

Supplementary Materials: Development and Validation of Liquid Chromatography-Based Methods to Assess the Lipophilicity of Cytotoxic Platinum(IV) Complexes

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Table S1. List of five platinum(IV) complexes bearing ionisable groups for determining distribution coefficients. The chromatographic lipophilicity parameters $\text{Log } k_w$ and ϕ_0 were additionally determined under acidic conditions (pH 2.5) using potassium iodide (KI) as dead time marker.

Nr.	Structure	$\text{Log } k_w$ (KI)	ϕ_0 (KI)
20		0.61	13.8
21		1.41	33.1
22		1.73	35.9
23		2.16	47.2
24		2.77	56.3

Table S2. List of 35 platinum(IV) complexes for converting ϕ_0 into calculated Log P (cLog P) based on the calibration curve described in the main text. The compounds were sorted according to increasing cLog P.

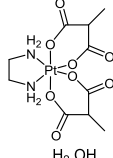
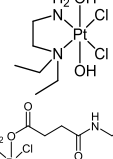
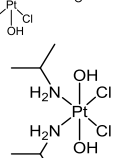
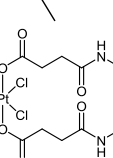
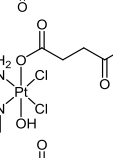
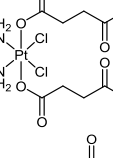
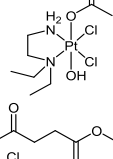
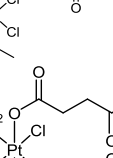
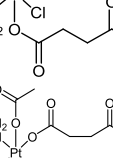
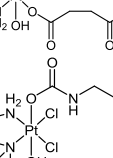
Nr.	Structure	Log k_w (KI)	ϕ_0 (KI)	cLog P (HPLC)
25		0.67	13.4	−1.9
26		0.80	17.6	−1.9
27		1.02	20.1	−1.9
28		0.93	24.6	−1.8
29		1.21	25.8	−1.8
30		1.29	27.6	−1.7
31		1.63	30.3	−1.7
32		1.13	31.8	−1.6
33		1.32	32.8	−1.6
34		1.43	34.0	−1.5
35		1.64	35.2	−1.5
36		1.34	37.8	−1.3

Table S2. Cont.

Nr.	Structure	Log k_w (KI)	ϕ_0 (KI)	cLog P (HPLC)
37		2.10	38.4	−1.3
38		1.61	38.8	−1.3
39		2.05	45.8	−0.9
40		1.94	49.1	−0.7
41		2.29	51.8	−0.5
42		2.13	52.1	−0.5
43		1.91	53.2	−0.4
44		2.03	53.2	−0.4
45		2.38	54.0	−0.3
46		2.23	56.3	−0.1
47		2.23	56.8	−0.1

Table S2. Cont.

Nr.	Structure	Log k_w (KI)	ϕ_0 (KI)	cLog P (HPLC)
48		2.58	57.4	0.0
49		2.48	58.8	0.1
50		2.61	59.0	0.1
51		2.70	60.7	0.3
52		2.89	61.3	0.3
53		2.72	63.8	0.6
54		3.57	67.2	0.9
55		3.07	67.8	1.0
56		3.34	68.2	1.1
57		3.56	70.8	1.3
58		3.37	71.4	1.4

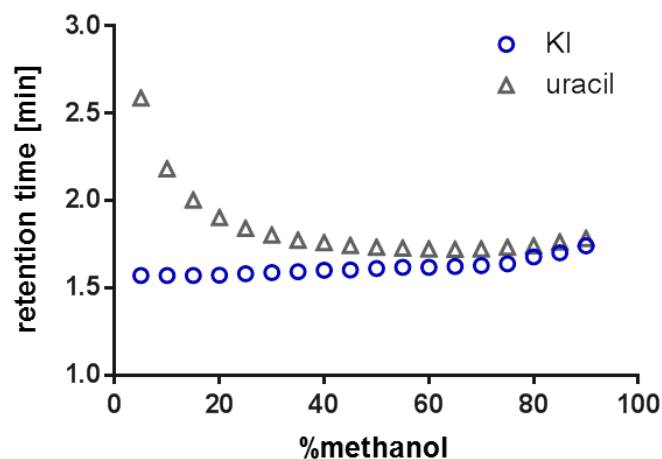


Figure S1. Comparison of the retention times of uracil (detection at 256 nm) and potassium iodide (KI, detection at 230 nm) at different percentages of methanol (ϕ) in the eluent.

