Supplementary Information

Brazilin inhibits α-synuclein fibrillogenesis, disrupts mature fibrils and protects against amyloid-induced cytotoxicity

Fufeng Liu&,#,‡*, Ying Wang†, Jingcheng Sang†, Wei Wei†, Wenping Zhao†, Beibei Chen†, Fang Zhao†, Longgang Jia†, Fuping Lu&,#,‡*

& Key Laboratory of Industrial Fermentation Microbiology, Ministry of Education, Tianjin, 300457, P. R. China;
# Tianjin Key Laboratory of Industrial Microbiology, Tianjin, 300457, P. R. China;
‡ College of Biotechnology, Tianjin University of Science & Technology, Tianjin 300457, China.

Corresponding Authors
‘Fufeng Liu, Phone: +86-22-60602717; Fax: +86-22-60602298; E-mail: fufengliu@tust.edu.cn
‘Fuping Lu, Phone: +86-22-60602271; Fax: +86-22-60602298; E-mail: lfp@tust.edu.cn
Fig. S1. The chemical structure of brazilin.
Fig. S2. Initial conformation of α-syn pentamer (L38-V95). The red region (E61-V95) represents the non-amyloid component (NAC) part of α-syn.
Fig. S3. The influence of pure brazilin on the ThT fluorescence. The ThT signal was measured at the excitation wavelength of 440 nm, the emission wavelength of 480 nm. ThT without brazilin or α-syn was set as negative control, and ThT with 50 µM α-syn was set as positive control.
Fig. S4. 3D AFM images of α-syn aggregates. Incubated without brazilin (a) and with 100 μM brazilin (b).
Fig. S5. ThT fluorescence of α-syn (50 μM) aggregates after incubation with various concentrations of different small-molecule inhibitors (i.e., EGCG, brazili


tin, vitamin B12, and dihydromyricetin). ThT fluorescence of pure α-syn aggregates was defined as 100%.
Fig. S6. Cytotoxicity of brazilin to the well-differentiated PC12 cells. The values represent means ± SD (n=6). * p < 0.05; *** p < 0.001.
Fig. S7. The root-mean-square deviation (RMSD) values of α-syn pentamer in water and 17 mM brazilin solution displayed as a function of the whole 100 ns simulation time.
Fig. S8. The solvent accessible surface area (SASA) values of α-syn pentamer in water and 17 mM brazilin solution displayed as a function of the whole 100 ns simulation time.
Fig. S9. Time-dependent of the secondary structure of α-syn pentamer in the absence (a) and presence of 17 mM brazilin (b).
Fig. S10. The number of contacts between α-syn pentamer and brazilin are displayed as a function of simulation time.
Fig. S11. The three binding regions (I, II and III) of α-syn pentamer directly interact with brazilin. In clarity, α-syn pentamer is shown as a NewCartoon model. The secondary structures of β-sheet, turn, random coil are colored by yellow, blue and white, respectively. Brazilin molecules were represented by Licorice model. The carbon, hydrogen and oxygen atoms are shown by gray, white and red, respectively.
Fig. S12. Number of hydrogen bonds formed between α-syn pentamer and brazilin displayed as a function of the whole 100 ns simulation time.
Fig. S13. Number of the intermolecular hydrogen bonds among α-syn monomers in water and 17 mM brazilin solution displayed as a function of the whole 100 ns simulation time.