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Evaluation of Parasite Resistance to Commonly Used Commercial Anthelmintics in Meat Goats on Humid Subtropical Pasture

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Abstract: Anthelmintic-resistant gastrointestinal nematode parasites are a threat to small ruminant industry sustainability. Meat goat does were administered one of four anthelmintics orally (ivermectin (n = 18), moxidectin (n = 18), levamisole hydrochloride (n = 17), or albendazole (n = 19)) or water (n = 18). Fecal samples were collected pretreatment and 12 days post-treatment. Fecal egg counts (FEC) were determined by the modified McMaster technique. The FEC reduction percentages (FECR%) were calculated using three equations. Log transformed FEC means were analyzed by treatment, sire breed of doe, and doe age. Sire breed affected ($P < 0.05$) pretreatment FEC, but not post-treatment FEC ($P = 0.12$). Pretreatment FEC did not differ ($P = 0.21$) by treatment group. Posttreatment FEC varied ($P < 0.05$) by treatment. Anthelmintic resistance determinations were based on FECR% falling below 90% or 80%, dependent on equation applied. Resistance was detected to all four anthelmintics using each equation. These results suggest the need for alternative methods of internal parasite control in goats.

Keywords: anthelmintics; resistance; internal parasites; meat goats; breeds; subtropical

Introduction

Producers are having trouble with sustainable goat production due to a primary reliance on a commercial anthelmintics to treat and prevent outbreaks of gastrointestinal nematode parasites (GIN) in their herds (Calvete and Uriarte, 2013). A major global threat goat producers now face is anthelmintic resistance (Coles et al., 2006; Howell et al., 2008). Reduced productivity and increased morbidity and mortality rates are consequences of anthelmintic resistance in goat herds in parasite-rich environments. The most common way to test for anthelmintic resistance is the Fecal Egg Count Reduction Test (Calvete and Uriarte, 2013; McKenna, 2014). There are different equations used to determine anthelmintic resistance and the most effective is still debated (McKenna, 2013; Falzon et al., 2014).

The main anthelmintic classes are benzimidazoles, imidazothiazoles, and macrocyclic lactones (Mortensen et. al., 2003; Coles et al., 2006). Some studies found GIN resistance to every class (Terrill et. al., 2001; Zajac and Gipson, 2000; Abubakar et. al., 2015). Macrocylic lactones (ivermectin, moxidectin), an imbazothiazole (levamizole), and a benzimidazole (albendazole) were compared on this study for resistance using different resistance equations.

Material and Methods

Study animals

In June and July, 90 young does were managed on pasture for determination of anthelmintic resistance. Herd management protocols were approved by the Tennessee State University Animal Care and Use Committee. Does were crossbred and straightbred progeny of

Boer (1 doe from 1 sire), Kiko (27 does from 8 sires), Myotonics (21 does from 4 sires), Savanna (28 does from 5 sires), and Spanish (13 does from 5 sires) sire breeds. The study population consisted of 22 primiparous 2-yr-old does (body weight = 27.6 kg (19.3-34.1 kg); packed cell volume = 21% (11-26%)) and 68 nulliparous yearlings does (body weight = 25.7 kg (18.6-33.2 kg); packed cell volume = 21.5% (13-27%)).

Does were semi-intensively managed in a humid subtropical area receiving 1,222mm of precipitation annually on the Tennessee State University research facility located along the Cumberland River (36°10′ N, 86°49′ W). The does grazed cool-season pastures containing predominantly tall fescue (*Festuca arundinacea*) and pastures consisting primarily bermudagrass (*Cynodon dactylon*) during the warm season. The collections for this experiment took place in June and July when they were grazing predominantly bermudagrass. Grazing areas also contained several additional species of grasses, clovers, broadleaf weeds, and woody browse species. The herd received water and minerals for *ad libitum* consumption. The goat mineral mix contained a minimum of 13.5% Ca, 7% P, 1,100 ppm Cu, 60 ppm Se, and 5,000 ppm Zn.

The 2-yr-old does were administered LEV at parturition per routine herd management protocol, roughly 3 months before the study. The yearlings had not been dewormed as a group since weaning per routine herd health management, 12 months prior to this study. A few individual yearling does were treated primarily with LEV and ALB secondarily on an as-needed basis from 12 months to 3 month before the study.

