J. Hyg., Camb. (1978), **80**, 77
Printed in Great Britain

Field trials of WBA 8119 (PP 581, brodifacoum*) against warfarin-resistant infestations of *Rattus norvegicus*

By B. D. RENNISON and A. C. DUBOCK

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

(*Received* 15 *June* 1977)

SUMMARY

Baiting with medium oatmeal or soaked wheat containing 0·002, 0·001 or 0·0005 % brodifacoum completely controlled infestations of warfarin-resistant rats on farms when the poisoned baits were maintained until rats ceased to feed on them. The concentration of brodifacoum did not affect the duration of these treatments which lasted from 11 to 25 days.

Poison baiting with 0·002 % brodifacoum for only 1, 4 and 7 days achieved, respectively, only about 41, 51 and 68 % control of similar farm infestations, and so emphasized the need to continue baiting for longer periods.

INTRODUCTION

The anticoagulant, brodifacoum [3-(-3(4′-bromobiphenyl-4-yl)-1,2,3,4-tetrahydronaphth-1-yl)-4-hydroxycoumarin], was tested under laboratory conditions by Redfern, Gill & Hadler (1976) and found to be more active than other known anticoagulants against warfarin-resistant and susceptible Norway rats. Concentrations in bait between 0·002 and 0·0005 % killed a high proportion of the rats tested even when fed for only 1 or 2 days. The demonstration of this greater activity gave rise to speculation that brodifacoum might be an effective 'single application' anticoagulant to use, for example, for crop protection or for sewer rat control, where re-baiting might be inconvenient or too costly. This possibility was investigated, along with more normal use of brodifacoum in field trials that were conducted against rat infestations in farm buildings in Powys (Montygomeryshire District) and Salop (Shropshire), the area of the Anglo-Welsh border country in which warfarin-resistant rat populations are most plentiful.

METHODS

Trial with unrestricted poison baiting

This trial was designed to determine an optimum field concentration of brodifacoum for control of warfarin-resistant rats using baits and methods of baiting similar to those generally recommended in the U.K. for anticoagulant rodenticides (P.I.C.L., 1976).

* Proposed common name.

Three concentrations of the anticoagulant were tested; 0·002, 0·001 and 0·0005 %. Nine control treatments were carried out with each concentration of bait applied in medium oatmeal or, where the dry cereal could have been insufficiently attractive, on whole wheat that had been soaked for 12 h in water. The poison baits were made up by mixing the appropriate proportions of laboratory prepared mastermixes containing the active ingredient into oatmeal or soaked wheat.

The methods for testing for anticoagulant resistance in the field, described by Drummond & Rennison (1973) and also used previously to test candidate rodenticides (Rennison, 1974; Rennison & Hadler, 1975), were used again to test brodifacoum. Thus in all infested buildings, bait points were prepared and wooden trays for bait placed in them 2–4 days before the poisoned baits, weighing 200–300 g, were laid for the first time on a Monday. Baiting then continued with sites being visited and baits replenished to the schedule described by Drummond & Rennison (1973) either until the takes of bait and other signs of rat activity ceased or until takes of bait had been recorded at significantly ($P < 0·05$) greater proportions of bait points than would have been expected after an equivalent period of effective baiting with 0·025 % warfarin, i.e. until the proportions crossed the upper 95 % confidence limit on the monitoring graph.

Before any of the above treatments began, the presence of warfarin-resistant rats on the farms was confirmed either by demonstrably unsuccessful poison baiting with 0·025 % warfarin or by trapping samples of live rats and feeding them for 6 days in the laboratory on oatmeal containing 0·005 % warfarin (Drummond & Wilson, 1968).

