The Use of Proftril[R] Boluses in Weaner Red Deer Hinds (*Cervus elaphus*): a Seven Month Study

K.A. Waldrup, C.G. Mackintosh, A P. Rhodes and R.E. Labes

Abstract

Three groups of weaner red deer hinds were treated with oral albendazole solution at either 35 day intervals (Control, n=10) or 21 day intervals (Albezol, n=25) or with a single albendazole-based sustained release bolus (Proftril, n=25). The Proftril group had significantly higher weight gains (11.4 g ± 2 8) compared with the Control or Albezol group (7.9 kg ± 2.9, SED 1.1 and 8.1 kg ± 4.3, SED 0.8 respectively) for the initial 91 days of the trial but had significantly lower gains from 91 to 203 days (5.7 kg ± 0.6, 8.8 kg ± 0.6, 10.5 kg ± 1 1 for Proftril, Albezol and Control groups respectively). The Proftril group had nil faecal larval counts (FLC) for lungworms between 14 and 91 days post-treatment (PI) while the other groups had mean FLCs up to 483 larvae per gram All Proftril treated animals were shedding lungworm larvae by 161 days (PI). At slaughter of some animals 91 days PI, there was no significant difference in the numbers of lungworms (adults and immatures) recovered from all 3 groups The Albezol group had significantly ($P<0.05$) fewer adult abomasal worms, and the Proftril group had significantly ($P<0.01$) higher numbers of *Ostertagia*-type L_4 larvae recovered from abomasal digests. At slaughter 203 days PI, there was no significant difference in the numbers of lungworms recovered from any group, but the Proftril group still had significantly greater numbers of *Ostertagia*-type larvae recovered from the abomasum

Introduction

Lungworms (*Dictyocaulus eckerti*, also classified as *D viviparus*) are recognised as important production-limiting parasites of young farmed deer in New Zealand and especially in their first autumn-early winter period (1) Recognition of parasitism by gastrointestinal nematodes as a production-limiting factor is emerging (2), and autumn is the season in which ingested larvae of the *Ostertagia*-type nematodes can become hypobiotic or inhibited in the abomasum of ruminants, including deer (3) With benzimidazole anthelmintics (white drenches), it is recommended to treat young deer at 21 day intervals for the most efficient control of lungworm infection (1). Albendazole is a benzimidazole derivative, the liquid oral formulation (Albezol DC[R], SmithKline Beecham Animal Health) of which is licensed for use in farmed deer in New Zealand. Albendazole has recently been formulated in a sustained-release intraruminal bolus for sheep (Proftril[R], SmithKline Beecham Animal Health). In sheep, the Proftril bolus is formulated to last to 100 days It is effective against established adult gastrointestinal nematodes and also is effective against ingested L_3 larvae (4). The potential advantages of a sustained-release bolus would include persistent protection of stock against parasites leading to greater production and reduction of stress and potential injury by a lessened need for yarding and handling An earlier trial using Proftril in red deer weaners showed decreased larval shedding and increased liveweight gain in treated deer compared with untreated or orally drenched deer over a 103 day period (5).

The present study is a long-term investigation on the effect of Proftril as a parasiticide in young red deer. The objectives of this study were: 1) to compare the growth rates, serum biochemistry and faecal larval output of weaned red deer hinds treated with either Albezol DC or Proftril for a 91 day period following the initiation of treatment (presumably during the

functional life of the bolus), 2) to compare the growth rates, serum biochemistry and faecal larval output of weaner red deer hinds from 91 to 203 days following the initiation of treatment, 3) to compare the total number of lungworms and abomasal worms recovered at necropsy at 91 days following initiation of treatment and 4) to compare the total number of lungworms and abomasal worms recovered at necropsy from 203 to 213 days following the initiation of treatment.

