The history of decoquinate in the control of coccidial infections in ruminants

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Decoquinate is a quinolone derivative that has been used for over 20 years in the control of coccidiosis in domestic ruminants. Decoquinate treats coccidiosis in lambs and calves and prevents coccidiosis in lambs when administered in feed at a dosage of 1 mg decoquinate/kg bodyweight (b.w.) daily for at least 28 days. It prevents coccidiosis in calves and aids in the prevention of coccidiosis in lambs when administered in calf and ewe feed, respectively, at a dosage of 0.5 mg/kg b.w. daily for at least 28 days. Decoquinate also aids in the prevention of abortions and perinatal losses owing to toxoplasmosis by medication of ewe feed at a dosage of 2 mg/kg b.w. daily, fed continuously for 14 weeks prior to lambing. Several field studies have reported reductions in cryptosporidial oocyst shedding. Decoquinate acts early in the life cycle of Eimeria on sporozoites, released from ingested oocysts, and on first-generation meronts, arresting development and release of merozoites and thus preventing further damage to the intestines owing to the gametocyte stages. Production benefits associated with the use of decoquinate are due mainly to its action as a coccidiostat rather than any effects on diet utilization or ruminal fermentation.

INTRODUCTION

Decoquinate (6-ethyl-(decycloxy)-7-ethoxy-4-hydroxy-3-quinolinecarboxylate) is a quinolone derivative developed initially as an anticoccidial for poultry in 1967 (Williams, 2006). It has been used in the control of coccidiosis in domestic ruminants for over 20 years (Laval & Rémy, 1994; Daugschies & Najdrowski, 2005). The compound is almost entirely coccidiostatic with activity against sporozoites and trophozoites of Eimeria spp. and is used in the treatment for and prevention of coccidiosis in calves (Miner & Jensen, 1976; Conlogue et al., 1984; Foreyt et al., 1986b; Fitzgerald & Mansfield, 1989; Mage et al., 1996) and lambs (Spelman et al., 1989; Mage et al., 1995a). Decoquinate has also been shown to prevent coccidiosis in young goats (Foreyt et al., 1986a; Mage et al., 1995b). It is administered by medication of feed to calves, lambs and kids and, in some countries, is licensed as for the medication of feed to be given to ewes as an aid in the control of coccidiosis in lambs.

Decoquinate is also active against Toxoplasma in sheep (Buxton et al., 1996) and is licensed in some countries as an aid in the prevention of abortions and perinatal losses owing to toxoplasmosis by medication of ewe feed. There is no reported activity against Cryptosporidium in vitro (Lindsay et al., 2000). However, field studies have reported reduction in clinical cryptosporidiosis in suckler calves (Navetat et al., 2002, 2004; Cameron & Richard, 2008; Bremner & Richard, 2010) and lambs (Navetat et al., 2002, 2004) by medicating the feed of the dam from 4 weeks preparturition to 1 week postparturition, and in young goats by medicating milk replacer (Mancassola et al., 1997). Research has also shown decoquinate to have in vitro activity against intracellular tachyzoites of Neospora caninum (Lindsay et al., 1997), which may have application for the prevention of associated abortions and neonatal infections by the medication of feed during pregnancy (Journel et al., 2002). However, decoquinate was not effective against experimentally induced sarcocystosis (Foreyt, 1986).

Decoquinate is registered and commercialized for use in ruminants in multiple countries worldwide, including the USA and several countries in Latin America, Europe and the Middle East. There is some variation between countries in the indications for use and the target species of ruminant.

The target dosage is usually expressed as the individual daily dose in mg/kg b.w., and the final dose in the feed, in parts per million (ppm), is calculated according to bodyweight and expected feed intake during the medication period. It is poorly absorbed by the target species when administered orally and is
largely eliminated in faeces unchanged. Consequently, tissue residues are low and deplete rapidly with time. A recent study in cattle showed that only small quantities of decoquinate become available systemically and the drug is rapidly eliminated with negligible residues in milk (Quintero-de Leonardo et al., 2009). In addition, toxicity by the oral route is low. Therefore, decoquinate is in Annex II of the EU Council Regulation No. 2377/90, which means it is not subject to maximum residue levels and therefore has a meat withdrawal time of zero days in cattle and sheep in Europe (EMEA, 2000).

Eimeria infections in ruminants have a typical coccidian life cycle (Taylor & Catchpole, 1994). Decoquinate arrests the development of coccidia by acting on sporozoites that are released from ingested sporulated oocysts during the first day of their life cycle (Joyner & Norton, 1971; Fitzgerald & Mansfield, 1986). It also acts on first-generation meronts, arresting development and release of merozoites (Fitzgerald & Mansfield, 1986), disrupting electron transport in the mitochondrial cytochrome b system (Wang, 1975), thus preventing further damage to the intestines caused by the gametocyte stages (Taylor et al., 2007). Because of its action on the very early stages of the development cycle of coccidia, it has been suggested that decoquinate may have a positive effect on growth performance in calves (Heinrichs et al., 1990; Heinrichs & Bush, 1991; Reynal et al., 1995; Jurjanz et al., 1997; Bagg et al., 2000) and lambs (Mage et al., 1995a). Treatment with decoquinate has been reported to improve milk production and weight gain in sheep (Morand-Fehr et al., 2005), to increase both weight gain and lactation performance in young female goats (Morand-Fehr et al., 2002) and to enhance productivity in lactating dairy cows (Quintero-de Leonardo et al., 2009).

