Zn^{2+} and Cu^{2+} binding to the extramembrane loop of Zrt2, a zinc transporter of *Candida albicans*

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Supplementary Information

Table S1. EPR parameters for Cu^{2+} complexes with the studied peptides at *I*=0.1 M (KCl) and M:L molar ratio = 0.8:1. C_L = $1.00 \cdot 10^{-3}$ M ($0.79 \cdot 10^{-3}$ M for L5).

pH	L1					L2					L3				
	$A_{//}$ [G] (A_z)	$g_{//}$ (g_z)	$g_{\perp}$ (g_x=g_y)	MW Frequency [GHz]	Coordination	$A_{//}$ [G] (A_z)	$g_{//}$ (g_z)	$g_{\perp}$ (g_x=g_y)	MW Frequency [GHz]	Coordination	$A_{//}$ [G] (A_z)	$g_{//}$ (g_z)	$g_{\perp}$ (g_x=g_y)	MW Frequency [GHz]	Coordination
3	125	2.42	2.08	9.58		122	2.41	2.08	9.57		121	2.41	2.08	9.58	
4	123	2.41	2.08	9.59		123	2.41	2.08	9.58		121	2.41	2.08	9.58	
5	167	2.30	2.06	9.59	2N	168	2.30	2.06	9.58	2N	163	2.30	2.06	9.58	2N
6	189	2.26	2.05	9.59	3N	186	2.25	2.05	9.58	3N	170	2.27	2.06	9.58	2N
7	201	2.24	2.05	9.58	3N	189	2.25	2.04	9.58	3N	175	2.27	2.06	9.57	3N
8	206	2.20	2.05	9.59	4N	198	2.20	2.04	9.58	4N	183	2.23	2.05	9.57	3N
9	206	2.20	2.05	9.58	4N	199	2.20	2.03	9.58	4N	200	2.18	2.05	9.58	4N
10	206	2.20	2.05	9.58	4N	199	2.20	2.03	9.58	4N	200	2.18	2.05	9.58	4N
11	206	2.20	2.05	9.58	4N	199	2.20	2.03	9.58	4N	200	2.18	2.04	9.58	4N

pH		L4					L5				
		$A_{//}$ [G] (A_z)	$g_{//}$ (g_z)	$g_{\perp}$ (g_x=g_y)	MW Frequency [GHz]	Coordination	$A_{//}$ [G] (A_z)	$g_{//}$ (g_z)	$g_{\perp}$ (g_x=g_y)	MW Frequency [GHz]	Coordination
3		123	2.42	2.08	9.58		122	2.42	2.08	9.58	
4		119	2.42	2.08	9.57					9.58	
5		167	2.30	2.06	9.57	2N	140	2.36	2.07	9.58	1N
6		172	2.28	2.06	9.58	2N	140	2.36	2.07	9.57	1N
7		174	2.27	2.05	9.58	3N	140	2.36	2.07	9.57	1N
8		176	2.25	2.05	9.57	3N				9.58	
9		192	2.19	2.05	9.58	4N				9.58	
10		195	2.19	2.05	9.58	4N				9.58	
11		195	2.19	2.05	9.58	4N	186	2.24	2.07	9.58	3N

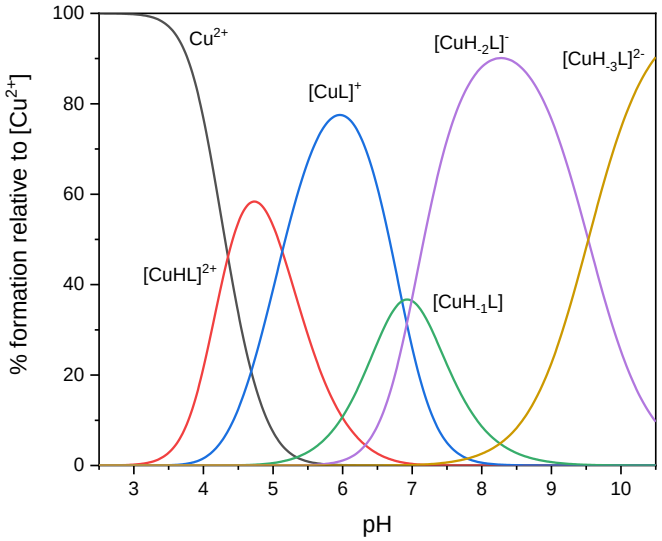


Figure S1. Species distribution diagram of Cu^{2+}/Ac-GPHTHSHFGD-Am; M:L ratio 0.8:1, C_M = $0.79 \cdot 10^{-3}$ M.

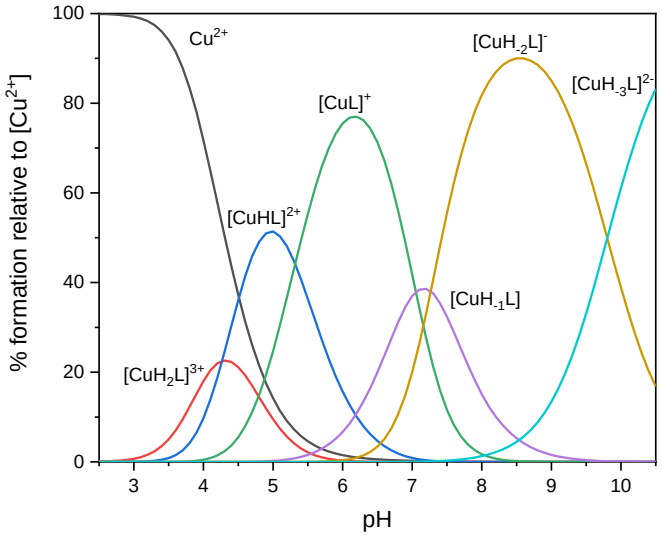


Figure S2. Species distribution diagram of Cu^{2+}/Ac-GPHTHAHFGD-Am; M:L ratio 0.8:1, C_M = $0.79 \cdot 10^{-3}$ M.

