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Field trials of bromadiolone against infestations of warfarin-resistant *Rattus norvegicus*

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SUMMARY

Baiting with 0·005% bromadiolone in medium oatmeal or soaked wheat completely controlled infestations of warfarin-resistant rats on farms when surplus amounts of the poisoned baits were maintained until rats ceased to feed on them. The speed with which control was achieved was the same as with other anticoagulants that have been tested in this way.

Poison baiting with 0·005% bromadiolone for only 1, 4 or 7 days achieved respectively about 49, 77 and 81% control of similar farm rat infestations.

INTRODUCTION

The anticoagulant rodenticide bromadiolone (3-[-4′-bromo[1,1′-biphenyl]-4-yl)-3-hydroxy-l-phenylpropyl]-4-hydroxy-2H-l-benzopyran-2-one) was first marketed in France in 1977 and is now sold in North America under the trade name 'Maki'. It has been shown in laboratory tests to be toxic to a wide range of rodents (Grand, 1976; Marsh, 1977). Limited field trials with 0·005% bromadiolone suggest that it is effective against *Rattus norvegicus* on farms (Fradois, 1976; Meehan, 1978). Warfarin-resistant rats are also killed but, as with difenacoum, the lethal dose is higher than for non-resistant rats (Redfern & Gill, 1980).

The high toxicity to rodents of bromadiolone and another new hydroxycoumarin derivative, brodifacoum, has led to the suggestion that these compounds could be used as 'single dose' poisons (Marsh, 1977; Dubock & Kaukeinen, 1978). Farm rat treatments in which poison baiting with brodifacoum was restricted to 1, 4 and 7 days, however, gave only limited control (Rennison & Dubock, 1978).

This paper describes field trials of bromadiolone against warfarin-resistant *R. norvegicus* infestations in and around farm buildings in Powys and Salop, employing both restricted periods of baiting and unrestricted surplus baiting.

METHODS

Trials with unrestricted poison baiting

Bromadiolone is recommended by the manufacturer for use at a concentration of 0·005% and poisoned baits were made up to this concentration in medium

oatmeal (or soaked wheat where oatmeal was not being eaten) from laboratory prepared master-mixes containing the active ingredient. Treatments were carried out on nine farms where the presence of warfarin-resistant rats had been confirmed by laboratory examination of the blood-clotting activity of live-trapped specimens, using the technique of Martin *et al.* (1979). To facilitate comparison with other anticoagulants, the field methods devised by Drummond & Rennison (1973) and developed by Rennison (1974), Rennison & Hadler (1975) and Rennison & Dubock (1978) were used. In all infested farm buildings, poisoned baits weighing about 100 g were laid on Monday, on wooden trays that had been placed the previous Thursday or Friday. Sites were then visited every day (Monday–Friday) to count the number of trays which had been visited by rats and to replenish the bait. Baiting continued until the takes of bait and other signs of rat activity had ceased or until bait takes had been recorded at significantly ($P < 0{\cdot}05$) greater proportions of bait points than would have been expected after an equivalent period of baiting with 0·025% warfarin against anticoagulant-susceptible rats (Drummond & Rennison, 1973).

Trials with restricted poison baiting

Three restricted periods of poison baiting (1, 4 and 7 days) were tested, each on four farms, as described by Rennison & Dubock (1978). The treatments were conducted and monitored as in the trials with unrestricted baiting, except that dry whole wheat was substituted for poisoned bait after the prescribed period. Baiting with dry wheat was continued until day 18, i.e. 18 days after the start of poisoning. A fourth set of four farms was baited for 11 days with dry whole wheat only, to estimate the rate at which takes of unpoisoned bait increased after day 2.

The treatments were allocated randomly to the farms, which were treated in rotation until the 16 had been completed.

RESULTS

Trials with unrestricted poison baiting

The numbers of bait trays visited daily by rats in the nine treatments in which surplus baiting was unrestricted were summed and plotted on the monitoring graph (Drummond & Rennison, 1973) as proportions of the number of takes recorded on day 2 (Fig. 1*a*). Complete control was achieved on eight of the farms in from 11 to 25 days. On the ninth farm, however, the proportion of points with takes did not start to decrease until day 8 and so remained consistently higher than that expected for a non-resistant rat population from day 5 to day 18. Although a small number of bait takes were still being recorded after 25 days, the treatment was discontinued because it was evident that the slowness of the fall in bait takes was due not to resistance but to rats which were coming into the farm buildings from adjacent waste ground beyond the scope of the poison baiting.

