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Fire Research Note No 1035

ON THE NON-EXISTENCE OF SYNERGISM BETWEEN INHALED HYDROGEN CYANIDE AND CARBON MONOXIDE

by

R D LYNCH

May 1975

FIRE RESEARCH STATION

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SUMMARY

Rats were exposed either to hydrogen cyanide, or carbon-monoxide, or various mixtures of these two gases to determine the degree of synergism, if any, with respect to the inhalation L Ct_{50}s. Within the sensitivity of the measurements, the toxicities of the two gases appear to be purely additive, ie no synergism exists.

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Department of the Environment and Fire Offices' Committee
Joint Fire Research Organization

FOREWORD

This note reports part of a study of the toxicity of the combustion products of wood and plastics carried out at the Chemical Defence Establishment, Porton Down, under contract to the Fire Research Station.

A complete account of the work under the contract, and discussion of its implications, is to be published elsewhere. All enquiries concerning the work described in this note should be directed to the Fire Research Station.

The principal objective of the study has been to determine whether or not the inhalation toxicity of the combustion products from wood, and from a selection of plastics materials commonly present in buildings, can be accounted for entirely by the carbon monoxide present. The inhalation toxicity has been measured in terms of the LCt_{50}* with respect to the carbon monoxide present for half-hour exposures of rats and guinea pigs.

The work reported in this note is an ancillary study designed to determine whether mixtures of two known toxic components of combustion products, carbon monoxide and hydrogen cyanide, exhibit positive synergism when present together; that is to say, whether the toxicity of mixtures is greater than is to be expected from the summation of the individual toxicities adjusted for relative potency. No evidence for such synergism has been found.

P.C.B.

*Product of concentration and exposure time giving a mortality of 50 per cent. Estimated by probit analysis of experimentally observed mortalities for a range of concentrations and a given exposure time.

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INTRODUCTION

At the request of the Joint Fire Research Organisation of the Department of the Environment and Fire Offices' Committee, an attempt was made to measure the degree of synergism, if any, between hydrogen cyanide and carbon monoxide when inhaled by rats. The only effect noted in this series of experiments was mortality.

Synergism between HCN and CO might be important in the case of atmospheres evolved from fires from certain materials as both gases are evolved in large quantities from some organic materials.

METHODS

Hydrogen cyanide was generated continuously by reacting potassium cyanide (1 M solution in 0.1 M NaOH) with 3 M phosphoric acid in aqueous solution. The two solutions were pumped continuously into a heated reactor flask; wherein the evolved HCN was stripped out using a stream of laboratory air. (Fig. 1)

HCN was sampled into Neale bubblers containing 5 mls of 1.0 M NaOH using an air flow of 1 l/m. The resultant NaCN was estimated using a CN electrode. Carbon monoxide was obtained from cylinders and monitored using a calibrated infra-red CO monitor.

Either or both gases were introduced into a chamber of approximately 125 l, with an air stream of 100 l/m for dilution purposes.

Randomised male Charles River albino rats were used for all exposures. Ten animals were used for each exposure of 30 minutes. Deaths were counted at plus 24 hours, although the results were always stable after about 1 hour from the end of the exposure.

RESULTS AND DISCUSSION

The crude mortalities for the two pure gases and those for mixtures of the two gases are given as a function of Ct in Tables 1-3. These results were analysed to find the LCt_{50}'s and limits.

The two sets of exposures using pure gases only gave the following results.

For HCN:

LCt_{50} = 3500 mg min/m^3: 95 per cent limits = 3800 → 3100

the regression equation is

$Y - 5.289 = 10.07 (x - 3.571)$

For CO:

LCt_{50} = 158200 mg min/m^3: 95 per cent limits = 168000 → 147000

the regression equation is

$Y - 5.247 = 9.879 (x - 5.244)$

Because b in each regression equation was almost identical (10.07 and 9.879) it was worthwhile submitting both sets of results to a potency ratio analysis. This gave slightly different results for the LCt_{50}.

