Effects of berberine on human rheumatoid arthritis fibroblast-like synoviocytes.


Source

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Abstract

Activated rheumatoid arthritis fibroblast-like synoviocytes (RAFLSs) play an important role in the initiation and progression of rheumatoid arthritis (RA). Rapid proliferation and defective apoptosis of RAFLSs are two main mechanisms contributing to synovial hyperplasia. Berberine, the major constituent of Coptidis Rhizoma, has been widely used as an antitumor and anti-inflammation agent. Here we show that berberine significantly inhibited cell proliferation of serum-starved human RAFLSs in a dose-dependent manner. Cell cycle analysis of berberine-treated RAFLSs indicated a cell cycle arrest at the G0/G1 phase. The inhibitory effects of berberine correlated with an induction of cyclin-dependent kinase (CDK) inhibitors Cip1/p21 and Kip1/p27 and a reduction of CDK2, CDK4 and CDK6, and cyclins D1, D2 and E. Furthermore, an apoptosis assay showed that berberine treatment increased apoptotic death of RAFLSs, which was associated with an increased expression of proapoptotic protein Bax and decreased expression of antiapoptotic proteins Bcl-2 and Bcl-xl, disruption of mitochondrial membrane potential, and activation of caspase-3, caspase-9 and poly (ADP-ribose) polymerase. Taken together, these results demonstrate that berberine exerts antiproliferative effects against RAFLSs, likely through deregulation of numerous cell cycle and apoptosis regulators, thus having potential therapeutic implications in the treatment of RA.

PMID:21676922