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Short Communication

THE TOXICITY OF METHYLISOCYANATE FOR RATS

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The toxicity of methylisocyanate has become an important subject because of the recent poisoning disaster in Bhopal in India. A literature search resulted in only one reference, from Kimmerle et al. [1]. However, this reference contained sufficient data to enable one to derive a concentration—time mortality-response relationship. In this short note the experimental data of Kimmerle et al. [1] will be summarized and the derived relationship between mortality and exposure conditions discussed.

Experimental exposure of rats to methylisocyanate

Kimmerle et al. [1] exposed rats to different concentrations of methylisocyanate and also varied the duration of exposure. The experimental conditions are summarized in Table 1. Only well-controlled exposures were included in the derivation of the relationship.

Derivation of concentration—time-mortality response-relationship

Using the method of probit analysis described by Finney [2] for the case with two independent parameters, concentration and time, the mortality relationship was derived from the experimental data in Table 1. The results are summarized below.

$$y = b_0 + b_1 \ln c + b_2 \ln t$$

$$P = \int_{-\infty}^{y-5} \exp(-\tfrac{1}{2}u^2)\, du$$

where % mortality = 100 × P, y = probit, c = concentration in mg/m^3, t = exposure period in minutes, and b_0, b_1, b_2 = regression coefficients.

t_{b_x} = Student t as a criterion for testing the condition that b_x is different from zero, x = 0, 1, 2.

chi-square = 7.598

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TABLE 1

Exposure of rats to methylisocyanate (from Ref. [1])

Concentration (mg/m^3)	Exposure period (min)	Number of animals exposed	Number of animals dead
51	60	20	7
68	60	5	2
37	60	5	1
49	120	20	10
50	120	20	10
5	120	20	0
54	240	20	20
21	240	20	16
12	240	20	10

degrees of freedom = 6

$b_0 = -6.640$ $tb_0 = -3.049$
$b_1 = 1.069$ $tb_1 = 4.296$
$b_2 = 1.637$ $tb_2 = 5.207$

variance $b_0, b_0 = 4.7417$
covariance $b_0, b_1 = -0.4450$
covariance $b_0, b_2 = -0.6483$
variance $b_1, b_1 = 0.0619$
covariance $b_1, b_2 = 0.0470$
variance $b_2, b_2 = 0.0988$

Student t for 95% confidence at 6 degrees of freedom = 2.45

$b_1/b_2 = 0.653$ (95% confidence limits: 0.344—0.962)

On the basis of the derived mortality relationship the LC_{95}, the LC_{50}, the LC_5 and the lower 95% confidence limit of the LC_5 were plotted against the duration of exposure. This is presented in Fig. 1.

Discussion

The derived relationship may be useful in risk analysis of processing and storage of methylisocyanate. The relationship has to be transformed for that purpose into the following equation

$$\text{Probit} = 1.637 \ln (C^{0.653} t) - 6.64$$

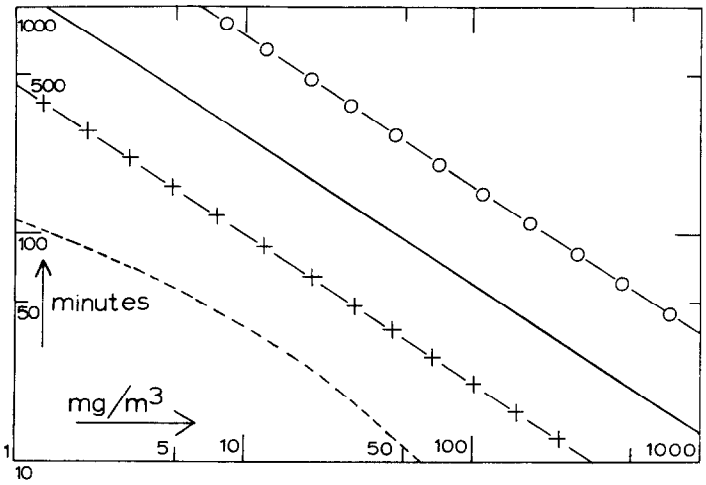

Fig. 1. Exposure of rats to methylisocyanate. Plot of lethal concentrations against duration of exposure: —o—o—: LC_{95}; ————: LC_{50}; —×—×—: LC_5; and — — — — —: lower 95% confidence limit of LC_5.

The term $(C^{0.653}\ t)$ may be considered as a dose factor. In case of varying concentration during the exposure period this term should be converted into

$$\int_{t_1}^{t_2} [C(t)]^{0.653}\, dt$$

where t_1 = time of start exposure, t_2 = time of end exposure, and $C(t)$ = concentration as function of time during exposure.

It is remarkable that the exponent of the concentration is smaller than 1. This is exceptional compared with other gases like chlorine and ammonia [3]. The significance of this small exponent in the case of methylisocyanate is that the duration of exposure is dominant in determining the mortality response. On the contrary, the exponent in the case of ammonia and chlorine is equal to or greater than 2, and the concentration dominates in determining the mortality response.

A prolonged exposure to methylisocyanate may be the cause of the high number of victims in Bhopal in India. One should consider in this connection that methylisocyanate does not have a well recognizable odor at concentrations up to 24 mg/m^3 [1].

References

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