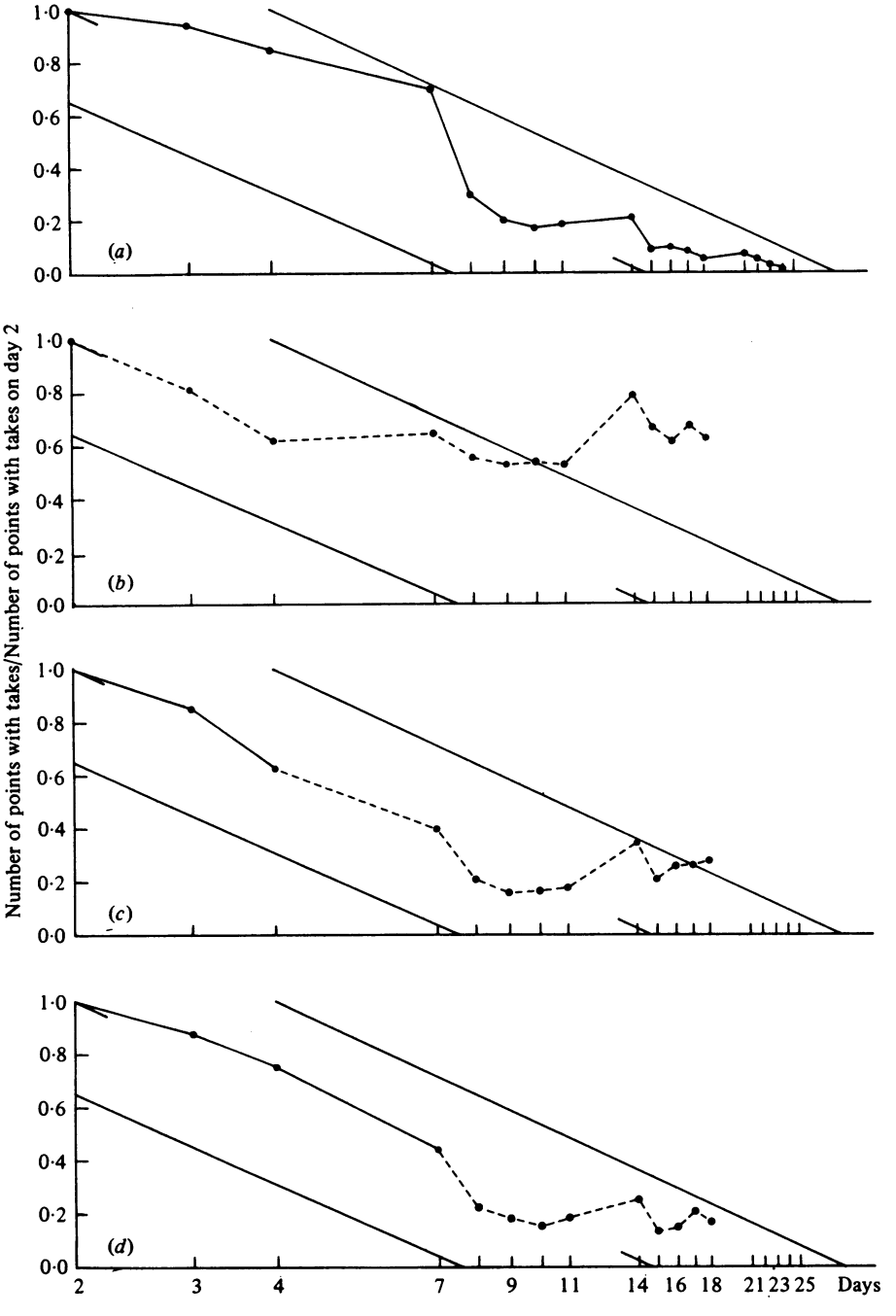

Fig. 1. Results, from the second day, of poison baiting trials with 0·005% bromadiolone in medium oatmeal; the oblique lines are the 95% confidence limits between which the plotted proportions should fall when a warfarin-susceptible rat population is treated with 0·025% warfarin. (*a*): Unrestricted poison baiting (Mean of 9 treatments). (*b*, *c* and *d*): Restricted poison baiting (solid lines) for 1, 4 and 7 days respectively and then baiting with unpoisoned whole wheat (dashed lines). (Means of 4 treatments in each case.)

