



Anthelmintic resistance in Creole horses in the South of Rio Grande do Sul, Brazil

[Resistência anti-helmíntica em equinos da raça Crioula no sul do Rio Grande do Sul, Brasil]

J.S. Lignon¹, N.F. Gonçalves², L.L. Cunha³, T.A. Antunes⁴, M.S. Leão², J.L.T. Camassola²,
T.G. Pellegrin², P.K. Ripoll⁴, F.G. Pappen⁴, D.M. Pinto⁴

¹Aluno de pós-graduação - Universidade Federal de Santa Maria - Santa Maria, RS

²Aluno de graduação - Universidade Federal de Pelotas - Pelotas, RS

³Aluno de pós-graduação - Universidade Federal do Rio Grande do Sul - Porto Alegre, RS

⁴Universidade Federal de Pelotas - Pelotas, RS

ABSTRACT

The objective of the study was to evaluate the antiparasitic resistance against horse nematodes in the South of Rio Grande do Sul, Brazil. The results concerning the tests of anthelmintic efficacy on horses, stored in the database of the Parasitic Diseases Study Group (GEEP) - Veterinary Faculty, at the Federal University of Pelotas (UFPe), were carried out in the laboratory from 2018 to 2019. Stool samples were received from farms with breeding of adult female and male Criollo horses naturally infected, located in municipalities in the country's southern region. The antiparasitic agents tested were Triclorfon + Fenbendazole, Closantel + Albendazole, Ivermectin + Praziquantel, Fenbendazole, Ivermectin, Doramectin, Mebendazole and Moxidectin. Techniques such as Gordon and Whitlock, Coproculture and Fecal Egg Count Reduction Test were performed. Of all the antiparasitic drugs tested, it was observed that only treatments with Ivermectin 2% showed desired values. The observed results indicate that resistance to macrocyclic lactones is usual in equine parasites in this Brazilian region, despite the results with isolated Ivermectin.

Keywords: anthelmintic resistance, equinoculture, FECRT, helminths, vermifuge

RESUMO

O objetivo deste estudo é avaliar a resistência antiparasitária contra nematodeos de equinos no sul do Rio Grande do Sul, Brasil. Os resultados referentes aos testes de eficácia anti-helmíntica em cavalos, armazenados no banco de dados do Grupo de Estudos de Doenças Parasitárias (GEEP) - Faculdade de Veterinária, da Universidade Federal de Pelotas (UFPe), foram realizados em laboratório, no período de 2018 a 2019. Amostras de fezes foram recebidas de fazendas com criação de cavalos Crioulos adultos fêmeas e machos naturalmente infectados, localizadas em municípios da região Sul do país. Os agentes antiparasitários testados foram triclorfon + fenbendazol, closantel + ivermectina + praziquantel, fenbendazol, ivermectina, doramectina, mebendazol e moxidectina. Técnicas como Gordon e Whitlock, coprocultura e teste de redução da contagem de ovos fecais foram realizadas. De todos os antiparasitários testados, observou-se que apenas os tratamentos com ivermectina 2% apresentaram os valores desejados. Os resultados indicam que a resistência às lactonas macrocíclicas é comum em parasitas equinos nessa região brasileira, apesar dos resultados com ivermectina isolada.

Palavras-chave: resistência anti-helmíntica, equinocultura, FECRT, helmintos, vermífugo

INTRODUCTION

In Brazil, the horse market provides financial incomes of approximately R\$ 15 billion per year through a population of more than 5 million animals, being 9.2% of this amount located in Rio Grande do Sul state (RS) (Brasil, 2016). In RS,

besides linked activities (e.g. leisure, sport, work), equine breeding, especially Criollo horse, is highly related to cultural traditions of native people (i.e. gaúchos) (Costa *et al.*, 2014). Horse management in RS is mainly extensive, wherein animals remain in pastures – natural or cultivated - often maintained with high animal

density increasing propensity to intestinal parasitism and favoring constant infections by presence of parasites in these pastures (Reinemeyer, 2008).

Horses are considered one of the most susceptible animals to a wide variety of gastrointestinal parasites, being able to host several species at the same time (Rehbein *et al.*, 2013), and endoparasitosis problems which limit considerably the productive performance of these animals. The control of parasitic infections in horses is extremely important to maintain animal health. Nevertheless, parasitic control keeps being based on exclusive and regular use of anthelmintics mainly due to its easy application, purchase, and cost-benefit for breeders (Molento, 2005).

