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## Activation of c-Jun N-terminal kinase 1 (JNK1) in mistletoe lectin II -induced apoptosis of human myeloleukemic U937 cells.

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Extracts of mistletoe (*Viscum album* var. *coloratum*) have been used for several decades as an anticancer immunomodulating agent in clinical fields. However, the mechanism by which the plant extracts kill tumor cells has remained elusive. We investigated the direct effects of beta-galactoside- and N-acetyl-d-galactosamine-specific mistletoe lectin II in inducing apoptotic death of U937 cells. Three distinct components of mistletoe, including beta-galactoside- and N-acetyl-D-galactosamine-specific lectin II (60 kDa), polysaccharides, and viscotoxin (5 kDa), induced apoptotic cell death, characterized by DNA ladder pattern fragmentation of U937 cells at 12 hr after treatment. Consistent with apoptosis of the cells, mistletoe extracts markedly increased the phosphotransferase activity of c-Jun N-terminal kinase 1 (JNK1)/stress-activated protein kinase (SAPK) in U937 cells. Among the three components, lectin II was the most potent in inducing apoptosis as well as JNK1 activation of U937 cells in a dose- and time-dependent manner. Catalytic activation of JNK1 induced by mistletoe lectin II was inhibited by the addition of peptide aC-DEVD-CHO, but not by aC-YVAD-CHO. In addition, mistletoe lectin II induced apoptosis in a variety of cell types including Jurkat T cells, RAW 264.7 cells, HL-60 cells, DLD-1 cells, and primary acute myelocytic leukemic cells.