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EFFECTS OF ACETONE ON THE CAPACITY OF o-XYLENE AND TOLUENE TO INDUCE SEVERAL FORMS OF CYTOCHROME P450 IN RAT LIVER

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SUMMARY

The influence of acetone on the induction of P450 in lung, kidney and liver by toluene and xylene was studied in an attempt to estimate more precisely the range of P450 which are proposed to function in the activation of xylenes and toluene to toxic metabolites in the conditions of combined exposures. The addition of acetone potentiated the induction of CYP1A1/2 to 4 times ethoxyresorufin deethylation that from control animals after pretreatment with toluene. The level of this enzymatic activity (0.4 nmol/min/mgP) estimated in this study is consistent with the turnover number for the purified CYP1A1 (0.45 nmol/min/mgP). The enzymatic assay activity results were confirmed by immunoblotting detection of the CYP1A1/2 levels. Oppositely, the addition of acetone in the inhalation protocol using o-xylene lead to a lower ethoxyresorufin deethylation activity as that in rat livers from rats pretreated with xylene alone. Pentoxyresorufin deethylation activity was enchanced strongly by toluene (3.5 times the controls) and by xylene (4 times the controls) and the addition of acetone potentiated the induction of CYP2B1 both after xylene and toluene. A 4 fold induction of CYP2E1 dependent chlorzoxazone hydroxylation after exposure to toluene and 2.5 fold after xylene corresponded to the enzyme levels of P4502E1 detected by immunobloting. The addition of acetone consequently potentiated the induction effect of toluene and xylene and increased its levels more markedly in the case of xylene, which is a weaker inducer of CYP2E1.

Key words: P450 forms, xylene, toluene acetone, combined exposure, immunodetection

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