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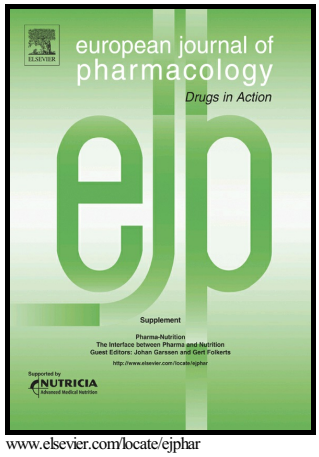

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Antineoplastic activity of isoliquiritigenin, a chalcone compound, in androgen-independent human prostate cancer cells linked to G2/M cell cycle arrest and cell apoptosis

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Abstract

Isoliquiritigenin is a natural chalcone derived from *Glycyrrhiza*, which has been reported to have anti-tumor activity in recent years. Here, we investigate the anticancer efficacy and associated mechanisms of isoliquiritigenin in human prostate cancer PC-3 and 22RV1 cells. Isoliquiritigenin (25-50 μM) inhibited cell proliferation, induced cell apoptosis, and caused G2/M cell cycle arrest in vitro. This agent also repressed the growth of PC-3 xenograft tumors in vivo with the results of hematoxylin/eosin staining and immunohistochemistry staining showing differences between isoliquiritigenin-treated groups and control group. Next, we used microarray transcriptional profiling to identify isoliquiritigenin-regulated genes on PC-3 prostate cancer cells. Multiple genes involved in cell cycle, DNA damage, and apoptosis signaling pathways were changed remarkably with the treatment of isoliquiritigenin. Molecular studies revealed that G2/M arrest was associated with a decrease in cyclin B1, cyclin-dependent kinase 1 (CDK1), and phosphorylated CDK1 (Thr14, Tyr15, and Thr161), whereas the expression of 14-3-3σ and growth arrest and DNA damage-inducible 45 alpha (GADD45A) was increased. The complexes of cyclin B1–CDK1 were also examined to show a decrease in the binding of CDK1 with cyclin B1. In addition, treatment with relatively high concentrations of isoliquiritigenin induced apoptosis, mainly associated with enhancing apoptosis regulator (Bax/Bcl-2) ratio. Collectively, these findings indicate that isoliquiritigenin modulates cyclin B1–CDK1 for G2/M arrest, together with an alteration of cell cycle regulators and apoptotic factors in human prostate cancer cells. However, we observed pleiotropic effects for isoliquiritigenin in microarray results, suggesting that other biological mechanisms also contribute to its efficacy, which could be of interest for future investigations.

Keywords:

prostate cancer; isoliquiritigenin; cell cycle arrest; CDK1; microarray profiling