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Laboratory tests of 5-*p*-chlorophenyl silatrane as a rodenticide*

By J. H. GREAVES, R. REDFERN and H. TINWORTH

Pest Infestation Control Laboratory,
Ministry of Agriculture, Fisheries and Food,
Hook Rise South, Tolworth, Surbiton, Surrey

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SUMMARY

The properties of 5-*p*-chlorophenyl silatrane as a rodenticide against *Rattus norvegicus* and *Mus musculus* were investigated in the laboratory. The high oral toxicity of the compound was confirmed. When the compound was given to laboratory rats and mice by stomach tube at lethal dosages, signs of poisoning were observed within a minute. When caged wild rats and mice were given a choice between plain and poisoned baits the optimum rodenticidal concentration in the bait was about 0·5 % for both species, producing 50 % mortality in wild rats and 95 % mortality in wild mice. The results are discussed in relation to safety in use and the probable effectiveness of the compound as a rodenticide in field conditions.

INTRODUCTION

In the United Kingdom the problems encountered in rodent control with the appearance and spread of resistance to the widely-used anticoagulant rodenticides have given increased emphasis to the need for new rodenticides that are both safe and effective in use (Greaves, 1971). The compound 1-(*p*-chlorophenyl) 2,8,9-trioxa-5-aza-1-silabicyclo (3,3,3) undecane, commonly known as 5-*p*-chlorophenyl silatrane, has been developed as a quick-acting rodenticide by M & T Chemicals Inc., and proposed for use against several rodent species in the United States. Two substantial assets have been claimed for the compound from the point of view of safety in use. First, though it has high acute oral toxicity, its percutaneous toxicity is very low. Second, the compound hydrolyses to non-toxic products after a short time in the presence of moisture, in prepared baits and in the bodies of poisoned rodents, which minimizes the hazard of persistent residues to wild-life and domestic animals (Beiter, Schwarcz & Crabtree, 1970).

This report describes laboratory trials carried out with 5-*p*-chlorophenyl silatrane on the Norway rat (*Rattus norvegicus*) and the house mouse (*Mus musculus*). The main aim of the study was to determine suitable bait concentrations of the compound for use in the field trials described in the two accompanying papers (Rennison, 1974; Rowe, Swinney & Bradfield, 1974).

METHODS

The animals employed included male laboratory rats (Wistar) and mice (LAC Grey) and wild rats and mice of both sexes. The wild mice were laboratory-bred, first or second generation descendants of wild-caught mice. The wild rats included warfarin-susceptible animals, caught in a Midlands refuse destructor and held in the laboratory for at least three weeks before use, and also warfarin-resistant rats caught on farms in the Welshpool area that had survived for at least two weeks in the laboratory after a single subcutaneous dose of 200 mg/kg of warfarin.

Doses of 5-*p*-chlorophenyl silatrane were given by stomach tube to the laboratory animals grouped five to a cage. The compound was ground finely in a mortar, suspended in a 5 % solution of powdered acacia B.P. and then administered to the animals within 15 min. A watch was kept on the treated animals and the time of onset of signs of poisoning was recorded.

Feeding experiments were carried out with singly-caged wild rodents. Each animal was presented with a choice for 48 hr. between plain and poisoned, but otherwise identical, baits. The bait base consisted of 90 % pinhead oatmeal, 5 % wholemeal wheat flour and 5 % corn oil. The two baits, mixed freshly each day, were provided in similar amounts and in sufficient quantity to permit each animal to feed exclusively on the unpoisoned bait without going hungry. The positions of the two baits in each cage were interchanged after the first 24 hr. in order to minimize any effects that place preference might have had on bait consumption. Mortality and the amounts of bait eaten were recorded daily. Animals that died were autopsied and survivors were kept under observation for 7 days after their last exposure to the poison.

We are indebted to M & T Chemicals Inc., Rahway, New Jersey, U.S.A. for providing a supply of 5-*p*-chlorophenyl silatrane. A sample of the compound was returned to the supplier midway through the work and was found to have suffered no significant decomposition in storage.