Long-term, continuous use of anticoccidials has led to ineffective treatment owing to drug resistance in Eimeria populations in some host species. For example, resistance to all chemical groups has emerged rapidly in intensive poultry production (Abbas et al., 2011). By contrast, reports of suspected anticoccidial resistance in ruminants are extremely rare and unproven. This may be because the discontinuous use of anticoccidials in ruminants results in a lower selection pressure for resistant strains.

**ACTIVITY OF DECOQUINATE AGAINST EIMERIA INFECTIONS (COCCIDIOSIS)**

**Cattle**

Bovine coccidiosis is one of the most common and important disease of cattle worldwide (Daugschies & Najdrowski, 2005). *Eimeria* infections have been observed in almost all areas where cattle are raised and are usually of greatest importance in calves <1 year of age. Cattle reared under conventional cattle farming systems are exposed and become infected early in life. All age groups of cattle are susceptible to infection, but clinical signs of diarrhoea, often bloody, are most common in young calves reared under intensive husbandry conditions, and more common in housed animals than those on pasture. At least 13 different species of *Eimeria* have been described in cattle (Joyner et al., 1966; Taylor et al., 2007), of which two species are considered pathogenic. Clinical signs of diarrhoea are associated with the presence of *Eimeria zuernii* or *Eimeria bovis*, which occur in the lower small intestine, caecum and colon (Ernst & Benz, 1986; Taylor & Catchpole, 1994; Taylor, 2000b). *Eimeria alabamenensis* has been reported to cause enteritis in first-season grazing calves in the first week following turnout, in some European countries (Gräfner et al., 1985; Svensson et al., 1994).

Outbreaks of disease are usually associated with a previous stressful situation such as shipping, overcrowding, feed changes, severe weather or concurrent infections. Some animals with coccidiosis develop concurrent nervous signs, including tremors, nystagmus, opisthotonus and convulsions. The cause of these clinical signs is unknown, although the possibility of the neurological signs being induced by a toxin has been suggested (Iser et al., 1987).

Outbreaks of clinical coccidiosis can appear suddenly and may prove troublesome to resolve as they often occur in intensive farming systems, particularly where good husbandry and management are lacking. If deaths are occurring, early confirmation of the diagnosis is vital and should be based on the history, postmortem examination and examination of intestinal smears for the presence of coccidial stages. Affected calves should be treated and moved to a cleaner environment or uncontaminated pasture as soon as possible. Normally, all animals in a group should be treated as even those showing no clinical signs may be infected. Several compounds have been shown to be effective in controlling or reducing the severity of coccidiosis in cattle (Miner & Jensen, 1976; Conlogue et al., 1984; Fitzgerald & Mansfield, 1986; Hoblet et al., 1989; Epe et al., 2005; Mundt et al., 2005; Daugschies et al., 2007). Decoquinate is licensed in several countries for the treatment for and prevention of coccidiosis in calves and is administered in feed for at least 28 days at the recommended dosage of 1 mg/kg b.w./day or 0.5 mg/kg b.w./day, respectively.

Studies to determine anticoccidial efficacy depend to a great extent not only on the levels of coccidia challenge, but also on the species composition and levels of challenge with the pathogenic species, *E. zuernii* and *E. bovis*. In a series of studies to determine the efficacy of decoquinate in the control of experimentally induced coccidiosis, male Holstein Friesian calves were challenged with 100 000 oocysts of both *E. bovis* and *E. zuernii*. Treatments were started 3 days before, and for 21–28 days after oral challenge, at dosages ranging between 0.1 and 1 mg decoquinate/kg b.w./day in feed. Decoquinate effectively controlled levels of oocyst excretion to zero, clinical signs of diarrhoea and death at dose levels of 0.5 mg/kg b.w./day and above (Miner & Jensen, 1976).

A study to investigate the effects of medication with decoquinate, or lasalocid, on the development of immunity to *Eimeria* infections in calves was conducted on 20 coccidia-free Holstein bull calves prechallenged with 2000 oocysts per day of *Eimeria* spp., and later challenged with 200 000 oocysts. Calves that received medicated diets at a dosage of 1.2 mg/kg b.w./day excreted significantly fewer oocysts than did untreated controls following initial challenge. Pre-exposure to coccidia did not...
prevent clinical signs in untreated calves, whilst treated calves that were subsequently challenged with the second higher dose of oocysts did not develop diarrhoea, unless the drugs were withdrawn. The results suggested that pre-exposed, untreated calves were no more resistant than treated calves and that medication with either decoquinate or lasalocid was effective in controlling coccidiosis and protected calves for as long as the medicated feeds were administered (Conlogue et al., 1984).

