SUPPORTING INFORMATION

for

N-Alkylamino Stilbene Compounds as Amyloid β Inhibitors for Alzheimer's Disease Research

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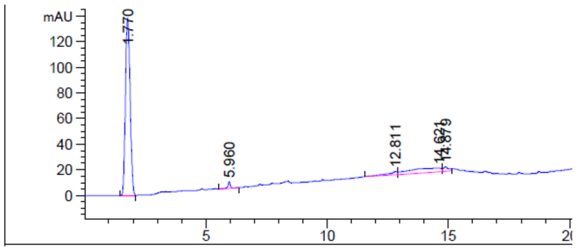
1. HPLC Chromatograms

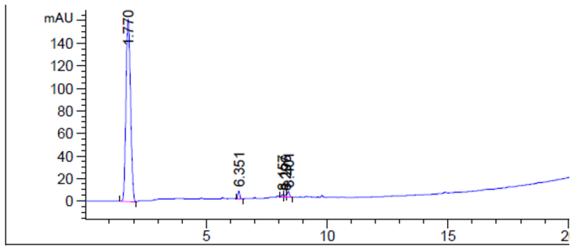
L1: VWD Wavelength = 230 nm

Purity: 80%



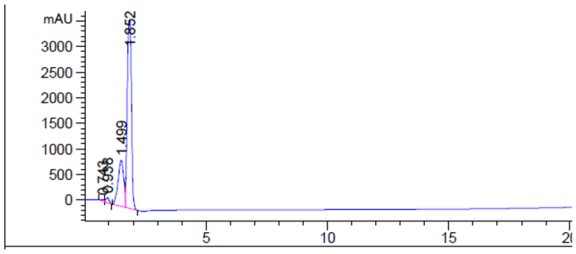
L2: VWD Wavelength = 230 nm

Purity: 96%



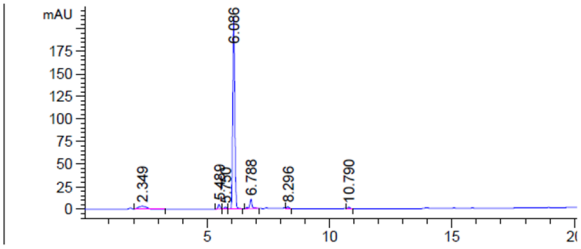
L3: VWD Wavelength = 230 nm

Purity: 74%



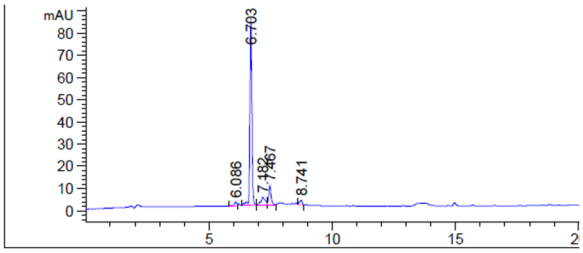
L4: VWD Wavelength = 260 nm

Purity: 85%



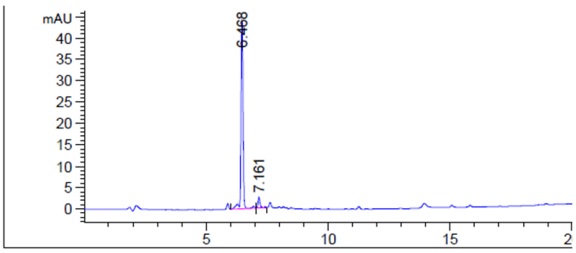
L5: VWD Wavelength = 260 nm

