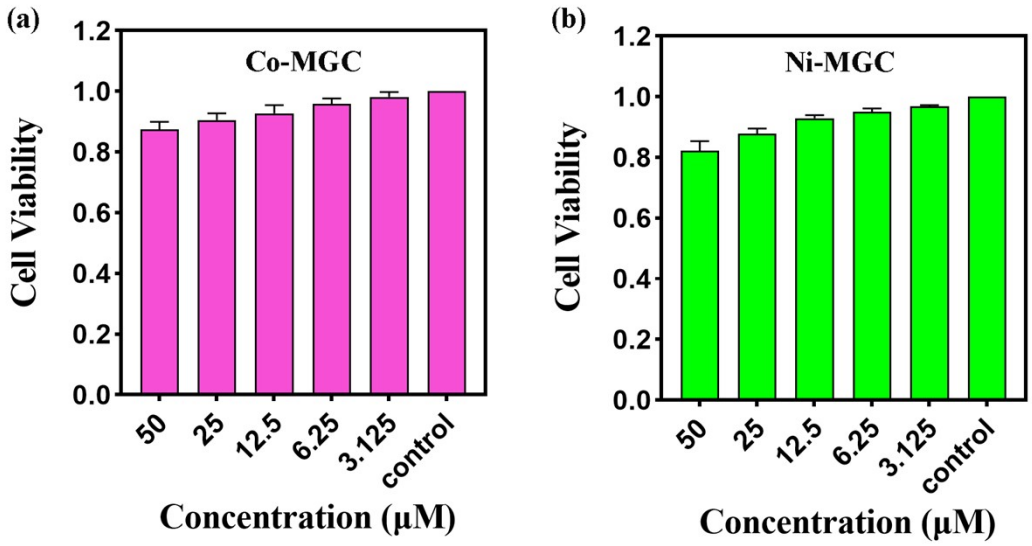

Fig. S6. Schematic diagram of cytotoxicity of Co-MGC and Ni-MGC on L929 cells

Tab. S4. Cytotoxicity of Co-MGC, Ni-MGC, in BxPC-3 and Panc-1 cells.

Complex	BxPC-3[IC_{50} (μM)]	Panc-1[IC_{50} (μM)]
Co-MGC	8.28±2.32	37.98±6.76
Ni-MGC	10.23±2.89	58.2±13.64

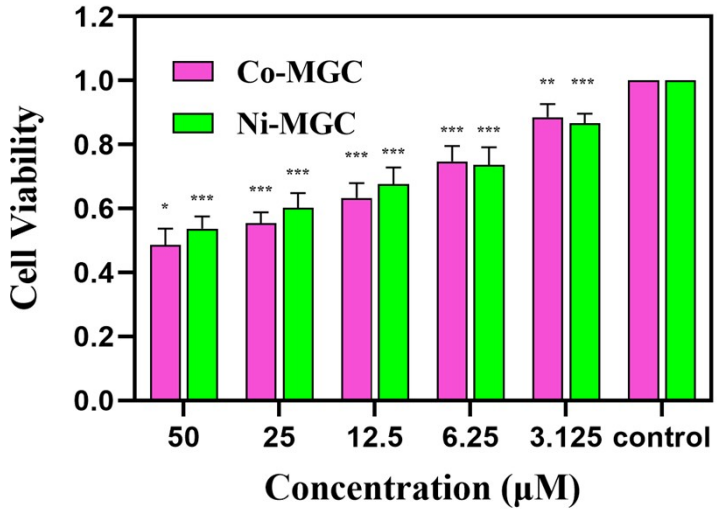

Fig. S7. Schematic diagram of cytotoxicity of Co MGC and Ni MGC on Panc-1 cells Values are expressed as mean ± SD. *p < 0.05, **p < 0.01, ***p < 0.001.

