Med Chem (Los Angeles) 2017, 7:11 (Suppl)
DOI: 10.4172/2161-0444-C1-037

Investigations on structure-activity relationships and anti-proliferative activities of some bis-benzimidazole derivatives

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As cancer chemotherapy has not yet reached the desired level, intensive studies are being conducted to develop more potent, more selective and less toxic novel anticancer drugs. In anticancer drug development studies, the effect of novel compounds on apoptotic and anti-apoptotic gene expressions is very important. In our preliminary studies, a series of 2-substituted benzimidazole derivatives were synthesized and tested for their cytotoxic effect against leukemic cell lines. These compounds were particularly found to be quite selective against the hepatocellular carcinoma cell line. Then, the effect of bis-benzimidazol derivative compounds on apoptosis and their mechanism of action was investigated in hepatocellular carcinoma in rats. In this study, anti-proliferative activities of twelve bis-benzimidazole derivatives was evaluated. The synthesized bis-benzimidazole derivatives were used to determine the potency and specificity against five different cancer cells (Human Lung Adenocarcinoma Epithelial Cells (A549), Human Renal Cancer Cells (A498), Human Cervical Cancer cells (HeLa), Human Skin Malignant Melanoma Cells (A375), Human Hepatocellular Carcinoma Cells (HepG2) lines) compared to methotrexate (MTX). In conclusion, bis-benzimidazole derivatives exhibited higher anti-proliferative than 2-substituted benzimidazoles.

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