Induction of G1 arrest and apoptosis by Scutellaria barbata in the human promyelocytic leukemia HL-60 cell line.


Source

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Abstract

Scutellaria barbata has been used to treat cancer in Chinese medicine. The responsible anticancer mechanism, however, is not clear. Here we demonstrated an inhibitory mechanism due to a Scutellaria barbata extract (SBE) on a human promyelocytic leukemia cell line (HL-60) that has a mutation in the tumor suppressor gene p53. HL-60 cells were incubated with various concentrations of SBE. After a 24-h incubation, cytotoxicity and apoptosis were determined by MTT and DNA fragmentation assay, respectively. After treatment with SBE, cell cycle arrest was determined by measuring the cell number stained by 5'-bromo-2'-deoxyuridine (BrdU) and 7-amino-actinomycin D (7-AAD). Treatment of cells with SBE resulted in a concentration- and time-dependent inhibition of growth and a G1 phase arrest of the cell cycle. This effect was associated with a marked decrease in the protein expression of cyclin A, D1, D2, D3, and E and their activating partners, cyclin-dependent kinases (CDK) 2, 4, and 6 with concomitant upregulation of p21, cyclin-dependent kinase inhibitor. Downstream of the CDK inhibitory protein-CDK/cyclin cascade, SBE decreased phosphorylation level of retinoblastoma protein. SBE treatment also resulted in apoptosis evidenced by an increase of sub-G1 phase cells, DNA fragmentation and degradation of the inhibitory protein for the caspase-activated deoxyribonuclease. The molecular mechanism during SBE-mediated growth inhibition in HL-60 cells may be due to modulation of the cell-cycle machinery and the induction of apoptosis.

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