Supplementary Information (SI)

Two Zn(II) coordination polymers with anticancer drug norcantharidin as ligands: for cancer chemotherapy

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Drug release of DMCA-Zn1 NPs

The drug release of DMCA-Zn1 NPs was evaluated by dialysis. The release experiments were performed in PBS at two different pH values (7.4 and 5.5). Briefly, 2 mL aqueous solution of DMCA-Zn NPs (0.5 mg mL^{-1}) was transferred into a dialysis bag (MWCO = 3500). Then it was incubated in 55 mL PBS at 37 °C and gently stirred by a magnetic bar at 60 rpm. At a specified time, 3 mL external PBS were extracted and 3 mL fresh PBS was added simultaneously. The cumulative release amount of DMCA was calculated by measuring the UV absorption intensity of DMCA at 207 nm. All the drug release experiments were carried out in triplicate and the results were the averaged values.

As a comparison, the drug release of DMCA-Zn1 crystal was also investigated, i.e., 10 mg DMCA-Zn1 was dispersed in 5 mL PBS and transferred into a dialysis bag (MWCO = 3500) and then processed by the same procedure as above. Drug release of DMCA-Zn2 NPs was use the same method.

Table S1 Crystallographic parameters and refinement details for DMCA-Zn1 and DMCA-Zn2.

Compound	**DMCA-Zn1**	**DMCA-Zn2**
Empirical formula	$C_{96}H_{96}O_{72}Zn_{18.14}$	$C_8H_{12}O_7Zn$
Formula weight	3587.91	285.57
Temperature / K	173 K	297 K
Crystal system	Triclinic	Monoclinic
Space group	P -1	P 21/ c
a / Å	16.9434(5)	11.0956(3)
b / Å	17.4308(5)	8.5168(2)
c / Å	17.7700(5)	10.9183(3)
α / °	107.588(1)	90
β / °	102.592(2)	107.151(1)
	117.115(1)	90
γ / °	4042.7(2)	985.89(4)
V / Å3	1.064	1.092
Goodness of fit on F^2	1	4
Z	1.474	1.910
Dcalc (g/cm3)	3.579	3.710
U (Mo Ka) / mm-1	1792.0	1168
F (000)	20.21.21	13, 10,13
h, k, l_{max}	14902	1807
Nref	0.0539	0.0304
R (int)	1.064	1.092
S	R1 = 0.0388 wR2 = 0.1166	R1 = 0.0271 wR2 = 0.0803
Final R indices [I > 2sigma(I)]	R1 = 0.0473 wR2 = 0.1217	R1 = 0.0279 wR2 = 0.0812
R indices (all data)		

$R_1 = \sum||F_o|-|F_c||/\sum|F_o|$. $wR_2 = [\sum[w(F_o^2-F_c^2)^2]/\sum[w(F_o^2)^2]]^{1/2}$

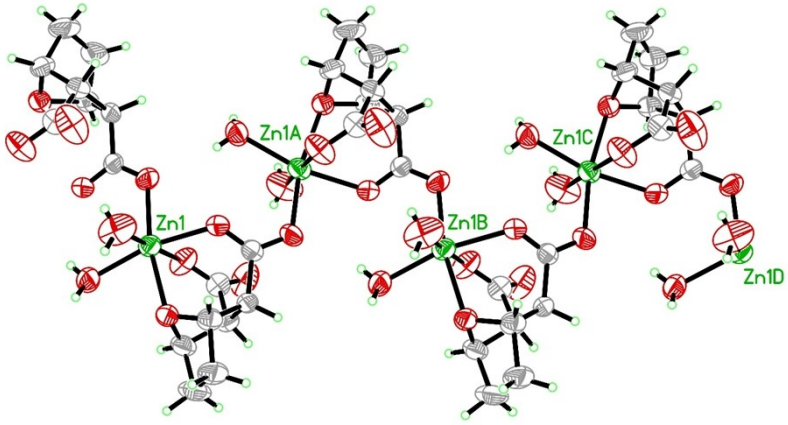

Fig. S1 The structural drawing showing atomic displacement parameters of DMCA-Zn2.