Data collection and Analysis

Does within each age group were divided into 5 similarly sized treatment groups balanced across sire breed. Groups orally received 795.2 mg (7 ml) of albendozole (n = 19, ALB,

Valbazen Cattle, Sheep, and Goat Drench®, Zoetis Inc. Kalamazoo, MI), 30mg (3ml) of ivermectin (n = 18, IVE, Ivomec Cattle Injectable®, Merial Ltd., Duluth, GA), 417 mg (3 ml) of levamosole (n = 17, LEV, Prohibit Cattle and Sheep Drench®, Agrilabs Ltd., St. Joseph, MO.), 15 mg (3 ml) of moxidectin (n = 18, MOX, Cydectin Cattle Pour-on®, Boehringer Ingelheim Inc., St. Joseph, MO), and 5ml of non-medicated water (n = 18). On average animals were administered anthelmintics dosages above recommended levels (IVE, 303%; MOX, 153%; LEV, 129%; ALB, 162%; Kaplan and Scharko, 2014). All goats on the study received anthelmintic dosages that exceeded recommended levels.

Fecal samples were collected immediately before treatment and 12 days after treatment. A small number of does (approximately 10%) were collected between 13 and 14 days due to inability to obtain sample after 12 days. The fecal samples were processed using the McMaster technique (Coles et al., 2006) to determine FEC with a detection limit of 50 eggs/g. Initial FEC (FEC1) and the post FEC (FEC2) were evaluated for significant differences based on treatment, age, and sire breed. The FEC values were transformed by log 10 (FEC + 1) for statistical analysis and back-transformed to geometric means. The FEC changes post-treatment were compared using three equations:

$$RT1 = 100(1 - [T2 / T1]) \quad (1)$$

$$RT2 = 100(1 - [T2 / T1] * [C1 / C2]) \quad (2)$$

$$RT3 = 100(1 - [T2 / C2]) \quad (3)$$

where T1 is FEC1 for a given treatment, T2 is FEC2 for a given treatment, C1 is FEC1 for the control group, and C2 is FEC2 for the control group. Each equation (Eq. 1, McKenna, 2013; Eq. 2, Dash et al., 1988; Eq. 3, Coles et al., 1992) has been recommended as a means of determining

anthelmintic resistance. Anthelmintic resistance was considered present if Eq. 1 or Eq. 3 was ≤ 90%. For Eq. 2, resistance was present if the reduction was ≤ 80%.

Statistical modeling was used to further evaluate treatment responses. Mixed model procedures of SAS (Cary, NC) were used to evaluate log transformed FEC1 and FEC2, relative change in log transformed FEC, and treatment responses using each reduction test. Doe age, sire breed of doe, and treatment were sources of variation tested. The Boer-sired doe was classified as Savanna, since the two breeds represent the same biological type of South African origin. For significant sources of variation, means were separated using the Tukey-Kramer test ($\alpha = 0.05$). Chi-square was used to assess the proportion of does meeting the threshold value for each reduction test equation.

Results

Sire breed of doe affected ($P < 0.01$) FEC1, but did not affect ($P = 0.12$) FEC2 (Figure 1). Savanna sired does had higher FEC1 than Kiko or Myotonic. Age of doe did not affect FEC1 or FEC2 (data not shown). Treatment did not affect ($P = 0.21$) FEC1, but was an important source of variation ($P < 0.001$) for FEC2. Water control group had higher FEC2 means than MOX, IVE, and ALB (Figure 2). The IVE group had a significantly lower FEC2 mean than LEV.

Treatment affected ($P < 0.001$) reduction values for log transformed FEC, but age and breed had no effect ($P > 0.2$). The water control group had lower ($P < 0.01$) FEC reduction value (-9.5%; [FEC increased by 9.5%]) than MOX (45.85%), IVE (50.54%), and ALB (32.48%). No other groups differed ($P > 0.1$) from each other (LEV = 20.49%) for FEC reduction.

Resistance was evident to the four anthelmintics tested (Table 1**)**. The minimum reduction threshold for Eq. 1 and Eq. 3 was 90% to show susceptibility to a test drug. For Eq. 2, the threshold was 80%. None of the anthelmintics tested met the threshold for any of the equations. For Eq. 1, water significantly differed from the other treatment groups for FEC change post-treatment; FEC increased for the water control group post-treatment (Table 1). Equation 2 showed no differences ($P = 0.28$) among the treatment groups. Equation 3 showed LEV had a lower ($P < 0.05$) FEC reduction than the other treatments (Table 1).

