EFFECTS OF SELEGILINE ON THE IN VITRO AGGREGATION OF A30P a-SYNUCLEIN: NEW PERSPECTIVES IN PARKINSON´S THERAPY

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Parkinson`s disease (PD) is a chronic disorder characterized by the formation of intraneuronal inclusions called Lewy bodies mainly composed of α-synuclein (α-syn). Alpha-syn is a natively-unfolded protein with unknown function and its implication in PD is due to the fact that two mutations (A30P and A53T) are linked to early-onset forms of PD. Selegiline (R(-)-deprenyl) is a noncompetitive monoamino oxidase-B inhibitor which has neuroprotective effects. It has been administered to PD patients either as monotherapy or in combination with L-dopa. However, the mechanism by which Sel works in unknown. We evaluated the effect of Sel in the *in vitro* aggregation of A30P?either in the presence or absence of amyloid seeds (small fibrils acting as a nucleus). We observed that Sel (1:10 protein:Sel) delays fibril formation by enhancing the nucleation phase. Sel effects on fibril formation are abolished when previously added seeds are present. Also, Sel in combination with dopamine (DA) favors fibril formation. These results suggest that in the presence of DA, Sel favors the conversion of the toxic protofibrils into the non-toxic fibrils, alleviating the dopaminergic neurons from toxic effects. In the non-dopaminergic neurons, Sel would slow down the fibrillation process, probably by forming large spherical aggregates. The toxicity of these aggregates is under observation by our group.
Keywords: Parkinson, synuclein, selegiline.