J. Hyg., Camb. (1961), **59**, 335
Printed in Great Britain

The toxicity and acceptability of the sodium salt of pindone, an anti-coagulant rodenticide, to the house-mouse (*Mus musculus* L.)

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(*Received* 20 *February* 1961)

INTRODUCTION

In large food stores in Great Britain, the house-mouse (*Mus musculus* L.) is more difficult to exclude and control than the common rat (*Rattus norvegicus* Berkenhout). The amount of free water in these stores however is usually limited to gutters and uncovered fire buckets and although mice exist in dry environments with extremely little drinking water, they are known to prefer damp to dry baits in such places (Southern, 1954). Poison baiting permanently with damp baits suffers from the disadvantage that the baits have to be changed frequently and the control of mice by liquid baits has therefore been suggested (Rowe, 1957; Chew, 1958).

Liquid baits which have been most commonly used against rats, particularly in the United States, are thallium sulphate, sodium fluoracetate and the sodium salts of the anti-coagulants warfarin [3-(α-acetonyl benzyl)-4 hydroxycoumarin] and pindone [2-pivalyl-1:3-indandione] (Spencer, 1954). The first two are somewhat dangerous for general use and solutions of anti-coagulant poisons are to be preferred. There is little information available however on the effectiveness of liquid anti-coagulants against mice. Some cage and field tests have been carried out (Crabtree & Robinson, 1953), but the published data are scanty, and further evidence on the toxicity and palatability of the sodium salt of pindone ('Na-pindone') is given below.

METHODS

The sodium salt of pindone used in the tests to be described was a proprietary brand marketed under the name of 'Pivalyn' by Motomco Ltd., N.Y., U.S.A., and was known to contain a chelating compound ('Versene') to prevent precipitation in the presence of the metallic ions normally present in tap water. It was presented to the test animals at a concentration of 0·005% in 20 ml. specimen tubes fitted with a rubber cap carrying a glass drinking spout. Each tube was inverted and clipped to the outside of a cage so that the tip of the spout just projected through the wire mesh into the cage. In a preliminary experiment a number of charged tubes were weighed (to the nearest 0·1 g.), attached to an empty cage and reweighed 24 hr. later. No loss by evaporation or leakage occurred.

In all tests wild mice were kept in individual cages (6 in. × 6 in. × 6 in.) in a room

at 70° F. and fed on wheat. During choice tests mice were offered two tubes placed on opposite sides of the cage, and in order to minimize any effects of place or container preference the positions of the two tubes were reversed each day. In tests lasting more than 2 days the drinking spouts were also exchanged on the third and every alternate day thereafter.

RESULTS

Toxicity tests

Information regarding the toxicity of Na-pindone to house-mice was obtained by allowing five mice deprived of other water to drink the poison *ad lib*. The mice died between the 4th and 6th day (Table 1).

It is possible that these mice continued to drink after they had ingested a fatal dose and therefore, to obtain some information on minimum lethal doses, a further seven were offered Na-pindone for 2 days (Table 2). Three of these survived, but as two ingested larger doses than those that died, it is clear that considerable individual variation in tolerance to Na-pindone can occur. The smallest lethal dose was 6·6 mg./kg. body weight.

Table 1. *The consumption of* 0·005 % Na-*pindone by male house-mice in the absence of drinking water*

Mouse no.	Wt. (g.)	Na-pindone drunk per day (g.)	Total (g.)	Dosage (mg./kg.)	No. of days to death
1	16·2	2·4, 4·3, 1·3, 0·8	8·8	27·1	4
2	17·6	0·5, 1·9, 0·7, 0·4, 0·0	3·5	10·0	5
3	14·5	0·3, 2·0, 0·2, 0·6, 0·4, 0·1	3·6	12·4	6
4	13·6	2·7, 0·0, 0·2, 0·6	3·5	12·9	4
5	7·8	1·3, 2·6, 1·1, 0·3	5·3	34·0	4

Table 2. *Results of offering* 0·005 % Na-*pindone for* 2 *days*

Mouse no.	Sex	Wt. (g.)	Na-pindone drunk per day (g.)	Total	Dosage (mg./kg.)	Result
6	M.	15·7	2·1, 1·7	3·8	12·1	Dead after 4 days
7	F.	16·6	0·3, 0·3	0·6	1·9	Survived
8	F.	17·5	1·1, 1·2	2·3	6·6	Dead after 6 days
9	F.	14·3	2·5, 0·5	3·0	10·5	Dead after 6 days
10	F.	17·6	4·4, 2·3	6·7	19·0	Survived
11	M.	16·8	1·1, 1·0	2·1	6·3	Dead after 7 days
12	M.	14·0	4·1, 1·9	6·0	21·4	Survived

