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J Clin Trials 2018, Volume 8
DOI: 10.4172/2167-0870-C2-026

Joint Event on

Global Pharmacovigilance and Advanced Pharmacy July 16-17, 2018 Sydney, Australia

Antitumor and acute toxicity studies of 4-(pyridin-4-yl)-6-(thiophen-2-yl)pyrimidin-2(1*H*)-one against Ehrlich ascites carcinoma and sarcoma-180

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In an effort to discover an effective and selective anti-tumor agent, 4,6-diarylpyrimidones as constrained chalcone analogues have been synthesized were evaluated against a panel of human cancer cell lines. Striking selectivity was displayed by the compounds against MiaPaca-2 (breast) cell lines while PC-3 (prostate) and A-549 (lung) cell lines were almost resistant to the exposure of the test compounds. Compound SK-25 exhibited remarkable cytotoxicity against MiaPaca-2 cell line with an IC50 value of 1.95 μM and was found to induce apoptosis evidenced through phase contrast microscopy, DAPI staining, mitochondrial membrane potential loss. The cell phase distribution studies indicated that the apoptotic population increased from 1.79% in control sample to 30.33% in sample treated with 20 μM compound SK-25. The anti-tumor efficacy of SK-25 was investigated on Ehrlich ascites tumor (solid), sarcoma 180 (solid) tumors and Ehrlich ascites carcinoma. The compound was found to inhibit tumor development by 94.71% in Ehrlich Ascites Carcinoma (EAC), 59.06% in Ehrlich Tumor (ET, solid) and 45.68% in Sarcoma-180 (solid) at 30 mg/kg dose. Additionally, SK-25 was established to be non-toxic at a maximum tolerated dose of 1000 mg/kg in acute oral toxicity in Swiss-albino mice. The current study provides insight for further investigation of the anti-tumor potential of the molecule.

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