Repurposing CNI-1493 to Treat Alzheimer's Disease: Attenuation of Intracellular Amyloid Beta in vitro and in vivo

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The purpose of this study was to investigate the anti-amyloid and anti-inflammatory properties of CNI-1493 as a treatment for intracellular amyloid beta toxicity and chronic neuro-inflammation. Three types of studies were performed in this study: a cell free model of amyloid beta aggregates were treated with CNI-1493 to measure the formation of fibrils and oligomers; an in vitro analysis using human neuroblatoma cells and microglia cells to test for the presence of intracellular amyloid beta and effects of CNI-1493 on inflammation; an in vivo analysis using C. elegans strain CL2006, which genetically expresses human amyloid beta in its muscle wall and phenotypically expresses paralysis, to determine the effects of CNI-1493 on ntracellular amyloid beta plaque destruction. Data was analyzed using a student’s t-test where ($p<.05$). Results show that the drug directly interacts with amyloid beta. CNI-1493 reduced fibril and oligomer formation by 21.5% and 45.83% ($p<.02$) respectively. In a cell free system CNI-1493 changes the structure of soluble and insoluble amyloid beta aggregates. Additionally, CNI-1493 attenuates intracellular amyloid beta toxicity in vivo in the transgenic C. elegans strain CL2006 where worms treated with CNI-1493 had 50% of the population move over 79.722 units with only 43.64 units for the untreated group ($p=.0017$). Lastly, CNI-1493 significantly reduced inflammation levels in inflammatory microglia cell. By mitigating inflammation and amyloid beta aggregation, CNI-1493 targets two major pathways of AD. Taken together, CNI-1493 represents a future drug candidate to be repurposed for the treatment of a-beta-mediated inflammatory diseases.

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