OFFICIAL ABSTRACT and CERTIFICATION

Linarin and Luteolin Elicit Anti-Aβ Cytotoxicity and Inflammation Properties as Novel Treatments for Alzheimer's Disease

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Alzheimer's Disease (AD) is a dementia-associated neurodegenerative disease characterized by amyloid-beta (Aβ) aggregation and tau protein hyperphosphorylation. Synthetic AD treatments often have adverse side effects, prompting the need for natural treatments. This study examined linarin and luteolin, two plant-derived substances, as potential AD treatments. Linarin and luteolin, individually and combined, were tested on the survival rates of GT1-7 murine neuronal cells and RAW264.7 murine immune cells to investigate the cytotoxic and neuroprotective against Aβ effects, as well as potential synergistic effects. The effects of linarin and luteolin on SK-N-SH human neuroblastoma cell counts were investigated, in addition to the impacts on amyloid precursor protein (APP) concentration in SK-N-SH cells and interleukin-1-beta (IL-1β) concentration in RAW264.7 cells. Results demonstrated that while short-term treatments against Aβ-induced cytotoxicity significantly increased the survival of neuronal ($p<0.01$) but not immune cells, long-term treatments significantly increased survival of neuronal ($p<0.001$) and immune ($p<0.01$) cells. Combined treatments did not significantly increase neuroprotective effects from individual treatments, indicating that linarin and luteolin do not have synergistic effects. Treatments significantly increased the cell count of Aβ-treated cells ($p<0.05$), demonstrating neuroprotective properties against Aβ on human neuronal cells. Linarin and luteolin decreased the concentrations of APP and IL-1β in neuronal and immune cells treated with Aβ, respectively, indicating that they ameliorate Aβ-induced cytotoxicity by decreasing both the source of Aβ plaques and proinflammatory cytokines. Therefore, while both linarin and luteolin are neuroprotective against Aβ-induced cytotoxicity and inflammation, which makes them promising novel AD treatments, they have not demonstrated synergistic effects.

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