Magnolol induces apoptosis in human leukemia cells via cytochrome c release and caspase activation.

李文森

Wen-Bin Zhong;Chih-Yuan Wang;Kuo-Jang Ho;Fung-Jou Lu;Tien-Chun Chang;Wen-Sen Lee

Abstract

Magnolol, isolated from the stem bark of Magnolia officnalis, was found to inhibit proliferation of human HL-60 cells and Jurkat T leukemia cells via inducing apoptosis in a dose- and time-dependent manner. By contrast, magnolol did not cause apoptosis in neutrophils and peripheral blood mononuclear cells of healthy donors. Apoptosis was determined by detection of DNA fragmentation in gel electrophoresis, morphological alternations by flow cytometry, quantification of phosphatidylserine externalization by Annexin V labeling and oligonucleosomal DNA content by TUNEL labeling. Activation of caspase-9, -3 and -2, and the proteolytic cleavage of poly(ADP-ribose) polymerase were found during apoptosis induced by magnolol. In addition, both pan-caspase and selective caspase-9 inhibitor blocked magnolol-induced apoptosis. The apoptosis could also be partially attenuated by caspase-3 and -2 inhibitors. Magnolol induced the reduction of mitochondrial transmembrane potential and the release of cytochrome c into cytoplasm. In conclusion, our findings indicate that magnolol-induced apoptotic signaling is carried out through mitochondria alternations to caspase-9 and that then the downstream effector caspases are activated sequentially. Magnolol could be a potentially effective drug for leukemia with low toxicity to normal blood cells and it merits further investigation.