Supporting Information

Dialing in on pharmacological features for a therapeutic antioxidant small molecule

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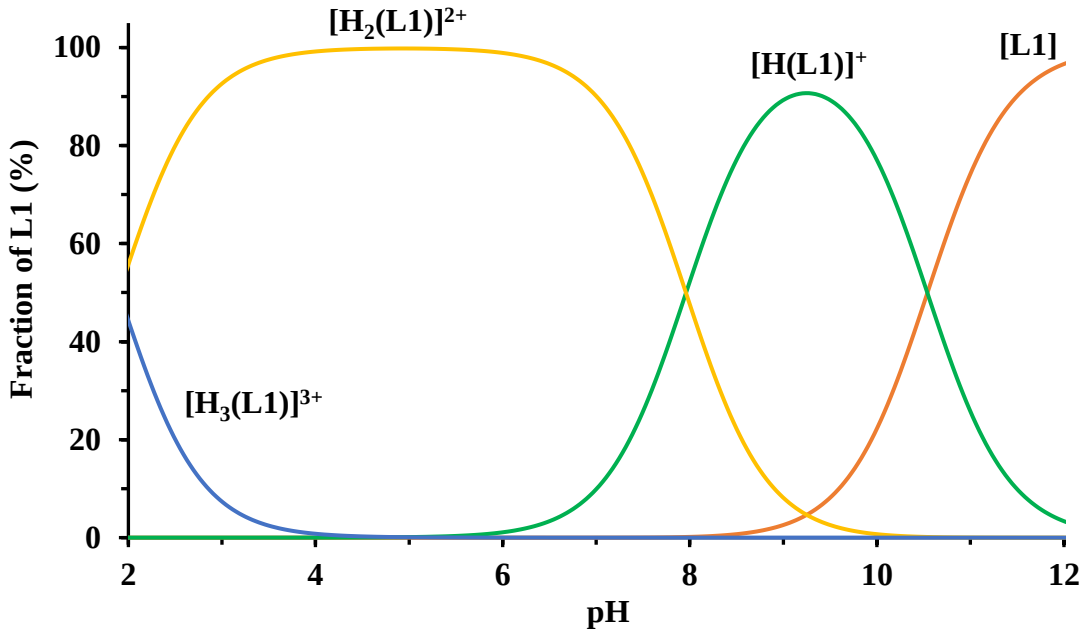

Figure S1. Equilibrium distribution diagram of **L1** based on ref [46] (c_L = 2.5 mM, I = 0.1 M KNO_3, T = 298 K).

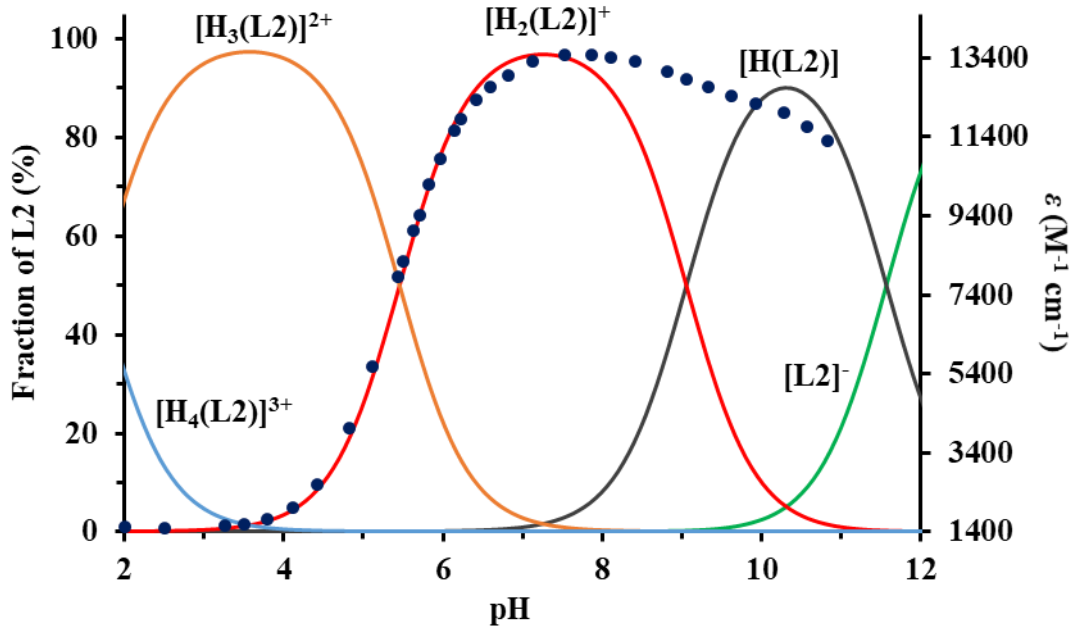

Figure S2. The equilibrium distribution curves for **L2**, calculated using the protonation constants obtained from pH-potentiometric titrations along with the molar extinction coefficients at 255 nm from UV spectrophotometric titrations (c_L = 0.1 mM, I = 0.15 M NaCl, T = 298 K).

