Genistein Induces G2/M Cell Cycle Arrest and Apoptosis in Rat Neuroblastoma B35 Cells; Involvement of p21waf1/cip1, Bax and Bcl-2

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Abstract:

Background: The effect of genistein on different types of cells has been investigated. However, its effect on the nervous system is still unclear. The aim of the present work is to explore the effect of genistein on rat neuroblastoma B35 cells.

Methods: The effect of genistein on the proliferation of B35 cells, its cytotoxicity, the cell-cycle distribution, the ultra-structural changes and the induction of apoptosis were determined using MTT assay, LDH assay, Flow-cytometric analysis, transmission electron microscopy and Hoechst staining, respectively. Furthermore, Real-time quantitative RT-PCR and Western blotting were used to examine the transcriptional and post-translational alterations of the G2/M cell-cycle arrest marker cyclin-dependent kinase inhibitor p21waf1/cip1 and the apoptosis-related genes after genistein treatment.

Results: Genistein significantly inhibits cell survival, slightly elevates the release of lactate dehydrogenase and induced apoptosis in B35 cells. Genistein increased the number of cells at S-phase and induced cells to accumulate at the G2/M phase. These G2/M arrested cells are associated with a marked up-regulation of p21waf1/cip1 at both the mRNA and protein levels. We observed that genistein up-regulates pro-apoptotic Bax with concurrent down-regulation of the anti-apoptotic Bcl-2 protein.

Conclusion: These observations suggest that the anticancer effect of genistein on B35 neuroblastoma cells is mediated through multiple cellular pathways including G2/M cell-cycle arrest and the induction of apoptosis.

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