Trial with restricted poison baiting

The purpose of this second trial was to test the possibility that a single application of bait containing 0·002 % of brodifacoum would be sufficient to control the rats. Three restricted periods of poison baiting, 1, 4 and 7 days, were carried out, each on four farms. However, because it might have been unnecessarily hazardous in the test environments to lay enough bait to last for 4 or 7 days, the treatments were conducted and monitored as in the preceding trial except that after the poisoned bait had been down for the prescribed period on a farm, it was replaced by dry whole wheat. The baiting with wheat then continued until bait takes ceased or the proportions of points with 'takes' crossed the upper line of the monitoring graph. The rat infestations on a fourth set of four farms were baited from the beginning until day 11 with dry whole wheat so that the rate at which takes of unpoisoned bait increased after day 2 could be measured.

The treatments were randomly allocated to the farms and carried out in rotation until the 16 had been completed.

RESULTS AND DISCUSSION

Trial with unrestricted poison baiting

The results of the unrestricted baiting with 0·002, 0·001 and 0·0005 % brodifacoum respectively are shown in Fig. 1*a–c*; which are simplified versions of the

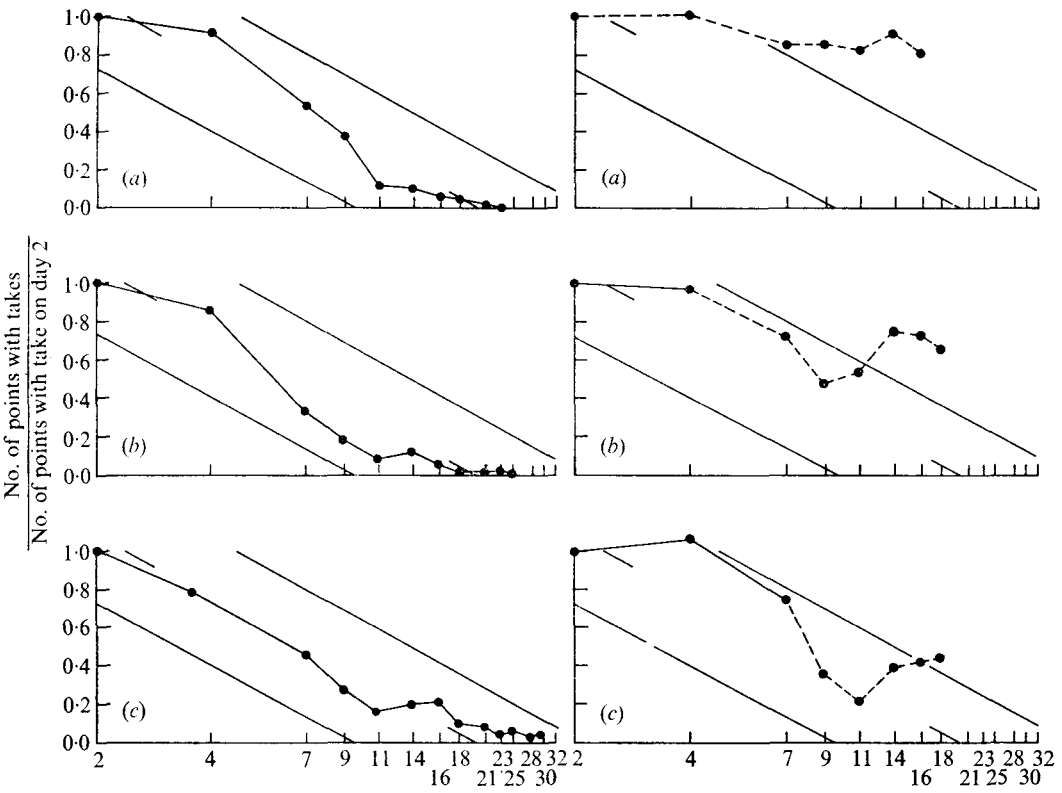

Fig. 1 Fig. 2

Fig. 1. Results, from the second day, of poison baiting with brodifacoum at 0·002% (*a*), 0·001% (*b*) and 0·0005% (*c*) in stabilized medium oatmeal. (Means of 9 treatments in each case.)

