Supporting Information

Natural flavonoid hesperetin blocks amyloid β-protein fibrillogenesis, depolymerizes preformed fibrils and alleviates amyloid-caused cytotoxicity

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Figure S1

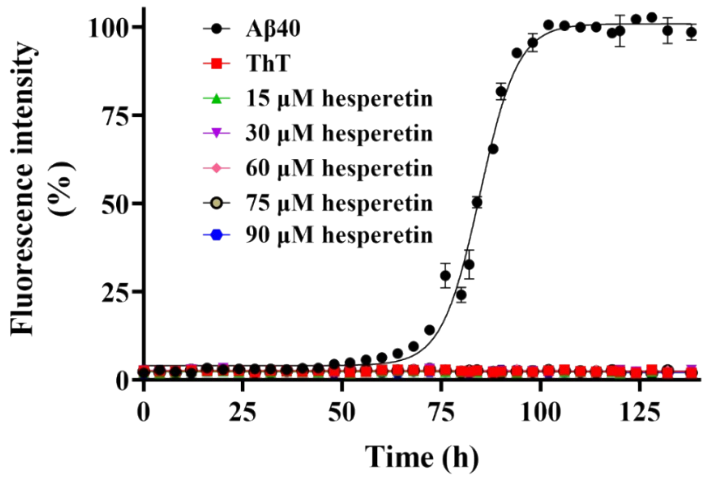

Figure S1 Effect of different concentrations of hesperetin on ThT fluorescence intensity.ThT without hesperetin and Aβ40 was negative control, while 30 μM ThT and 30 μM Aβ40 were positive control.

Figure S2

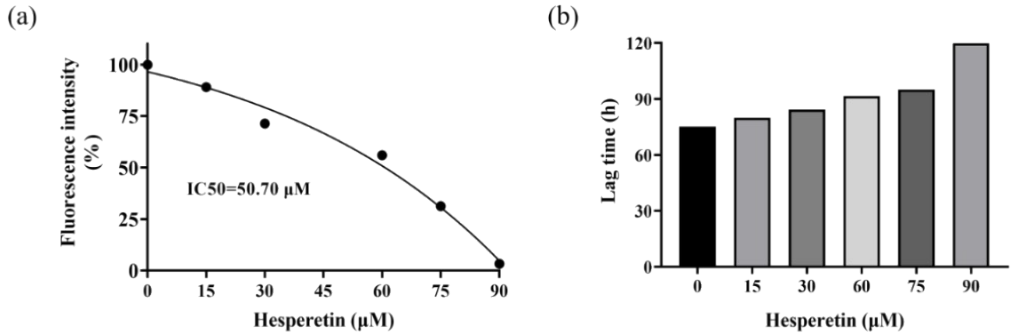

Figure S2 (a) The half-maximal inhibitory concentration (IC50) of hesperetin against Aβ40 fibrillation. (b) The lag time of Aβ40 kinetics curve with and without different concentrations of hesperetin.

Figure S3

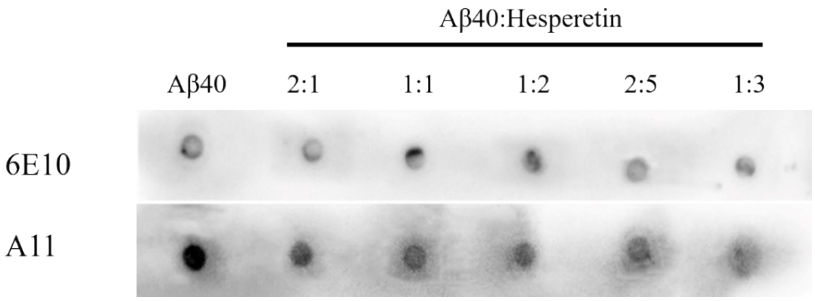

Figure S3 Dot blot of Aβ40 co-cultured with hesperetin. From left to right, Aβ40 treated with different concentrations of 0, 15, 30, 60, 75 and 90 μM hesperetin.

