Involvement of PI3-K Pathway and β-catenin Signaling in curcumin Protecting Against Aβ1-42-Induced Neurotoxicity

Hoppe, J.B., Lisbôa, L.M., Frozza, R.L., Meneghetti, A.B., Silva, T., Salbego, C.G.

Departamento de Bioquímica, UFRGS, RS, Brazil.

Alzheimer’s disease (AD) is the most prevalent form of dementia. New treatments to manage this complex illness will require full understanding of the pathophysiological mechanisms involved, which include amyloid β (Aβ)-induced toxicity. Substantial evidence indicates that curcumin has neuroprotective properties in AD; however, the molecular mechanisms involved in this process remain poorly understood. The aim of this study was investigate whether curcumin possesses a neuroprotective effect against Aβ-induced toxicity organotypic hippocampal cultures. Slices were exposed to Aβ, curcumin and/or LY294002, an inhibitor of phosphoinositide-3-kinase (PI3-K) pathway. Cell death was measured by propidium iodide uptake and some cell signaling pathways were investigated by Western blot assay. Moreover, we measured the synaptophysin expression, involved in the regulation of synaptic plasticity. Our results show that Aβ caused about 30% of cell damage in hippocampal slices, a significant increase when compared to controls cultures. The treatments with 5 and 10 µM of curcumin decreased the cell death significantly. The curcumin treatment prevented the decreased in synaptophysin expression after exposure to Aβ peptide. Aβ treatment increased the phosphorylated (Ser45) β-catenin and decreased β-catenin immunocontent, and the curcumin treatment prevented this β-catenin destabilization. Additionally, the curcumin neuroprotection was prevented by LY294002 and curcumin induced the phosphorylation/activation of Akt and the phosphorylation/inactivation of glycogen synthase kinase-3β (GSK-3β). These results reinforce the neuroprotective effect of curcumin and add some evidence that its mechanism may involve the PI3-K pathway and β-catenin signaling, a key transducer of the Wnt signaling pathway.

Word Keys: Alzheimer, Amyloid-β, Curcumin, Organotypic Cultures, Neuprotective, Neurotoxicity.
Supported by: CNPq and CAPES