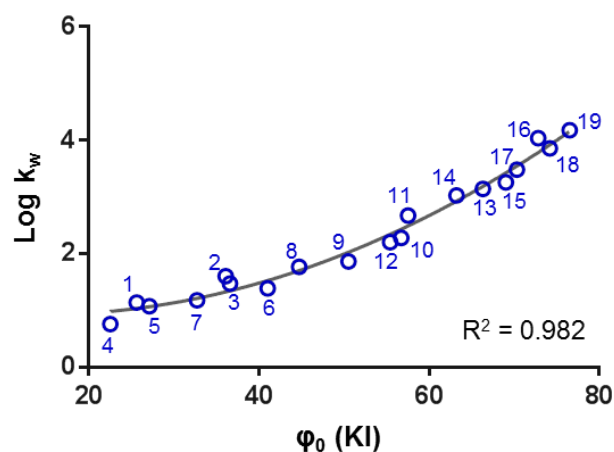


Figure S2. The correlation between the chromatographic lipophilicity parameters ϕ_0 and $\text{Log } k_w$ is quadratic polynomial (using potassium iodide as dead time marker) with $R^2 = 0.982$ for the standard set of 19 platinum compounds.

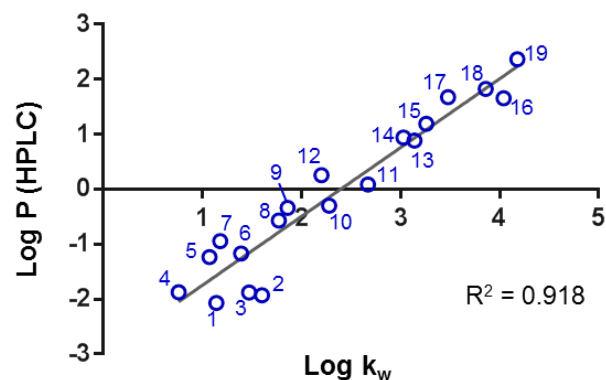


Figure S3. The correlation between $\text{Log } P$ by the shake flask method (using HPLC-UV/Vis) and the chromatographic $\text{Log } k_w$ is linear (using potassium iodide as dead time marker) with $R^2 = 0.918$ for the standard set of 19 platinum compounds. $\text{Log } P (\text{HPLC}) = 1.250 \cdot \text{Log } k_w - 3.000$.

Compound	ϕ_0 (Kl)	Log(IC ₅₀)
1	25,6	-5,0
2	36,1	-5,2
3	36,6	-5,2
7	32,7	-4,7
8	44,7	-3,8
9	50,5	-6,5
10	56,7	-4,6
11	57,5	-5,7
12	55,4	-7,0
13	66,3	-4,8
14	63,2	-7,2
15	69,0	-4,6
17	70,3	-8,3
18	74,2	-4,6
19	76,5	-5,0

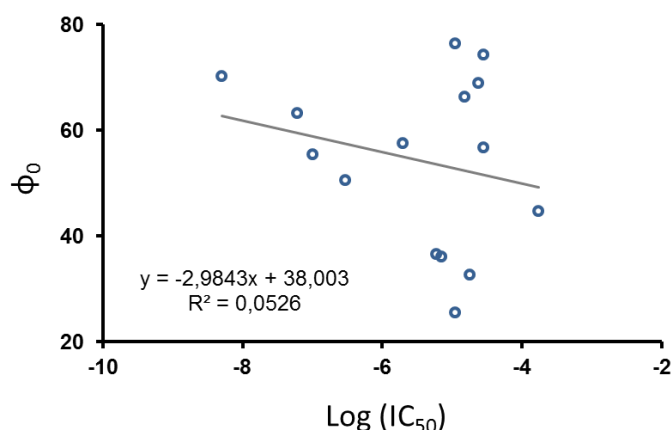


Figure S4. The cytotoxicity expressed as the concentration of 50% growth inhibition (IC₅₀) in the PA-1 cancer cell line (formerly CH1 cancer cell line) did not directly correlate with lipophilicity parameters (exemplified by ϕ_0) in the reference set of 19 structurally diverse platinum compounds. The cytotoxicities of 4–6 were not determined in these studies. Taken from refs [1–6].

References

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