The effect of faecally excreted ivermectin and fenbendazole on the insect colonisation of cattle dung following the oral administration of sustained-release boluses

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Received 18 April 1995; accepted 18 July 1995

Abstract

The effects of faecal drug residues following the administration of anthelmintics in the form of sustained-release boluses, on dung-colonising Coleoptera and Diptera are reported. In blind field trials, pats of standard weight and size were prepared from the dung of cattle treated with an ivermectin (Ivomec SR Bolus®, MSD Agvet) or a fenbendazole (Panacur Bolus®, Hoechst) sustained-release bolus, and from a third control group of cattle that received no treatment. Pats were recovered after 7, 14, 21 and 42 days in the field and searched for invertebrates. There were no differences in the numbers of adult beetles found in the pats from the three treatment groups. Pats made from the dung of ivermectin-treated animals contained no larval Diptera Cyclorrhapha and significantly fewer larval Scarabaeidae than pats made from the dung of the other two groups. Furthermore, larval Scarabaeidae in the ivermectin pats were inhibited in their development. The pats from fenbendazole-treated animals contained similar numbers of larval Scarabaeidae and Diptera to the pats from untreated animals throughout the trial. At 42 days, the solid matter of the control and fenbendazole-containing cow pats was reduced to a crumbling, granular texture, while the pats from the ivermectin-treated animals were solid and compacted. Pitfall trapping, using traps baited with dung from the three groups, showed no significant difference between the numbers of adult Scarabaeidae attracted, though a trend towards higher numbers attracted to the dung of both anthelmintic-treated groups was evident. The results provide evidence of the toxic effects of excreted ivermectin on key dung-colonising families of insects, and show that fenbendazole lacks such toxic effects.

Keywords: Cattle-Nematoda; Dung-insects; Fenbendazole; Ivermectin; Controlled-release technology

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1. Introduction

For the control of endoparasitic nematodes of ruminants, the development of sustained-release bolus technology for the administration of anthelmintics is viewed as an important advance (Zimmerman and Hoberg, 1988). The use of a bolus allows a measured quantity of drug to be delivered directly to the rumeno-reticulum over an extended time period. This allows for a reduction in labour costs to the farmer and handling stress to the animal while giving sustained anthelmintic cover. However, for all classes of anthelmintic, a proportion of the administered drug is excreted either in the faeces or urine, often in a largely unmetabolised form (Strong and Wall, 1990). Concern has been expressed by many authors about the impact of excreted anthelmintics on insects of the dung community and the potential effects on dung degradation and nutrient recycling (Herd et al., 1993).

The concentrations of excreted drug in dung over time are dependent, amongst other things, on the mode of administration and may be higher for considerably longer following implantation of a sustained-release bolus than after more conventional delivery routes, such as subcutaneous injection, drench or pour-on. This is because a bolus usually releases a significant proportion of the dose directly into the gut and out in the faeces without having been absorbed, in addition to that resecreted into the gut from the blood system. In one trial in which cattle were dosed with an experimental sustained-release bolus delivering 8 mg of ivermectin daily, the faeces were shown to be highly toxic to dung insects, the absence of which significantly retarded the rate of dung-pat degradation (Wall and Strong, 1987). A commercial ivermectin bolus appeared on the UK market in 1993 (Ivomec® SR bolus, MSD Agvet) releasing 12 mg ivermectin daily; 50% more than the earlier device tested. Recently, the benzimidazole anthelmintic, fenbendazole, has also been marketed in the form of a sustained-release bolus (Panacur® bolus, Hoechst). Fenbendazole is also excreted in the dung of treated animals and there is little published work on its impact on dung-community insects.

The aim of this work, therefore, was to carry out a comparative field study to evaluate the effects of fenbendazole and ivermectin after administration by sustained-release bolus on dung colonising Coleoptera and Diptera.

2. Materials and methods

2.1. Livestock and treatments

Twelve helminth-naive calves aged one year (Limousin × Friesian crosses) weighing 278 ± 14.5 kg and of both sexes were separated at random from the Langford stock. The animals were further divided into three groups of four. Each group was housed in a separate pen at the School of Veterinary Science, Langford, Bristol. Animals were fed hay, concentrate (Cowpride Super Rearing Nuts 252, Dalgety), and water ad libitum. The pens were cleaned and all dung removed daily. On 18th May 1994, one group of four animals was treated with an ivermectin-releasing bolus, and identified subsequently as group A. Four animals were left untreated and identified as group B (controls). The
final four calves were treated with a fenbendazole bolus, and identified as group C. The principal investigators were not present when the calves were dosed and knew the groups only by their code letters until the end of the trial. The animals were checked daily by a veterinarian for two weeks after treatment; none rejected a bolus and no adverse reactions were noted.