In another study, calves challenged with 275 000 oocysts, predominantly E. bovis and E. zuernii, were fed either decoquinate at 0.5 mg/kg b.w./day, monensin or lasalocid at 1 mg/kg b.w./day, from 7 days pre- to 46 days postchallenge. Calves given medicated rations had significantly fewer oocysts in their faeces and fewer clinical signs of coccidiosis than did calves given nonmedicated rations, but no significant differences were seen in daily weight gain and feed conversion ratios among treated and nontreated groups (Foreyt et al., 1986b).

Decoquinate was subsequently shown to be most effective in preventing coccidial infections in calves when fed continuously in feed for at least 28 days at a dosage of 0.5 mg/kg b.w./day during periods of exposure to coccidia or when cattle are considered to be at risk (Fitzgerald & Mansfield, 1989).

The polyether ionophores, lasalocid and monensin, which are used to increase feed efficiency and weight gains, are also effective in preventing coccidiosis (McDougal, 1978; Waggoner et al., 1994). Monensin has a lower threshold for toxicity, and cattle must be gradually introduced to it in their diet to prevent diarrhoea, feed refusal or toxicity (Potter et al., 1984). The other compounds used in the treatment and control of bovine coccidiosis are the triazines, toltrazuril and dicyclazuril, which are available in several countries worldwide. Studies with these two newer anticoccidial compounds indicate that single metapyllactic treatments prior to anticipated periods of risk can control coccidiosis in calves (Epe et al., 2005; Mundt et al., 2005; Daugschies et al., 2007), but there is potential that the level of protection against subclinical infection may not be as high as that provided by an in-feed medication administered continuously throughout the risk period.

Sheep

Fifteen species of Eimeria have been reported in sheep, of which 11 are commonly identified based on oocyst morphology. Although the majority of sheep, particularly those under 1 year old, carry coccidia, only two species, Eimeria ovinoidalis and Eimeria crandallis, are known to be highly pathogenic (Taylor & Catchpole, 1994; Taylor, 2000b; Taylor et al., 2007).

Coccidiosis in young lambs at pasture has become a significant problem particularly with increased stocking densities and intensive sheep management systems. In spring lambing flocks raised on pasture, coccidiosis generally affects young twin lambs in spring when they are between 3 and 8 weeks of age, with a peak incidence of clinical disease around 6 weeks of age (Taylor & Catchpole, 1994). Disease can occur earlier under intensive production systems in which lambs from dairy ewes are weaned shortly after birth and reared indoors (Saratsis et al., 2011).

Strategic treatments in these situations can be with either diclozuril or toltrazuril, administered prior to anticipated periods of risk, based on the farm history, prevailing management and husbandry systems and knowledge of the epidemiology of the disease. Intervention treatments should aim to limit clinical signs and subclinical production losses but not prevent sufficient exposure to coccidia oocysts to enable the development of protective immunity (Taylor et al., 2011).

An alternative approach to coccidiosis control in young lambs is the administration of decoquinate in creep feed for 28 days at a dosage of 1 mg/kg b.w./day (Taylor, 2005). This dosage requires 100 ppm in feed, which equates to 100 g/10 kg of feed. Decoquinate can also be administered for use prophylactically by medicating ewes in late pregnancy for a period of 28 days at 0.5 mg/kg b.w./day (Taylor, 2005).

There are several studies reporting the effects of feeding decoquinate to lambs to control coccidiosis. In a series of clinical field trials, effective prevention of coccidiosis, under commercial conditions, was observed by medication of ewes in feed for 28 days prior to lambing with decoquinate at 0.5 mg/kg b.w./day, and then by providing creep feed medicated with decoquinate at the same daily dosage to lambs from about 2 weeks old for 28 days. Faecal oocyst output from medicated lambs was reported rapidly and significantly reduced to very low numbers, whilst liveweight gains were improved in the decoquinate-medicated groups compared with untreated control groups. The same authors also conducted an artificial challenge study with decoquinate-treated and untreated control groups of lambs challenged with 10 000 oocysts of both E. ovinoidalis and E. crandallis. At 14 days postchallenge, 50% of the lambs in both the treated and the untreated control groups were slaughtered and necropsied; with remaining lambs assessed for coccidial output and liveweight gain for a further 7 weeks. Decoquinate was shown conclusively to prevent severe coccidiosis. All artificially challenged and unmedicated lambs showed gross and histological lesions of severe coccidiosis, whilst medicated lambs showed no lesions, or only mild lesions detected histologically. Oocyst output was significantly reduced and bodyweights improved in the decoquinate group compared to the unmedicated control group of lambs. The overall conclusions from these studies were that decoquinate demonstrated good efficacy in preventing coccidiosis in lambs under a wide range of husbandry conditions, and also showed positive results in the treatment of clinically affected lambs (Spelman et al., 1989). Additional abstracts and posters, presented at International conferences reporting effective control of coccidiosis in lambs, are summarized in Table 2.

