MEDIAN LETHAL DOSE OF 3-AMINO-1,2,4-TRIAZOLE

BY

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ABSTRACT

3-Amino-1,2,4-triazole has been reported to inhibit the liver catalase and the kidney catalase but not the blood catalase, though even its median lethal dose has not been known still.

In the present study, the median lethal dose of 3-amino-1,2,4-triazole in mice was found to be 5.47 g/kg by intraperitoneal administration and 5.54 g/kg by subcutaneous administraiton.

INTRODUCTION

The liver catalase activity of tumor-bearing hosts has been reported to show a remarkable decrease[1]. Since Heim showed that 3-amino-1,2,4-triazole inhibits the liver catalase and the kidney catalase but not the blood catalase[2], triazole has been studied mainly in connection with the mechanism of depression of the liver catalase activity in tumor-bearing animals[3].

On the other hand, triazole has been found to inhibit phenol formation from benzene in rat liver[4,5]. It was thus applied to the study of the mechanism of intoxication in benzene poisoning. It was found that intraperitoneal administration of triazole prevented benzene poisoning of rats[6]. From this fact, it was postulated that hemopoietic disturbace in benzene poisoning was caused by phenol formation from benzene in the animal body.

Triazole promises to be a rather important and useful medical material, not only in research, but also in the clinical medicine of the future though even its median lethal dose has not been known. Accordingly, the median lethal dose of 3-amino-1,2,4-triazole was determined in this study.

MATERIALS AND METHODS

Experimental animals used were four week old male mice of ICR-JCL strain, weighing 20 grams. Fifty four mice were used in each experiment. They were fed with commercial pelleted food and water *ad libitum,* in

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cages at 21±2°C and 55±5% relative humidity.

The 3-amino-1,2,4-triazole used was made by Tokyo Chemical Industrial Company. In the first experiment, 10% aqueous solution of triazole (disinfected at 100°C for 10 minutes) was administered to fifty four mice intraperitoneally. In a second experiment, the same solution was administered to fifty four mice subcutaneously on the back. The mice in each experiment were divided into six groups, each group receiving a different dose of triazole.

Five days after the administration, the number of dead mice were counted, and each median lethal dose was calculated using the modification of Behrens method.

Results

As shown in the tables, either intraperitoneal or subcutaneous administration of triazole to mice showed a similar median lethal dose.

Tables MEDIAN LETHAL DOSE of 3-AMINO-1,2,4-TRIAZOLE

1. Intraperitoneal Injection

Dose (g/kg)	Number of Animals			Rate of Cumulative Mortality
	Tested Mice	Survived Mice	Dead Mice	
3.0	9	9	0	0/28
4.0	9	8	1	1/19
5.0	9	5	4	5/15
6.0	9	4	5	10/15
7.0	9	1	8	18/19
8.0	9	0	9	27/27

LD_{50}=5.47 g/kg

2. Subcutaneous Injection

Dose (g/kg)	Number of Animals			Rate of Cumulative Mortality
	Tested Mice	Survived Mice	Dead Mice	
3.0	9	9	0	0/30
4.0	9	7	2	2/21
5.0	9	7	2	4/16
6.0	9	2	7	11/16
7.0	9	3	6	17/20
8.0	9	0	9	26/26

LD_{50}=5.54 g/kg

Experimental animals died of triazole intoxication, neither of peritonitis nor other diseases.

Experimental animals, especially those surviving, showed no abnormal behavior except lethargy.

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References

1) Greenstein, J. P., Jentrette, W. V. and What, J.: J. Nat. Cancer Inst., **2**: 283 (1941).
2) Heim, W. G., Appleman, D. and Pyfrom, H. T.: Science, **122**: 693 (1955).
3) Sugimura, T.: Gann, **47**: 159 (1956).
4) Nomiyama, K.: Med. J. Shinshu Univ., **7**: 27 (1962).
5) Nomiyama, K.: Bull. Tokyo Med. Dent. Univ., **11**: 297 (1964).
6) Nomiyama, K.: Med. J. Shinshu Univ., **7**: 41 (1962).