



Evaluation of macrocyclic lactones efficacy against gastrointestinal nematodes in double purpose calves from Chone, in the ecuadorian low tropic

Evaluación de la eficacia de lactonas macrocíclicas frente a nematodos gastrointestinales en terneros doble propósito del cantón Chone, en el trópico bajo

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Resumen

With the objective of evaluating the current efficacy of macrocyclic lactones against gastrointestinal nematodes in dual-purpose calves from Chone Canton, Manabí Province, located in the Ecuadorian lowland tropics. A total of 27 calves were used, divided into three experimental groups: one treated with 1% Doramectin, another with 1% Ivermectin, and a third untreated control group. The parasitic load, estimated by eggs per gram of feces (EPG), was determined using the McMaster coprological technique, and the anthelmintic efficacy was assessed through the percentage reduction of EPG in the treated groups compared to the control (%RH). Efficacy was evaluated on day zero (before treatment) and at 3, 7, 14, 21, and 28 days post-treatment (DPT), respectively. Data were analyzed using non-parametric statistics. Pre-treatment EPG values ranged from 616.67 to 750. The group treated with 1% Ivermectin showed mean EPG values of 761.11, 400, and 172.22, and efficacies of 61.81%, 49.2%, and 56.94% at 3, 7, and 14 DPT, respectively. The group treated with 1% Doramectin presented EPG values of 616.17, 638.89, and 555.56, and efficacies of 48.11, 20.40, and 0% on different sampling days. Significant differences ($p < 0.05$) were observed in efficacy between the treatments with macrocyclic lactones and the untreated control during the trial. The results indicate low efficacy of both 1% Ivermectin and 1% Doramectin and suggest partial anthelmintic resistance of gastrointestinal nematodes to the macrocyclic lactone mechanism of action at the study site..

Keywords: efficacy, macrocyclic lactones, nematodes, cattle.

Resumen

Con el objetivo de evaluar la eficacia actual de lactonas macrocíclicas, frente a nematodos gastrointestinales en terneros doble propósito del Cantón Chone, provincia de Manabí, ubicado en el trópico bajo ecuatoriano. Se utilizaron 27 terneros divididos en tres grupos experimentales, los cuales consistieron en: grupo tratado con Doramectina 1%, grupo con Ivermectina 1%, y grupo no tratado (testigo). Los valores de huevos por gramo de heces (HPG), se determinó mediante la técnica coprológica de McMaster, y la eficacia del antihelmíntico, a través del porcentaje de reducción de HPG de los grupos tratados frente al testigo (%RH). La eficacia se midió antes del tratamiento, y a los 3, 7, 14, 21 y 28 días postratamiento (DPT); siendo los datos analizados a través de estadística no paramétrica. Los HPG se encontraban en un rango entre 616,67 a 750, previo al tratamiento. El grupo tratado con Ivermectina 1%, mostró los DPT 3, 7, 14, 21 y 28, valores promedios de HPG de 761,11, 400 y 172,22, y eficacias de 61,81; 49,20 y 56,94 de %RH, respectivamente. Los valores de HPG y %RH del grupo tratado con Doramectina 1%, fueron 616,17, 638,89 y 555,56 HPG y 48,11; 20,40 y 0%, mostrando diferencias estadísticas ($p < 0,05$) en las eficacias entre los grupos tratados, y de estos con el control. Los resultados indican baja eficacia de la Ivermectina 1% y Doramectina 1% e indicios de resistencia antihelmíntica parcial por parte de nematodos gastrointestinales, al mecanismo de acción de lactonas macrocíclicas en el lugar del estudio.

Palabras clave: eficacia, macrocyclic lactones, nematodes, cattle.



Introduction

Gastrointestinal parasitoses, especially those caused by nematodes, are of great importance because they affect the health, welfare, and production of cattle (*Bos taurus*), particularly young animals whose feeding is based on grazing (Urdaneta et al. 2011). Due to their location and pathogenic effects, these nematodes cause syndromes of poor digestion and nutrient absorption; likewise, some species are hematophagous, which leads to cases of anemia (Angulo et al., 2010a).

To prevent the harmful effect of gastrointestinal nematodiasis (GIN) on bovine health and production, anthelmintic drugs are used as part of control strategies, including macrocyclic lactones. These are a group of drugs used in veterinary medicine, with efficacy against nematodes and ectoparasites, because they have a broad active spectrum against adult and immature forms (Lifschitz et al., 2024), with active ingredients such as doramectin and ivermectin being the most widely used. However, due to their continuous use and long persistence, parasite resistance to these drugs has been reported in several parts of the world (Muñoz et al., 2008; Pacheco et al., 2023).

