Biochanin-A, an isoflavon, showed antiproliferative and anti-inflammatory activities through the inhibition of iNOS expression, p38-MAPK and ATF-2 phosphorylation and blocking NFκB nuclear translocation.


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Abstract
Biochanin-A, an isoflavone, existing in red clover, cabbage and alfalfa, has an inhibitory and apoptogenic effect on certain cancer cells. However, the actual mechanism by which this compound inhibits proliferation and induces apoptosis in cancer cells and the mechanism of its anti-inflammatory activities have not been well characterized. In this study, we have investigated the anti-inflammatory and anti-proliferative activity of Biochanin-A. The effects of Biochanin-A on RAW 264.7, HT-29 cell lines and mouse peritoneal macrophages have been investigated in vitro. Cell proliferation and anti-inflammatory effects were analyzed by 3-(4,5-dimethylthiazol-2-yl)2,5-diphenyl-tetrazolium bromide (MTT) assay, (3)H-thymidine incorporation assay, Western blot, cytokines estimation, Luciferase assay, Electrophoretic mobility shift assay (EMSA) and Kinase assay. Present investigation demonstrated that, Biochanin-A inhibited lipopolysacharide (LPS)-induced nitric oxide(NO) production in macrophage and showed dose dependent inhibition of inducible nitric oxide synthase (iNOS) expression. The induction of NF-κB binding activity by LPS was inhibited markedly by co-incubation with different doses of Biochanin-A. Biochanin-A inhibited the LPS-induced IκB kinase (IKK) activity and nuclear factor kappa beta (NF-κB) activation associated with the inhibition of iNOS expression. LPS-induced phosphorylation of IκBα and p38 MAPK was blocked by Biochanin-A and it inhibited IL-6, IL-1β and TNF-α production in RAW264.7 cells indicating its anti-inflammatory activity in association with anti-proliferation. Biochanin-A is important for the prevention of phosphorylation and degradation of IκBα, thereby blocking NF-κB activation, which in turn leads to decreased expression of the iNOS, thus preventing proliferation and inflammation.

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