Diosgeninblocks neuroinflammation in LPS-activated BV2 microglia through mechanisms involving NF-κB

Neuroinflammation is the first line of defence of the central nervous system (CNS) against harmful substances. The pathological mechanism sinneuroinflammation are caused by complex pathological processes including microglial activation (1). Diosgenin is a plant-derived steroidal saponin found in fenugreek (*Trigonellafoenumgraecum*), and roots of wide yam (*Dioscoreavillosa*) (*2*).Some studies have suggested that diosgenin induced anti-inflammatory activity against lipopolysaccharide (LPS)-induced inflammation in mouse primary peritoneal macrophage (3) and mouse lung injury (4). Our previous results howed that diosgenin has an anti-neuroinflammatory effect in LPS-stimulated BV2 cells (5),However, the mechanism of this effect has not yet been determined. In this study the anti-neuroinflammatory effects of diosgenin on LPS-induced nuclear factor kappa beta(NF-κB) andp38 activation were investigated. BV2 cells were pre-incubated with diosgenin (5, 10, and20 μM) prior to stimulation with LPS(100 ng/ml).The effects of diosgenin on the main components of NF-κB signalling pathway were evaluated using western blotting analysis, EMSA and luciferase reporter assay. In addition, protein expression of phospho-p38 was also determined. Diosgenin significantly ($p < 0.001$) decreased the phosphorylation of inhibitory kappaBalpha (IκB-α) and the subsequent nuclear translocation of NF-κB in LPS-activatedBV2 cells. Pretreatment of BV2 cells with diosgeninat a concentration of 20 μMresulted in 34.8 ± 8.5 phsopho-IκB-α and 30.8 ± 5.1 phsopho-NF-κBp65 protein expression when compared to LPS control. In addition, diosgenin significantly ($p < 0.01$) inhibited TNF-α-induced transcriptional activity of NF-κB in HEK293 cells. At 20 μM, diosgenin decreased the TNF-α-induced transcriptional activity of NF-κBby 40.0 ± 6.6 when compared to the TNF-α control. Diosgenin reduced the LPS-induced DNA binding activity of NF-κB in BV2 cells when compared to the LPS control. This compound did not inhibit the phosphorylation of p38 in LPS-stimulatedBV2 cells. The results showed that diosgenin exhibits anti-neuroinflammatory activity through interference with NF-κB signalling pathway in LPS-activated BV2 cells. Taken together, these results suggest that diosgenin might be useful inneurodegenerative diseases that are mediated by microglial hyperactivation.

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