題名:In vitro and in vitro study of phloretin-induced apoptosis in human liver cancer cells involving inhibition of type II glucose transporter

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摘要:Phloretin (Ph), a natural product found in apples and pears with glucose transporter (GLUT) inhibitory activity, exerts antitumor effects. However, little is known about its effects on human liver cancer. The purpose of this study is to test the cytotoxic effects of Ph on HepG2 cells and to identify the underlying molecular pathways. Human hepatocellular carcinoma specimens and HepG2 show a high level of GLUT2 transporter activity in the cell membrane. Real-time PCR and MTT assays demonstrate that Phinduced cytotoxicity correlates with the expression of GLUT2. Flow cytometry and DNA fragmentation studies show that 200 1M Ph induces apoptosis in HepG2, which was reversed by glucose pretreatment. GLUT2 siRNA knockdown induced HepG2 apoptosis, which was not reversed by glucose. Western blot analysis demonstrates that both intrinsic and extrinsic apoptotic pathways in addition to Akt and Bcl-2 family signaling pathways are involved in Ph-induced cell death in HepG2 cells.

Furthermore,
using flow cytometry analysis, a mitochondrial membrane potential
assay and Western blot analysis, we show that cytochalasin B,
a glucose transport inhibitor, enhances the Ph-induced apoptotic
effect on HepG2 cells, which was reversed by pretreatment with
glucose. Furthermore, we found significant antitumor effects in
vivo by administering Ph at 10 mg/kg intraperitoneally to severe
combined immune deficiency mice carrying a HepG2 xenograft. A
microPET study in the HepG2 tumor-bearing mice showed a 10-
fold decrease in 18F-FDG uptake in Ph-treated tumors compared
to controls. Taken together, these results suggest that Ph-induced
apoptosis in HepG2 cells involves inhibition of GLUT2 glucose
transport mechanisms.