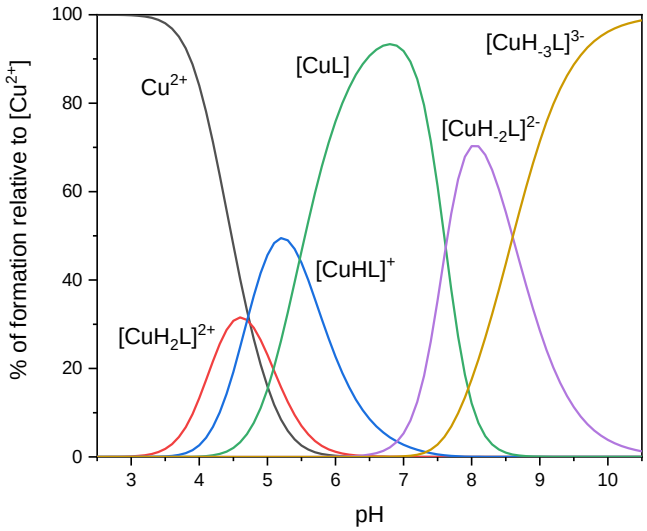


Figure S3. Species distribution diagram of Cu^{2+}/Ac-PSHFAHAQEHQDP-Am; M:L ratio 0.8:1, C_M = $0.79 \cdot 10^{-3}$ M.

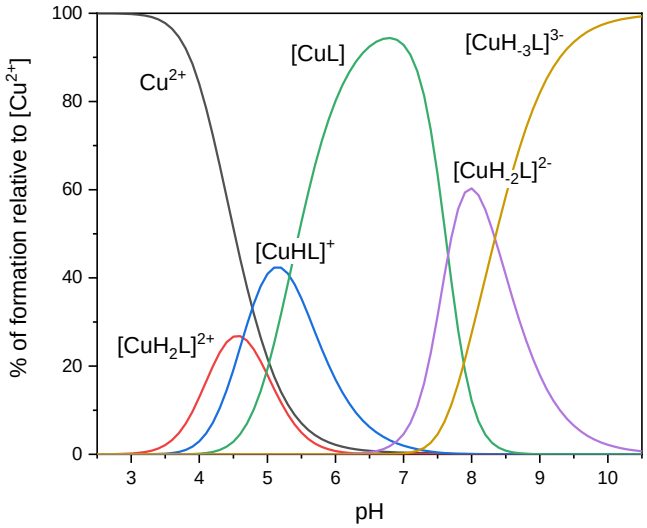


Figure S4. Species distribution diagram of Cu^{2+}/Ac-PAHFAHAQEHQDP-Am; M:L ratio 0.8:1, C_M = $0.79 \cdot 10^{-3}$ M.

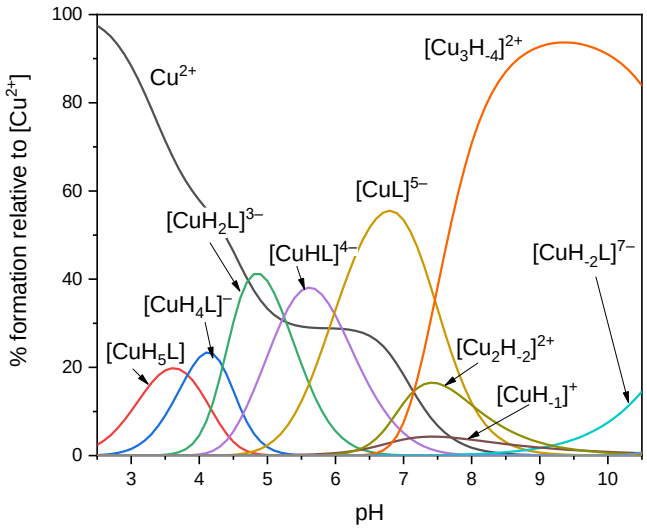


Figure S5. Species distribution diagram of Cu^{2+}/Ac-DDEEEDLE-Am; M:L ratio 0.8:1, $C_M = 0.79 \cdot 10^{-3}$ M.

