

**Copper complexes as imaging agents for the diagnosis of Alzheimer's disease:  
Copper complexes of hybrid thiosemicarbazone-HYNIC ligands that target A $\beta$   
plaques.**

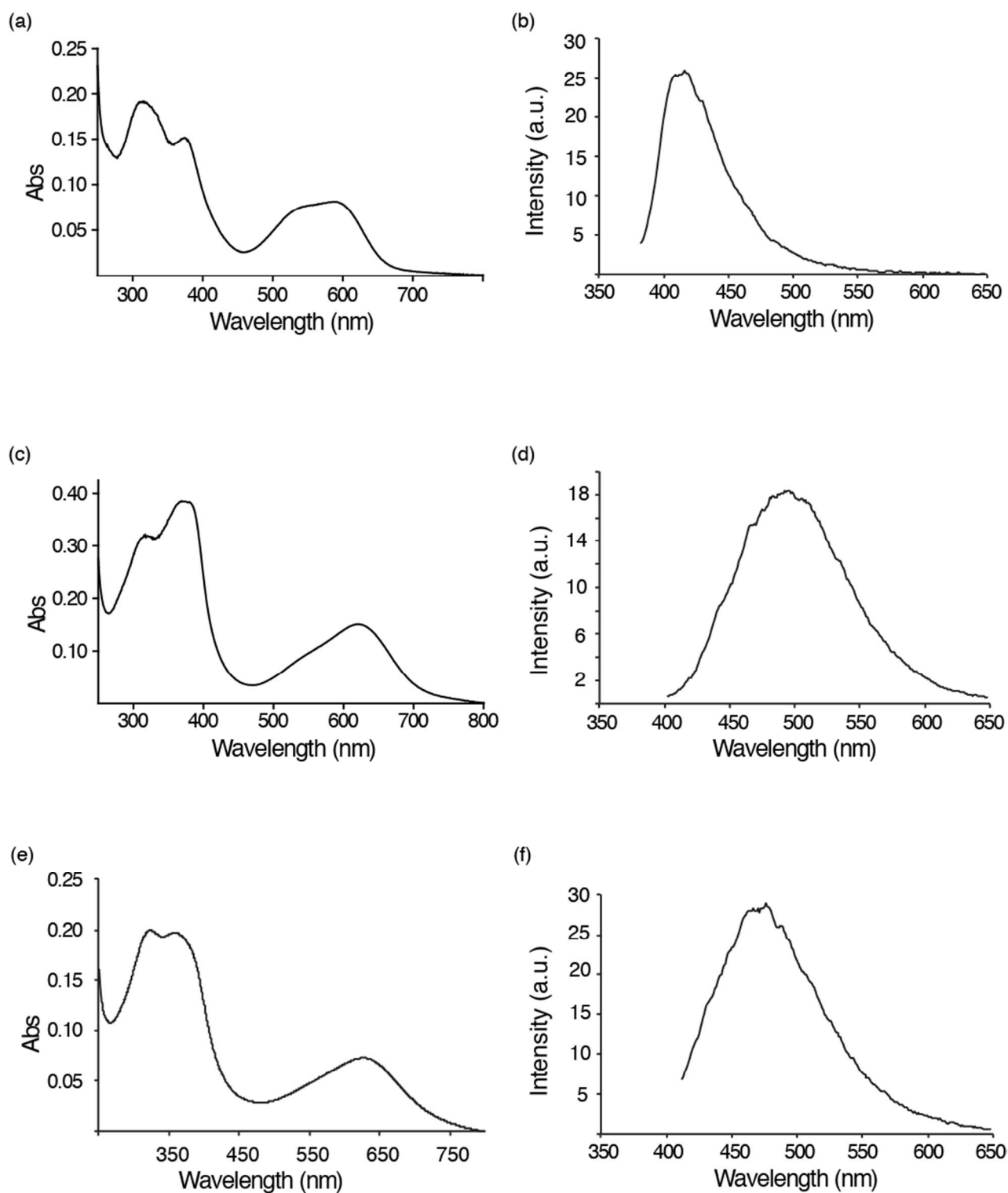
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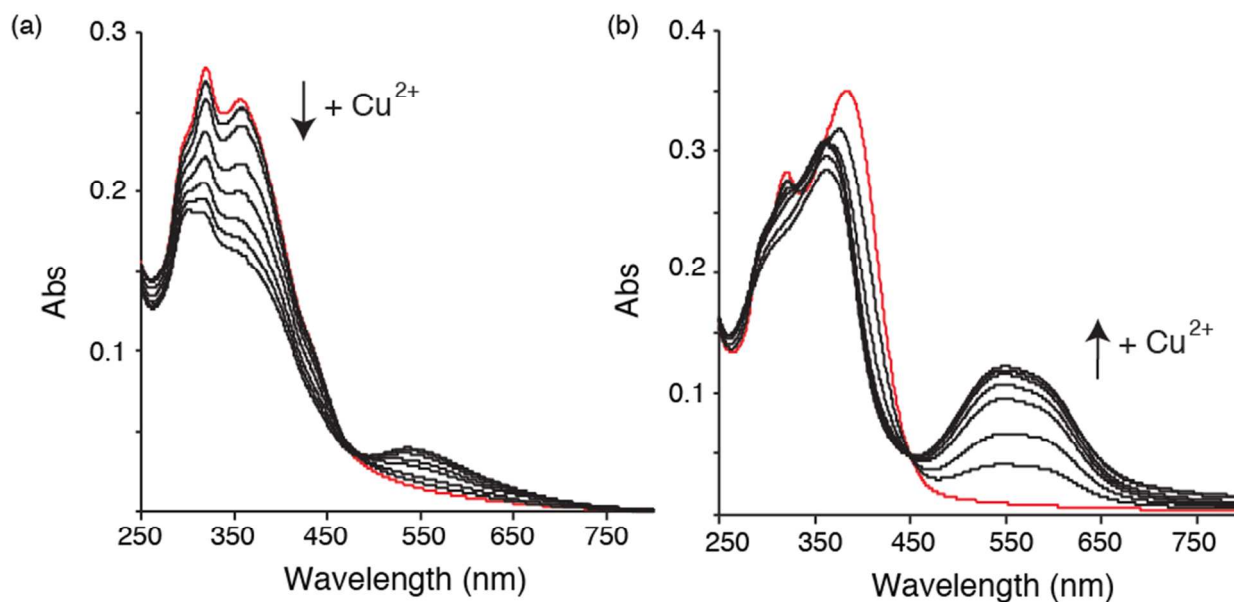
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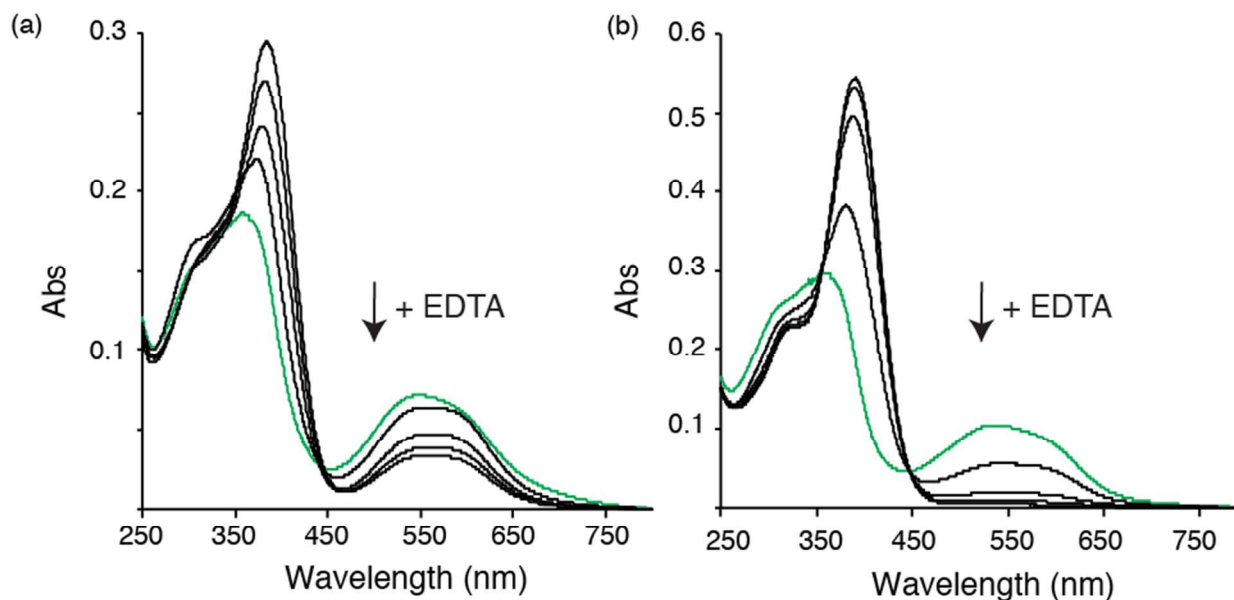
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**Figure S1.** (a) UV/Vis and (b) Fluorescence spectra ( $\lambda_{\text{ex}} = 370$  nm,  $\lambda_{\text{em}} = 420$  nm) of 10  $\mu$ M Cu<sup>II</sup>L<sup>1</sup> in CH<sub>3</sub>CN. (c) UV/Vis and (d) Fluorescence spectra ( $\lambda_{\text{ex}} = 390$  nm,  $\lambda_{\text{em}} = 480$  nm) of 10  $\mu$ M Cu<sup>II</sup>L<sup>2</sup> in CH<sub>3</sub>CN. (e) UV/Vis and (f) Fluorescence spectra ( $\lambda_{\text{ex}} = 390$  nm,  $\lambda_{\text{em}} = 465$  nm) of 10  $\mu$ M Cu<sup>II</sup>L<sup>3</sup> in CH<sub>3</sub>CN.



