

CHAPTER VI

CONCLUSION

In the present study, the effects of genistein supplementation at the human consumption dose and its mechanism on NMU-induced tumorigenesis and mammary tumor growth in adult female rats could be summarized as follows;

1. Long-term supplementation of phytoestrogen at a human consumption dose, 1 mg/kg BW of genistein, to adult female rats could stimulate the NMU-induced mammary tumorigenesis. It is represented by the increasing of tumor multiplicity, tumor cross-sectional area and the metastases of cancer to other organs.
2. Genistein at the dosage of 1 mg/kg BW does not exhibit reproductive effects on the ovary, uterus and the serum estradiol levels, while it shows the carcinogenic effects on the breast tissues. In turn, it may conclude that cancer cells are more sensitive to phyto/estrogen than the gonadal cells.
3. Genistein stimulates the mammary tumor growth, possibly by upregulating the IGF-1 mRNA expression, not via the estrogen receptor pathway.
4. GPR54, an orphan receptor of metastasis suppressor gene, may play a role in the metastatic potential of cancer cells to other organs, which it is decreased in expression after genistein treatment.
5. Tamoxifen, an estrogen antagonist, inhibits the mammary tumor growth by downregulating the ER α mRNA expression or via the estrogen receptor pathway.
6. The antagonistic effect of genistein on tamoxifen could be observed only at the molecular levels (by the induction of the IGF-1 mRNA expression), not in the cellular levels (by determination of tumor growth).
7. Tamoxifen treatment affects on reproductive organs and functions via its estrogen antagonistic activity. It increases the serum estradiol levels and then decreases the rat body weight.
8. Although NMU-tumor induction can not be compared directly with the human breast cancer, the results of this study suggest that the supplementation of soy isoflavone,

especially the purified or concentrated forms of genistein, to premenopausal women with breast cancer or high risk in breast cancer should be avoided.