Sanguinarine induced apoptosis in human leukemia U937 cells via Bcl-2 downregulation and caspase-3 activation.


Source

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Abstract

BACKGROUND:

Sanguinarine is a benzophenanthridine alkaloid derived from the root of Sanguinaria canadensis, which induces apoptosis in human cancer cells, but the underlying action mechanisms are not completely understood. We investigated the mechanisms of sanguinarine on the induction of apoptosis using U937 leukemia cells.

METHODS:

Cytotoxicity was evaluated by MTT assay. Apoptosis was detected using DAPI staining, agarose gel electrophoresis and flow cytometry. The protein levels were determined by Western blot analysis. Caspase-3 activity was measured using a colorimetric assay.

RESULTS:

Exposure of U937 cells to sanguinarine resulted in growth inhibition and induction of apoptosis. Apoptosis by sanguinarine treatment was associated with the activation of caspase-3 and degradation of poly-(ADP-ribose) polymerase (PARP) and phospholipase C-gamma 1 protein. Induction of apoptosis by sanguinarine was also accompanied by upregulation of pro-apoptotic Bax and downregulation of anti-apoptotic Bcl-2 expression. Sanguinarine-induced caspase-3 activation and apoptosis were significantly
attenuated in Bcl-2-overexpressing U937/Bcl-2 cells. Furthermore, a caspase-3-specific inhibitor blocked caspase-3 activation as well as PARP degradation, and increased the survival rate of sanguinarine-treated U937 cells.

**CONCLUSIONS:**

These results demonstrated that the induction of apoptosis by sanguinarine in U937 cells was associated with altering the balance of Bcl-2 and Bax protein expression and activation of the caspase-3 pathway.

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