2.2. Dung collection and pat preparation

Twenty-one days after bolus administration (8th June 1994), dung deposited in the previous 24 h was collected from each of the experimental pens, using separate equipment for each pen to avoid cross contamination. The dung was held at 0°C overnight. The fresh dung was again removed from the pens 24 h later and combined with the previous day’s collection. Thus the dung used in the trials was produced over 2 days. The dung from each group was then mixed thoroughly to ensure homogeneity.

Triplicate samples of the dung, 10–20 g wet weight, were collected from each treatment group for measurement of water content. For this, each dung sample was weighed fresh on a Mettler AE200 electronic balance, dried overnight at 80°C in a fan-assisted oven, cooled in a desiccator and re-weighed.

At the University of Bristol’s Wyndhurst Farm, an 18 × 12 m area, within a sheep and cattle paddock, was fenced off and a 12 × 10 m grid marked out using labelled garden canes inserted into the ground at 1 m intervals. At this site, the mixed dung was weighed into 1 kg aliquots using a spring balance and fashioned into experimental pats, each in a cardboard former 15 cm in diameter and 5 cm deep. Each experimental pat was placed on the ground over a square of 1 cm² mesh, plastic netting. Pats were protected from the possible foraging attention of birds or mammals by a cover of 2.5 cm² mesh pen wire (Strong and Wall, 1994a). Forty ivermectin pats, 40 fenbendazole pats and 40 control pats, labelled with group numbers, were set out in this way at positions in the marked grid allocated by random numbers.

2.3. Dung-pat analysis

Seven days after setting out the pats in the field, 10 group A, 10 group B, and 10 group C pats were collected, transferred to polythene bags and taken to the laboratory. Five-hundred ml of 5% formalin were added to the bags which were sealed and stored at 0°C until sorting. This procedure was repeated at 14, 21 and 42 days after pat preparation. When analysed for invertebrates, the pats were gently broken up in a 12 l bucket fitted with a spout of plastic tubing 5 cm in diameter. Water from a tap flowed into the bucket and the effluent flowed from the spout through two stacking sieves of mesh size 2 mm and 1 mm respectively. The material trapped in the finer sieve was washed repeatedly with running water to remove small particles of dung material. At intervals the contents of the finer sieve were transferred into a large white enamel tray containing approximately 1 cm depth of water. The tray was searched for invertebrates, which were transferred into labelled specimen jars containing 70% ethanol to await identification. The invertebrates were examined under a binocular microscope, sorted and identified into phyla, order and family before being counted (Strong and Wall, 1994a).
2.4. Pitfall trapping

Eighteen pitfall traps were set out in the same area of pasture as the artificial dung-pats. Each trap consisted of an identical plastic bowl, 20.5 cm in diameter and 10 cm in depth, sunk in the ground so that its rim was flush with the surrounding grass. Traps were distributed at intervals of approximately 2 m. Each trap was covered by a square of wire of approximately 2 cm² mesh. The traps were filled with water, to a depth of 2–3 cm and a small quantity of liquid detergent added.

Fresh dung, less than 12 h old, was collected from the three treatment pens in labelled buckets, 45 days after cattle treatment. This experiment was initiated after the dung-pat analysis test was started, which explains why the dung was collected after that used for the dung-pat analysis test. The dung from each pen was thoroughly mixed before being transported to the field site. Aliquots of dung, each of approximately 375 ml, were formed into a standard shape using a plastic bowl as a mould, and each was placed into the centre of one of the squares of wire mesh over a pitfall trap. Traps were emptied and baited again with fresh dung every 48 h.

Pats from the three treatments were put out in a standard sequence and the position of each treatment was rotated one place clockwise at each 48 h collection. At each collection the contents of the pitfall traps were sieved and subsequently stored in 5% formalin in screw-top plastic jars at 4°C to await analysis. With 18 traps, six pats from each treatment were present at any one time and the experiment was continued for 8 days. In the laboratory the adult Scarabaeidae present in each trap catch were identified to genus level and counted.

