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# The volatile compounds α-asarone and β-caryophyllene promote disassembly and dis-aggregation of tau fibrils and natural aggregates

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## Abstract

Aggregation and assembly of hyperphosphorylated tau into neurofibrillary tangles (NFTs) is one of the main pathological hallmarks of Alzheimer's disease (AD) and other tauopathies. A critical step in the formation of NFTs involves the conversion of soluble tau into insoluble fibrils and aggregates. Disassembly and disaggregation of tau fibrils and aggregates into the non-toxic tau oligomeric species is recognized as a viable therapeutic strategy. In the current study, the effects of the volatile compounds α-asarone (ASA) and β-caryophyllene (BCP) were assessed for their potential to promote the disassembly and dis-aggregation of tau fibrils and aggregates. SDS-PAGE analysis revealed that both ASA and BCP, at certain concentrations, could convert the high molecular weight tau species into their low molecular weight counterparts or monomeric forms. The ThT fluorescence intensities of the pre-formed tau fibrils and aggregates diminished in the presence of the volatile compounds ASA and BCP. Furthermore, circular dichroism spectroscopy analysis indicated that ASA and BCP substantially diminished the β-sheet structure of the tau samples, concomitantly increasing the α-helix or random coil contents. Additionally, atomic force microscopy images illustrated that ASA and BCP possess the capacity to convert tau fibrils or aggregates into tau intermediate oligomers. MTT assays indicated that these tau oligomers formed in the presence of ASA and BCP were less toxic to the SH-SY5Y neuroblastoma cells, in comparison to the not-treated positive control sample. All results revealed the potential protective effects of ASA and BCP on tau fibrils and aggregates. Consequently, the volatile

compounds ASA and BCP warrant further investigation due to their neuroprotective and therapeutic activities against AD and other tauopathies.

**Keywords:** α-asarone, β-caryophyllene, Disassembly, Dis-aggregation, tau protein, Alzheimer's disease