ABSTRACT

Charles University

Faculty of Pharmacy in Hradec Králové

Department of Biochemical Sciences

Candidate: Zlata Slavíčková

Supervisor: prof. Ing. Barbora Szotáková, Ph.D.

Title of diploma thesis: Liver slices – model system for studying the effect of sesquiterpenes on detoxifying enzymes

Sesquiterpenes are naturally occurring substances, mainly in higher plants as secondary metabolites. Together with monoterpenes, represent the main components of plant essential oils. Sesquiterpenes are biologically active compounds, among their biological activities belong anti-inflammatory, anti-carcinogenic, antioxidant, antibacterial and antimycotic effects.

The aim of this diploma thesis was to find out the influence of three structurally similar acyclic sesquiterpenes *cis*-nerolidol, *trans*-nerolidol, and farnesol on the activity of selected biotransformation enzymes – aldo-keto reductase (AKR1A1, AKR1C9), carbonyl reductase 1 (CBR1), NAD(P)H-quinone oxidoreductase 1 (NQO1), cytochrome P450 (CYP1A1, CYP1A2, CYP2B, CYP3A), sulfotransferase (SULT), glutathione-S-transferase (GST), and UDP-glucuronosyltransferase (UGT) in rat liver. The influence of sesquiterpenes on selected enzymes was studied in precision-cut liver slices. The precision-cut tissue slices were obtained from rat liver (*Rattus norvegicus*, tribe *Wistar*). The thickness of the slices was approximately 200-250 μm and diameter 8 mm. The precision-cut liver slices were incubated for 8 and 24 hours in the medium containing the test substances in concentration 10 μM. The incubation was performed in a 12-well plate at 37 ˚C in the atmosphere of pneumoxide. The slices affected by CNER showed an increase in activity of AKR1A1 after 24 hours of incubation. AKR1C activity in slices affected by FAR showed a decrease in activity after 8 hours of incubation. TNER caused decrease in activity of SULT after 8 hours and inactivity of CYP2B/3A after 8 and 24 hours incubation. The activity of CBR1, NQO1, and GST in slices affected by the tested sesquiterpenes did not show any significant change in comparison to control. The activities of cytochrome P450 isoforms CYP1A1, CYP1A2, and conjugating enzyme UGT were not detected.