For HCN:

LCt_{50} = 3480 mg min/m^3

CO:

158250 mg min/m^3

with a calculated potency ratio of 45.5 (95 per cent limits 50.7 → 40.9).

From this potency ratio one may examine each set of combined exposures as if they were to one gas only of an equivalent total toxicity.

For example, from exposure set which consisted of a mixture of gases in the concentration ratio 10:1 (Table 3) take experimental result line 1.

Ct of CO (mg min/m^3)	Ct of HCN (mg min/m^3)	Mortality
36000	3600	10/10

By multiplying the HCNCt ty 45.5 and summing with the CO Ct one obtains a result as if all the gas were CO; ie

CO Ct = 36000 mg min/m^3

HCNCt x 45.5 = 163800 mg min/m^3

Total Ct expressed as CO = 199800 mg min/m^3

Similarly, by dividing the Ct of CO by 45.5 and summing with the Ct of HCN one obtains a result as if the gas were all HCN; ie

Ct of CO ÷ 45.5 = 791

Ct of HCN = 3600

Total Ct expressed as HCN = 4391 mg min/m^3

The three groups of experiments with combined exposures to HCN and CO were calculated for equivalent total toxicity to one gas using the above conversion; the results are given in Table 4. Probit analyses were made on these results to compare with those for the pure gases; the results are given in Table 5. The result for the various gas mixtures always fits in the range for single gases. It is obvious, therefore, that for the mixture ratios used, and within the sensitivity of the method, there is no synergism between CO and HCN.

Table 1

Mortality data for rats inhaling hydrogen cyanide (nine sets of exposures)

Ct of HCN (mg min/m^3)	Mortality (No. dying/No. exposed)
5760	10/10
5040	10/10
4980	9/10
3450	8/10
4320	7/10
3600	4/10
2700	1/10
1800	0/10
2025	0/10

Table 2

Mortality data for rats inhaling carbon monoxide
(twelve sets of exposures)

Ct of CO (mg min/m^3)	Mortality (No. dying/No. exposed)
116700	1/10
140700	5/10
140700	6/10
185100	5/10
205200	10/10
185100	7/10
185100	6/9
161100	3/10
141000	1/10
185100	7/10
205200	10/10
225370	10/10

Table 3

Mortality data for rats inhaling mixture of
hydrogen cyanide and carbon monoxide

Concentration ratio (CO/HCN)	Ct of CO (mg min/m^3)	Ct of HCN (mg min/m^3)	Mortality (No. dying/No. exposed)
10:1	36000	3600	10/10
	30000	3000	7/10
	24000	2400	3/10
25:1	63000	2550	9/10
	55500	2250	6/10
	49500	1950	3/10
50:1	87000	1800	8/10
	75000	1500	6/10
	67500	1350	3/10
	60000	1200	1/10

Table 4

Ct values in the combined exposure to HCN and CO converted to single gas equivalent total toxicity, (using potency ratio)

Exposure ratio (CO/HCN)	Calculated equivalent single gas Ct (mg min/m^3)		Mortality (No. dying/No. exposed)
	as CO	as HCN	
10:1	199800 166500 133200	4391 3659 2927	10/10 7/10 3/10
25:1	179025 157875 138225	3935 3470 3038	9/10 6/10 3/10
50:1	168900 143250 128925 114600	3712 3148 2834 2519	8/10 6/10 3/10 1/10

Table 5

Results of probit analysis for single gas equivalent total toxicity in combined exposures to CO and HCN, and a comparison with the measured pure gas toxicities

Concentration ratio (CO:HCN)	Calculated equivalent single gas toxicity	
	LCt_{50} with 95% confidence limits expressed as CO	LCt_{50} with 95% confidence limits expressed as HCN
10:1	147391 (162000–126000)	3239 (3600–2800)
25:1	150217 (163000–129000)	3302 (3600–2800)
50:1	141457 (159000–130000)	3109 (3500–2800)
Measured LCt_{50} with 95% confidence limits for pure gases.	158200 (168000–147000)	3500 (3100–3800)