Figure S4

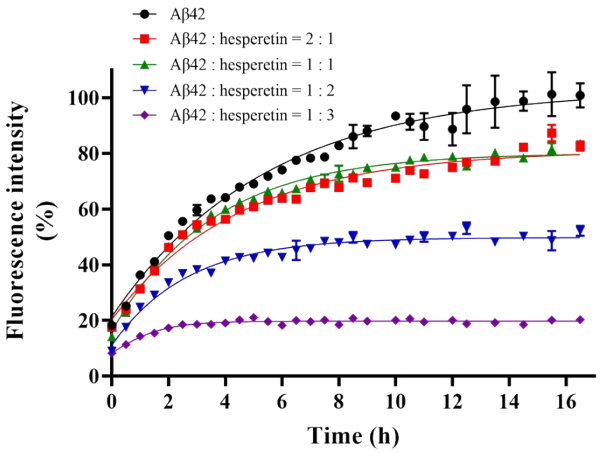

Figure S4 ThT fluorescence of different concentrations of hesperidin co-cultured with Aβ42.

Figure S5

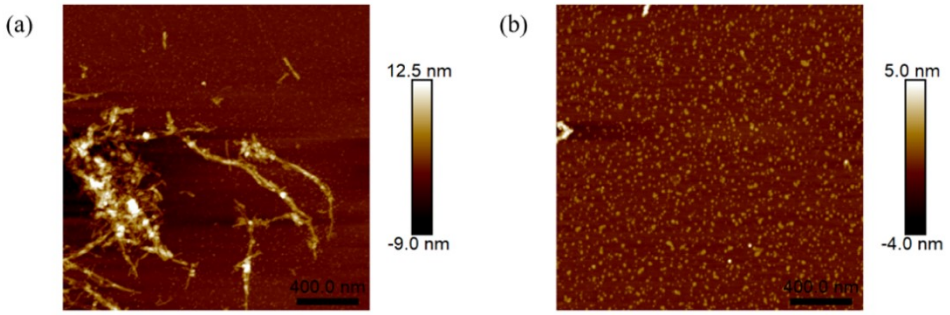

Figure S5 AFM images of Aβ42 co-cultured with hesperetin 30 μM Aβ42 was cultured to plateau stage with (b) or without (a) 90 μM hesperetin, scale:400 nm.

Figure S6

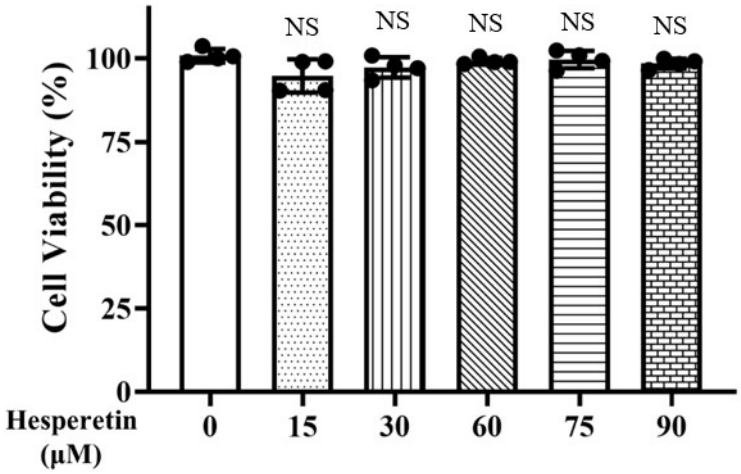

Figure S6 Cytotoxicity of hesperetin at different concentrations. NS, not significant.

