Abstract

Charles University
Faculty of Pharmacy in Hradec Králové
Department of Biochemical Sciences

Candidate: Bc. Michaela Smolíková, DiS.
Supervisor: doc. PharmDr. Iva Boušová, Ph.D.
Advisor: Mgr. Michaela Šadibolová
Title of diploma thesis: Effect of camphor isomers on the expression of drug-metabolizing enzymes in human liver cells

Camphor is a cyclic ketone from the group of monoterpenes. Two camphor isomers occur in nature. Currently, camphor is used as an antiseptic, analgesic, rubefacients, and anti-inflammatory drug. Camphor is sed mainly in preparations for topical use, where it has a mild anesthetic effect and a feeling of warmth together with its characteristically strong fresh scent. Most camphor intoxications are caused by improper use or dosing. The aim of the diploma thesis was to determine the effect of isomers (+)-camphor and (-)-camphor on the expression of selected phase I and II biotransformation enzymes. The precision-cut human liver slices prepared from a total of three patients, two men and one woman at the age range of 46 - 49 years, were used as biological material. Liver slices were incubated with 10 μM and 50 μM (+)-camphor and (-)-camphor for 24 hours at 37°C. Protein expression of phase I (cytochrome P450 (CYP) 3A4, CYP2C, aldo-keto reductase (AKR) 1C3), and phase II enzymes (glutathione S-transferase (GST) A) was determined using the western blot technique. The mRNA expression of phase I (CYP3A4, CYP1A2, CYP2C, CYP2B6, AKR1C, and NAD(P)H:quinone oxidoreductase (NQO1) and phase II enzymes (GSTA1, GSTP1, UDP-glucuronosyl transferase (UGT) 1A6, and sulfotransferase (SULT) 1A1) was determined by real-time polymerase chain reaction. The most significant changes at protein levels occurred in patient L48, where induction of CYP3A4 ((+)-camphor 10 and 50 μM) and inhibition of CYP2C and AKR1C3 ((+)-camphor 50 μM, (-)-camphor 10 and 50 μM) were noticeable. At the mRNA level, induction of several enzymes by (-)-camphor 50 μM in patient L48 (CYP3A4, AKR1C, GSTA, and UGT1A6) and by (+)-camphor 50 μM in patient L49 (NQO1) was found. Both isomers at both concentrations caused inhibition of GSTP1 (patient L48) and SULT1A1 (patient L49) mRNA. Camphor could therefore affect the efficacy of concomitantly administered drugs.