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INDUCTION OF CASPASE 3 AND MODULATION OF SOME APOPTOTIC GENES IN HUMAN ACUTE PROMYELOCYTIC LEUKEMIA HL-60 CELLS BY CARBOPLATIN WITH AMIFOSTINE

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Induction of caspase 3 and modulation of some apoptotic genes in human acute promyelocytic leukemia HL-60 cells by carboplatin with amifostine. M. MIROWSKI, M. RÓŻALSKI, U. KRAJEWSKA, E. BALCERCZAK, W. MŁYNARSKI, R. WIERZBICKI. Pol. J. Parmacol., 2003, 55, 227–234.

The influence of carboplatin alone and carboplatin in combination with cytoprotective agent amifostine on the growth, caspase 3 activity and some apoptotic genes expression was investigated *in vitro* in human acute promyelocytic leukemia HL-60 cells. Proliferation of HL-60 cells exposed to carboplatin dropped down with increasing dose of the drug. This effect was slightly higher when carboplatin was used in combination with amifostine. The cytotoxic index (IC_{50}) was estimated as 6.6 and 4.4×10^{-4} M (after 24 h) and 3.3 and 2.5×10^{-5} M (after 48 h) for carboplatin and carboplatin with amifostine, respectively. This effect was accompanied by induction of caspase 3 activity. HL-60 cells treated with carboplatin alone showed about 120-fold increase in caspase 3 activity. Combination of carboplatin with amifostine induced the enzyme activity up to 280 times. Furthermore, the expression of *bcl-2*, *c-myc* and *bax* genes involved in apoptosis as well as *p65*, which function in this process is unknown, were determined. Semi-quantitative RT-PCR showed a decrease in *bcl-2* and an increase in *bax, c-myc* and *p65* expression in HL-60 cells treated with carboplatin in combination with amifostine as compared to the cells treated only with carboplatin.

We conclude that amifostine may potentiate carboplatin therapeutic efficiency towards human acute promyelocytic leukemia cells.

Key words: *HL-60 cell line, carboplatin, amifostine*

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