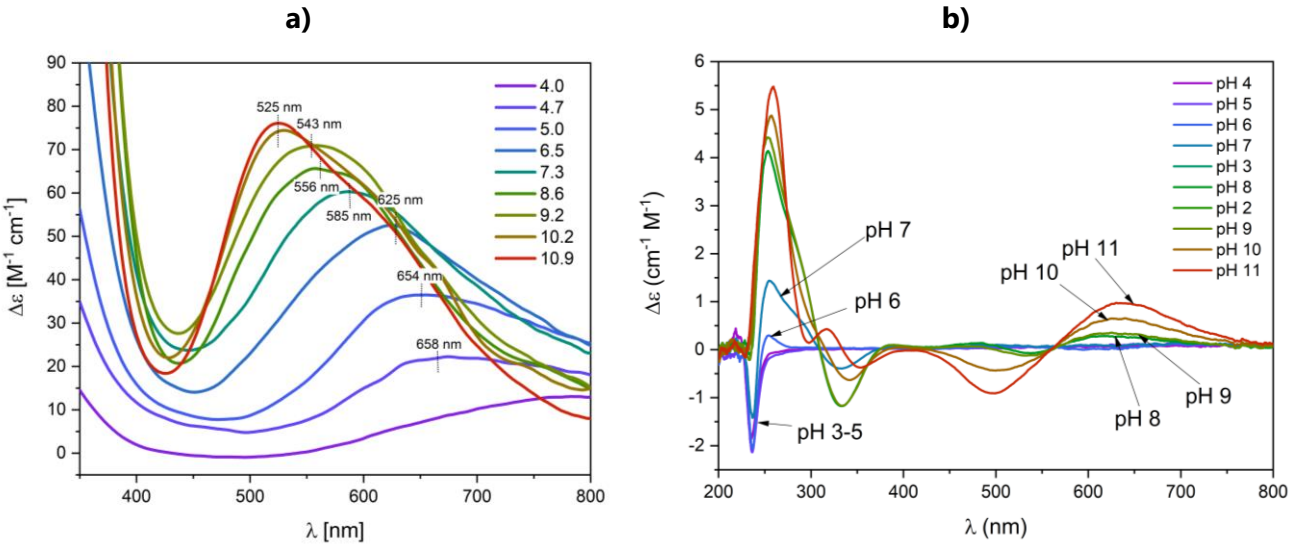


Figure S6. (a) Vis absorption spectra, (b) CD spectra of Cu^{2+}/Ac-GPHTHAHFGD-Am system; M:L ratio 0.9:1. $C_M = 0.63 \cdot 10^{-3}$ M, optical path 1 cm.

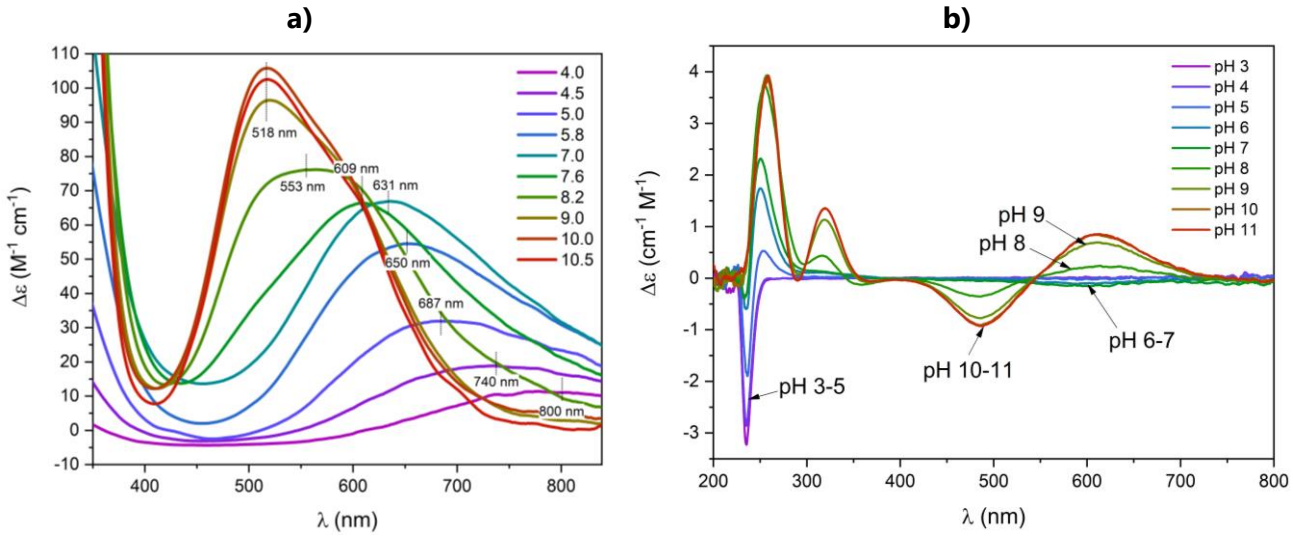


Figure S7. (a) Vis absorption spectra, (b) CD spectra of Cu^{2+}/Ac-PAHFAHAQEHQDP-Am system; M:L ratio 0.9:1. CM = $0.63 \cdot 10^{-3}$ M, optical path 1 cm.

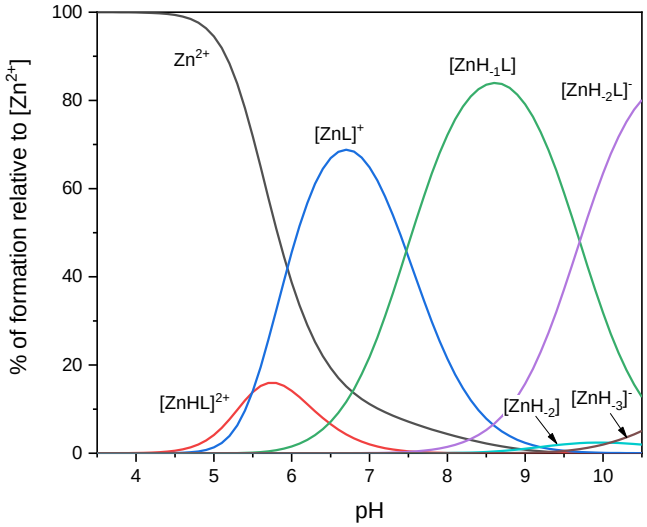


Figure S8. Species distribution diagram of Zn^{2+}/Ac-GPHTHSHFGD-Am; M:L ratio 0.8:1, C_M = $0.79 \cdot 10^{-3}$ M.

