특강

Anti-proliferative effects of ginsenoside on human cancer cells

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The roots of *Panax ginseng* C.A. Meyer (Araliaceae) has been traditionally used as an oriental medicine in Korea for more than 5,000 years for various disease, such as liver dysfunction, hypertension, cerebrovascular diseases, atherosclerosis and postmenopausal disorder. Ginseng saponins isolated from the root have been reported to be the main effective ingredients. Some components of ginsenoside, such as Rh2 (G-Rh2), isolated from the root of *Panax ginseng* has been shown to have anti-cancer proliferation, differentiation and chemopreventive effects in certain cancer cell types. We first investigated the mechanism of G-Rh2-induced growth inhibition in MCF-7 human breast carcinoma cells. G-Rh2 significantly inhibited the cell growth in a concentration-dependent manner, which effect was reversible, and induced a G1 arrest in cell cycle progression. G-Rh2 treatment down-regulated the protein level of cyclin D3 but upregulated the expression of cyclin-dependent kinase (Cdk) inhibitor $p21^{WAF1/CIP1}$. The increased levels of p21 were associated with increased binding of p21 and Cdk2 concomitant with marked decrease in Cdk2 and cyclin E-dependent kinase activities with no changes in Cdk2 and cyclin E expression. G-Rh2 markedly reduced the phosphorylated retinoblastoma protein (pRb) and enchanced association of unphosphorylated pRb and the transcription factor E2F-1. These data suggest that G-Rh2 inhibited the growth of MCF-7 cells, by inducing protein expression of p21 and reducing the protein levels of cyclin D which resulted in the down-regulation of cyclin/Cdk complex kinase activity, decreasing phosphorylation of pRb, and inhibiting E2F release. We also tested a crude extract of Panax ginseng produced by a certain boiling method on human U937 leukemia cells. The extract also efficiently inhibited the proliferation of leukemia cells, produced apoptotic body, and increased the size of sub-G1 fraction with flow cytometry analysis. Western blotting demonstrated the presence of PARP, PLCγ1, and β-catenin cleavages. Caspase-3, -8, and -9 were also induced after the treatment of the extracts on leukemia cells dose-dependently. The extracts also showed modulation on the expression levels of Bcl-2 and IAP family proteins. Moreover, several genes involved in the regulation of iNOS/COXs and telomere length were modulated after the treatment. The results will be discussed the effectiveness of a ginsenoside or a certain extracts on human breast cancer cells and leukemia cells.