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Anticancer activity of coumarin hydrazide-hydrazone derivatives bearing five-membered heterocyclic rings

Tamer Nasr^{1,2}, Samir Bondock^{1,3} and Mahmoud Youns²

¹King Khalid University, King Saudi Arabia

²Helwan University, Egypt

³Mansoura University, Egypt

Drug-resistance is the main problem in cancer treatment, to solve this problem we designed and synthesized some hybrid compounds having both coumarin, hydrazide hydrazone, and biologically active five-membered heterocyclic rings in one molecule and evaluated them against human pancreatic carcinoma (Panc-1), hepatic carcinoma (Hep-G2) and leukemia (CCRF) cell lines in vitro. Some of the synthesized coumarin derivatives were significantly more potent than doxorubicin (DOX) against Panc-1 cells. 6- Bromocoumarins were able to activate caspases 3/7 and induce apoptosis in resistant Panc-1 cells. Microarray analysis revealed that the 6-bromocoumarins were able to induce the expression of apoptotic- and cell cycle arrest (G2/M)- genes in resistant Panc-1 cells. Moreover, they induced the up-regulation of CDKN1A, DDIT4, GDF-15 and down-regulation of CDC2, CDC20, CDK2 genes. Based on our results, we conclude that our target compounds could be potent anticancer drugs to overcome drug resistance in cancer and they could be highly beneficial for patients in the clinic.

Biography

Tamer Nasr has earned his PhD in Medicinal Chemistry by synthesizing non-natural nucleoside analogues and evaluating their therapeutic applications, in one of the world renowned university (Kyushu University), Japan. Post his doctorate, he joined as an Assistant Professor to teach Medicinal Chemistry in one of the top universities in his home country; Helwan University, Egypt. He moved to Saudi Arabia and joined as an Assistant Professor in King Khalid University (KKU). Due to his hard work and excellent teaching abilities; in short span he was promoted from staff to Chair of the Pharmaceutical Chemistry Department, KKU.