Supplementary Data

Development of An Oral Satraplatin Pharmaceutical Formulation by Encapsulation with Cyclodextrin

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1. XRD analysis

The lack of crystallinity is an added piece of evidence for the formation of inclusion complex. **Fig. S1** shows the XRD patterns of satraplatin, β-CD and their inclusion complex. In **Fig. S1**, satraplatin (**Fig. S1(a)**) and β-CD (**Fig. S1(b)**) indicated sharp, intense peaks showing that both of them were in crystalline form. The complexe is not a superimposition of the patterns of the pure satraplatin. Some diffraction patterns were dramatically affected in the inclusion complexe, which formed a new crystal structure of the solid complexe. Additionally, the diffraction pattern of the physical mixture (**Fig. S1(c, d)**) is different from the complexe, indicating that there was an interaction between satraplatin and β-CD.

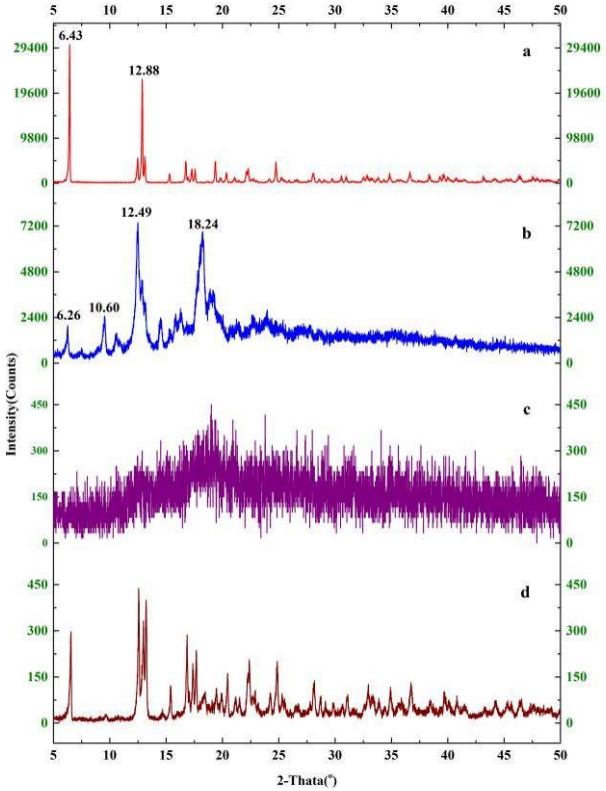

Figure S1 XRD patterns: (a) satraplatin, (b) β-CD, (c) satraplatin/β-CD inclusion complex, (d) satraplatin/β-CD physical mixture

2. FTIR analysis

The FTIR spectra provided detailed information about the functional groups involved in the interaction when the complex was formed. The spectra of pure satraplatin, β-CD, their physical mixture, and the inclusion complex are shown in **Fig. S2**. The FTIR spectrum of β-CD showed prominent absorption bands at 3390 cm^{-1} (for O-H stretching vibrations), 2931 cm^{-1} (for C-H stretching vibrations), 1641 cm^{-1} (for H-O-H bending), 1153 cm^{-1} (for C-O stretching vibrations) and 1035 cm^{-1} (for C-O-C stretching vibrations), as indicated by previous studies. The sharp and strong absorption bands, observed at 3249, 3054 and 1249 cm^{-1} due to N-H and C-H stretching vibrations and bending vibrations in cyclohexane (**Fig. S2(a**)), respectively, in satraplatin were considerably reduced in the inclusion complex owing to complexation (**Fig. S2(c)**). For the inclusion complex (**Fig. S2(c)**), an additional key observation was an increase in the intensity and a slight redshift of the peak from 3500-3000 cm^{-1} in the spectrum of the inclusion compound. In agreement with earlier reports, vibrational modes in the region of 3500-3300 cm^{-1} have been correlated with of host-guest interactions as a result of water release upon inclusion. In addition, no additional peaks were detected in the spectrum of the inclusion complex, indicating the absence of any chemical reactions between satraplatin and β-CD. The spectrum of the physical mixture was equivalent to the simple combination of satraplatin and β-CD, and some characteristic absorption peaks of satraplatin at 3243, 3064, 2846, 1357, 1301 and 705 cm^{-1} were easily observed (**Fig. S2(d)**), suggesting that the natural structure of satraplatin still existed without any interactions with β-CD. These results indicate that a satraplatin/β-CD inclusion complex was obtained and that the large cyclohexane ring of satraplatin entered the cavity of β-CD during the formation of the inclusion complex.