The pure DMCA-Zn2 were confirmed by PXRD measurement in which the diffraction peaks of experimental pattern (black line) was in excellent agreement with the simulated pattern (red line) from single-crystal X-ray data by Materials Studio 7.0 (Fig. S1(a)). The thermal stability of DMCA-Zn2 were investigated by TGA measurement in the air. As show in Fig. S1(b), two weight loss stages were observed in the TGA curve of DMCA-Zn2. The first weight loss of 19.03% occurred below 200 ^{o}C was ascribed to the removal of two coordinated H_2O molecules (calcd. 19.96%). The second weight loss of 53.95% occurred from 300 to 500 ^{o}C was attributed to the removal of most DMCA ligands (calcd. 53.13%), which resulted in the decomposition of the coordination polymer DMCA-Zn2. The last residual weight of 27.02% was attributed to the formation of ZnO (calcd. 26.91%).

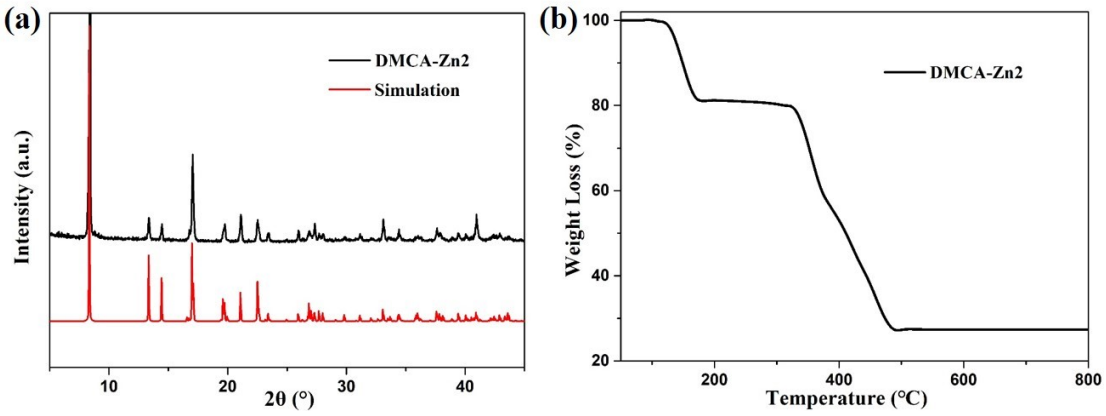

Fig. S2 (a) PXRD patterns of DMCA-Zn2, (b) The TGA curve of DMCA-Zn2 in air.

Preparation of DMCA-Zn2 NPs

The formation of DMCA-Zn2 NPs was identified by DLS and TEM measurements. Fig. S2(a) gives the DLS curve of DMCA-Zn2 NPs solution and confirms the formation of nanoparticles with a unimodal size distribution (PDI = 0.182) and an average hydrodynamic diameter about 162 nm. At the same time, DLS measurement was also used to monitor the size change of DMCA-Zn2 NPs in five days and the results indicates they are basically stable in aqueous solution (Fig. S2(b)-(c)). Furthermore, the TEM image in Fig. S2(d) shows that DMCA-Zn2 NPs have spherical morphology with an average size of approximately 160 ± 40 nm, which is consistent with the size given by DLS measurement.

