

A NOVEL SERIES OF BIOACTIVE 2, 4, 7'-TRISUBSTITUTED ISOFLAVONES INDUCE G₀-G₁ ARREST AND APOPTOSIS IN HORMONE-DEPENDENT AND HORMONE-INDEPENDENT BREAST CANCER CELLS.

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Bioactive 2, 4, 7'-trisubstituted isoflavones, derivatives of genistein with unknown mechanisms of action, are currently being evaluated in hormone-independent and hormone-dependent breast cancer cell lines by our lab. Dose-dependent studies have shown several compounds to be potent inhibitors of proliferation in both MCF-7 and MDA-MB-231 breast cancer cells. ELISA ssDNA screening suggested that apoptosis may be another mechanism in addition to antiproliferative and cytotoxicity activity involved in these targeted compounds. In search of other antiproliferative effects, we assessed the ability of these compounds to influence cell cycle arrest. A significant G₀-G₁ arrest $\geq 25\%$ with respect to control was observed by 24 hours of exposure to 10 μ M of the compounds in MCF-7 and MDA-MB-231 breast cancer cells, indicating ability of these compounds to block cell cycle progression. To serve as an independent validation that these compounds induce programmed cell death we turned to another methodology, flow cytometry. Annexin V, a known assay to measure early apoptosis, along with 7-AAD a method to assess cell viability was used to quantitatively determine the percentage of cells within a population that are actively undergoing apoptosis. By 24 hours, several compounds induced apoptosis at 10 μ M treatment as measured by cells that stained positive for Annexin V-PE and negative for 7-AAD in both MCF-7 and MDA-MB-231 cell lines. Currently, research investigating breast cancer therapeutics is leaning towards a better understanding of the microenvironment of the cell in response and resistance to treatment. These data indicate that several compounds in these series of 2, 4, 7'-trisubstituted isoflavones promote cell cycle arrest at G₀-G₁ and apoptosis in MCF-7 and MDA-MB-231 breast cancer cell lines and thereby represent a promising candidate in the treatment of hormone-dependent as well as hormone-independent breast cancer.

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