Electronic Supplementary Information Associated with

A novel water-soluble Ni(II) complex as a prototype of metallodrug to treat toxoplasmosis

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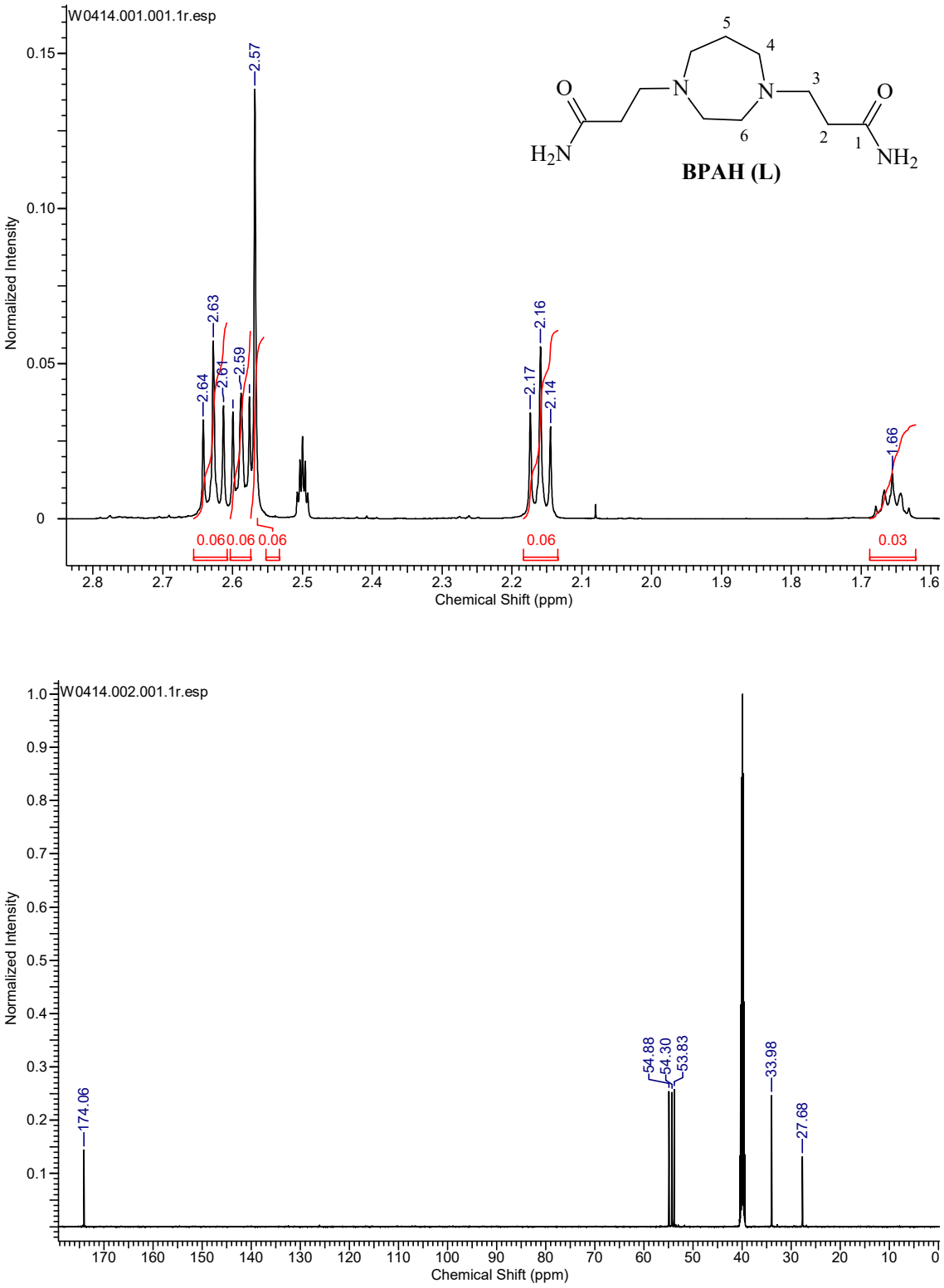