**Figure S2.** (a) Change in the UV/Vis spectrum of a solution containing  $\text{H}_2\text{L}^2$  ( $10\ \mu\text{M}$ ) in 30% dmso/PB (20 mM, pH 7.4) upon titration with  $\text{Cu}^{2+}$  (1 mM). (b) Change in the UV/Vis spectrum of a solution containing  $\text{H}_2\text{L}^3$  ( $10\ \mu\text{M}$ ) in 30% dmso/PB (20 mM, pH 7.4) upon titration with  $\text{Cu}^{2+}$  (1 mM).



**Figure S3.** (a) Change in the UV/Vis spectrum of a solution containing  $\text{Cu}^{\text{II}}\text{L}^3$  ( $10\ \mu\text{M}$ ) in 30% dmso/PB (20 mM, pH 7.4) upon 24 hour incubation with increasing EDTA (10, 50, 100, 150  $\mu\text{M}$ ). (b) Change in the UV/Vis spectrum of a solution containing  $\text{Cu}^{\text{II}}\text{L}^3$  ( $10\ \mu\text{M}$ ) in 30% dmso/MES (20 mM, pH 6.5) upon 24 hour incubation with increasing EDTA (10, 50, 100, 150  $\mu\text{M}$ ).

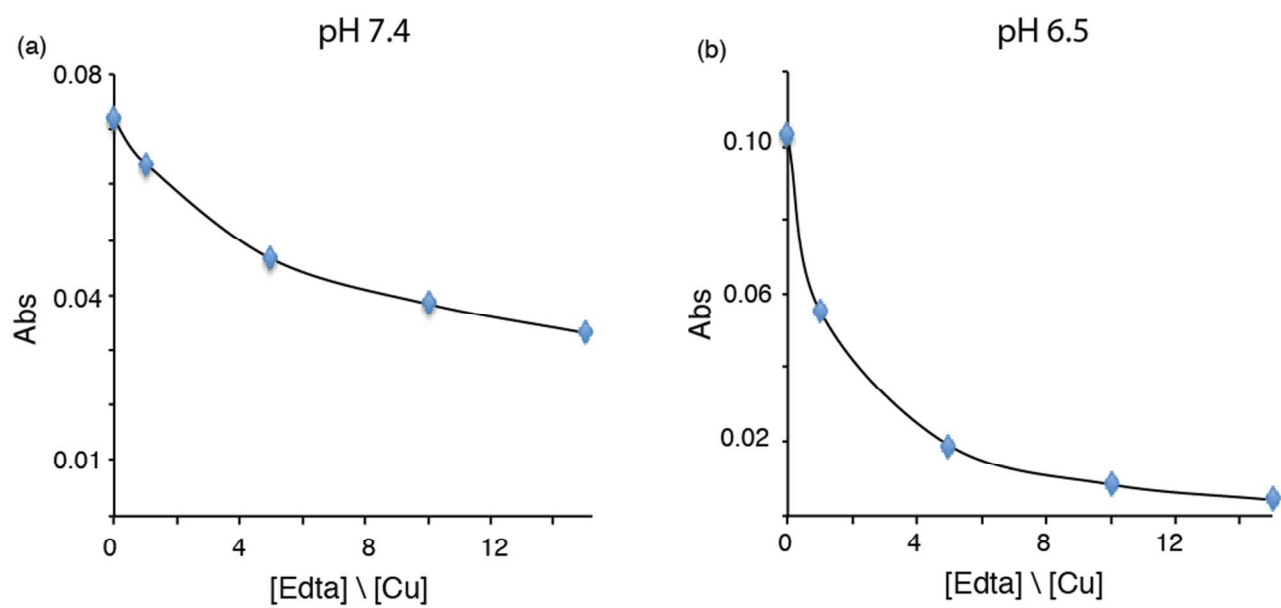
**Table S1. Estimation of  $K_D$  ( $\text{Cu}^{\text{II}}\text{L}^3$ ) for  $\text{H}_2\text{L}^3$  ligand by competition with Edta in 30% dmso/PB (20 mM, pH 7.4)<sup>a</sup>**

