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EVALUATION OF AN HERBAL FEED SUPPLEMENT (ANIMUNIN POWDER®) IN NURSING LAMBS FOR GROWTH AND HEALTH

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ABSTRACT

Enteric and respiratory infections cause lamb death during and after weaning, resulting in economic losses in intensive ovine production systems. These infections have been treated with antibiotics, but their inadequate use has resulted in bacterial resistance. Plant-derived secondary metabolites can be used as an alternative to antibiotics in lambs. We hypothesized that Animunin could improve lamb performance and immunological response during and after weaning. The objective of this study was to see how Animunin supplementation affected the profile of blood metabolites related to health status and weight changes in nursing lambs. The experimental design was completely randomized, with treatments consisting of supplementation with Animunin gel caps at doses of 0.0, 0.25, 0.50, and 1.0 g d^{-1} for 60 d. Treatments were assigned at random to 40 male Hampshire x Suffolk nursing lambs (initial body weight (IBW) 10.8±2.6 kg, 25 d old). Weight at weaning (WW) was determined on day 83±2. During lactation, the lambs were offered pre-starter feed and water *ad libitum*, in addition to nursing. SAS GLM procedure was used to analyze the data. The level of polyherbal mixture had no effect on most blood components. However, as the dose of Animunin in the gel caps increased, glucose, urea, and creatinine levels decreased. In contrast, the levels of alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) in the blood of lambs given the 1 g dose increased by 39.4 and 45.9 %, respectively, compared to lambs given 0 g. The final body weight and daily gain were not affected ($p > 0.05$). In conclusion, the phytogenic Animunin had hypoglycemic effects while having no affecting lamb growth.

Keywords: feed plant additive, metabolites, phytobiotics.

INTRODUCTION

In intensive ovine production systems, lambs with deficient immunological protection who are fed colostrum without specific antibodies may become sick during lactation (Zhang *et al*., 2015) and die during and after weaning, resulting in economic losses. Antibiotics have been used in the prophylactic management of diarrhea and as growth promoters, but their continuous indiscriminate use causes bacteria to become resistant (Economou and Gousia, 2015) and results in antibiotic residues in meat, which has a negative impact on food safety, human health, and the environment.

In the European Union and several other countries, the use of antibiotics has been prohibited. For this reason, recent emphasis has been placed on the development of safe and effective antibiotic alternatives, such as the use of herbal additives (Valenzuela-Grijalva *et al*., 2017). Supplementation with polyherbal additives containing bioactive compounds could be a good strategy to improve productivity and animal health (Hashemzadeh *et al*., 2022).

Natural plant products, such as phytogenic supplements, are used as sources of secondary metabolites in ruminant nutrition to improve performance, rumen fermentation, and health (Kosina *et al*., 2010; Naumann *et al*., 2017; Orzuna-Orzuna *et al*., 2021). The polyherbal mixture of parts from various plants, such as *Adhatoda vasica, Solanum xanthocarpum, Curcuma longa, Hedychium spicatum, Boerhavia diffusa, Piper longum,* and *Albezia lebbek,* contains a high concentration of phenolic and flavonoid compounds (Sánchez *et al*., 2021).

The inclusion of a polyherbal mixture in the diet of dairy calves has shown positive results (Lee-Rangel *et al*., 2022). In ruminants, previous studies have shown that herbal products can improve performance and carcass characteristics (Razo-Ortiz *et al*., 2020; Lozano-Sánchez *et al*., 2021; Dorantes-Iturbide *et al*., 2022). It has been reported that secondary metabolites (saponins or tannins) of several plants at low to moderate dosages (tannins, 1–4 % or 10–40 g kg^{-1} DM) have a positive effect on ruminant production and health, inhibiting the proliferation of pathogenic bacteria in the gastrointestinal tract, improving rumen fermentation, and mitigating rumen methane production, while reducing the environmental impact of livestock production (Naumann *et al*., 2017), enhancing productivity, and promoting anti-microbial and anti-parasitic activities in ruminants (Huang *et al*., 2018). However, high levels of tannins (> 5 % or 50 g kg^{-1} DM) in the diet reduce fiber digestibility and, consequently, voluntary intake.

