Trials of the anticoagulant rodenticide WBA 8119 against confined colonies of warfarin-resistant house mice (*Mus musculus* L.)

BY F. P. ROWE AND A. BRADFELD

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

(Received 24 June 1976)

SUMMARY

The efficacy of the newly developed anticoagulant rodenticide WBA 8119 was evaluated against the house mouse (*Mus musculus* L.) using individual and family groups of warfarin-resistant animals. WBA 8119 at 0.002%, 0.005% and 0.01% in pinhead oatmeal bait gave complete kills of mice in 'no-choice' feeding tests carried out in cages and small pens. In replicated 21-day treatments on families of mice confined in larger pens and conditioned to feeding on plain foods, the overall mortalities obtained using the three formulated poison baits were 71/72, 62/63 and 57/57 respectively.

The results of the WBA 8119 toxicity tests are considered in relation to previous findings on other anticoagulant rodenticides, particularly difenacoum. In equivalent tests, WBA 8119 performed better than difenacoum. The data thus support the laboratory findings that WBA 8119 is the most active anticoagulant so far tested for the control of warfarin-resistant house mice.

INTRODUCTION

The problem of resistance to warfarin and to other well-known anticoagulant rodenticides in house mouse (*Mus musculus* L.) populations has reduced the use of these compounds in urban areas of Britain. A recent outcome of work on alternative rodenticides that has been in progress at Pest Infestation Control Laboratory was the development of the new anticoagulant difenacoum (Hadler, Redfern & Rowe, 1975). Laboratory tests showed that difenacoum was more toxic to mice than other longer established anticoagulant rodenticides. Nevertheless, it was found that a few warfarin-resistant animals could withstand 21 days feeding on difenacoum-treated bait and on this evidence it was concluded that difenacoum treatments would probably not succeed in eradicating all warfarin- or other anticoagulant-resistant infestations of mice. More recently the related compound, WBA 8119, 3-(3-[4'-bromobiphenyl-4-yl]-1,2,3,4-tetrahydronaphth-1-yl)-4-hydroxycoumarin, has also been evaluated (Redfern, Gill & Hadler, 1976). In the laboratory WBA 8119 was found to be more toxic than difenacoum to rats and mice, including warfarin-resistant animals. Further information on the toxicity of WBA 8119 to warfarin-resistant mice is presented in this paper.

METHODS

Laboratory feeding tests were conducted using individually caged and family groups of penned mice. The mice employed in the feeding tests were the descendants of wild stock drawn from a single building located near Cambridge (Wallace & MacSwiney, 1976) and from another in Loughborough, in both of which prolonged warfarin treatments had failed to gain control. They were not screened for resistance to warfarin before treatment with WBA 8119 since 21-day 0.025% warfarin feeding tests on earlier progeny had shown that both strains were highly resistant to warfarin (94.3% and 100% survival in 244 Cambridge and 47 Loughborough mice respectively).

The feeding tests undertaken were of the 'no-choice' and 'choice' type. In each test WBA 8119 treated bait was presented for a maximum of 21 days. Preliminary tests with individually caged animals were carried out for two reasons. First, the response of the Cambridge and Loughborough mice to WBA 8119 had not been investigated in the laboratory by Redfern *et al.* (1976). Second, the fact that both strains had been employed in earlier cage tests using difenacoum and the similar WBA 8119 tests enabled comparison of the performance of the two compounds. In each test, adult mice, of equal sexes and known weight, were fed plain bait (95% pinhead oatmeal, 5% corn oil) for 1 day before they were offered WBA 8119 in the same bait-base. Similar 'no-choice' tests were carried out on laboratory reared family groups of mice, comprising sub-adult and adult animals (weight range 10–23 g), enclosed in circular metal pens, 1.7 m in diameter. As in earlier work on difenacoum (Rowe & Bradfield, 1975), family groups were also housed in larger pens ($7\frac{1}{2} \times 2\frac{1}{4}$ m) and the mice provided with two plain foods (whole wheat and diet 41B) 7 days prior to and throughout the WBA 8119 treatment period.

