STUDY OF EFFECTIVENESS OF ANTICOAGULANT RODENTICIDES USED IN SLOVAK REPUBLIC

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Abstract - The toxic effects, diagnosis and post-mortem picture of anticoagulant rodenticides were tested in *Rattus norvegicus* according to OEPP/EEPO No 13, series 10, 1982 method. Experimental animals were fed by a single dose (30 mg/animal) of tested rodenticides. Warfarin in concentrations 50 g/kg, 100 g/kg, 150 g/kg and 200 g/kg in bait. Bromadiolone and brodifacoum bait concentrations were 0.005%. The effectiveness of the tested rodenticides was compared also according to the occurrence of the first clinical symptoms and the day of death in experimental animals. The first clinical symptoms after administration of all three compounds appeared from the 3rd to the 4th day. We observed some similar clinical symptoms as: apathy, somnolence, immobility, food deprivation, later bleeding from nose, eyes, mouth and genitalia. Warfarin: dyspnoe and typical bleeding from nose, eyes, ears, mouth and genitalia. Death occurred from 7th to 15th day in conc. 50 g/kg in bait, from 6th to 15th day (100 g/kg in bait), from 7th to 15th day (150 g/kg in bait), from 8th to 15th day (200 g/kg in bait). Bromadiolone: strong pruritus, which caused several bleeding wounds and later scabs on neck and back. Death occurred from 4-8 day. For the post-mortem picture, large haemorrhages around vena jugularis and in abdominal cavum, normal size of liver and spleen and slight anemia of tissues were typical. Brodifacoum: did not differ from those of warfarin. The death appeared from 5th to 8th day and was caused by rupture of venas. The post-mortem picture was characterised by partly coagulated blood in thoracal and abdominal cavum, several haematomas in muscle around jugular, axillar, femoral venas and mesenterical venas, vena cava caudalis, truncus pulmonaris. Haematomas were observed also in testicular parenchyma and venas of epididymides.

Key words - Warfarin, bromadiolone, brodifacoum, clinical symptoms, post-mortem

INTRODUCTION

Rodenticides are a common cause of poisoning in companion animals. Of these agents, anticoagulants are of high incidence because of their availability to household owners and their important role in urban and agricultural rodent control programs. Warfarin has been the dominant rodenticide since 1940. But the evolution of warfarin - resistant rats has resulted in the introduction of more effective anticoagulant rodenticides, specifically brodifacoum and bromadiolone (Thijssen, 1995). All the anticoagulant rodenticides act by interfering with the synthesis of vitamin K which is essential for normal blood coagulation because it is a cofactor for the postribosomal synthesis of clothing factors II, VII, IX and X (Bell, 1978), suppression of the hepatic formation of prothrombin and of factors VII, IX and X produces the clotting defects. In addition, anticoagulant rodenticides cause direct capillary damage.

In Slovak Republic the anticoagulant baits used in commensal rodent control are rodenticides of first generation - warfarin (Kumatox, RODOSTOP Z) and the second generation rodenticides with the effective agents of brodifacoum (TALON G, TALON H, VOLID) and of bromadiolone (LANIRAT, RATREX M, RATREX P, RODENTIC FAST, TOPIN 2B) (List of permitted preparations for protection of plants, stores and DDD, 1998). The purpose of this paper is the comparison of the toxic effect, clinical symptoms, post-mortem picture, effectiveness and sensory features of tested rodenticides.

MATERIALS AND METHODS

Animals

Thirty six male and 36 female rats *Rattus norvegicus* weighing 200 - 220 g were used. Rats were maintained in single polycarbonate cages and had free access to water, and the poison bait and the Larsen diet were administered *ad libitum.* We used Choice tests on singly - caged rodents, according to OEPP/EEPO No 13, series 10, 1982 method.

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Tested substances

Warfarin was administered in concentrations 50, 100, 150 and 200 g/kg in bait. Bromadiolone (TOPIN 2B) and brodifacoum (TALON G) bait concentration were 0.005%. Warfarin and TALON G baits had the form of granules. TOPIN 2B had a dough form with good smell and special taste (fish, cheese, vanilla and other special odours). The baits were packed into special 10g small sacks.

Experimental animals were fed by a single dose (30 mg/animal) of tested rodenticides. The effectiveness and clinical symptoms of the anticoagulant were observed within 14 days. Before testing animals were adapted the laboratory conditions for ten days, and during this period health condition and food consumption were observed (Ondrašoviè *et al.*, 1993). The results were statistically evaluated according to Student's t-test.

RESULTS

In the first three days of the experiment rats preferred the baits to Larsen's diet. The average bait consumption for all rodenticides during a fourteen-day test is shown in Table 1. The first clinical symptoms after administration of all three compounds appeared from the 3rd to the 4th day. We observed some similar clinical symptoms as: apathy, somnolence, immobility, food deprivation, later bleeding from nose, eyes, mouth and genitalia.