Goats

Coccidiosis is one of the most common conditions in young growing goats with the disease occurring either as an acute clinical form, causing diarrhoea and sometimes death, or as a subclinical form which is common on many goat farms (Chartier et al., 1991). The subclinical form results in decreased growth rates by causing the destruction of epithelial cells in the small intestine with impaired digestive function (Yvoré et al., 1981).
Nine species of coccidia have been identified in goats based on oocyst morphology and predilection site. *Eimeria ninakohlyakimovae* and *Eimeria caprina* cause widespread denudation of the mucosa in the upper and lower large intestine in young kids. *Eimeria arloingi* is probably the most commonly encountered coccidia causing polyp formation and focal hyperplasia of the mucosa. Other species that are considered pathogenic in goats are *Eimeria christenseni* and *Eimeria hirci* (Taylor et al., 2007).

Given the variability in goat husbandry and management systems, and the limited amount of research on goat coccidia, there have been only a limited number of studies on coccidiosis control in goats. The situation is further compounded by the fact that there are currently no licensed anticoccidial products available in many countries.

In one study conducted in the USA, 50 goat kids <4 months of age were artificially challenged with 30,000 oocysts, mainly *E. christenseni* (74%) and *E. ninakohlyakimovae* (20%), at 19 days of age, and randomized into five groups of 10. Four groups were then treated for 87 days with 0.3, 0.5, 1.0 or 4.0 mg decoquinate/kg b.w./day in feed and compared to an untreated control group. Nontreated goats developed profuse watery diarrhoea and tenesmus and gained weight poorly, and two animals died. Treated goats did not develop clinical coccidiosis and gained significantly more weight regardless of the dose used. Decoquinate-treated goats also had significantly fewer oocysts in faeces than nontreated controls. It was concluded that decoquinate was a safe and effective drug for the prevention of clinical coccidiosis in goats. (Foreyt et al., 1986a).

In a study in France to evaluate the efficacy of decoquinate in the prevention of subclinical coccidiosis, weaned, female Alpine goats, aged 6–8 weeks old, were fed 1 mg decoquinate/kg b.w./day for 30 days. Oocyst counts of *E. ninakohlyakimovae* and *Eimeria faurei* were reduced by 86% during the treatment period, and improvement in growth rate and feed conversion was observed compared to untreated control animals (Mage et al., 1995b).

**EFFECTS OF DECOQUINATE ON GROWTH AND PERFORMANCE**

**Cattle**

Whilst coccidiosis can cause significant mortality and economic loss in young calves (Fitzgerald, 1980; Fitzgerald & Mansfield, 1986), the effect of subclinical coccidiosis on feed conversion and growth in neonatal calves is frequently overlooked (Daugschies et al., 2007). Feeding of decoquinate, or the ionophore coccidiostats, lasalocid and monensin, has been shown to be effective in controlling coccidia and improving growth rates in young calves (Foreyt et al., 1986b; Stromberg et al., 1986; Watkins et al., 1986; Fitzgerald & Mansfield, 1989, Heinrichs & Bush, 1991). Improved growth performance, achieved mainly through increased efficiency of feed utilization, has been observed in older cattle treated with ionophores (Bergen & Bates, 1984). A growth effect has not always been shown in young dairy calves fed ionophores (Hoblet et al., 1989; Heinrichs & Bush, 1991; Waggoner et al., 1994). The reason for inconsistent benefits from ionophores has not been completely clarified, but a possible explanation might be that the young calf is in a transition period, changing from a nonruminant to a ruminant, and the effect of the ionophores on performance is dependent on a fully functioning microbial population in the rumen (Nussio et al., 2002). Heinrichs and Bush (1991) suggested that it depends on starter intakes, as the calves have to consume the optimal dosage of the product.

Several performance studies have been reported with decoquinate, mainly from the USA, but also other countries around the world. Studies on ruminal fermentation, diet digestibility and growth performance indicate that improvements in performance from the addition of decoquinate were probably owing to its activity as a coccidiostat and not owing to any modification in diet utilization or ruminal fermentation characteristics (Harmon et al., 1987).

In a 24-week growth study conducted in Pennsylvania, USA, 41 Holstein and Brown Swiss calves were raised under conditions in which they were naturally exposed to sporulated coccidia oocysts at a very early age. Calves were assigned randomly at birth to treatment groups of decoquinate (0.5 mg/kg b.w./day) or lasalocid (1 mg/kg b.w./day), or to an unmedicated control group. Faecal oocyst counts were reduced in the calves fed decoquinate, and both treated groups had higher weight gains than untreated calves, indicating that in-feed medication with decoquinate reduced the severity of coccidiosis and improved growth in young calves where early natural exposure to coccidia occurred (Heinrichs & Bush, 1991).