Purity: 79%



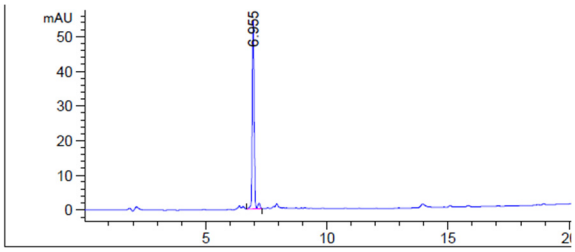
L6: VWD Wavelength = 260 nm

Purity: 94%



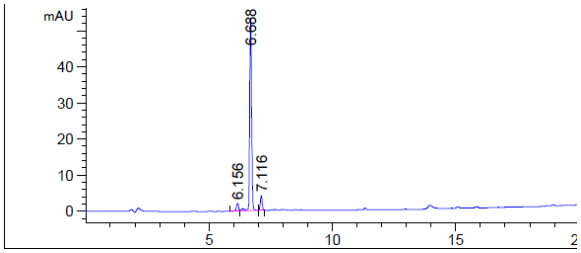
L7: VWD Wavelength = 260 nm

Purity: 100 %



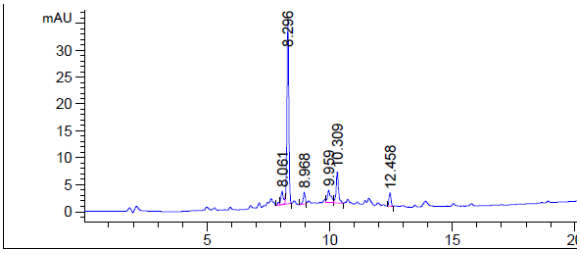
L8: VWD Wavelength = 260 nm

Purity: 90%



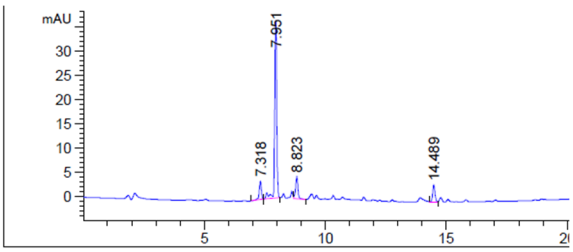
L9: VWD Wavelength = 260 nm

Purity: 90%



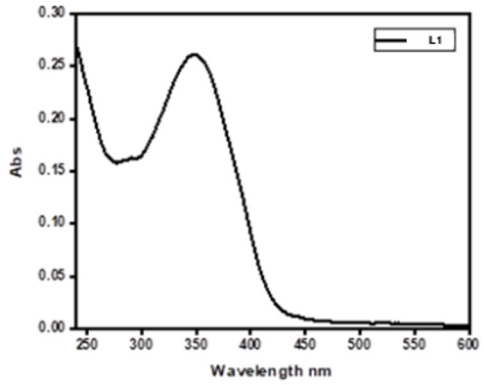
L10: VWD Wavelength = 260 nm

Purity: 84%

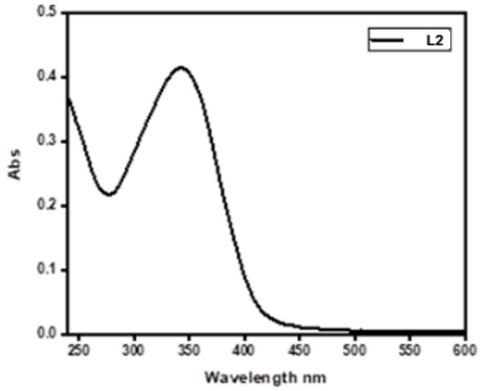


2. Absorbance Spectra

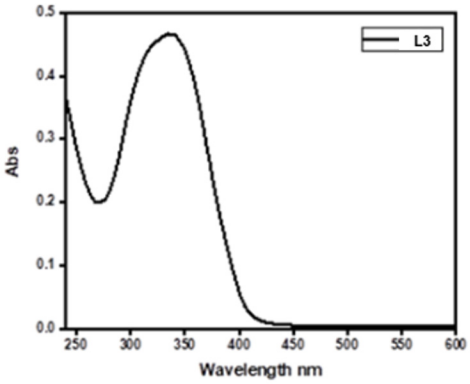
L1



L2



L3



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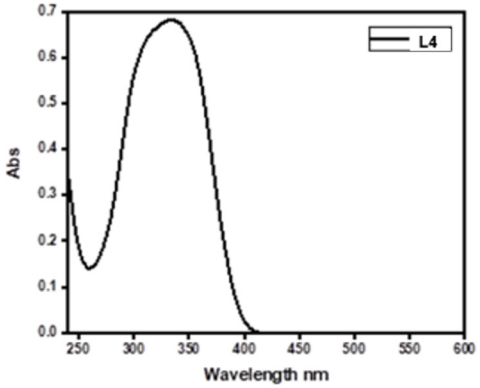