Isoquinoline alkaloids such as sanguinarine, chelerythrine, and alocriptopine showed antimicrobial, anti-inflammatory, and immunomodulatory effects (Kosina *et al*., 2010). Alkaloids can improve carcass yield and reduce ruminal acidosis injuries to rumen walls in cattle fed with high-energy diets (Michels *et al*., 2018). The addition of phenols and flavonoids to lamb diets promotes weight. Nevertheless, secondary metabolite effects on the animal response appear to be dose and source dependent. Polyherbal feed additives have been shown to improve lamb performance in small ruminants (Orzuna *et al*., 2021; Sánchez-Torres *et al*., 2022), but there is limited information about their effects on nursing lambs.

We hypothesized that supplementation with secondary metabolites contained in Animunin can improve lamb health and yield during lactation. The objective of this study was to evaluate the effects of increasing dietary concentrations of the phytogenic Animunin on blood metabolites related to health status and live weight changes in nursing lambs.

MATERIALS AND METHODS

Location

Lamb care and management procedures were carried out according to the guidelines established by the Animal Welfare Committee of the *Colegio de Postgraduados*. The study was conducted at the *Colegio de Postgraduados* experimental farm in Montecillo, Mexico (19° 27′ 38″ N, 98° 54′ 11″ W, altitude 2250 m). The climate is temperate subhumid (Cwb) with summer rains, dry winters (wo) (w), and moderate humidity (i′) g, with average annual temperatures and precipitation of 15.2 °C and 665 mm, respectively.

Animals, diet, and housing

Forty male Hampshire x Suffolk nursing lambs (initial body weight 10.8±2.6 kg, average age of 25 d) were assigned, according to a completely randomized design, to one of four treatments, which included dosages (0.0, 0.25, 0.50, and 1.0 g d^{-1}) of the polyherbal mixture supplement "Animunin" administered orally in gel capsules (Animunin Powder®, Nuproxa S. de R.L. de C.V., Mexico). The supplement is a polyherbal mixture composed of plant parts from *Solanum xanthocarpum (*antioxidant activity), *Hedychium spicatum* (antimicrobial, anti-inflammatory, and antioxidant activities), *Curcuma longa* (antioxidant and anti-inflammatory effects), *Piper longum* (antioxidant activity), *Albizia lebbek,* and *Adhatoda vasica* (Orzuna-Orzuna *et al*., 2021; Sánchez *et al*., 2021).

The lambs were allowed to suckle freely all day and stayed with their mothers for 24 h until weaning. During lactation, in addition to nursing, the lambs were offered pre-starter feed (Lamb Tech®, Agribrands Purina, Mexico) *ad-libitum*. The pre-starter diet for the lambs consisted of pelleted feed (2.99 Mcal metabolizable energy (ME) kg^{-1} DM, with 20 % crude protein (CP)). Water was provided with a nipple drinker. Lambs were weaned at an average age of 83±2 d, and their weights were recorded. The experimental phase lasted 60 d. During lactation, each ewe was fed 300 g d^{-1} of a commercial concentrate (Ovina Reproductores, Purina®, Mexico, 14 % CP), 500 g d^{-1} alfalfa hay (16 % CP), and 1000 g d^{-1} oat hay (9 % CP) once a day at 08:00 h, with water available *ad libitum*.

Animal performance

Lamb weight was recorded at the start and end of the experimental period. The average daily gain (ADG, g d^{-1}) by dividing the difference between the final and initial weights (08:00 h) by the number of days in the experiment. Weight at weaning (WW) was recorded on day 83±2.

