Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

Pyrogallol, Corilagin and Chebulagic Acid target the "fuzzy coat"of Alpha-Synuclein to inhibit the fibrillization of the protein

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Supporting Methods

UV-Visible spectrophotometric measurements

In order to check if any of the three catechols, Pyrogallol, Corilagin, Chebulagic acid, interfere with the ThT fluorescence assay, UV-Visible spectrophotometric measurements were performed. Now, in the ThT fluorescence experiment (see Materials and Methods in the Main text), the final concentration of ThT in the cuvette while performing the measurements was 15 μM, whereas, the concentration of each catechol was 3 μM each (For details, see Materials and Methods in the Main text). Therefore, the UV-Visible spectrum of each of ThT, Pyrogallol, Corilagin and Chebulagic acid was recorded in the wavelength range 350-500 nm.

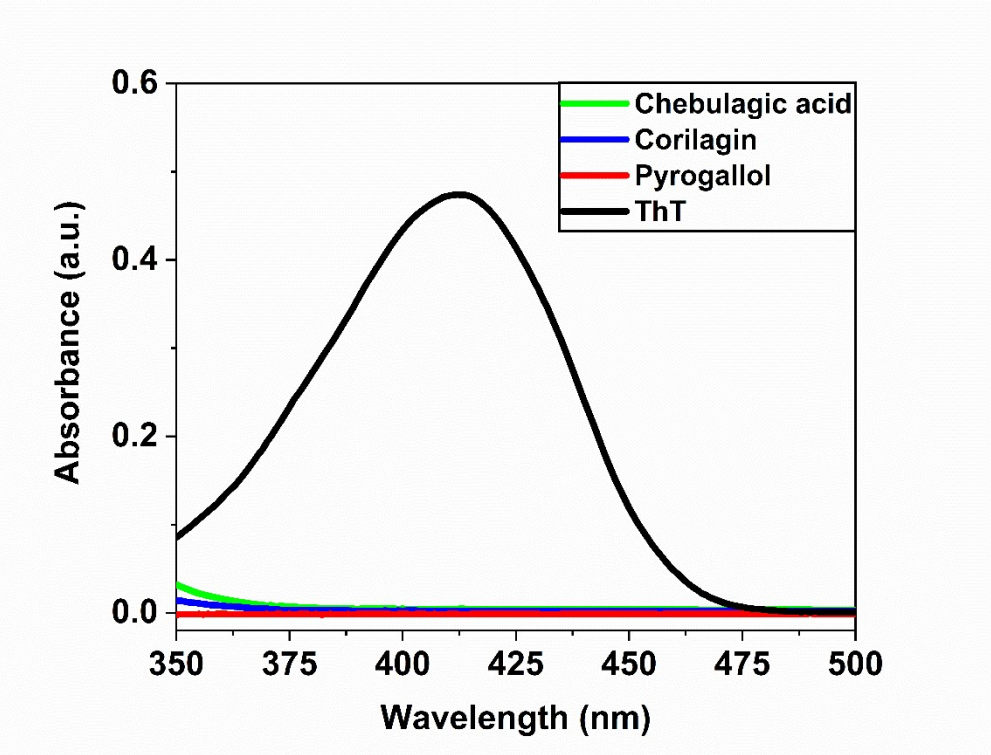

Figure S1. Comparison between the electronic absorption profile of ThT and the three catechols. The UV-Visible absorption spectra of 15 μM ThT, 3 μM Pyrogallol, 3 μM Corilagin and 3 μM Chebulagic acid in the wavelength range of 350 - 500 nm are shown.

