Supporting Information

Brazilin Inhibits Fibrillogenesis of Human Islet Amyloid Polypeptide, Disassembles Mature Fibrils, and Alleviates Cytotoxicity

Jingjing Guo[a#], Wanqi Sun[b#], Li Li[c], Fufeng Liu[a, d*], Wenyu Lu[a*]

[a] Department of Biochemical Engineering and Key Laboratory of Systems Bioengineering of Ministry of Education, School of Chemical Engineering and Technology, Tianjin University, Tianjin 300072, China

[b] Department of Chemical and Biological Engineering, The University of Alabama, Tuscaloosa, AL, USA

[c] College of Marine and Environmental Sciences, Tianjin University of Science & Technology, Tianjin 300457, China

[d] Key Laboratory of Industrial Fermentation Microbiology of Ministry of Education; Tianjin Key Laboratory of Industrial Microbiology; National Engineering Laboratory for Industrial Enzymes; National and Local United Engineering Lab of Metabolic Control Fermentation Technology; College of Biotechnology, Tianjin University of Science & Technology, Tianjin 300457, P. R. China

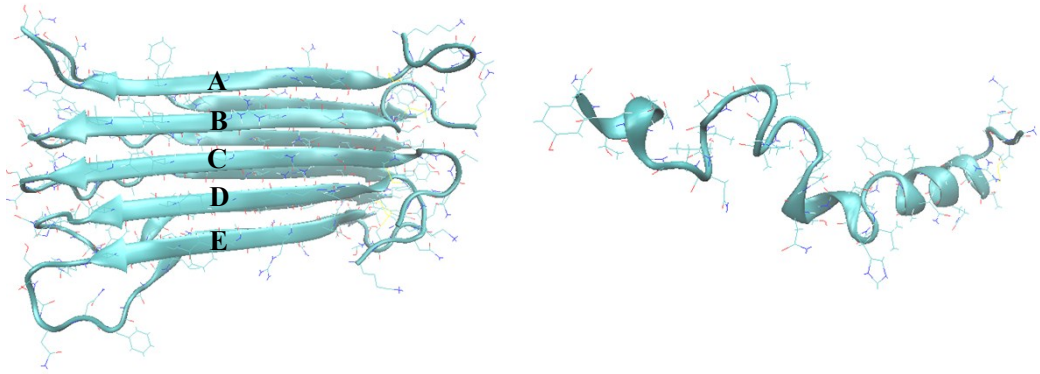
Corresponding Authors

[*]Phone: +86-022-60602717; Fax: +86-022-60602298; E-mail: fufengliu@tust.edu.cn; wenyulu@tju.edu.cn

Author Contributions

[#] These authors contributed equally to this work.

(A) **(B)**



(C)

KCNTATCATQ$_{10}$ RLANFLVHSS$_{20}$ NNFGAILSST$_{30}$ NVGSNTY$_{37}$

Figure S1. (A) The 3D structure model of human Islet Amyloid Polypeptide (hIAPP) pentamer including monomers A, B, C, D and E (B) the 3D structure model and (C) the amino acid sequences of hIAPP monomer. The backbones and side chains of hIAPP are shown by a blue NewCartoon and thin sticks, respectively. Atoms are colored red for oxygen, blue for nitrogen, white for hydrogen, and green for carbon. The snapshots are plotted with the visual molecular dynamics (VMD) software.