In the last decade, reduction in antiparasitic drug's effectiveness has become a serious threat to animal health mainly through parasitic resistance, which selects more resistant individuals and eliminate most susceptible ones from a population by a selective pressure factor (e.g. anthelmintic compounds) (Molento, 2005). Given the importance related to losses caused by parasitic diseases and the lack of a new anthelmintic chemical group for horses, the objective of the study is to evaluate the effectiveness of antiparasitic against equine nematodes in the south of the state of Rio Grande do Sul, Brazil - where Livestock and horse-related activities are directly related to native traditions.

MATERIALS AND METHODS

This study was performed by analyzing results from diagnoses made by Parasitic Diseases Study Group (GEEP), at the Faculty of Veterinary Medicine, Federal University of Pelotas (UFPel), Brazil, during the years 2018 and 2019, as part of an extension project elaborated to provide scientific basis for landowners decisions regarding horse sanitary management. This work was approved by the Animal Experimentation Ethics Committee (CEEA) of the UFPel under registration number 7888 and was carried out in accordance with the rules and relevant regulations to animal care. Stool samples from 235 animals were used, received from 12 farms (numbered from 1 to 12, Table 1) with Criollo horses breeding, adults, males and females, naturally infected and located in the southern region of Rio

Grande do Sul state, Brazil. Included properties were from Camaquã (30° 51' 04" S; 51° 48' 44" W), Pelotas (31° 46' 19" S; 52° 20' 33" W), Capão do Leão (31° 46' 3" S; 52° 26' 55" W), São Lourenço do Sul (31° 21' 55" S; 51° 58' 42" W), Arroio Grande (32° 14' 15" S; 53° 05' 13" W) and Rio Grande (32° 1' 60" S; 52° 5' 55" W) municipalities.

All applied extensive properties have similar management systems with high stocking rates (> 1 animal unit per hectare), being pastures (native and/or exotic) the main forage source for animals and carrying out antiparasitic treatment every three months with active principles rotation. The drugs used in this study were administered orally according to recommended doses by manufactures of each product, based on animal weight. Antiparasitic agents tested were: Triclorfon + Fenbendazole 10% (22.5mg/kg + 7.5mg/kg), Closantel 10% + Albendazole 5% (20mg/kg + 5mg/kg), Ivermectin 1% + Praziquantel 7.5% (0.2mg/kg + 2.5mg/kg), Fenbendazole 10% (7.5mg/kg), Ivermectin 2% (0.2mg/kg), Doramectin 1% (0.2mg/kg), Mebendazole 2% (10mg/kg) and Moxidectin 2% (0.2mg/kg). There was no influence on our part in the choice of anthelmintics used in each property, only the antiparasitic management of each one was followed. All properties had a veterinarian responsible for antiparasitic management and they requested the effectiveness test.

Fecal samples were analyzed using the technique proposed by Gordon and Whitlock (1939) and the result was expressed in eggs per gram of feces (EPG). In the parasitological analysis, the characteristics of the eggs were analyzed according to Hoffmann (1987). The evaluation of the efficacy of treatments was based on the Fecal Egg Count Reduction Test (FECRT), according to which assess helminth egg count per gram of feces before and after treatment (Coles *et al.*, 1992). FECRT is the main method to detect parasitic resistance and, to be considered effective, treatment must reduce the EPG count by at least 95% (Molento, 2005). Stool samples were collected on the day of treatment and 14 days after the use of anthelmintics to quantify eggs. In addition, before and after treatment, coproculture (Roberts & O'Sullivan, 1950) was performed to generate third-stage larvae (L3) for Strongylidae species differentiation. Morphological characteristics of Cyathostomins were performed

according to Santos *et al.* (2018) and large strongyles were identified based on Bevilacqua *et al.* (2000).

RESULTS

Each treatment efficacy is presented in Table 1, wherein it was observed that only treatments with Ivermectin 2% (0.2mg / kg) showed efficacy within the desired level. In properties “8” and “9”, where this active ingredient was used without

association with another drug, they obtained an efficiency of 95% and 98.9% respectively. In parasitological analysis, only morulated eggs characteristic of parasites from Strongylidae family were observed in all samples. Results from coproculture before and after treatment are shown in Table 2, revealing that in all properties wherein anthelmintic drugs were resistant, there was presence of Cyathostomins.