Table 1. *The numbers of bait points on four farms at which takes of unpoisoned bait were recorded*

		Days					
		2	3	4	8	9	10
Farm	*a*	38	52	41	51	52	46
	b	13	15	13	8	10	8
	c	10	8	7	1	2	5
	d	23	28	26	24	23	27
Total		84	103	87	85	87	86

Trials with restricted poison baiting

After a single day of poison baiting, followed by baiting with wheat, the proportions of bait points with takes decreased until day 4, when they were on average 0·62 of the second day's value (Fig. 1*b*). This was the same level as that recorded on day 4 in the trials with unrestricted baiting (Fig. 1*a*). Although there was a further slight fall during the second week, this was followed by a compensatory rise in the third week. The takes on day 18 were on average 0·63 of the second day's value.

Following poison baiting for 4 or 7 days, the proportions of bait takes reached a minimum on day 9 or 10 (Fig. 1*c*, *d*), which was again similar to the levels which were recorded at the same point in the trials with unrestricted baiting (Fig. 1*a*). On both groups of farms, the proportions of takes increased from this minimum point, with the result that the average proportions of takes on day 18 were 0·28 and 0·23 of the second day's value for 4 and 7 days' baiting respectively.

DISCUSSION

In the successful treatments, unrestricted poison baiting with 0·005 % bromadiolone achieved complete control of the farm rat infestations in the same time as treatments of anticoagulant-susceptible infestations with 0·025 % warfarin and with other anticoagulant poisons that have been tested in the same way (Drummond & Rennison, 1973; Rennison, 1974; Rennison & Hadler, 1975; Rennison & Dubock, 1978).

Rennison & Dubock (1978) pointed out that the values recorded on day 18 in trials of restricted poison baiting underestimate the success of the poison because they do not take into account the increase in bait takes which normally occurs after the second day of baiting if rats are not being poisoned. The results can be corrected for this effect by using the results (Table 1) from the four farms on which the rats were baited only with whole wheat. The sum of the bait takes on all of these farms on day 2 was 0·815 of the maximum number of takes, which was reached on day 3. The final proportions of takes recorded in Fig. 1*b–d* should therefore be multiplied by 0·815 so that the corrected proportions of takes on day 18 were 0·51, 0·23 and 0·19 of the second day's value. This represents kills of 49, 77 and 81 % for each baiting period. Restricted baiting with 0·002 % brodifacoum

achieved approximately 41, 51 and 68% control with 1, 4 and 7 days' baiting respectively (Rennison & Dubock, 1978). The difference between these two poisons, however, is well within the limits of the experimental error inherent in the method and bromadiolone cannot be said to have performed better than brodifacoum.

The continued fall in the number of bait takes after the poisoned baits had been picked up following restricted periods of baiting can be explained by the laboratory observation that rodents take several days to die after they have ingested a lethal dose of any anticoagulant (see e.g. Redfern & Gill, 1980). The limited control achieved by restricted baiting, even with a highly toxic anticoagulant, can probably be explained in terms of social interactions within the rat populations (Rennison & Dubock, 1978). Rat social behaviour may also account for the fact that, with surplus baiting, the speed of control is apparently not influenced by the toxicity of the anticoagulant used.

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REFERENCES

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

Dubock, A. C. & Kaukeinen, D. E. (1978). Brodifacoum (Talon rodenticide), a novel concept. *Proceedings of the Eighth Vertebrate Pest Conference, Sacramento, California*, 1978, pp. 127–37.

Fradois, G. (1976). Qu'est-ce que la bromadiolone? *La Défense des Végétaux* **182**, 279–88.

Grand, M. (1976). Experimental data on a new anticoagulant raticide: bromadiolone. *Phytiatrie-Phytopharmacie* **25**, 69–88.

Marsh, R. E. (1977). Bromadiolone, a new anticoagulant rodenticide. *E.P.P.O. Bulletin* **7** (2), 503–8.

Martin, A. D., Steed, L. C., Redfern, R., Gill, J. E., & Huson, L. W. (1979). Warfarin resistance genotype determination in the Norway rat. *Laboratory Animals* **13**, 209–14.

Meehan, A. P. (1978). Rodenticidal activity of bromadiolone – a new anticoagulant. *Proceedings of the Eighth Vertebrate Pest Conference, Sacramento, California*, 1978, pp. 122–6.

Redfern, R. & Gill, J. E. (1980). Laboratory evaluation of bromadiolone as a rodenticide against warfarin-resistant and non-resistant rats and mice. *Journal of Hygiene*, **84**, 263–8.

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. & Dubock, A. C. (1978). Field trials of WBA 8119 (PP 581, brodifacoum) against warfarin-resistant infestations of *Rattus norvegicus*. *Journal of Hygiene* **80**, 77–82.

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