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Short communication

Examination of commercially available copper oxide wire particles in combination with albendazole for control of gastrointestinal nematodes in lambs

J.M. Burke[a,*], J.E. Miller[b], T.H. Terrill[c], E. Smyth[a], M. Acharya[d]

[a] Dale Bumpers Small Farms Research Center, USDA, ARS, Booneville, AR 72927, USA
[b] Department of Pathobiological Sciences, School of Veterinary Medicine and Departments of Animal Science and Veterinary Science, Louisiana State University, Baton Rouge, LA 70803, USA
[c] Fort Valley State University, Fort Valley, GA 31030, USA
[d] University of Arkansas, Fayetteville, AR 72702, USA

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ABSTRACT

Control of gastrointestinal nematodes (GIN) remains a critical issue due to the prevalence of anthelmintic resistance. The objective of the experiment was to determine the efficacy of copper oxide wire particles (COWP) from three commercial sources and a combination of COWP and albendazole to control GIN and/or *Haemonchus contortus* in lambs. Naturally infected Katahdin lambs in early June 2014 and 2015 were randomly assigned to receive no COWP (CON; $n = 9$ and 12) or 2 g COWP in a gel capsule as Copasure® (COP; $n = 4$ and 17; Animax Ltd.), copper oxide—wire form (AUS; $n = 7$ in 2014 only; Pharmplex), Ultracruz™ (ULT; $n = 8$ and 15; Santa Cruz Animal Health™), no COWP and albendazole (CON + alb; $n = 10$ in 2015 only; 15 mg/kg BW; Valbazen®; Zoetis Animal Health), or COWP + alb ($n = 7$ and 11; in 2014, lambs were administered alb on day 3). Lambs grazed grass pastures as a group and were supplemented with 227 g/lamb daily of a commercial grain mix (15% crude protein) and the same amount of alfalfa pellets. Feces were collected on days 0 (day of COWP treatment), 7, and 14 for determination of fecal egg counts (FEC). Pooled (2014) or pooled treatment group feces were cultured on days 0, 7, and 14 (2015 only) to determine GIN genera. Data were analyzed using repeated measures in a mixed model, and FEC were log transformed. The predominant GIN on day 0 was *H. contortus* (87%) in 2014, and there was a mixed population in 2015. The mean FEC was reduced by day 7 in AUS and ULT lambs (treatment × day, $P = 0.001$), and all of the COWP products were similar. By day 14, the AUS FEC were lower than the CON and COP groups. When examining the combination of COWP and synthetic anthelmintic, the FEC of COWP + alb were reduced to nearly 0 eggs/g (back-transformed) and lower than the other groups (treatment × day, $P = 0.001$). The percentage of *H. contortus* in cultured feces was reduced to a greater extent in the COWP than CON or CON+alb groups of lambs. In a mixed GIN population, the COWP products appeared to be similar in efficacy and using a combination of COWP + alb increased the efficacy not only against *H. contortus*, but all GIN genera present, offering options in the face of resistance to benzimidazoles.

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1. Introduction

Gastrointestinal nematodes (GIN) are the greatest health and production challenge for small ruminants in warm, humid climates. *Haemonchus contortus* or barber pole worm is a blood feeder that can cause severe anemia and death if left untreated. A recent study conducted on U.S. sheep flocks found *H. contortus* in nearly every state in the U.S. examined (United States Department of Agriculture, 2014a; R. Kaplan, personal communication). The exploration of alternatives to synthetic anthelmintics for the control of *H. contortus* in small ruminants remains critical because of the prevalence of anthelmintic resistance (Kaplan et al., 2005; Howell et al., 2008). Not only do organic farms need to worry about anthelmintic resistance, but also a means of control that is acceptable to the USDA National Organic Program (United States Department of Agriculture, 2014b) is paramount. Some organic certifiers in the US allow the use of copper oxide wire particles (COWP) as an anti-parasitic agent. Our laboratory (Burke et al.,

* Corresponding author. Fax: +1 479 675 2940.
E-mail address: joan.burke@ars.usda.gov (J.M. Burke).