Methods and Materials

In mid-March 1993, 60 weaned female red deer (*Cervus elaphus*) were randomly allocated to 3 different groups which were run together at all times. Group 1 (Control) consisted of 10 deer in which moderate parasitic infections were maintained. Past experience at Invermay has shown that untreated weaned deer often develop very severe parasitic disease For humane reasons to prevent debilitating infections over the extended time frame of this study, these animals were routinely drenched with a white drench but on a 35 day schedule instead of 21 days. These animals were randomly allocated into 5 pairs at the start of the trial, and one pair was drenched each week on a rotating schedule. In addition to the collection of reference data from these animals, they were intended to provide sufficient pasture contamination for an adequate parasite challenge to the other groups Group 2 (Albezol) consisted of 25 animals which were orally drenched at 21 day intervals with Albezol DC at the rate suggested by the manufacturer (based on 10 mg/kg liveweight, the actual dose was 5 ml of Albezol DC if less than 51 kg liveweight and 10 ml of Albezol DC if greater than 51 kg liveweight). Treatment dosage was based on the previous (7 days prior) liveweight of the individual animal. Group 3 (Proftril) consisted of 25 animals which were dosed with a single Proftril bolus on day 0 (10 March 1993).

Liveweights and faecal samples (for faecal larval counts) were taken from all animals at 7 day intervals until day 91 PI (post initiation) when the first slaughter was done After that time, the remaining animals were sampled at 14 day intervals until slaughter beginning at day 203 PI. Blood samples were taken for serum from all animals at day 0 and then at 21 day intervals until day 84 PI for analysis of total serum protein, serum albumin, serum pepsinogen and SGOT (serum glutamic oxalacetic transaminase). After day 84 PI, blood samples were taken from the remaining animals at monthly intervals until slaughter. All animals were twice vaccinated with Yersiniavax^{R} and a multivalent clostridial vaccine and were treated with a 4 gm capsule of copper oxide wire particles (Copper Needles^{R}, Bayer New Zealand Ltd) on day 0. Selenium supplementation was given monthly until June by oral solution at the rate of approximately 1 mg/10 kg liveweight. No further supplementation was given after June 1993

After an average of 91 days, 5 control (1 randomly chosen from each pair), 10 Albezol treated (randomly chosen) and 10 Proftril treated animals (randomly chosen) were humanely slaughtered. The remaining 35 animals (5 Control, 15 Albezol and 15 Proftril) were maintained on the same paddocks and monitored biweekly for a further 4 months. Due to a limited capacity to process all the samples simultaneously, 7 animals were killed at 90 days PI, 7 were killed at 91 days PI and 11 were killed at 92 days PI Pre-slaughter live weight and hot carcass weights were recorded. The abomasum was isolated, tied and removed as quickly as possible after slaughter. The respiratory tract was removed, and the abomasum and respiratory tract were processed for adult and 5th stage larval nematode parasites (6). Fluid from the abomasum was collected as the contents were strained to recover abomasal nematodes The contents were further washed and fixed in 10% formalin for analysis (6). The

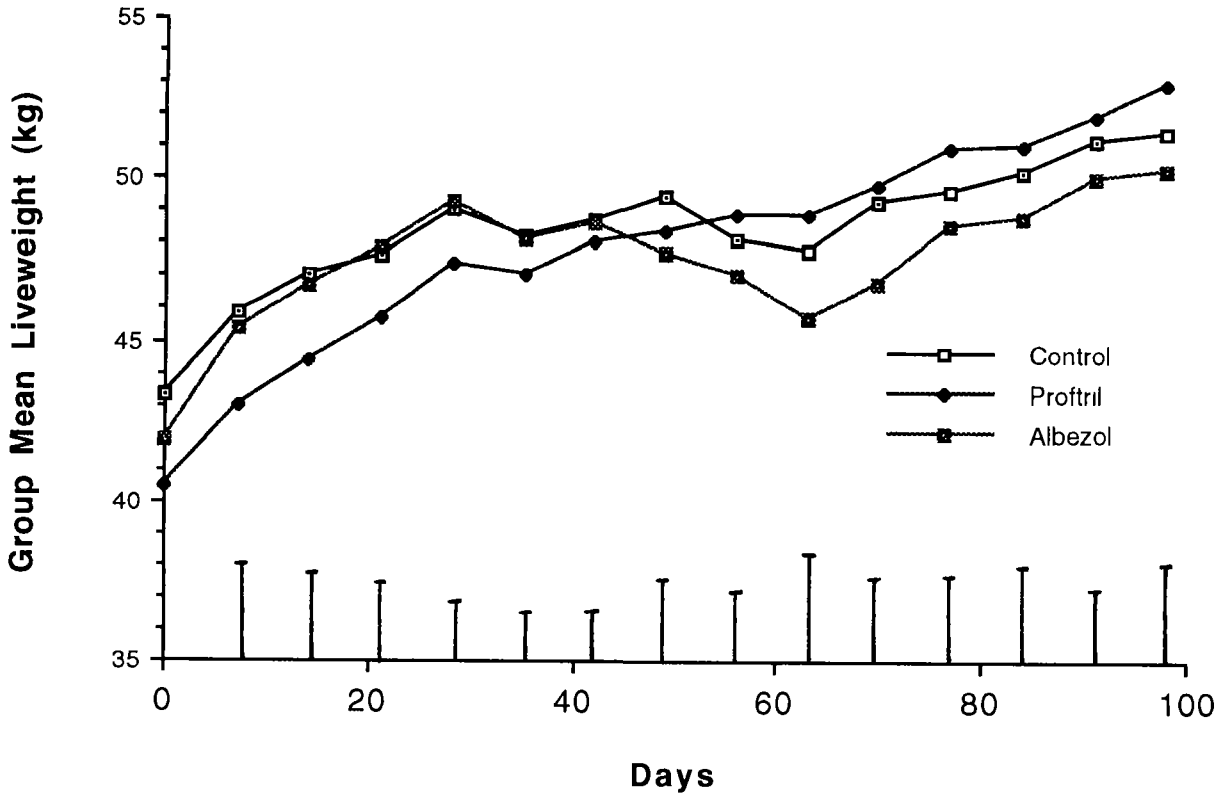
abomasal mucosa was removed by scraping and processed (by acidic enzymatic digestion) for the recovery of 4th stage *Ostertagia*-type larvae (6). The pH of the abomasal fluid was analyzed with an electronic pH meter. Liver sections from each animal were analyzed for copper and selenium concentrations. The boluses were recovered from treated animals and sent for analysis.

