THE 6-(METHYLSULFINYL)HEXYL ISOTHIOCYANATE AS NEUROPROTECTIVE AGENT IN A MURINE MODEL OF ALZHEIMER'S DISEASE

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Alzheimer's disease (AD) is considered the most frequent neurodegenerative disease age-related and the main cause of dementia in elderly patients. AD is characterized by the progressive loss of cognitive capacities, in the beginning it involves the short term memory ability and then all intellectual functions are compromised. The principal morphological abnormalities that could be observed in the evolution of AD are the formation of neuritics plaques of β-amyloid (Aβ) protein and the intracellular neurofibrillary agglomerates of tau protein hyperphosporylated, beyond microgliosis, dystrophic neuritis and neuronal and synaptic death. Though AD etiology is still unknown, the most common hypothesis involved the activation of amyloid cascade, where the crucial event may be an imbalance between production and degradation of Aβ peptide. Isothiocyanates are natural compounds that have already shown interesting neuroprotective properties, especially through an antioxidant activity, and in AD, an anti-amyloidogenic property. The 6-(methylsulfinyl)hexyl isothiocyanate (6-MSITC), abundant in the rizome of Wasabia Japonica, has shown interesting anti-inflammatory and antioxidant activities.

The aim of the present study is to investigate the potential neuroprotective properties of 6-MSITC in an experimental murine model of AD. We utilized male mice C57BL/6, that received an intracerebroventricular (i.c.v.) injection of Aβ1-42 oligomers and the treatment with 6-MSITC (5 mg/kg) started 1 hour after the surgery for the next 10 days. At the end of the treatment, mice were tested to assess the cognitive function with Morris Water Maze. After the sacrifice, the hippocampus was analyzed through Western Blotting for Akt, Erk1/2 and Gsk3 proteins and cognitive decline was also associated with increased oxidative stress and caspase activation.

In conclusion, results of the present study shows that our AD model is good to create a temporal window to investigate the potential neuroprotective action of novel compounds as 6-MSITC, that is not only able to restore a physiological oxidative status and to interfere positively with Nrf2-pathway, but also to slow down neuronal death and protect neurons to the damage.

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