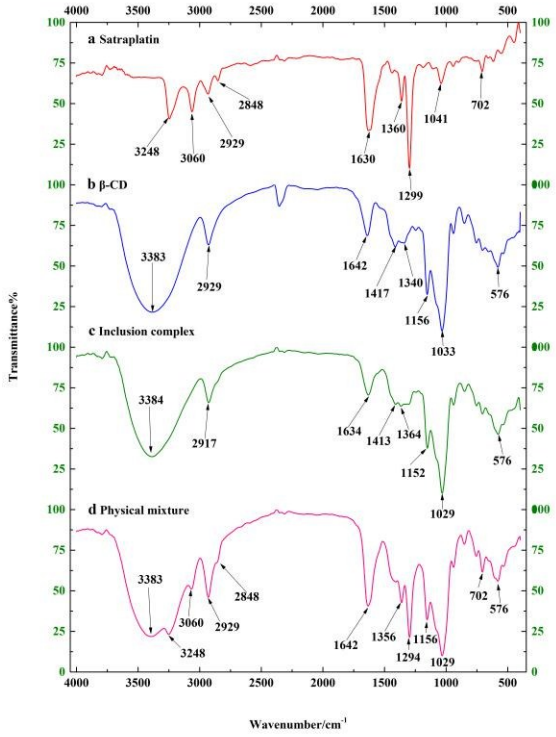

Figure S2 FTIR spectra of **(a)** satraplatin, **(b)** β-CD, **(c)** the satraplatin/β-CD inclusion complex in a 1:1 molar ratio and **(d)** the satraplatin and β-CD physical mixture in a 1:1 molar ratio.