2.5. Weather records

Air and ground temperature were recorded throughout the trial by an automatic weather station in a field approximately 3 km from the field site. Figures for rainfall were obtained from the Bristol weather centre.

2.6. Statistical treatments

Insect numbers collected from cow pats were logₑ transformed (+1) prior to analysis of variance, with dung treatment and duration of exposure in the field as factors (Statgraphics®, Manugistics). The numbers of insects caught in pitfall traps were also logₑ transformed (+1) prior to analysis of variance in which dung treatment was included as a factor and 48 h exposure period and the sequence of dung treatment types included as blocking factors. All means in the text are presented ± their standard error.

3. Results

3.1. Weather

The day of artificial pat preparation was sunny and dry with a mean air temperature of 14.2°C. The entire trial was characterised by a relatively warm, dry period with a
mean air temperature of 15.4°C ± 0.3°C. Thirty-three of the 42 days that the pats were in the field were without rain, and the remaining 9 days experienced an average rainfall of 3.4 ± 1.6 mm per day. During the pitfall trapping experiments the mean air temperature was 15.9 ± 0.7°C.

3.2. Water content of the dung samples

The mean percentage water contents for ivermectin, fenbendazole and control dung were 83.20% ± 0.08, 82.47% ± 0.01 and 83.34% ± 0.06 respectively. There were no significant differences between the three treatments.

3.3. Scarabaeidae adults

The most numerous adult Coleoptera present in the dung pats were Scarabaeidae (Fig. 1). They were only present in pats exposed for 7 and 14 days in the field and were found in similar numbers in all pats regardless of treatment. Adult Hydrophilidae and Staphylinidae were also present in low numbers but again their numbers were not significantly different between the three treatments.

3.4. Scarabaeidae eggs

Eggs of Scarabaeidae were found in pats of all ages and from all three treatment groups (Fig. 2). There was a significant effect of time in the field (P < 0.001) with the
Fig. 2. The mean log$_e$ ( + 1) (with 95% confidence limits) of the number of Scarabaeidae eggs found in 1 kg artificial pats. Pats were made from the dung of cattle treated with ivermectin, cattle given no treatment (control), or cattle treated with fenbendazole. Groups of 10 pats were recovered from the field after 7, 14, 21 or 42 days.

greatest number of eggs found in pats exposed for 14 days. There was a significant interaction between treatment and time in the field (\( P = 0.02 \)), with the control dung containing the greatest numbers of eggs at 7 and 14 days, the smallest number at 21 days and an equivalent number of eggs to the dung from the fenbendazole-treated animals at 42 days. The dung pats from ivermectin-treated cattle contained lower numbers of eggs than pats from the animals in the other two treatments in at all exposure times except 21 days.

3.5. Scarabaeidae larvae

No larval Scarabaeidae were present in any pats after 7 days in the field (Fig. 3). Larval numbers increased in the pats exposed for 14 and 21 days and then declined in pats which had remained in the field for 42 days (\( P < 0.001 \)). There was a highly significant effect of treatment on the numbers of larvae found in pats (\( P < 0.001 \)) and a significant interaction between treatment and time in the field (\( P = 0.01 \)). The numbers of larvae in the dung from ivermectin-treated animals were consistently lower than in either of the other two treatments. However, while the control dung contained the highest numbers of larvae at 14 days, the dung from the fenbendazole-treated animals contained the highest number of larvae at 21 and 42 days.

After 14 days, the larvae in the fenbendazole and control pats had developed to the second instar, and were brown in colour because of the dung filling their guts (Figs. 4
Fig. 3. The mean log₁₀ (+1) (with 95% confidence limits) of the number of larval Scarabaeidae found in 1 kg artificial pats. Pats were made from the dung of cattle treated with ivermectin, cattle given no treatment (control), or cattle treated with fenbendazole. Groups of 10 pats were recovered from the field after 7, 14, 21 or 42 days.

and 5). At 21 days, the larvae were third instar and were 15 mm long. By 42 days, most were fully grown (20 mm). Larval Scarabaeidae in the 14-day-old ivermectin pats were less than 5 mm long; these larvae were first instars and showed no growth from hatching. They were also transparent or white because their empty guts contained no dung (Fig. 6). At 21 days, larvae were no more advanced in development and, by 42 days, a solitary Scarabaeidae larva (<5 mm long) was found in the 10 ivermectin pats. These data show that ivermectin does not simply reduce numbers of larval Scarabaeidae; it also inhibits the post-embryonic development of those that hatch.