Figure 1SM. ^{1}H NMR (500 MHz, DMSO-D_6, top) and ^{13}C NMR (125 MHz, DMSO-D_6, bottom) spectra of the ligand BPAH

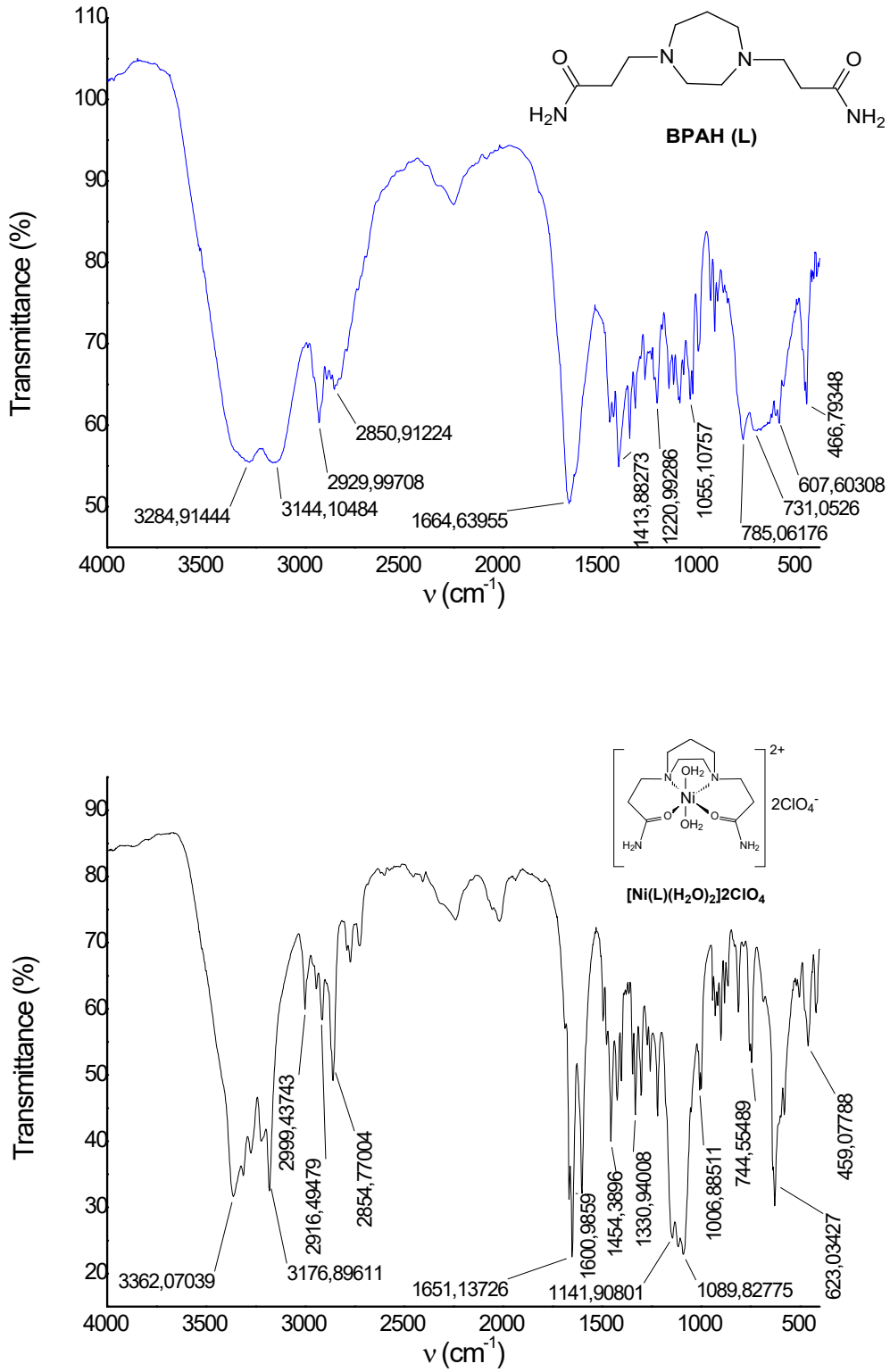


Figure 2SM. IR spectra of the ligand BPAH (top) and the nickel(II) complex (bottom).