Anthelmintic product influenced ($P < 0.05$) the percentage of does that met the threshold values for effective treatment response using the FEC reduction test equations. The MOX, IVE, ALB groups were statistically similar according to the three equations and had the greatest number of does meeting threshold (Table 2). The ALB and LEV groups were statistically similar according to the three equations. The Eq. 1 showed IVE and MOX had a higher success rate than LEV and water (Table 2). The Eq. 2 showed MOX had higher efficacy than LEV. Using Eq. 3, IVE had a higher positive response rate than LEV (Table 2).

Discussion

Previous studies reported that goat breeds can differ for FEC (Baker et al., 1998; Browning et al., 2011). In the current study, Savanna-sired does had higher FEC than Myotonic- or Kiko-sired does. There were no prior reports found in the literature of relative FEC for Savanna goats. The Savanna breed has a similar South African origin to the Boer breed (Campbell, 2003). Boer goats had higher FEC than Kiko or Spanish in other studies (Browning et al., 2011; Nguluma et al., 2013). There is a growing interest in using non-chemical approaches

to control GIN (Burke et al., 2007; Luginbuhl et al., 2011). Genetic management is one such approach (Baker et al., 1998; Mandonnet et al., 2006; Bishop, 2012). The current study suggests that Savanna may not be a preferred breed choice for enhancing FEC under these test conditions.

Anthelmintic resistance was shown for the four anthelmintics tested (MOX, IVE, LEV, ALB). Prior studies in the geographic region of the current study found resistance to multiple anthelmintics (Zajac and Gipson, 2000; Terrill et. al., 2001; Mortensen et al., 2003; Howell et al., 2008; Courter et al., 2012). Two studies sampled commercial herds (Mortensen et al., 2003; Howell et al., 2008). The other three studies were similar to this project in testing institutional herds (Zajac and Gipson, 2000; Terrill et. al., 2001; Courter et al., 2012). The oldest four of the five regional studies showed resistance to ALB and IVE as did the current study. The LEV was found to have suspected resistance in the commercial herd surveys (Mortensen et al., 2003; Howell et al., 2008). The current results of verified resistance to LEV were in agreement with the other institutional herd studies (Zajac and Gipson, 2000; Terrill et. al., 2001; Courter et al., 2012). Earlier studies that tested MOX found it effective (Terrill et. al., 2001; Mortensen et al., 2003). The current outcomes concurred with Howell et al. (2008) in observing MOX resistance. The current study was the only test that had verified resistance to all four of the anthelmintics tested. This problem of resistance to multiple anthelmintics is becoming more evident globally (Byaruhanga et al., 2013; Nabukenya et al., 2014; Abubakar et al., 2015).

Despite the demonstrated level of resistance for all of the anthelmintics, each product except for LEV reduced FEC significantly compared to the control group. In addition IVE was more effective than LEV in lowering FEC. Over the course of several production years, LEV was the primary anthelmintic used in the study herd this may in part explain the relative ineffectiveness compared to the other anthelmintics. The annual use of LEV was infrequent. The

breeding herd was scheduled for group treatment only at kidding over the last several years (Browning et al., 2011). Doelings were only treated at weaning with a combination of LEV and ALB. On occasion groups of late lactating does or yearling doe groups were treated if severe internal parasitism was evident. Otherwise outside of the scheduled once a year deworming, does were treated individually as needed.

In 2010, approximately 160 does were added to the research herd (60% of the total inventory) from numerous (approximately 40) source herds across the region. Those source herds likely utilized various deworming protocols thus introduced GIN with varied anthelmintic resistance profiles. This infusion of new GIN germplasm should have diluted the concentration of GIN with anthelmintic resistance to LEV resulting from the research herd deworming program up to 2010. However, the current results indicated that the infusion of GIN germplasm did not prevent the expressed resistance to LEV or any of the other anthelmintics. Perhaps the widespread reports of resistance to multiple anthelmintics in this region is reflected in the multiproduct resistance in the current study population despite introducing new GIN germplasm and the relatively infrequent use of anthelmintics, primarily LEV, in the research herd.

