

## **ABSTRACT**

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Title of diploma thesis: The effect of alpha-humulene and caryophyllene oxide in ovarian cancer cells.

Sesquiterpenes  $\alpha$ -humulene and  $\beta$ -caryophyllene oxide are substances with antiproliferative activity against number of tumor cell lines. In this study, the antiproliferative effect of  $\alpha$ -humulene and  $\beta$ -caryophyllene oxide was tested alone and in combination with doxorubicin, using neutral red uptake assay. Doxorubicin-sensitive cell line A2780 was more sensitive to the action of doxorubicin and sesquiterpenes than SKOV3 cell line, which is naturally doxorubicin-resistant. To determine the interactions between sesquiterpenes and doxorubicin, software program CalcuSyn which is based on Chou-Talay method was used. The combination indexes of sesquiterpenes with doxorubicin were determined. Both sesquiterpenes had antagonistic effect on doxorubicin in A2780 cell line and synergistic effect on SKOV3 cell line. The mechanism of the antiproliferative effect of all three tested substances is explained by the production of ROS. For the determination of pro-oxidant effects of the tested substances the DCF assay was used. Our results showed good pro-oxidant properties of doxorubicin increasing ROS production in both tested cell lines. Sesquiterpenes showed only slight pro-oxidant effect on A2780 cell line. Furthermore, we tested the ability of  $\alpha$ -humulene and  $\beta$ -caryophyllene oxide to increase intracellular concentrations of doxorubicin using UHPLC method. Both substances showed the ability to increase intracellular concentration of doxorubicin in both tested cell lines,  $\beta$ -caryophyllene oxide being more efficient. When determining the intracellular distribution of doxorubicin in cells by confocal microscopy, the results were inconclusive.