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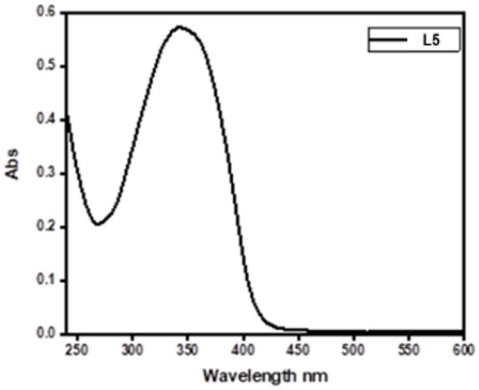

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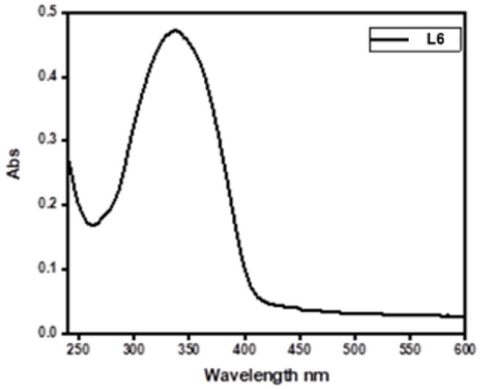

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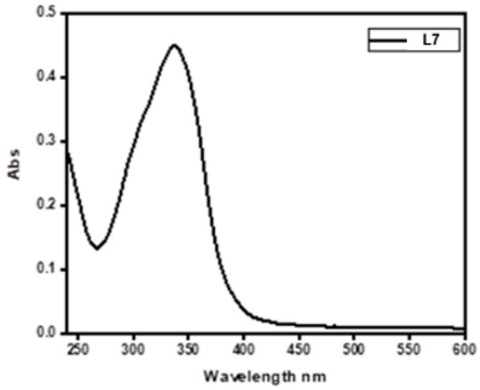

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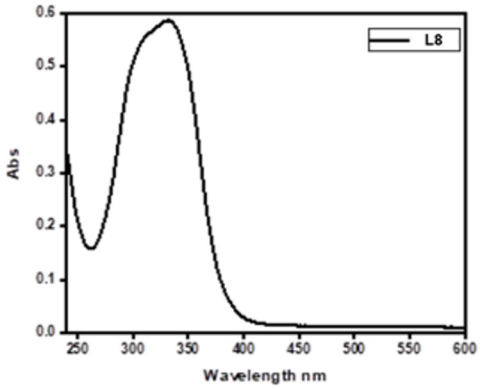

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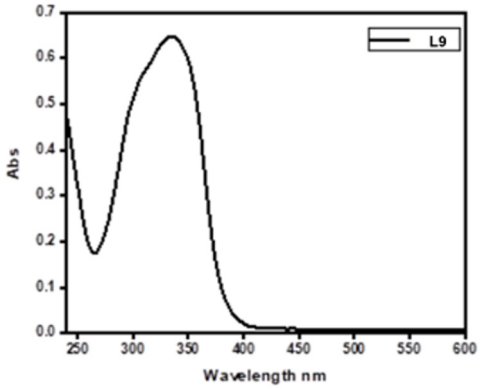
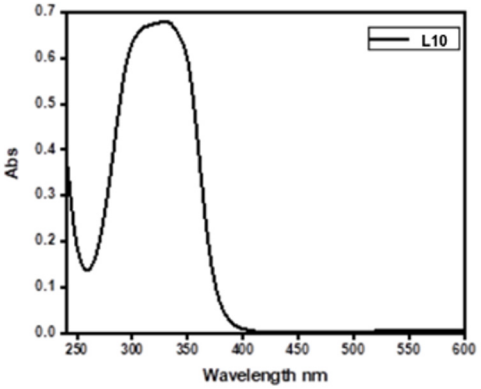