It has been proposed by Cole et al. (2006) that the interval from treatment to post-treatment fecal sampling should vary by anthelmentic product. It was suggested that LEV have a 3 to 7 day test period, 8 to 10 days for benzimidazoles such as ALB, and that macrocyclic lactones be tested 14-17 days post treatment. In this study, samples were collected 12 days after the anthelmintic treatments following outreach recommendations to farmers. Modified collection times as suggested by Cole et al. (2006) may have yielded modified responses leading to different results for anthelmintic resistance on the current study. Collecting LEV on the later date might have influenced its appearance to have greater amount of GIN resistance than the other

products tested because LEV only attacks adult worms. By 12-14 days after LEV treatment resident larva in the gastrointestinal tract might have matured and started producing eggs.

Regardless of what equation was used, resistance was found to MOX, IVE, LEV, and ALB. The only differences amongst the equations were minor re-rankings that affected which treatment differed from LEV for relative efficacy. Some studies have found different results for resistance based on equation (Falzon et al., 2014; Pena-Espinosa et al., 2014). This was suggested to be because of a lower level of resistance to the anthelmintics tested. The equation that is the most accurate for determining anthelmntic resistance remains undetermined and is an area of investigation (Calvete and Uriarte, 2013; McKenna, 2013, 2014; Falzon et al., 2014; Pena-Espinosa et al., 2014).

Anthelmintic resistance remains prevalent in this geographic area with no new anthelmintics coming onto the market. This is a serious threat to goat producers (Coles et al., 2006). Anthelmintics not approved for goats are already being relied. The dosage rates in the current study were well above recommended levels as offered by Kaplan and Scharko (2014). Anthelmintic resistance can be lessened through more rigorous standards of anthelmintic use. Reliance on commercial anthelmintics to control parasites is too great. Approaches involving grazing management, nutritional management, and goat genetic management may be effective in lowering GIN loads in goat herds (Tsotetsi et. al., 2012; Shalaby, 2013).

Conclusion

Current study results show resistance to LEV, ALB, MOX, and IVE. This suggests an ongoing issue with relying solely on anthelmintics to control GIN. Other methods of control

need to be considered and investigated for suitable solutions. This study also suggests that Savanna germplasm may not be a preferred choice for controlling GIN populations through breed selection. Further studies on alternative animal and environmental management options to control GIN in goat production systems are warranted.

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References

Abubakar, F., Kari, A., Zawawi, I., Usman, T.H., Baba, A.R., 2015. Preliminary study of nematode resistance to anthelmintic drugs in two goat farms in Terengganu. J. Teknologi. 77, 13-16.

Baker, R.L., Mwamachi, D.M., Audho, J.O., Aduda, E.O., Thorpe, W., 1998. Resistance of Galla and Small Eastern African goats in the sub-humid tropics to gastrointestinal nematode infections and the peri-parturient rise in fecal egg counts. Vet. Parasitol. 79, 53-64.

Bishop, S.C. 2012. Possibilities to breed for resistance to nematode parasite infections in small ruminants in tropical production systems. Animal. 6, 741-747.

Browning, R., Leite-Browning, M.L., Byars, M., 2011. Reproductive and health traits among Boer, Kiko, and Spanish meat goats does under humid, subtropical pasture conditions of the southeastern United States. J. Anim. Sci. 89, 648-660.

Burke, J.M., Terrill, T.H., Kallu, R.R., Miller, J.E., Mosjidis, J., 2007. Use of copper oxide wire particles to control gastrointestinal nematodes in goats. J. Anim. Sci. 85, 2753-2761.

Byaruhanga, C., Okwee-Acai, J., 2013. Efficacy of albendazole, levamisole, and ivermectin against gastro-intestinal nematodes in naturally infected goats at the National Semi-arid Resources Research Institute, Serere, Uganda. Vet. Parasitol. 195, 183-186.

Calvete, C., Uriarte, J., 2013. Improving the detection of anthelmintic resistance: Evaluation of faecal egg count reduction test procedures suitable for farm routines. Vet. Parasitol. 196, 438-452.

Courter, A.D., Hutchens, T.K., Andries, K., Miller, J.E., Tower, J.E., Neary, M.K., 2012. Efficacy of garlic juice, copper oxide wire particles, and anthelmintics to control gastrointestinal nematodes in goats. Sheep and Goat Res. J. 27, 19-25.