No anthelmintic treatments were given to any animals after 98 days PI unless faecal larval counts from an individual animal were over 50 larvae per gram Animals thus identified were treated with Albezol DC at the next sampling period. The remaining animals were humanely slaughtered beginning at 203 days PI. Nine animals were killed at 203 days, 9 animals were killed at 205 days, 9 animals were killed at 210 days and 8 animals were killed at 213 days PI. All samples were collected as analyzed as before Statistical analysis was done by ANOVA or regression analysis using Genstat 5 (2 2) (copyright 1990). Statistical analysis of worms recovered was done with log transformation of the actual numbers.

Results

Changes in liveweight from day 0 to day 91 PI: Figure 1 shows the pattern of weekly liveweight change of the 3 groups over the 91 day evaluation. Over this period the Proftril group gained 11.4 kg which was significantly more than the 7.9 kg gain (SED 1.1; $P<0.01$) of the Control group or the 8.1 kg gain (SED 0 8; $P<0.01$) of the Albezol group. It is noteworthy that between days 40 and 70 PI (during May) both the Control (5 weekly Albezol) and the Albezol (3 weekly) groups declined in weight (0.9 kg and 2.9 kg respectively) compared to an increase in the Proftril group of 0.6 kg (SED 0.61 and 0.45 respectively).

Figure 1. Changes in liveweight of weaner red deer hinds on three different anthelmintic programs from 10 March to 9 June.



Serum biochemistry. The mean serum pepsinogen values for the control and Albezol groups were not significantly different at any time (see Table 1) during the first 91 days PI, except for day 84, and this difference is probably not of clinical significance. The Proftril group however had a significantly elevated mean value on day 0. There was no significant difference among the mean serum pepsinogen values of the 3 groups on day 21 and day 42. The mean serum pepsinogen value of the Proftril group was significantly different from the Albezol group on day 63 PI. On day 84 PI, the serum pepsinogen value for the Proftril group was significantly elevated in comparison to the other groups ($P<0.01$). There was no significant difference in serum pepsinogen values for the remaining animals for any dates after day 84 PI until the second slaughter.

Table 1. Mean serum pepsinogen values (Units/litre) for weaner red deer hinds at 21 day intervals on different anthelmintic regimes over 91 days.

