

Andrographolide recovers cognitive impairment in a natural model of Alzheimer's disease (*Octodon degus*)

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Abstract

The social species *Octodon degus* (degu) is the only wild-type South American rodent that develops Alzheimer's-like pathology with age. Here, we evaluated the ability of a natural product (Andrographolide, ANDRO), a diterpene of the labdane family obtained from the Asian plant *Andrographis paniculata*, to recover the cognitive decline in this long-lived animal model. We administered ANDRO to aged degus (56-month old) for 3 months. In addition, in 2 control groups (young degus: 12-month old and aged degus: 56-month old), we administered saline solution as a vehicle. We evaluated cognitive performance through several behavioral tests. We also performed a series of physiological and biochemical analyses (e.g., electrophysiological and immunoblotting assessment) to identify possible mechanisms underlying cognitive performance associated with age. Our results suggest that there is an effect of aging on the loss of cognitive function, and this decrease in cognitive function was also related to a decrease in the synaptic functions and an increase in the main hallmarks of Alzheimer's disease (AD). More importantly, ANDRO treatments showed the following beneficial effects: (1) recovery of spatial memory and learning performance; (2) recovery of synaptic basal transmission; (3) partial or complete protection of certain synaptic proteins; and (4) a specific neuroprotective effect, including the reduction of phosphorylated tau protein and amyloid beta aggregate maturation in aged degus. Taken together, our results suggest that ANDRO could be used as a potential therapy for AD and support the use of *O. degus* as a natural model in which to study both neural damage associated with aging processes and the behavioral and neuropathological hallmarks of aging-related diseases such as AD..