Parkinson’s Disease: Evaluating the Effects of Possible Anti-parkinsonian Compounds on Alpha-Synuclein Aggregation and Neurotoxicity.

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The aggregation of many proteins and polypeptide chains is the hallmark of many diseases called collectively as amyloidosis. Parkinson’s disease (PD) is a chronic disorder characterized by the formation of intraneuronal inclusions called Lewy bodies mainly composed of α-synuclein (AS), a natively-unfolded protein. Up to now, the only available treatment administered to PD patients is L-dopa, the precursor of dopamine.

Selegiline (Sel) is a monoamino oxidase-B inhibitor with neuroprotective effects. It has been administered to PD patients either as monotherapy or in combination with L-dopa. Our group has evaluated the effect of Sel in the in vitro aggregation of wt and A30P α-syn. We could not map any specific interaction of Sel with monomeric AS but our data showed that Sel was able to delay AS fibril formation leading to the formation of an aberrant aggregate of AS, which showed to be non-toxic to dopaminergic neurons in culture. Our data showed that Sel acts specifically in the nucleation phase of AS aggregation. Taken together these data suggest that administration of Sel to PD patients abolished the formation of toxic aggregates in route to fibril formation.

Edaravone (ED) has anti-oxidant properties and has neuroprotective effects against 6-hidroxidopamine induced neurodegeneration. We also tested the effect of ED on AS aggregation. Our data shows that ED seems to interact with WT AS, as observed in NMR experiments, modulating its aggregation and is neuroprotective against the toxicity of α-syn oligomers.

These data will be discussed in the light of possible therapies against PD.