A study on the metabolism of aromatic organic solvents and their interaction

(Benzene, Toluene and Xylene)

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- Abstract -

We studied the effects of a single, combined and mixed exposure of benzene, toluene and xylene on P-450-mediated metabolizing capacity, and the activities, other related enzymes and the excretion of their metabolites.

1. The contents of cytochrome P-450 and b_5 in liver microsomes derived from treated groups were slighly higher than those from the control group: The increases of P-450 contents were prominent in B3, TX and mixed groups (M)($p<0.05$) and that of b_5 contents were also prominent B1, X3, TX and M groups ($p<0.05$).

2. The activities of NADPH-P-450 reductase in liver microsomes derived from treated groups were increased: The activity of TX group was prominent.

The activity of NADH b_5 reductase showed same tendency as NADPH-P-450 reductase: The activities of B1, T2, BT and TX groups were prominent ($p<0.05$).

3. The prominent increase of EROD activity was observed with single treatment of B, T, X ($p<0.05$), but not the with combined and mixed treatment. Also the prominent increase of PROD activities were observed with the treatments except BT and TX groups ($p<0.05$).

4. Western blotting with monoclonal antibodies against P4502B1/2 isozymes showed the presence of cytochrome P4502B1 in liver microsomes from rats treated with xylene and T3, and color densities of bands were corelated with the injected xylene amounts. The color density against P4502E1 were slightly increased in benzene, T1 and T2 groups compared with xylene treated groups.

5. The amounts of urinary metabolites of the organic solvents by single treatments were significantly higher than those by combined and mixed treatment ($p<0.01$).

These results suggested that P4502E1 isozyme might be responsible for the metabolism of benzene and toluene, and P4502B1 isozyme is for xylene. We also found that P-4502B1 was inducible by xylene. When we compared the results of single treatments with those of combinatory and mixture treatments for the activities of P-450 dependent monooxygenase, the activities were reduced in the groups of combined and mixed reatments. Therefore, there must be some interactions of the organic solvents in inductions of P4502E1 and P4502B1 and in their action in the metabolism.

Key Words: Benzene, Toluene, Xylene, CYP2B1/2, CYP2E1/2, CYP1A1/2, Cytochrome P-450 dependent monooxygenase, Metabolites

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Abbreviation: B, benzene; T, toluene; X, xylene; BT, benzene+toluene; BX, benzene+xylene; TX, toluene+xylene; M, benzene+toluene+xylene