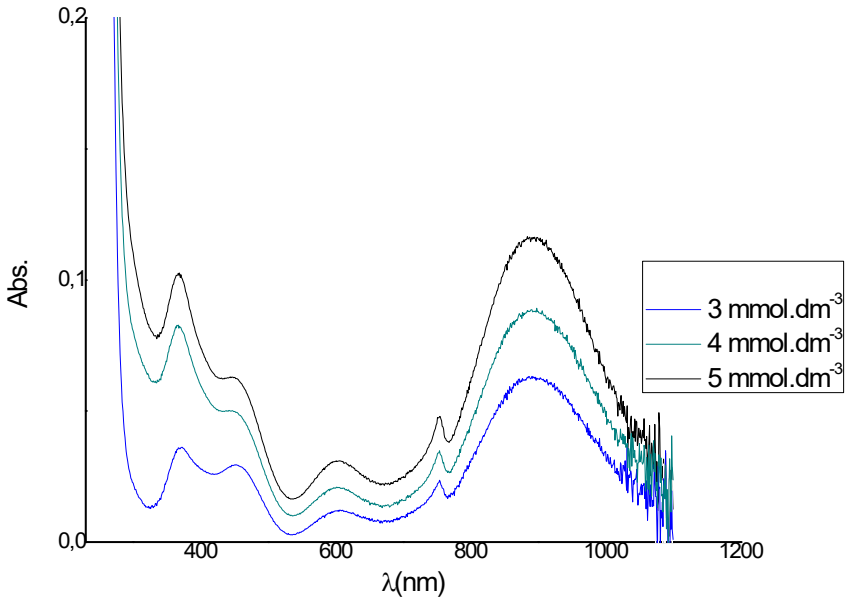


Figure 3SM. Electronic spectra of the nickel(II) complex at different concentrations in aqueous solution.

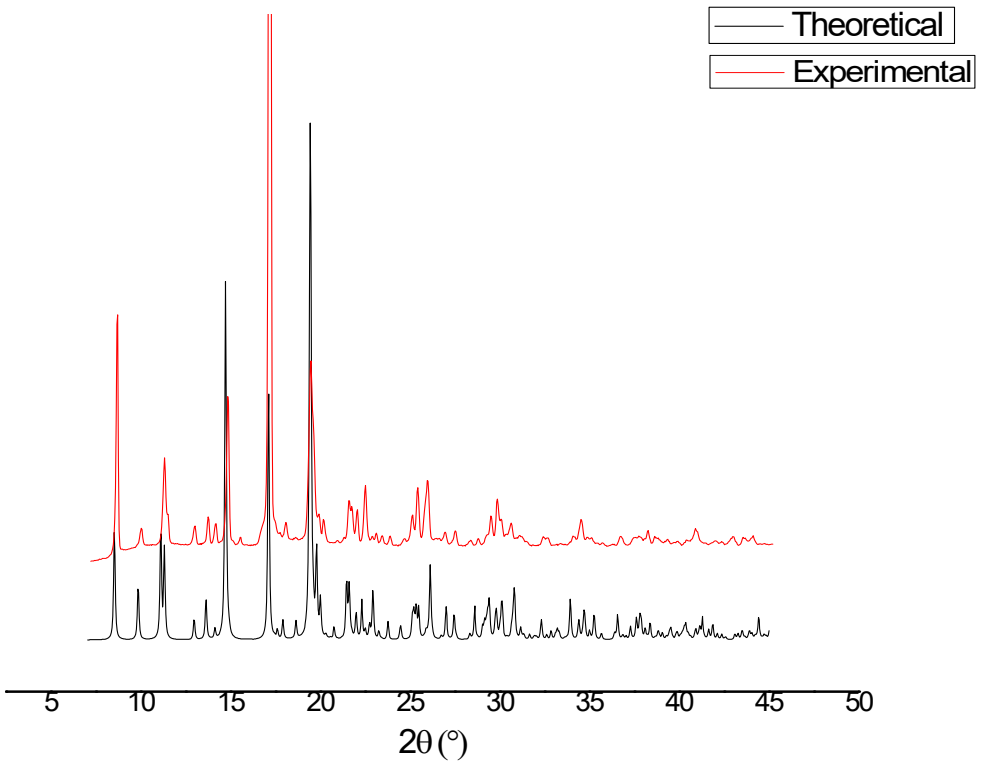


Figure 4SM. Experimental and theoretical diffractograms for the nickel(II) complex.

