

ABSTRACT

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Title of diploma thesis: The effect of flubendazole on the efficacy of paclitaxel in breast cancer cells

Flubendazole (FLU) is a common anthelmintic drug for veterinary and human use. Its molecular mechanism of action is based on binding to β -tubulin subunit of microtubules. FLU was previously identified to have antitumor activity. The aim of this study was to evaluate the effect of FLU on antiproliferative efficacy of paclitaxel (PTX) in breast cancer cells.

For this study, three breast cancer cell lines were used – non-metastatic line MCF-7 and two metastatic cell lines, MDA-MB-231 and BT-474. The effects of FLU, PTX and FLU + PTX combination on viability of the cells (determined using WST-1 analysis) and on the expression of molecules involved in cell adhesion, migration and proliferation on mRNA (RT-PCR analysis) and protein levels (western blotting) were studied and compared. The activity of caspases after PTX and FLU treatment was evaluated using luminescence measurement.

FLU has significant antiproliferative effect in all tested cell lines. MCF-7 and MDA-MB-231 have been shown as the most sensitive to PTX and FLU treatment. However, combination of PTX + FLU had not higher effect on cell viability as well as the levels of molecules involved in cell adhesion, migration and proliferation than PTX alone. Moreover, FLU decreased the accumulation of PTX within cells. On the other hand, higher activity of the caspase 2 and caspases 3/7 were observed in cells treated with PTX + FLU combination. FLU alone also increased the activity of caspases significantly.