Fig. 2. Results, from the second day, of poison baiting with 0·002% brodifacoum in stabilized medium oatmeal (solid lines) for 1 day (*a*), 4 days (*b*) and 7 days (*c*), and then baiting with unpoisoned whole wheat (dashed line). (Means of 4 treatments in each case.)

monitoring graph (Drummond & Rennison, 1973) and show average values for each set of nine treatments.

No difficulties were experienced in the treatments with either 0·002 or 0·001% brodifacoum and all 18 followed the expected course defined by the monitoring graph to terminate with complete control after, on average, 23–25 days baiting (Fig. 1*a*, *b*). Eight of the treatments with 0·0005% of the poison also achieved complete control within 11–18 days, but on one farm takes were still occurring at a few bait points near a deep litter poultry house after 30 days (Fig. 1*c*, days 21–30). The treatment was discontinued, but 14 live rats were trapped to be tested for resistance to brodifacoum in the laboratory. Eleven of these died showing characteristic symptoms of anticoagulant poisoning shortly after capture and the three survivors died after 3 days feeding in the laboratory on 0·002% brodifacoum in oatmeal. The continued infestation on the farm was, therefore, not due to

https://doi.org/10.1017/S0022172400053419 Published online by Cambridge University Press

Table 1. *The numbers of bait points on four farms at which takes of bait by rats were recorded 2, 4, 7, 9 and 11 days after baiting with whole wheat commenced*

	Days				
	2	4	7	9	11
	No. of bait points with takes				
Farms	13	15	20	15	18
	14	19	20	18	21
	10	12	13	13	12
	13	16	16	17	19

resistance and it was subsequently traced to rats coming into the farmstead from an unofficial refuse tip on adjacent overgrown waste ground. But for this immigration, the treatment would probably have succeeded within 18–21 days.

Since the successful treatments, irrespective of the concentration of poison used, achieved complete control within the same time as treatments of farm rat infestations with 0·025 % warfarin, the lowest concentration of brodifacoum, 0·0005 %, would be the best and safest to use for Norway rat control where a continuous baiting schedule can be followed.

Trials with restricted poison baiting

The single day of poison baiting followed by baiting with wheat resulted in the proportions of points with takes being reduced on day 7 to an average of 0·86 of the second day's value (Fig. 2*a*). Although the proportion on day 7 was therefore significantly higher than it would have been at the same stage of a normal warfarin treatment, the baiting with wheat was continued until day 16 in case the numbers of takes increased as possibly unbaited or sub-lethally poisoned rats started to feed.

Poison baiting for 4 or 7 days led to takes at decreasing proportions of points from day 4 until days 9 or 11 (Fig. 2*b*, *c*). On both groups of farms, the proportions of bait points at which rats fed increased and levelled off after 14–18 days, during which time they crossed the upper 95 % confidence limit of the monitoring graph.

At first sight, the last values recorded in Fig. 2*a–c* indicate that 1, 4 and 7 days poison baiting reduced the target rat populations to, on average, respectively 0·82, 0·68 and 0·43 of their original size. However, such an assumption fails to recognize that numbers of takes of unpoisoned bait normally increase and after only 2 days baiting are less closely related to rat population size than the numbers recorded after 16 days. Corrections are, therefore, necessary and can be made from the results (Table 1) obtained on the four farms on which the rats were baited only with whole wheat.

The average rate at which rat feeding on the unpoisoned baits increased can be deduced by converting the numbers of points in each line of Table 1 to proportions of the maximum numbers and calculating the linear regression of proportions (y) on $\log_{10}$ days (x); the logarithms being necessary for linearity. The equation $y = 0{\cdot}32\ (\log_{10}x) + 0{\cdot}62$ that expressed the very significant ($P < 0{\cdot}001$) positive relationship between the proportions and days showed that on day 2 takes of bait

https://doi.org/10.1017/S0022172400053419 Published online by Cambridge University Press

