Anti-parasitic use of sericea lespedeza and copper oxide wire particles in small ruminants

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Abstract

Management of gastrointestinal parasitism in sheep and goats is a major challenge in many parts of the world, particularly in the current age of multi-drug anthelmintic resistance. *Haemonchus contortus* has gained substantial notoriety for its pathogenicity, as well as for its ability to develop resistance to all currently available classes of anthelmintics. As conventional pharmaceuticals continue to lose efficacy, alternative anti-parasitic strategies, such as feeding sericea lespedeza, a plant rich in condensed tannins, and administration of copper oxide wire particles, are gaining popularity in the United States.

Key words: sericea, lespedeza, anthelmintic, parasites, small ruminants

Résumé

La gestion du parasitisme gastro-intestinal chez le mouton et la chèvre représente un grand défi dans plusieurs parties du monde surtout dans le contexte de l'émergence de multi-résistance aux anthelminthiques. Le nématode *Haemonchus contortus* est bien reconnu pour sa pathogénicité et son aptitude à développer une résistance contre toutes les classes d'anthelminthiques présentement disponibles. Alors que les produits pharmaceutiques continuent de perdre de leur efficacité, des stratégies alternatives de contrôle des parasites, comme l'utilisation de particules de métal d'oxyde cuprique et l'inclusion de la lespedeza de Chine (une plante riche en tannins condensés) dans l'alimentation, gagnent en popularité aux États-Unis.

Introduction

Gastrointestinal nematode parasites are the most important health threat to small ruminants in many parts of the world.[15] Many gastrointestinal nematodes infect sheep and goats, but *Haemonchus contortus* is by far the most pathogenic and prevalent nematode in parts of the United States where there is sufficient warmth and moisture to support its life cycle. *Haemonchus contortus* causes blood loss during feeding activity in the abomasum. When infection intensity is high in vulnerable hosts, symptoms such as anemia, weakness, weight loss, and death can ensue. This disease state is referred to as haemonchosis. The 2 next most prevalent nematode parasites in small ruminants are *Trichostrongylus colubriformis* and *Teladorsagia circumcincta*; appetite reduction, loose feces, and weight loss occur in heavily parasitized hosts.[15]

Over the past 16 years, anthelmintic resistance has increased rapidly in both prevalence and magnitude, particularly in *H. contortus* populations. From 2000 to 2003, multi-drug resistant (benzimidazole, imidazothiazoles/tetrahydropyrimidine, and ivermectin[a]-resistant (but moxidectin[b]-sensitive) *H. contortus* were documented in goat herds in Virginia and Georgia.[22,25,32] In 2008, a study conducted on 48 small ruminants in the southeastern United States demonstrated that *H. contortus* was the most prevalent parasite on 44 of the 46 farms.[14] Resistance to all 3 classes of anthelmintics was present on 22 (48%) of the farms, and resistance to all 3 anthelmintic classes and moxidectin[b] was detected on 8 farms (17%).[14] Since that study was published, total anthelmintic resistance has been recognized with increasing frequency.[15] In response to the rapid evolution of anthelmintic resistance, renewed interest in alternative parasite control solutions has stimulated research efforts to characterize the efficacy and safety of condensed tannins, copper, nematophagous fungi, and *H. contortus* vaccines.