3. Other spectroscopy and spectra

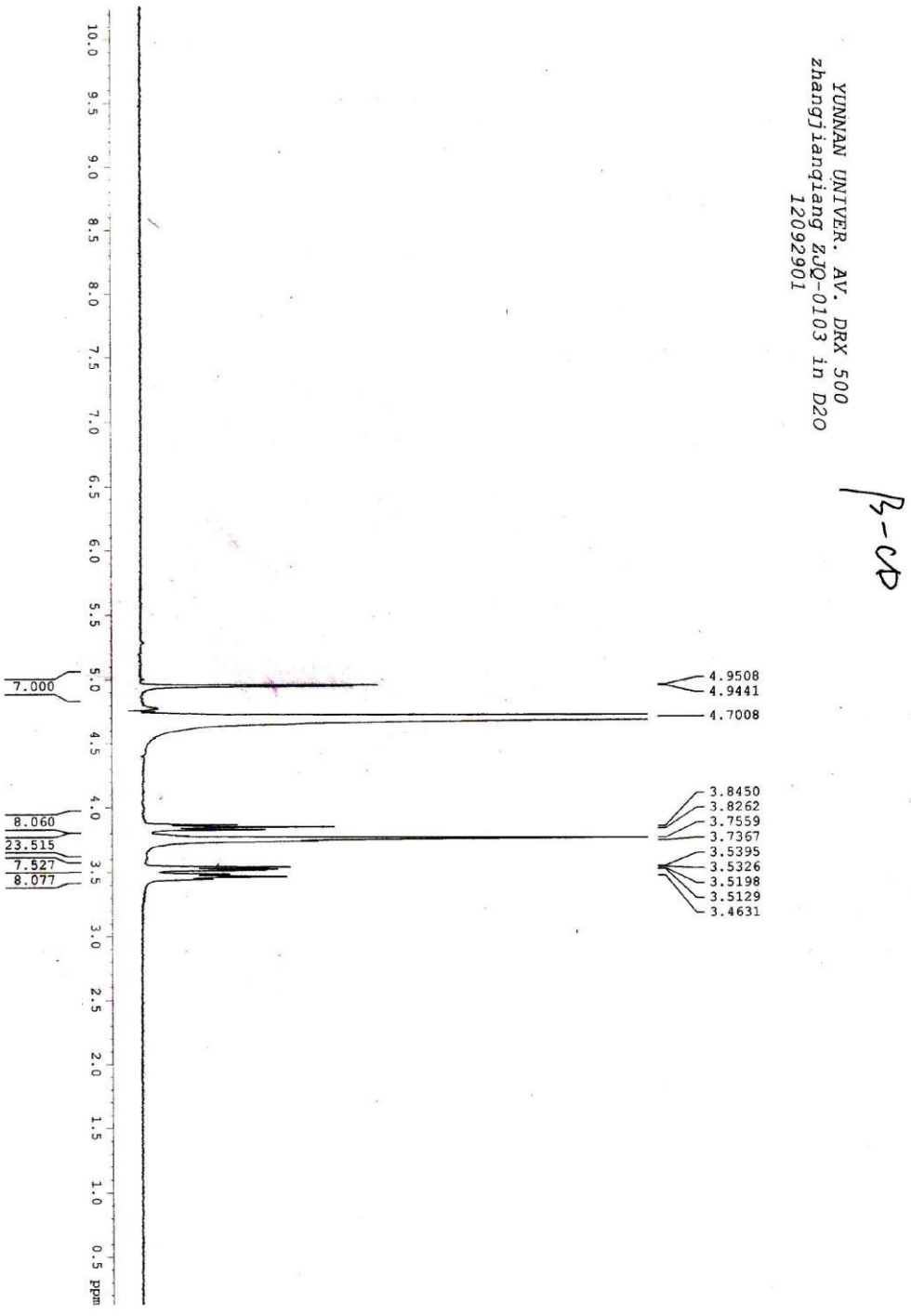

Figure S3 1H NMR spectra of β-CD in D_2O.

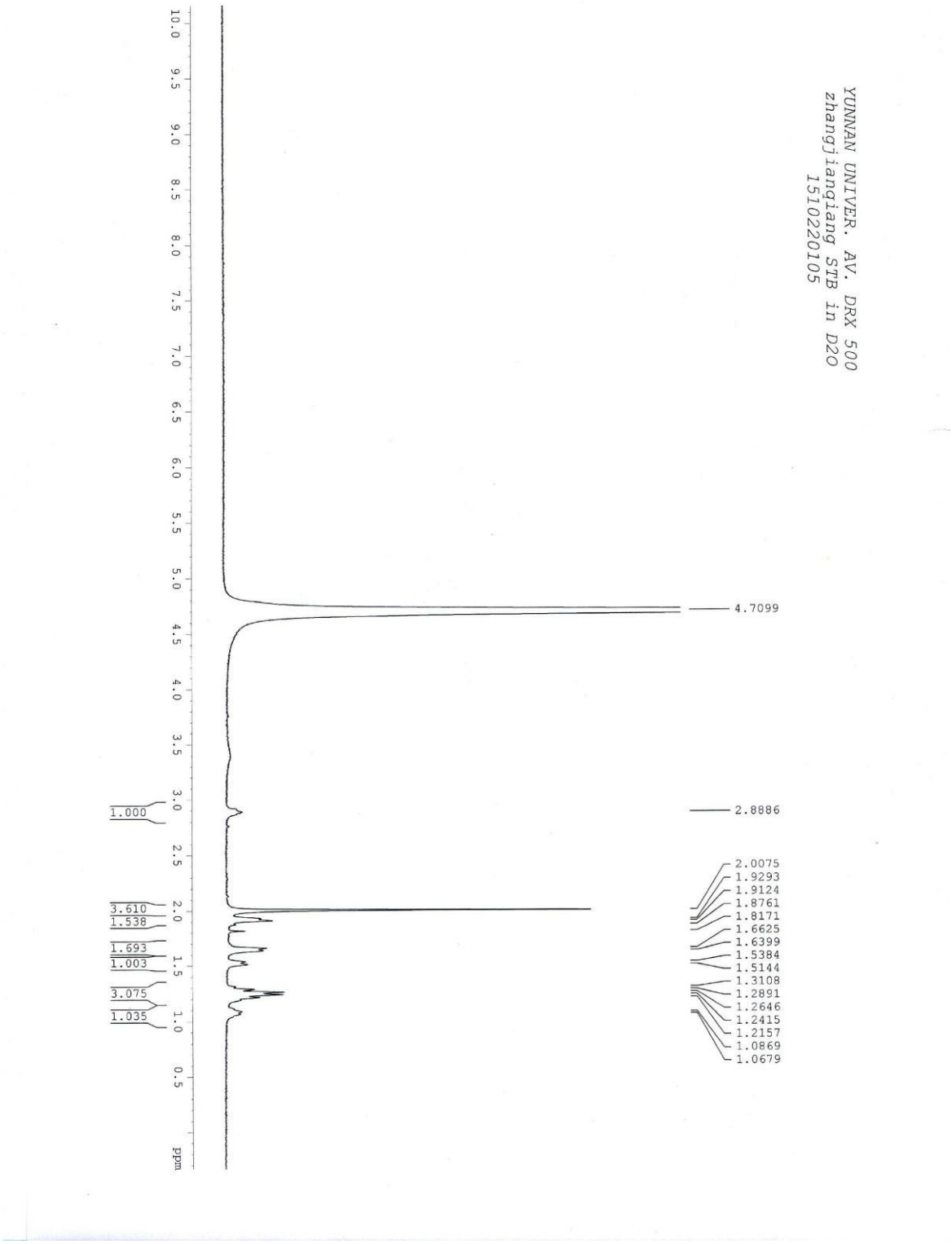

Figure S4 1H NMR spectra of Satraplatin in D_2O.

