Protodioscin

Protodioscin (PD) is a steroidal saponin with anti-cancer effects on a number of cancer cells, but the anti-tumor effects and mechanism of action of PD on human cervical cancer cells is unclear.

METHODS: We determined cell viability using the MTT assay. Cell death, mitochondrial membrane potential (MMP), intracellular reactive oxygen species (ROS) generation, and endoplasmic reticulum (ER) stress were measured on a flow cytometry. Caspase activation, ER stress, and MMP-dependent apoptosis proteins in cervical cancer cells in response to PD were determined by Western blot analysis. The ability of ATF4 binding to ChIP promoter was measured using the ChIP assay.

RESULTS: We demonstrated that PD inhibits cell viability, causes a loss of mitochondrial function, and induces apoptosis, as evidenced by up-regulation of caspase-8, -3, -9, -PARP, and Bax activation, and down-regulation of Bcl-2 expression. PD was shown to induce ROS and the ER stress pathway, including GRP78, p-eIF-2α, ATF4, and CHOP. Pre-treatment with NAC, a ROS production inhibitor, significantly reduced ER stress and apoptosis-related proteins induced by PD. Transfection of GRP78/CHOP-siRNA effectively inhibited PD-induced ER stress-dependent apoptosis. Moreover, treatment with PD significantly increased p38 and JNK activation. Co-administration of a JNK inhibitor (SP600125) or p38 inhibitor (SB203580) abolished cell death and ER stress effects during PD treatment. In addition, PD induced the expression of nuclear ATF4 and CHOP, as well as the binding ability of ATF4 to the CHOP promoter.

CONCLUSION: Our results suggest that PD is a promising therapeutic agent for the treatment of human cervical cancer [1)]

1)
Lin CL, Lee CH, Chen CM, Cheng CW, Chen PN, Ying TH, Hsieh YH. Protodioscin Induces Apoptosis Through ROS-Mediated Endoplasmic Reticulum Stress via the JNK/p38 Activation Pathways in Human Cervical Cancer Cells. Cell Physiol Biochem. 2018 Mar 22;46(1):322-334. doi: 10.1159/000488433. [Epub ahead of print] PubMed PMID: 29590661.