

# 1 ABSTRACT

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Title of diploma thesis: Modulatory effect of humulene, caryophyllene and caryophyllene oxide on selected biotransformation enzymes in human liver cells

Sesquiterpenes are substances of natural origin, produced mainly by higher plants. They are mainly found in food supplements and natural medicines. Large structural diversity is a feature of these substances. The anti-inflammatory, antiparasitic and anti-cancer effects were also reported. The aim of this diploma thesis was to investigate the effect of selected sesquiterpenes,  $\alpha$ -humulene (HUM),  $\beta$ -caryophyllene (KAR) and  $\beta$ -caryophyllene oxide (CAO), on gene and protein expression of selected phase I drug-metabolizing enzymes, which were carbonyl reductase 1 (CBR1), aldo/keto reductase 1C (AKR1) and several cytochrome P450 isoforms, namely CYP3A4, CYP2B6 and CYP2C.

The effect of sesquiterpenes on the gene and protein expression of enzymes was studied using precision-cut human liver slices (8 mm diameter, 150-180  $\mu$ m thickness). Liver samples were received from hepatic surgery of five subjects of both sexes and at 58-69 years of age. Liver slices were incubated with studied compounds (HUM, KAR, CAO) at 10  $\mu$ M concentration in a 12-well plate in a pneumoxide atmosphere (95% O<sub>2</sub>/5% CO<sub>2</sub>) for 24 hours. The mRNA and protein expression of individual enzymes was detected using quantitative PCR and Western blot, respectively.

HUM caused significant inhibition in CBR1 and AKR1C mRNAs in one liver sample. Protein expression of CBR1 was remarkably inhibited by HUM in all liver samples, while that of AKR1C3 was markedly increased in three samples. The results of this work showed that effects of studied sesquiterpenes are inconsistent, and they reflected rather inter-individual variability among liver donors.