Group (n)	Day 0	Day 21	Day 42	Day 63	Day 84
Control (10)	0.75^{a}	$0\ 78^{a}$	0.57^{a}	$0\ 54^{ab}$	$0\ 68^{A}$
Albezol (25)	$0\ 80^{a}$	$0\ 77^{a}$	0.46^{a}	0.38^{a}	0.59^{B}
Proftril (25)	3.31^{b}	$1\ 01^{a}$	0.54^{a}	0.63^{b}	0.95^{C}
SED Control vs Albezol & Proftril	1 40	0.17	0.07	0 12	0.08
SED Albezol vs Proftril	1.06	0.12	0 05	0.09	0.06

In columns, similar superscripts indicate no significant difference Different lowercase superscripts indicate $P<0\ 05$ and different uppercase superscripts indicate $P<0\ 01\ 01$

The mean total serum protein values were not statistically different among the 3 groups at any time during the first 91 day evaluation and ranged from 61 to 71 g/l. However the Albezol group had a significantly lower mean serum albumin value than the Proftril group on Day 84 PI ($P<0.05$), and over the period from Day 0 to Day 84 PI the mean serum albumin value for the Proftril group declined significantly less than that of the Albezol group ($P<0.001$) and the Control group ($P<0.05$) (see Table 2). From Day 91 to Day 203 PI, there was no significant difference in the serum albumin levels among the three groups.

The serum SGOT levels were within the normal range for all animals in all groups for both the initial 91 day period and the entire 203 day period.

At necropsy on Day 91 PI, lungworms were recovered from animals from all 3 groups despite the fact that the Proftril group had not shed larvae for approximately 77 days. The mean numbers of lungworm adults recovered were 2, 2 and 10 from the Control, Albezol and Proftril groups respectively (not significantly different-NS) The mean numbers of immature lungworms recovered were 70, 30 and 70 from the Control, Albezol Proftril groups respectively (NS). It was noted that some of the adult female lungworms from Proftril- treated deer appeared patent at approximately one half the normal adult female size (M. Taylor, pers. comm.). The boluses were recovered from the rumens of all 10 treated animals.

Ostertagia-type nematodes were the only abomasal parasites recovered. The geometric group means of abomasal worms recovered are shown in Table 3 For adult *Ostertagia*-type worms all three groups were significantly different from each other ($P<0.05$) with Albezol the lowest (7) and Proftril the highest (553). There were no significant differences in the number of 5th stage larvae (L5) between groups. However all three groups had significantly different numbers of 4th stage larvae (L4) again with Albezol the lowest (444) and Proftril the highest (12,288) ($P<0.05$).

There was a significant correlation between the number of adult *Ostertagia*-type worms and the abomasal pH ($r=0.55$; $P<0.01$).

Table 3. Geometric means of abomasal *Ostertagia*-type nematodes recovered from three treatment groups of 8 month old red deer hinds at slaughter.

Group (n)	Adult Worms	L_5 Larvae	L_4 Larvae	Abomasal pH
Control (5)	135^a	38	1777^a	4.4^a
Albezol (10)	7^b	0	444^b	3.8^a
Proftril (10)	553^c	32	12288^c	4.4^a
Std error ratios for Control v Albezol & Proftril	1 4	1 3	1.6	0.5
Std error ratios for Albezol v Proftril	1.4	1.2	1.5	