A 56-day growth study compared the effects of decoquinate and lasalocid, or a combination of the two, on rate of weight gain and control of naturally occurring coccidiosis in weaned Holstein calves (Waggoner et al., 1994). In this study, 64 calves were randomly assigned to one of three treatments groups with decoquinate (0.5 mg/kg b.w./day), lasalocid (1 mg/kg b.w./day) or sequential decoquinate and lasalocid, and an untreated control group. For the sequential treatment, decoquinate was fed for 28 days, followed by lasalocid for the remaining 28 days of the study. In this study, under conditions of natural exposure to coccidiosis and normal management practices, there was little advantage in gain and performance for calves medicated with lasalocid or decoquinate at recommended dosages compared with nonmedicated control calves. No improvement in performance was found for calves administered a sequence of decoquinate and lasalocid compared with single agents administered throughout the study. Although unmedicated calves had higher oocyst shedding than did medicated calves, lack of differences in rate of gain and efficiency of gain was attributed to the low levels of natural coccidia infection, as evidenced by low rates of oocyst shedding. In addition, only a small percentage of calves were infected and shedding oocysts of the two pathogenic species, *E. bovis* and *E. zuernii*.

The effectiveness of decoquinate on the health and growth of neonatal dairy calves in early weaned (4 weeks) and conventional
(7 weeks) weaning systems was investigated in another US study. Treatment with decoquinate reduced numbers of coccidia oocysts shed in the faeces. In addition to improved feed intake for a 3-week period, treatment improved weight gains, height at withers and heart girth circumference. There were no long-term effects of early weaning over the more conventional weaning at 7 weeks of age, and treatment affected both weaning groups similarly (Heinrichs et al., 1990).

A natural exposure study was conducted on female Holstein calves, raised as herd replacements under conditions of a well-managed, mid-western US dairy farm to determine the anticoccidial effects of decoquinate (0.5 mg/kg b.w./day) and lasalocid (1 mg/kg b.w./day) fed over a 90-day period. Weight gains were significantly greater in medicated calves although not statistically significant. Faecal oocyst counts were also significantly reduced. Mild diarrhoea was noticed in all calves but treated calves had a healthier appearance (Hoblet et al., 1989). In a similar comparison study, the effects of decoquinate and monensin on feed intake, height and weight gain in dairy calves prior to weaning age were observed on Holstein heifer calves medicated in feed with either decoquinate (0.5 mg/kg b.w./day) or monensin for 42 days prior to weaning. There were no significant differences between treatments in feed intake, weight gain or height gain, suggesting that decoquinate and monensin have equivalent effects on these parameters in preweaned dairy heifers (Begg et al., 2000).

Another study was undertaken to determine whether treatment of cattle with decoquinate could enhance nonspecific immune function in cattle affected with coccidiosis. This followed observations that feeding decoquinate to coccidiosis-infected cattle has been associated with reduced morbidity and mortality from respiratory diseases (Roth et al., 1989). One group of cattle aged 10–12 months of age were fed decoquinate at 0.5 mg/kg b.w./day for 30 days, and a second group remained as untreated controls. After 30 days, half of the cattle in each group were treated with dexamethasone for 5 days. Dexamethasone-treated steers in the nonmedicated group developed clinical coccidiosis, whereas decoquinate-treated cattle remained clinically normal. It was also shown that the feeding of decoquinate influenced neutrophil function in both dexamethasone-treated and nonmedicated cattle. It was not clear whether decoquinate had a direct on neutrophil function or whether changes were attributable to decreased coccidia burdens and any suppressive effect on the immune system.

Additional studies, presented as abstract or posters at international conferences, report improved performance effects with in-feed decoquinate and are summarized in Table 1.

**Sheep**

Several studies have been conducted to determine the production benefits from feeding decoquinate to lambs. In a study in France to evaluate the efficacy of decoquinate in the prevention of subclinical coccidiosis, cross-bred lambs were weaned at 60 days old and then reared indoors on feed medicated with decoquinate at a dosage of 1 mg/kg b.w./day for 30 days. Improvement in growth rate, feed conversion and carcass quality was observed compared to untreated control animals (Mage et al., 1995a). Abstracts and posters with reported growth effects from feeding decoquinate in feed as presented at international conferences are summarized in Table 2. Any lamb performance benefits observed have depended to some extent on

