New Journal of Chemistry

Enhanced cytotoxicity by benzothiazole- containing cisplatin derivative in breast cancer cells

Chaoqun You^a, Jia Yu^a, Yu Sun^a, Yanghui Luo^a, Xiangyang Zhang^b, Jin Zhu^c, Baiwang Sun^{a,*}

^a School of Chemistry and Chemical Engineering, Southeast University, Nanjing 210089, PR China. Fax: +86 25 52090614, Tel: +86 25 52090614, E-mail address: chmsunbw@seu.edu.cn

^b Laboratory of Organic Chemistry, ETH Zurich, 8093 Zurich, Switzerland

^c Key Laboratory of Antibody Technique of Ministry of Health, School of Pathology, Nanjing Medical University, Nanjing 210093, PR China

Supplementary data

General. ¹HNMR spectra were recorded on a Bruker AMX-400 (400 MHz) or Bruker DPX-300 (300 MHz). Chemical shifts are reported in ppm from tetramethylsilane with the residual solvent resonance as the internal standard (DMSO: δ 2. 54). Data are reported as follows: chemical shift, multiplicity (s: singlet, d: doublet, dd: double doublet, td: triplet of doublets, t: triplet, q: quartet, br: broad, m: multiplet), couping constants (J in Hz), integration and assignment. All reactions were conducted in flame-dried glassware under an inert atmosphere of argon.

Synthesis and characterization

1. CJM 126



The synthesis procedure in a similar manner according to previous literature as the manuscript described. The light green product was subsequently purified from ethanol, and dried in vacuo with a yield of 45%. ¹HNMR (DMSO-d6), δ (ppm) 8.007 (d, 1H, H₄), 7.901 (d, 1H, H₁), 7.881 (d, 2H, H₅,H₇), 7.745 (dt,1H, H₃), 7.452 (dt, 1H, H₂), 6.674 (d, 2H, H₆,H₈), 5.886 (brs, 2H, H₉). ESI-MS (m/z): 227.06 [M+H]⁺.

2. CJM-COOH

Briefly, Malonyl dichloride (375mg, 2.66mmol) was dissolved in DCM (20ml) and stir vigorously under ice-water bath to a mixture solution , and then CJM (300 mg, 1.33mmol) dissolved in DCM (10ml) was add by drop with a 80 mL constant pressure funnel. After the drop add finished, the mixture was continue stir under ice-water bath for 2 h and after CJM-COOH formed precipitation, filter to obtain pale yellow residue at room temperature.



The pale yellow product was subsequently purified from methanol, and dried in vacuo with a yield of 83%. ¹HNMR (DMSO-d6), δ (ppm) 10.601 (s, 1H, H₁₀), 8.141 (d, 1H, H₄), 8.093 (d, 1H, H₁), 8.072 (d, 2H, H₅,H₇), 7.949 (dt, 1H, H₃), 7.753 (dt, 1H, H₂), 6.684 (d, 2H, H₆,H₈), 3.686 (d, 2H, H₉). ESI-MS (m/z): 313.06 [M+H]⁺.

3. CJM-Pt

Briefly, cisplatin (100 mg, 0.33 mmol) was suspended with an equimolar amount of silver sulfate for 24 h in distilled water stirred at room temperature in the dark. The AgCl precipitate was removed by filtration. Then the filtrate of (dach)PtSO4 was reacted with the equimolar barium salt of CJM-COOH in 20 mL for 5 h at room temperature. After BaSO4 was filtered off, the filtrated was evaporated to dryness

under reduced pressure.



CJM-Pt

The yellowish green product was subsequently purified from methanol, and dried in vacuo with a yield of 22%. 1H NMR (DMSO-d6): δ (ppm) 8.136 (d, 2H, H₄,H₈), 8.118 (d, 2H, H₁,H₅), 8.097 (d, 4H, H₉,H₁₁,H₁₃,H₁₅), 8.063 (dt, 2H, H₃,H₇), 8.041 (dt, 2H, H₂,H₆), 7.841 (d, 4H, H₁₀,H₁₂,H₁₄,H₁₆), 3.956 (d, 4H, H₁₇,H₁₈). ESI-MS (m/z): 882.16 [M+H]⁺.ESI-MS (m/z): 904.16 [M+Na]⁺.



Fig. S1. ¹HNMR spectra contrast figure of CJM126, CJM-COOH and CJM-Pt.

Li p o-CJM-Pt	PEG-PCL/SP	Particle size/nm	PDI	EE,%	DLC,%	
Lipo-1	2:60	73.39	0.244	81.34	27.49	-
Lipo-2	2:45	97.95	0.172	75.27	31.32	
Lipo-3	2:30	117.30	0.289	67.16	30.28	

Table S1. Characterization of the CJM-Pt loaded liposomes with different proportion contents.

Sample	MGC-803	SGC-7901	MCF-7	MDA-MB-231
Cis-Pt	32.55±0.02	15.12±0.04	13.73±0.15	17.49±0.12
СЈМ	36.72±0.13	40.05 ± 0.02	49.22±0.08	29.95±0.03
CJM-Pt	31.60±0.01	59.91±0.23	15.21 ± 0.12	10.78±0.05

Table S2. IC_{50} [µg/ml] for the 24 h of action of investigated drugs on MGC-803, SGC-7901, MCF-7 and MDA-MB-231 determined by MTT assay.



Fig. S2. **A**. UV absorption spectrum of CJM and CJM-Pt. **B**. CJM-Pt calibration curve by detected absorption peak at 293 nm on HPLC. **C**. The different peak times of CJM126, CJM-Pt and Lipo-CJM-Pt at 293 nm.