البحث الرابع

5-fluorouracil Synergized with Raloxifene and Cytosineβ-Darabinofuranoside to Combat Colorectal Cancers *in vitro* via Controlling Lipolysis

Authors: Ahmed A. Abd-Rabou, **Marwa A. Mwaheb**, Ola N. Sayed, Safaa H. Mohamed and Mohamed S. Kishta

Journal of Pharmacology and Toxicology. 2016. 12 (1), 14-32

Abstract

Background: Colorectal cancers (CRCs) are the 3rd leading mortality cause in the states. Raloxifene (RX) was recently approved for cancer prevention. Therefore, 5-flurouracil (FU), a DNA blocker, stimulates apoptotic cascade in CRC cells. Unfortunately, many of the therapies that use FU and RX are likely to become ineffective due to drug resistance. Therefore, providing cytosine-β-D-arabinoside (CYT), an S-phase specific chemotherapeutic drug, may be of great support. Lipases are principally elaborated in energy metabolism and cancer aggressiveness. Human colorectal cells (HCT 116 and Caco-2) were cultivated in their proper conditions. Materials and Methods: These cells were seeded to perform cell proliferation assay using MTT upon RX, FU and CYT combinations. Moreover, cells were proceeded for measuring lipase expression in the supernatant using appropriate lipase assay kit. **Results:** This study observed that RX alone has the most effective cytotoxicity against Caco-2 cells, scoring a very low IC_{50} equal 19.8 μ M. Intriguingly, the triple therapy of RX+FU+CYT was the most effective against HCT 116 cells at 100 µM which kills approximately 90% of the cells and scoring a very low IC_{50} equal 38.4 μ M. **Conclusion:** This study concluded that the synergistic effect of the triple therapy in the aggressive HCT 116 cells has the potential to kill those cells by inhibiting lipase activity. Killing colorectal cancer cells using FU combinations.