

Concentrations of phenol, *o*-cresol, and 2,5-xyleneol in the urine of workers employed in the distillation of the phenolic fraction of tar

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Abstract

Phenol (87.3 mg/l), *p*-cresol (58.6 mg/l), *o*-cresol (76.9 mg/l), and 2,5-xyleneol (36.7 mg/l) were detected in the urine of workers employed in the distillation of the high temperature phenolic fraction of tar (carbolic oil). The concentrations of these compounds in the urine of non-exposed male workers was 11.7 mg/l, 25.7 mg/l, 68.1 µg/l, and 69 µg/l respectively. The excretion rates were 4.20 mg/h for phenol, 2.4 mg/h for *p*-cresol, 3.3 mg/h for *o*-cresol; and 1.5 mg/h for 2,5-xyleneol. The highest concentrations of the mentioned compounds were detected in urine collected between eight and 10 hours from the beginning of exposure. The kinetics of excretion are considered.

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Phenol is a normal constituent of human urine^{1,2} and concentrations above the physiological level have been found in the urine of people that have contact with benzene¹⁻⁴ or phenol.^{5,6} *p*-Cresol also occurs in the urine of non-exposed people and its concentration can reach 50 mg/l.⁷ Small amounts of *o*-cresol have been detected in the urine of workers in contact with toluene.⁸⁻¹²

After exposure to *p*-xylene, 2,5-xyleneol was found in urine.¹³

Because high concentrations of *o*-cresol and 2,5-xyleneol were found in hydrolysates of urine from workers in a carbochemical plant, measurement of excretion of these compounds in successive portions of urine collected during 24 hours was undertaken.

Materials and methods

The investigation was carried out on 106 male workers employed in the distillation of the

high temperature phenolic fraction of tar (carbolic oil) and exposed mainly to phenol, cresols, xyleneols, and other phenolic derivatives. Control urine specimens were collected from 26 male subjects not exposed professionally to phenol, cresols, or xyleneols. All men were smokers.

URINE SAMPLING

Urine samples were collected as follows: (1) voids collected after four hours at work (examined directly after the end of the work shift) from exposed male workers and non-exposed subjects. (2) Successive voids, collected for 24 hours from 16 exposed male workers.

URINE ANALYSIS

The concentrations of phenol, *p*-cresol, *o*-cresol, and 2,5-xyleneol in the hydrolysate of urine were determined spectrophotometrically after separation by means of thin layer chromatography on polyamide gel with the developing solvent chloroform-methanol (99:1 v/v).¹⁴ The concentrations were corrected for a specific gravity of 1.024 and for creatinine concentration in the urine.

Because of the low concentrations of *o*-cresol and 2,5-xyleneol in urine of occupationally non-exposed workers, gas chromatographic techniques were used for these compounds.

STATISTICS

Geometric mean and geometric SD were calculated. Toxicokinetic calculations were made according to the methods of Piotrowski.¹⁵

Results

The metabolite concentrations were assumed to distribute log normally. Table 1 gives the concentrations of phenol, *p*-cresol, *o*-cresol,

Table Concentration and excretion rate of phenol, *p*-cresol, *o*-cresol, and 2,5-xyleneol in urine

Urinary metabolite	Group	No of subjects	Observed value (mg/l)	Value corrected for		Excretion rate (mg/h)
				Creatinine (mg/g)	Specific gravity* (mg/l)	
Phenol	A	89	67.8 (2.483)	38.2 (2.212)	87.3 (2.182)	4.20 (2.281)
	B	26	13.8 (1.604)	8.3 (1.531)	11.7 (1.486)	0.53 (1.876)
<i>p</i> -cresol	A	106	54.3 (1.722)	32.5 (1.784)	58.6 (1.841)	2.43 (2.064)
	B	26	28.2 (1.514)	17.8 (1.515)	25.7 (1.430)	1.32 (1.785)
<i>o</i> -cresol	A	77	58.9 (3.031)	38.8 (2.243)	76.9 (1.614)	3.31 (2.204)
	B	24	75.0 (1.684)†	62.2 (1.594)†	68.1 (1.567)†	3.75 (2.862)†
2,5-Xyleneol	A	64	30.4 (2.775)	17.4 (1.720)	36.7 (1.614)	1.50 (1.794)
	B	15	79.1 (2.636)†	54.5 (2.366)†	69.0 (2.178)†	3.92 (2.263)†

Values are geometric means (geometric SD); A = workers employed in the distillation of carbolic oil; B = non-exposed male workers.

*Specific gravity of urine 1.024.

†Values in µg/l, µg/g, µg/l, and µg/h for *o*-cresol and 2,5-xyleneol in non-exposed workers.

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and 2,5-xyleneol in the four hour samples of urine from the workers and non-exposed subjects.