Acceptance tests

To assess the relative acceptability of Na-pindone solution and tap water, eight mice were allowed to choose between them for 8 days. Since one mouse died on the 5th day and the consumption of liquid by others was then falling, only the amounts drunk over the first 4 days are shown in Table 3. The difference in acceptance of the two liquids is clearly not significant. Four of the mice died, the last

21 days after the test began, this being the slowest period to death recorded in all experiments.

An attempt was then made to increase the palatability of Na-pindone to mice by adding 1 % sugar. This formulation was offered to ten mice for 4 days, with tap water as an alternative (Table 4). Since one mouse died on the 3rd day, consumption during the first 2 days only is considered. Again no significant preference for either liquid was shown.

Table 3. *Comparative acceptance of* 0·005 % Na-*pindone and tap water during first* 4 *days of an* 8-*day test*

Mouse no.	Sex	Wt. (g.)	Water drunk over first 4 days	Na-pindone drunk over first 4 days	Difference	Total dosage of Na-pindone (mg./kg.)	Result
13	M.	15·5	2·8	1·0	−1·8	8·0	Dead after 21 days
14	M.	14·7	4·1	1·3	−2·8	10·5	Survived
15	M.	16·2	4·1	2·8	−1·3	4·9	Survived
16	M.	19·3	4·1	0·7	−3·4	3·6	Survived
17	F.	16·0	2·8	0·4	−2·4	3·8	Survived
18	F.	17·6	6·7	10·7	4·0	35·5	Dead after 8 days
19	F.	15·5	2·1	3·1	1·0	44·5	Dead after 5 days
20	F.	18·3	2·7	4·5	1·8	13·4	Dead after 9 days
Total	—	—	29·4	24·5	−4·9	—	—

Table 4. *Comparative acceptance of tap water and* 0·005 % Na-*pindone* + 1 % *sugar during the first* 2 *days of a* 4-*day exposure*

Mouse no.	Sex	Wt. (g.)	Water drunk in 2 days	Na-pindone drunk in 2 days	Difference	Total dosage Na-pindone (mg./kg.)	Result
21	M.	14·0	0·5	3·9	3·4	14·9	Dead after 3 days
22	M.	13·3	1·9	0·2	−1·7	11·3	Dead after 7 days
23	M.	12·2	3·3	0·3	−3·0	4·9	Survived
24	M.	14·8	0·6	15·6	15·0	84·5	Dead after 5 days
25	M.	16·5	1·9	1·1	−0·8	8·5	Survived
26	F.	14·0	1·0	2·6	1·6	13·2	Dead after 5 days
27	F.	14·6	2·1	1·2	−0·9	5·5	Survived
28	F.	17·7	5·1	0·5	−4·6	2·5	Survived
29	F.	14·7	3·9	0·6	−3·3	3·1	Survived
30	F.	16·5	3·1	1·0	−2·1	3·9	Survived
Total	—	—	23·4	27·0	3·6	—	—

The result of a similar test in which the sugar content of the Na-pindone solution was increased to 10 % is shown in Table 5. This test was continued until all the mice had died.

Five of the mice used in this test drank more of the Na-pindone/sugar solution from the 1st day. Nos. 35, 37, 38 and 39 however drank more water, and there was no over-all preference of any significance ($P = 0·5$). By the 5th day, all mice that

https://doi.org/10.1017/S0022172400038997 Published online by Cambridge University Press

were still drinking (including nos. 35, 37, 38 and 39) clearly preferred the sugar solution and maintained this preference to the end.

In a similar experiment in which six mice were offered tap water or Na-pindone plus 10 % sugar for 2 days only, all the mice drank more Na-pindone solution than water from the beginning (Table 6). Mouse no. 43 showed an extraordinary taste for Na-pindone and sugar solution, consuming 20·4 g. in 2 days, whilst mouse no. 41, which took the smallest dose, died first.

