Diosgenin induces cell cycle arrest and apoptosis in HEL cells with increase in intracellular calcium level, activation of cPLA2 and COX-2 overexpression.

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Source

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Abstract

Many natural components of plant extracts are studied for their beneficial effects for health and particularly on carcinogenesis chemoprevention. In the present study, we investigated the effects of diosgenin on erythroleukemia HEL cells. Our results demonstrated that diosgenin induced G2/M arrest of cell cycle progression through p21 up-regulation in a p53-independent pathway and strong induction of apoptosis in HEL cells. Apoptosis induction was accompanied by an increase in Bax/Bcl-2 ratio, PARP cleavage and DNA fragmentation. Moreover, we showed for the first time that diosgenin provoked a collapse of mitochondrial membrane potential with an increase in intracellular calcium levels. It is well known that [Ca2+]i increase is one of the major activators of cytosolic PLA2. In our study, we demonstrated that diosgenin treatment induced cPLA2 activation through translocation to the cellular membrane. Moreover, arachidonic acid metabolism activation led to cyclooxygenase-2 (COX-2) but not lipoxygenase overexpression. Surprisingly, we observed a COX-2 up-regulation associated with apoptosis induction by diosgenin. These findings suggest that diosgenin has a potential chemopreventive effect; future studies should evaluate the mechanism of COX-2 activation during diosgenin-induced apoptosis in cancer cell lines.

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