Researchers such as Packianathan et al. (2023) reported an efficacy of less than 72% for doramectin against GIN. Likewise, parasite resistance to multiple drugs has been reported in parasitic species of the genera *Cooperia*, *Trichostrongylus*, and *Haemonchus* (Ramos et al., 2016). In the case of ivermectin and moxidectin, resistance has been detected in 100% of the farms evaluated in areas of Brazil (Bezerra et al., 2021). In this regard, Muñoz et al. (2008) reported low efficacy of ivermectin against nematode larvae present within the mucosa, but better efficacy against adults, both in species located in the abomasum and in the intestine.

It is important to indicate that, although a wide variety of antiparasitic drugs is available, the compounds doramectin and ivermectin, owing to their endectocidal properties, long pharmacokinetic persistence, and broad efficacy, as well as their low cost and ease of use, have been used irrationally, which may result in helminth resistance to antiparasitic mechanisms of action (Angulo et al. 2010b). In the province of Manabí, located in the coastal region of Ecuador, there is no information on the efficacy of these drugs against the helminth fauna affecting local cattle. In view of this, the present study aimed to evaluate the current efficacy of 1% doramectin and 1% ivermectin against gastrointestinal nematodes in cattle from a dual-purpose commercial cattle production system.

Materials and Methods

Área of study

The research was conducted in a cattle production system located in the parish of San Antonio, Chone canton, province of Manabí, Ecuador. Its geographical location is at the coordinates 0°35'12" S and 80°14'15" W. The area is located at an altitude of 205 m a.s.l., with a temperature of 27 °C and an average annual precipitation of 1,200 mm³, with a tropical semi-humid climate (Barros and Troncoso, 2010).

Animal units

Twenty-seven crossbred calves (crosses of the Holstein, Brown Swiss, Brahman, and Gyr breeds) from a dual-purpose (DP) production system were used. The animals were between four and seven months of age and were naturally infected with GIN at the beginning of the trial. Their feeding was based on lactation, through milking in the presence of the calf, and grazing on pastures of forage species (*Megathyrsus maximus*), with water provided ad libitum and supplementation with mineral salts. At the beginning of the trial, at least three months had elapsed since the animals had been dewormed with benzimidazoles, or they had not been treated with any anthelmintic.

Experimental design

The 27 animals were divided into three groups of nine calves each. The first experimental group was treated with 1% ivermectin, the second with 1% doramectin, and the third was kept untreated as the control group. The drugs were administered subcutaneously (SC), with a single therapeutic dose for both drugs of 200 µg·kg⁻¹ of live weight (LW). Fecal samples were taken directly from the rectum using disposable plastic gloves; they were labeled and transported under refrigeration to the Veterinary Parasitology Laboratory of the Universidad Técnica de Manabí for processing. Coproparasitological sampling was carried out on day zero, before treatment, and on days 3, 7, 14, 21, and 28 post-treatment (DPT).

Sample analysis was performed using the quantitative McMaster technique (Sandoval et al., 2011). The parasite burden was estimated by counting the number of eggs per gram of feces (EPG), and the efficacy of the treatments against GIN was determined by the percentage reduction in EPG (% reduction) in the treated groups relative to the control group (Geurden et al. 2022), using the following formula:

$$\% \text{ EPG reduction} = 100 \times (1 - \bar{x} \text{ EPG T} / \bar{x} \text{ EPG C})$$

Where:

% EPG reduction was the percentage in eggs in the treated groups relative to the control group.

$\bar{x}$ EPG T was the mean EPG of each treated group

$\bar{x}$ EPG C was the mean EPG of the control group.

The dependent variable was drug efficacy, measured as a percentage, and the independent variable was the treatments or experimental groups

Data Analysis

The data were analyzed using descriptive statistics and nonparametric tests, because EPG values have a negative binomial distribution (Kruskal-Wallis), to determine differences among the experimental groups on the different sampling days, with respect to their efficacy and the mean EPG of each experimental group, with a significance level of $p \leq 0.05$, using the InfoStat statistical software (Di Rienzo et al., 2015).

Results and Discussion

When evaluating the current efficacy of the application of 1% doramectin and 1% ivermectin in calves from a dual-purpose cattle production system against gastrointestinal nematodes, the animals in the experimental groups presented parasite burdens, measured as mean EPG before the trial (0 DPT), ranging from 483 to 611 EPG, as shown in Figure 1. The group treated with 1% ivermectin showed EPG values of 611, 761, 450, 194, 306, and 369 on sampling days 0, 3, 7, 14, 21, and 28 DPT, respectively (Figure 1). Likewise, the group treated with 1% doramectin showed EPG values of 544, 639, 611, 556, 439, and 583 on the different DPT (Figure 1). The EPG values of the control group during the trial ranged from 450 to 1,231 (Figure 1). Anthelmintic efficacy, measured as % EPG reduction, is shown in Figure 2. In the case of 1% ivermectin, the highest efficacy was observed at 14 DPT, with 58.09%, followed by a subsequent reduction to 18% at the end of the trial. In the case of 1% doramectin, the highest efficacy was observed on day 3 DPT, with 48.09%, decreasing to 0% by day 14 DPT (Figure 2).