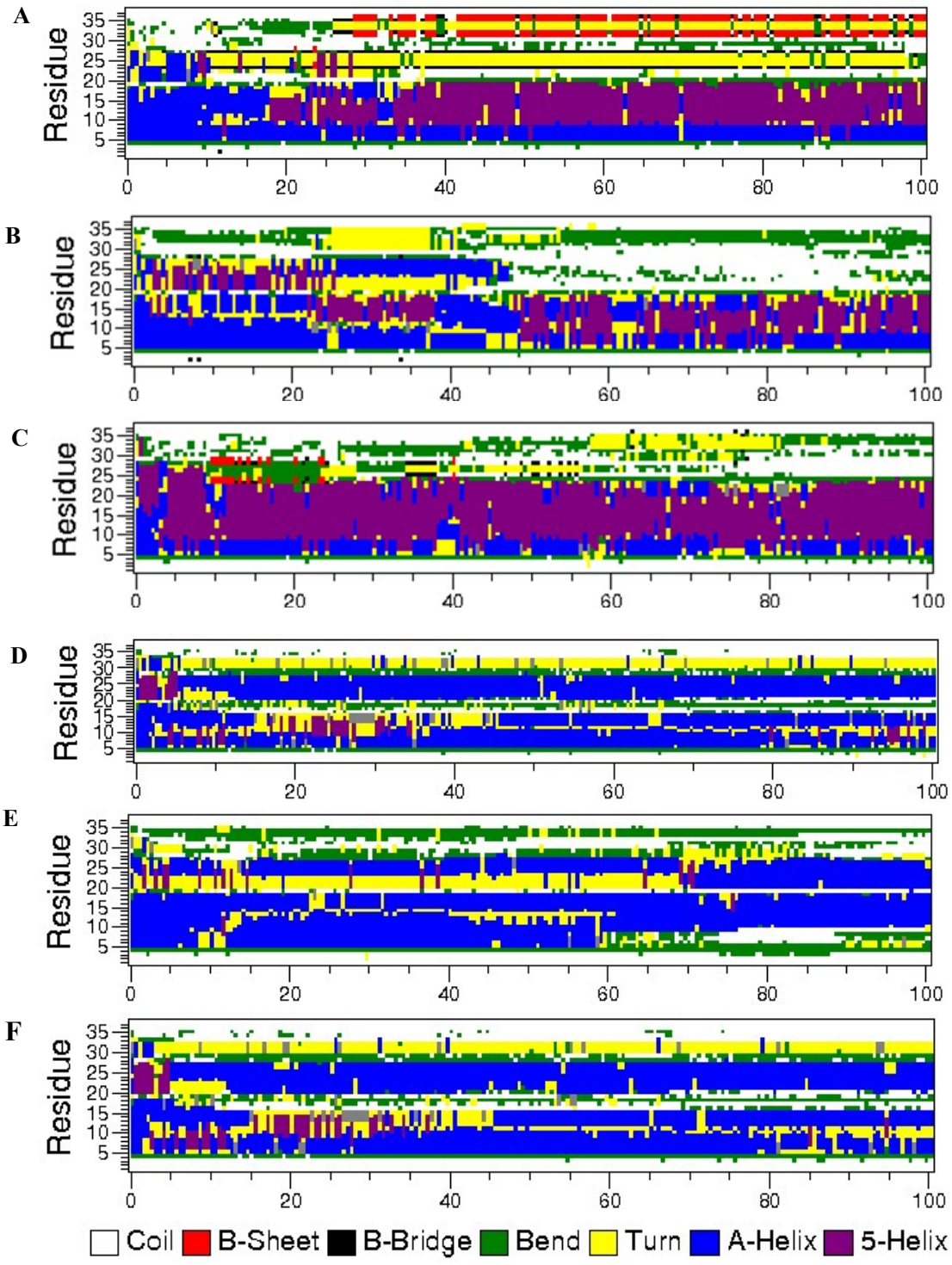


Figure S2. Secondary structures as a function of simulation time for hIAPP monomer calculated by DSSP in the absence (A, B and C) and presence (D, E and F) of brazilin. The vertical coordinate represents the residue number of hIAPP monomer, and the secondary structure is color-coded. The structures are analyzed every 0.2 ns.

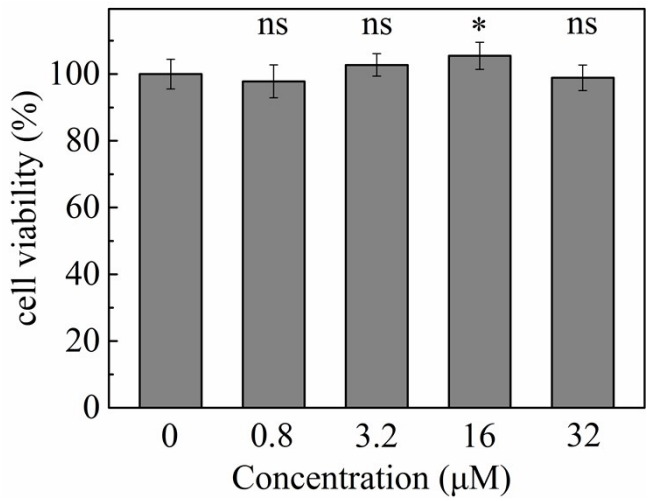


Figure S3. Viability of INS-1 cells after addition of different concentrations of brazilin. The cell viability treated with PBS buffer only was used as a control. The error bars were standard deviations of four different replicates. ns, no significant. *$p<0.05$ compared to control group.