The large increase in molar extinction coefficients between pH 4 and 7 aligns well with the deprotonation of the hydroxyl group (log *K* = 5.45) and the consequent increase of electron delocalization in the 7-center 8-electron π-system. From pH 7 a slow decrease in absorbance can be observed which is caused by the deprotonation of the pyridine N-atom (log *K* = 9.05). These changes support the proposed protonation order shown in Figure 3.

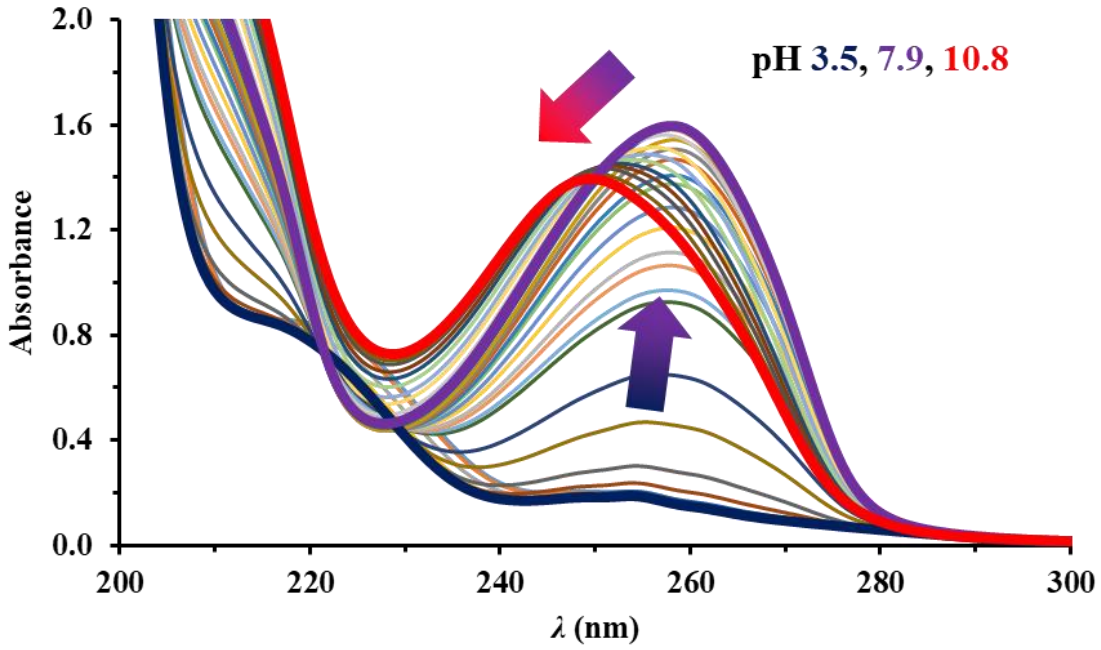

Figure S3. pH dependence of UV spectra in aqueous solution of **L2** (c_L = 0.1 mM, pH varied between 1.683 and 10.835).