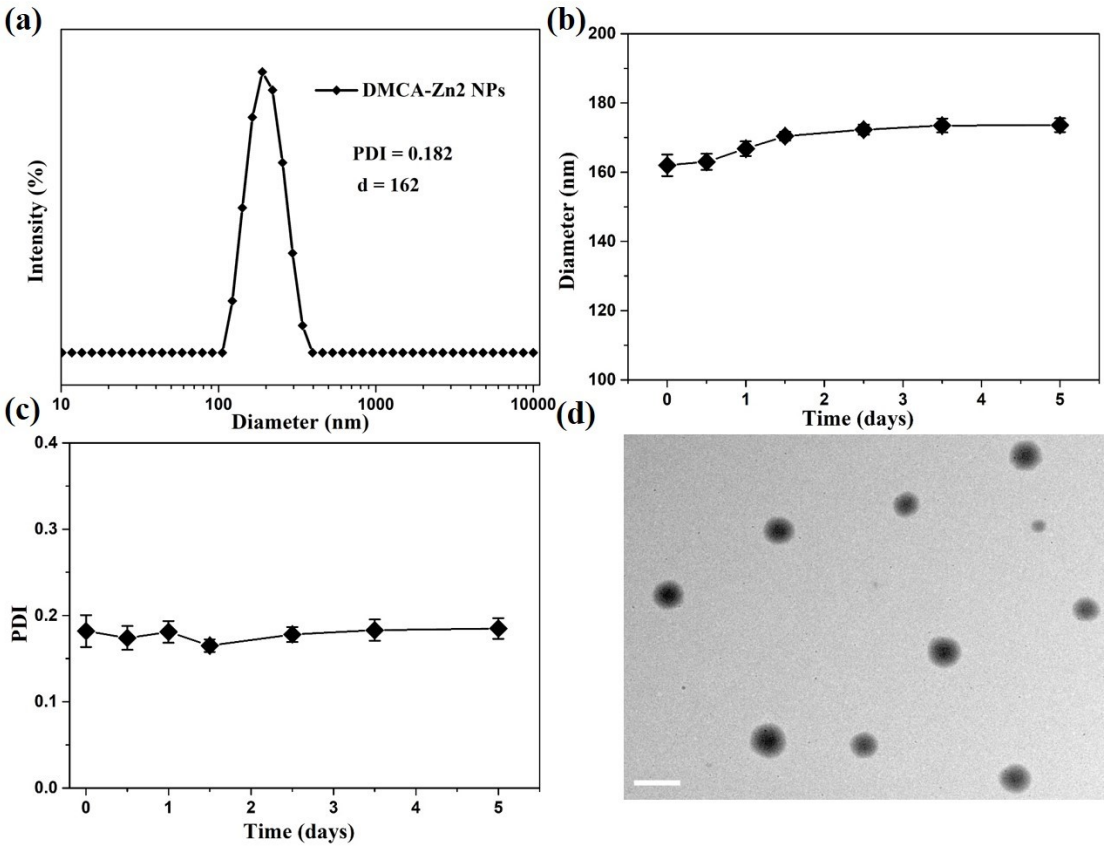

Fig. S3 (a) DLS curve of DMCA-Zn2 NPs, (b) The diameter changes of DMCA-Zn2 NPs vs the storage time, (c) The particle size distribution index (PDI) of DMCA-Zn2 NPs vs the storage time, (d) TEM image of DMCA-Zn2 NPs, Scale bar: 200 nm.

The calibration standard curve of DMCA measured by UV-Vis spectrum

A series of PBS solution with various concentration of DMCA was prepared to measure their UV-Vis spectra. Then the calibration standard curve of DMCA was obtained by plotting the absorbance to the concentration as shown in Fig. S3.

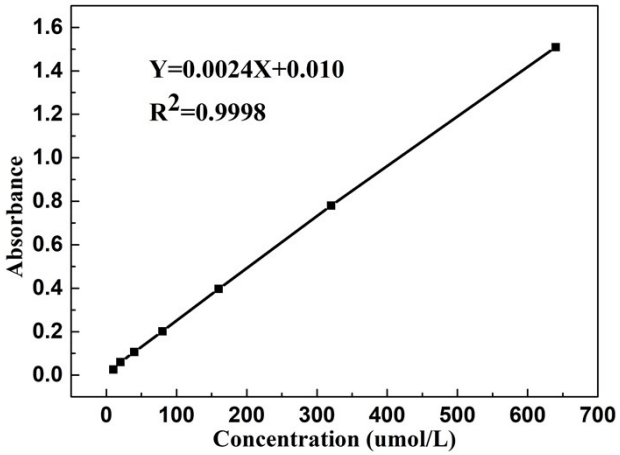

Fig. S4 The calibration standard curve of DMCA in PBS.