Campbell, Q.P., 2003. The origin and description of southern Africa's indigenous goats. S. Afr. J. Anim. Sci. 33, 18–22.

Coles, G., Bauer, C., Borgsteede, F., Geerts, S., Klei, T., Taylor, M., Waller, P., 1992. World Association for the Advancement of Veterinary Parasitology (W.A.A.V.P.) methods for the detection of anthelmintic resistance in nematodes of veterinary importance. Vet. Parasitol. 44, 35–44.

Coles, C.G., Jackson, F., Pomroy, W.E., Prichard, R.K., Samson-Himmelstjerna, G., Silvestre, A., Taylor, M. A., Vercruysse, J., 2006. The detection of anthelmentic resistance in nematodes of veterinary importance. Vet. Parasitol. 136, 167-185.

Dash, K., Hall, E., Barger, I., 1988. The role of arithmetic and geometric mean worm egg counts in faecal egg count reduction tests and in monitoring strategic drenching programs in sheep. Aus. Vet. J. 65, 66–68.

Falzon, L.C., Leeuwen, J., Menzies, P.I., Jones-Bitton, A, Sears, W., Jansen, J.T., Peregrine, A.S., 2014. Comparison of calculation methods used for the determination of anthelmintic resistance in sheep in a temperate continental climate. Parasitol. Res. 113, 2311-2322.

Holm, S.A., Sorensen, C.R.L., Thamsborg, S.M., Enemark, H.L., 2014. Gastrointestinal nematodes and anthelmintic resistance in Danish goat herds. Parasite. 21, 1-10.

Howell, S.B., Burke, J.M., Miller, J.E., Terrill, T.H., Valencia, E., Williams, M.J., Williamsons, L.H., Zajac, A.M., Kaplan, R.M., 2008. Prevalence of anthelmintic resistance on sheep and goat farms in the southern United States. J. Am. Vet. Med. Assoc. 233, 1913-1919.

Kaplan, R.M., Scharko P., 2014. Dewormer Chart for Goats. https://ahdc.vet.cornell.edu/docs/GoatDewormerChart.pdf (accessed 20.06.2015).

Luginbuhl, J.M., Pietrosemoli, S., Howell, J.M., Anderson, K.L., 2011. Alternatives to traditional anthelmintics to control gastrointestinal nematodes in grazing meat goats. Archivos Latinoamericanos de Producción Animal. 18, 3-4.

Mandonnet, N., Menendez-Buxadera, A., Arquet, R., Mahieu, M., Bachand, M., Aumont, G., 2006. Genetic variability in resistance to gastro-intestinal strongyles during early lactation in Creole goats. Anim. Sci. 82, 283-287.

McKenna, P.B., 2013. Are multiple pre-treatment groups necessary or unwarranted in fecal egg count reduction tests in sheep? Vet. Parasitol. 196, 433-437.

McKenna, P.B., 2014. Future studies on the necessity or otherwise of multiple pre-treatment groups in fecal egg count reduction tests in sheep. Vet. Parasitol. 200, 212-215.

Mortensen, L.L., Williamson, L.H., Terrill, T.H., Kircher, R.A., Larsen, M., Kaplan, R.M., 2003. Evaluation of prevalence and clinical impactions of anthelmintic resistance in gastrointestinal nematodes in goats. J. Am. Vet. Med. Assoc. 223, 495-500.

Nabukenya, I., Rubaire-Akiiki, C., Olila, D., Muhangi, D., Hoglund, J., 2014. Anthelmintic resistance in gastointestinal nematodes in goats and evaluation of FAMACHA diagnostic marker in Uganda. Vet. Parasitol. 205, 666-675.

Nguluma, A., Leite-Browning, M.L., Browning, R., 2013. Comparison of Boer-Cross and foundation breeds for meat goat doe fitness in the humid subtropics. Livest. Res. Rural Dev. 25, 3.

Pena-Espinoza, M., Thamsborg, S.M., Demeler, J., 2014. Field efficacy of four anthelmintics and confirmation of drug-resistance nematodes by controlled efficacy test and pyrosequencing on a sheep and goat farm in Denmark. Vet. Parasitol. 206, 208-215.

Shalaby, H.A., 2013. Anthelmintics Resistance; How to Overcome it? Iran J. Parasitol. 8, 18-32.