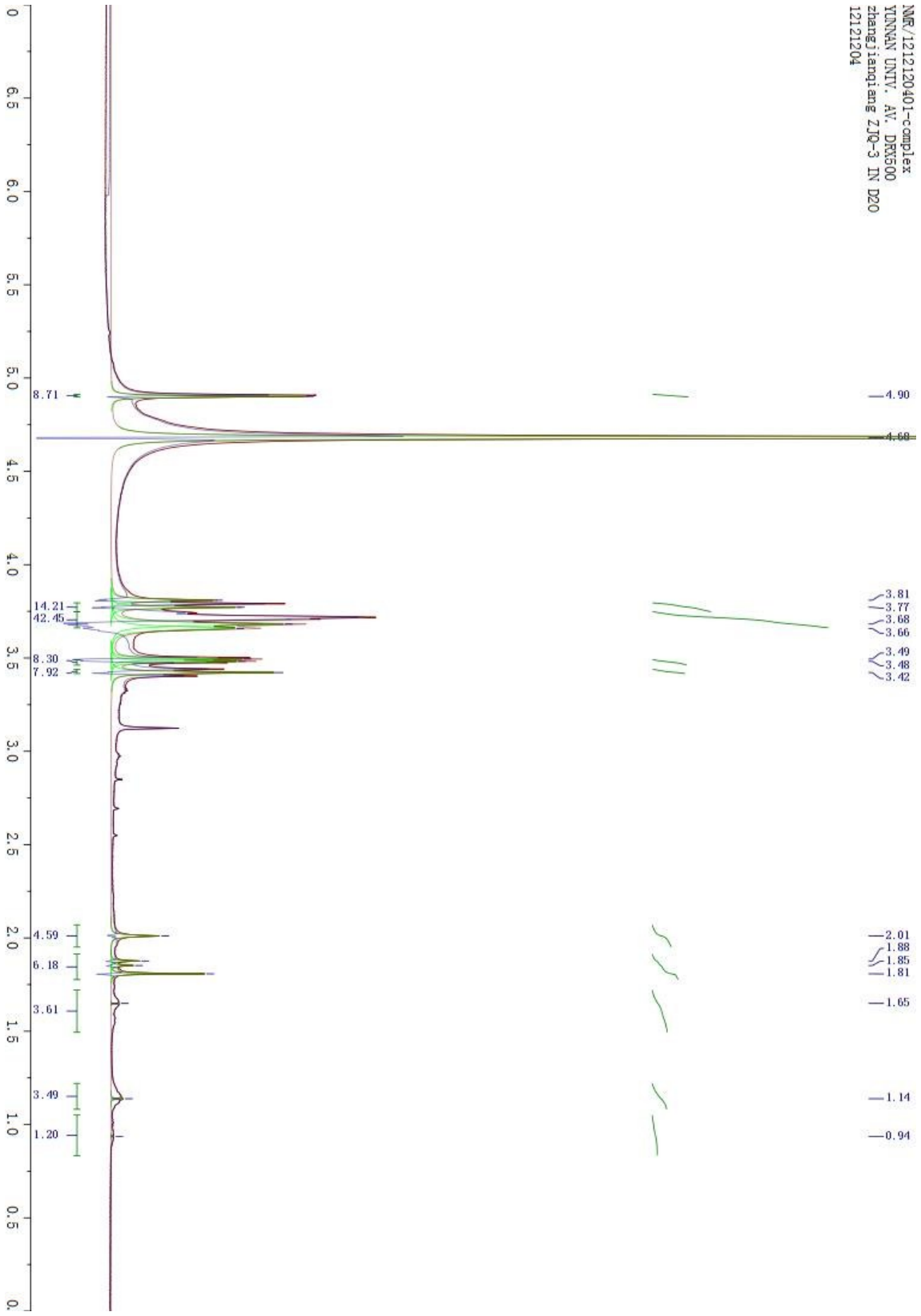

Figure S5 1H NMR spectra of Satraplatin/β-CD complex in D_2O.

