Effect of Diclofenac on Doxorubicin-Induced Apoptosis in Breast Cancer

Introduction and Research Problem

Statistic studies show that breast cancer is the most common cancer diagnosed among women worldwide. Scientists find a drug repurposing as a solution for drug development to overcome the adverse effects of the chemotherapeutic treatment.

Materials and Methods

Effect of Diclofenac (DICLO) on Doxorubicin (DOX) cytotoxicity effect on MCF-7 and discover the possible underlying mechanisms with respect to cell cycle disturbance, apoptosis, cellular uptake and P-glycoprotein activity

Summary of Results

Addition of DICLO (10 and 100 µg/mL) to DOX resulted in a significant reduction of IC_{50} by 16.24% and 86.55%, compared to DOX-alone treated cells.

Cell Cycle analysis showed that DICLO (100 µg/mL) significantly increased the percentage of apoptotic cells of DOX (0.25 µg/mL) 3.5% to 10.9%, In addition, markedly increased the DOX (1 µg/mL) apoptotic cells to (40.2 %), compared to DOX alone (15.6 %).

Apoptosis assay showed that Co-treatment of DICLO with DOX (0.25, 1µg/mL) resulted in significant increase in early apoptosis percentage to more than 12 folds, 3 folds compared to DOX-alone of corresponding DOX-alone.

DICLO increased the cellular uptake of DOX significantly by about 44% compared to DOX alone (5 µg/mL) and 63% of DOX alone (10 µg/mL). This is explained by P-glyc protein inhibition of DICLO treatment with DOX (10 µg/mL) equal to the effect of Verapamil (10 µM) that is a well-known p-glycoprotein inhibitor).

Conclusion and Recommendations

Diclofenac significantly increased the cytotoxicity of the Doxorubicin. The suggested mechanism is apoptosis induction and increase the cellular uptake of DOX by P –glycoprotein activity inhibition.

Further studies is needed to confirm the effect of Diclofenac invivo and the possible underlying mechanisms