3.6. Larval Hydrophilidae

Larval Hydrophilidae were present in similar numbers at 14 days in the fenbendazole (mean 5.0 ± 2.58 per pat) and control pats (mean 3.20 ± 1.21 per pat). No Hydrophilidae larvae were found in the dung from ivermectin-treated cattle.

3.7. Diptera

Larvae of Diptera Cyclorrhapha occurred in the pats from both fenbendazole-treated and control animals after 7, 14 and 21 days in the field (Fig. 7). However, no cyclorrhaphous dipteran larvae were found in any of the ivermectin pats. No cyclorrhaphous larvae were found in any of the pats recovered after 42 days in the field. The
Fig. 4. Whole mount of a typical Scarabaeidae larva found in the control dung after 14 days in the field. Note the greater size of the larva (2nd instar) and gut filled with dung, by comparison with the larva found in ivermectin dung (Fig. 6). Scale bar = 1 mm.

effects of treatment and exposure time on the number of cyclorrhaphous larvae were highly significant ($P < 0.001$) as was the interaction between these factors ($P < 0.001$). Control pots contained the highest number of cyclorrhaphous larvae at 14 days exposure, but dung from the fenbendazole-treated animals contained the greatest number at 7 and 21 days exposure.

Fig. 5. Whole mount of a typical Scarabaeidae larva found in the fenbendazole dung after 14 days in the field. Note the greater size of the larva (2nd instar) by comparison with the larva found in the ivermectin dung (Fig. 6) and the dung-filled gut. Scale bar = 1 mm.
Fig. 6. Whole mount of a typical Scarabaeidae larva found in the ivermectin dung after 14 days in the field. Note the small size of the larva (1st instar) and the empty gut. Scale bar = 1 mm.

Throughout the trial, larvae of Diptera Nematocera were distributed irregularly amongst the pats and there were no significant differences between their numbers in each treatment group.

Fig. 7. The mean log$_e$ (+1) (with 95% confidence limits) of the number of larvae of Diptera Cyclorrhapha found in 1 kg artificial pats. Pats were made from the dung of cattle treated with ivermectin, cattle given no treatment (control), or cattle treated with fenbendazole. Groups of 10 pats were recovered from the field after 7, 14, 21 or 42 days.
3.8. Physical condition of the pats

For the first 21 days, no differences were noticed in the physical condition of the samples when they were collected: all pats were relatively intact and easy to lift from the surface of the pasture, using the netting. On the final day of collection (day 42), clear differences were noted. The control and fenbendazole pats were alike, and both had been reduced to a thin crust (about 5 mm thick) covering a loose, black, granular material. To avoid losing or damaging Scarabaeidae larvae, this material had to be scooped carefully into the polythene bags. By contrast, the dry, solid pats from the ivermectin-treated cattle showed none of the above changes and were picked up intact.

When the fenbendazole and control pats were processed, recovery of the Scarabaeidae larvae was easy because the loose granular material fell through the sieves, leaving only the thin crust and a small volume of granular material. To process the ivermectin samples, it was necessary to break up the solid pats by hand, producing large volumes of fibrous dung matter to be washed and sieved for invertebrates.

3.9. Pitfall trapping

There was no significant difference in the number of adult Scarabaeidae (predominantly *Aphodius* spp.) caught in the pitfall traps by the three different dung treatments (*P* = 0.16, *n* = 54, Fig. 8). There were no significant interactions between dung treatment type and the exposure period (*P* = 0.59) or dung treatment type and the sequence in which pats were put out (*P* = 0.18).

![Fig. 8. The mean log$_2$ (+ 1) (with 95% confidence limits) of the number of adult Scarabaeidae found in pitfall traps baited with the dung of cattle treated with ivermectin, cattle given no treatment (control), or cattle treated with fenbendazole.](Image)
4. Discussion

In these trials, pats of standard weight and size were prepared from the dung of animals treated either with rumen-rectal boluses of ivermectin, fenbendazole or given no treatment. The work was designed to allow comparative and quantitative data to be obtained on the numbers of families of key, dung-colonising of insects in the artificial pats.

