

Mechanistic insights into the chemomodulatory effects of Caffeic acid phenethyl ester in colon cancer cells

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Colorectal cancer (CRC) is the third common cause of cancer deaths. Chronic inflammation plays an important role in the pathogenesis of CRC. Cyclooxygenase-2 is overexpressed in several human cancers including CRC. Estrogen receptor- β (ER- β) is a subtype of estrogen receptors (ER) that possesses anti-inflammatory effects. It is the prevalent ER in normal colon mucosa and its level is significantly reduced in CRC. Caffeic acid phenethyl ester (CAPE) is an active component of honey bee propolis that possesses potent anti-inflammatory and selective estrogen receptor modulatory activities. The current work aims at investigating the potential modulatory effects of CAPE on the cytotoxicity of 5-Fluorouracil (5-FU) in colon cancer cells and exploring the possible underlying mechanisms. Our data indicated that CAPE synergized the cytotoxicity of 5-FU in HT-29 cells as confirmed via Calcusyn synergy analyses. CAPE treatment significantly reduced cyclin D1 and increased p27 expressions compared to control. FACScan revealed an increased percentage of cells at pre-G phase with CAPE treatment. Bax/Bcl-2 ratio was significantly increased in the same group. CAPE increased the expression of ER- β and its downstream tumor suppressor FOXO1. Furthermore, CAPE treatment significantly reduced the level of COX-2, PGE2 and VEGF in HT-29 cells compared to control. In conclusion, CAPE synergized 5-FU cytotoxicity and antiproliferative activity in HT-29 cells. This can be, at least partly, attributed to CAPE pro-apoptotic effects, in addition to ER- β and COX-2 modulatory effects. Further investigations are needed in order to evaluate the potential merit of CAPE/5-FU combinations for the management of colorectal cancer in humans.

Biography:

Dr. Mai F Tolba is an Assistant Professor of Pharmacology and Toxicology at Ain Shams University and The American University in Cairo. She is a post-doctoral member of the Society of Toxicology (SOT). Dr. Tolba is interested in investigating the role of estrogen signaling in cancer for which she has co-authored 3 publications. The cancer transforming role of catechol estrogens in prostate cells [PMID23685341]. The use of CAPE, a phytoestrogen, as a sensitizer for prostate cancer cells to taxanes [PMID23847086]. The effect of the obesity mediator leptin on estrogen metabolism and the proliferation of prostate cells [PMID25433128]