

Andrographolide suppresses endothelial cell apoptosis via activation of phosphatidyl inositol-3-kinase/Akt pathway

蕭哲志

Chen JH;Hsiao G;Lee AR;Wu CC;Yen MH

摘要

Abstract

Andrographolide (Andro), an active component isolated from the Chinese official herbal *Andrographis paniculata*, which has been reported to prevent oxygen radical production and thus prevent inflammatory diseases. In this study, we investigated the molecular mechanisms and signaling pathways by which Andro protects human umbilical vein endothelial cells (HUVECs) from growth factor (GF) deprivation-induced apoptosis. Results demonstrated that HUVECs undergo apoptosis after 18 hr of GF deprivation but that this cell death was suppressed by the addition of Andro in a concentration-dependent manner (1-100 microM). Andro suppresses the mitochondrial pathway of apoptosis by inhibiting release of cytochrome c into the cytoplasm and dissipation of mitochondrial potential ($\Delta\psi(m)$), as a consequence, prevented caspase-3 and -9 activation. Treatment of endothelial cells with Andro-induced activation of the protein kinase Akt, an anti-apoptotic signal, and phosphorylation of BAD, a down-stream target of Akt. Suppression of Akt activity by wortmannin, by LY-294002 and by using a dominant negative Akt mutant abolished the anti-apoptotic effect of Andro. In contrast, the ERK1/2 activities were not affected by Andro. The ERK1/2 inhibitor, PD98059 failed to antagonize the protective effect of Andro. In conclusion, Andro exerts its anti-apoptotic potential via activation of the Akt-BAD pathway in HUVECs and thus may represent a candidate of therapeutic agent for atherosclerosis