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EFFECT OF DIFFERENT GENISTEIN CONCENTRATIONS ON EXPRESSION OF $p21^{WAF1}$, p53, CYCLIN B_1 AND BAX; ESTROGEN AGONIST AND ANTAGONIST ACTIONS IN MCF-7 CELLS

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Genistein, a phytoestrogen derived from soy isoflavone, has been shown to exert anti-proliferative activities, and have cell arrest and apoptotic effects in cultured tumor cells. However, these properties may not show at the low concentrations of genistein. Present study examined the effect of different concentrations of genistein on cell proliferative proteins, cell cycle regulators or apoptosis related protein in comparison with different concentrations of estrogen or co-treatment with estrogen. MCF-7 cells were treated with either genistein (25 μM, 50 μM and 100 μM) or 17-beta estradiol (12.5 nM, 25 nM and 50 nM) or genistein and estradiol for 48 hr and western blot analysis of the proteins were carried out. Genistein increased $p21^{WAF1}$ and p53 protein expressions at 50 and 100 μM concentrations. The lowest concentration co-treatment of genistein and estrogen, 25 μM and 12.5 nM respectively, showed the least amount of protein expression even less than the estrogen treatments. With the dose-depedent manner, expression of Cyclin B1 was down-regulated in genistein treated cells. The high concentration of genistein co-treatment with estrogen markedly decreased the estrogen-induced up-regulation of Cyclin B1. Bax expression was increased by genistein at all of the three different concentrations of genistein. Estrogen stimulation of Bax protein was noticeable at the higher concentrations. Co-treatment of genistein with estrogen resulted in down-regulation of this protein. These results indicate that genistein, at the low concentration (25 μM), acts as an agonist of estrogen, and at the higher concentrations (50 or 100 μM), as an antagonist of estrogen.