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TOXIC EFFECTS OF ACUTE EXPOSURE TO PARTICULAR XYLENE ISOMERS IN ANIMALS

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Abstract. The effect of exposure to particular xylene isomers at a concentration of 3000 ppm on rotarod performance in rats and the respiratory rate in mice was investigated. Rotarod performance was tested in rats immediately after termination of a 6-hour exposure, and the respiratory rate in mice was recorded during a short 6 minute exposure to individual xylene isomers. In both rats and mice the toxic effects of exposure to ortho- and meta-xylene were more pronounced than that of para-xylene.

INTRODUCTION

Commercial xylene or "xylol" is a mixture of xylene (dimethylbenzene) isomers. Depending on whether it is derived from petroleum or coal tar sources, xylol may have varying ratios of three xylene isomers and thereby different toxicity. Toxicity data, such as LD_{50}, LC_{50} vary for particular xylene isomers (1, 2, 3) and may indicate different degrees of their toxic effect.

The toxic effect of exposure to xylene is chiefly on the nervous system and respiratory tract (4).

The aim of the present study was to compare the acute toxic effects of particular xylene isomers on the nervous system in rats and the respiratory system in mice.

MATERIALS AND METHODS

Ortho-, meta-, para-xylene (reagent grade) were supplied by Reachim and the Polish Chemical Company. In the experiments, rotarod performance was tested in rats and respirtory rate was measured in mice.

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Male Wistar rats of body weight 200—250 g were exposed to the vapours of individual xylene isomers at a concentration of 3000 ppm, in a dynamic inhalation chamber (1.3 m^3 volume) for 6 hours. Vapours of xylene isomers were generated by heating liquid solvents in washers. The required concentrations of vapours were obtained by appropriate air influx. Concentrations of xylene isomers in the air of inhalation chambers were measured with gas chromatography. Determination of solvents was carried out using 3 m column with 10% FFAP (2-nitroterephtalate polyethylene glycol) on chromosorb WAW DMCS as a stationary phase; temperature of column 150°C. Measurements were made by means of gas chromatograph type Varian 1400 with a flame-ionization detector.

Rotarod performance was tested before and immediately after termination of exposure according to the method described by Kaplan and Murphy (5). Each exposure and control group consisted of 10 rats. The rotarod apparatus used consisted of a 8 cm diameter wooden rod rotated at 12 rpm, and suspended horizontally 20 cm above the floor which was constructed from metal bars connected to a power source of 80 V and 2 mA. Before the experiment, animals were trained, and only those rats which could perform normally on the rotarod for at least one week, were used in testing. The ability of rats to remain on the rotating rod for 2 min was taken as an index of normal neuromuscular function. In both sham-exposed and exposed groups rotarod performance test was carried out before and immediately after termination of a 6-hour exposure.

The respiratory rate was measured in Balb/C male mice of body weight 25—30 g by means of the plethysmographic method (6). Each animal was placed in a body plethysmograph attached to a small dynamic inhalation chamber (2.3 l volume). A Stattham's pressure transducer was attached to each plethysmograph. The respiratory pattern was recorded with a Beckman's polyphsiograph. Respiratory rate was recorded continously before the exposure to solvents, during 6 min exposure and 3 min after termination of exposure.

Mice were exposed to the vapours of each xylene isomer at a concentration of 3000 ppm. The concentration of 3000 ppm for inhalation exposure was arbitrarily settled. It was near LD_{50} value which was found for changes in respiratory rate and motorcoordination disturbances caused by exposure to the mixture of xylene isomers (7). Each exposure group consisted of 6 mice.

RESULTS AND DISCUSSION

All rats exposed for 6 hours to individual xylene isomers, at a concentration of 3000 ppm survived the exposure. Under the same conditions of inhalatory exposure (3000 ppm) all xylene isomers caused disturbances in rotarod performance in rats. The effects of ortho- and meta-xylene were more clearly pronounced than that of para-xylen (Table 1).

Each tested xylene isomer at a concentration of about 3000 ppm caused a decrease in respiratory rate in mice (Fig. 1). The maximum decrease of respiratory rate was always observed in the first or second min of exposure. In the first minute of exposure to para-xylene the respiratory rate amounted 54% of control value, whereas exposure to ortho- and meta-xylene caused the decrease in the respiratory rate to 46% and 43% of the control values, respectively. The toxic effect of exposure to ortho-xylene took a longer time, and 3 minute after exposure the respiratory rate still amounted only 68% of control value whereas 3 minute after exposure to para- and meta-xylene the respiratory rate reached 95% and 106% of control values, respectively. The observed changes in respiratory rate during exposure to individual xylene isomers indicated that the irritant effect of ortho- and meta-xylene was more pronounced than that of para-xylene.

Acute inhalation exposure to individual xylene isomers, at a concentration of about 3000 ppm caused depression of the central nervous system in rats and irritation of the respiratory tract in mice.

Under conditions of inhalatory exposure to individual xylene isomers, the rotarod performance test in rats and measurement of respiratory rate in mice demonstrated similar potency of action of ortho- and meta--xylene. Their toxic effects were clearly more pronounced than that of para-xylene.