The cumulative release amount of DMCA from DMCA-Zn was calculated according to the following formula:

$$CR\% = \frac{50 \times C_{drug(n)} + 3 \times \sum_{n=1}^{n-1} C_{drug(n-1)}}{W_0} \times 100\%$$

Here,

CR%: the cumulative release amount of DMCA

W_0: the total amount of DMCA loaded in DMCA-Zn

$C_{drug(n)}$ and $C_{drug(n-1)}$: the concentration of DMCA in the buffer taken out at the n and n-1st times

Drug release of DMCA-Zn2 NPs

According to the cumulative release curves of DMCA-Zn2 NPs in Fig. S4(a), the release rate of DMCA at pH = 5.5 was much higher than that at pH = 7.4. For example, more than 87.9% DMCA was released form DMCA-Zn1 NPs at pH = 5.5, whereas only about 38.8% DMCA was released at pH = 7.4 after 98 h. In order to further analyze the drug release of DMCA-Zn2 NPs, the drug release of DMCA-Zn1 was also evaluated at the same condition. The test results show in Fig. S4(b), the release rate of DMCA at pH = 5.5 was also much higher than that at pH = 7.4 for DMCA-Zn2. However, compared with DMCA-Zn2, DMCA-Zn2 NPs have achieved the effect of sustained release. That means DMCA-Zn2 NPs are promising candidate for drug delivery.

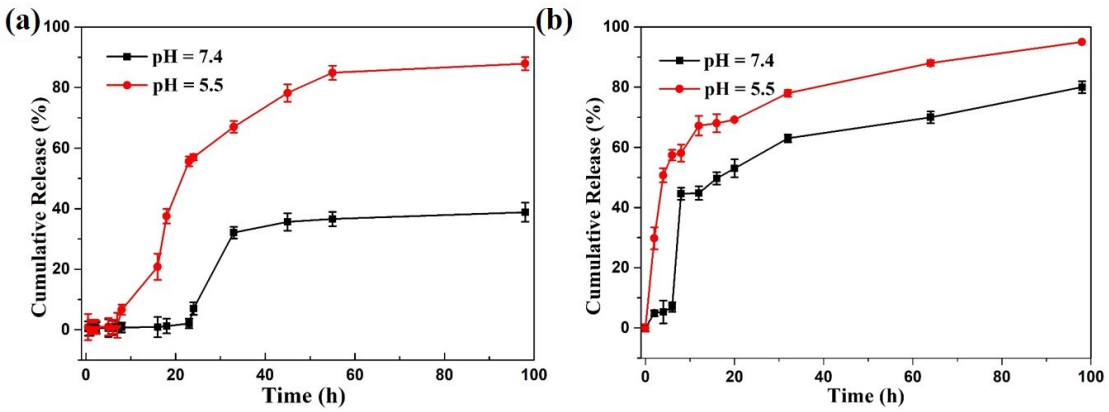

Fig. S5 The DMCA release profiles of DMCA-Zn2 NPs (a) and DMCA-Zn2 (b) in the simulated physiological conditions (37 °C, PBS solution at pH = 7.4 and pH = 5.5).

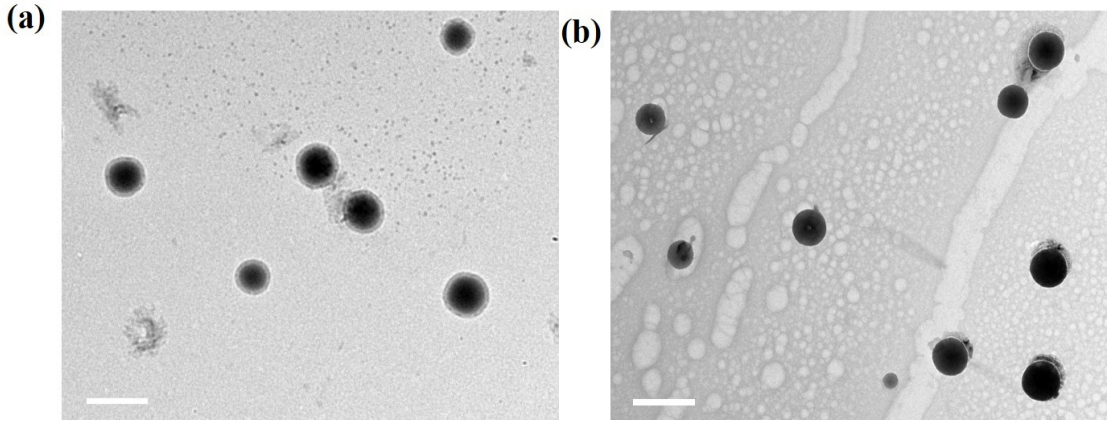

Fig. S6 The TEM image of (a) Nile red loaded DMCA-Zn1 NPs and (b) Nile red loaded DMCA-Zn2 NPs, Scale bar: 200 nm.

