P11

Bcl-2 overexpression prevents β-sitosterol-induced apoptosis in U937 cells by inhibition of caspase-3 activity and XIAP expression

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β-sitosterol is the main dietary phytosterol found in plants, and has been shown to induce anti-proliferation and apoptosis of human cancer cell lines. This study investigated the mechanism of apoptosis induced by β-sitosterol in human leukemic U937 cells. β-sitosterol induced cytotoxicity and apoptosis in U937 cells in a concentration dependent manner and the increase in apoptosis by β-sitosterol was correlated with the down-regulation of XIAP, degradation of PARP and PLC-γ1 protein and activation of caspase-3 without changes in the expression of the Bcl-2 family members. z-DEVD-fmk, a caspase-3 specific inhibitor, blocked caspase-3 activation and PARP degradation, and increased the survival rate of β-sitosterol-treated U937 cells. This suggests that caspase-3 activation is essential for β-sitosterol-induced apoptosis. Although β-sitosterol did not alter Bcl-2 expression, Bcl-2 overexpression significantly blocked caspase-3 activation, the decrease in XIAP and PARP cleavage by β-sitosterol, and effectively attenuated the apoptotic response to β-sitosterol. These results show that βpotently induces apoptosis in U937 cells, and βapoptosis is related to the selective activation of caspase-3 and the down-regulation of XIAP.

Keywords : β-sitosterol, apoptosis, caspase-3, Bcl-2, XIAP

P12

Growth inhibition and apoptosis of human colon cancer cells by sanguinarine, a benzophenanthridine alkaloid

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Sanguinarine, derived from the root of *Sanguinaria canadensis* and other poppy fumaria species, is known to exhibit anti-microbial, anti-inflammatory and anti-oxidant properties. However, the mechanism by which sanguinarine induced-apoptosis is not completely understood. In the present study, we investigated the biochemical mechanisms of apoptosis induction by sanguinarine in human colon cancer cells. At a 0.6-1.2 microM dose-level, sanguinarine significantly enhanced apoptosis measured by flow cytometry analysis. Sanguinarine caused apoptosis in HCT-116 cells through the down-regulation of Bcl-2 and Bcl-xL, and the cleavage of Bid. Sanguinarine also activated caspases-3, -8 and -9 and increased cleavage of PARP, PLC-γ1 and β-catenin proteins. Furthermore, sanguinarine-induced apoptosis might be due to an increase in NAG-1 and tumor suppressor p53 proteins. Our results indicated that the apoptotic processes caused by sanguinarine are mediated by the regulation of the Bcl-2 and caspase families in human colon cancer cells. Our data also suggested that sanguinarine may have chemotheraputic benefits for colon cancer patients.

Keywords : sanguinarine, apoptosis, colon cancer cells, NAG-1