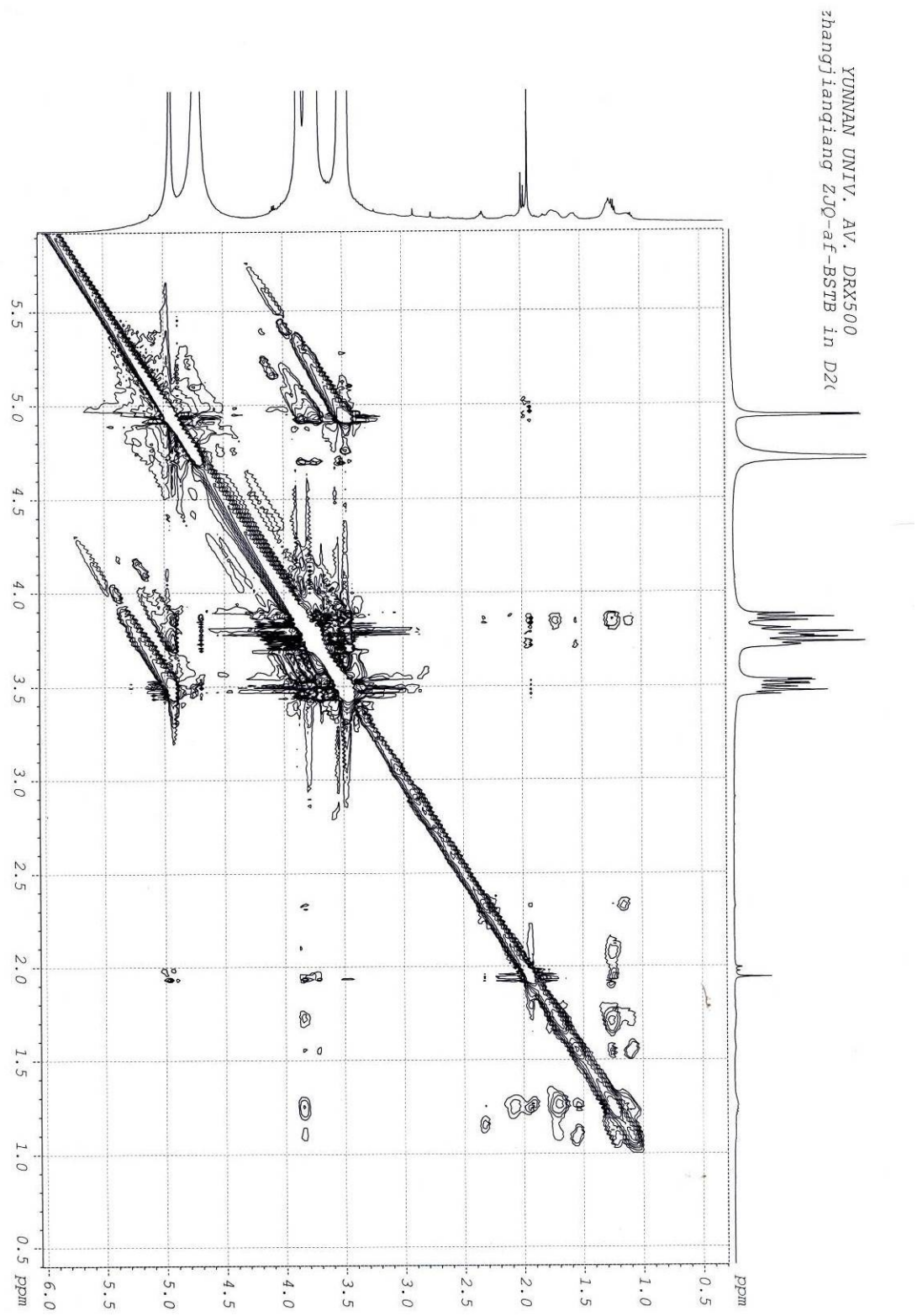

Figure S6 ROESY spectrum of satraplatin/α-CD complex in D_2O.