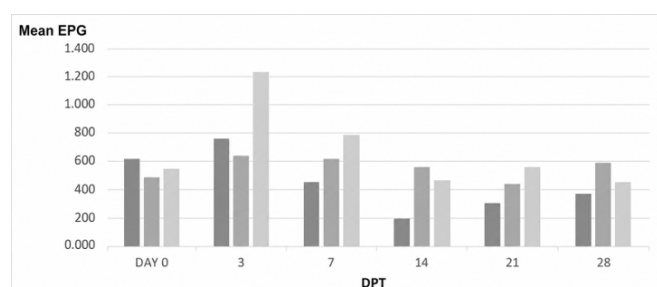


Figure 1. Mean EPG values for the different experimental groups during the trial. Days post-treatment (DPT); eggs per gram of feces (EPG).

Días post tratamiento (DPT), Huevo por gramo de heces (HPG).

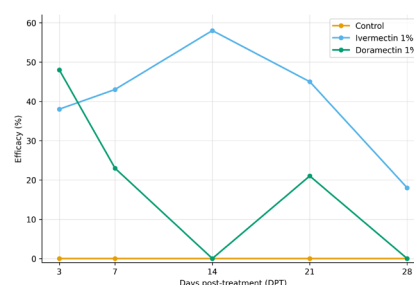


Figure 2. Mean efficacy, expressed as RH (%), in the experimental groups at different days post-treatment (DPT).

These results showed efficacies below 90%, the threshold for identifying antiparasitic efficacy (Geurden et al., 2022), indicating that there was evidence of partial resistance of GIN to the mechanism of action of these drugs. In both cases, as macrocyclic lactones, they presented the same mechanism, which consisted of the inhibition of nematode-specific glutamate-gated chloride channels, inhibiting nerve impulses and causing flaccid paralysis and death of the parasite (Atif et al. 2017).

When comparing the efficacy of both drugs, it was recorded that 1% ivermectin showed relatively better efficacy than 1% doramectin, although neither active ingredient reached the required efficacy threshold. This study revealed, for the first time in Ecuador, the presence of anthelmintic resistance of GIN to the mechanism of action of macrocyclic lactones. Different studies have reported anthelmintic efficacy values of macrocyclic lactones against GIN ranging from 72 to 100%, indicating that the possible differences may be due to GIN populations that are sensitive or resistant to the mechanisms of action of these drugs (Bezerra et al., 2021; Packianathan et al., 2023). Parasite resistance to multiple drugs has been reported in the GIN genera *Cooperia*, *Trichostrongylus*, and *Haemonchus* (Ramos et al., 2016)..

Several authors have reported the phenomenon of anthelmintic resistance in various regions of the world, revealing a concerning trend of multiple resistance to different classes of anthelmintics (Angulo et al., 2011; Geurden et al., 2015; Bezerra et al., 2021), which poses significant challenges for the control of nematode infections in cattle.

The factors that contributed to the development of resistance were diverse, including the frequency and timing of anthelmintic treatment, drug dose, drug efficacy, lifespan, and fecundity of adult nematodes, among others (Geurden et al., 2022). Mauger et al. (2022), in a study with doramectin, achieved adequate efficacy, unlike the present study, in which the results may have been influenced by the number of animals sampled, their body condition, and geographical location. Other authors evaluating drugs such as albendazole and macrocyclic lactones observed anthelmintic resistance (Angulo et al., 2011; Geurden et al., 2015; Bezerra et al., 2021).

Conclusion

La eficacia de los tratamientos utilizados, Doramectina 1% e Ivermectina 1%, estuvo por debajo del umbral de eficacia de los fármacos antihelmínticos, con moderados porcentajes de reducción de huevos de los grupos tratados respecto al control, mostrando indicios de resistencia antihelmíntica parcial de los NGI frente a lactonas macrocíclicas en el lugar del ensayo.

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Conflict of interest

The authors declare that they have no conflicts of interest in any phase of the present publication.

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Declaration of contribution according to CRediT

Ramón Jair García-Zambrano: investigation, methodology, writing - original draft **Juan Zambrano-Villacís:** unding acquisition, project administration, resources, supervision, validation. **Francisco Angulo-Cubillán:** onceptualization, data curation, formal analysis, investigation, methodology, supervision, validation, writing, review, editing - original draft