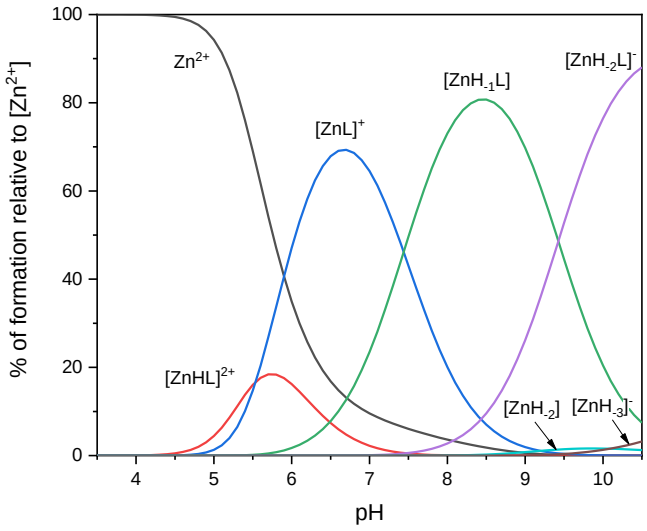


Figure S9. Species distribution diagram of Zn^{2+}/Ac-GPHTHAHFGD-Am; M:L ratio 0.8:1, C_M = $0.79 \cdot 10^{-3}$ M.

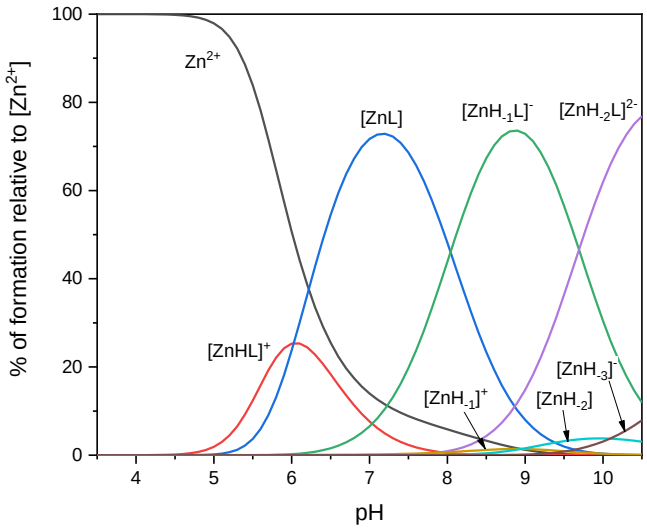


Figure S10. Species distribution diagram of Zn^{2+}/Ac-PSHFAHAQEHQDP-Am; M:L ratio 0.8:1, C_M = $0.79 \cdot 10^{-3}$ M.

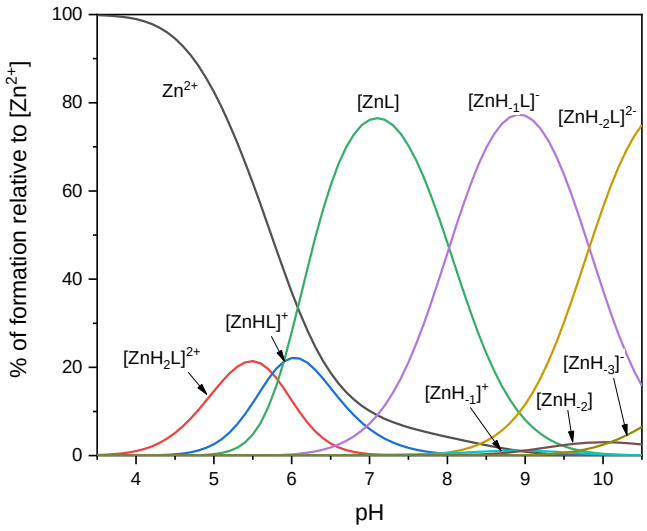


Figure S11. Species distribution diagram of Zn^{2+}/Ac-PAHFAHAQEHQDP-Am; M:L ratio 0.8:1, C_M = $0.79 \cdot 10^{-3}$ M.

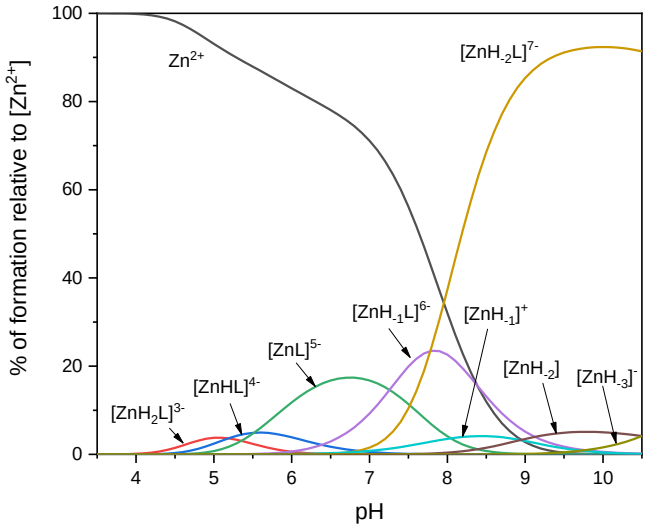


Figure S12. Species distribution diagram of Zn^{2+}/Ac-DDEEEDLE-Am; M:L ratio 0.8:1, C_M = $0.79 \cdot 10^{-3}$ M.

