

Natural and synthetic effectors of alpha-synuclein: features and interplays

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Parkinson's disease (PD) and α -synucleinopathies are characterized by the progressive loss of neuronal cells and the decline of cognitive and motor functions. Oxidative stress, dyshomeostasis of metal ions and α -synuclein (α Syn) should be key factors in the development of these disorders^{1,2}. Moreover, the aggregation of α Syn is a crucial event in the pathogenesis of α -synucleinopathies. Metal-protein interactions play an important role in α Syn aggregation and might represent a link between the pathological processes of protein aggregation, oxidative damage, and neural death. High Copper concentration is detected in the cerebrospinal fluid of PD patients, as well as in the Lewy bodies, the intracellular aggregates of α Syn. Moreover, Copper regulates α Syn intracellular localization and cytotoxicity². Lipoxidation and carbonylation have also been observed in neurodegenerative diseases. α Syn seems to induce lipid peroxidation and, conversely, α Syn carbonylation has been found in PD. In particular, acrolein (ACR) and 4-hydroxy-nonenal (HNE) have been reported to affect the aggregation process of α Syn³. The interplay between ACR, copper, and α Syn has been recently investigated⁴. Moreover, we comprehensively assessed the interaction with α Syn 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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