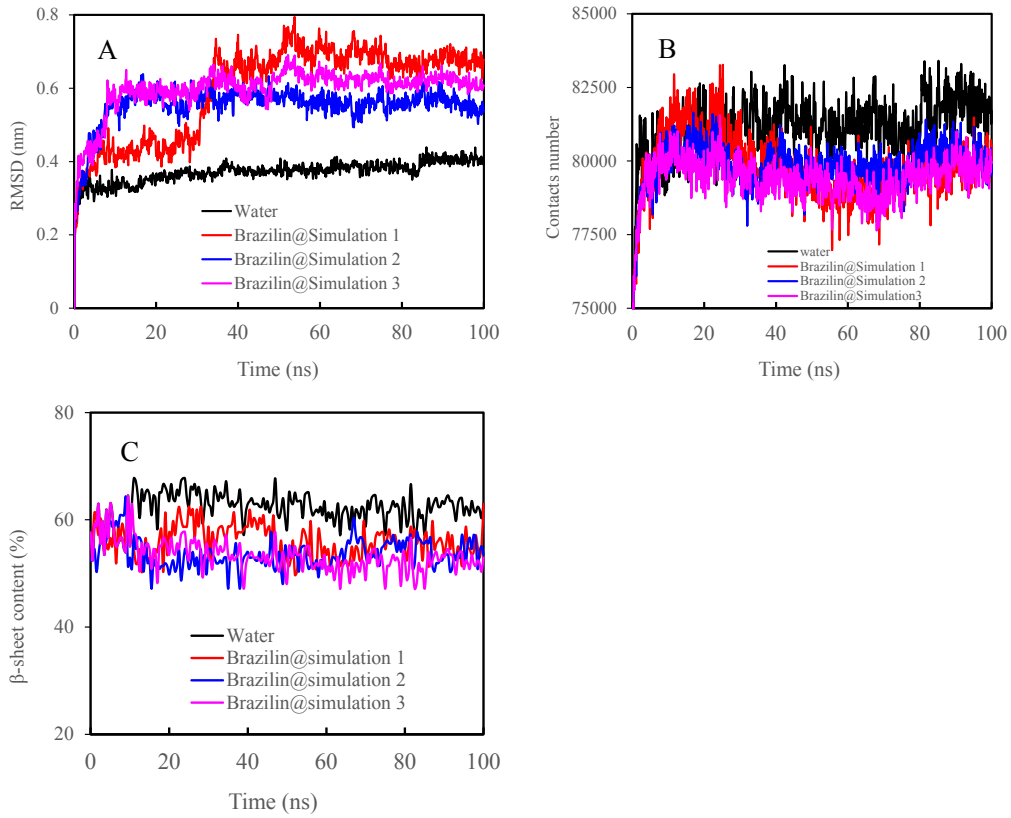


Figure S4. Time evolution of (A) root mean square deviation (RMSD) of Cα atoms of hIAPP pentamer, (B) the total inter-chain contact number of hIAPP pentamer, and (C) β-sheet content of hIAPP pentamer.

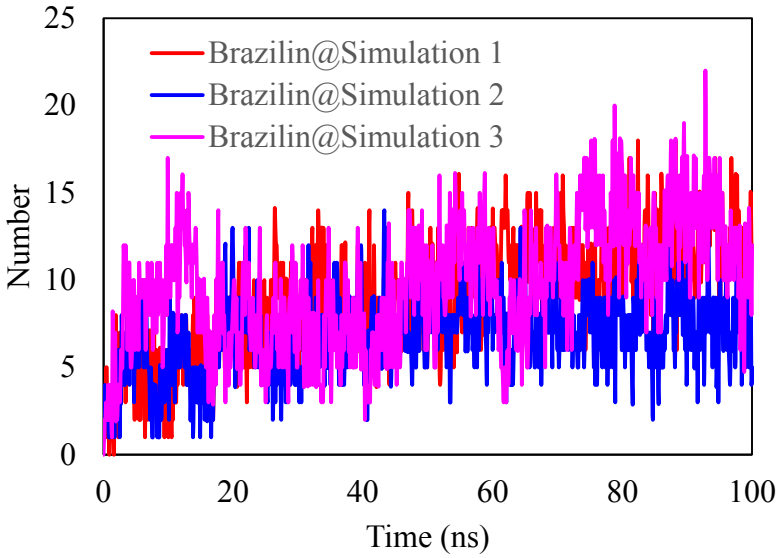


Figure S5. The number of hydrogen bonds between brazilin molecules and hIAPP pentamer.