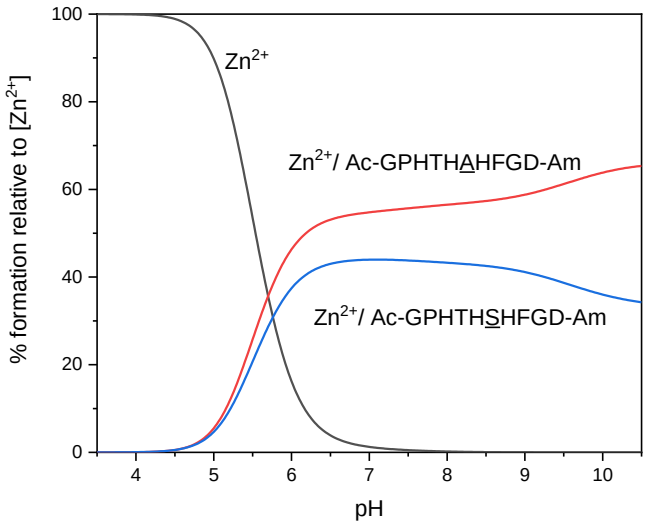


Figure S13. Competition plots for a solution containing equimolar concentrations ($1 \cdot 10^{-3}$ M) of Ac-GPHTHSHFGD-Am, Ac-GPHTHAHFGD-Am and Zn^{2+}.

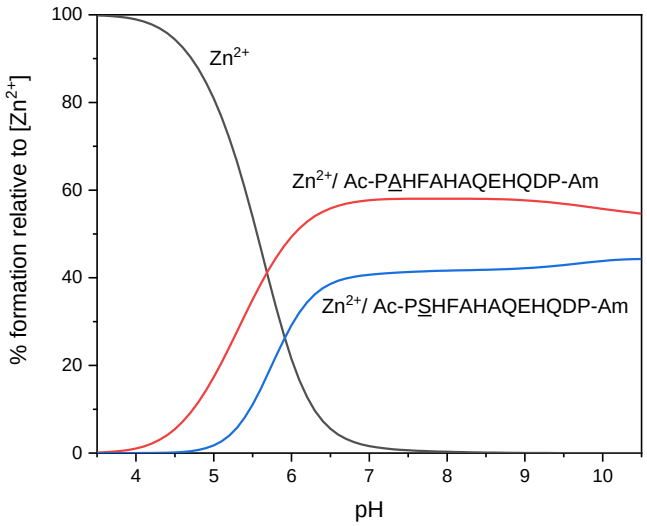
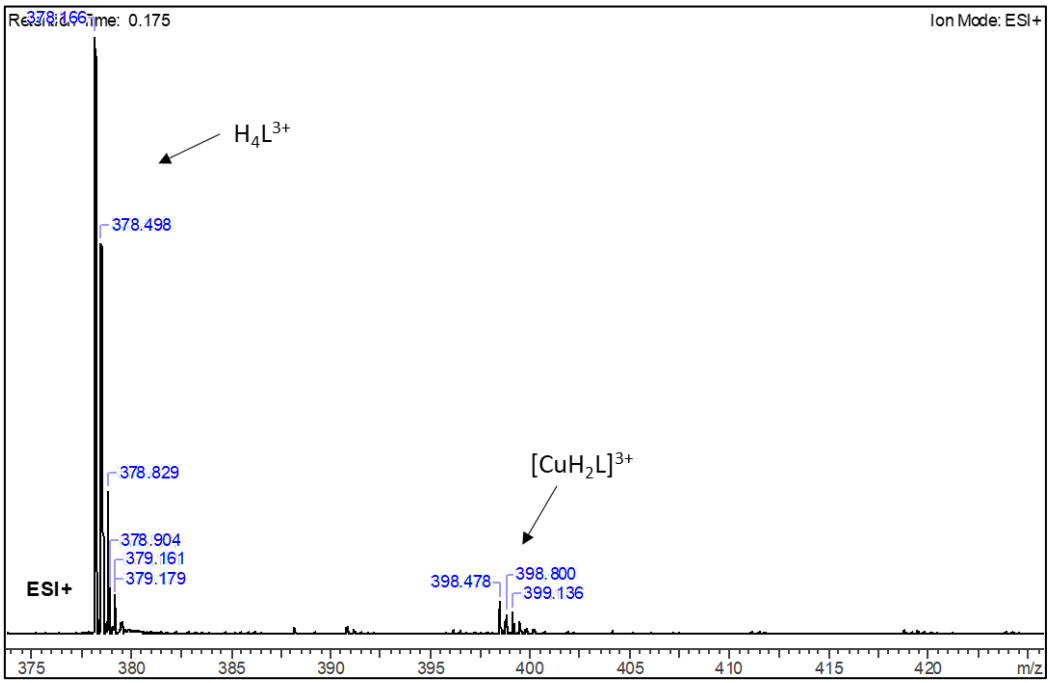


Figure S14. Competition plots for a solution containing equimolar concentrations ($1 \cdot 10^{-3}$ M) of Ac-PSHFAHAQEHQDP-Am, Ac-PAHFAHAQEHQDP-Am and Zn^{2+}.