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2004; Burke and Miller, 2006) and others (Bang et al., 1990; Knox, 2002) have examined the use of COWP to control *H. contortus*. We have used a product marketed to alleviate copper deficiency in cattle (Copasure®; Animax Ltd., Suffolk, England). Recently, similar products have become available for small ruminants to treat copper deficiency. Producers may be using these products as an anthelmintic without any knowledge of their efficacy.

The objective of the experiment was to determine the efficacy of COWP from three commercial sources and a combination of COWP and albendazole to control a natural infection of *H. contortus* or mixed GIN in lambs.

2. Materials and methods

All husbandry practices and experimental procedures were approved by the USDA, ARS Animal Care and Use Committee. The experiment was conducted at the Dale Bumpers Small Farms Research Center, Booneville, AR, in June (summer) of 2014 and 2015. This sheep flock is certified as Animal Welfare Approved (http://animalwelfareapproved.org).

Naturally infected Katahdin ewe (2014) and ewe and ram (2015) lambs that were 106 ± 1.3 days of age (born February; $n = 35$) and 21.6 ± 1.3 kg in 2014 and 149.4 ± 5.6 days of age (born December to January; $n = 65$) and 28.0 ± 1.4 kg in 2015 were randomly assigned to receive a gel capsule (NOW® Foods Single "0" VCAPS™, Bloomingdale, IL) filled with soybean meal (**CON**; $n = 9$ and 12) or 2 g COWP as Copasure® (**COP**; $n = 4$ and 17; Animax Ltd.), copper oxide—wire form (**AUS**; $n = 7$ in 2014 only; Pharmplex), Ultracruz™ (**ULT**; $n = 8$ and 15; Santa Cruz Animal Health™), no COWP and albendazole (CON + alb; $n = 10$ in 2015 only; 15 mg/kg BW; Valbazen®, Zoetis Animal Health, Kalamazoo, MI), or COWP + alb ($n = 7$ and 11). In 2014, the COWP + alb were 4COP, 2 AUS, and 1 ULT lambs treated on day 3. In 2015, all COWP + alb were treated with COP as the COWP source. The intent of the albendazole treatment in 2014 was to eliminate *Trichostrongylus* spp. or other non-*H. contortus* GIN as lambs developed diarrhea (thus, these lambs were not randomly assigned). The *H. contortus* in this flock were determined to be resistant to benzimidazole according to Drenchrite (R. Kaplan, University of Georgia), which was thought to minimize the effect of deworming on *H. contortus*, the GIN of interest. Previous studies determined that COWP was primarily effective in reducing *H. contortus* (Bang et al., 1990; Knox, 2002).

When blood packed cell volume (PCV) fell below 19%, lambs were dewormed with levamisole (12 mg/kg BW, AgriLabs, St. Joseph, MO). This occurred on day 7 in 3CON and 1 ULT in 2014 and 1COP in 2015. The *H. contortus* in this flock was determined to have suspected resistance to levamisole according to the Drenchrite, but a recent fecal egg count (FEC) reduction test indicated a 98% reduction in FEC (Burke, unpublished results). Rather than penalize the lambs that were not dewormed by deleting the day 14 FEC of levamisole treated lambs, the day 7 value was also used for day 14 in these 4 lambs in 2014 and 1 lamb in 2015. This would be a conservative estimate because if left untreated, the FEC would most likely have increased by day 14. Because it is difficult to predict the PCV on day 14, these 5 observations were deleted for that analysis.

