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Role and interplay of copper(II) and related ligands as effectors of α-synuclein

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The progressive loss of neuronal cells, as well as the decline of cognitive and motor functions are common features of several neurodegenerative disorders, such as Parkinson's disease (PD) and α-synucleinopathies. Other key factors in the development of these disorders should be oxidative stress, dyshomeostasis of metal ions and α-synuclein (αSyn)(1,2). Moreover, the abnormal aggregation process of αSyn is considered a crucial event in the pathogenesis of α-synucleinopathies. Metal-protein interactions play an important role in αSyn aggregation and might represent a link between the pathological processes of protein aggregation, oxidative damage, and neural death. High Copper concentration is detected the cerebrospinal fluid of PD patients, as well as in the Lewy bodies, the intracellular aggregates of αSyn. Moreover, Copper regulates αSyn intracellular localization and cytotoxicity(2). Lipoxidation and carbonylation have also been observed in neurodegenerative diseases. αSyn seems to induce lipid peroxidation and, conversely, αSyn carbonylation has been found in PD. In particular, acrolein (ACR) and 4-hydroxy-nonenal (HNE) have been reported to affect the aggregation process of αSyn(3). The interplay between ACR, copper, and αSyn has been recently investigated(4). Moreover, we comprehensively assessed the interaction with αSyn ability and inhibitory properties in preventing α-Syn aggregation of a series of glyco- and dipeptide-conjugates of 8-hydroxyquinoline, well-known molecules that provide neuroprotection in neurodegenerative disorders.

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