Condensed Tannins

Plants such as sulla, sainfoin, birdsfoot trefoil, big trefoil, chicory, and sericea lespedeza contain condensed tannins which have been shown to have antiparasitic benefit.[13] Tannins are plant polyphenols that are divided into 2 groups based on their structure: hydrolyzable and condensed tannins.[13] Hydrolyzable tannins are degraded in the ruminant digestive tract to absorbable, potentially toxic metabolites. In contrast, condensed tannin metabolites are poorly absorbed after degradation in the digestive tract. Condensed tannins remain in the ingesta bound to macromolecules such as protein and polysaccharides. Consumption of low to moderate concentrations of condensed tannins has nutritional benefit because the protein binding allows some dietary protein to bypass the rumen, and undergo digestion in the small intestines. However, consumption of high levels of condensed tannins can negatively impact rumen microbiota, and cause a decline in appetite.[13] Other benefits of condensed tannins in ruminant nutrition included decrease in bloat and reduction in methane gas formation.[26] Condensed tannins bind and disrupt the protein-rich parasitic cuticle in vitro and, presumably, in vivo.[13] Anti-parasitic benefits include reduction in nematode numbers, reduced worm fecundity, and decreased fecal egg output.[13]

Sericea lespedeza (SL) is a non-bloating perennial legume that is rich in condensed tannins.[26] It is especially well adapted to the southeastern United States. It grows well in a variety of soils, including otherwise infertile acidic soils. In addition, SL is also drought tolerant and insect resistant. For the past century, SL has mainly been used for soil stabilization, and as a livestock forage.[27] Many SL cultivars exist, but AU Grazer®[c] is the primary cultivar used in the United States for feeding livestock.[27] The anti-parasitic benefits of SL were only recently discovered. Min et al published one of the first reports that highlighted this anthelmintic effect.[21] Naturally parasitized goats on SL-rich pasture had had a 57% reduction in fecal egg count (FEC) compared to goats grazing grass pasture.[21] In a subsequent experiment, Angora does that grazed on SL pasture for 81 days had a 76% reduction in their total adult worm burden compared to controls on crabgrass/fescue pasture.[20] Adult *H. contortus* were reduced by 94%, *T. circumcincta* by 100%, and *Trich. colubriformis* populations by 45% in goats on SL pasture.[20] Min's research group later demonstrated that goats ingesting SL pasture not only had decreased FEC, but parasitic larval development was also impaired. In addition, goats grazing SL had higher packed cell volumes (PCV), and improved immunologic function, compared to goats on crabgrass/tall fescue pasture.[19] Lambs grazing SL pasture also had lower FEC than their counterparts on bermudagrass pasture.[5] Unlike goats, sheep appear to require an adjustment period to acclimate to the astringency of fresh SL.[5,26]

Further studies were conducted to evaluate whether the condensed tannins in SL would retain anti-parasitic benefits when fed as hay and as pellets. Shaik et al[23] trickle-infected 20 Boer bucks with *H. contortus* larvae to mimic natural infection, and fed the goats a diet that consisted of either 75% Bermuda grass hay (control group) or 75% SL hay, in confinement for 7 weeks.[23] The ration was balanced between groups for protein and calories with a supplemental feed that made up the remaining 25% of the diet. By the last 2 weeks of the trial, goats eating SL had an 88% decrease in FEC from pre-trial data.[23] The SL group maintained higher PCV than the control group, and ova collected from the SL group were less likely to develop into infective larvae. At slaughter, significantly fewer abomasal worms (*H. contortus* and *T. circumcincta*) and intestinal worms (*Trich. colubriformis*) were recovered from the SL group compared to the control group; the anthelmintic effect was highest against *H. contortus*.[23] Similarly, lambs fed SL hay had 67 to 98% lower FEC during the feeding trial, and the FEC remained significantly lower than controls on Bermuda grass hay throughout the feeding period.[18] The FEC increased quickly after SL feeding ceased, indicating that the reduction in FEC was in part stemming from reduced worm fecundity.[18] These studies demonstrated that SL maintains its anti-parasitic properties after being dried and made into hay, and that the hay was highly palatable to goats and sheep. A subsequent titration study in goats concluded that 75% of the diet needed to be comprised of SL hay to achieve the greatest benefit, but feeding it as 50% of the diet also reduced FEC compared to controls.[24]

Since pellets are more convenient to store and ship than hay, research was conducted determine if pelleting diminished the anti-parasitic effect of SL hay. Terrill et al compared the effect of SL hay and pellets in goats, using a bermudagrass hay control group.[28] The SL hay and pellets effectively lowered FEC compared to controls, and the effect was most pronounced in the goats receiving the SL pellets. Worm burdens, especially *H. contortus*, were significantly reduced in the SL groups compared to controls.[28] These studies showed that SL effectively reduced gastrointestinal nematodes when fed fresh, as hay or as a pelleted preparation.

