MEDICINAL PLANT EXTRACTS INDUCED DNA DAMAGE AND APOPTOSIS THROUGH OXIDATIVE STRESS IN TRANSGENIC MOUSE MODEL

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Abstract: One of the most frightening events that women will ever face is being diagnosed with breast cancer. One in eight women in the United States will be diagnosed with this life-threatening disease during her lifetime. Even with all the advances in pharmaceutical technology, mortality rates for breast cancer have remained stagnant for the past few decades. The development of new drugs from natural products is considered important. The specific aim of the present study was to use transgenic mouse mammary tumors as a test model to explore the therapeutic mechanisms of a novel natural product as an anti-cancer agent in the treatment of breast cancer. To achieve our specific aim, we performed both in vitro and in vivo studies. Acridine orange and propidium iodide (AO/PI) staining were used to visualize live and dead cells with the means of Cellometer Vision. Tumor volume and weight were measured. Tumor histology was assessed by immunohistochemistry, and enzymatic activities were determined by spectrophotometry. The extent of DNA damage was evaluated by the Comet assay. Cell/tissue apoptosis was measured by the flow cytometry. Data obtained from the AO/PI dye assessment indicated that the tested natural product significantly reduced the number of live cells in a dose-dependent manner, showing a gradual increase in the loss of viability in treated cells. We observed tumor growth inhibition after 4 weeks of daily intraperitoneal administration of plant extracts to transgenic mice. There was a significant increase in DNA damage in treated mice compared to the control mice. Flow cytometry data showed a strong dose-response relationship between plant extracts treatment and annexin V/PI positive cells. Similarly, a statistically significant and dose-dependent increase (p < 0.05) was recorded with regard to caspase 3 activity. Data from enzyme analysis (alanine transaminase, aspartate transaminase, and creatinine) revealed that plant extract administration is not toxic to treated mice. These results suggest that induction of cell death, DNA damage, and cell/tissue apoptosis may be involved in the therapeutic mechanisms of plant extracts in breast cancer. Collectively, the findings from this study provide convincing evidence that the tested plant extracts may represent a potential anticancer candidate against breast cancer.

Keywords: Medicinal Plant extracts, MCF-7 cells, transgenic mouse tumor, breast cancer

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