Diosgenina inibe a proliferação de células K562 da leucemia mielógena parando o ciclo celular em G2/M e aumenta a apoptose via mitocondria

Diosgenin induces cell cycle arrest and apoptosis in human leukemia K562 cells with the disruption of Ca2+ homeostasis.

Liu MJ, Wang Z, Ju Y, Wong RN, Wu QY.

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Source

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Abstract

PURPOSE:

Diosgenin is a steroidal sapogenin with estrogenic and antitumor properties. In order to elucidate the mechanism of its antiproliferative activity, we investigated its effects on the cell cycle and apoptosis in human chronic myelogenous leukemia K562 cells.

METHODS:

Cell viability was assessed via an MTT assay. Apoptosis was investigated in terms of nuclear morphology, DNA fragmentation, and phosphatidylserine externalization. Cell cycle analysis was performed via PI staining and flow cytometry (FCM). Western blotting and immunofluorescence methods were used to determine the levels of p53, cell cycle-related proteins and Bcl-2 family members. FCM was also used to estimate the changes in mitochondrial membrane potential (MMP), intracellular Ca2+ concentration and reactive oxygen species (ROS) generation.

RESULTS:

Cell cycle analysis showed that diosgenin caused G2/M arrest independently of p53. The levels of cyclin B1 and p21Cip1/Waf1 were decreased, whereas cdc2 levels were increased. Subsequent apoptosis was demonstrated with the dramatic activation of caspase-3. A dramatic decline in intracellular Ca2+

concentration was observed as an initiating event in the process of cell cycle arrest and apoptosis, which was followed by the hyperpolarization and depolarization of MMP. Generation of ROS was observed in the progression of apoptosis. The antiapoptotic Bcl-2 and Bcl-xL proteins were downregulated, whereas the proapoptotic Bax was upregulated.

CONCLUSIONS:

Diosgenin inhibits K562 cell proliferation via cell cycle G2/M arrest and apoptosis, with disruption of Ca2+ homeostasis and mitochondrial dysfunction playing vital roles.

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