The data from this trial confirm the initial observations of Wall and Strong (1987) that faecally excreted ivermectin has a marked suppressive effect on many insects that colonise the dung pats. The data also show that the dung from fenbendazole-treated animals has no obvious impact on the coleopteran or dipteran species encountered in this study, and that the pats from the fenbendazole-treated animals were not consistently different from the pats of untreated animals.

Information on the concentrations of ivermectin in the faeces of bolus-treated cattle has not been published, the maximal faecal concentration of ivermectin measured after injection being about 0.4 $\mu$g g$^{-1}$ fresh dung (Sommer et al., 1992). Much lower concentrations of drug can have severe effects on the abundance of some dung-breeding insects, for example Scathopaga stercoraria L. (Strong, 1992, 1993). The impact of dung contamination with ivermectin following bolus usage is more intense and of longer duration than after injection (Barth et al., 1993), and one might anticipate faecal levels of the drug to be higher than 0.4 $\mu$g g$^{-1}$. Assuming that only 50% of the given daily dose eventually reaches the faeces, a concentration of at least 0.5 $\mu$g g$^{-1}$ would be expected in the pats (Strong and Wall, 1994b). A bioassay with the dung fly Neomyia cornicina (F.), estimated the concentration of ivermectin in the dung used in this study to be 0.66 $\mu$g g$^{-1}$ (J. Gover and L. Strong, unpublished observations, 1994). At this stage, one cannot predict whether such levels are maintained for the life of the bolus.

Plasma levels of ivermectin in bolus-treated livestock appear to fall by about 50% from 14–35 days after dosing (Barth et al., 1993; Stuedemann et al., 1994). However, analysis of the relationship between faecal drug output and blood plasma levels may be complicated by growth of the treated animals over the life of the bolus. Ivermectin shows little degradation in whole cow pats exposed on pasture land for 45 days (Sommer et al., 1992).

The reduced number of Scarabaeidae larvae in the ivermectin-containing pats noted in previous studies (Wall and Strong, 1987; Strong and Wall, 1994a) may be explained in terms of larval mortality or avoidance of these pats by colonising adults. The data presented here now allow the latter explanation to be rejected. Adult Scarabaeidae were found in the dung pats from ivermectin-treated animals in the same density as in uncontaminated dung and dung from fenbendazole-treated animals. In addition, there was no significant difference between the numbers of adult Scarabaeidae caught by pitfall traps baited with dung from control animals or animals treated with ivermectin of fenbendazole. Clearly, therefore, neither anthelmintic treatment repelled colonising adult beetles.

Although not significant at the 5% probability level, the pitfall-trap data suggest that there may have been a trend towards the opposite effect. Dung from both anthelmintic treatments caught greater numbers of Scarabaeidae than the control dung. Enhanced
attractiveness of the dung of ivermectin-treated sheep to five species of scarabaeid adult beetles has been recorded previously (Wardhaugh and Mahon, 1991). Increased attractiveness of ivermectin-contaminated dung to some, but not all the species of beetle examined, was recorded by Holter et al., (1993). Wardhaugh and Mahon (1991) suggested that the effect might be attributable to the effects of anthelmintic therapy on the gut flora of the treated animal and only indirectly to the drug itself. The fact that the present data suggest some increased attractiveness to the dung of both ivermectin and fenbendazole-treated animals would support the explanation proposed by Wardhaugh and Mahon (1991).

The demonstration that neither ivermectin nor fenbendazole repels colonising dung beetles is confirmed by the presence of Scarabaeidae eggs in the dung from all treatment groups. The reduced numbers of eggs in the pats from ivermectin-treated animals suggests that colonising females laid fewer eggs than in dung from the other two treatment groups. This finding is readily explained by the fact that ivermectin-induced reproductive deficiencies in dung beetles have been documented previously (Wardhaugh and Rodriguez-Menendez, 1988; Ridsdill-Smith, 1993; Wardhaugh et al., 1993). Wardhaugh and Rodriguez-Menendez (1988) also observed mortality in some adult beetles after contacting the dung of cattle injected with ivermectin. Considering the anticipated concentrations of ivermectin in the dung of bolus-treated cattle, it would be of value to investigate the subsequent survival rates of adult Scarabaeidae that have visited the dung of these cattle.

