Effect of co-ultramicronized PEALut treatment in a murine model of autism spectrum disorder

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Autism spectrum disorders (ASDs) are pervasive neurodevelopmental disorders characterized by neurological deficits, especially as related to cognitive function. Although its pathogenesis remains unknown, the major hypothesis at present posits that autism is a multifactorial disorder with a genetic predisposition. Brain inflammation can be a key element in the pathogenesis of neuropsychiatric disorders, including a significant proportion of subjects with ASD. N-palmitoylethanolamide (PEA) is considered to be the parent molecule of ALIAmides, known for its anti-inflammatory, analgesic and neuroprotective properties. PEA inhibits peripheral and central neuroinflammation as well as associated symptomatology. Flavonoids, such as luteolin, possess neuroprotective actions in central nervous pathophysiological conditions. Moreover, the association of PEA with Luteolin (co-ultra PEALut) is more effective in eliciting neuroprotective and anti-inflammatory actions in different models of CNS pathologies, than the molecule taken alone**.**

Our goal was to evaluate the effects evoked by orally administration of co-ultra PEALut in the management of inflammatory and neuroregenerative events associated with ASD using a well established experimental model. A multidisciplinary approach was employed to study: behavioral taks; neuroinflammatory pathways; neurogenesis and neuroplasticity alterations.

On P14, C57BL/6 mice were injected with 400 mg/kg sodium valproate. Two different set of experiments were conducted. In the first, on P15 mice were administered with co-ultraPEALut (1mg/kg, daily) and on P30 the behavioral and neuroinflammatory studies were assessed. In the second, at P120, mice started treatment with co-ultraPEALut (2 weeks) and then were sacrified for neurogenesis and neuroplasticity investigations.

Co-ultraPEALut ameliorated aggressive behavior and improved spatial learning memory in the valproic acid-induced autistic mice. Moreover, our results revealed the ability of co-ultraPEALut to reduce the level expression of NF-κB, GFAP and nitrotyrosine; also modulate apoptosis in hippocampus and cerebellum. Moreover co-ultraPEALut increases neurogenesis and neuroplasticity in the hippocampus of the autistic mice.