especially tau oligomers, have been shown critical roles in connection with synaptic impairment and cognition decline in AD. Consequently tau-directed drug discovery has been emerging as a new direction for development of effective AD-modifying agents, especially given the unsuccessful clinical trials of Ab targeted therapies. Methods: A rationally designed small molecule bivalent compound, ZCM-I-1, from the structures of curcumin and melatonin was characterized to inhibit the aggregation of tau441, remodel the aggregates of tau441, and rescue MC65 cells from tau-induced cytotoxicity by biochemical, biophysical and cellular assays. Results: Our studies demonstrated that ZCM-I-1 efficiently remodeled the tau441 aggregates at a 1:2 ratio in a Thioflavien T fluorescence based assay. When compared to EGCG, a known tau aggregation inhibitor, ZCM-I-1 exhibited significantly improved efficacy. Transmission electron microscopy studies also confirmed the remodeling effects of ZCM-I-1 on tau441 fibrils. Notably, our studies on the aggregation of tau441 also identified ZCM-I-1 as an aggregation inhibitor with an IC_{50} of 20.05 uM. In a cellular AD model, ZCM-I-1 efficiently protected MC65 cells from extracellular tau441 fibril induced cytotoxicity. Conclusions: Our studies established that ZCM-I-1 exhibits promising inhibitory activity on tau aggregation. ZCM-I-1 also shows activity to restructure tau441 aggregates to less toxic species. Combining the results of our previous studies of ZCM-I-1 on Ab and oxidative stress, the results strongly encourage further development of ZCM-I-1 and analogs as novel and effective disease modifying agents for AD.