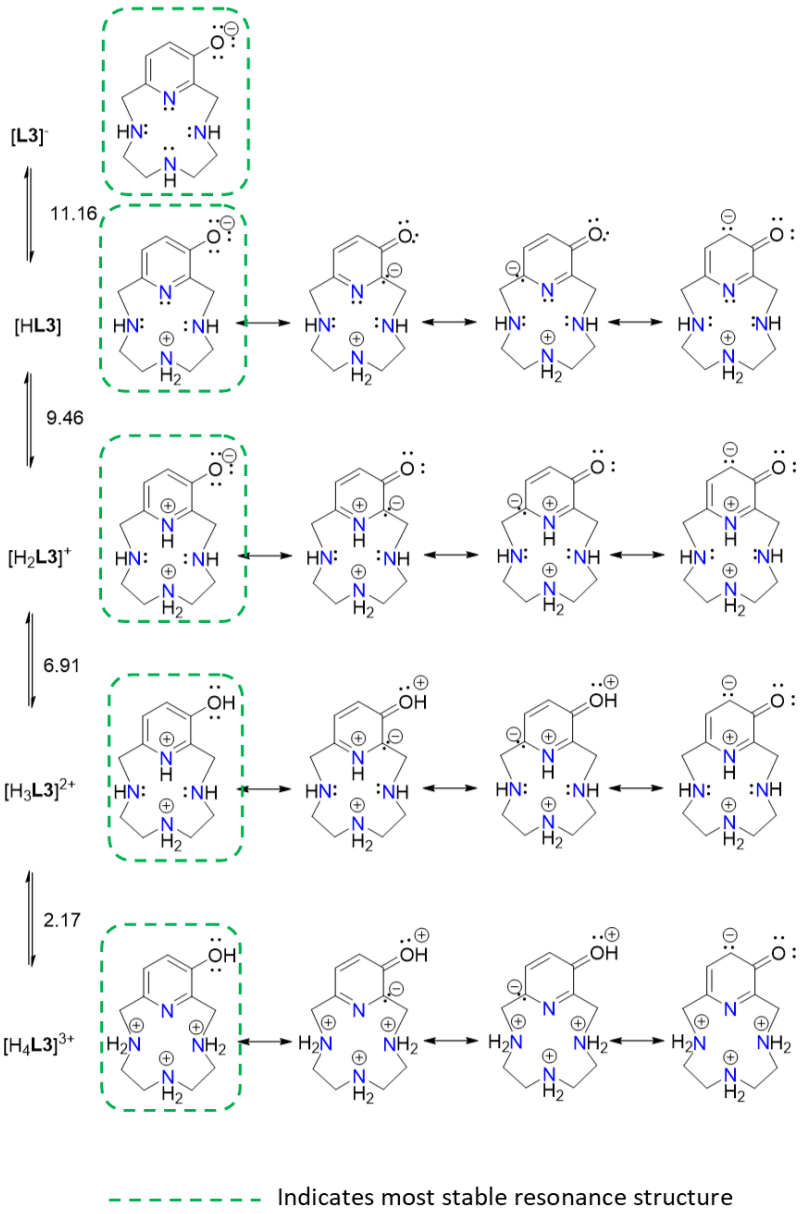

Figure S4. pH dependent resonance structures of **L3**.

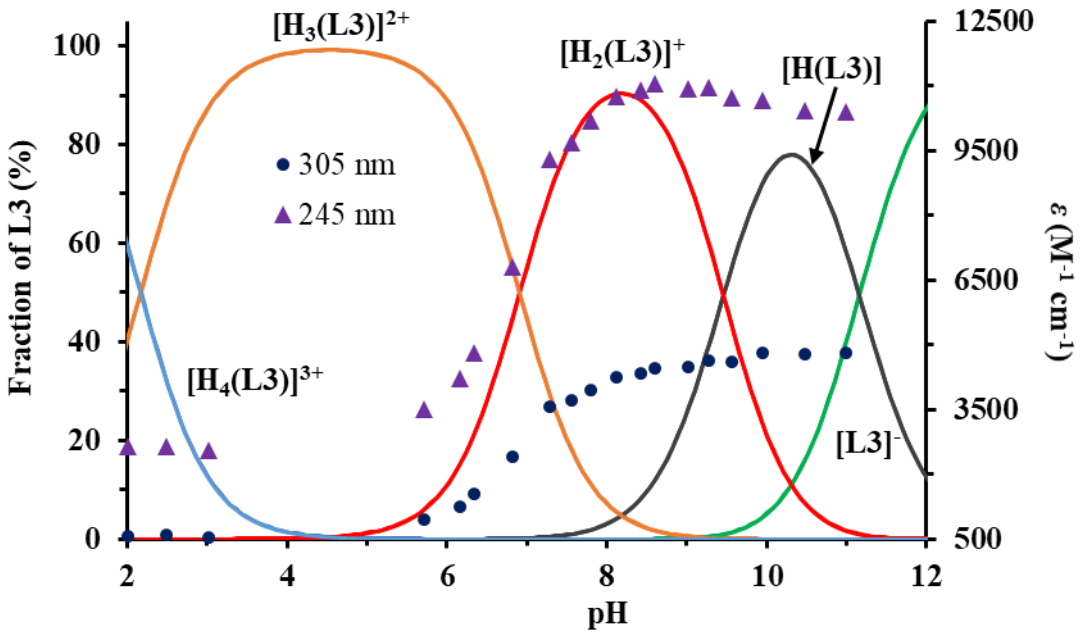

Figure S5. The equilibrium distribution curves for **L3**, calculated using the protonation constants obtained from pH-potentiometric titrations along with the molar extinction coefficients at 245 and 305 nm from UV spectrophotometric titrations (c_L = 0.03 mM, I = 0.15 M NaCl, T = 298 K).