Figure S7

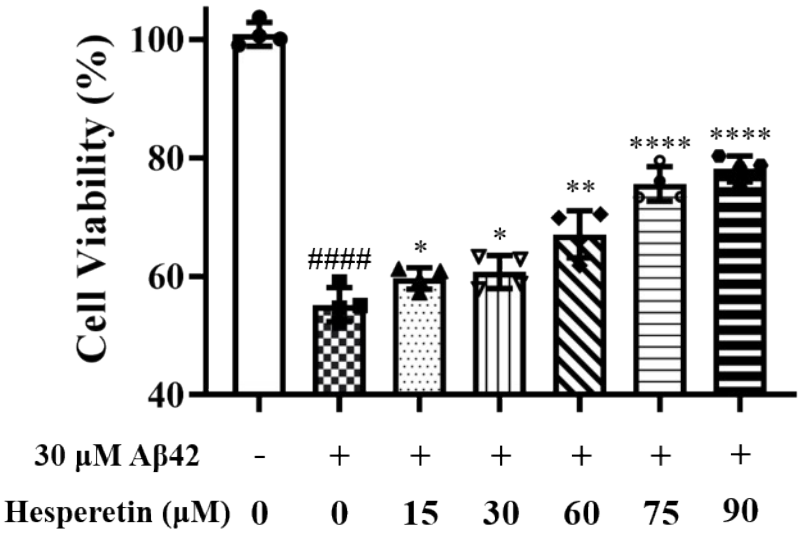

Figure S7 Cytotoxicity of different concentrations of Aβ42 co-cultured with hesperetin.

Figure S8

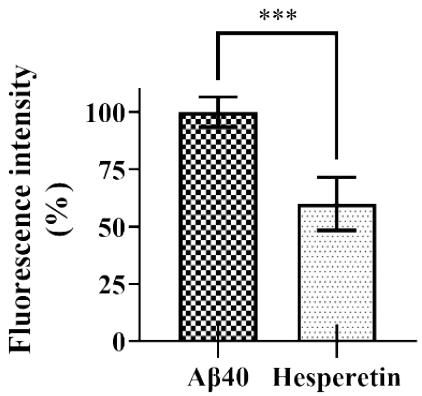

Figure S8 Quantitative fluorescence analysis of PI-DNA in PC12 cells induced by Aβ40 aggregates.

Figure S9

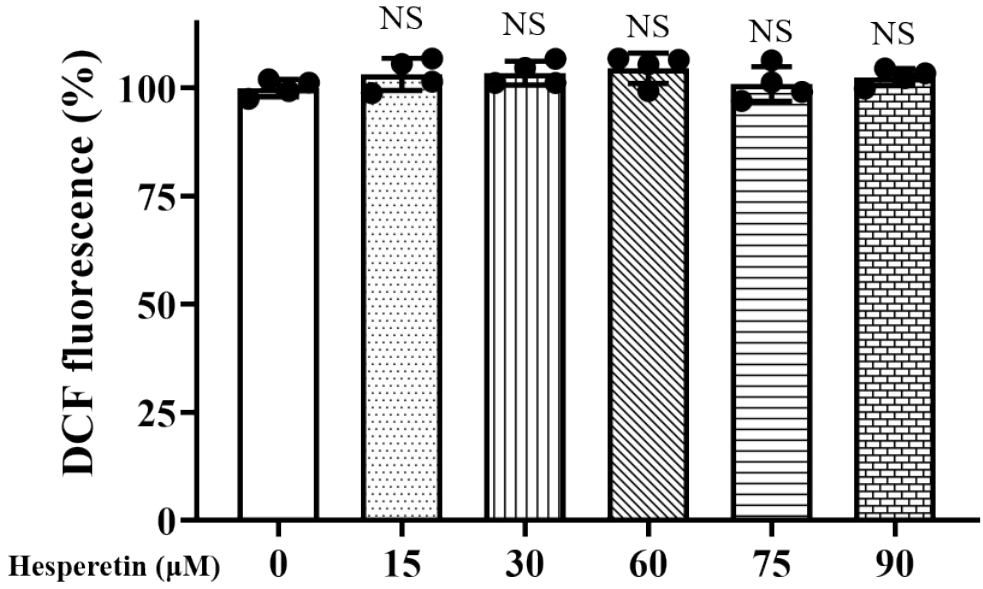

Figure S9 The effect of hesperetin at different concentrations on ROS level.