L10



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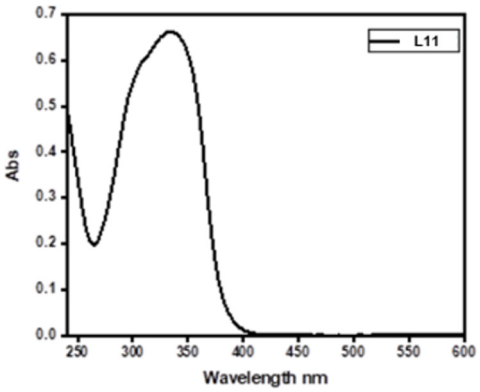
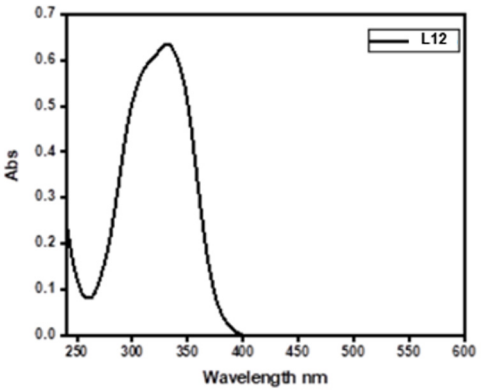