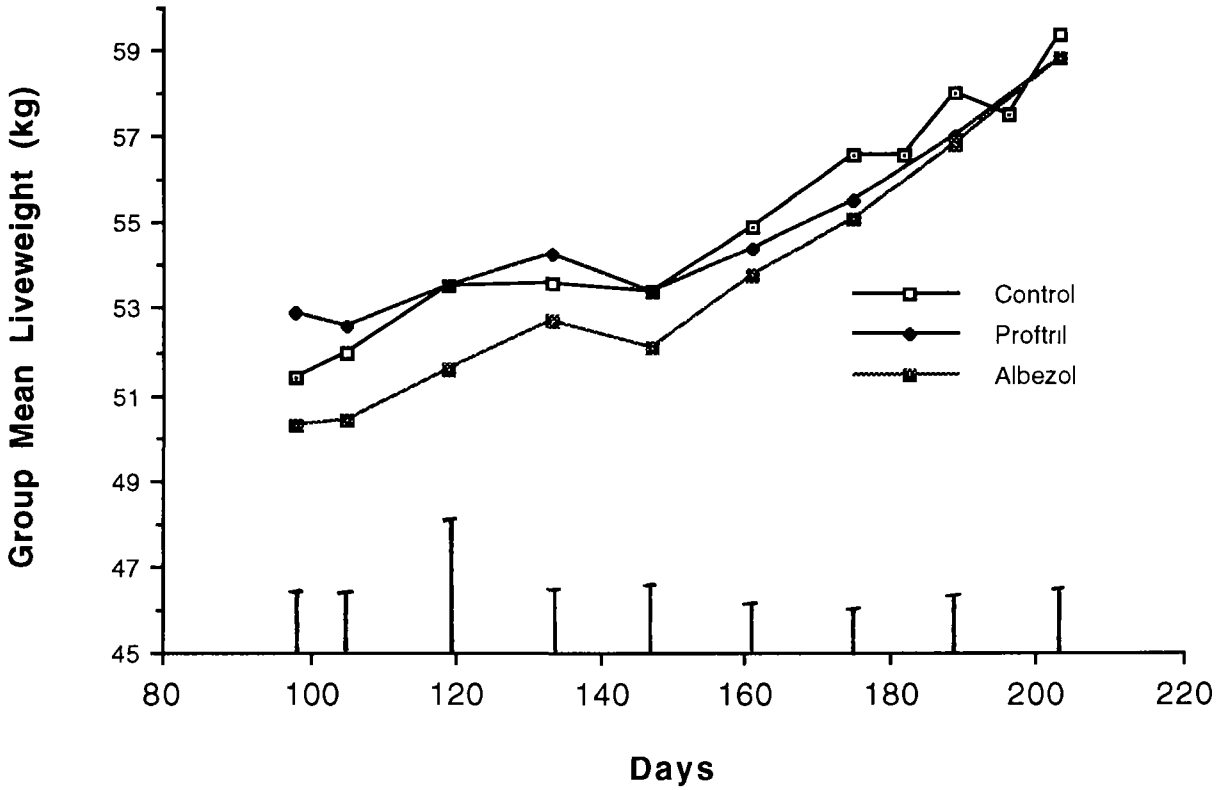
In columns, similar superscripts denote no significant difference Different superscripts denote a significant difference ($P<0$ 05)

Capsule kinetics. The mean liveweight for the Proftril-treated animals which were slaughtered after 91 days was 50 3 kg. The mean release rate of the recovered boluses was 0 51 mm/day (std. deviation 0 016) as compared with the expected release rate of sheep of 0.57 mm/day This release rate would deliver 32.3 mg of albendazole to the animal per day. On a mean live weight basis of these animals, the daily deliver was calculated to be 0.64 mg/kg per day. This exceeds the minimum designed dose of 0 5 mg/kg per day for sheep (4) At this rate, the mean expected life of a Proftril bolus in a red deer weaner would be approximately 119 days.

Changes in liveweight from 91 to 203 ays PI: Figure 3 shows the pattern of biweekly liveweight of the remaining deer in the 3 groups over winter into early spring

The mean live weight gain of the Proftril group was significantly less (P<0 05) than the Control or Albezol groups (5 7 kg, 10.6 kg, SED 1.24, and 8.8 kg, SED 0.875, respectively).

Figure 3. Changes in liveweight of red deer hinds on three different anthelmintic programs from 9 June to 27 September



Parasitology from the second slaughter. Lungworms were recovered from all three treatment groups. There were significantly fewer adult lungworms recovered from the Albezol group than the Proftril group (P<0 05) The Albezol group had significantly fewer (P<0.05) immature lungworms than the Control group but not the Proftril group. *Ostertagia*-type species were the only worms recovered from the abomasa of animals in these groups. The mean numbers of worms recovered is listed in Table 4. There were significantly (P<0.05) fewer numbers of early (EL4) and late (LL4) fourth stage larvae recovered from the Albezol group than from the Control or the Proftril group.

Table 4. Arithmetic means of lungworms and abomasal *Ostertagia*-type nematodes recovered from three treatment groups of 11 month old red deer hinds at slaughter.