Table 1. The average bait consumption of tested rodenticides during a fourteen-day test (g/animal).

Rodenticide	Warfarin				Bromadiolone (TOPIN 2B)	Brodifacoum (TALON G)
	50g/kg	100g/kg	150g/kg	200g/kg		
bait consumption (g/animal)	24	22.5	21	23.5	17.5	25

Warfarin

The clinical symptoms were represented by dyspnoe and typical bleeding from nose, eyes, ears, mouth and genitalia. Death occurred from 7th to 15th day in conc. 50 g/kg in bait, from 6th to 15th day (100 g/kg in bait), from 7th to 15th day (150 g/kg in bait), from 8th to 15th day (200 g/kg in bait) (Fig. 1).

Bromadiolone

The symptoms were similar to those after warfarin administration. We observed also strong pruritus, which caused several bleeding wounds and later scabs on neck and back. Death occurred from 4-8 day (Fig. 2). For the post-mortem picture, large haemorrhages around vena jugularis and in abdominal cavum, normal size of liver and spleen and slight anaemia of tissues were typical.

Brodifacoum

Clinical symptoms did not differ from those of warfarin. The death appeared from 5th to 8th day (Fig. 3) and was caused by rupture of venas. The post-mortem picture was characterised by partly coagulated blood in thoracal and abdominal cavum, several haematomas in muscle around jugular, axillar, femoral venas and mesenterical venas, vena cava caudalis, truncus pulmonaris. Haematomas were observed also in testicular parenchyma and venas of epididymides.

DISCUSSION

Control of certain rodent pests in urban environments is essential to human and animal health. Of all rodenticidal compounds, one of the most widely used has been the anticoagulant rodenticides. As

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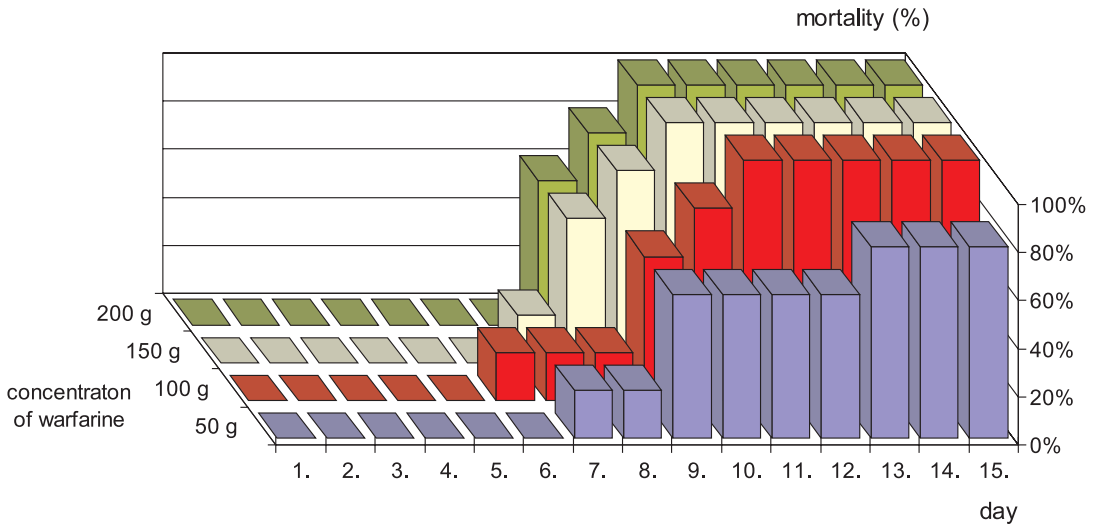

Figure 1. Mortality of experimental rats after administration of warfarin in concentration of 50, 100, 150 and 200 g/kg bait.

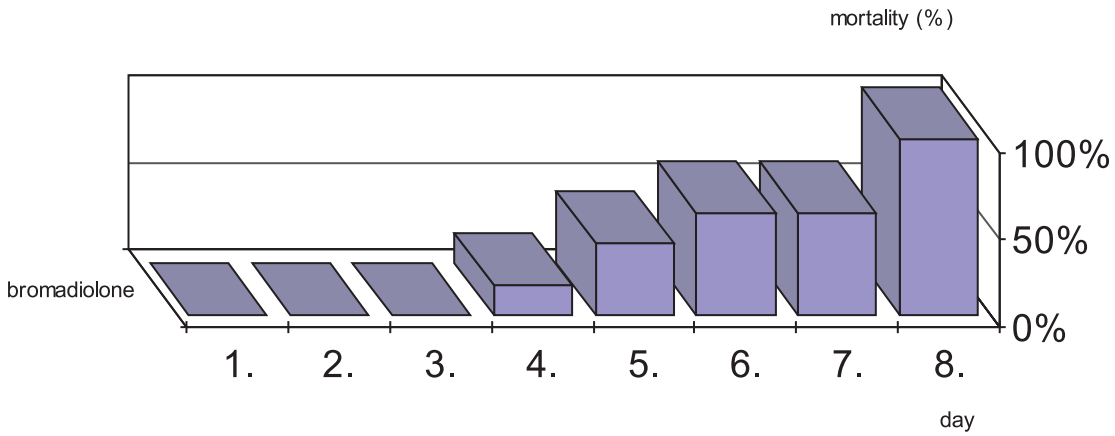

Figure 2. Mortality of experimental rats after administration of bromadiolone (TOPIN 2B).