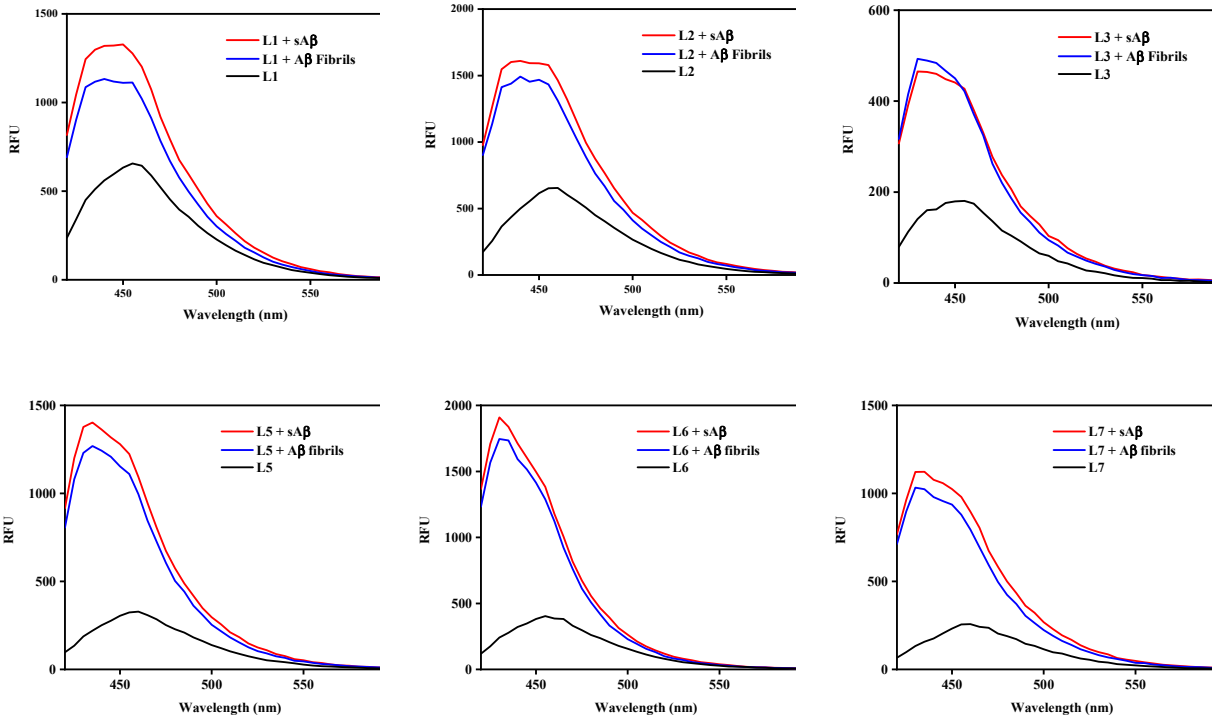
L12



3. Fluorescence Spectra

Table S1. λ_{max} of emission at excitation 380 nm for compounds, compounds with Aβ fibrils, and compounds with soluble Aβ aggregates.

Compound	Compound λ_{em} (nm)	Compound+Fibrils λ_{em} (nm)	Compound+sAβ λ_{em} (nm)
L1	455	455	455
L2	460	440	440
L3	455	430	430
L4	455	435	435
L5	460	435	435
L6	455	430	430
L7	460	430	430
L8	460	430	430
L9	455	450	455
L10	455	435	435
L11	455	450	450
L12	450	435	430



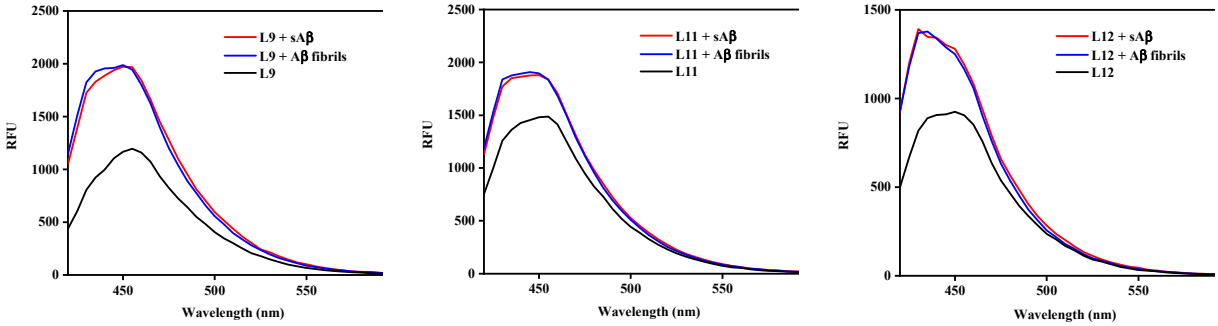


Figure S1. Fluorescence spectra of L1, L2, L3, L5, L6, L7, L9, L11, and L12 (black trace). Turn-on fluorescence of compounds with soluble (sAβ, red trace) and fibrillar (blue trace) Aβ aggregates.