<table>
<thead>
<tr>
<th>Country</th>
<th>Breed/type</th>
<th>Dosage (mg/kg)</th>
<th>Period of administration</th>
<th>Effect</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>England</td>
<td>Dairy</td>
<td>1</td>
<td>Daily in milk replacer</td>
<td>Improved growth (+0.2 kg/day)</td>
<td>Potter &amp; Drysdale (2011)</td>
</tr>
<tr>
<td>France</td>
<td>Freisian</td>
<td>1</td>
<td>59 days</td>
<td>Improved growth rate in dairy heifers and young Limousin bulls</td>
<td>Mage et al. (1996)</td>
</tr>
<tr>
<td>France</td>
<td>Limousin</td>
<td>0.5</td>
<td>28 days</td>
<td>Improved growth rate in dairy heifers</td>
<td>Jurjana et al. (1997)</td>
</tr>
<tr>
<td>France</td>
<td>Holstein</td>
<td>0.5</td>
<td>90 days</td>
<td>Improved growth rate in dairy heifers</td>
<td>Richard et al. (2008)</td>
</tr>
<tr>
<td>France</td>
<td>Charolais</td>
<td>0.5</td>
<td>28 days</td>
<td>Improved performance in fattening unit (11.2 kg) and feed conversion (−0.13 kg)</td>
<td>Richard &amp; Labar (2008)</td>
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<tr>
<td>France</td>
<td>Limousin</td>
<td>0.5</td>
<td>28 days</td>
<td>Improved growth (+14 kg) in indoor fattening cattle</td>
<td>Richard &amp; Charrier (2011)</td>
</tr>
<tr>
<td>Turkey</td>
<td>Holstein</td>
<td>0.5</td>
<td>5 to 6 months of age</td>
<td>Improvement of fattening calves in-feed conversion (−0.79) ratio and growth(=3 kg)</td>
<td>Erkan &amp; Richard (2010)</td>
</tr>
<tr>
<td>USA (Texas)</td>
<td>Feedlot</td>
<td>0.5</td>
<td>28 days</td>
<td>Improved growth (0.5 kg) and increased feed conversion (24%)</td>
<td>Fox (1989)</td>
</tr>
<tr>
<td>USA (Oklahoma)</td>
<td>Stocker calves</td>
<td>0.5</td>
<td>60 days</td>
<td>Improved growth (0.2 kg/day)</td>
<td></td>
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<tr>
<td>USA (Oklahoma)</td>
<td>Weaned dairy calves</td>
<td>0.5</td>
<td>56–58 days</td>
<td>Improved growth (0.2 kg/day)</td>
<td></td>
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<td>Mexico</td>
<td>Dairy heifers</td>
<td>2.5</td>
<td>30 days in milk replacer</td>
<td>Improved growth (0.09 kg/day)</td>
<td>Richard et al. (2006)</td>
</tr>
</tbody>
</table>
Spain Merino lambs 1 32 days Improved weight gain when administered with Spain Merino lambs 1 49 days Improved feed conversion and weight gain et al.

Israel Awassi lambs 1 89 days Improved growth rate and food conversion rate Leibovich

France Lacaune lambs 1 28 days Reduced oocyst shedding 21 days postweaning Le Scouarnec et al.

France Ile de France lambs Not specified Dosage (mg/kg) Period of administration Effect References

Table 2. Studies on coccidiosis control and growth effects of decoquinate fed to sheep (short papers, abstracts, posters presented at international conferences)

<table>
<thead>
<tr>
<th>Country</th>
<th>Breed/type</th>
<th>Dosage (mg/kg)</th>
<th>Period of administration</th>
<th>Effect</th>
<th>References</th>
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<tr>
<td>Brazil</td>
<td>Santa Ines lambs</td>
<td>Not specified</td>
<td>56 days</td>
<td>Both decoquinate and monensin reduced oocyst output but no differences in performance observed</td>
<td>Susin et al. (2004)</td>
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<td>France</td>
<td>Lacaune ewe lambs</td>
<td>1</td>
<td>30 and 75 days from weaning</td>
<td>Improved growth rate, food conversion rate and subsequent milk production on the 75-day treatment</td>
<td>Morand-Fehr et al. (2005)</td>
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<tr>
<td>France</td>
<td>Lacaune lambs</td>
<td>1</td>
<td>84 days</td>
<td>Indoor-reared lambs had reduced oocyst shedding and +2.4 kg in autumn born lambs; +1.5 kg in winter born lambs</td>
<td>Morand-Fehr et al. (2010)</td>
</tr>
<tr>
<td>France</td>
<td>Lacaune lambs</td>
<td>1</td>
<td>28 days</td>
<td>Reduced oocyst shedding 21 days postweaning</td>
<td>Le Scouarnec et al. (2003)</td>
</tr>
<tr>
<td>Israel</td>
<td>Awassi lambs</td>
<td>1</td>
<td>89 days</td>
<td>Improved growth rate and food conversion rate</td>
<td>Leibovich et al. (2008)</td>
</tr>
<tr>
<td>Spain</td>
<td>Merino lambs</td>
<td>1</td>
<td>49 days</td>
<td>Improved feed conversion and weight gain compared with lambs fed plant extracts</td>
<td>Carrasco &amp; Richard (2010)</td>
</tr>
<tr>
<td>Spain</td>
<td>Merino lambs</td>
<td>1</td>
<td>32 days</td>
<td>Improved weight gain when administered with sulphonamides compared with sulphonamides alone</td>
<td>Habela et al. (2011)</td>
</tr>
</tbody>
</table>

the sheep management system, and the length of time feed supplementation was provided.

Monensin has been used in sheep and has been shown to reduce oocyst output but has no significant effect on lamb growth rate (Gregory et al., 1983). When given to ewes for a month before lambing, it appeared to confer some advantages to the offspring of medicated ewes but it has been suggested that it may have acted by raising ewe milk output or by raising lambs’ selenium status (Anderson et al., 1983).