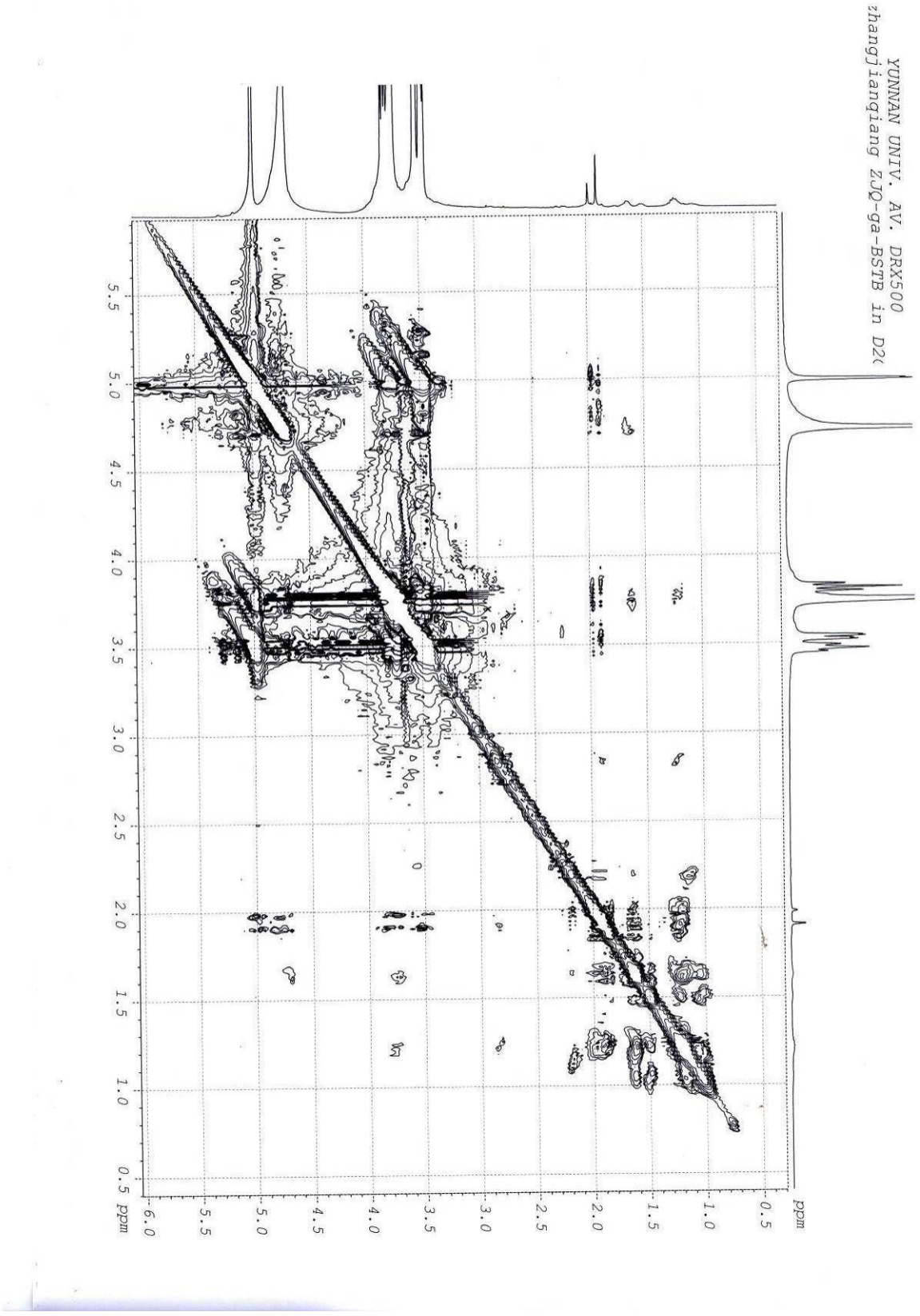

Figure S7 ROESY spectrum of satraplatin/γ-CD complex in D_2O.

