ABSTRACT

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Title of diploma thesis: Cytostatic effect of new paclitaxel derivatives in selected cancer lines

Paclitaxel (PTX) is antiproliferative drug used for therapy of some types breast, lung and ovarian cancer. It stabilizes microtubules and as a result, cause inhibition of the normal cell division. Unfortunately it makes no difference between normal and malignant cells and affect all proliferating cells. To increase selectivity of effect of PTX on cancer cells, conjugates of PTX with gonadotropin-hormon (Gn-RH) were prepared in Institute of experimental botany of Czech Academy of Sciences in Prague.

The aim of our study was to compare effect of PTX conjugates and PTX alone on cell viability and proliferation of cell lines MDA-MB-231 and CaCo2. Cell line MDA-MB-231 is human breast adenocarcinoma line which express receptors for GnRH. CaCo-2 cell line is derived from epithelial colorectal adenocarcinoma cells which don`t express receptors for Gn-RH. Antiproliferative effect of tested substances was monitorated by two different tests of cell viability and real-time cell analysis by system x-CELLigence. For appointment of cytotoxic effect was used primary culture of rat hepatocytes.

Obtained results showed lower antiproliferative effect of derivat MP264 in comparation of PTX. Comparable antiproliferative effect of derivates MP265 and MP394 with PTX on cell line MDA-MB-231. Derivat MP 264 showed lower cytotoxic effect in primary cell culture of rat hepatocytes and lower antiproliferative effect in CaCo-2 cell line. Stability tests proved fast degradation of MP 265 derivat in growth medium.