4. $A\beta_{40}$ Inhibition Assays

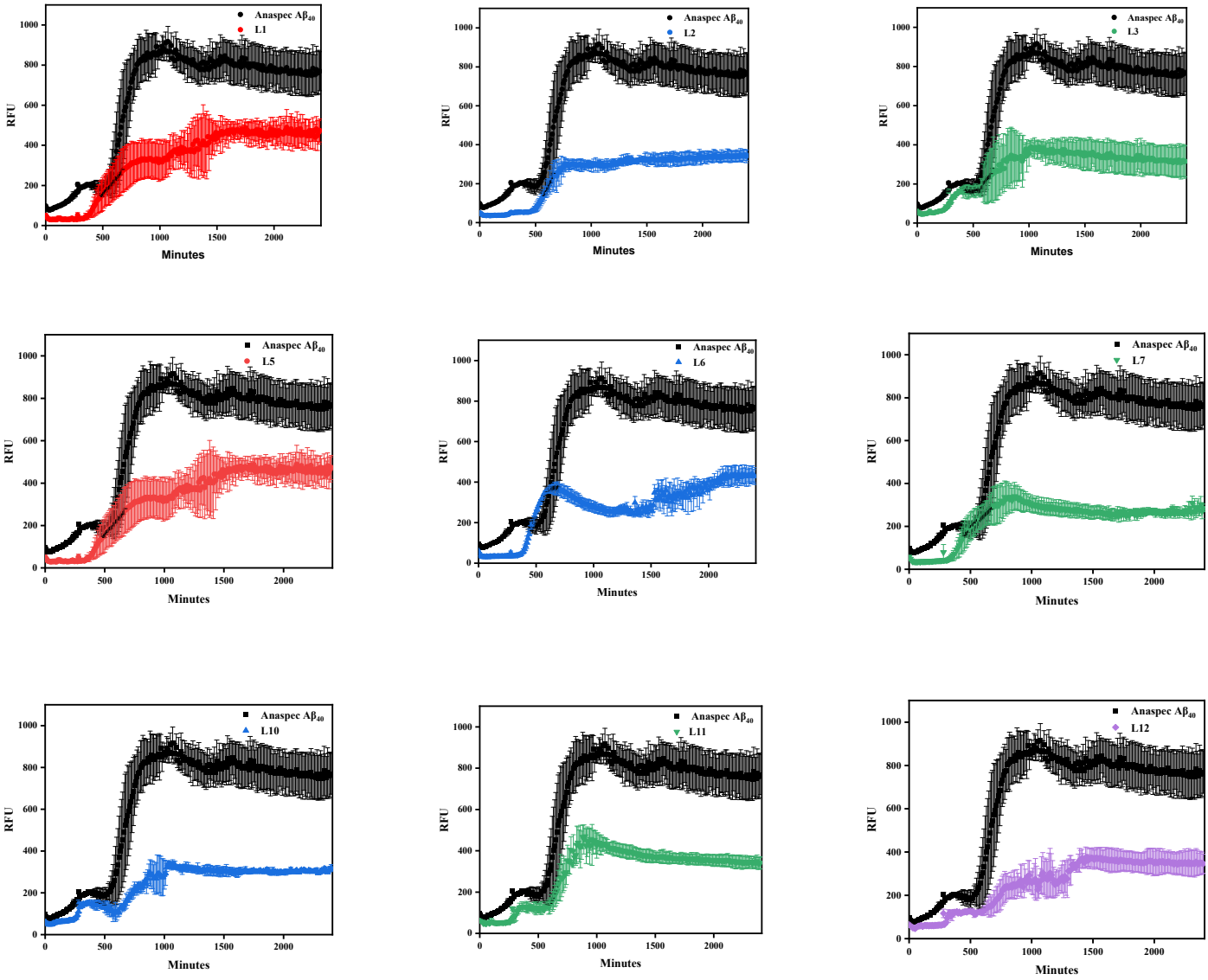
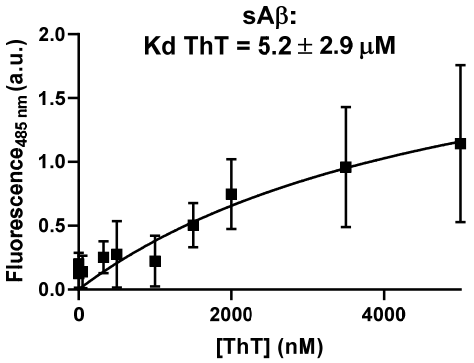
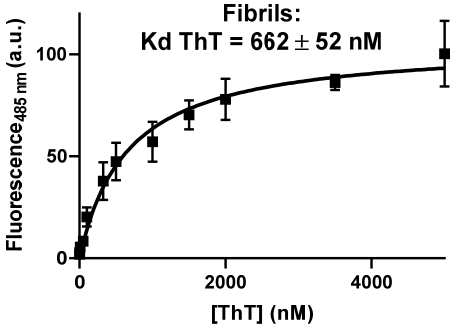


