題名:Anti-tumor potential of 15; 16-dihydrotanshinone I against breast adenocarcinoma through inducing G1 arrest and apoptosis

作者:梁有志

Tsai1 SL; Suk FM; Wang CI; Liu DZ; Hou WC; Lin PJ; Hung LF; Liang YC

貢獻者:醫學檢驗暨生物技術學系

上傳時間:2009-08-25T02:37:53Z

摘要:Chemotherapeutic drugs are usually designed to induce cancer cell death via cell cycle arrest and/or apoptosis pathways. In this study, we used the chemical drug 15,16-dihydrotanshinone I (DHTS) to inhibit breast cancer cell proliferation and tumor growth, and investigate the underlying molecular mechanisms. Human breast cancer cell lines MCF-7 and MDA-MB-231 were both used in this study, and DHTS was found to significantly decrease cell proliferation by a dose-dependent manner in both cells. Flow cytometry indicated that DHTS induced G1 phase arrest in synchronous MCF-7 and MDA-MB-231 cells. When analyzing the expression of cell cycle-related proteins, we found that DHTS reduced cyclin D1, cyclin D3, cyclin E, and CDK4 expression, and increased CDK inhibitor p27 expression in a dose-dependent manner. In addition, DHTS inhibited the kinase activities of CDK2 and CDK4 by an immunocomplex kinase assay. In addition, DHTS also induced apoptosis in both cells through mainly mitochondrial apoptosis pathways. We found that DHTS decreased the anti-apoptotic protein Bcl-xL level and increased the loss of mitochondria membrane potential and the amount of cytochrome c released. Moreover, DHTS activated caspase-9, caspase-3, and caspase-7 and caused

cell apoptosis. The fact that
DHTS-induced apoptosis could be blocked by pretreating cells with pan-caspase inhibitor
confirmed that it is mediated through activation of the caspase-3-dependent pathway. In a
nude mice xenograft experiment, DHTS significantly inhibited the tumor growth of MDAMB-
231 cells. Taken together, these results suggest that DHTS can inhibit human breast
cancer cell proliferation and tumor growth, and might have potential chemotherapeutic
applications.