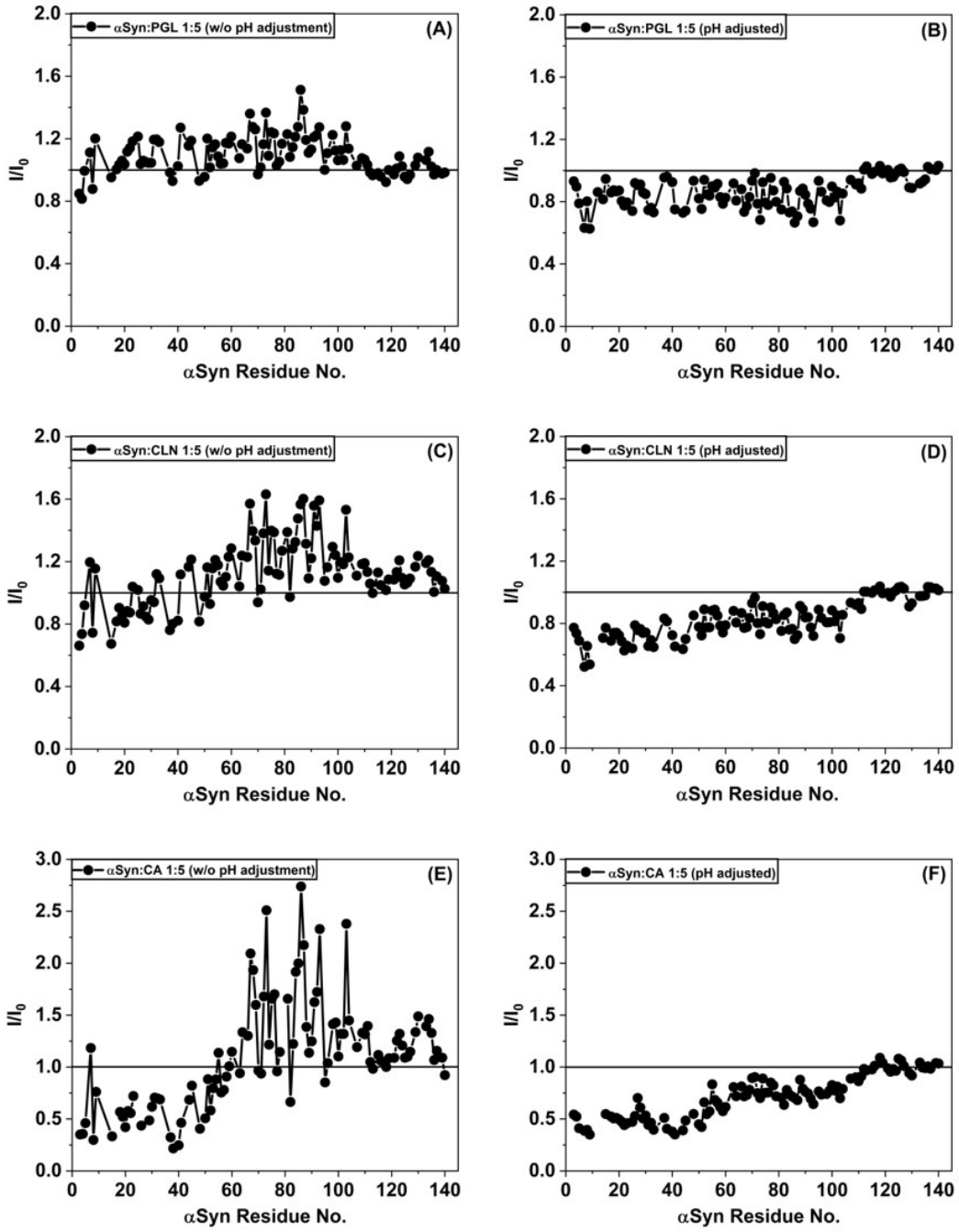

Figure S2. α-Synuclein (αSyn) backbone amide ^{1}H-^{15}N resonances are highly susceptible to pH changes. (A, **C** and **E)** ^{1}H-^{15}N HSQC signal attenuation (I/I_0) of αSyn in the presence of 5 times molar equivalent concentration of Pyrogallol (PGL), Corilagin (CLN) and Chebulagic acid (CA) respectively, without adjusting the solution pH changes that occur due to the addition of each of these compounds. It was observed the pH difference between the 'protein + ligand' solution and the protein solution was ~0.3, ~0.5 and ~0.7 in the case of PGL, CLN and CA respectively. **(B**, **D** and **F)** I/I_0 of αSyn in the presence of 5 times molar equivalent concentration of PGL, CLN and CA respectively, with pH adjustment prior to the experiments such that both the 'protein + ligand' solution and the protein solution, containing only protein had the same pH. The horizontal solid line indicates an I/I_0 ratio of 1.

Table S1. Pairwise statistical analyses (using unpaired Student's t-test) for the distribution of ^{1}H-^{15}N HSQC signal attenuation (I/I_0) values of different domains of αSyn.

Experiment	*p-value* for (N-terminus vs NAC)	*p-value* for (NAC vs C-terminus)	*p-value* for (N-terminus vs C-terminus)
αSyn : Pyrogallol (1:5)	0.46	1.5×10^{-6}	1.1×10^{-6}
αSyn : Corilagin (1:5)	2.3×10^{-6}	2.9×10^{-8}	4.6×10^{-17}
αSyn : Chebulagic acid (1:5)	1.4×10^{-18}	2.5×10^{-10}	1.0×10^{-26}