Only Cambridge-derived mice were employed in the pen experiments because the Loughborough stock failed to reproduce satisfactorily.

WBA 8119 was used at 0.002%, 0.005% and 0.01% in bait. The poison bait was prepared by thoroughly mixing the appropriate amount of the pure compound in corn oil (5%) with pinhead oatmeal (90%) and wholemeal flour (5%). Difenacoum, supplied as a 0.2% concentrate in a polyethylene glycol/glycerine solution, was included in the same bait-base and used at 0.005% and 0.01% in the cage tests. With rare exception, the amount of poison bait eaten was measured each day. The pens were also searched daily for dead mice and poisoned animals were autopsied for evidence of anticoagulant poisoning.

Difenacoum and WBA 8119 were supplied by Sorex (London) Ltd.

RESULTS AND DISCUSSION

The caged mice of both strains died after feeding on WBA 8119 at each of the three concentrations at which the poison was included in bait (Table 1). Two males (one from each strain) survived the 21-day feeding period on 0.005% difenacoum bait but both individuals died on the following day.

Table 1. *The toxicity of difenacoum and WBA 8119 to individually caged warfarin-resistant Mus musculus in 21-day 'no-choice' feeding tests*

Source	Poison	Concentration (%)	Mortality	Dosage range that killed (mg/kg)	Days to death	
					Range	Mean
Cambridge	Difenacoum	0.005	10/10	23.1-140.6	6-22	12.3
		0.01	10/10	45.1-157.8	4-17	8.0
	WBA 8119	0.002	10/10	5.9-26.1	4-15	8.5
		0.005	10/10	25.0-88.7	5-17	9.7
		0.01	10/10	43.3-124.1	5-18	9.6
Loughborough	Difenacoum	0.005	8/8	24.9-157.7	6-22	10.5
		0.01	10/10	48.9-115.0	5-13	9.8
	WBA 8119	0.005	8/8	30.5-60.6	4-12	7.5
		0.01	10/10	21.3-129.6	3-11	8.7

Table 2. *The toxicity of WBA 8119 to family groups of warfarin-resistant Mus musculus in 'no-choice' feeding tests*

Poison bait eaten (g) on day	Concentration of poison (%)		
	0.002	0.005	0.01
1	34.2	45.7	28.3
2	31.9	42.0	20.7
3	28.5	28.0	12.4
4	9.6	13.0	2.5
5	2.5	5.5	0.9
6	0.2	2.2	1.0
7	0.0	1.5	0.4
8	0.2	0.0	0.0
9	0.8	1.5	0.0
10	0.2	—	—
11	0.0	—	—
12	0.0	—	—
Mortality	12/12	16/16	10/10
Days to death			
Range	3-12	3-9	3-9
Mean	6.6	5.3	4.9

Similarly, there were no survivors in any of the Cambridge family groups given WBA 8119 bait in the 'no-choice' feeding tests carried out in the small pens. In each treatment feeding was minimal after 7 days and all animals were dead by day 12 (Table 2). In previously conducted tests using Cambridge mice (Hadler *et al.* 1975) the kills obtained employing four other anticoagulant rodenticides - difenacoum (at 0.005%), coumatetralyl (0.05%), chlorophacinone (0.025%) and diphacinone (0.0125%) were 14/15, 3/13, 6/13 and 0/9 respectively.