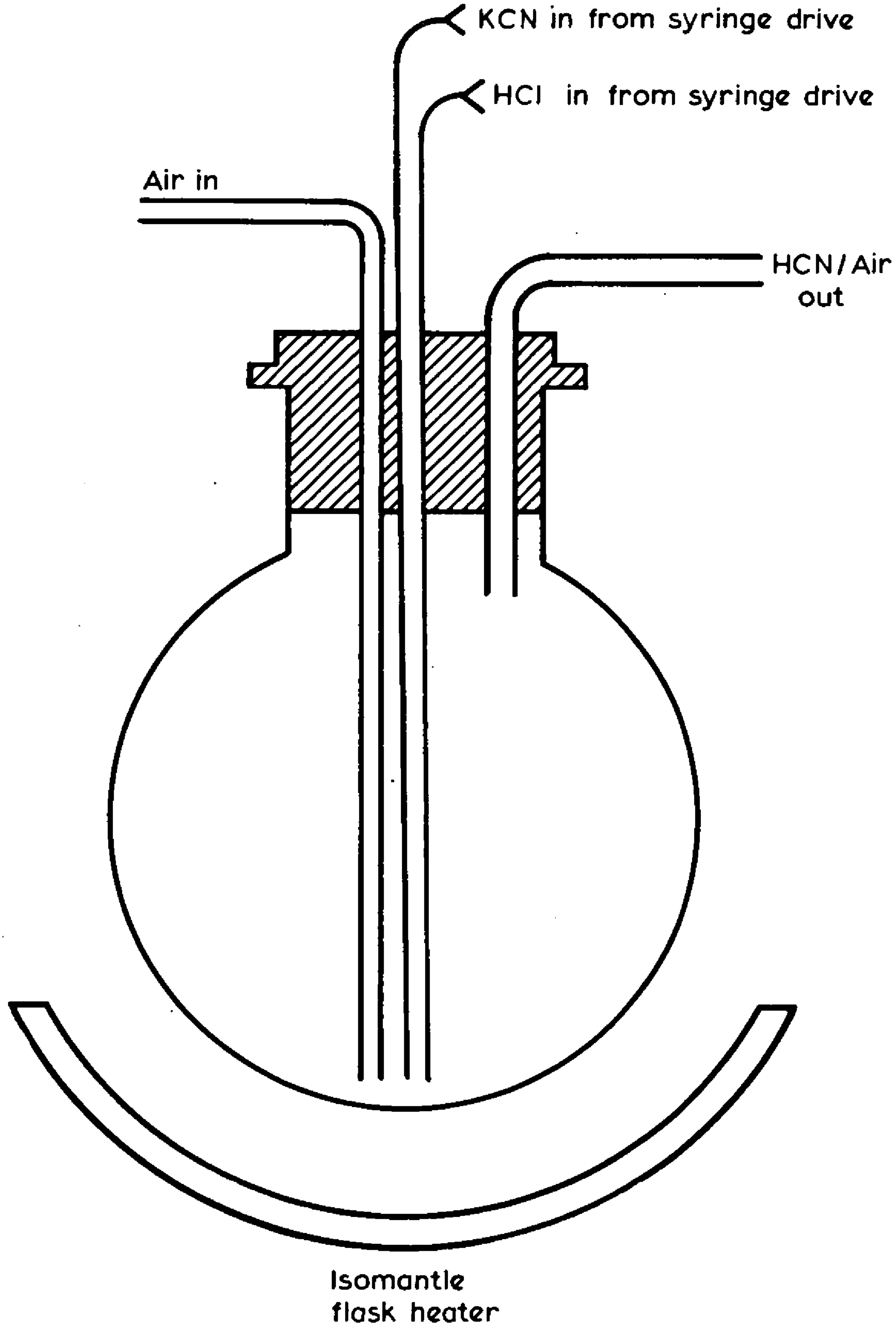

Figure 1 HCN generator

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