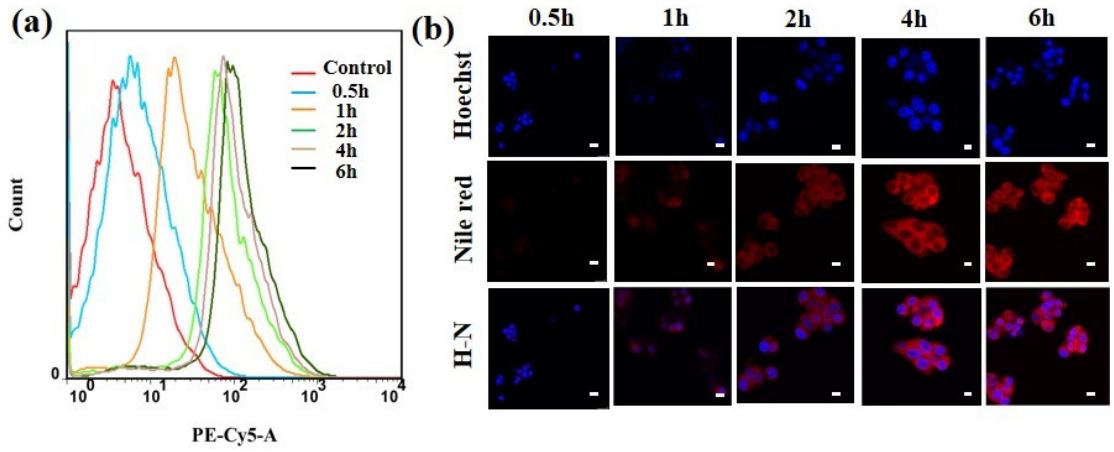

Fig. S7 (a) Flow cytometry analysis for cell uptake of DMCA-Zn2 NPs by Hep3B cells. The time-dependent mean fluorescence intensity of Hep3B cells cultured with DMCA-Zn2 NPs, (b) The CLSM images of Hep3B cells incubated with DMCA-Zn2 NPs for 0.5 h, 1 h, 2 h, 4 h and 6 h at 37℃.

DMCA-Zn1 and DMCA-Zn2 have a good stability in pH = 7.4 aqueous solution as shown in Fig. S7. (a) DMCA-Zn1 and (b) DMCA-Zn2 can stay in pH = 7.4 aqueous solution for 5 hours without being damaged.

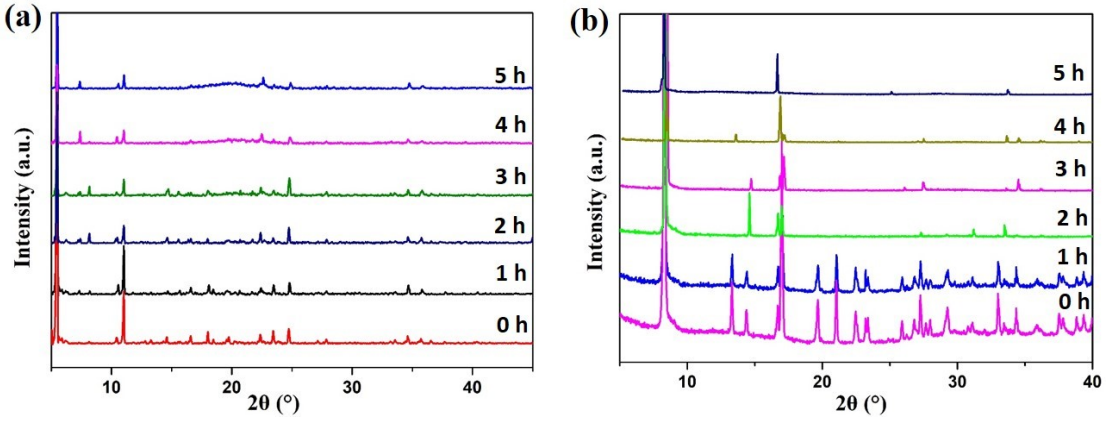

Fig. S8 The PXRD spectra of (a) DMCA-Zn1 and (b) DMCA-Zn2 in pH = 7.4 aqueous solution.

