

Estrogenic effects of genistein on the growth of estrogen receptor-positive human breast cancer (MCF-7) cells in vitro and in vivo.

Hsieh CY, Santell RC, Haslam SZ, Helferich WG.

Abstract

Genistein, found in soy products, is a phytochemical with several biological activities. In the current study, our research focused on the estrogenic and proliferation-inducing activity of genistein. We have demonstrated that genistein enhanced the proliferation of estrogen-dependent human breast cancer (MCF-7) cells in vitro at concentrations as low as 10 nM, with a concentration of 100 nM achieving proliferative effects similar to those of 1 nM estradiol. Expression of the estrogen-responsive gene pS2 was also induced in MCF-7 cells in response to treatment with a concentration of genistein as low as 1 microM. At higher concentrations (above 20 microM), genistein inhibits MCF-7 cell growth. In vivo, we have shown that dietary treatment with genistein (750 ppm) for 5 days enhanced mammary gland growth in 28-day-old ovariectomized athymic mice, indicating that genistein acts as an estrogen in normal mammary tissue. To evaluate whether the estrogenic effects observed in vitro with MCF-7 cells could be reproduced in vivo, MCF-7 cells were implanted s.c. in ovariectomized athymic mice, and the growth of the estrogen-dependent tumors was measured weekly. Negative control animals received the American Institute of Nutrition (AIN)-93G diet, the positive control group received a new s.c. estradiol (2 mg) pellet plus the AIN-93G diet, and the third group received genistein at 750 ppm in the AIN-93G diet. Tumors were larger in the genistein (750 ppm)-treated group than they were in the negative control group, demonstrating that dietary genistein was able to enhance the growth of MCF-7 cell tumors in vivo. Increased uterine weights were also observed in the genistein-treated groups.

In summary, genistein can act as an estrogen agonist in vivo and in vitro, resulting in the proliferation of cultured human breast cancer cells (MCF-7) and the induction of pS2 gene expression. Here we present new information that dietary genistein stimulates mammary gland growth and enhances the growth of MCF-7 cell tumors in ovariectomized athymic mice.