Blood metabolites

At the end of the experiment, blood samples were collected from each lamb before the morning feeding (pre-prandial 08:00 h; 5 mL) by jugular vein venipuncture using anticoagulant-free vacutainer tubes (BD Vacutainer). The samples were immediately refrigerated (4 °C) and then centrifuged (Sigma 2-16 k, Germany) at 3500 g for 20 min, and the blood serum obtained was stored in Eppendorf tubes and kept in a freezer (Sanyo MDF-436, USA) at -20 °C until analysis (one sample per lamb). The concentrations of blood metabolites such as glucose, urea, uric acid, creatinine, total protein, globulin, albumin, cholesterol, bilirubin, alkaline phosphatase (ALP), lactate dehydrogenase (LDH), aspartate amino transferase (AST), Ca, and P were determined using a blood auto-analyzer (EasyVet, KontroLab ES-300, Mexico) and Spinreact kits (Barcelona, Spain).

Statistical analysis

The Shapiro-Wilk and Levene tests were used to verify the normal distribution and variance homogeneity of variables. The data were analyzed using the GLM procedure (SAS, 2012). Initial body weight was used as the covariate by final and average daily gain. Tukey's test ($p \leq 0.05$) was used to compare treatment means. A completely randomized design was used for the model:

$$Y_{ij} = \mu + \tau_i + £_{ij}$$

where μ is the mean value, τ_i is the treatment effect (fixed), and $£^{ij}$ is the error term.

RESULTS AND DISCUSSION

There were no effects ($p > 0.05$) on the final body weight and average daily gain by the phytogenic supplement (Table 1).

Evaluations of the polyherbal mixture have shown its ability to improve lamb feedlot performance (Dorantes-Iturbide *et al.*, 2022). However, lamb growth and live weight were not modified in our study. Orzuna-Orzuna *et al*. (2021) and Lozano-Sánchez *et al*. (2021) observed that, as the dose of polyphenols and flavonoids increased (3 g kg^{-1} DM), daily weight gain (DWG) and body weight (BW) decreased, similar to our

Table 1. Least square means for the effects of herbal phytogenic on nursing lamb performance.

Item	Animunin Powder® (g d^{-1})†				SEM
	0.00	0.25	0.50	1.00	
Initial weight (kg)	10.86	10.68	10.04	10.76	0.857
Final weight (kg)	21.26	21.34	21.01	20.20	1.597
ADG (kg d^{-1})	0.184	0.190	0.178	0.168	0.0184

ADG: average daily gain; SEM: standard error of the mean. †Nuproxa México, Querétaro, México.

results. In another study, Razo-Ortiz *et al*. (2020) used a polyherbal mixture (0, 0.1, 0.2, and 0.3 % DM) and found that lambs supplemented with high doses had lower DWG than lambs in the other treatments. In a similar study, Dorantes-Iturbide *et al*. (2022) investigated the effects of a polyherbal additive (0, 1, 2, and 3 g kg^{-1} DM) containing hydrolyzable tannins, flavonoids, and essential oils on the productive performance of finishing lambs and observed a higher DWG in lambs supplemented with only 1 g kg^{-1} DM of polyherbal additive. However, as the dose increased, DWG decreased, which is consistent with our findings. In contrast, Sánchez-Torres *et al*. (2022) noticed no effect of the highest dose of Animunin (0, 1, 2, and 3 g kg^{-1} DM) on the productive performance of lambs.

These results suggest that the effects of the secondary metabolites present in the polyherbal mixture at low doses can improve productivity, but at high doses they can affect growth rate, probably due to the toxic effects of saponins, alkaloids, terpenes, and tannins. Moreover, flavor and palatability can vary depending on the type and dose of the phytogenic source, the composition and secondary metabolites in each plant, as well as administration time, diet composition, productive stage, and lamb characteristics. Therefore, the response to Animunin is influenced by the dosage, species, and physiological state. In lactating animals, the effects of the phytogenic supplement may have been limited since they feed mainly on milk and the rumen has not developed; thus, secondary metabolites were unable to have positive effects on microbiota or digestion.

The results of the blood metabolite analysis on lambs supplemented with the polyherbal mixture (Table 2) showed no effect of daily Animunin dosages on the

Table 2. Least square means for the effects of herbal phytogenic on the biochemical profile of nursing lambs.