RESULTS AND DISCUSSION

Oral intubation tests

The results of oral intubation tests with laboratory animals are given in Table 1. The mortality data are consistent with the acute oral LD 50 estimates given by Beiter *et al.* (1970) of 1–4 mg/kg for rats and 0·9–2·0 mg/kg for mice. After a single dose of 10 mg/kg all animals had convulsions within 1 min. and died within 5 min. There was no evidence of subacute toxicity in the animals given successive daily doses and the two rats that died did so immediately after the second dose was administered. No symptoms of illness were seen in any of the animals that survived and at autopsy there were no obvious signs attributable to the poison.

The short interval between dosing and the onset of illness may be compared with corresponding estimates obtained by various techniques of 15 min. for norbormide (Greaves, 1966), 47 min. for sodium fluoroacetate and zinc phosphide and 157 min. for fluoroacetamide (Bentley & Greaves, 1960). These intervals provide a measure of the time available to a rodent for the continued ingestion of

Table 1. *Results of oral intubation tests on male laboratory rats and mice with* 5-p-*chlorophenyl silatrane*

Animals	Mean body weight (g)	Single dose		Four daily doses	
		10 mg/kg	1 mg/kg	1 mg/kg	0·1 mg/kg
Rats	105	5/5	0/5	2/5	0/5
Mice	20	5/5	0/5	0/5	0/5

Table 2. *Results of giving wild rodents a choice for two days between plain bait and bait containing* 5-p-*chlorophenyl silatrane*

Type of animal	Mean body weight (g)	Sex	Conc (%)	Mortality	Mean bait intake (g)		Mean and range of doses (mg/kg) of active ingredient taken by animals that:			
					Poison	Plain	Died		Survived	
Rat (non-resistant)	284	M	1·0	4/10	0·5	9·7	15	4–28	17	3–30
	213	F	1·0	5/10	0·2	2·2	9	3–16	9	0–21
	254	M	0·5	4/10	0·6	14·6	13	9–20	12	6–19
	306	F	0·5	7/10	0·6	5·0	7	3–15	19	10–27
Rat (resistant)	162	M	1·0	5/10	0·2	3·1	14	0–42	16	6–33
	103	F	1·0	9/10	0·2	1·6	23	1–43	0	—
	238	M	0·5	5/10	0·3	6·0	6	0–17	8	0–23
	245	F	0·5	4/10	0·3	9·3	5	3–7	5	0–9
Mouse	17	M	0·5	9/10	0·06	0·1	22	0–71	0	—
	13	F	0·5	10/10	0·06	0·2	27	0–111	—	—
	18	M	0·25	8/10	0·07	0·4	9	0–50	16	13–19
	13	F	0·25	9/10	0·07	0·1	14	0–63	21	21
	14	M	0·1	6/10	0·3	1·4	18	7–25	22	8–35
	15	F	0·1	6/10	0·2	1·0	9	7–15	17	0–35

poisoned bait. Since, as the above figures show, the onset of illness is relatively early with 5-*p*-chlorophenyl silatrane the opportunity for a rodent to ingest a lethal dose is correspondingly less than with the other rodenticides mentioned. This disadvantage may however be countered if the rate of ingestion of the compound can be increased by increasing its concentration in the bait.

Feeding tests with wild rodents

Preliminary feeding experiments with laboratory strains had indicated that the lowest concentrations worth testing in bait were 0·5% for rats and 0·1% for mice. These concentrations were therefore the first to be tried with the wild strains. Successively higher concentrations were then tested with further groups of animals until no appreciable increase in mortality was obtained.