Table 5. *The consumption of* 0·005 % Na-*pindone* + 10 % *sugar and tap water until death*

Mouse no.	Sex	Wt. (g.)	Total water drunk (g.)	Total Na-pindone drunk (g.)	Water drunk in 2 days (g.)	Na-pindone drunk in 2 days (g.)	Difference	Total dosage of Na-pindone (mg./kg.)	No. of days to death
31	M.	13·7	0·1	7·9	0·1	5·2	5·1	28·9	4
32	M.	15·5	1·2	26·5	0·4	12·0	11·6	95·5	11
33	F.	15·0	3·2	4·8	2·4	3·2	0·8	16·0	3
34	F.	15·0	2·0	17·6	0·8	8·9	8·1	68·6	6
35	F.	17·7	4·8	16·3	3·4	1·9	−1·5	45·9	6
36	M.	18·1	3·5	9·5	2·0	3·8	1·8	26·2	8
37	M.	18·6	7·2	15·4	4·3	0·5	−3·8	41·4	8
38	M.	12·6	5·7	6·3	3·5	0·6	−2·9	25·0	6
39	F.	19·6	17·7	6·9	8·2	0·3	−7·9	17·6	6
Total	—	—	45·4	111·2	25·1	36·4	11·3	—	—

Table 6. *Comparative acceptance of* 0·005 % Na-*pindone* + 10 % *sugar and water over* 2 *days*

Mouse no.	Sex	Wt. (g.)	Total water drunk (g.)	Total Na-pindone drunk (g.)	Difference	Dosage of Na-pindone (mg./kg.)	Result
40	M.	17·4	0·4	3·8	3·4	10·9	Dead on day 5
41	M.	16·3	0·3	2·8	2·5	8·6	Dead on day 5
42	M.	19·8	0·1	6·8	6·7	17·1	Dead on day 7
43	F.	16·2	2·3	20·4	18·1	62·9	Dead on day 7
44	F.	13·0	1·7	3·1	1·4	11·9	Survived
45	F.	13·9	2·2	2·8	0·6	10·1	Survived
Total	—	—	7·0	39·7	32·7	—	—

It is important where permanent baiting is practised that the acceptability of the poison solution should not be affected by ageing. Ten mice were therefore offered a choice for 2 days of water or a Na-pindone + 10 % sugar solution which had been prepared 4 months previously. The Na-pindone/sugar solution had been kept since its preparation in a brown bottle and during storage it had become cloudy. A further six mice were given the same choice until death.

In the 2-day test (Table 7) seven mice drank more Na-pindone/sugar solution than water but the difference in consumption was not very marked ($P = > 0{\cdot}2$).

In the test which continued until all mice had died (Table 8) five of the six mice

drank more Na-pindone/sugar solution and this preference was shown from the 1st day. The totals for the first 2 days of this test when combined with those of the previous one gave a probability of $< 0{\cdot}05$. Thus there is no evidence of any appreciable change in the palatability to house-mice of a 0·005 % Na-pindone/sugar solution after 4 months' storage.

Table 7. *Comparative acceptance of a* 0·005 % Na-*pindone* + 10 % *sugar solution* (4 *months old*) *and tap water over* 2 *days*

Mouse no.	Sex	Wt. (g.)	Total water drunk (g.)	Total Na-pindone drunk (g.)	Difference	Na-pindone dosage (mg./kg.)	Result
46	F.	15·4	0·2	3·5	3·3	11·4	Dead on day 5
47	F.	10·1	1·1	2·4	1·3	11·8	Dead on day 7
48	F.	19·1	4·0	1·1	−2·9	2·9	Dead on day 7
49	F.	15·2	1·8	9·1	7·3	30·0	Killed after 16 days
50	F.	15·6	1·7	2·5	0·8	8·0	Dead on day 12
51	M.	21·5	1·7	3·0	1·3	7·0	Survived
52	M.	19·3	2·7	0·2	−2·5	0·5	Survived
53	M.	17·0	0·4	4·5	4·1	13·2	Dead on day 4
54	M.	16·2	1·9	3·5	1·6	10·8	Dead on day 6
55	M.	20·3	1·6	0·4	−1·2	1·0	Survived
Total	—	—	17·1	30·2	13·1	—	—

Table 8. *The consumption of* 0·005 % Na-*pindone* + 10 % *sugar solution* (4 *months old*) *and tap water* (*until death*)