Table 1. Properties, active principles tested, doses used and their respective efficacy rates

Property	Active principle	Dose	Average EPG pre-treatment	Average EPG after treatment	Efficacy index (%)
1	Triclorfon + Fenbendazole 10%	22.5mg/kg+7.5mg/kg	1243	507	59.2%
2	Closantel 10% + Albendazole 5%	20mg/kg+5mg/kg	429.5	227.2	47%
3	Ivermectin 1% + Praziquantel 7.5%	0.2mg/kg+2.5mg/kg	627.1	168.7	73%
4	Ivermectin 1% + Praziquantel 7.5%	0.2mg/kg+2.5mg/kg	615.2	69.4	89%
5	Ivermectin 1% + Praziquantel 7.5%	0.2mg/kg+2.5mg/kg	1694	114	93.2%
6	Ivermectin 1% + Praziquantel 7.5%	0.2mg/kg+2.5mg/kg	2785.1	2048.1	26.4%
7	Fenbendazole 10%	7.5mg/kg	1104.5	840.9	23%
8	Ivermectin 2%	0.2mg/kg	2055	110	95%
9	Ivermectin 2%	0.2mg/kg	2316.6	25	98.9%
10	Doramectin 1%	0.2mg/kg	865	750	13.3%
11	Mebendazole 2%	10mg/kg	881.9	866.89	1.2%
12	Moxidectin 2%	0.4mg/kg	550.7	103.9	81.1%

Table 2. Results of coprocultures performed before and after treatment, according to the anthelmintic drug used in each property

Property	Active principle	Number of Animals	Coproculture before treatment	Coproculture after treatment	Result
1	Triclorfon + Fenbendazole 10%	12	<i>Strongylus vulgaris</i> , Cyathostomins	Cyathostomins	Resistant
2	Closantel 10% + Albendazole 5%	20	<i>S. vulgaris</i> , Cyathostomins	Cyathostomins	Resistant
3	Ivermectin 1% + Praziquantel 7.5%	12	<i>S. vulgaris</i> , <i>S. equinus</i> , Cyathostomins	Cyathostomins	Resistant
4	Ivermectin 1% + Praziquantel 7.5%	15	<i>S. vulgaris</i> , Cyathostomins	Cyathostomins	Resistant
5	Ivermectin 1% + Praziquantel 7.5%	75	<i>S. vulgaris</i> , Cyathostomins	Cyathostomins	Resistant
6	Ivermectin 1% + Praziquantel 7.5%	20	<i>S. equinus</i> , Cyathostomins	Cyathostomins	Resistant
7	Fenbendazole 10%	13	<i>S. vulgaris</i> , <i>S. equinus</i> , Cyathostomins	Cyathostomins	Resistant
8	Ivermectin 2%	17	<i>S. vulgaris</i> , Cyathostomins	-	Effective
9	Ivermectin 2%	15	<i>S. vulgaris</i> , Cyathostomins	-	Effective
10	Doramectin 1%	10	<i>S. equinus</i> , Cyathostomins	Cyathostomins	Resistant
11	Mebendazole 2%	10	<i>S. equinus</i> , Cyathostomins	Cyathostomins	Resistant
12	Moxidectin 2%	16	<i>S. vulgaris</i> , Cyathostomins	Cyathostomins	Resistant

DISCUSSION

In properties “8” and “9” treatments with Ivermectin 2% were effective and these results are similar to those obtained by Godeski *et al.* (2017) that obtained 100% efficacy in horses treated with Ivermectin (0.2mg/kg, orally) in three farms in Major Videira, Santa Catarina state. In a farm located in Uberlândia city, Minas Gerais state, Barbosa *et al.* (2018) found 99.7% effectiveness on the 14th day after Ivermectin dosage. Currently, Ivermectin is the most widely used drug in horses and still maintain good effectiveness levels (Canever, 2012), although some reports of resistance have been described years ago (Molento *et al.*, 2008; Traversa *et al.*, 2009), after almost three decades of widespread. One of the main reasons for the delay in the resistance development in this compound can be explained by its chemical property that has no action on encysted larvae in the intestinal mucosa, considered as a large refugee population (Kaplan, 2002).