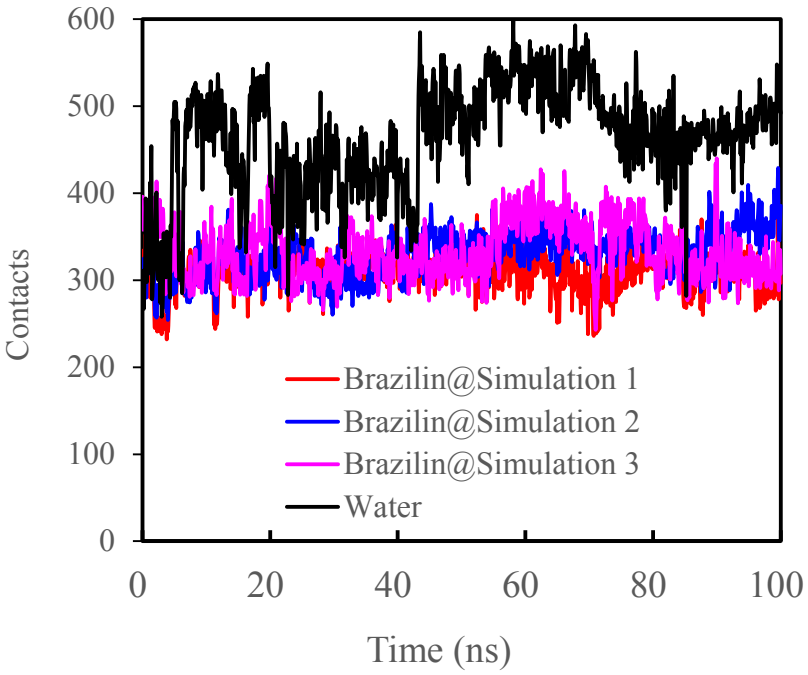


Figure S6. Time evolution of contact number between residue Asn3 of monomer C and other residues of hIAPP pentamer.