Group (n)	Adult lungworms	Immature lungworms	Adult Ostertagia	Early L4 Larvae	Late L4 Larvae	Abomasal pH
Control (5)	11.2[a]	12.6[a]	1120[a]	740[b]	12960[b]	4.88[a]
Albezol (15)	6.1[b]	7.5[b]	1433[a]	167[a]	5273[a]	3.99[a]
Proftril (15)	15.3[a]	9 6[ab]	1513[a]	760[b]	17820[b]	4.35[a]
SED	4 1	2 53	406	171	2495	0.429

In columns, similar superscripts denote no significant difference Different superscripts denote a significant difference (P<0 05)

There was no significant difference in the mean abomasal pH of the three groups due to the variance within each group. Unlike the first slaughter, there was not a correlation with any abomasal worm counts

Discussion

The initial results of this trial were similar to an earlier trial using Proftril in weaner red deer with respect to weight gain and faecal larval counts (5) for the first 91 day period. The Proftril treated deer had significantly higher liveweight gains and had virtually no shedding of lungworm larvae during this initial period. Shedding of lungworm larvae in Proftril-treated deer began on Day 112 PI and all animals in that group had shed larvae by Day 161 PI. The high FLC for the Albezol group occurred at the end of May and in the previous 4-5 weeks both groups receiving Albezol drench had lost weight (see Fig. 1), compared with the rise in liveweight in the Proftril group. This suggests that the entire group was heavily challenged by parasites over this period and Proftril prevented the uptake and development of parasitic burdens, whereas the other groups developed burdens which were then cleared by periodic Albezol treatment. Though 21 day treatment is considered to be a standard with white drenches, it has been shown in cattle that biochemical changes indicative of *Ostertagia* infection can occur within 17 days of treatment with oxfendazole, another white drench (7). These results also show that a lack of liveweight gain and biochemical changes occurred in red deer calves drenched with albendazole at 21 day intervals The difference in FLCs at Day 63 PI between the 3 weekly Albezol group and the 5 weekly Albezol (Control) is probably due to the fact that the treatment in the control group was rotated so that only 2/10 of the group were at the same stage of treatment. Thus, if by chance there was a particularly heavy challenge around the time of the previous Albezol treatment 3 weeks earlier, all 25 animals would have developed burdens at the same time, compared with only 2 animals in the Control group treated at that time. The scheduled drench on Day 63 PI brought a decrease in FLC and an increase in liveweight. It can therefore be inferred that the parasite challenge to the Proftril group was sufficient to have caused disease had the bolus not been functioning.

The number of worms recovered from the Albezol-treated animals 7 days after treatment indicates that albendazole is an efficacious drug for the removal of lungworms and abomasal

worms in deer. The number of lungworms and abomasal worms present in the Proftril-treated deer at slaughter is a matter of concern, as these numbers are equivalent to those previously reported to have caused loss of production in farmed red deer (2). This may have contributed to the significantly lower live weight gain seen in the Proftril-treated deer as compared with the Control and Albezol groups over winter.

It is apparent that the Proftril treatment did not completely prevent the infection of the treated deer by parasitic nematodes for the initial 91 days of this trial, although it did seem to offer protection from the loss of liveweight and serum albumin as observed in the Control and Proftril groups. However the increased serum pepsinogen level in the Proftril-treated deer could be indicative of a developing abomasal problem and was associated with much greater numbers of 4th stage *Ostertagia*-type larvae. In spite of the differences in mean number of 4th stage larvae recovered from the abomasa of the 3 groups at the first slaughter, there was no statistical difference in the mean abomasal pH. Whether these numbers of 4th stage larvae are indicative of a recent massive challenge or whether the Proftril treatment had a suppressive effect on the larvae which promoted inhibition is still in question. The correlation of abomasal pH with the numbers of adult *Ostertagia* present is inconsistent with studies done in cattle with transplanted *Ostertagia* adults where adult worms did not cause a change in abomasal pH (8). In these deer however, increased numbers of adult worms should suggest that more worms have completed the full patent cycle and may have caused more mucosal damage or affected some change by secretagogues (9). With respect to inhibited larvae, the numbers of fourth stage larvae recovered from the abomasa of the Proftril group at the end of the trial would indicate that whatever factors were at work in the initial 91 days after bolus administration were still present. It has been suggested that sustained-release anthelmintic therapy could reduce immunity through a lack of exposure While there may be immunologic interactions here, it is not through a lack of exposure to infectious larvae.

The analysis of the boluses recovered at 91 days post-treatment indicated that these devices were functioning adequately relative to the designed release target of 0 5 mg/ kg per day and that the bolus probably functioned out to 119 days. Therefore the presence of lungworms in the Proftril-treated deer at the first slaughter (91 days) was not due to malfunction Whether those lungworms were accrued during the treatment period or had survived from infections prior to treatment is in question. Though there were significant mathematical differences in the numbers of lungworms recovered from the Albezol and Proftril groups at the second slaughter, these numbers were probably not clinically significant.

