

## Diphacinone and coumatetralyl persistence in deer and implications for wildlife management

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### Abstract

Because of the concerns regarding wildlife contamination following the field use of anticoagulants the hepatic persistence of diphacinone and coumatetralyl has been compared in deer. Initial coumatetralyl concentrations in liver following oral dosing with 8.25 mg/kg coumatetralyl were similar on day 1 to those achieved by administration of diphacinone at 1.5 mg/kg. Coumatetralyl was more slowly eliminated ( $t_{1/2}$  14 days) than diphacinone ( $t_{1/2}$  6 days) and residues were still present in liver tissue after 50 days versus 12 days for diphacinone. Bioaccumulation on repeated field use is unlikely.

Keywords: coumatetralyl, deer, diphacinone, persistence, pharmacokinetics, residues

### Introduction

The pharmacokinetics of rodenticides determines their tendency to bioaccumulate on repeated exposure. Pharmacokinetic research involves dosing animals and taking blood or tissue samples for analysis. In this study liver samples were taken for analysis of diphacinone or coumatetralyl since it is well known that the highest concentration of these compounds occurs in the liver. Diphacinone is reported to have a short hepatic half-life of 3 days in rats (Fisher et al., 2003), and shorter than the 55 days reported for coumatetralyl in rats (Fisher et al., 2003). The aims of this study were to investigate the comparative persistence of diphacinone versus coumatetralyl in deer. The persistence of anticoagulants has not previously been reported in deer which could come into contact with rodenticide baits if they are used on or near deer farms or in conservation settings to kill predators of ground dwelling birds.

### Methods

Six young male red deer weighing from 77 to 89 kg were split into two groups of three. Deer were fed palatable feed containing 8.25 mg/kg coumatetralyl or 1.5 mg/kg diphacinone. The doses of 8.25 mg/kg coumatetralyl and 1.5 mg/kg diphacinone represented  $\frac{1}{2}$  the published single dose LD50 in rats for coumatetralyl, namely 16.5 mg/kg and for diphacinone, 3.0 mg/kg (Buckle and Smith, 1994). No acute toxicity data exists for either of these compounds in deer. Liver biopsies were undertaken with the same lobe of the liver sampled on each occasion with repeat samples taken in very close proximity to each other. The incision site was located through the 11th intercostal space on the right hand side of each deer. A 1-2 g liver biopsy was taken. To minimise trauma a sedative and local anaesthetic was administered as outlined in West and Vermut (1995). Analyses of residue concentrations were undertaken on liver samples by an established hplc technique. Animal Ethic Approvals were obtained. The half-lives ( $t_{1/2}$  days) for diphacinone and coumatetralyl were determined from the regression as  $(\log_e(2)/b)$ , where b is the slope of the regression of  $\log_e(\text{concentration})$  against time.

### Results

Diphacinone concentrations deer liver decreased to below or at the level of detection of 0.05  $\mu\text{g/g}$  within 29 days (see Table 1). The depletion half-life for diphacinone in liver tissue in deer was 6.3 days ( $\pm 0.8$  SEM). Initial coumatetralyl concentrations in deer liver following dosing with 8.25 mg/kg coumatetralyl were similar on day 1 to those achieved by administration of diphacinone at 1.5 mg/kg. However residues of coumatetralyl were still present after 50 days in one animal (see Table 2). The depletion half-life for coumatetralyl in deer was 14.4 days ( $\pm 3.6$  SEM). MDL=0.02  $\mu\text{g/g}$ .

**Tab. 1** Liver concentrations following oral administration of diphacinone (1.5 mg/kg).

Day after dosing	Individual conc. in µg/g	Average concentration µg/g
1	0.48, 1.26, 0.22	0.69
5	0.24, 0.40, 0.29	0.31
12	0.41, 0.00, 0.00	0.14
29	0.00, 0.00, 0.00	0.00

**Tab. 2** Liver concentrations following oral administration of coumatetralyl (8.25 mg/kg).

Day after dosing	Concentration in µg/g	Average concentration µg/g
1	0.39, 0.66, 0.37	0.47
8	0.49, 0.49, 0.41	0.46
15	0.47, 0.09, 0.09	0.22
29	0.50, 0.09, 0.00	0.20
50	0.08, 0.00, 0.00	0.03
85	0.00, 0.00, 0.00	0.00

## Discussion

Assessments of the persistence of diphacinone and coumatetralyl have been completed in deer and the depletion half-life calculated in liver tissue. Coumatetralyl was more slowly eliminated in deer ( $t_{1/2}$  14 days) than diphacinone ( $t_{1/2}$  6 days) and residues were still present in liver tissue after 50 days versus 12 days for diphacinone. Both compounds appear to be more suited for repeated field use versus the more persistent second generation anticoagulants with diphacinone being less likely to bioaccumulate than coumatetralyl. In contrast with the results obtained with these compounds in deer brodifacoum and all other second-generation anticoagulants have unusually long hepatic half-lives in liver in all species tested (Laas et al., 1985; Parmar et al., 1987; Huckle et al., 1989a and b). Not surprisingly, given the unusual persistence of brodifacoum, residues have been found in game animals such as pigs and deer and a range of avian species (Eason et al., 2001). This paper confirms that coumatetralyl and diphacinone are quickly eliminated from mammals including deer, which is important in areas where deer may be game for hunters. An understanding of the persistence of rodenticides is important when considering rodenticides for field use for conservation and in an agricultural setting. Furthermore we believe that the idea of revisiting synergists such as low dose cholecalciferol with diphacinone and coumatetralyl, whilst presenting registration challenges, has scientific merit in terms of producing rodenticides as potent as brodifacoum with reduced hazards to non-target wildlife resulting from bioaccumulation.

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