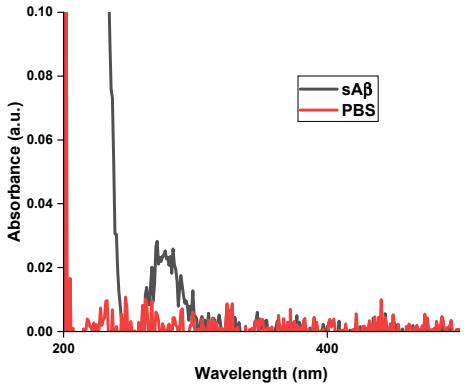
Figure S2. $A\beta_{40}$ Inhibition with L1, L2, L3, L5, L6, L7, L10, L11, and L12 tracked in minutes from nucleation to fibrilization.

5. ThT Control Studies

Table S2. The $A\beta_{42}$ fluorescence turn-on assay with ThT (em = 485 nm, ex = 435 nm) for soluble $A\beta_{42}$ and $A\beta_{42}$ fibrils was used to control for soluble vs. insoluble amyloid. [$A\beta_{42}$] = 5 μM; [ThT] = 1, 5, 10, 50, 100, 325, 500, 1000, 1500, 2000, 3500, 5000 nM). Using the protocol from the main text to prepare soluble and fibrillar $A\beta_{42}$, the UV-vis absorbance was measured for the soluble $A\beta_{42}$ used in the control. In a cuvette, 100 μL of [$A\beta_{42}$] = 20 μM. Soluble $A\beta_{42}$ control shows $A\beta_{42}$ signature absorbance band at 280 nm (bottom) which confirms the existence of amyloid species for soluble amyloid.[1] The Kd was taken for both fibrils and soluble amyloid with ThT. ThT does not bind to non-amyloids and will not exhibit a fluorescence enhancement. Soluble $A\beta_{42}$ control shows negligible turn-on (top left) compared to the fibrillar control, 6 nM, (top right) which matches the reported Kd for ThT and $A\beta_{42}$.[2]







6. Molecular Docking Data

Table S2. Molecular docking summary for 5OQV docked compounds. Ranking based on docking score.

Compound	Docking Score	Glide e-model (kcal/mol)
L7	-7.749	-72.099
L11	-7.749	-53.999
L5	-7.708	-71.690
L6	-7.696	-69.227
L8	-7.515	-64.145
L12	-7.374	-54.522
L1	-7.239	-67.812
L4	-7.140	-62.917
L10	-6.975	-66.622
L9	-6.943	-65.236
L2	-6.685	-62.721
L3	-6.681	-61.783

Table S3. Molecular docking summary for 6RHY docked compounds. Ranking based on docking score.

Compound	Docking Score	Glide e-model (kcal/mol)
L2	-5.055	-46.608
L6	-4.572	-45.696
L3	-4.395	-52.13
L7	-4.312	-49.4
L4	-4.132	-49.385
L10	-4.123	-45.857
L12	-3.97	-48.282
L9	-3.967	-48.275
L5	-3.961	-45.516
L11	-3.776	-50.625
L1	-3.436	-42.099
L8	-3.126	-38.738

7. Log D Measurements

Table S4. Log D values for the compounds.

Compounds	Log D
L1	1.33 ± 0.01
L2	1.48 ± 0.02
L3	0.98 ± 0.01
L4	1.44 ± 0.01
L5	1.39 ± 0.01
L6	1.37 ± 0.01
L7	1.35 ± 0.02
L8	1.29 ± 0.01
L9	0.93 ± 0.02
L10	1.03 ± 0.01
L11	0.85 ± 0.01
L12	0.81 ± 0.01

8. References

1. Xue, C.; Lee, Y. K.; Tran, J.; Chang, D.; Guo, Z., A mix-and-click method to measure amyloid-β concentration with sub-micromolar sensitivity. *R. Soc. Open Sci.* **2017,** *4* (8), 170325.
2. Groenning, M., Binding mode of Thioflavin T and other molecular probes in the context of amyloid fibrils—current status. *J. Chem. Biol.* **2010,** *3* (1), 1-18.