Recent studies discovered that feeding sericea lespedeza also provides significant anti-coccidial benefit in kids and lambs. Lambs naturally infected with nematodes and coccidia that received SL pellets 30 days before and 21 days after weaning, had lower FEC, and shed up to 98% fewer *Eimeria* oocysts than controls on a conventional creep feed.[6] In addition, none of the lambs on the SL pelleted rations needed treatment for clinical coccidiosis, whereas 33% of controls had symptoms significant enough to warrant treatment.[6] Similarly, feeding SL leaf meal pellets to recently weaned goats significantly reduced both the FEC (66%) and fecal oocyst count (FOC) (91%).[17] In contrast to what was noted with FEC, the FOC did not increase when the SL feeding was discontinued, indicating a direct and permanent effect on the coccidian parasites.[6]

In summary, SL is a non-bloating legume that can provide substantial benefit for control of gastrointestinal nematodes, as well as *Eimeria* spp in small ruminants. For this reason, it has been referred to as "smart man's alfalfa (lucerne)".[27] For control of *H. contortus*, and to a lesser extent other gastrointestinal nematodes, SL can be fed at approximately 50% (or more) of the diet in any of its various forms (fresh forage, hay, pellets, silage) during periods of high risk. Once SL feeding is discontinued, however, small ruminants should be closely monitored for signs of parasitism from gastrointestinal nematodes. When using it for natural coccidian control, SL can be fed to youngsters as 50% or more of the diet, 2 weeks before weaning. The SL creep feed can be continued for up to 6 weeks after weaning, but not indefinitely, as micronutrient deficiencies have been noted in youngsters with long-term feeding.[27] This micronutrient issue has not been noted in adults on long-term SL supplementation.[27] Practical obstacles to feeding SL are availability and cost. Sericea lespedeza grows well in warm climates, and it can be grown separately, or mixed with other forages. Certified AU Grazer® sericea lespedeza seed and pellets are commercially available.[d] Demand for the products continues to increase, so manufacturer supplies are often limited.[e]

Copper Oxide Wire Particles

Copper oxide wire particles[c] (COWP) are currently marketed as 12.5 g boluses for cattle, and as 2 and 4 g boluses for small ruminants to treat copper deficiency. Over 15 years ago, researchers noted that COWP also had an anthelmintic effect.[1] Administration of 5 grams of COWP to 10-week-old lambs 5 days prior to inoculation with either *H. contortus*, *T. circumcincta*, and *Trich. colubriformis* reduced parasitic establishment by 96, 56, and 0%, respectively.[1] This study indicated that COWP has the most profound impact on *H. contortus*. After administration, copper oxide wire particles mix with ingesta in the forestomachs, and subsequently lodge in the abomasal mucosa. Copper dissolves from the particles in the acidic environment.[1] Dissolved copper interacts with susceptible parasites, causing expulsion or death. If abomasal pH is raised to 3 to 4 by *Teladorsagia circumcincta* infection, dissolution of copper from COWP is significantly decreased.[2] Ionic copper released from COWP is absorbed in the small intestine. Copper concentration peaks at day 4 in the proximal duodenum, and after 10 days it steadily declines.[2]

