(b) (4)

CONFIDENTIAL

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Tox. Konzern

ACUTE ORAL TOXICITY TO RATS

OF (b) (4)

TINUVIN 770

(b) (4)

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Authors:

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We, the undersigned, hereby declare that the work was performed under our supervision, according to the procedures herein described, and that this report provides a correct and faithful record of the results obtained.

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Division of Toxicology

Sample Designation: (b) (4)

Examination for: Acute oral toxicity to rats.

Date examined: April-June 1972.

EXPERIMENTAL PROCEDURE

Rats of the CFY strain, in the weight range 93 to 127g were starved overnight before treatment with (b) (4)

(b) (4) was prepared as a 30% suspension in 0.5% carboxy methyl cellulose and administered at a maximum dosage volume of 16.7ml/kg bodyweight. Rats dosed with the vehicle alone (16.7ml/kg) served as controls.

During the observation period of 14 days, a record was kept of all mortalities and signs of toxicity. All rats that died were examined macroscopically in an attempt to identify the target organs, and those animals surviving terminally were similarly examined to detect possible residual damage.

From the mortality data recorded in Table 2, the LD_{50} and its 95% confidence limits were calculated by the method of Litchfield J.T., and Wilcoxon, F. (1949), J. Pharmac. exp. Ther, 96, 99.

RESULTS

Ten rats (five males and five females) were treated with (b) (4) at a level of 5g/kg bodyweight. Nine rats died, indicating that the median lethal dose (LD_{50}) was less than 5g/kg bodyweight. Results of further range finding tests indicated that the median lethal dose lay in the region of 2.5 to 5.0g/kg bodyweight (Table 1).

Dosing was then extended to further groups of rats (five males and five females) in order to locate the median lethal dose more precisely (Table 2).

Signs of reactions to treatment, observed shortly after dosing, consisted of salivation, diarrhoea and diuresis.

Death occurred between one hour and four days after dosing. Autopsy revealed pale patches on all liver lobes.

Recovery of survivors, as judged by external appearance and behaviour was apparently complete within two days. Bodyweight increases were depressed during the first week of the observation period compared with controls, but were normal during the second week (Table 2). Autopsy findings were normal.

CONCLUSION

The acute median lethal oral dose (LD_{50}) and its 95% confidence limits to rats of (b) (4) [redacted] was calculated to be:

3.7(3.1 to 4.4)g/kg bodyweight.

TABLE 1

Mortality data for groups of rats dosed orally with (b) (4)

Range finding screen

Dosage (g/kg)	Mortality ratio (No. of deaths / No. dosed)			Time of death after dosing (Days)
	♂	♀	Combined	
0	$^{0}/_{2}$	$^{0}/_{2}$	$^{0}/_{4}$	-
1.25	$^{0}/_{2}$	$^{0}/_{2}$	$^{0}/_{4}$	-
2.5	$^{1}/_{2}$	$^{0}/_{2}$	$^{1}/_{4}$	4

TABLE 1

Mortality ratio and group mean bodyweight (g) of rats dosed orally with (b) (4)

Full scale test

Sex	Dosage (g/kg)	Bodyweight (g) at			Mortality ratio (No. deaths / No. dosed)	Time of death after dosing (hours)
		Dosing	1 week	2 weeks		
♂	0	97	195	232	0/5	-
	2.5	112	178	243	2/5	<4 days
	3.2	112	167	238	2/5	<42
	4.0	108	151	225	3/5	<42
	5.0	97	died	-	5/5	<43
♀	0	97	165	181	0/5	-
	2.5	106	151	186	0/5	-
	3.2	105	148	181	0/5	-
	4.0	106	159	187	2/5	<42
	5.0	102	146	166	4/5	<67