Table S2. Stoichiometry, molecular formula and average *m/z* value for the species present in ESI-MS spectra of Cu^{2+} and Zn^{2+} complexes with the studied ligands; L:M molar ratio = 1:1 in water/methanol 50:50 solution.

	Species	**Formula**	**Average *m/z***
L1	H_4L^{3+}	C49H68N17O15	378.4
Positive mode	$([H_3L] \cdot Na)^{3+}$	C49H67N17O15Na	385.7
	$([H_3L] \cdot K)^{3+}$	C49H67N17O15K	391.1
	$[CuH_2L]^{3+}$	C49H66N17O15Cu	398.9
	$[ZnH_2L]^{3+}$	C49H66N17O15Zn	399.2
	$([ZnHL] \cdot K)^{3+}$	C49H65N17O15ZnK	412.2
	$([CuL] \cdot NaK)^{3+}$	C49H64N17O15CuNaK	418.9
L2	H_4L^{3+}	C49H68N17O14	373.1
Positive mode	$([H_3L] \cdot Na)^{3+}$	C49H67N17O14Na	380.4
	$([H_3L] \cdot K)^{3+}$	C49H67N17O14K	385.8
	$[CuH_2L]^{3+}$	C49H66N17O14Cu	393.6
	$[ZnH_2L]^{3+}$	C49H66N17O14Zn	394.2
	$([CuHL] \cdot K)^{3+}$	C49H65N17O14CuK	406.3
	$([ZnHL] \cdot K)^{3+}$	C49H65N17O14ZnK	406.9
	$([CuL] \cdot NaK)^{3+}$	C49H64N17O14CuNaK	413.6
	$([ZnL] \cdot K_2)^{3+}$	C49H64N17O14ZnK2	419.6
L3	H_5L^{3+}	C67H95N22O21	514.9
Positive mode	$([H_4L] \cdot Na)^{3+}$	C67H94N22O21Na	522.2
	$([H_4L] \cdot K)^{3+}$	C67H94N22O21K	527.6
	$[CuH_3L]^{3+}$	C67H93N22O21Cu	535.4
	$[ZnH_3L]^{3+}$	C67H93N22O21Zn	536.0
	$([CuH_2L] \cdot K)^{3+}$	C67H92N22O21CuK	548.1
	$([ZnH_2L] \cdot K)^{3+}$	C67H92N22O21ZnK	458.7
	$([CuHL] \cdot NaK)^{3+}$	C67H91N22O21CuNaK	555.4
	$([ZnHL] \cdot NaK)^{3+}$	C67H91N22O21ZnNaK	556.0
L4	H_5L^{3+}	C67H95N22O20	509.5
Positive mode	$([H_4L] \cdot Na)^{3+}$	C67H94N22O20Na	516.9
	$([H_4L] \cdot K)^{3+}$	C67H94N22O20K	522.2
	$[CuH_3L]^{3+}$	C67H93N22O20Cu	530.0
	$[ZnH_3L]^{3+}$	C67H93N22O20Zn	530.7
	$([CuH_2L] \cdot K)^{3+}$	C67H92N22O20CuK	542.7
	$([ZnH_2L] \cdot K)^{3+}$	C67H92N22O20ZnK	543.4
	$([CuHL] \cdot NaK)^{3+}$	C67H91N22O20CuNaK	550.1
L5	H_5L^{2-}	C40H57N9O23	516.0
Negative mode	$([H_4L] \cdot Na)^{2-}$	C40H56N9O23Na	527.0
	$([H_3L] \cdot Na_2)^{2-}$	C40H55N9O23Na2	537.9
	$[CuH_3L]^{2-}$	C40H55N9O23Cu	546.7
	$([H_2L] \cdot Na_3)^{2-}$	C40H54N9O23Na3	548.9
	$([CuH_2L] \cdot Na)^{2-}$	C40H54N9O23NaCu	557.7
	$([ZnH_2L] \cdot Na)^{2-}$	C40H54N9O23ZnNa	558.6
	$([CuH_2L] \cdot K)^{2-}$	C40H54N9O23CuK	565.8
	$([CuHL] \cdot Na_2)^{2-}$	C40H53N9O23CuNa2	568.7

A)



B)