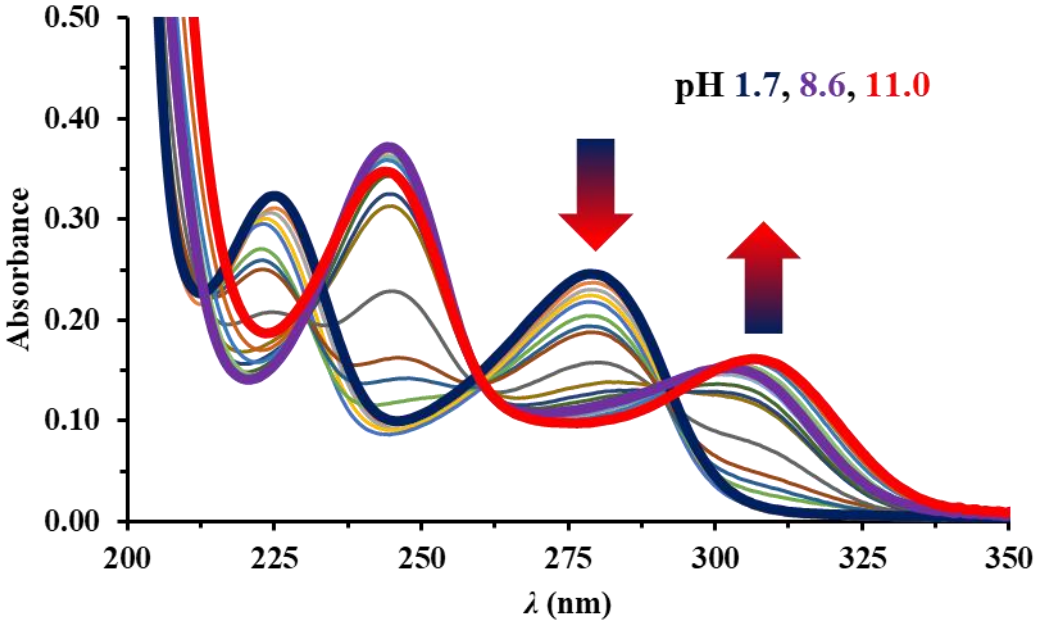

Figure S6. pH dependence of UV spectra in aqueous solution of **L3** (c_L = 0.03 mM, pH varied between 1.706 and 11.000).

