IN Volvement of B-Catenin SIGNALING IN CURCUMIN PROTECTING AGAINST AB1-42" INDUCED NEUROTOXICITY


Biochemistry, Federal University of Rio Grande do Sul (UFRGS), Porto Alegre, Brazil

Introduction: Alzheimer's disease (AD) is a neurodegenerative disorder, which is probably caused by the neurotoxic effect of the amyloid β-peptide (Aβ). Substantial evidence indicates that curcumin has neuroprotective properties in AD. However, the molecular mechanisms remain far from established.

Aims: The aim of this study was investigate whether curcumin possesses a neuroprotective effect against Aβ1-42-induced toxicity in both in vitro and in vivo models of the disease.

Methods: For this purpose, organotypic hippocampal cultures were exposed to Aβ1-42 (2 µM) for 48 hours with or without curcumin (0.5, 1, 5 and 10 µM). Cell death was measured by propidium iodide uptake in the slices. In vivo study was designed to investigate the beneficial effect of curcumin (100mg/kg/day, i.p.; 10d) on bilaterally intracerebroventricular Aβ1-42 (2nmol)-induced memory dysfunction in male Wistar rats (object recognition test). Cell signaling pathways were investigated by performing Western blot assay.

Results: Our results show that Aβ1-42 caused about 30% of cell damage in hippocampal slices, a significant increase when compared to controls cultures. The treatment with curcumin (5 and 10 µM) decreased the cell death significantly. The administration of Aβ1-42 in rats caused, 2 weeks later, memory impairment and the curcumin treatment prevented this decreased performance in object recognition test. In both models, Aβ1-42 neurotoxicity resulted in an increased in phosphorylated (Ser45) β-catenin and curcumin treatments prevented this β-catenin destabilization.

Conclusions: These findings suggest that curcumin may provide an effective neuroprotection against Aβ1-42 peptide by modulating β-catenin levels, a key transducer of the Wnt signaling pathway.