Fulvic Acid Inhibits Aggregation and Promotes Disassembly of Tau Fibrils Associated with Alzheimer's Disease.

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Source

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Abstract

Alzheimer's disease is a neurodegenerative disorder involving extracellular plaques (amyloid-β) and intracellular tangles of tau protein. Recently, tangle formation has been identified as a major event involved in the neurodegenerative process, due to the conversion of either soluble peptides or oligomers into insoluble filaments. At present, the current therapeutic strategies are aimed at natural phytocomplexes and polyphenolics compounds able to either inhibit the formation of tau filaments or disaggregate them. However, only a few polyphenolic molecules have emerged to prevent tau aggregation, and natural drugs targeting tau have not been approved yet. Fulvic acid, a humic substance, has several nutraceutical properties with potential activity to protect cognitive impairment. In this work we provide evidence to show that the aggregation process of tau protein, forming paired helical filaments (PHFs) in vitro, is inhibited by fulvic acid affecting the length of fibrils and their morphology. In addition, we investigated whether fulvic acid is capable of disassembling preformed PHFs. We show that the fulvic acid is an active compound against preformed fibrils affecting the whole structure by diminishing length of PHFs and probably acting at the hydrophobic level, as we observed by atomic force techniques. Thus, fulvic acid is likely to provide new insights in the development of potential treatments for Alzheimer's disease using natural products.