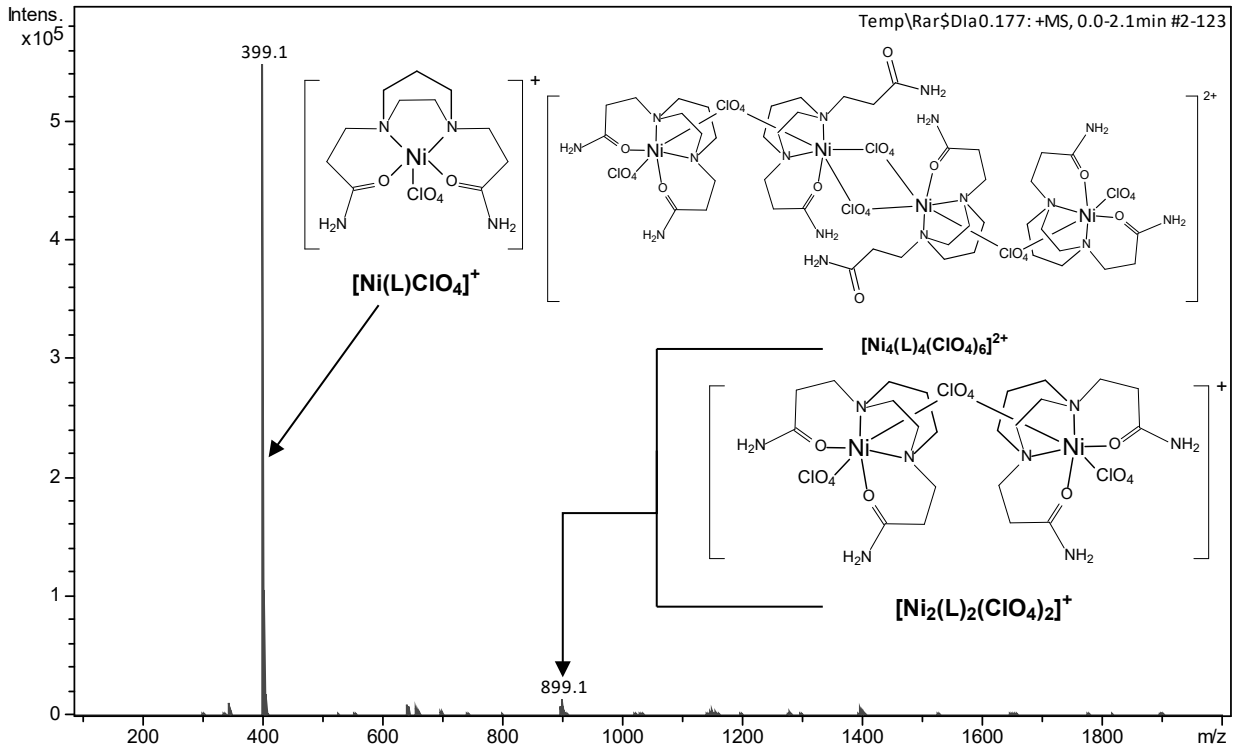


Figure 5SM. ESI-(+)-MS spectrum of complex $[Ni(BPAH)(H_2O)_2]^{2+}$, in H_2O/MeOH.

