Molecular Mechanisms of Magnolol-Induced Apoptosis in Human Hepatoma Cells.

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Abstract

Magnolol has been reported to have anticancer activity. In this study we found that treatment with 100 microm magnolol induced apoptosis in cultured human hepatoma (Hep G2) and colon cancer (COLO 205) cell lines but not in human untransformed gingival fibroblasts and human umbilical vein endothelial cells. Our investigation of apoptosis in Hep G2 cells showed a sequence of associated intracellular events that included (a) increased cytosolic free Ca(2+); (b) increased translocation of cytochrome c (Cyto c) from mitochondria to cytosol; (c) activation of caspase 3, caspase 8, and caspase 9; and (d) downregulation of bcl-2 protein. Pretreatment of the cells with the phospholipase C inhibitor 1-[6-[[(17 beta)-3-methoxyestra-1,3,5(10)-trien-17-yl]amino]hexyl]-1 H-pyrrole-2,5-dione (U73122) or the intracellular chelator of Ca(2+) 1,2-bis(2-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid acetoxymethyl ester (BAPTA/AM) inhibited the subsequent magnolol augmentation of [Ca(2+)](i) and also the activation of caspase-8 and caspase-9, so that the occurrence of apoptosis in those cells was greatly reduced. Pretreatment of the cells with ZB4 (which disrupts the Fas response mechanism) also decreased the subsequent magnolol-induced caspase-8 activation and reduced the occurrence of apoptosis. We interpreted these findings to indicate that the above-listed sequence of intracellular events led to the apoptosis seen in Hep G2 cells and that [Ca(2+)](i), Cyto c, and Fas function as intracellular signals to coordinate those events.