The Diarylheptanoid (+)-*S*-Myricanol from *Myrica cerifera* (Bayberry) and its Derivatives Destabilize the Microtubule-Associated Protein Tau.

Alzheimer Disease (AD) is a neurodegenerative disorder and the most common form of dementia that affects approximately 5.1 million americans and this number is rising in line with the aging population. The cause of the AD is not well known and to rationale a target pathway the cholinergic, amyloid and tau hypotheses were proposed. Target-based drug discovery for AD based on the acetylcholine production and modulation of the amyloid plaques formation have not been effective. The overlooked approach focused on tau aggregation was used in our previous bioassay-guided fractionation of a reducing tau root bark extract of *Myrica cerifera* (bayberry) and lead to the identification *S*-(+)-myricanol as a tau destabilizer agent. This diarylheptanoid compound may represent a novel scaffold for drug development efforts targeting tau turnover in Alzheimer's disease. A larger scale extraction from the bayberry root bark provided enough pure *S*-(+)-myricanol to generate semi-synthetic derivatives. All the myricanol analogs have been screened for their tau level and cytoxicity evaluation.