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INTERACTION OF STYRENE AND ETHYLMETHYLKETONE IN THE INDUCTION OF CYTOCHROME P450 ENZYMES IN RAT LUNG, KIDNEY AND LIVER AFTER SEPARATE AND COMBINED INHALATION EXPOSURES

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SUMMARY

The present study compares the induction of different cytochrome P450 forms (CYP1A1/2, 2B1, 2E1) after pretreatment with styrene, ethylmethylketone separately or in combined exposures. Combined exposures lead to cumulative elevation of CYP levels, except for CYP1A1 and 2B1. Induction of CYP1A1 was higher in liver and kidney respectively and did not change significantly with the pretreatment mode. Styrene produced two times higher induction of CYP1A2 in the lung and kidney than ethylmethylketone. The simultaneous application of both inducers lead to significantly higher induction of CYP1A2 than that estimated after pretreatment with each of the inducers separately. CYP2B1 was induced by styrene to higher extent in the liver, where it was almost indetectable in controls. Major form of cytochrome P450 induced by styrene proved to be CYP2E1 - about 3-fold induction of chlorzoxazone hydroxylation activity in the liver and 2.5 times in the lung. Ethylmethylketone significantly potentiated the CYP2E1 induction ability of styrene. This induction of CYP2E1-dependent catalytic activity correlates with the enzyme levels detected by immunoblotting.

Key words: P450 forms, styrene, ethylmethylketone, combined exposure, immunodetection

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