Terrill, T.H., Kaplan, R.M., Larsen, M., Samples, O.M., Miller, J.E., Gelaye, S., 2001. Anthelmintic resistance on goat farms in Georgia: efficacy of anthelmintics against gastrointestinal nematodes in two selected goat herds. Vet. Parasitol. 97, 261-268.

Tsotetsi, A. M., Njiro, S., Katsande, T. C., Moyo, G., Baloyi, F., Mpofu, J., 2012. Prevalence of gastrointestinal helminths and anthelmintic resistance on small-scale farms in Gauteng Provence, South Africa. Trop. Anim. Health Prod. 45, 751-761.

Zajac, A.M., Gipson, T.A., 2000. Multiple anthelmintic resistance in a goat herd. Vet. Parasitol. 87, 163-172.

Figure 1. Effect of sire breed on geometric mean fecal egg counts (FEC). FEC1= Pretreatment FEC; FEC2 = Post-treatment FEC. [a,b,c]Means without a common superscript differ ($P < 0.05$).

Figure 2. Effect of treatment on geometric mean fecal egg counts (FEC). FEC1= Pretreatment FEC; FEC2 = Post-treatment FEC. IVE, ivermectin; MOX, moxidectin; LEV, levamizole; ALB, albendazole; H2O, water. [a,b,c]Means without a common superscript differ ($P < 0.05$).

Table 1. Anthelmintic efficacy in meat goat does according to different equations for fecal egg count (FEC) reduction.[1]

Average FEC reduction (%)			
Treatment[2]	RT1	RT2	RT3
MOX	67[a]	43[a]	85[a]
IVE	75[a]	57[a]	85[a]
LEV	37[a]	-10[a]	42[b]
ALB	64[a]	38[a]	78[a]
Water	-120[b]	-	-

Does meeting equation threshold for anthelmintic efficacy (%)			
Treatment[2]	RT1	RT2	RT3
MOX	44[a]	61[a]	44[ab]
IVE	50[a]	44[ab]	56[a]
LEV	11[b]	24[b]	18[b]
ALB	26[ab]	37[ab]	32[ab]
Water	6[b]	-	-

[a,b]Means without a common superscript within a column and test differ ($P < 0.05$).

[1]Anthelmintic resistance (i.e., reduced efficacy) was present if Reduction Test (RT) 1 (McKenna, 2013) or RT3 (Coles et al., 1992) showed ≤ 90% FEC reduction. Resistance for RT2 (Dash et al., 1988) was present if FEC reduction was ≤ 80%.

[2]IVE, ivermectin; MOX, moxidectin; LEV, levamizole; ALB, albendazole.