Figure S10

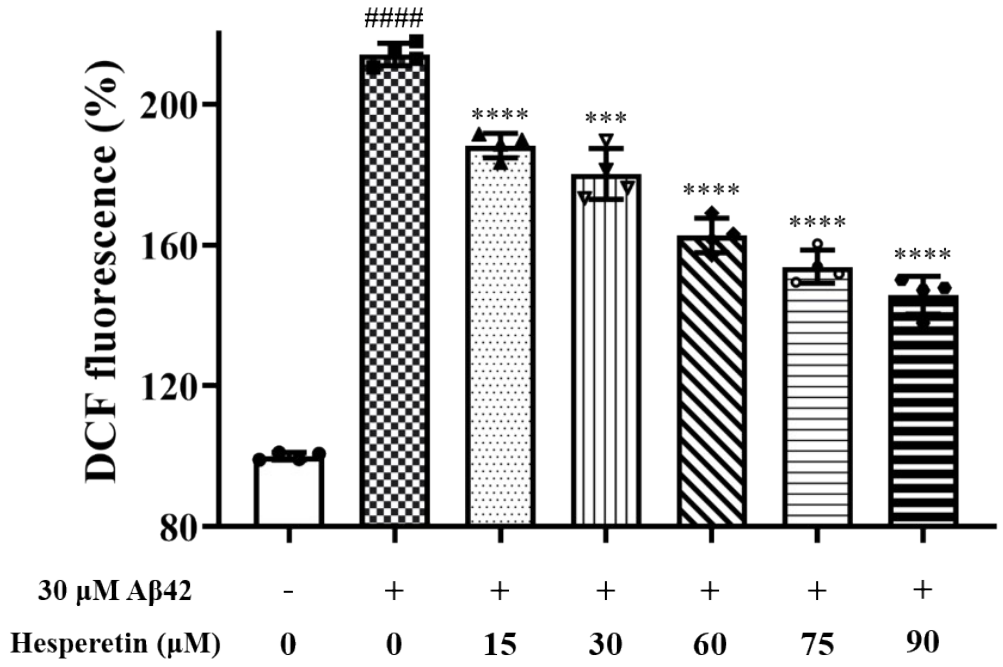

Figure S10 Oxidative stress of different concentrations of hesperetin co-cultured with Aβ42.

Figure S11

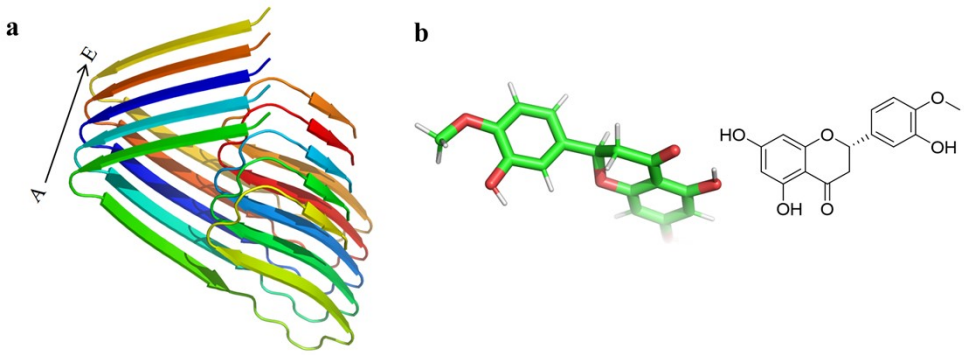

Figure S11 The fibrillary structure of Aβ42 pentamer and hesperetin. (a) The three-dimensional structure of Aβ42 pentamer. (b) The three-dimensional structure (left) and structural formula (right) of hesperetin.