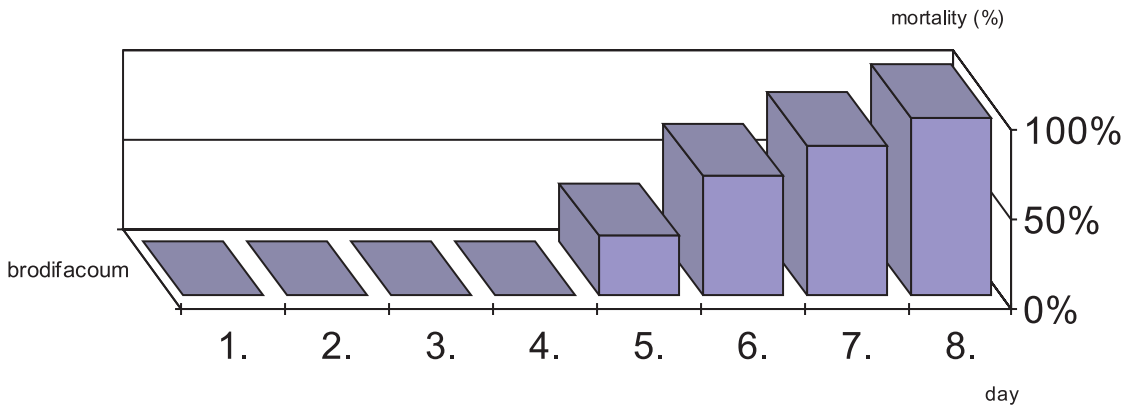

Figure 3. Mortality of experimental rats after administration of brodifacoum (TALON G).

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compared to classical rodenticide warfarin, many newer formulations are more hazardous to nontarget species of animals in urban and suburban environments. They cause prolonged suffering, necessitate expensive and often ineffective therapies and can induce permanent organ damage (Beasley, 1992).

Warfarin has proved to be an ideal rodenticide in that its effect is cumulative and usually the common three - day delay before the onset of clinical sings often allows time for the owner to discover evidence of exposure and to present the animal for veterinary care (Beasley and Buck, 1983). In our experiment we observed the first common clinical symptoms such as apathy, somnolence, immobility, food deprivation, later bleeding from the external openings after administration of all three anticoagulants from the 3rd to the 4th day which correspond to paper data (Radeleff, 1970). But the time of the death was different. After warfarin intoxication death occurred from 6th to 15th day with dependence on the concentration of the effective substance in bait. The effect of the superwarfarins is considered to be 100 times more potent than that of warfarin (Bryson, 1996), characterised by greater prolongation of clotting and prothrombin times (Hoffman *et al.*, 1988). Therefore we assume that it was the reason of the observation of several special clinical symptoms, necropsy and the time of death after their administration.

After bromadiolone intoxication strong pruritus which caused bleeding wounds and later scabs were observed. Death occurred from 4-8 day. More potent effect of brodifacoum reflected in post-mortem picture especially (rupture of venas, haematomas in muscle around jugular, axillar, femoral venas and mesenterical venas, vena cava caudalis and truncus pulmonaris). The death appeared from 5th to 8th day. We can conclude that the effectiveness of super warfarins is greater, with earlier time of death but with more severe permanent organ damages.

The long time use of warfarin has resulted in the selection of warfarin-resistant rat strains in various geographic locations (Lund, 1967). The resistance appeared to be inheritable and to contain a single autosomal gene (Greaves and Ayres, 1967). The introduction of the second-generation rodenticides provided a tool to eradicate infestations of warfarin - resistant rats. Unfortunately, selection for resistance does not end with warfarin and rats which are also resistant to some super-warfarins have been discovered (Greaves *et al.*, 1982). A second point of concern is the potential ecological persistence of the superwarfarins (Huckle *et al.*, 1989).

Rodenticide poisoning of pets, domestic and wildlife animals and their risk exposure for human and animals is a common problem for which ethical behaviour demands control. Control can be achieved by means of increased consideration of likely patterns of exposure prior to product formulation and marketing, thorough testing of final formulations in species likely to be accidentally overexposed in urban and suburban environments, and reevaluations of the safety of such products in pets through implementation of routine monitoring of illness in exposed or overexposed pets, domestic and wild animals.

ACKNOWLEDGEMENTS

This work was supported by the VEGA Grant No. 1/51-50/98 and the VEGA Grant No. 2/4003/97.

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