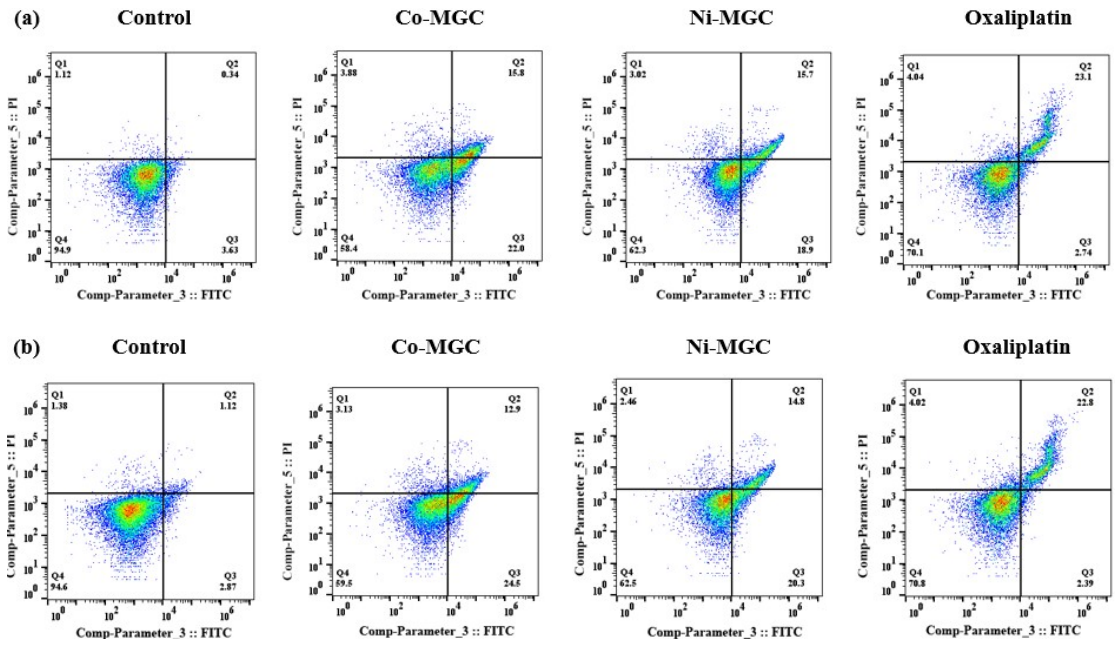

Fig. S8. Apoptosis induction in BxPC-3 cells after 24-hour incubation with Co-MGC, Ni-MGC, and Oxaliplatin: (a) Cycle 2; (b) Cycle 3.

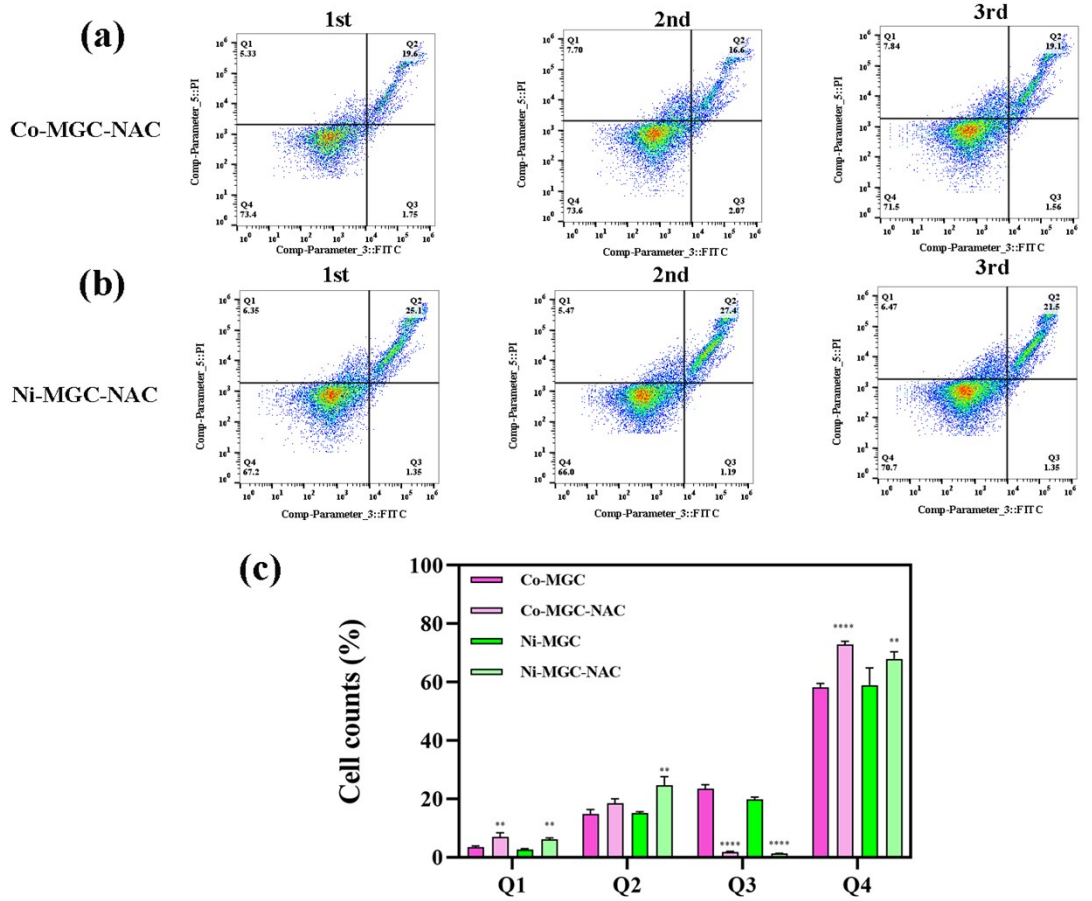

Fig. S9. Apoptosis and cell cycle distribution of BxPC-3 cells after co incubation with Co MGC, Ni MGC, and NAC for 24 hours. Values are expressed as mean ± SD. *p < 0.05, **p < 0.01, ***p < 0.001.