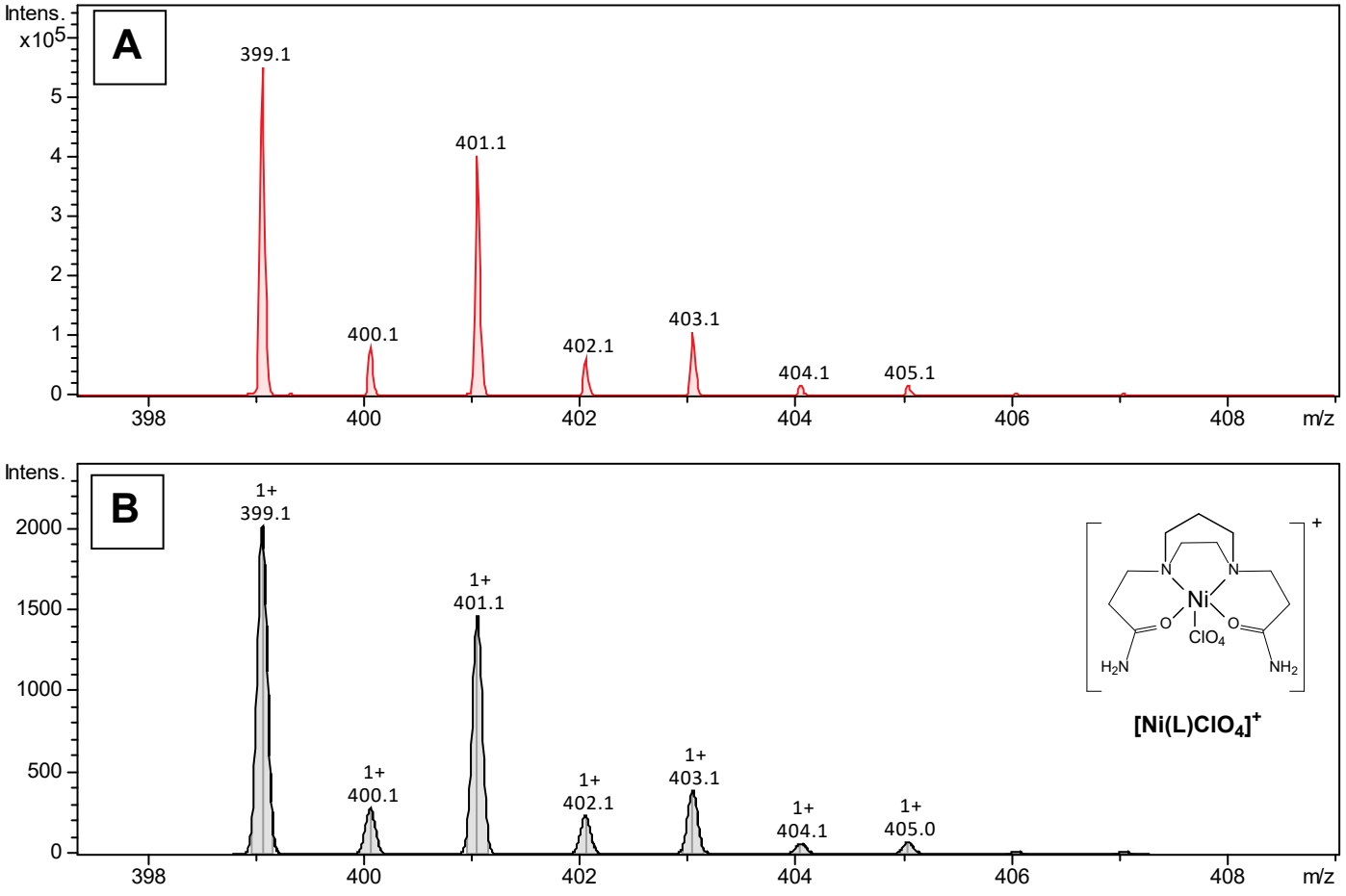


Figure 6SM. ESI-(+)-MS in the positive mode for a water:methanol 1:1 solution of complex $[Ni(BPAH)(H_2O)_2](ClO_4)_2$. [A] Experimental and [B] calculated isotopic patters for the ion of *m/z* 399.1 ≡ $[Ni(BPAH)(ClO_4)]^+$.