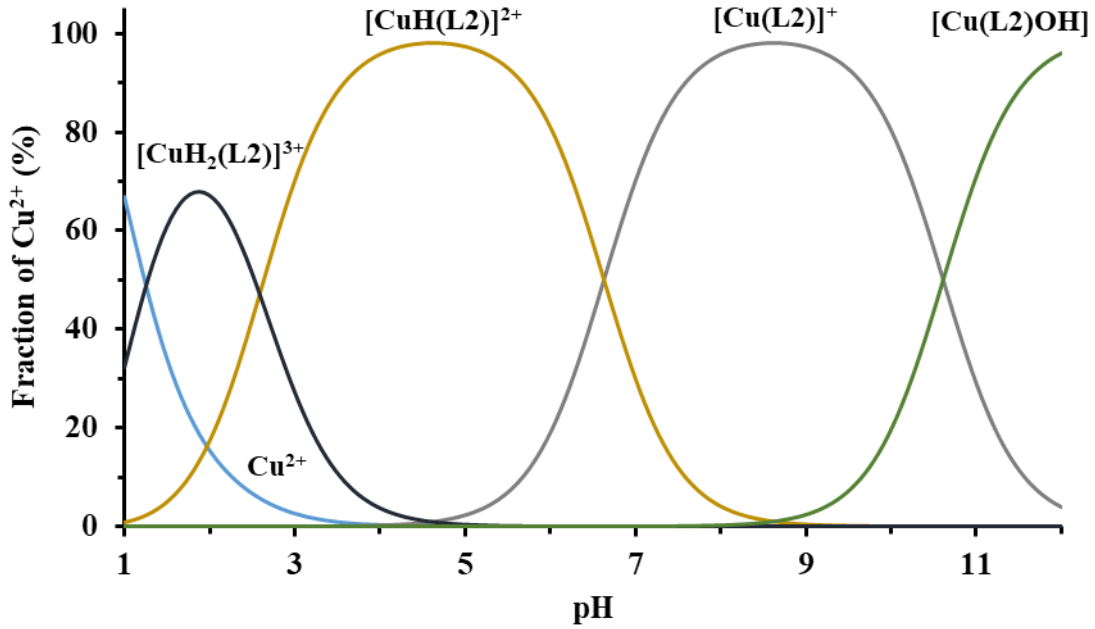

Figure S7. Equilibrium distribution diagram in the Cu^{2+}-**L2** system calculated by using 2.00 mM concentration of Cu^{2+} ion and the ligand.

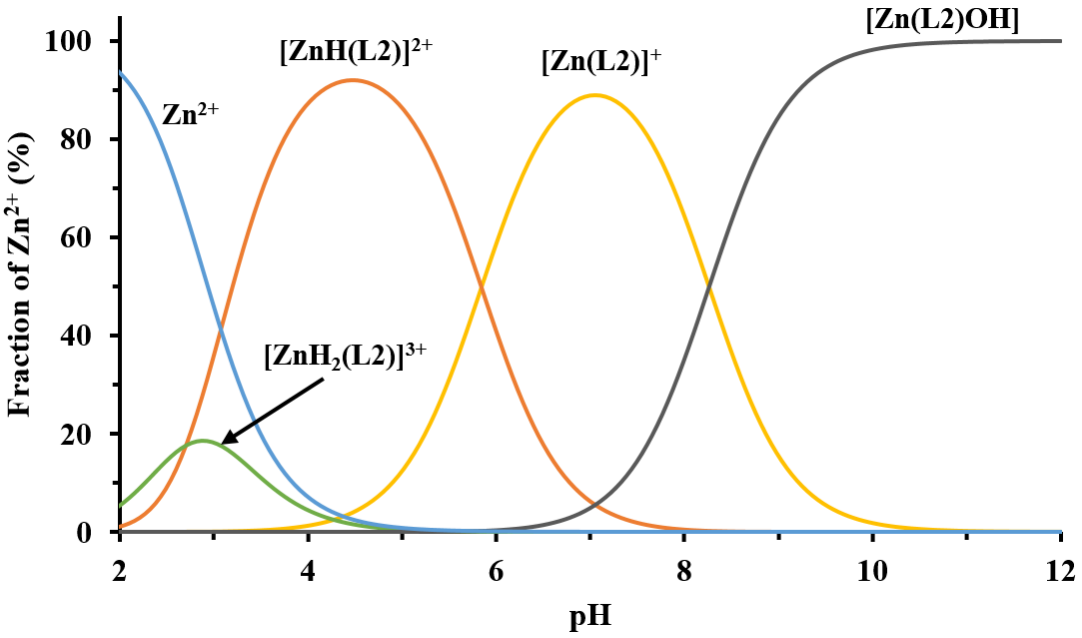

Figure S8. Equilibrium distribution diagram in the Zn^{2+}-**L2** system calculated by using 2.00 mM concentration of Zn^{2+} ion and the ligand.