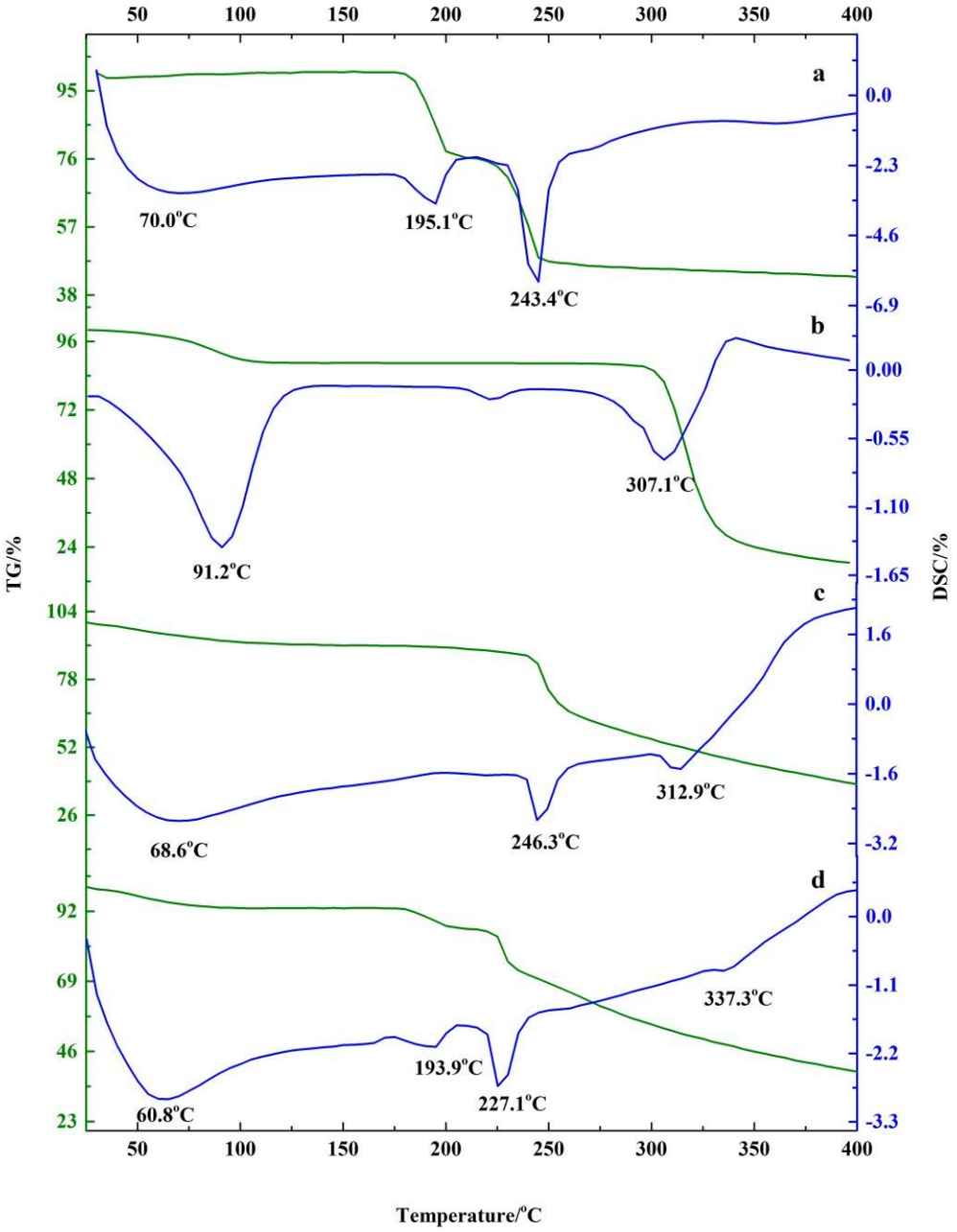

Figure S8 DSC thermograms (blue Line) and TG (green line): (a) satraplatin, (b) β-CD, (c) satraplatin/β-CD inclusion complex, (d) satraplatin/β-CD physical mixture.

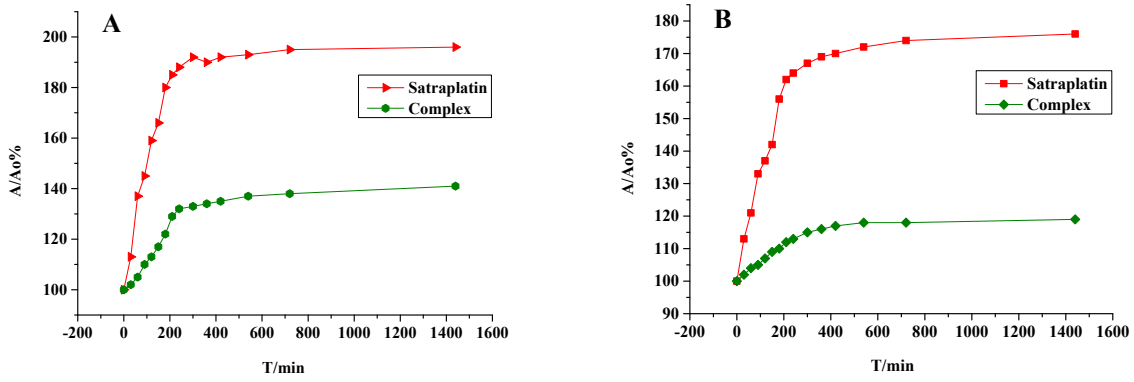

Figure S9 Degradation profiles of satraplatin decomposition, **(A)** in pH 2.2 aqueous solution; and **(B)** in pH 7.3 aqueous solution.