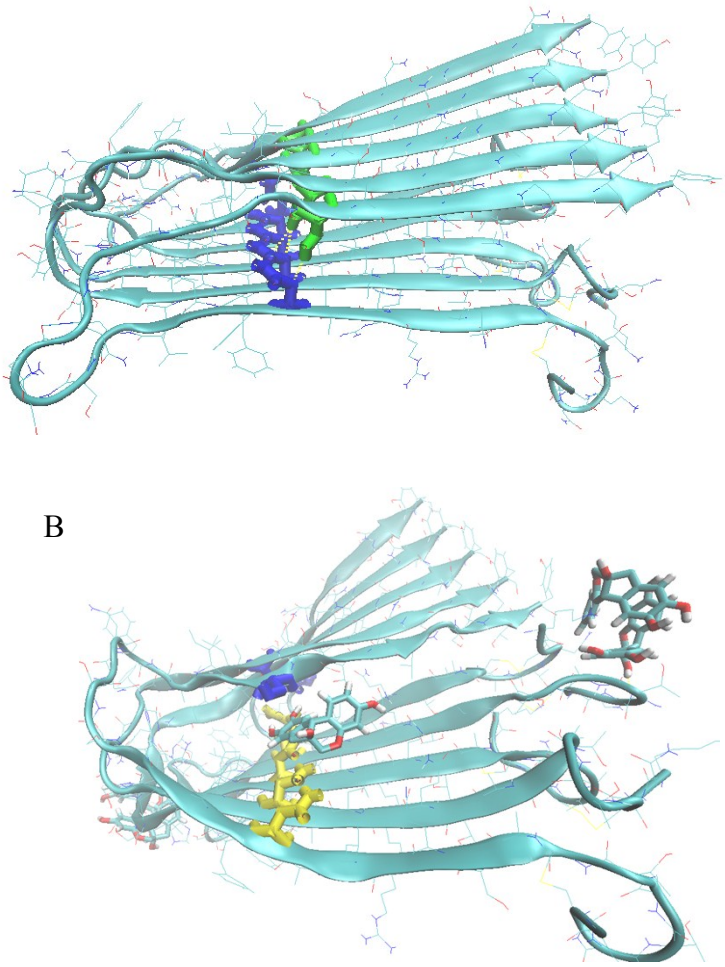


Figure S7. The typical interacting model between residues Asn14 and Ser28 in the initial structure of hIAPP pentamer (A) and the structure disrupted by brazilin molecules based on the MD simulations (B). Residues Asn14 and Ser28 are represented by the yellow and blue Bonds model, respectively. Brazilin molecules are shown in Licorice model. Hydrogen bonds are shown in a yellow dotted lines. The illustrations of the snapshot are the same as those described in the caption to Figure S1.

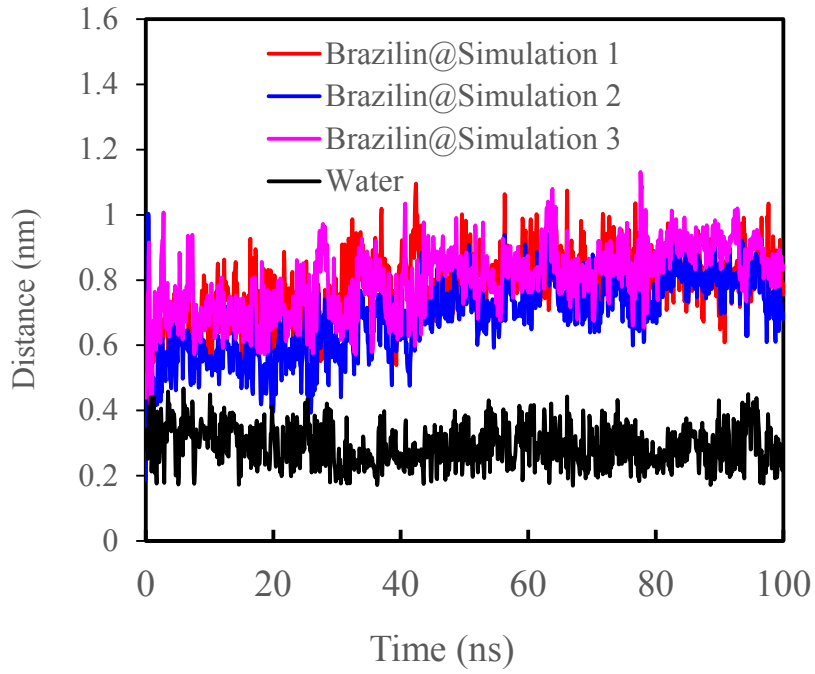


Figure S8. Time evolution of distance between Asn14 and Ser28 of monomer C was studied in the absence and presence of brazilin.

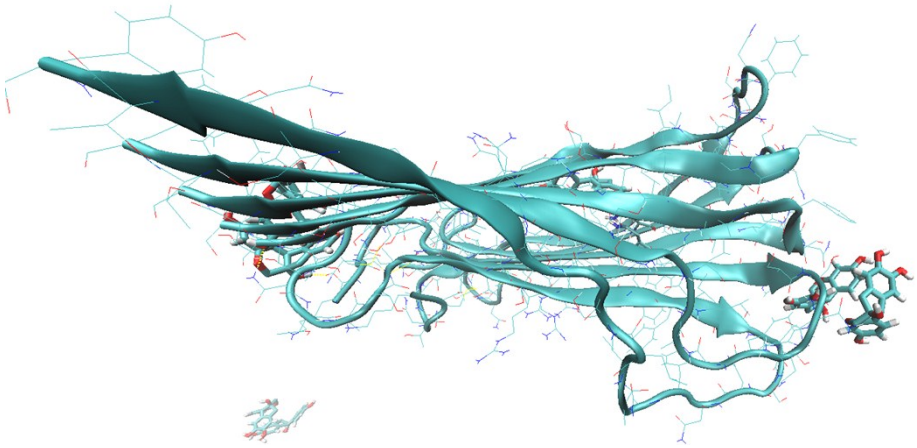


Figure S9. The initial β-sheet structure of hIAPP pentamer was disrupted by brazilin molecules based on the MD simulations. The illustrations of the snapshot are the same as those described in the caption to Figure S1.