

The traditional Chinese herb medicine formulation, modified Gexiazhuyu decoction , induces apoptosis in hepatic stellate cells

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Background :

The traditional Chinese herb Modified Gexiazhuyu decoction is an effective regimen that is usually used in outpatients with chronic liver disease (including fibrosis and cirrhosis). However, the underlying mechanism for the therapeutic effect of Modified Gexiazhuyu decoction is not yet clear. Since activation of hepatic stellate cells (HSCs) is a key feature of liver fibrosis, our goal in this study is to investigate the effects and the possible mechanism of Modified Gexiazhuyu decoction on the LX-2 cells.

AIM :

To investigate the effects of apoptosis and its possible mechanism of Chinese herb Modified Gexiazhuyu decoction on LX-2 cell line.

Methods :

Cell proliferation was estimated by cell viability. LX-2 cell apoptosis was detected by TdT Labeling reaction(TUNEL assay). The intracellular calcium ion concentration ($[Ca^{2+}]$) was measured by flow cytometry with fluo-4 Ca^{2+} -indicator dyes. Western blotting analysis was performed to investigate the underlying mechanism of Modified Gexiazhuyu decoction with LX-2 cells.

Results:

Our study showed that the Modified Gexiazhuyu decoction induces apoptosis and resulted in a decrease in LX-2 cell proliferation in a dose- and time-dependent manner (excepted experimental group with 100 μ g/ml at 24 hr). The concentration of Ca^{++} was increased in cytosol. The expression of Calpain 1 following exposure of LX-2 cells to Modified Gexiazhuyu decoction, the active form (75 kD) was increased at 48hr, and at 72hr the active form was decreased with dose dependent. The active form expression of caspase-12 was increased at 72hr.

Conclusion :

Our result demonstrates that the traditional Chinese herb medicine formulation, Modified Gexiazhuyu decoction, induces hepatic stellate cell apoptosis through increasing intracellular Ca^{++} levels, upregulation of the Ca^{++} -dependent protease calpain, preceding the caspase activation.