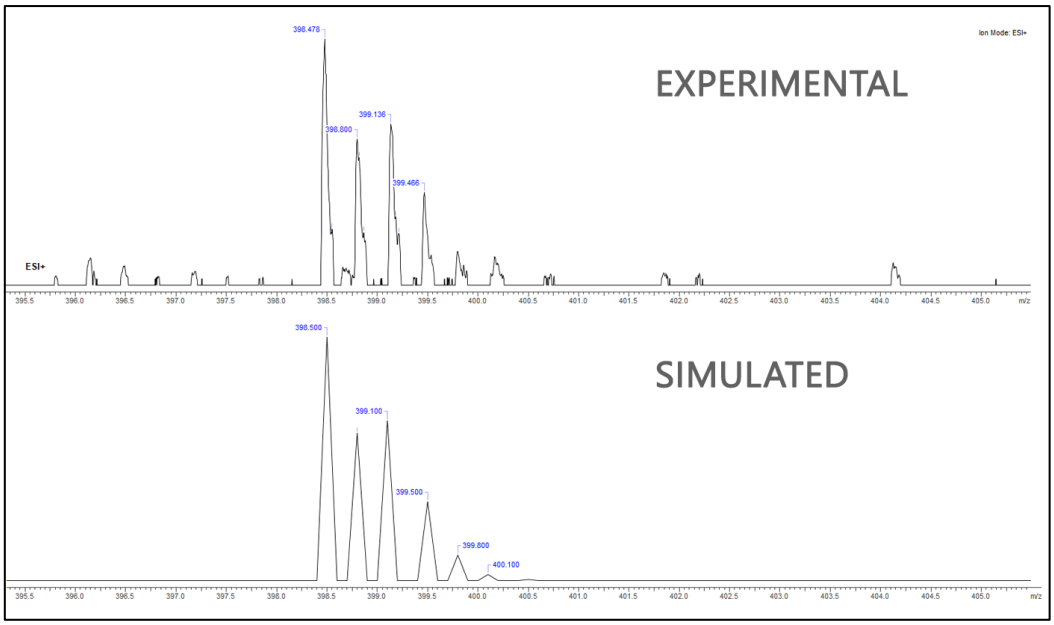
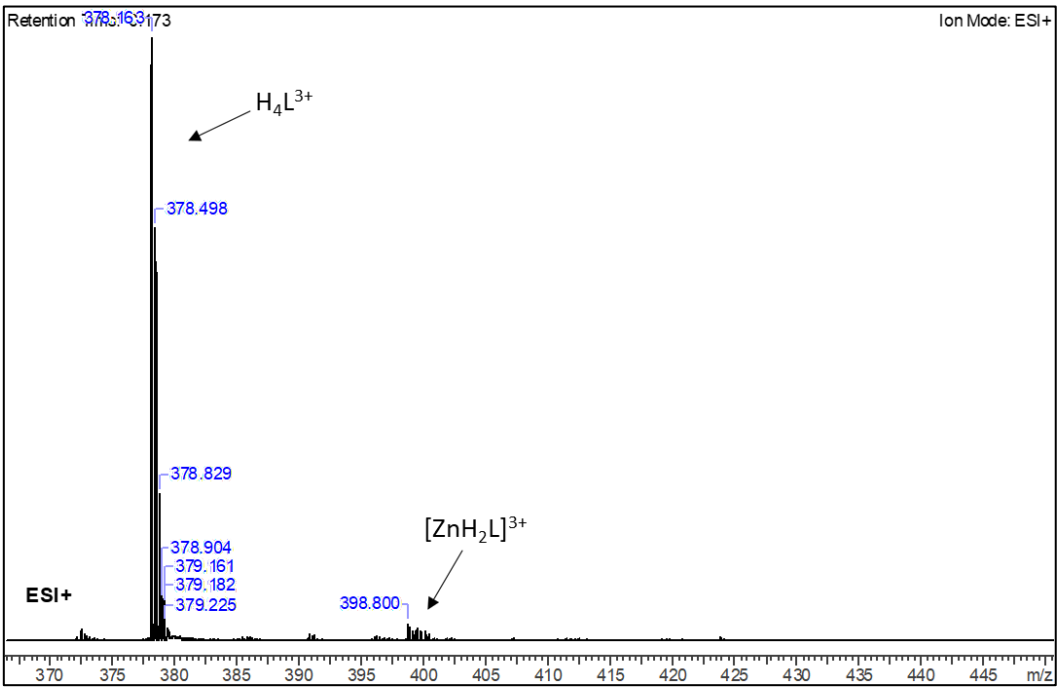


Figure S15. A) ESI-MS spectrum for Cu^{2+}/L1 system at L:M molar ratio=1:1 in MeOH:H_2O (1:1) mixture solution. B) Comparison of experimental and simulated isotopic pattern of the chosen metal complex $[CuH_2L]^{3+}$.

A)