Scarabaeidae larvae were present in the ivermectin pats on days 14 and 21 in lower numbers than in control pats of the same age which would be expected if fewer eggs were laid in the ivermectin dung. In addition, after hatching, larvae in dung from ivermectin-treated animals had empty guts and were inhibited in their development. Wardhaugh et al. (1993) recorded that adults of Euoniticellus fulvus Goeze failed to feed normally after ingesting the dung of sheep drenched with ivermectin one day previously. There are reports that ivermectin has anti-feedant properties, but it is equally possible that insects contacting the ivermectin are simply incapable of feeding (Strong, 1992, 1993). Sommer et al. (1993) described how ivermectin affects the mouth parts and feeding activity in two species of dung beetles. While mouth parts were not examined in the present study, the empty guts of the ivermectin-treated larvae confirm that they had not fed. The fact that dung-feeding had not occurred suggests that ivermectin was taken in by an alternative route: consumption of contaminated egg shells or across the larval integument. The consequence is that ivermectin in the dung of bolus-treated cattle reduces the number of eggs laid by Scarabaeidae adults, and terminates the development of those larvae that do hatch. These observations illustrate the disruptive effect of ivermectin action, and show that the presence of adult Coleoptera in cow pats (Barth et al., 1993) does not indicate normal pat colonisation.

The control dung supported a variety of higher dipteran larvae. These were absent from the dung of ivermectin bolus-treated cattle. Many species of Diptera Cyclorrhapha are highly sensitive to very low concentrations of ivermectin residues in cattle dung (Strong, 1992, 1993).

Fenbendazole and its metabolites are also excreted in the dung of treated cattle (Short et al., 1987). However, in the present study the colonisation of the fenbendazole pats
followed closely that of the controls and few consistent differences could be shown between these two groups. Adult Scarabaeidae colonised the pats and laid eggs in similar numbers to those found in control dung. The larvae hatching from the eggs fed and developed at a similar rate to those in control dung, and fully grown larvae were found in the 42-day pats. Also, higher dipteran larvae were abundant in the fenbendazole dung 7, 14 and 21 days after treatment. These data confirm previous findings on cattle and horses treated orally with fenbendazole: higher Diptera and adult Scarabaeidae were not suppressed following such treatments (Lumaret, 1986; Madsen et al., 1988). By contrast, Wardhaugh et al. (1993) noted some mortality in larval Musca vetustissima Walker reared on sheep dung 1–2 days after drenching with oxfendazole. It might be that M. vetustissima is very sensitive to oxfendazole, or that higher levels of the anthelminthic occurs in the dung of recently drenched sheep. This is a clear demonstration of the value of knowing faecal drug concentrations when trying to compare data from various trials.

This trial compared the effects of ivermectin and fenbendazole, when administered in a similar manner, on dung colonisation by Diptera and Coleoptera. Quantification of dung decomposition was not attempted, but the considerable qualitative differences in the physical nature of the pats call for comment. After 42 warm days in the field, the control and fenbendazole pats had a loose granular texture and disintegrated on collection. The absence of larval Coleoptera or Diptera in pats from ivermectin-treated animals was consistent with their solid and dried-out nature. Whatever external factors contribute to the breakdown of dung in the field (Strong 1992, 1993; Barth, 1993; Barth et al., 1993), there can be little doubt that the breakdown of pats by insect activity may be considerably retarded, if not prevented by ivermectin residues in the dung. Fenbendazole administered in a similar manner did not have similar effects, an observation made previously by Madsen et al (1988).

It can be concluded that, 21 days after administering an ivermectin sustained-release bolus into cattle, faecal drug residues prevent the colonisation of the dung by larval Cyclorrhapha and Scarabaeidae. This lack of colonisation by Coleoptera is not caused by repellency to colonising adults. Fenbendazole, administered in a similar way using a sustained-release bolus at the same time, is without measurable impact on either Diptera or Coleoptera that colonise the dung, which has a similar insect fauna to dung containing no anthelminthic residues.

Acknowledgements

We are grateful to Geoff Davies for providing livestock and facilities at Wyndhurst Farm, Langford, and Mark Hillyer and staff in the School of Clinical Veterinary Medicine, Langford, for dosing and checking the cattle during the trial. We also wish to thank Professor G. Gettinby for helpful statistical advice, and Dr. E.M. Abbott for comments on the manuscript. The research was undertaken in support of regulatory requirements on behalf of Hoechst VG.
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