Goats

In France, with its intensive goat milk production systems, female goats are mated as early as 7–8 months old so that they kid when they are 1 year old with the objective of achieving a high first lactation. Any disruption of growth during the first 7–8 months may have consequences on subsequent reproductive or production performance of the young goat and therefore on flock productivity (Morand-Fehr et al., 1996). A study was conducted to investigate whether decoquinate treatments in a goat flock with no clinical coccidiosis could improve the growth and milk performances of replacement goats. Over a 5-year period, groups of young female Alpine goats were treated for coccidiosis, either twice daily with sulphadimerazine for 3 days or with 1 mg decoquinate/kg b.w. daily from 8 days prior to weaning, and for either 30 or 75 days postweaning. Animals in the decoquinate-treated groups had consistently higher bodyweights at 7 months of age by 1.4–4.8 kg, compared with the sulphadimerazine-treated group. The 75-day decoquinate treatment was more effective in terms of weight gain than the 30-day treatment. In all the cases, feed efficiency was improved. The 100- or 200-day milk production for the first lactation was improved with the 75-day treatment, but not with the 30-day treatment. The effect on milk production was attributed to heavier live weight at mating and parturition in the decoquinate-treated goats (Morand-Fehr et al., 2002).

ACTIVITY AGAINST CRYPTOSPORIDIOsis

Parasites of the coccidial genus Cryptosporidium are small intracellular parasites that occur throughout the animal kingdom (Fayer & Ungar, 1986). The importance of Cryptosporidium infections was for a long time overlooked, until infection in young livestock, and the role that Cryptosporidium parvum played as a primary pathogen in calf diarrhoea was recognized (Trápori et al., 1980). Cryptosporidiosis is now one of the most common causes of calf diarrhoea throughout the world. Although several species of Cryptosporidium have been reported from cattle, C. parvum is the most important species, as it is highly prevalent in ruminants, and zoonotic transmission has been reported from calves and lambs, particularly following educational visits to farms (Taylor, 2000a). More recent studies suggest that C. bovis is the most prevalent species in cattle aged 3–11 months (Santin et al., 2007). As with other coccidia, infection is by ingestion of oocysts, which are shed into the environment by other infected calves, and by adult cows (Mann et al., 1986; Villacorta et al., 1991; Scott et al., 1994; Faubert & Litvinsky, 2000; Huetink et al., 2001). However, unlike other coccidia, sporulation takes place within the host so that oocysts passed in the faeces are immediately infective (Taylor et al., 2007).

Cryptosporidiosis is usually characterized by low mortality but high morbidity with clinical signs of dehydration, diarrhoea and weight loss. Few therapeutic or prophylactic measures are effective against cryptosporidiosis, and control depends mainly on disinfection, hygiene and attention to husbandry. Halofuginone has reported efficacy in the treatment for cryptosporidiosis in calves (Joachim et al., 2003) and it is licensed for the treatment for and prevention of diarrhoea owing to diagnosed C. parvum in several countries. Because of the narrow therapeutic index, treatment must begin within 24 h of the onset of diarrhoea, before the onset of dehydration, and should not be given to animals on an empty stomach. Paromomycin has also been shown to be effective in reducing both oocyst output and
clinical signs in lambs (Viu et al., 2000) and kids (Chartier et al., 1996).

Calves

Studies have reported inconsistent results from the use of decoquinate for the treatment for and prevention of cryptosporidiosis in young calves. Redman and Fox (1994) indicated in a small number of experimentally challenged calves, oral administration of decoquinate was effective in delaying the time from challenge to shedding, reducing the number of days of shedding and improving the faecal consistency. However, a study in neonatal calves artificially infected with C. parvum and treated with 2 mg/kg b.w./day for 28 days in milk replacer showed no effect on oocyst shedding or clinical signs associated with cryptosporidiosis (Moore et al., 2003). Similarly, veal calves medicated in milk replacer at a dosage of 2.5 mg/kg b.w./day for 21 days showed no reduction in oocyst shedding or diarrhoea (Lallemand et al., 2006).

Several field studies have reported reduction in clinical cryptosporidiosis in suckler calves by medicating the feed of the dam from 4 weeks preparturition to 1 week postparturition at a dosage of 1.25 mg/kg b.w./day (Navetat et al., 2002, 2004; Cameron & Richard, 2008; Bremner & Richard, 2010). This suggests that environmental loading of oocysts from the dam could be reduced, leading to lower levels of challenge to the calf, which has potential to prevent the onset of clinical signs whilst allowing the development of immunity.

During an outbreak of clinical cryptosporidiosis in weaned Holstein calves on a dairy farm in the UK, 80% morbidity with 20% mortality was reported. Affected calves were treated with decoquinate added to the milk replacer to provide a daily dose of 2.5 mg/kg b.w./day, and treatment was continued for at least 2 weeks. Milk was withheld from dehydrated calves, and instead an oral rehydration solution was administered to which 2.5 mg decoquinate/kg b.w. was added. No further deaths occurred following the start of treatment (Vine, 2006).