Item	Animunin Powder® (g d^{-1})†				
	0.00	0.25	0.50	1.00	SEM
Cholesterol (mg dL^{-1})	67.20	67.20	65.50	64.80	3.48
Glucose (mg dL^{-1})	97.70ab	98.90a	96.20ab	87.60b	2.75
Urea (mg dL^{-1})	45.00ab	45.40a	45.80a	35.30b	2.62
Uric acid (mg dL^{-1})	0.47	0.43	0.42	0.47	0.04
Creatinine (mg dL^{-1})	1.00a	0.97a	0.88ab	0.81b	0.03
Total protein (g dL^{-1})	7.78	7.64	7.78	7.70	0.12
Albumins (g dL^{-1})	4.01	3.91	3.89	3.87	0.08
Globulins (g dL^{-1})	3.77	3.73	3.89	3.83	0.11
Albumins/Globulins	1.08	1.06	1.01	1.01	0.04
Bilirubin (mg dL^{-1})	0.31	0.37	0.32	0.44	0.05
ALP (IU L^{-1})	38.80b	54.10a	38.40b	55.00a	3.84
LDH (IU L^{-1})	75.10c	109.60ab	80.40bc	120.0a	8.46
Calcium (mEq L^{-1})	8.87	8.86	9.17	9.30	0.22
Phosphorus (mEq L^{-1})	4.73	5.04	5.30	4.96	0.23

ALP: alkaline phosphatase; LDH: lactate dehydrogenase; SEM; standard error of the mean. †Nuproxa Mexico, Querétaro, Mexico. abc Means in each row with different superscripts are statistically different ($p \leq 0.05$).

cholesterol, uric acid, total protein, albumins, globulins, and bilirubin concentrations ($p > 0.05$). Blood glucose, urea, and creatinine ($p \leq 0.05$) were reduced with the 1.0 g d^{-1} Animunin dietary supplementation dose. Liver enzyme levels increased ALP and LDH ($p \leq 0.05$) in response to the 1.0 g d^{-1} dose. Serum calcium and phosphorus levels ($p > 0.05$) were not affected.

Blood biochemistry was used as an indicator of changes in health status and protein and energy metabolism as a result of the phytogenic effect (Kiran *et al.,* 2012). In the experiment with dairy calves, Animunin improved health and immune response (Sánchez *et al*., 2021), but not in lambs in our study. In general, most serum biochemical parameters were not affected by the level of Animunin used. This is consistent with the findings of Orzuna-Orzuna *et al.* (2021) and Sánchez-Torres *et al*. (2022), who found that serum concentrations of cholesterol, protein, albumin, globulin, and bilirubin were not affected by the level of Animunin in the diet. Higher liver enzyme values have been reported in lambs infected with various etiological conditions (Lipecka *et al.,* 2010). Increases in bilirubin can be associated with polyphenolic compounds that inhibit glucuronidation (Mohamed and Frye, 2011).

An increase in ALP and LDH was observed with the 1.0 g d^{-1} phytobiotic dose of 39.4 and 45.9 %, respectively, compared to lambs that received the treatment control (0 g), which are usually indicators of liver damage and renal diseases such as nephrosis. A mild elevation may also be seen in young, growing animals, but lamb health and growth were not affected in other studies (Das *et al*., 2017; Hrkovic-Porobija *et al*., 2017). Higher ALP values were reported in calves after intake of Animunin (Sánchez *et al*., 2021). Hepatic ALP can be affected by nutrition (Hrkovic-Porobija *et al*., 2017). Nevertheless, in our study, blood biochemistry changes were not reflected in improved performance productivity.

According to our findings, the highest Animunin dosage reduced blood glucose, which is required to activate immune cells and provide an adequate energy supply for the immune system (Palsson-McDermott and O'Neill, 2013). The reduction in glucose due to the phytogenic effect could have an effect on insulin signaling and release, glycogen synthesis, and gluconeogenesis, affecting genes involved in glucose metabolism (El-Barky, 2017). Urea and creatinine concentrations in lambs may indicate a better immune response to environmental stress. Higher doses of the phytogenic supplement reduced these concentrations.

