Apple polyphenol phloretin potentiates the anticancer actions of paclitaxel through induction of apoptosis in human hep G2 cells.

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摘要

Abstract

Phloretin (Ph), which can be obtained from apples, apple juice, and cider, is a known inhibitor of the type II glucose transporter (GLUT2). In this study, real-time PCR analysis of laser-capture microdissected (LCM) human hepatoma cells showed elevated expression (>5-fold) of GLUT2 mRNA in comparison with nonmalignant hepatocytes. In vitro and in vivo studies were performed to assess Ph antitumor activity when combined with paclitaxel (PTX) for treatment of human liver cancer cells. Inhibition of GLUT2 by Ph potentiated the anticancer effects of PTX, resensitizing human liver cancer cells to drugs. These results demonstrate that 50-150 microM Ph significantly potentiates DNA laddering induced in Hep G2 cells by 10 nM PTX. Activity assays showed that caspases 3, 8, and 9 are involved in this apoptosis. The antitumor therapeutic efficacy of Ph (10 mg/kg body weight) was determined in cells of the SCID mouse model that were treated in parallel with PTX (1 mg/kg body weight). The Hep G2-xenografted tumor volume was reduced more than fivefold in the Ph + PTX-treated mice compared to the PTX-treated group. These results suggest that Ph may be useful for cancer chemotherapy and chemoprevention.