The results are summarized in Table 2. Several animals, particularly mice, died after eating undetectably small quantities of poisoned bait and often these animals also appeared to have eaten no plain bait. However, only two mice and four rats

Table 3. *Chi square analysis of mortality in wild rodents (data from Table 2)*

Species	Source of variation	χ^2	D.F.	P
Mouse	Concentration	8·124	2	0·01–0·02
	Sex	0·414	1	0·5–0·7
	Sex × concentration	0·212	2	0·8–0·9
	Total	8·750	5	0·1–0·2
Rat	Sex	2·464	1	0·1–0·2
	Concentration	0·452	1	0·5–0·7
	Resistance	0·452	1	0·5–0·7
	Sex × concentration	0·457	1	0·3–0·5
	Sex × resistance	0·055	1	0·8–0·9
	Resistance × concentration	2·469	1	0·1–0·2
	Sex × resistance × concentration	2·458	1	0·1–0·2
	Total	8·807	7	0·2–0·3

survived without eating measurable amounts of poisoned bait and, of these, only one mouse had failed to eat at least some of the plain bait. It should be noted that overnight increases in the moisture content of bait of the order of 0·1 g can occur, which may account for some of the apparent failures to eat. Thus the majority, and probably all of the surviving animals did in fact eat a sublethal dose of the rodenticide and then avoided eating a further, lethal dose either by feeding preferentially on the plain bait or by virtually refraining from eating at all for the remainder of the experiment. A previous study of the feeding behaviour of rats in similar experiments indicated that these responses characterized the development of a learned aversion towards the poison and bait material (Greaves, 1966). It seems likely therefore, that if sublethal feeding on the bait were to occur in field conditions, the rodents would tend as a result to avoid eating further amounts of bait containing 5-*p*-chlorophenyl silatrane.

A chi square analysis of the mortality data is given in Table 3. Mortality was not significantly influenced by sex in either species or by resistance to warfarin in the rat. In mice the effect of increasing the concentration of poison in the bait was significant. Kills of 12/20, 17/20 and 19/20 were obtained at concentrations of 0·1, 0·25 and 0·5 % respectively. Since the mortality of 19/20 produced in mice by 0·5 % 5-*p*-chlorophenyl silatrane could scarcely be bettered, it seems likely that this concentration would be near-optimal for the control of house mice in field conditions. In rats the increase in mortality (from 20/40 to 23/40) obtained by increasing the concentration from 0·5 to 1·0 % was insignificant, which is consistent with the conclusion of Beiter *et al.* (1970) that a bait concentration of about 0·5 % is also optimal for the control of this species.

The very obvious difference between the two species in the mortality that occured in tests with the compound at 0·5 % suggests that it is likely to be more effective for the control of mice than of rats. Inspection of Table 2 shows that at this concentration rats generally ate less of the active ingredient (in terms of mg/kg) than did mice. The difference may be attributable to a species difference in ability to taste or smell the compound, though there is no direct evidence of

this. It seems at least as likely that a greater acuity on the part of the rats in detecting the earliest symptoms of poisoning may have contributed to their more frequent survival.

There remains the question of how 5-*p*-chlorophenyl silatrane is likely to perform in field conditions in comparison with other quick-acting rodenticides. As far as the mouse is concerned no comparable data appear to have been published for other rodenticides. The high kill obtained in the feeding test at a concentration of 0·5 % suggests however that in the field the success of treatments against mice is less likely to be limited by any failing of the rodenticide at this concentration than by the general difficulty of attracting the mice away from their normal food supplies to eat rodenticidal baits. Regarding the rat, the relation between the results of laboratory tests of the type used here and those of field trials have been discussed by Rennison, Hammond & Jones (1968) in the context of studies with the rodenticides zinc phosphide and norbormide. These authors report that mean kills of 54 % (13/24) with zinc phosphide and 29 % (7/24) with norbormide in laboratory feeding experiments with wild rats were reflected in the superior performance of zinc phosphide in field trials. The mean kill of 54 % (43/80) obtained here with 0·5 and 1·0 % 5-*p*-chlorophenyl silatrane suggests therefore that the compound is likely to be about as effective as zinc phosphide against rats in the field.

From the point of view of safety in use, it has been mentioned that 5-*p*-chlorophenyl silatrane has advantages over other rodenticides from the standpoints of the low toxicity of bait residues, low secondary poisoning hazard and low percutaneous and subacute toxicity. Nevertheless, the acute toxicity of the compound to non-rodents appears to be at least as great as that of other rodenticides (Beiter *et al.* 1970). It should therefore be realized that the hazard due to accidental ingestion of fresh bait is likely to be no less with this than with most other rodenticides.

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