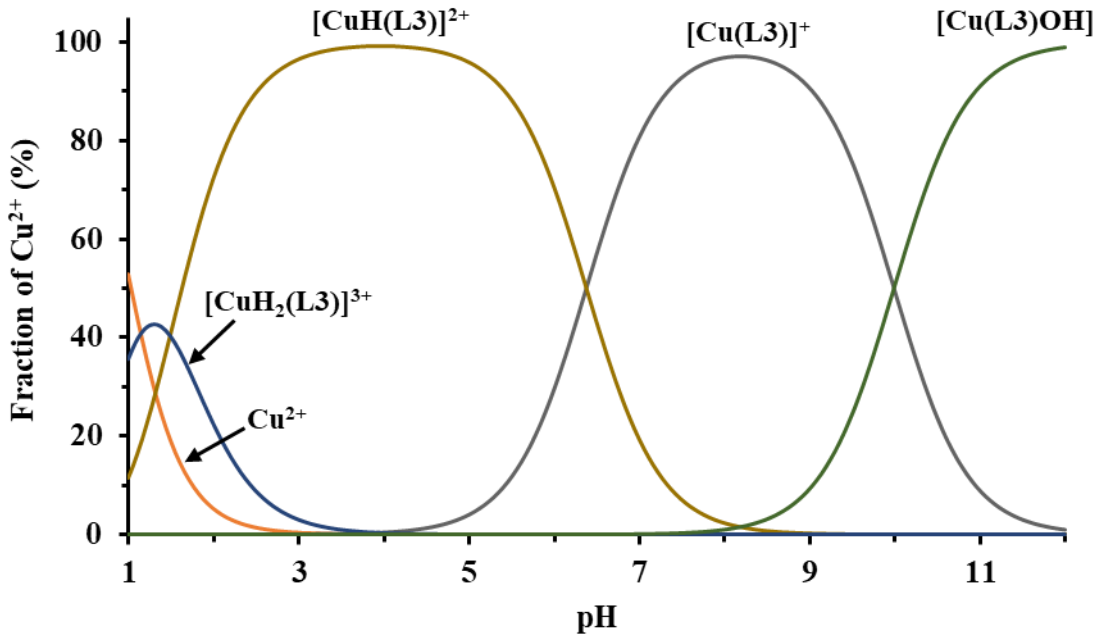

Figure S9. Equilibrium distribution diagram in the Cu^{2+}-**L3** system calculated by using 2.00 mM concentration of Cu^{2+} ion and the ligand.

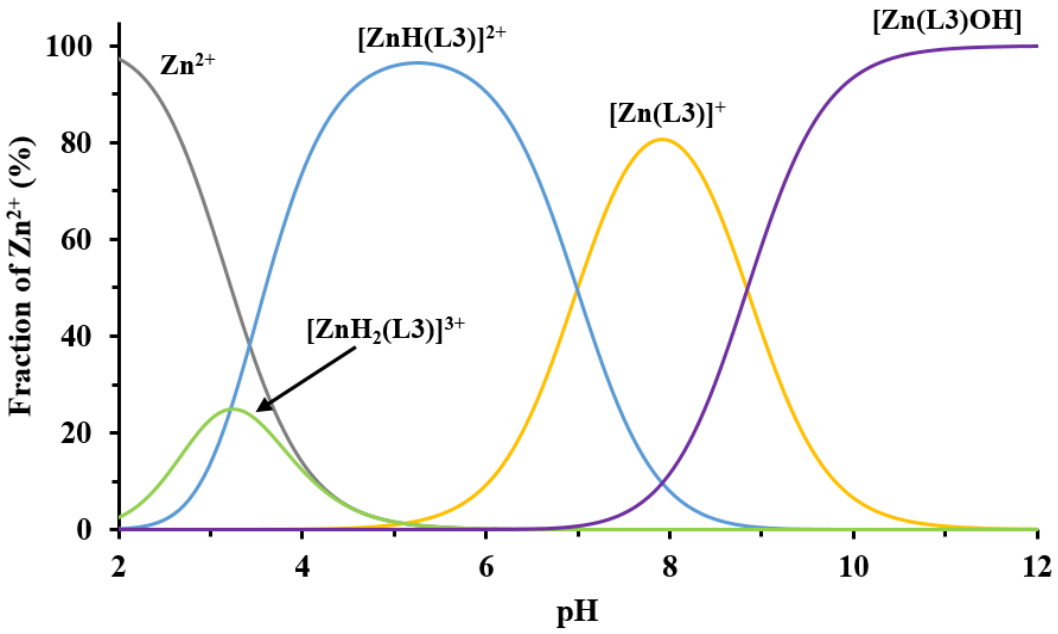

Figure S10. Equilibrium distribution diagram in the Zn^{2+}-**L3** system calculated by using 2.00 mM concentration of Zn^{2+} ion and the ligand.

Table S1. Fitting parameters for cellular toxicity studies of cyclen, **L1**, and **L2** with HT-22 cells.

	Cyclen	**L2**	**L1**
log(inhibitor) vs. normalized response			
Best-fit values			
$LogIC_{50}$	1.867	2.474	2.365
IC_{50}	73.63	298.0	231.8
Std. Error			
$LogIC_{50}$	0.05372	0.05707	0.07932
95% Confidence Intervals			
$LogIC_{50}$	1.760 to 1.974	2.362 to 2.586	2.207 to 2.524
IC_{50}	57.50 to 94.29	230.3 to 385.6	160.9 to 334.0
Goodness of Fit			
Degrees of Freedom	63	159	63
R square	0.9422	0.7962	0.9086
Absolute Sum of Squares	5788	33402	11727
Sy.x	9.585	14.49	13.64
Number of points Analyzed	64	160	64