$[\text{H}_2\text{L}^3]_{\text{tot}}$ ( $\mu\text{M}$ )	$[\text{Edta}]_{\text{tot}}$ ( $\mu\text{M}$ )	$[\text{Cu}]_{\text{tot}}$ ( $\mu\text{M}$ )	$A_{550}^b$	$[\text{CuL}^3]$	$[\text{CuEdta}]$ ( $\mu\text{M}$ )	$\text{Cu}^{\text{II}}$ occupancy on Edta	$K_D(\text{CuL}^3)^c$ ( $10^{-18}$ M)
12	0.00	10	0.072	10.0	0.0		
12	10.00	10	0.064	8.9	1.1	0.113	4.46
12	50.00	10	0.047	6.5	3.5	0.071	6.48
12	100.00	10	0.038	5.3	4.7	0.047	6.12
12	150.00	10	0.033	4.6	5.4	0.036	6.02
						<b>Average</b>	<b>5.77</b>

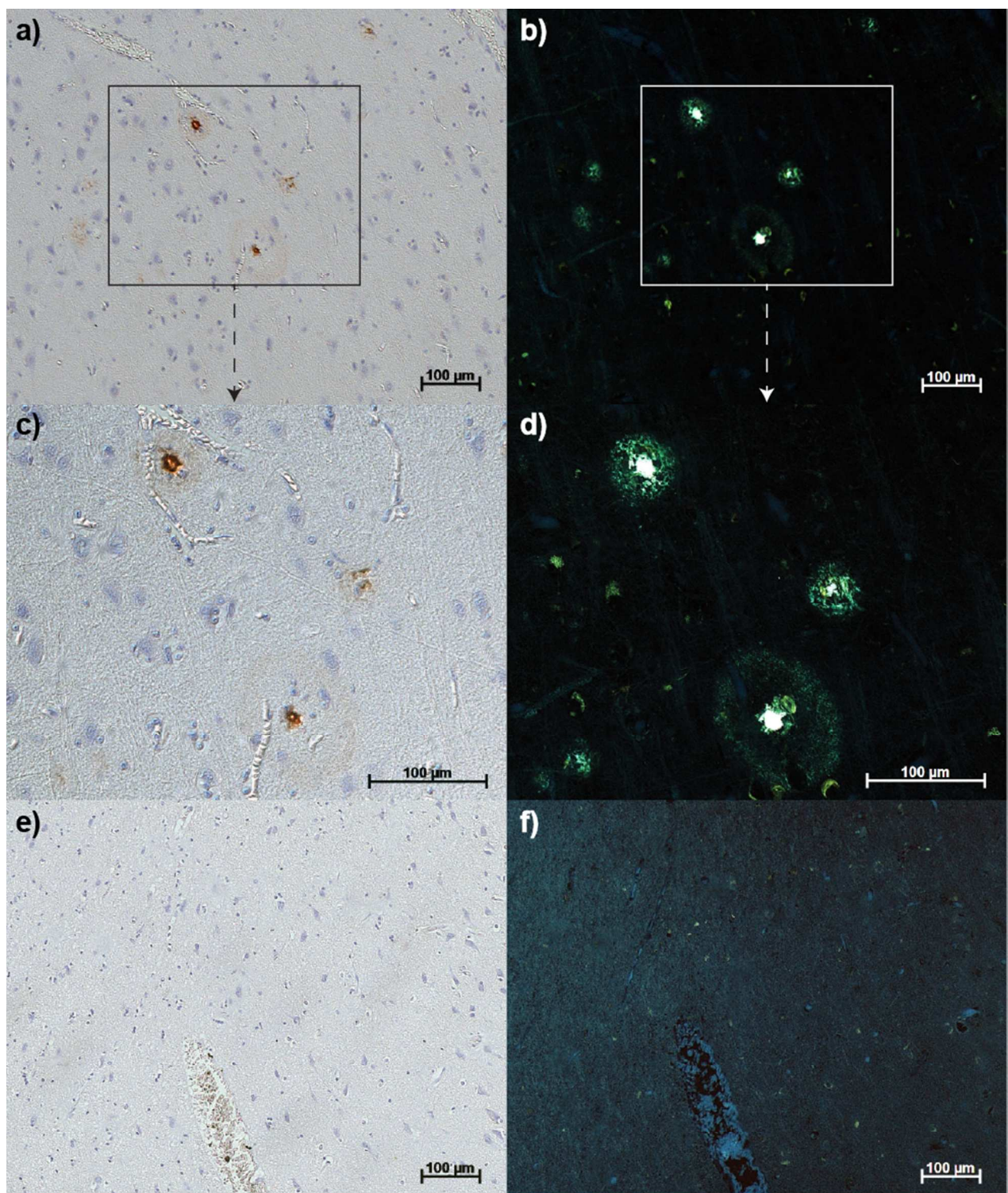
<sup>a</sup> Values measured at  $\mu\text{M}$  concentrations.<sup>b</sup> Values recorded after the reaction mixtures were equilibrated at room temperature for 24 hours.<sup>c</sup> Value obtained from a curve-fitting of the experimental data to eq 14 based on  $K_D(\text{Cu-Edta}) = 8.61 \times 10^{-15}$  M at pH 7.4 using eq 22. (see Xiao, Z.; Wedd, A. G. *Nat. Prod. Rep.* **2010**, 27, 768)**Table S2. Estimation of  $K_D$  ( $\text{Cu}^{\text{II}}\text{L}^3$ ) for  $\text{H}_2\text{L}^3$  ligand by competition with Edta in 30% dmso/MES (20 mM, pH 6.5)<sup>a</sup>**