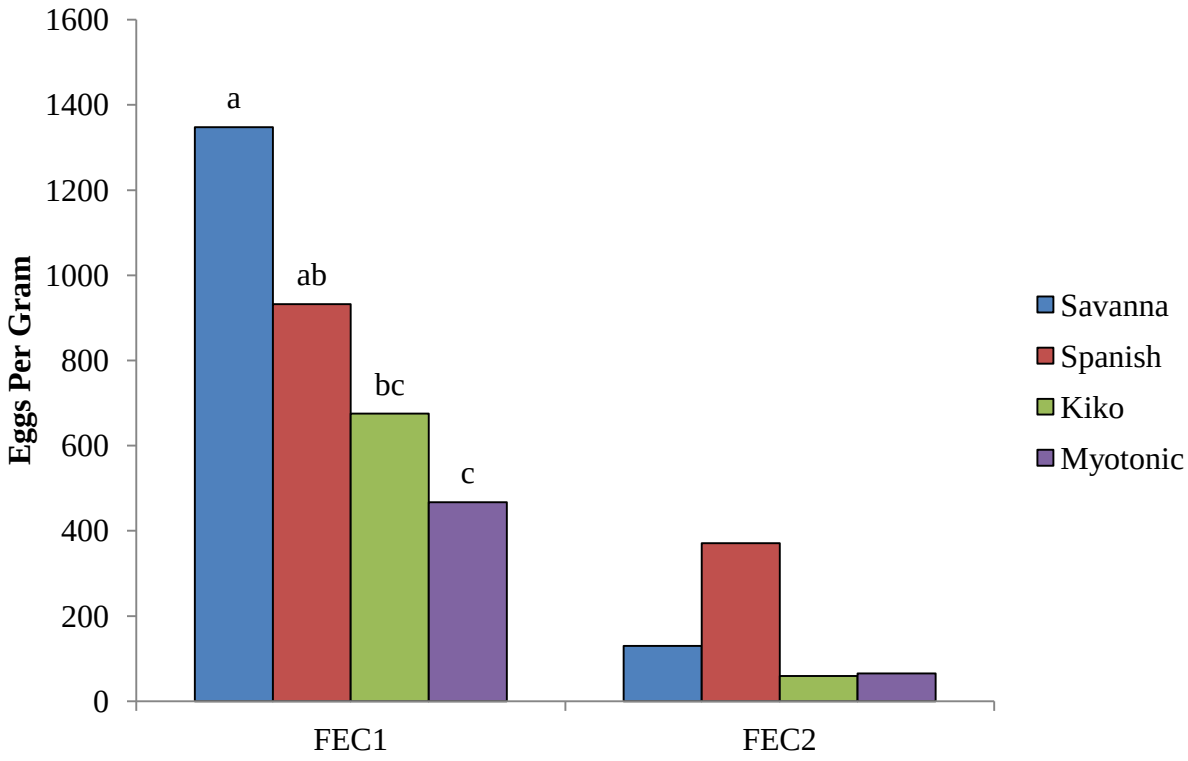

Figure 1.

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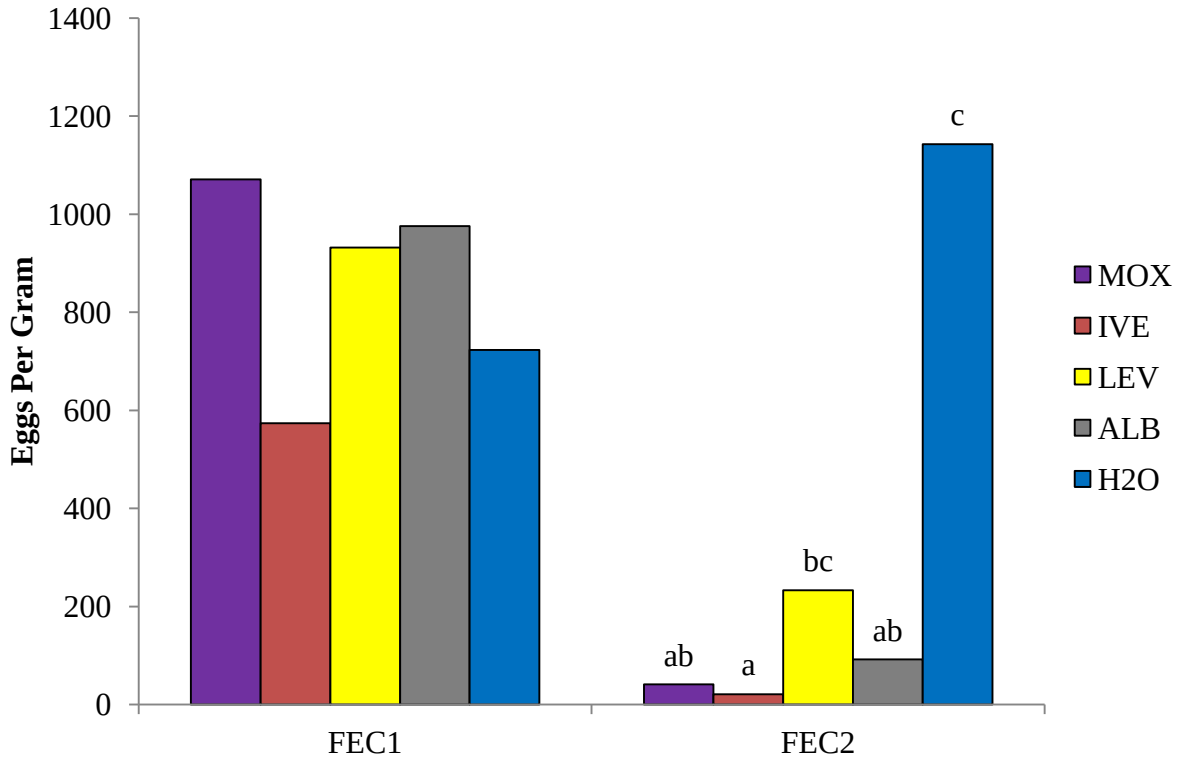

Figure 2.

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