In 2000, research on dairy goats demonstrated that COWP (2 and 4 g) reduced experimentally established *H. contortus* infections by 75%, and lowered fecal egg counts up to 95%.[11] *Teladodorsagia circumcincta* and *Trich. colubriformis* burdens were only reduced by 28% and 15%, respectively, at necropsy.[11] Copper oxide wire particle treatment was not very effective at preventing establishment of new *H. contortus* infections, however.[11] Similarly, COWP treatment (either 2.5 or 5 g) significantly reduced established *H. contortus* infections in yearling sheep, but did not effectively limit establishment of experimental new infections over the 8-week study period.[16] In a subsequent experiment on 4-month-old Zulu goat kids, neither a 2 or 4 g COWP treatment prevented establishment of new *H. contortus* infections.[31] These findings indicate that COWP treatment is most effective against established *H. contortus* infections, and has minimal prophylactic benefit. Anthelmintic benefit of COWP only persists for 28 days.[30]

Administration of copper from any source, including COWP, increases hepatic copper concentration. Depending on individual, nutritional, and environmental factors, copper supplementation can potentially lead to copper toxicity in small ruminants, especially sheep.[29] Hepatic copper stored safely in lysosomes is slowly released into bile, and excreted in feces. If the liver becomes overloaded with copper, any stressor can lead to release of free copper from lysosomal storage. Unbound copper wreaks oxidative damage on the liver and other tissues, and causes hemolysis in in circulation.[29] Sheep are more prone to copper toxicity than goats because they are less efficient at eliminating stored hepatic copper.[29] In order to reduce the risk of copper toxicity, several research efforts focused on identifying the lowest COWP dose that would provide anthelmintic benefit in sheep and goats. In 2004, Burke et al administered 0, 2, 4, or 6 g COWP to 6-month-old lambs, 28 days after administration of *H. contortus* third stage larvae.[4] All doses of COWP resulted in much lower FEC, higher PCV, and a significant reduction in abomasal worms at necropsy compared to untreated controls.[4] Liver copper concentrations 28 days after COWP administration were 62.2, 135.7, 161.1, and 208.4 ppm (wet matter basis) in the 0, 2, 4, and 6 g groups, respectively.[4] Although none of lambs showed signs of copper toxicity in this study, the hepatic copper was twice as high as controls at 28 days, and above the normal hepatic copper reference levels. A subsequent study in weaned lambs showed that even lower doses (0.5 and 1 g COWP) had anti-parasitic benefit.[3] Further, these lower doses were safely administered 3 times at 6-week intervals to lambs within the same grazing season.[3] In goat kids, 0.5 and 1 g COWP improved FEC and PCV, compared to untreated controls.[10] The 0.5 g dose was considered the optimal dose for goat kids.[10]

A COWP dose titration trial was performed in mature Polypay ewes with natural parasite infections (70% *H. contortus*) to determine the lowest effective dose.[8] The ewes received either 0, 0.5, 1, or 2 g doses of COWP 60 days after lambing.[8] Seven days after administration, ewes treated with 1 or 2 g COWP had lower FEC than ewes treated with either 0 or 0.5 g COWP. Although PCV declined in all groups, ewes that received either the 1 or 2 g COWP bolus were less anemic than the sheep in the control and 0.5 g dose groups. Hepatic copper concentrations were not measured; aspartate aminotransferase activity did not differ among groups. The 0.5 g COWP dose had little anti-parasitic effect in the ewes. The 1 and 2 g COWP doses were deemed effective, but the 2 g dose gave slightly better results.[8] Unfortunately, extensive dose titration studies have not been performed in mature goats. Interestingly, Chartier et al were 1 of the few researchers to take body size into account when dosing COWP. In that study, mature Saanen goats weighing 141 to 167 lb (64 to 76 kg) received 4 g COWP, and goats weighing 92 to 101 lb (42 to 46 kg) received 2 g COWP; both doses achieved anthelmintic benefit.[11]