Regarding serum urea concentrations, Orzuna-Orzuna *et al*. (2021) reported a decrease with the highest dose of Animunin (3 g kg^{-1} DM). In contrast, Razo-Ortiz *et al*. (2020) and Sánchez-Torres *et al*. (2022) found no difference in this metabolite in lambs supplemented with a polyherbal mixture containing polyphenols and flavonoids. Some studies report a decrease in serum creatinine in lambs as the polyherbal dose increases (Orzuna-Orzuna *et al*., 2021). In contrast, other authors do not report changes in the concentration of this serum metabolite when including polyphenols and flavonoids (Razo-Ortiz *et al*., 2020; Sánchez-Torres *et al*., 2022).

Creatinine is an indicator of kidney function; in cases of chronic and acute kidney failure, its concentration increases in the body. In our study, there was a small

reduction, but values were within the normal range, suggesting that the polyherbal phytogenic supplement used had no effect on kidney health. Orzuna-Orzuna *et al.* (2021) reported similar results in lambs supplemented with Animunin. However, Razo-Ortiz *et al.* (2020) and Sánchez-Torres *et al*. (2022) investigated the effects of supplementation with a polyherbal mixture containing polyphenols and flavonoids and found no effect on serum creatinine concentration.

The increase in serum concentrations of liver enzymes such as alkaline phosphatase and aspartate aminotransferase found in our study likely indicates that some secondary metabolites in the herbal mixture may be causing liver stress (Mahgoub *et al*., 2008). Giannini *et al*. (2005) mentioned that these enzymes can be used as an indicator of liver function. When liver cells damage occurs, blood levels of alkaline phosphatase and aspartate aminotransferase increase (Braun *et al*., 2010). In contrast, Lozano-Sánchez *et al*. (2021), Dorantes-Iturbide *et al*. (2022), and Sánchez-Torres *et al*. (2022) did not report an effect of the polyherbal phytogenic supplement on these liver enzymes, which is likely a result of differences in the source and dose of the supplement provided, feeding management, and physiological status of the animal.

According to research on the plants used to make Animunin supplements, each may benefit animal health. *Adhatoda vasica* has been reported to have antifungal, antiviral, hepatoprotective, antibacterial, anti-inflammatory, cardiovascular protective, hypoglycemic, antitubercular, antioxidant, and antimutagenic properties (Kumar *et al.*, 2017). The addition of curcumin, a component of *Curcuma longa*, to the diet of lactating ewes improved milk production and had antioxidant and anti-inflammatory effects (Jaguezeski *et al.*, 2018). In nursing lambs, it improved antioxidant capacity and anti-inflammatory response (Molosse *et al*., 2019).

Piperine, the main component of *Piper longum*, an alkaloid used in traditional Indian medicine, has shown immunomodulatory and antioxidant properties (Kumar *et al.*, 2015). *Boerhavia diffusa* phytochemicals include alkaloids, flavonoids, rotenoids, and phytosterols with various pharmacological properties such as analgesic, anti-inflammatory, hepatoprotective, immunomodulatory, and nephroprotective effects (Kumar *et al.*, 2018), although their nutraceutical properties have not been evaluated in ruminants. *Solanum xanthocarpum* has hypoglycemic, hepatoprotective, antibacterial, and antioxidant properties (Nithya *et al.*, 2018), while *Hedychium spicatum* is used for respiratory disorders, as an analgesic, and for its anti-inflammatory, antimicrobial, antioxidant, antifungal, and cytotoxic activities (Sravani and Paarakh, 2011), although studies on animals are limited.

The differences in serum metabolite concentrations reported in the literature and those obtained in the current study are most likely due to nutritional factors, the polyherbal mixture (type of plants, dose, administration time), and lambs characteristics (breed, sex, age, health status). The serum metabolite levels found in our study are within the normal range described for nursing lambs (Braun *et al*., 2010), indicating that the animals were clinically healthy and unaffected by pathology caused by hygienic-sanitary conditions, feeding, and handling during the experimental phase.

CONCLUSIONS

The polyherbal phytogenic supplement had no effect on weight changes or immune response metabolites in nursing lambs. Other possible beneficial effects deserve further study during the pre-ruminant to weaning period, as the diet transitions from liquid to solid form and the immune system matures.

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