Magnolol suppresses proliferation of cultured human colon and liver cancer cells by inhibiting DNA synthesis and activating apoptosis

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摘要

Abstract

Magnolol, a hydroxylated biphenyl compound isolated from the Chinese herb Hou p'u of Magnolia officinalis, has been reported to have anti-cancer activity. In the present study, magnolol at very low concentrations of 3-10 microM inhibited DNA synthesis and decreased cell number in cultured human cancer cells (COLO-205 and Hep-G2) in a dose-dependent manner, but not in human untransformed cells such as keratinocytes, fibroblasts, and human umbilical vein endothelial cells (HUVEC). Magnolol was not cytotoxic at these concentrations and this indicates that it may have an inhibitory effect on cell proliferation in the subcultured cancer cell lines. [(3)H] thymidine incorporation and flow cytometry analyses revealed that magnolol treatment decreased DNA synthesis and arrested the cells at the G0/G1 phase of the cell cycle. Moreover, the magnolol-induced cell cycle arrest occurred when the cyclin-CDK system was inhibited, just as p21 protein expression was augmented. When magnolol concentration was increased to 100 microM, apoptosis was observed in COLO-205 and Hep-G2 cells, but not in cultured human fibroblasts and HUVEC. COLO-205 cells implanted subcutaneously in nude mice formed solid tumors; subsequent daily i.p.-injections of magnolol led to profound regression of these tumors of up to 85%. In these tumors, an increase in the expression of p21 protein level and the occurrence of apoptosis were observed. These findings demonstrate for the first time that magnolol can inhibit the proliferation of tumor cells in vitro and in vivo.