ABSTRACT

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Title of rigorous thesis: Effect of selected sesquiterpenes on carbonyl reductase 1 activity *in vitro*

Sesquiterpenes, the main components of plant essential oils, are integral parts of spices, traditional food and beverages. They are used in folk medicines, pharmaceutical industry as well as in cosmetics. Several sesquiterpenes possess interesting biological activities but they could interact with concurrently administered drugs via the modulation of activity and/or expression of drug-metabolizing enzymes. Enzyme carbonyl reductase 1 (CBR1) is one of the enzymes participating in the metabolism of a number of endogenous and xenobiotic compounds. One of the CBR1 substrates is chemotherapeutic agent doxorubicin, which is metabolized by this enzyme to the less effective metabolite doxorubicinol, which is responsible for the doxorubicin cardiotoxicity. The aim of this rigorous thesis was to find out the ability of five selected sesquiterpenes (i.e. valencene, β-caryophyllene oxide, α-humulene, *cis*-nerolidol and *trans*-nerolidol) to affect the activity of CBR1 *in vitro*. The effect of studied substances on the activity of this enzyme was monitored in cytosolic fraction obtained from rat liver and also on recombinant human CBR1. Activity of CBR1 was in both cases assessed by method of Maté et al. (2008) using menadion as a substrate. The highest inhibitory effect was found in case of *trans*-nerolidol, which decreased CBR1 activity in cytosol by 14,3 % compared to the control. In case of human recombinant CBR1, no significant change in activity was observed. Taken together, the results of this study indicate that the selected sesquiterpenes valencene, β-caryophyllene oxide, α-humulene, *cis*-nerolidol and *trans*-nerolidol do not express considerable inhibitory effect towards CBR1.