Lambs

Cryptosporidium infections in sheep have been described worldwide and it has been generally assumed that most Cryptosporidium infections were owing to C. parvum (Angus, 1990). Molecular methods have since been used to identify and confirm that C. parvum is important in neonatal lamb diarrhoea and is widespread in UK sheep flocks (McLauchlin et al., 2000) but other species and genotypes are also present in sheep (Ryan et al., 2005; Mueller-Doblies et al., 2008). Little is known about the epidemiology of cryptosporidiosis in sheep, particularly in lambs at pasture raised with their dams, but oocyst shedding has been shown to increase in ewes during the periparturient period and as such, the ewes may constitute an important source of environmental contamination of C. parvum oocysts (Ortega-Mora et al., 1999). It has been suggested that treatment of ewes with decoquinate at 1.5 mg/kg b.w./day for 28 days prior to lambing, and 8 days postlambing, will help control cryptosporidiosis in lambs by reducing oocyst shedding of ewes during the periparturient period (Navetat et al., 2002, 2004).

Goats

Studies on the efficacy of decoquinate for the prevention of and treatment for cryptosporidiosis in kids have given more positive results. Mancassola et al. (1997) found that decoquinate in milk replacer for 21 days at a dosage of 2.5 mg/kg b.w./day, started 3 days after inoculation with C. parvum, reduced the severity of cryptosporidiosis and oocyst excretion in kids compared to nonmedicated controls.

Ferre et al. (2005) investigated the efficacy of decoquinate at 2.5 mg/kg b.w./day to prevent cryptosporidiosis in kids by either dosing the kids for 21 days from 3 days of age or instead feeding the dams for 21 days prior to kidding. Both treated groups showed improvements over the untreated controls, including no deaths, lower faecal consistency scores and reduction in oocyst shedding. Treatment did not, however, eradicate naturally acquired cryptosporidiosis from the kids.

ACTIVITY AGAINST TOXOPLASMA INFECTIONS (TOXOPLASMOsis)

Toxoplasma gondii was first identified as a cause of abortion in sheep over 50 years ago (Cole et al., 1954; Hartley et al., 1954) and is now recognized as a major cause of abortion in ewes, and perinatal mortality in lambs. If infection of the ewes occurs early in gestation (<55 days), there is death and expulsion of the small foetus, which is seldom observed. If infection occurs in midgestation abortion is more readily detected, the organisms being found in the typical white lesions in the cotyledons of the placenta and in foetal tissues. Alternatively, the dead foetus may be retained, mummified and expelled later. If the foetus survives in utero, the lamb may be stillborn or, if alive, weak (Taylor et al., 2007).

In the UK, toxoplasmosis has been estimated to be the primary cause of loss in 10–20% of flocks with an abortion problem, with an estimated annual incidence in the breeding ewe population of 1–2% (Blewett & Watson, 1984; Blewett & Trees, 1987). The disease can be controlled in some countries such as New Zealand, the UK and Ireland by use of a live attenuated vaccine (O’Connell et al., 1988; Wilkins et al., 1988; Buxton et al., 1991, 1993). However, on farms where vaccination cannot be instigated, or where the vaccine is not available, the use of an effective drug to prevent or reduce the losses is a valuable control option. Monensin has been shown to be effective in the control of ovine toxoplasmosis (Buxton et al., 1988) but is not licensed for use in sheep and may be toxic if fed at high dosages (Nation et al., 1982).

In a study reported by Buxton et al. (1996), decoquinate was shown to reduce the effect of experimentally induced toxoplasmosis in pregnant ewes. In this study, sheep were challenged orally with T. gondii oocysts at 90 days of gestation. Decoquinate
was given in the feed daily, at either 1 or 2 mg/kg b.w/day from 10 days prior to oocyst challenge through to lambing. Feeding decoquinate at the higher rate of 2 mg/kg b.w./day was shown to cause a delay in the onset of the febrile response to infection, reduction in the overall severity of fever and delay in the production of antibodies to the parasite. This treatment also reduced the placental damage caused by the parasite, lengthened the mean gestation period and increased the number and weight of live lambs, in comparison with ewes not fed decoquinate, but challenged with *T. gondii* oocysts. These results support the licensed indication of decoquinate as an aid in the prevention of abortion and perinatal losses owing to toxoplasmosis for use during pregnancy, with a recommended dosage of 2 mg/kg b.w. fed continuously for the last two-thirds of pregnancy (i.e. 14 weeks prior to lambing).

CONCLUSIONS

Decoquinate is a quinolone coccidiostat that can be administered via the feed at a dosage of 0.5–1 mg decoquinate/kg b.w. daily for at least 28 days for the treatment and prevention of coccidiosis in ruminants. Decoquinate is also effective as an aid in the prevention of abortions and perinatal losses owing to toxoplasmosis by medication of ewe feed at a dosage of 2 mg/kg b.w. daily, fed continuously for 14 weeks prior to lambing. Reported effects on growth performance and improved milk production in ruminants are mainly owing to its action as a coccidiostat and not owing to any modification in diet utilization or ruminal fermentation. Decoquinate also has reported effects on cryptosporidial oocyst shedding in ruminants, which has potential to reduce environmental challenge. The uses of decoquinate referred to in this article may not be licensed in any particular country, and local product literature should always be consulted prior to use.

CONFLICTS OF INTEREST

Prof. Mike Taylor was commissioned by Pfizer Animal Health to research the publications and write the manuscript. David Bartram is a paid employee of Pfizer Animal Health who contributed to writing the manuscript and sourced several of the cited references.

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