The observed different degrees of toxic effects for xylene isomers seem to be concordant with that suggested by toxicity data (such as LD_{50}) for particular xylene isomers obtained after intraperitoneal exposure (2); they differ, however from those suggested by toxicity data (LD_{50}, LC_{50}) reported for individual xylene isomers after oral or inhalation exposure (1, 3).

The reason for observed different degree of toxic effects of particular xylene isomers is not known.

It may be assumed that the position of the methyl group at the benzene ring is crucial.

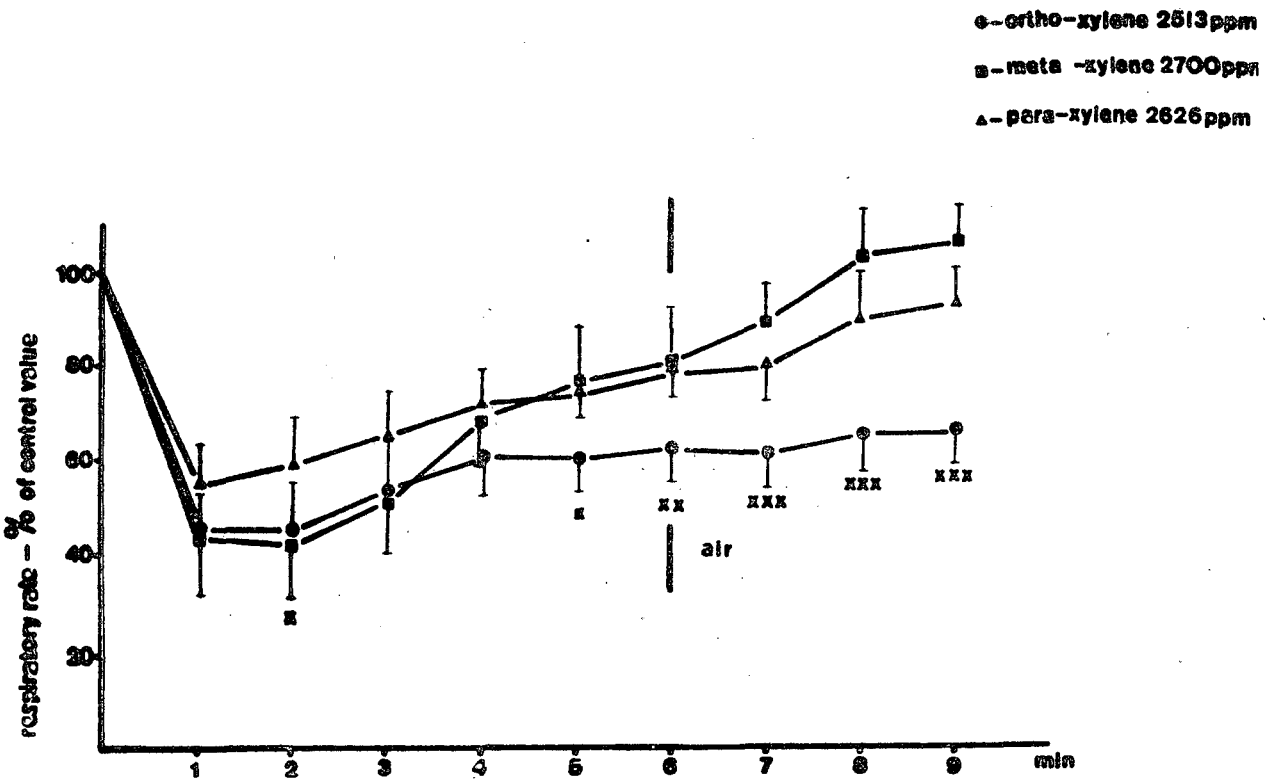

Fig. 1. Respiratory rate in mice exposed to ortho- meta-, and para-xylene at a concentration of 3000 ppm.
Each point represents the mean value of separate measurements in 6 mice ± SD.. Statistically significant difference in comparison to para-xylene $x-p \leqslant 0.05$, $xx-p \leqslant 0.01$, $xxx-p \leqslant 0.001$ (Analysis of variance (ANOVA) followed by the Tukey test for multiple comparisons).

TABLE 1. Rotarod performance of rats exposed to the vapours of individual xylene isomers for 6 hours. Rotarod performance was tested immediately after termination of exposure

Control	ortho-xylene		meta-xylene		para-xylene	
No of failures/ No of tested animals	Concentration ppm (mg/m^3)	No of failures/ No of tested animals	Concentration ppm (mg/m^3)	No of failures/ No of tested animals	Concentration ppm (mg/m^3)	No of failures/ No of tested animals
0/10	3017 (13123)	9/10	3141 (13663)	1/10	3109 (13524)	1/10
0/10	3038 (13215)	10/10	3045 (13245)	5/10	3021 (13141)	0/10
0/20		19/20**		6/20*		1/20

Statistically significant difference in comparison to para-xylene x—$p \leqslant 0.05$, xx—$p \leqslant 0.001$ (Fisher test)

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