Jordan University of Science and Technology

Caffeine inhibits paclitaxel?induced apoptosis in colorectal cancer cells through the upregulation of Mcl?1 levels.

Authors: Mhaidat NMAlzoubi KHAl-Azzam SIAlsaad AA.

Abstract: Colorectal cancer (CRC) cells have been previously observed to be resistant to paclitaxel?induced apoptosis by activation of the mitogen?activated protein/extracellular signal?regulated kinase (MEK)/ERK signaling pathway and increased expression of glucose?regulated protein 78 (GRP78). Caffeine, the most widely used neuroactive compound, has antiproliferative activity and the ability to induce cell cycle arrest and apoptosis. In the current study, the effect of concomitant use of caffeine on paclitaxel ?induced apoptosis in CRC cells was investigated. The results revealed that treatment of Colo205 cells with varying caffeine concentrations did not induce apoptosis. Pretreatment of CRC cells with caffeine significantly inhibited paclitaxel ?induced cytotoxicity by increasing the levels of the antiapoptotic Bcl?2 family member, Mcl?1. This effect was inhibited by pretreatment of Colo205 cells with the MEK?ERK chemical inhibitor, U0126. In addition to GRP78, these results indicated that Mcl?1 may be a downstream target of the MEK?ERK signaling pathway. Moreover, administration of caffeine may decrease chemotherapeutic responses to paclitaxel by the MEK?ERK mediated upregulation of Mcl?1. In conclusion, coadministration of cell cycle?modifying agents, including caffeine should be avoided in CRC patients treated with paclitaxel.