Title: Effect of Diclofenac on Doxorubicin-Induced Apoptosis in Breast Cancer

Name: Noha Eldeab Mohammed

King Abdulaziz University School of Medicine, Jeddah, KSA

Introduction: Breast cancer is the most common disease in women worldwide. Studies in Saudi Arabia recorded significant increase in breast cancer incidence and occur earlier than Western countries. Doxorubicin (DOX) is a type of chemotherapeutic drug known as anthracycline and is highly effective in advanced breast cancer in the 1970s. Unfortunately, the cytotoxic effects of DOX affect normal and secondary effects of cancer cells. Scientists find a reusable medication as a solution to the production of medicines to mitigate the adverse effects of the chemical therapy. Diclofenac (DICLO) is an anti-inflammatory non-steroidal drug used to treat inflammation and pain. Studies proof of the effect of DICLO treatment on anticancer. Therefore, the aim of the present study was to study the effect of DICLO co treatment with DOX on MCF-7 breast cancer cell line and investigate the possible mechanism by studying apoptosis, cell cycle phase distribution, cellular uptake and p-glycoprotein inhibition in breast cancer cells to overcome the side effects and multidrug resistance of Doxorubicin treatment.

Materials and methods: In order to assess these effects, we have investigated the DOX effect on cytotoxicity, cellular absorption, p-glycoprotein function, apoptosis induction and cell cycle phase distribution when DICLO is present with different concentrations.

Results: The addition of diclofenac (10 and 100 µg / ml) increased the effectiveness of doxorubicin as it led to a significant decrease in IC50 by 16.4% and 86.55% compared to the cells treated with doxorubicin only. Cell cycle analysis showed that diclofenac(100µg / ml)

significantly increased the percentage of programmed cell death from doxorubicin (0.25 µg / ml) 3.5% to 10.9% in addition to that significantly increased programmed cell death when adding diclofenac to doxorubicin to 40.2% compared to 15.6% doxorubicin.A programmed cell death test showed that combined treatment of diclofenac with doxorubicin (0.25 and 1) resulted in a significant increase in the rate of early programmed cell death to more than 12 times, 3 times greater than doxorubicin. Diclofenac increased the cellular absorption of doxorubicin significantly by 44% compared to doxorubicin alone (5 µg/ ml) and 63% from doxorubicin alone (10 µg/ ml). This is mediated by known p-glycoprotein inhibition.

Conclusion: In conclusion, diclofenac exhibits significant antitumor properties in the model of breast cancer that may lead to further advancement of treatment. Diclofenac's ability to induce apoptosis, enhance DOX cellular absorption and inhibit P-glycoprotein production. As an adjuvant to traditional therapies, DICLO has different potential benefits to reduce the adverse effects of many conventional therapies.