Copper oxide wire particles are typically administered within a gelatin capsule, using a balling gun. Since this method of administration involves individual handling, a simpler delivery method would provide a practical advantage. Burke et al demonstrated that administration of 2 g COWP in feed was as effective at reducing FEC in goats as 2 g COWP administered in a gelatin capsule.[9] The researcher advised that treatment be given on an individual basis rather than free choice to a group of animals to avoid inadvertent over- or under-dosing. This more convenient route of administration could be particularly advantageous to handlers of exotic hoof stock that are susceptible to *H. contortus*. Copper oxide wire particle treatment of oryx, roan antelope, blackbuck, and blesbok reduced FEC by over 90% for up to 28 days.[23]

In summary, COWP treatment effectively reduces established *H. contortus* infections in sheep and goats, based on decrease of FEC of up to 97%. However, it does not have much activity against other abomasal or intestinal parasites. Benefit appears to persist only about 28 days, and treatment does not effectively limit re-establishment of new infections. Treatment with COWP appears to have greater anti-parasitic benefit in lambs and kids than in mature sheep and goats, for reasons that are unclear.[10] Even though copper is slowly and incompletely released from COWP, studies demonstrated that treatment elevates hepatic copper concentration.[1,2,4,11,30,31] Although clinical copper toxicity was not induced in test subjects by COWP administration in any of the published studies, use of COWP in client-owned animals should be undertaken carefully. Assessment of copper and other minerals in hepatic tissue submitted from healthy animals, or from animals that die suddenly on farms, is recommended to determine if COWP benefits outweigh potential risks. The lowest effective dose of COWP should be used, and repeated dosing within the same grazing season discouraged if the micronutrient status of the herd or flock is unclear. Research supports the use of 0.5 to 1 g COWP in lambs and kids for anthelmintic effect.[3,8,10] In adult sheep, doses of 1 to 2 g COWP appear sufficient.[8] Doses of 2 to 4 g COWP are indicated for use in goats.[11] The lower end of the dosage range can be used for smaller breeds, and for animals where risks for copper toxicity are unknown. Treatment efficacy can be assessed using a fecal egg count reduction test. Researchers currently recommend selective (rather than whole herd or flock) use of COWP for anthelmintic purposes.[10] Since some worms survive exposure, it is possible that resistance to COWP treatment (as has been seen with conventional anthelmintic treatment) could develop.[10] Use of COWP can be combined with an anthelmintic to make treatment more broad-spectrum when infections are mixed.[18] The FAffa MAlan CHArt (FAMACHA) System can be used to detect small ruminants with clinically significant *H. contortus* burdens based on their degree of anemia.[7]

Conclusions

Alternative anti-parasitic strategies, such as use of sericea lespedeza and copper oxide wire particles, are promising additions to parasite control strategies on small ruminant farms. In particular, organic producers welcome non-pharmaceutical approaches to worm control. Sericea lespedeza's nutritional and parasite control advantages have few downsides other than product availability. Production of SL is an emerging agricultural opportunity, as demand for seeds, pellets and hay often exceeds supply, and demand is likely to continue to increase in the United States. In contrast, COWP are easily obtained through commercial channels. Although COWP products[c] are marketed as a treatment for copper deficiency, clear benefit has been demonstrated against established H. contortus infections. Producers require education in order to safely implement COWP into their integrated parasite management strategies to avoid copper toxicity. Since the smallest Copasure® bolus[f] on the market is 2 g, capsule content will have to be divided up in order to use lower doses, which is inconvenient for producers. Selective use of COWP at the lowest effective dose, and periodic assessment of micronutrient levels in hepatic tissues from healthy animals that are harvested for meat are several strategies that can be used to mitigate this risk.

Endnotes

[a]Ivomec®, Merial Ltd., Duluth, GA
[b]Cydectin®, Boehringer Ingelheim Vetmedica, Inc., St. Joseph, MO
[c]AU Grazer®, Auburn, AL
[d]Sims Brothers, Union Springs, AL
[e]Sims Brothers, personal communication
[f]Copasure®, Henry Schein Animal Health, Dublin, OH

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