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Promising Organochalcogens for the treatment of amyloid-beta related diseases: a preliminary study in *Caenorhabditis elegans*

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Amyloid-beta (A β) related diseases such as Alzheimer's disease (AD) are neurodegenerative diseases that have no cure and have a limited therapeutic scope. AD pathophysiology involves the formation of an insoluble peptide (amyloid beta), neuroinflammation, neuronal death and behavioral alterations that include cognitive deficits and locomotion impairment. Of note, it is not clear what triggers amyloid beta formation in the subjects, since genetic mutations are not the only cause of this disease and evidences point out to toxicants and microbiota involvement as well. The drugs currently used in the treatment are directed to only one therapeutic target, such as inhibition of acetylcholinesterase (AChE) activity or in reducing the formation and aggregation of A β plaques. Preliminary studies with organochalcogens from some classes indicated their multitarget potential, acting as antioxidants, antiinflammatory and AChE inhibitors. In this sense, our group has been screening new compounds using an *in vivo* model for A β aggregation with a paralysis phenotype, the nematode *Caenorhabditis elegans*. The transgenic animals used in the studies have a human mutated form of A β which causes oxidative stress, neurodegeneration, paralysis and reduced longevity, similar to the phenotype observed in humans. So far, we have identified promising selenoesters, selenoureas and a phenyltelluril-chloroquinoline that have antioxidant potential, modulate important antioxidant and antiinflammatory pathways such as DAF-16, modulate the expression of heat shock proteins, important for degrading malformed peptides as A β and also cause some inhibition in AChE activity. These compounds reduced paralysis rate in the treated worms and also prolonged their lifespan. These studies reduce and refine the use of rodents in drug screening for AD and provide molecular mechanisms to target and treat this neurodegenerative disease.