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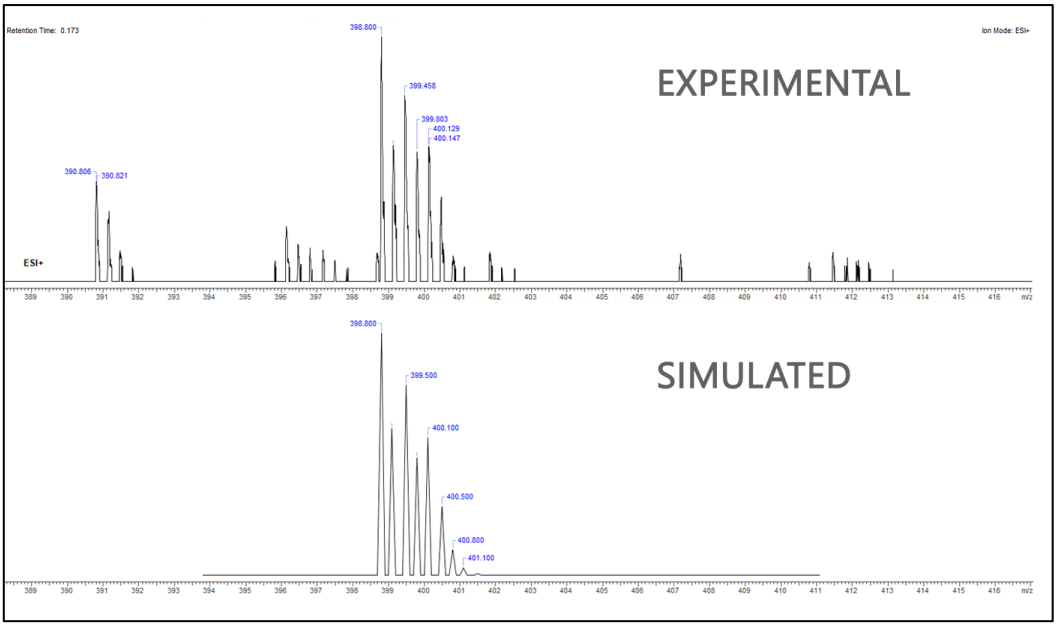
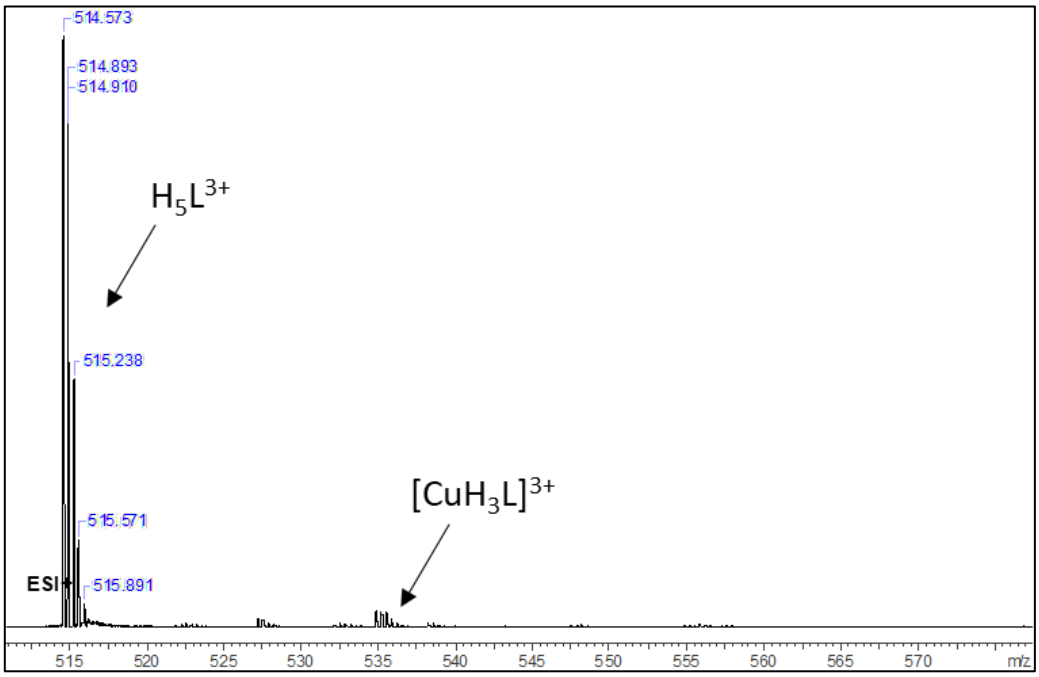


Figure S16. A) ESI-MS spectrum for Zn^{2+}/L1 system at L:M molar ratio=1:1 in MeOH:H_2O (1:1) mixture solution. B) Comparison of experimental and simulated isotopic pattern of the chosen metal complex $[ZnH_2L]^{3+}$.

A)



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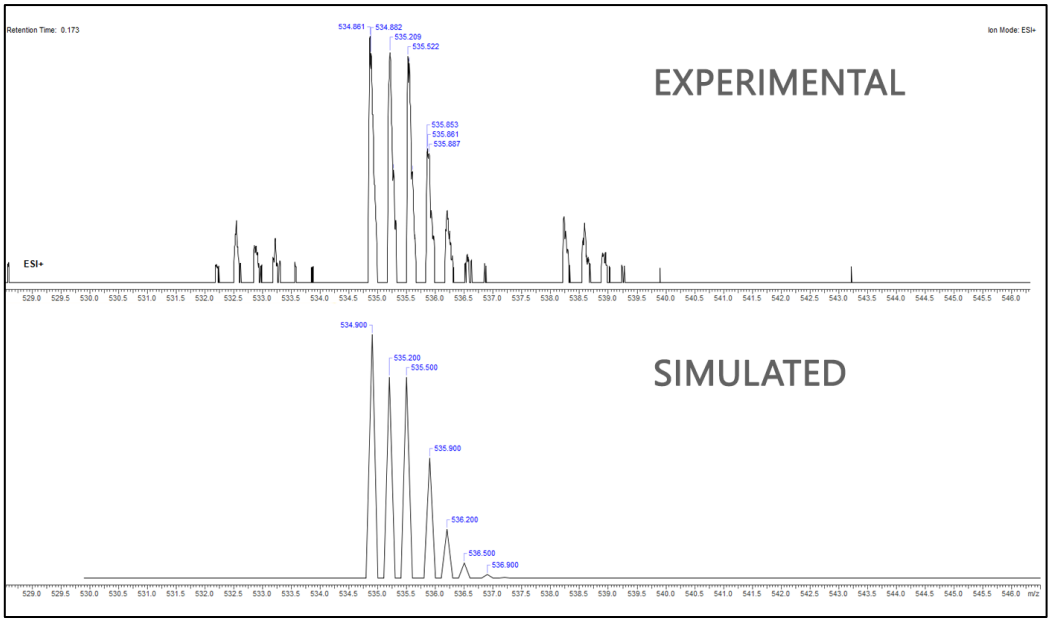

Figure S17. A) ESI-MS spectrum for Cu^{2+}/L3 system at L:M molar ratio=1:1 in MeOH:H_2O (1:1) mixture solution. B) Comparison of experimental and simulated isotopic pattern of the chosen metal complex $[CuH_3L]^{3+}$.