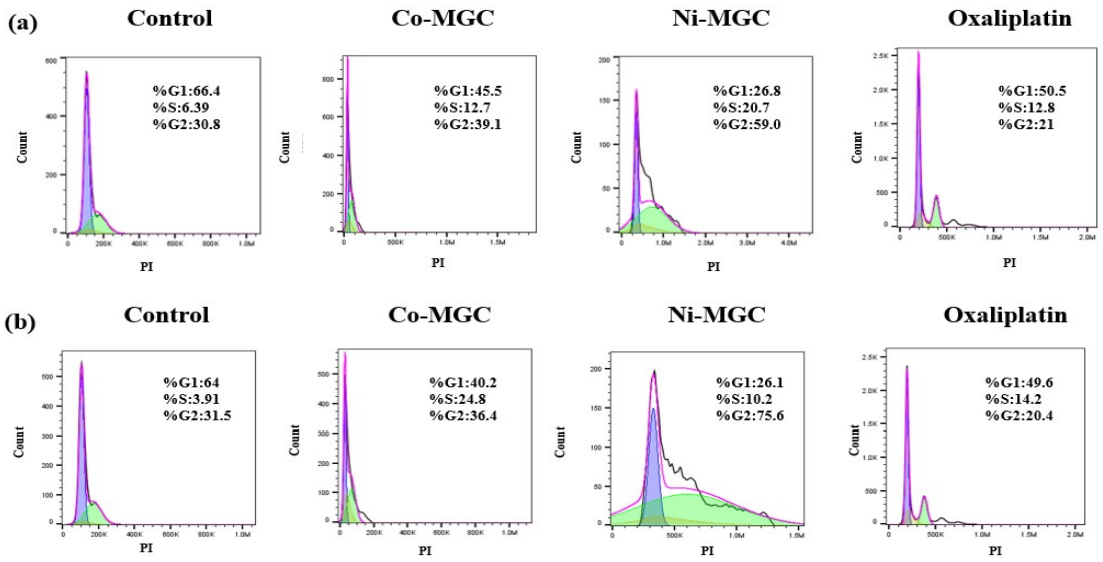

Fig. S10. Cell cycle distribution in BxPC-3 cells after 24-hour incubation with Co-MGC, Ni-MGC, and Oxaliplatin: (a) Cycle 2; (b) Cycle 3.

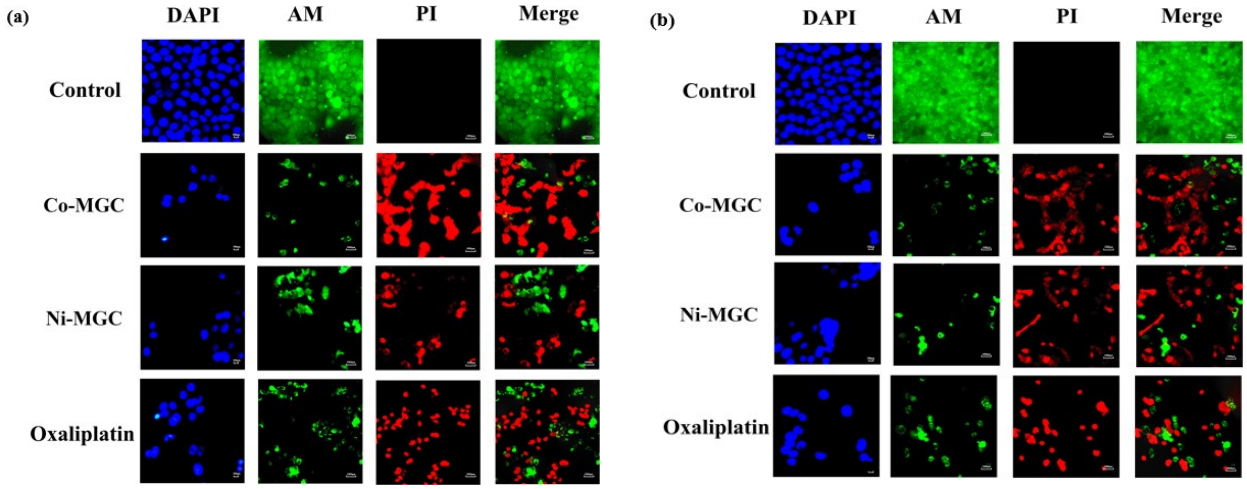

Fig. S11. Fluorescence images of BxPC-3 cells stained with DAPI (scale bar: 500 μm) and AM/PI co-staining images (scale bar: 1000 μm) following different treatments: (a) Cycle 2; (b) Cycle 3.