Effect of Flavonoids (ZGM1) on the Aggregation of Beta-amyloid Peptides and Mechanisms

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OBJECTIVE: To investigate the mechanism by which flavanol (ZGM1,2-(2,3-dihydroxyphenyl)-5,7-dimethoxychroman-4-one) changes the aggregation process of beta-amyloid (Abeta) and verify the protective effect of ZGM1 on cognitive function of APP/PS1 mice. METHODS: At the molecular level, the effect of ZGM1 on Abeta aggregation was observed by Western Blotting, and the direct binding force of ZGM1 to Abeta was determined by microscale thermophoresis (MST). After combining the results of Dot Blotting, Thioflavine T fluorescence spectroscopy (ThT), and transmission electron microscopy (TEM), the mechanism of ZGM1 mediated Abeta aggregation was analyzed. At the cellular level, the self-toxicity of ZGM1 was detected by MTT assay, and the intervention effect of ZGM1 on APP overexpressing cells was observed by long-term live cell imaging technique (Incucyte). At individual level, the maze test was used to explore the protection of ZGM1 on cognitive function of APP/PS1 mice, and the effect of ZGM1 on the formation of amyloid plaques in brains was studied using Thioflavine S (ThS) staining. RESULTS: ZGM1 binds to Abeta and promotes assembly of non-toxic aggregates. ZGM1 has low cytotoxicity and can improve the cytotoxicity of APP overexpression. Animal experiments have shown that low concentrations of ZGM1 improve cognitive impairment in APP/PS1 mice, but accelerate the increase of cerebral amyloid plaque formation. CONCLUSION: ZGM1 stabilizes the non-beta-sheet Abeta oligomers which are low toxic at 98.6 Fahrenheit, and acts as a seed to directly mediate the formation of amyloid plaques, crossing the stage of highly toxic soluble Abeta oligomers (AbetaOs). It reduces the neurotoxicity mediated by Abeta aggregation and provides a new idea for the treatment of Alzheimer's disease.

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