Mouse no.	Sex	Wt. (g.)	Total water drunk (g.)	Total Na-pindone drunk (g.)	Water drunk in 2 days (g.)	Na-pindone drunk in 2 days (g.)	Difference	Total dosage of Na-pindone (mg./k.g.)	No. of days to death
56	M.	19·5	3·2	17·3	2·2	6·3	4·1	44·3	6
57	F.	17·1	1·8	13·8	1·1	12·6	11·5	40·3	6
58	F.	15·6	0·9	14·0	0·7	6·7	6·0	44·8	5
59	F.	17·4	4·9	9·0	1·5	2·6	1·1	25·8	13
60	F.	21·0	5·2	3·4	2·0	1·5	−0·5	8·1	10
61	M.	17·3	1·2	7·1	0·5	3·5	3·0	20·5	8
Total	—	—	17·2	64·6	8·0	33·2	25·2	—	—

In addition to the laboratory tests further information on the relative acceptability of a 0·005 % Na-pindone/10 % sugar solution was obtained from an experiment with mice kept in less confined conditions. Two metal pens (area 36 sq.ft.) were erected in an unheated building and twelve mice were released in each pen. Both groups of mice were given a choice of water or Na-pindone/sugar solution. The solution offered in one pen had been freshly prepared but that offered to mice in the other was 2 months' old. After a fortnight the mortality in each pen was 11/12, and although the two survivors were left for a further 10 days they still showed no signs of illness. It must be presumed that if these two mice were drinking, they preferred water to Na-pindone/sugar solution, for we have no case of a mouse surviving dosing with 0·005 % Na-pindone for more than 6 days.

DISCUSSION AND CONCLUSIONS

The two toxicity tests showed that in the absence of other drinking water, access to 0·005% Na-pindone for only 2 days is not sufficient to bring about 100% mortality in wild house-mice (four died out of seven), but that a solution of the same concentration is lethal in 6 days. In all the remaining tests plain water was also available. In one of them, Na-pindone with 10% sugar gave a complete kill in 11 days (8/9 in 8 days) and in another test the same combination killed four out of six mice after only 2 days exposure. With 1% sugar the mortality was four out of ten in 4 days and, without any sugar, only four of eight mice died after 8 days. There was some indication that the success of 10% sugar compared with 1% sugar or plain water was partly because it caused an increase in total liquid intake, but the very high consumption noted in Table 6 is mainly due to the drinking of one animal. There was no apparent relation between the dose consumed and the length of the survival period. For instance mouse no. 41, which took 8·6 mg./kg. of Na-pindone, died on the 3rd day, whereas mouse no. 43 died on the 7th day, having taken 62·9 mg./kg over the same period of 2 days (Table 6).

The marked variability in tolerance of individual mice to 0·005% Na-pindone has been commented on already and is in line with the experiences of other authors with other anti-coagulants (Bentley & Larthe, 1959). This variability is well seen when the data of Tables 2, 6 and 7 are examined together. Mice survived (S) or were killed (D) by dosages equivalent to 0·5 mg./kg. of body weight (S), 1·0 (S), 1·9 (S), 2·9 (D), 6·3 (D), 6·6 (D), 7·0 (S), 8·0 (D), 8·6 (D), 10·1 (S), 10·5 (D), 10·8 (D), 10·9 (D), 11·4 (D), 11·8 (D), 11·9 (S), 12·1 (D), 13·2 (D), 17·1 (D), 19·0 (S), 21·4 (S), 30·0 (S) and 62·9 mg./kg. of body weight (D). The distribution of tolerance in these three experiments suggests the possibility that increasing the dosage above a certain level leads to increased survival.

It is difficult to predict results in the field from laboratory tests conducted at a temperature of 70° F. and in which no searching was necessary to find the drinking bottles. It seems reasonable to suppose however, that Na-pindone might be effective when offered in 10% sugar solution in environments where alternative drinking supplies are intermittent or non-existent.

SUMMARY

1. A 0·005% solution of the sodium salt of pindone was found to kill wild house-mice (*Mus musculus*) in 4–6 days. Mice offered a choice between this solution and water drank more water, but the difference in consumption was not statistically significant.

2. The addition of 1% sugar did not appreciably alter the palatability of a 0·005% solution, but a solution of the anti-coagulant containing 10% sugar was more readily accepted than water. This preference was maintained with solution 4 months old.

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