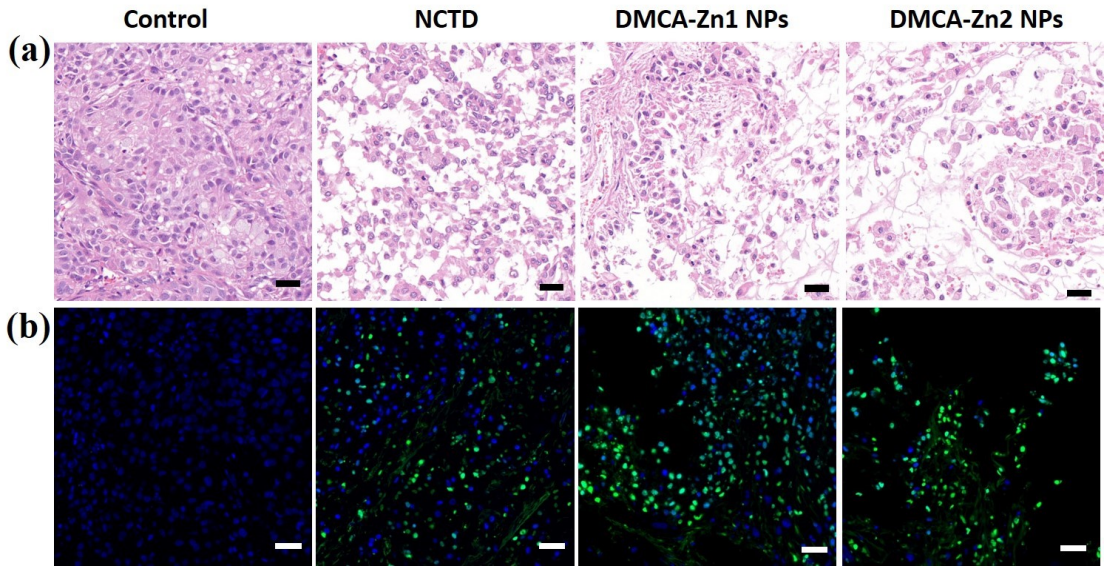

Fig. S9 (a) The H&E staining for the groups of control, NCTD, DMCA-Zn1 NPs and DMCA-Zn2 NPs, (b) The TUNEL staining for the groups of control, NCTD, DMCA-Zn1 NPs and DMCA-Zn2 NPs, scale bar: 50 μm.

Table S2 Liver function parameters.

Groups	ALT/U·L^{-1}	ALP/U·L^{-1}	AST/U·L^{-1}
PBS	47.26 ± 3.70	144.30 ±5.40	94.13 ± 3.73
NCTD	56.02 ± 3.03	162.52 ± 9.02	117.14 ± 9.47
DMCA-Zn1 NPs	43.70 ± 1.85	138.81 ± 5.87	94.95 ± 3.42
DMCA-Zn2 NPs	43.12 ± 1.19	146.88 ± 3.79	92.96 ± 5.25

Values are Mean ± SD, n = 3.

* Values are significantly different from the normal control group at ($p < 0.05$)

Table S3 Kidney function parameters.

Groups	UA/μmol·L^{-1}	CRE/μmol·L^{-1}	BUN/mg·dL^{-1}
PBS	133.99 ± 3.88	38.75 ± 0.60	22.80 ± 1.35
NCTD	106.76 ± 5.13	51.33 ± 5.13	31.27 ± 3.78
DMCA-Zn1 NPs	131.30 ± 1.50	35.10 ± 1.95	24.07 ± 1.69
DMCA-Zn2 NPs	129.00 ± 8.76	35.32 ± 3.57	24.67 ± 2.32

Values are Mean ± SD, n = 3.

*Values are significantly different from the normal control group at ($p < 0.05$)