A New Class of Antimetabolites: Pyridine Thioglycosides as Potential Anticancer Agents

Galal H. Elgemeie[a,*], Elsayed M. Mahdy[a], Mona A. Elgawish[b], Mohammad M. Ahmed[c], Wafaa G. Shousha[a], and Mohammad E. Eldin[a]

[a] Faculty of Science, Chemistry Department, Helwan University, Helwan, Cairo, Egypt. Fax: 0 02 02 25 55 24 68. E-mail: elgemeie@yahoo.com
[b] National Center for Radiation Research and Technology, Cairo, Egypt
[c] Cancer Biology Department, National Cancer Institute, Cairo University, Cairo, Egypt

* Author for correspondence and reprint requests

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The present study was designed for highlighting and focusing on the cytotoxic activity of a new class of antimetabolites both on human cell lines, namely liver carcinoma cell line (Hepg2), lung carcinoma cell line (H460), breast carcinoma cell line (MCF7), brain carcinoma cell line (U251), and animal cell line EAC (Ehrlich ascites carcinoma cells). The results revealed that some of these modified deazapyrimidine thioglycosides have significant cytotoxic activity against EAC cells with growth inhibition percentage ranged between 80% to 90%. The possible inhibitory mechanism of the pyridine thioglycosides was explored by studying the cell cycle perturbation of thioglycosides against human cell lines *(in vitro*) as well as the most suitable time for maximum compound cytotoxic activity after 6, 18, and 24 h of incubation. To confirm the cytotoxic activity of these compounds, they have been tested for their apoptotic and antiproliferative activity *in vivo* against solid Ehrlich tumours using five groups of Swiss albino mice for 37 days from inoculation and three treatments, 250, 500 and 1,000 μg/kg body weight. There was significant reduction in Ehrlich tumour size in case of the 500 and 1,000 μg/kg body weight group but mild significant tumour reduction in the 250 μg/kg body weight group. Histograms of DNA per cell for each treatment group indicated that there was a dose-dependent increase in the preG_1 phase with a corresponding complete arrest of cells from entering the G_2/M phase compared to the untreated EAC group.

In conclusion, pyridine thioglycosides have proven good cytotoxic effects against EAC cells and also significant cytotoxic activity against the four tested human cell lines. Flow cytometric DNA ploidy analysis of pyridine thioglcyosides against the Hepg2 and U251 cell lines revealed that the postulated mechanism of action of pyridine thioglcyosides is cell cycle arrest in the S phase. This is similar to antimetabolites and cell cycle arrest in the G_2/M phase (M phase) in the same way as microtubule inhibitors like pyridine thioglycosides are cell-cycle-specific in the S phase and the M phase (in case of human cell lines) and have apoptotic effects (in case of animal cell line).

Key words: Anticancer Agents, Antimetabolites, Pyridine Thioglycosides