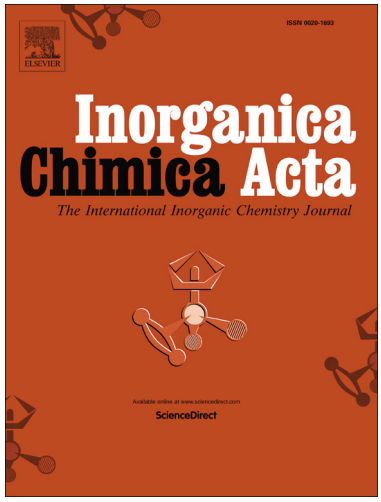

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Tau-peptide fragments and their copper(II) complexes: effects on Amyloid-β aggregation.

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Abstract

Recent studies suggest that the interaction of Aβ and Tau may be significant in the pathogenesis of Alzheimer's Diseases (AD). In addition, the potential influence of copper on Tau-related pathology in AD has not been previously addresseded and the interaction between Tau protein, Aβ and Copper has even more recently been associated with AD. While the copper(II) interaction with the Aβ peptide has exhaustively been studied, the few studies carried out on copper(II) complexes with peptide fragments from Tau protein have been focused on the pseudo-repeats of Tau protein in the microtubule-binding region. No data have been reported about the metal complexes with peptides derived from the N-terminal portion of Tau protein, outside the microtubule-binding domain, despite increased levels of peptide fragments from this region have been detected in the Cerebrospinal fluid (CSF) of AD patients. Here we examine the interaction of two peptides fragments, encompassing the 1-25 or 26-44 residues of the human Tau protein sequence, with Aβ as well as the Cu^{2+}-binding features of these two naturally occurring peptides. The CD experiments showed that copper(II) differently affects the peptide conformation of the two ligands and provided also insight into the donor atoms involved in metal coordination. Stoichiometry of copper(II) complexes was obtained by means of High Resolution ESI-MS. Finally, the influence of the studied peptide on Aβ's fibrillogenesis, either in the presence or absence of Cu^{2+}, was investigated by means of Th-T fluorescence coupled with turbidimetric measurements. The observed different effect on the *in vitro* Aβ's aggregation, was correlated with the affinity of copper(II) with the two peptide ligands. The overall results indicate that copper(II) can bind these peptides using the