

Abstract

Many exogenous and endogenous compounds are referred to as endocrine disruptors (EDCs), as they interfere with natural synthesis, signaling and metabolism of endogenous hormones. Common exogenous endocrine disruptors are benzo(a)pyrene (BaP) and 17 α -ethinylestradiol (EE2). Endogenous endocrine disruptor 17 β -estradiol (E2) is frequently present in the environment as well.

In this thesis, the effect of the mentioned EDCs and their combinations on gene and protein expression of CYP1B1, 3A1 and 3A2 in rat liver, kidney and lung was determined. Protein expression was studied using Western blot method and specific antibodies; gene expression was assessed by quantitative PCR. Moreover, the effect of tested EDCs and their combinations on BaP metabolism and CYP3A specific activity (measured as testosterone 6 β -hydroxylation) were studied in liver microsomal samples.

It was confirmed, that BaP significantly increases CYP1B1 expression in rat liver and lung both alone and together with EE2 or E2. Pretreatment of rat with E2 and BaP increases the ability of BaP to induce CYP1B1 expression. On the contrary, EE2, E2 and their combination decrease the CYP1B1 gene expression. The rate of BaP metabolites formed in liver microsomal samples increases in rats pretreated with BaP and its combinations. In liver, there was a decrease in expression of CYP3A1 and 3A2 in rats pretreated with EE2, E2 and its combinations. This corresponds with specific activity of CYP3A, which decreased after pretreatment of rat with EE2, E2 and its combination with BaP. On the contrary, pretreatment of rat with E2 caused an increase in CYP3A1 and 3A2 expression in kidney. In lung, BaP significantly increases the gene expression of CYP3A1 and 3A2. EE2 and E2 alone slightly increase the gene expression of CYP3A1 and 3A2 as well. Combinations of these EDCs significantly decrease CYP3A expression, the cause of this phenomenon waits to be further elucidated.

The changes in CYP1B1, 3A1 and 3A2 expression caused by studied EDCs can influence their metabolism and genotoxic effects in organism and subsequently affect their impact on environment as well.

(In Czech)

Keywords: endocrine disruptors, benzo(a)pyrene, 17 α -ethinylestradiol, 17 β -estradiol, cytochrome P450, expression