

ABSTRACT

Charles University in Prague

Faculty of Pharmacy in Hradec Králové

Department of Biochemical Sciences

Candidate: Erika Vyskočilová

Supervisor: PharmDr. Iva Boušová, Ph.D.

Title of diploma thesis: MODIFICATION OF SELECTED BIOTRANSFORMATION ENZYMES DURING AGEING (IN RAT)

Ageing is an inevitable biological process characterized by progressive functional decline of all organ systems with simultaneous increase in oxidative damage as a result of reactive oxygen species (ROS) accumulation. Increased activity of antioxidant enzymes, such as peroxidase and catalase, is related to increased production of ROS during ageing. Activity of biotransformation enzymes such as cytochrome P450 (CYP) and glutathion-*S*-transferase (GST) changes during ageing too. In general, activity of enzymes is lower in very young and very old individuals than in the period of adulthood. The aim of the present work was to study age-related changes in activities and expression of selected xenobiotic-metabolizing enzymes (GST, CYP 1A, CYP 2B, CYP 3A4) and antioxidant enzymes (catalase, peroxidase, superoxiddismutase) in rat liver. Male Wistar rats were sacrificed by decapitation under ether anesthesia at the age of 6 weeks and 21 months (6 individuals in each group). Subsequently, liver specimens were processed to obtain the subcellular fractions (microsomes and cytosol) in which the specific activities of enzymes were assessed by spectrofluorimetric and spectrophotometric methods. GST protein expression was also monitored by immunoblotting with specific antibody against GSTA and normalized to the amount of β -actin. Specific activity of GST was about 6-fold higher in 21-month-old rats, which was accompanied by an increase in the GST protein expression. In contrast, specific activity of CYP1A2, CYP2B and catalase significantly decreased with increasing age. Specific activity of CYP 2B was 4.5-fold lower in 21-month-old rats than in 6-week-old ones, while specific activity of CYP1A2 decreased by one fourth only. No significant changes in peroxidase and superoxiddismutase activity with age were observed. The obtained results can contribute to the understanding of age-related changes in xenobiotic metabolism, which can be caused by alterations in the activity and/or expression of these biotransformation and antioxidant enzymes.