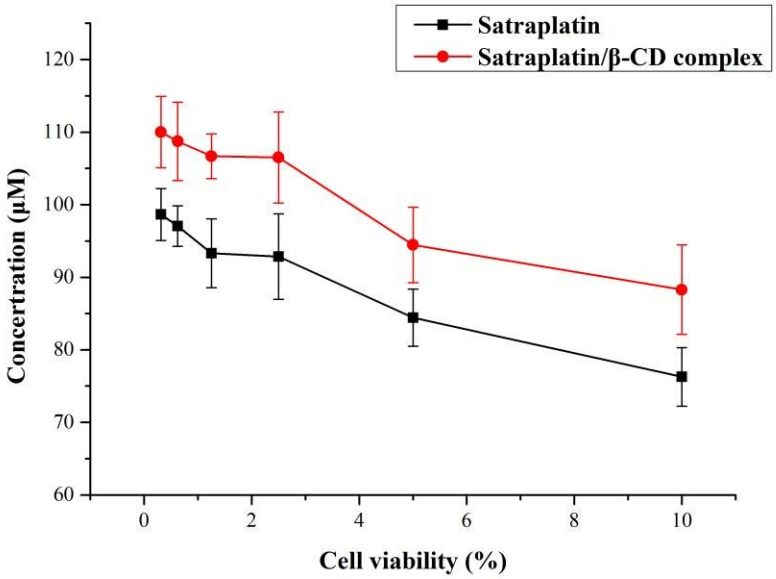

Figure S10 Cytotoxicity assays (Caco-2) for satraplatin and satraplatin/β-CD complex at different concertration.

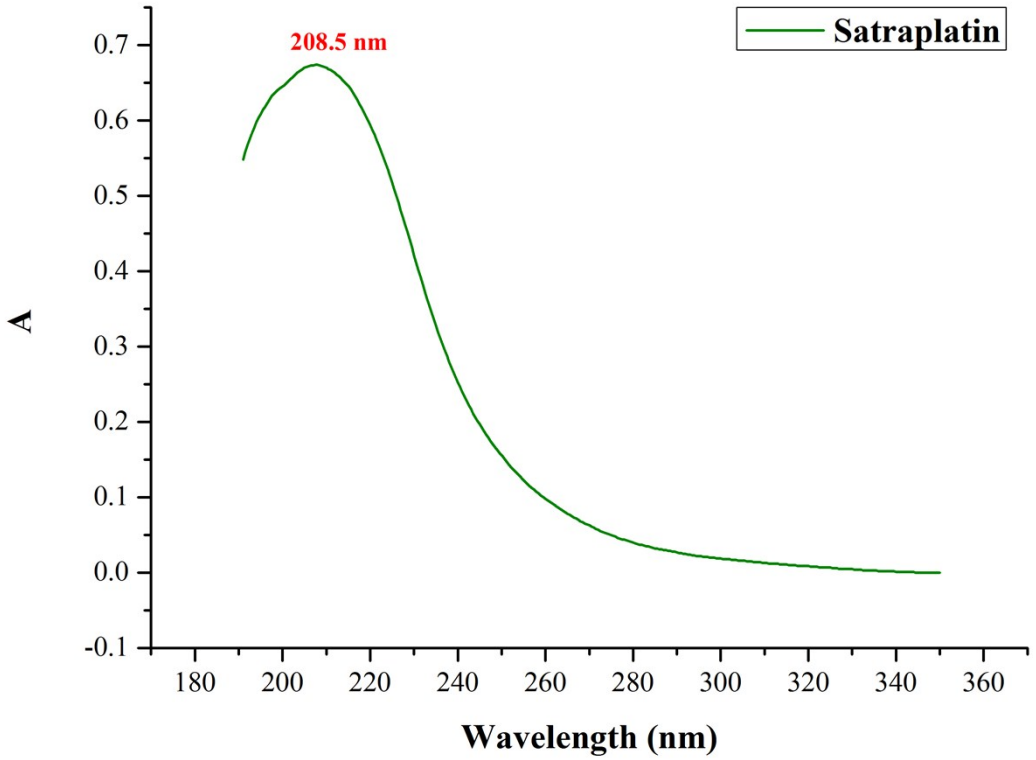

Figure S11 The UV-*vis* absorption spectra of satraplatin.

Table S1 Inhibitory concentration (IC50) (μM) values calculated for β-CD, satraplatin, satraplatin/β-CD complex, satraplatin/α-CD complex, and satraplatin/γ-CD complex for the two different cancer cell lines A549 and MCF-7.

Sample	IC_{50} (μM)	
	A549	MCF-7
β-CD	>500	>500
Satraplatin	10.12	0.25
Satraplatin/β-CD complex	6.09	0.14
Satraplatin/α-CD complex	45.12	56.38
Satraplatin/γ-CD complex	50.48	65.32

Table S2 Chemical Shifts of ^{1}H NMR of satraplatin Protons in the presence and absence of satraplatin.

protons		chemical shift (ppm)		
		$\delta_{satraplatin}$	$\delta_{satraplatin/\beta\text{-CD}}$	$\Delta\delta$
H-1, 2(CH_3)	m	2.008	2.060	0.052
H-3	s	2.889	2.978	0.089
H-4, 8(α-H)	m	1.698	1.872	0.174
H-5, 7(α-H)	m	1.589	1.698	0.109
H-6(α-H)	m	1.526	1.589	0.063
H-4, 5, 6, 7, 8(β-H)	m	1.264	1.202	-0.62