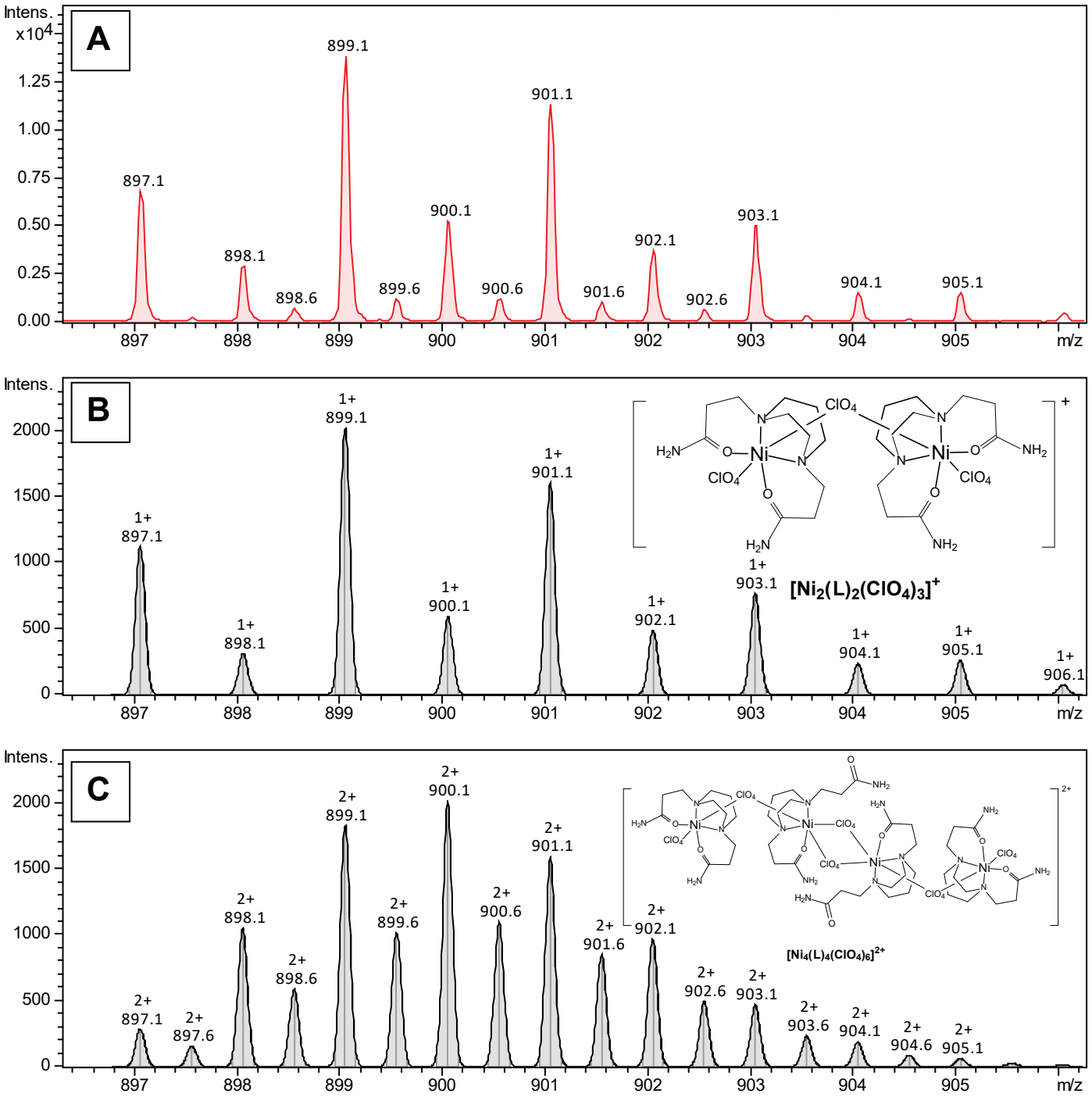


Figure 7SM. ESI-(+)-MS in the positive mode for a water:methanol 1:1 solution of complex $[Ni(BPAH)(H_2O)_2](ClO_4)_2$. [A] Experimental, [B] calculated isotopic patters for the ion of *m/z* 899.1≡ $[Ni_2(L)_2(ClO_4)_3]^+$ (dimer). [C] calculated isotopic patters for the ion of *m/z* 899.1≡ $[Ni_4(L)_4(ClO_4)_6]^{2+}$ (tetranuclear).