Conclusions

1. The use of Proftril boluses in weaner red deer hinds increased the mean liveweight gains as compared with the use of albendazole oral drench for the first 91 days after treatment.

2. The use of Proftril boluses in weaner red deer hinds protected against parasite-induced hypoalbuminemia as compared with albendazole oral drench.

3. The use of Proftril boluses in weaner red deer prevented the shedding of lungworm larvae from 14 to 112 days post-treatment

4. The use of Proftril boluses in weaner red deer hinds did not prevent infection by lungworms or abomasal worms Proftril treated animals had equivalent lungworm infections as controls and greater numbers of total abomasal worms than animals treated with albendazole oral drench.

5. Analysis of the boluses recovered after 91 days showed that the mean release rate was 0.64.mg/kg per day in weaner red deer hinds, and at that rate, the bolus would have lasted to 119 days.

6. In the 3 months following the expected effective life of the bolus (in this case, over winter), Proftril-treated red deer hinds gained less weight than red deer hinds treated with albendazole oral drench

7. At slaughter 203 days after treatment, Proftril-treated red deer hinds still harboured more total abomasal parasites than red deer hinds treated with albendazole oral drench

Acknowledgements

This work was funded in part by a grant from the Game Industry Board of New Zealand, and the authors wish to express their sincere thanks for that support. The authors wish to thank SmithKline Beecham Animal Health, in particular Mr Adrian Rhodes, for the contribution of the Proftril boluses and the Albezol DC used in this study. Thanks are extended to Tony Pearse, Ian Woodhouse, Frans Laas and Adam Whaanga and the Invermay Deer Crew for their help in collecting and processing samples Additional thanks are extended to Melanie Taylor and her helpers for their efforts in parasitology (MAF Quality Management, Invermay) and to Jan Blythe, Peter Johnstone and Ken Dodds for their help in computing and statistics. Further thanks and acknowledgement are extended to Mr David Biland of Captec, Ltd. for providing the analysis of the recovered Proftril boluses.

Literature Cited

(1) Mackintosh, C G., Mason P.C , Bowie J.Y., Beatson N S. Anthelmintics against lungworm (*Dictyocaulus viviparus*) in red deer (*Cervus elaphus*). *Proceedings of a Deer Course for Veterinarians*. Course No 1 Pp 69-77. Deer Branch of the New Zealand Veterinary Association, Wellington, 1984.

(2) Connan R.M. Type II ostertagiosis in farmed red deer. *Veterinary Record* 128, 233-235, 1991.

(3) Borgsteede, F.H.M. Studies on the epidemiological pattern and control of nematode infection in Cervidae In· The Management and Health of Farmed Deer Pp 13-22. Reid HW (ed) Kluwer Academic Publishers, Dordrecht, The Netherlands, 1988

(4) Anonymous Proftril[R] Captec Technical Manual SmithKline Beecham Animal Health, Auckland, New Zealand

(5) Rhodes, A.P. Efficacy of slow-release albendazole capsules in controlling lungworms and gastro-intestinal nematodes in red deer (*Cervus elaphus*). *New Zealand Veterinary Journal*, in press.

(6) Anonymous. Manual of Veterinary Parasitology Laboratory Techniques, third edition, Central Veterinary Laboratory, Weybridge, England 1986.

(7) Holmes, P.H., Bairden, K , McKechnie, D , Gettinby, G and McWilliam, P.N Effect of sustained release and pulse released anthelmintic intraruminal devices on development

of pathophysiological changes and parasite populations in calves infected with *Ostertagia ostertagi* and *Cooperia oncophora*. *Research in Veterinary Science* 51,223-226, 1991.

(8) McKellar, Q , Duncan, J.L., Armour, J., Lindsay, F.E.F., McWilliam,P. Further studies on the response to transplanted adult *Ostertagia ostertagi* in calves *Research in Veterinary Science*, 42,29-34, 1987

(9) Eiler, H., Baber, W., Lyke, W A , Scholtens, R. Inhibition of gastric hydrochloric acid secretions in the rat given *Ostertagia ostertagi* (a gastric parasite of cattle) extract. *American Journal of Veterinary Research*, 42,498-502, 1981.