Figure S12

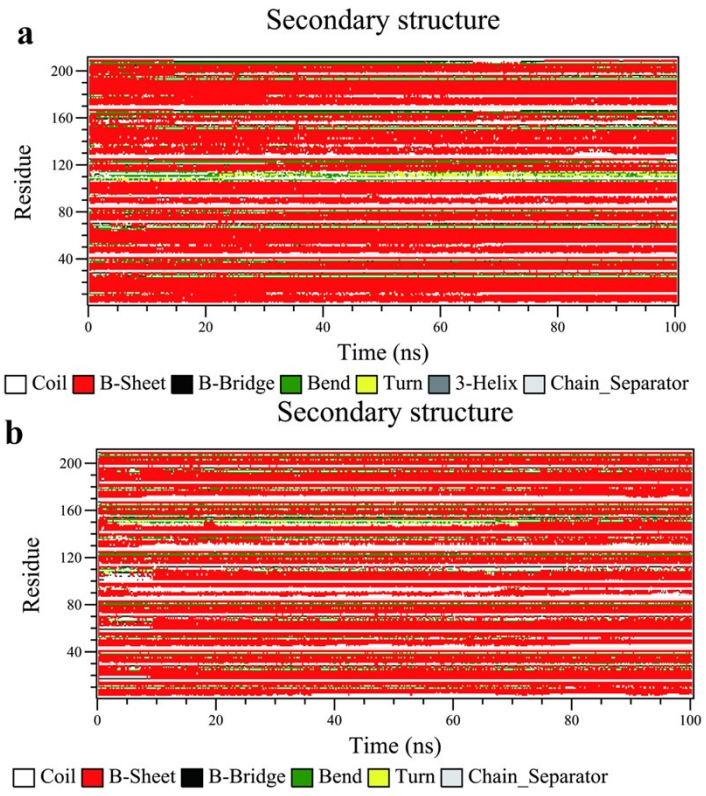

Figure S12 The changes of secondary structure of Aβ42 pentamer in the absence (a) and presence of hesperetin (b).

Figure S13

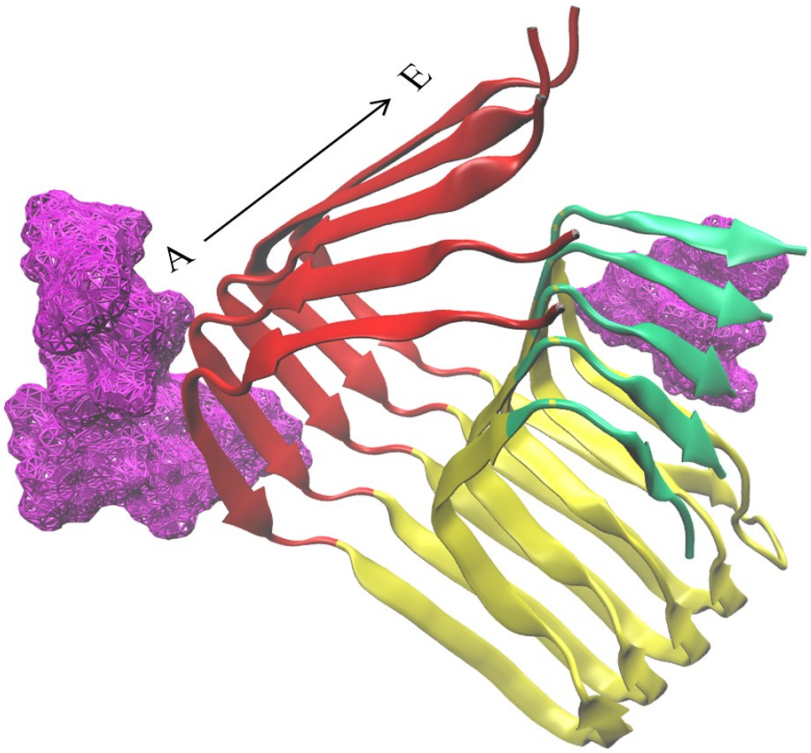

Figure S13 A typical configuration of the spatial distribution of hesperetin on Aβ42 pentamer. Among them, the Aβ42 pentamer is divided into three parts, the R1 region (Red) including residues D1−Q15; the R2 region (Yellow) formed by residues I16-G37 and the R3 region (Green) formed by residues G38-A42. In addition, hesperetin is expressed in purple Wireframe mode.

