

ABSTRACT

Apoptosis represents one of the cell death mechanisms which is realized after the application of taxanes in breast cancer cell lines. Apoptosis induction can be principally triggered either by outer or inner pathway.

The aim of the diploma thesis is to contribute to the elucidation of role and mechanisms of the inner mitochondrial pathway of apoptosis induction after taxane application (paclitaxel and SB-T-1216) employing a model of breast carcinoma cell lines SK-BR-3 (nonfunctional p53, functional caspase-3) and MCF-7 (functional p53, nonfunctional caspase-3). Specifically, we tested the effect of both employed taxanes on mitochondrial membrane potential, ROS level and the expression and localization of proteins regulating inner mitochondrial pathway. Taxane application resulted in mitochondrial membrane dissipation in SK-BR-3 cell line. However, this was not shown in MCF-7 cell line. We found no changes in Bax and Smac/DIABLO expression after taxane application in both tested cell lines. There was a decrease of Bid expression after taxane application in SK-BR-3 line, but not in MCF-7 line. Taxane application did not lead to the translocation of Bax and Bid (tBid) proteins from cytosol to mitochondria in both tested cell lines. Similarly, there was no Smac/DIABLO release from mitochondria to cytosol. We detected cytochrome c release from mitochondria into the cytosol after taxane application in SK-BR-3 cell line. This was not shown in MCF-7 line. Finally, we found significant downregulation of proteins of the IAP family after taxane treatment in both cell lines.

The results indicate that taxane application triggers inner mitochondrial pathway of apoptosis induction in SK-BR-3 cell line. However, the mechanisms of outer mitochondrial membrane permeabilization is not clear. In the case of MCF-7 cell line, taxane application triggers apoptosis induction by other mechanisms than mitochondrial pathway.

Key words: breast cancer cells, taxanes, apoptosis induction, mitochondrial membrane potential, ROS, Smac/DIABLO, proteins of the Bcl-2 family, proteins of the IAP family