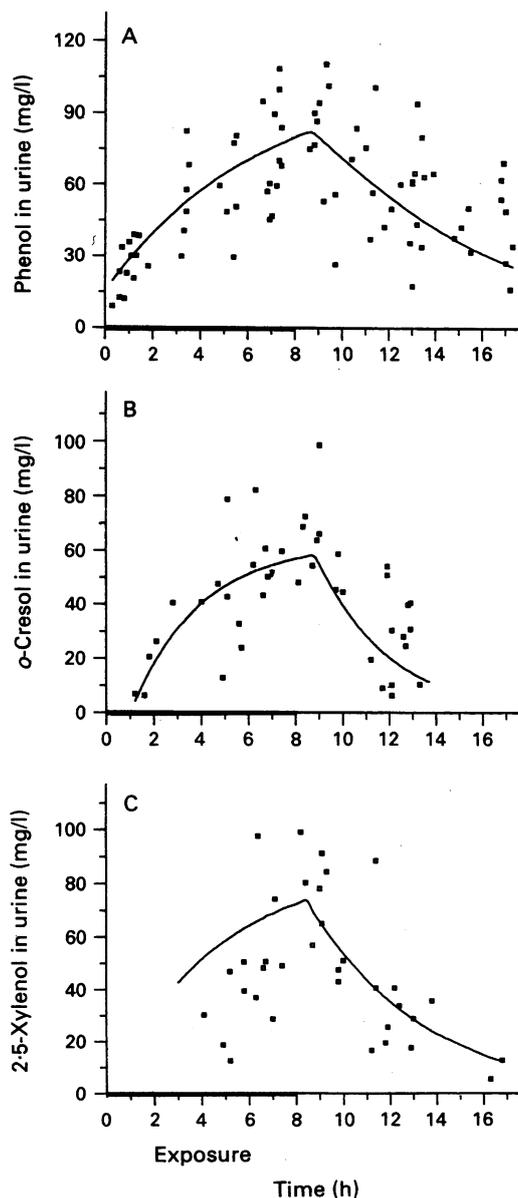
The necessity to use hydrolysates of urine is evidence that the compounds are excreted in urine in the form of conjugates, probably as glucuronides and sulphates.

In 16 workers employed in the distillation of carbolic oil, the excretion of phenol, *o*-cresol, and 2,5-xyleneol in successive voids of urine collected during 24 hours was determined. The highest concentrations of phenolic compounds were found during the first two hours after the end of the work shift.

The urinary excretion of phenol, *o*-cresol, and 2,5-xyleneol as a function of time from the beginning of exposure was examined mathematically. The elimination of phenol, *o*-cresol, and 2,5-xyleneol in the urine of workers can be described by the equations shown in the figure.

Because of considerable fluctuations in the concentration of *p*-cresol in urine of non-exposed persons, the excretion of *p*-cresol has not been considered here.

Urinary excretion as a function of time. (A) phenol; regression equation for $t \leq 8.8$, $c(t) = 105(1 - e^{-0.16(t+1)})$; for $t > 8.8$, $c(t) = 105(1 - e^{-0.16(t+1)})e^{-0.16(t-8.8)}$; $k = 0.16/h$, $t_{1/2} = 4.3$ hours. (B) *o*-Cresol; regression equation for $t \leq 8.8$, $c(t) = 62.68(1 - e^{-0.34(t-1)})$; for $t > 8.8$, $c(t) = 62.68(1 - e^{-0.34(t-1)})e^{-0.34(t-8.8)}$; $k = 0.34/h$, $t_{1/2} = 2.0$ hours. (C) 2,5-Xyleneol; regression equation for $t \leq 8.4$, $c(t) = 85.6(1 - e^{-0.23t})$; for $t > 8.4$, $c(t) = 85.6(1 - e^{-0.23t})e^{-0.23(t-8.4)}$; $k = 0.23/h$, $t_{1/2} = 3.0$ hours. c = concentration of compounds in urine; t = time from start of exposure. Note: *o*-cresol and 2,5-xyleneol were not found in some urine samples in which phenol was found. Hence there are fewer points on graphs B and C than on graph A.



Discussion

Considerable differences in the concentration of vapours of phenolic compounds at various sites of the work area, difficulties in defining time of the exposure of particular workers, and likely absorption of phenolic compounds through the skin are reasons why measurement of the mean metabolite concentration in the urine seems to offer the most rational solution for realistic estimation of exposure.

Technologically processed carbolic oil contains phenol (14%), *o*-cresol (4.8%), and 2,4- and 2,5-xyleneol (1.8%). High values for concentrations of phenol, *o*-cresol, and 2,5-xyleneol in the urine confirm that exposure to these compounds occurred. Because *o*-cresol has been detected in the urine of persons having contact with toluene⁸⁻¹² high concentrations of *o*-cresol in the urine of the workers might be the result of their exposure to both toluene and *o*-cresol present at the workplace.

For technical reasons, the data on urinary concentration of the phenolic compounds are not accompanied in this series of investigations by counterpart data on their concentrations in the air of the work premises. The data suggest, however, that in the absence of data on air concentrations, the determination of phenolic compounds in the urine may be valid as a comparative test of exposure.

The similar shape of the excretion curves presented in the figure suggests similarities in the metabolism of these phenolic compounds.

The phenol, *o*-cresol, and 2,5-xyleneol excretion curves found under conditions of exposure in a carbochemical plant are similar to the curve obtained by Piotrowski¹⁵ after experimental exposure of humans to phenol. With regard to phenol itself, the fit of the kinetic curve is only approximate. The real values suggest a more prolonged process of elimination, a phenomenon discussed earlier by Paradowski² in the case of workers with longstanding exposure to aromatic compounds. Such prolonged excretion does not occur in volunteers not previously exposed to aromatic compounds (unpublished data). With this reservation in mind the studied phenolic compounds are characterised by high turnover rates, which principally exclude their possible accumulation in the course of subsequent days of exposure.

The kinetic results presented here show that phenol, *o*-cresol, and 2,5-xyleneol are quickly excreted into the urine. Thus the results of the biological monitoring relate to exposure on the day of urine collection rather than on the preceding days.

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