Summary of the DVM thesis No 27212, Faculty of Veterinary Medicine, Urmia University.

The academic year: 2024-2025

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Title of thesis: Evaluating the effect of combined gallic acid and all-trans-retinoic acid on viability and oxidative stress biomarkers in MCF-7 breast cancer cell line.

Summary:

Breast cancer is the second leading cause of cancer-related death worldwide and the most common cancer among women. A significant proportion of breast cancer originate from breast epithelium and are generally classified into two categories: in-situ carcinoma and invasive carcinoma. The incidence of breast cancer is influenced by several factors, including genetic, gender, age, and lifestyle. Pro-oxidants are chemical compounds that induce oxidative stress and cell death, particularly in cancer cells, by generating reactive oxygen species or inhibiting the antioxidant system, while only marginally affecting healthy cells. There is currently considerable interest in utilizing the pro-oxidant properties of compounds in cancer treatment. Furthermore, given that carcinogenesis depends on multiple pathways, combination therapy with drugs and substances can reduce the risk of side effects by using lower-than-optimal doses. Therefore, combination therapy has emerged as a new approach in cancer treatment. Gallic Acid is a plant polyphenol, and All-Trans Retinoic Acid (ATRA), classified as a retinoid and derived from vitamin A, both possess pro-oxidant and anti-cancer properties. This study aims to investigate the combined effects of Gallic Acid and ATRA on cell viability and oxidative stress biomarkers in the human breast cancer cell line MCF-7, as well as to examine the expression changes of the apoptosis-related genes Bax, Bcl-2, and FOXO3a. According to the results, treatment of cells with Gallic Acid and ATRA significantly inhibited cell viability in a concentration-dependent manner, and we observed a greater reduction in cell survival with the combined treatment of Gallic Acid and ATRA compared to the individual treatments and the control group. The level of apoptosis in cells treated individually with Gallic Acid and ATRA increased in a concentration-dependent manner, and the level of apoptosis in the combined treatment was also significantly higher than that in the individual treatments. Individual treatment with Gallic Acid and ATRA resulted in a dose-dependent decrease in reduced glutathione (GSH) levels and an increase in malondialdehyde (MDA) levels compared to the control group. Additionally, the reduction in GSH and the increase in MDA in the group treated with the combination of ATRA and Gallic Acid, compared to their individual treatments, indicate an increase in oxidative stress. Meanwhile, the activity of the enzyme superoxide dismutase (SOD) in cells treated individually with gallic acid and ATRA compared to the control group, and in the combined treatment compared to the individual treatments, decreased insignificantly. Furthermore, in the individual treatment compared to the control group, there was a dose-dependent increase in the expression of Bax, Bax/Bcl-2 ratio, and FOXO3a, along with a decrease in Bcl-2 expression. The combined treatment also led to a further increase in the expression of Bax and FOXO3a and induced more apoptosis compared to the individual treatments in MCF-7 cells. The results of this study indicate that the combination of

Gallic Acid and All-Trans Retinoic Acid (ATRA) effectively induces apoptosis and increases oxidative stress in MCF-7 breast cancer cells. This combination not only reduces cell viability but also causes significant changes in the expression of apoptosis-related genes. Therefore, the combined treatment of these two compounds may be considered a promising approach in breast cancer therapy.

Keywords: Gallic Acid, All-Trans Retinoic Acid, apoptosis, pro-oxidant, oxidative stress.