The results of the WBA 8119 treatments on mice provided with alternative plain food in the large pens are summarized in Table 3. Each of four family groups was treated with WBA 8119 at 0.002%, 0.005% and 0.01% in bait and a complete or high kill was obtained in each case, 71/72 (98.6%), 62/63 (98.4%) and

Table 3. *The toxicity of WBA 8119 to family groups of warfarin-resistant Mus musculus in 21-day 'choice' feeding tests*

Concentration of poison (%)	Poison bait eaten (g)			Mortality	Mortality (%)	Days to death	
	Days 1-7	Days 8-14	Days 15-21			Range	Mean
0.002	54.0	8.3	—	11/11	100	3-15	6.6
	118.0	3.5	0.0	27/27	100	3- 9	5.9
	107.4	7.9	2.4	21/21	100	3-18	5.8
	92.3	49.7	4.9	12/13	92.3	4-13	7.1
0.005	38.1	—	—	11/11	100	3- 9	5.3
	92.3	10.9	9.4	14/15	93.3	3-11	6.6
	47.9	0.9	0.0	16/16	100	3-18	7.2
	137.0	16.2	12.0	21/21	100	4-26	8.5
0.01	66.6	0.3	—	16/16	100	3-11	4.9
	80.6	0.4	—	13/13	100	3-12	6.2
	57.3	6.5	0.0	14/14	100	3-15	6.2
	39.5	3.8	—	14/14	100	3-14	6.0

57/57 (100%) respectively. As in the small pen treatments, poison bait consumption declined considerably after 7 days and thereafter there was least feeding by mice offered bait containing WBA 8119 at the highest concentration (0.01%). Only three mice – one male and two females treated with 0.002% and 0.005% WBA 8119 bait respectively – survived the test period. One of the females was in a sick condition when the 0.005% WBA 8119 bait was withdrawn and it died 5 days later; the other was still active at the end of the treatment period and, 7 days later, it was subjected to a further 21-day 0.005% WBA 8119 treatment without alternative food. Although this animal fed inconsistently and bleeding occurred at a facial site, it ate 50.7 g of WBA 8119 bait (228.4 mg/kg) over the 21 days. It died 16 days later but no discernible poison symptoms were found on autopsy. The male survivor fed well over 21 days on 0.002% WBA 8119 bait alone, eating 58.7 g of bait (82.7 mg/kg), but it died 12 days later. During the test period bleeding sites on the tail and ears were observed and autopsy revealed subcutaneous haemorrhages.

In corresponding large pen trials (Rowe & Bradfield, 1975), difenacoum at 0.005% and 0.01% gave kills of 72/81 (88.9%) and 65/67 (97.0%) respectively, marginally lower than those obtained using WBA 8119 at these two concentrations in bait. Feeding also tended to be more prolonged in the case of the difenacoum treatments. Furthermore, 3 of the 9 mice (8 females, 1 male) which survived the 0.005% difenacoum treatment period also survived when fed the same poison bait alone for 21 days and did not die subsequently. The two 0.01% difenacoum survivors (1 male, 1 female) died on days 14 and 16 after feeding on the same poison bait alone.

The large pen trials in which excess supplies of alternative food were present, came nearest to resembling the conditions encountered in treating mouse infestations in the field. The results of the treatments of this kind add support to the conclusion reached by Redfern *et al.* (1976) that WBA 8119 is likely to be more

effective than difenacoum in treating mice resistant to warfarin or other anti-coagulant poisons. Field trials to determine the effectiveness of WBA 8119, at 0.005% in bait, against free-living mouse populations are in progress.

REFERENCES

- HADLER, M. R., REDFERN, R. & ROWE, F. P. (1975). Laboratory evaluation of difenacoum as a rodenticide. *Journal of Hygiene* **74**, 441-8.
- REDFERN, R., GILL, J. E. & HADLER, M. R. (1976). The evaluation of WBA 8119 as a rodenticide for use against warfarin-resistant and non-resistant rats and mice. *Journal of Hygiene* **77**, 419-26.
- ROWE, F. P. & BRADFIELD, A. (1975). Comparative acute and chronic toxicity tests on confined colonies of wild house mice (*Mus musculus* L.). *Proceedings of the 4th British Pest Control Conference, Jersey*, April 1975.
- WALLACE, M. E. & MACSWINEY, F. J. (1976). A major gene controlling warfarin resistance in the house mouse. *Journal of Hygiene* **76**, 173-81.