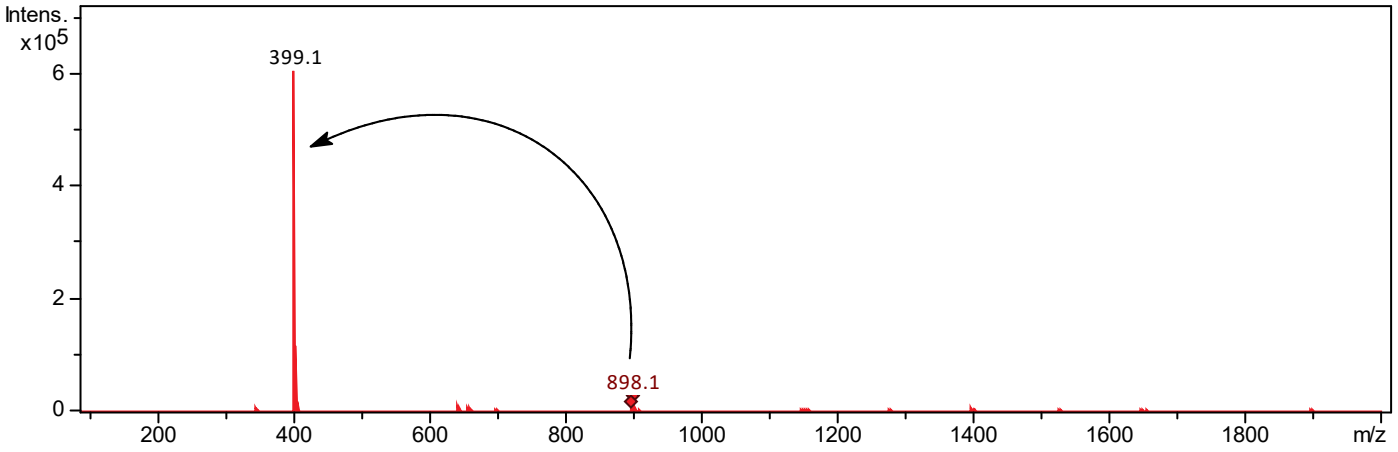


Figure 8SM. ESI(+)MS/MS of the ion of *m/z* 899.1, for a water:methanol 1:1 for complex $[Ni(BPAH)(H_2O)_2](ClO_4)_2$.

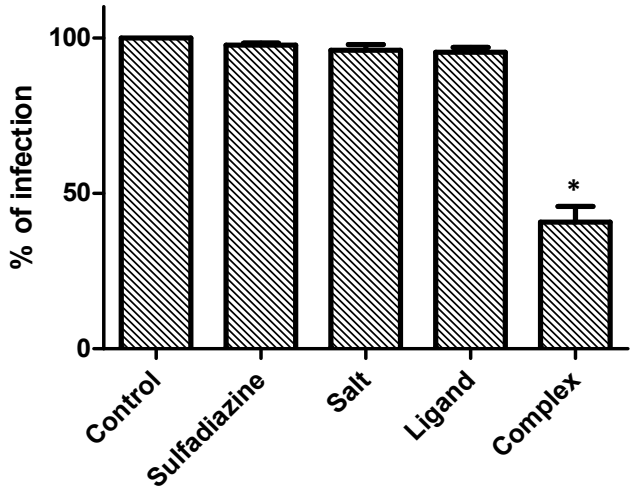
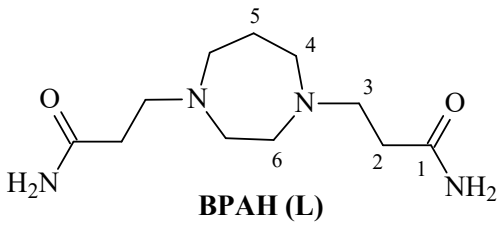


Figure 9SM. *Toxoplasma gondii* growth in LLC-MK2 cells for 24 h in the presence of 10 µmol L^{-1} of complex $[Ni(BPAH)(H_2O)_2](ClO_4)_2$, ligand BPAH, $[Ni(H_2O)_6](ClO_4)_2$ (salt) and sodium sulfadiazine. Untreated cells are the control. A representative experiment of three repetitions performed in triplicate. *Significant difference with $P < 0.001$.