In both years, lambs grazed bermudagrass (*Cynodon dactylon*) pastures as a group and were supplemented with 227 g/lamb daily of a grain mix (soyhull pellets, wheat middlings pellets, corn gluten pellets, cracked corn, dried distillers grain; 15% CP; Farmer's Cooperative, Van Buren, AR) and the same amount of alfalfa pellets (16% CP; Farmer's Cooperative, Van Buren, AR). On day of treatment, lambs were fed after COWP and/or albendazole was administered. Blood and feces were collected on days 0 (day of COWP treatment), 7, and 14 for determination of PCV and FEC (nematodes only), respectively, according to Whitlock (1948), and pooled (2014) or

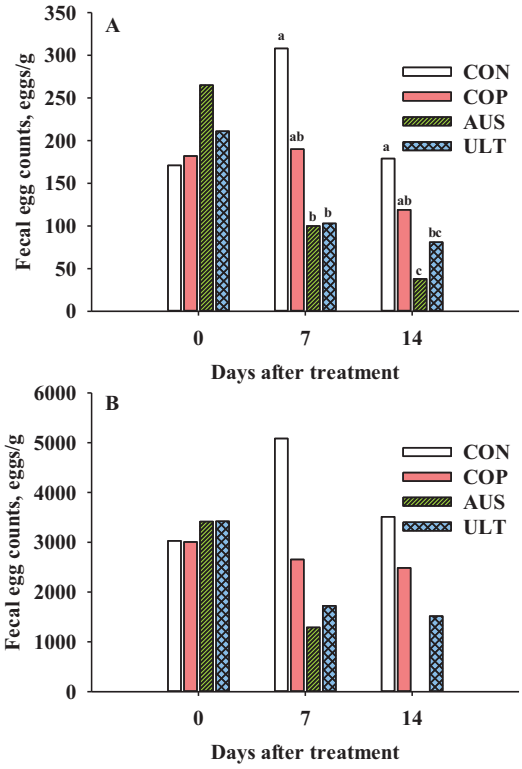

Fig. 1. Effect of administration of a gel capsule filled with soybean meal (CON; $n = 21$; white bars), or 2 g copper oxide wire particles (COWP) in a gel capsule as Copasure® (COP; $n = 21$; Animax Ltd.; solid orange bars), copper oxide—wire form (AUS; $n = 7$; Pharmplex; fine diagonal green bars), or Ultracruz™ (ULT; $n = 23$; Santa Cruz Animal Health™; checked blue bars) to lambs on days 0 (day of COWP treatment), 7, and 14. Statistical analyses of fecal egg counts were performed on log transformed values (treatment × day, $P = 0.001$) and back transformed least squares means are presented (Panel A). Within day of treatment, individual means with different letters differ ($P < 0.05$). The back transformed standard error is 0.14. Untransformed least squares means are presented in Panel B as some readers are more accustomed to these.

pooled treatment group feces were cultured on days 0, 7, and 14 (2015 only) according to Peña et al. (2002) to determine GIN genera.

The COWP diameter was measured on 16 particles of COP, AUS, and ULT by standing particles on end and determining the average of the longest and shortest width. PROC GLM was used to determine differences among means.

Individuals were removed from the data set if the FEC on day 0 was less than 400 eggs/g; numbers per treatment above reflect lambs that remained in the data set. Three lambs were removed in 2014 and 38 were removed in 2015. Data were analyzed as repeated measures (Littell et al., 1996) using mixed models (SAS 9.3, SAS Institute Inc., Cary, NC) and included the COWP treatment and year in the model. An autoregressive covariance structure was used and orthogonal contrasts (CON vs. COWP, COP vs. ULT, ULT vs. AUS). A second analysis was conducted to determine the effect of albendazole. For this, the COWP groups were pooled and orthogonal contrasts were CON vs. CON + alb, COWP vs. COWP + alb, and CON + alb vs. COWP + alb. In addition, means were separated using pre-planned pairwise comparisons using the *t*-test when treatment effect was $P < 0.05$. The FEC data were log transformed [ln(FEC + 10)] and presented as back-transformed means.

A FEC reduction for each COWP treatment per year was calculated using arithmetic means (2014) as discussed in Miller et al. (2006). First, post-treatment was considered on day 7 and day 14 using all eggs counted relative to the CON group of lambs: [100 × (1 − mean post-treatment/mean post-CON)]. Second, efficacy against *H. contortus* (using percentage *H. contortus* larvae counted on days 7 and 14) was considered on days 7