occurred at an expected $0{\cdot}72 \pm 0{\cdot}11$ of the maximum numbers of points at which takes were subsequently recorded. The final proportions recorded in Fig. 2*a–c* should probably be multiplied by 0·72; thus 1, 4 and 7 days poison baiting caused the death of 41, 51 and 68% respectively of the target populations. These are minimum estimates of the control that was achieved because it is unlikely that all the rats on the wheat baited farms would have been attracted to the baits by day 11 while competition for bait remained high in the absence of mortality. On the other hand, the poisoned baits were regularly replenished and so were probably more effective than they would have been if they had been laid at the start of the treatments and left unchecked for 4 or 7 days. Nevertheless, the estimates of control are probably comparable with those resulting from single applications, after pre-baiting, of 2·5% of zinc phosphide in oatmeal baits which killed 71% of farm rat populations (Rennison, Hammond & Jones, 1968).

Although the results of the restricted poisoning with brodifacoum were disappointing, they were of considerable interest because they illustrated the delayed response of Norway rat populations to baits in the field and emphasized the difficulty of extrapolating laboratory results to the field. In farm buildings 7 days baiting with 0·002% brodifacoum controlled only about 68% of the warfarin-resistant rats, whereas in the laboratory 2 days' baiting was sufficient to kill 100%. Thus it seems that under natural conditions a number of rats eat very little, if at all, from bait points during the first week or longer of a treatment, although eventually all must do so because 100% control is possible if baits are left down long enough – on average for 18 days. Presumably, the rats that are slow to feed on bait are the socially inferior animals that are prevented from feeding until their social superiors have succumbed to the poison. Therefore, the rise in the number of takes that occurred 5–7 days after 4 and 7 days poison baiting (Fig. 2*b*, *c*) was probably due to late starters as well as the possibility of rats recovering from sub-lethal poisoning.

There must be a period of baiting of between 7 and 18 days duration which, in most situations, will be long enough to ensure that late feeders eat a lethal dose of poison. However, the amount of bait to lay safely at the outset of a treatment to last for this period, will, in the majority of situations, be impossible to determine. Thus the most satisfactory method of using brodifacoum will be the same as it is for other anticoagulants, namely that involving regular visits to monitor and replenish baits until all takes cease.

The authors wish to acknowledge the parts played in these trials by Mr N. J. Wallace, Mr S. F. Pritchard, Mr G. E. Jones, Mr G. W. Long and Mr E. O. Pugh, and also to thank Mr M. R. Hadler of Sorex (London) Ltd. for providing the brodifacoum mastermixes.

REFERENCES

Drummond, D.C. & Rennison, B. D. (1973). The detection of rodent resistance to anticoagulants. *Bulletin of the World Health Organization* **48**, 239–42.

Drummond, D. C. & Wilson, E. J. (1968). Laboratory investigations of resistance to warfarin of *Rattus norvegicus* Berk. in Montgomeryshire and Shropshire. *Annals of Applied Biology* **61**, 303–49.

P.I.C.L. (1976). Control of rats and mice. In: *Reference Manual for Pest Control Personnel*. Ministry of Agriculture, Fisheries and Food, Pest Infestation Control Laboratory in co-operation with the Local Government Training Board.

REDFERN, R., GILL, J. E. & HADLER, M. R. (1976). Laboratory evaluation of WBA 8119 as a rodenticide for use against warfarin-resistant and non-resistant rats and mice. *Journal of Hygiene* **77**, 419–26.

RENNISON, B. D. (1974). Field trials of calciferol against warfarin-resistant infestations of the Norway rat (*Rattus norvegicus* Berk). *Journal of Hygiene* **73**, 361–7.

RENNISON, B. D. & HADLER, M. R. (1975). Field trials of difenacoum against warfarin-resistant infestations of *Rattus norvegicus*. *Journal of Hygiene* **74**, 449–55.

RENNISON, B. D., HAMMOND, L. E. & JONES, G. L. (1968). A comparative trial of norbormide and zinc phosphide against *Rattus norvegicus* on farms. *Journal of Hygiene* **66**, 147–58.