$[\text{H}_2\text{L}^3]_{\text{tot}}$ ( $\mu\text{M}$ )	$[\text{Edta}]_{\text{tot}}$ ( $\mu\text{M}$ )	$[\text{Cu}]_{\text{tot}}$ ( $\mu\text{M}$ )	$A_{550}^b$	$[\text{CuL}^3]$ ( $\mu\text{M}$ )	$[\text{CuEdta}]$ ( $\mu\text{M}$ )	$\text{Cu}^{\text{II}}$ occupancy on Edta	$K_D(\text{CuL}^3)^c$ ( $10^{-15}$ M)
12	0.00	10	0.103	10.0	0.0		
12	10.00	10	0.055	5.4	4.6	0.462	1.33
12	50.00	10	0.019	1.8	8.2	0.163	1.36
12	100.00	10	0.008	0.8	9.2	0.092	1.77
12	150.00	10	0.004	0.4	9.6	0.064	2.44
						<b>Average</b>	<b>1.72</b>

<sup>a</sup> Values measured at  $\mu\text{M}$  concentrations.<sup>b</sup> Values recorded after the reaction mixtures were equilibrated at room temperature for 24 hours.<sup>c</sup> Value obtained from a curve-fitting of the experimental data to eq 14 based on  $K_D(\text{Cu-Edta}) = 7.88 \times 10^{-14}$  M at pH 6.5 using eq 22. (see Xiao, Z.; Wedd, A. G. *Nat. Prod. Rep.* **2010**, 27, 768)



**Figure S4.** Determination of  $Cu^{II}$  dissociation constants ( $K_D$ ) of  $CuL^3$  with ligand Edta at differing pH in; **(a)** 30% dmsO/PB (20 mM, pH 7.4) and **(b)** 30% dmsO/MES (20 mM, pH 6.5) with ligand Egta. Decrease in  $A_{550}$  of solution containing  $[Cu^{II}]_{total} = 10 \mu M$  and  $[H_2L^3]_{total} = 12 \mu M$  with increasing amount of Edta.



**Figure S5.** AD human brain sections with 1E8 antibody stained A $\beta$  plaques **a)** x10, **c)** x 20 magnification; and epifluorescence microscopy of H<sub>2</sub>L<sup>3</sup> binding selectively to A $\beta$  plaques **b)** x10, **d)** x20 magnification measured at  $\lambda_{\text{ex}} = 359$  nm,  $\lambda_{\text{em}} = 461$  nm; controls consist of age-matched healthy brain sections treated with **e)** 1E8 antibody and **f)** H<sub>2</sub>L<sup>3</sup>.