Figure S14

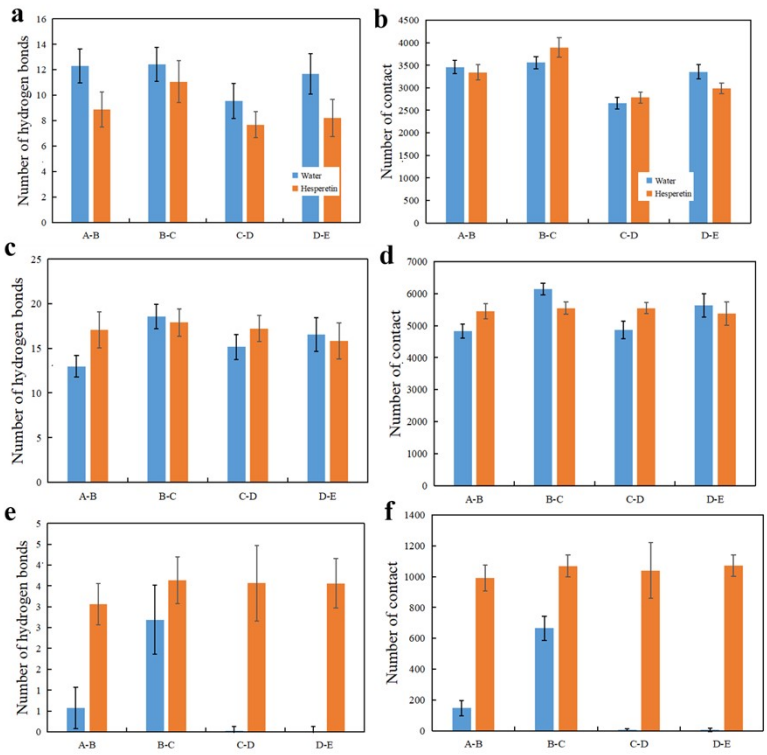

Figure S14 100 ns simulation period, the number of hydrogen bonds and the number of contacts between Aβ42 pentamer in aqueous solution and hesperetin system. The number of hydrogen bonds of the R1 region (a), the R2 region (c) and the R3 region (e). The number of contacts of the R1 region (b), the R2 region (d) and the R3 region (f).

Figure S15

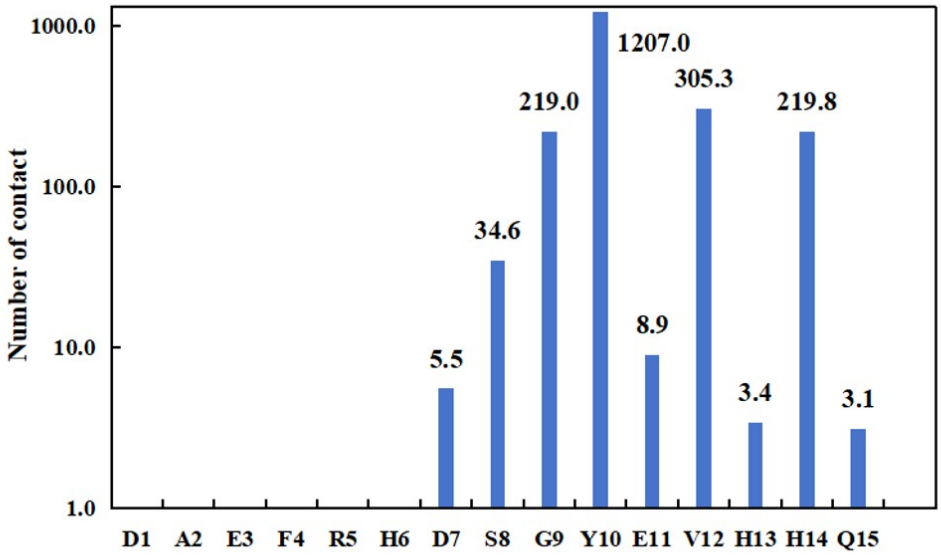

Figure S15 100 ns simulation period, the average number of contacts between each amino acid in the R1 region of Aβ42 pentamer and hesperetin system in aqueous solution.