Table 1SM. ^{13}C (125 MHz) and ^{1}H (500 MHz) NMR data of the BPAH (in DMSO-D_6), δ in ppm and J in Hz (in parenthesis), including results obtained by heteronuclear 2D shift-correlated HMQC ($^{1}J_{HC}$) and HMBC ($^{n}J_{HC}$ n = 2 and 3) *.



BPAH (L)

	HMQC		HMBC	
	δ_c	δ_H	$^{2}J_{HC}$	$^{3}J_{HC}$
C				
1	174.1	-	2H-2	2H-3
2	34.0	2.16 (*t*, 5)	2H-3	
3	54.3	2.59 (*t*,5)	2H-2	2H-4; 2H-6
4	54.9	2,63 (*t*, 10)	2H-5	2H-3; 2H-6
5	27.7	1.66 (*m*)	2H-4	
6	53.8	2.57 (s)		2H-3; 2H-4

Table 2SM. Crystal data and structure refinement for nickel(II) complex.

Empirical formula	$C_{11}H_{26}Cl_2N_4NiO_{12}$	
Formula weight	535.97	
Temperature	200(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 9.4387(3) Å	α= 90°.
	b = 15.9252(5) Å	β= 108.2210(10)°.
	c = 14.3529(4) Å	γ = 90°.
Volume	2049.25(11) $Å^3$	
Z	4	
Density (calculated)	1.737 Mg/m^3	
Absorption coefficient	1.276 mm^{-1}	
F(000)	1112	
Crystal size	0.22 x 0.20 x 0.16 mm^3	
Theta range for data collection	1.97 to 30.09°.	
Index ranges	-13<=h<=11, -22<=k<=22, -20<=l<=20	
Reflections collected	37963	
Independent reflections	6028 [R(int) = 0.0143]	
Completeness to theta = 30.09°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7460 and 0.7128	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6028 / 0 / 271	
Goodness-of-fit on F^2	1.048	
Final R indices [I>2sigma(I)]	R1 = 0.0311, wR2 = 0.0793	
R indices (all data)	R1 = 0.0340, wR2 = 0.0815	
Largest diff. peak and hole	0.917 and -0.991 $e.Å^{-3}$	

Table 3SM.Selected bond lengths [Å] and angles [°] for nickel(II) complex.

Ni(1)-O(2)	2.0413(11)
Ni(1)-O(1)	2.0469(11)
Ni(1)-N(1)	2.0791(13)
Ni(1)-N(4)	2.0800(13)
Ni(1)-O(2W)	2.1217(12)
Ni(1)-O(1W)	2.1222(12)
O(2)-Ni(1)-O(1)	88.75(4)
O(2)-Ni(1)-N(1)	173.61(5)
O(1)-Ni(1)-N(1)	96.65(5)
O(2)-Ni(1)-N(4)	96.57(5)
O(1)-Ni(1)-N(4)	174.03(5)
N(1)-Ni(1)-N(4)	77.87(5)
O(2)-Ni(1)-O(2W)	83.32(5)
O(1)-Ni(1)-O(2W)	87.17(5)
N(1)-Ni(1)-O(2W)	93.51(5)
N(4)-Ni(1)-O(2W)	90.77(5)
O(2)-Ni(1)-O(1W)	86.04(5)
O(1)-Ni(1)-O(1W)	83.44(5)
N(1)-Ni(1)-O(1W)	97.93(5)
N(4)-Ni(1)-O(1W)	99.57(5)
O(2W)-Ni(1)-O(1W)	165.95(5)
C(13)-O(1)-Ni(1)	125.00(10)
C(23)-O(2)-Ni(1)	125.69(10)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y+1,-z+1 #2 x-1,-y+3/2,z-1/2 #3 -x+1,y-1/2,-z+3/2

#4 -x,-y+1,-z+1 #5 x,-y+3/2,z-1/2