Godeski *et al.* (2017) evaluated Moxidectin efficacy after 14 days of treatment with a reduction of 100%. Among drugs used to control parasites in horses, this is the only one with some action against encysted cyathostominae, currently recommended for controlling this group with high efficacy rates (Barbosa *et al.*, 2018). However, reduced efficacy of Moxidectin against cyathostominae has already been reported in Brazil (Canever, 2012) like our result (81% in property “12”). Recently, Vera *et al.* (2020) analyzed the effectiveness of Ivermectin, Moxidectin and Febendazole in 10 properties located in São Paulo state, Brazil. According to the authors, they were the three most common anthelmintic drugs available on market for horse treatment. In their study, Moxidectin and Ivermectin had satisfactory rates (i.e. above 95% of efficiency) in all farms, indicating that macrocyclic lactones (Ivermectin and Moxidectin) are still highly effective in the studied region.

However, tests with Febendazole showed values below 95% of effectiveness in eight of 10 properties, presenting similar results to the present study. Rodrigues *et al.* (2020) found that animals treated with Febendazole showed, on average, a reduction of only 36% in the EPG count in a farm in Alegrete city, RS, similar to the property “7”

result (Table 1). The presence of resistant Febendazole cyathostomins was already expected in our study due to Febendazoles resistance reported in several countries, including Brazil (Canever, 2012; Molento *et al.*, 2008; Canever *et al.*, 2013). Maintenance of benzimidazoles anthelmintic efficacy become even more important in relation to the effect of cross-resistance leading parasites population resistant to all molecules of this class (Vera *et al.*, 2020).

Rodrigues *et al.* (2020) found that Doramectin showed an average reduction of 96% of eggs that differed from our study wherein efficiency was 13.3% (property “10”). The Doramectin used is an injectable antiparasitic with a wide spectrum with endo and ectoparasitic activities, suitable for bovine, swine and ovine. Currently, according to the inserted package of the drug, there is no recommendation to use in horses and there are few studies available regarding its efficiency, including dose and form of application. However, in a study by Pérez *et al.* (2002) considering its pharmacokinetic characteristics and anthelmintic efficacy over the main parasites of horses, showed that oral administration can be an alternative for the treatment and control of horse parasitic diseases. On the other hand, unsatisfactory levels have already been reported after deworming with Doramectin in horses (Madeira de Carvalho *et al.*, 2007).

Over the years resistance to antiparasitic drugs has been increasing and it seems that no new class of drugs is under development to use in horses in a short and medium term (Matthews, 2014), reinforcing the importance of strategic anthelmintic control programs. Early resistance detection can maintain effectiveness of certain drugs, avoiding suspension of active principles for many years. Even knowing this, the diagnosis of resistance or reduced efficacy of anthelmintics still remains poorly performed in the field as we could see in the evaluated properties in our study, wherein this monitoring has not been adopted. The horses from our study were treated every three months and different active principles were used in each deworming. Although the rapid rotation of active principles is suggested to prevent parasite resistance, no evidence was found to support it, furthermore this practice can mask the occurrence of resistance (Torres-Acosta *et al.*, 2012). Moreover, Kaplan *et al.* (2004) suggest that the greater frequency of antiparasitic

treatments, the greater likelihood of drug-resistant cyathostominae emergence.

As an alternative, drug associations have been used to control resistant parasites by increasing the effectiveness of antiparasitic treatments. When adopting treatments with associations of drugs, it is possible to maintain the recommended dosages for each drug and combine bases belonging to different chemical groups, with different action mechanisms. These differences make it difficult to adapt parasitic genotypes to treatments (Pink *et al.*, 2005). Our results, however, showed that the used drug associations were not effective (properties "1" to "6") which probably indicates that the parasitic populations of these properties have been largely exposed previously to the chemical molecules tested in this study. Association of Closantel + Albendazole, in horses, is not quite common, due to its reduced clinical safety margin and resistance to these compounds were reported in Brazil (Borges *et al.*, 2010), corroborating our results.

Regarding the combined use of Ivermectin + Praziquantel, despite results variation, no property obtained satisfactory rates with the drug, indicating anthelmintic resistance in these populations. This can be explained by the previous use of some other macrocyclic lactone, causing a cross reaction between the drugs. Still, it must be considered that Praziquantel is a broad spectrum anthelmintic against species of cestodes and trematodes, not influencing the action of Ivermectin. In contrast, in the properties where Ivermectin itself was effective, there was no use of other macrocyclic lactones previously, and there was no manifestation of the cross reaction (Molento, 2004; Molento *et al.*, 2008).

The combination of Triclorfon + Fenbendazole, despite the little use due to the narrow safety margin of Triclorfon causing episodes of colic was not effective as well. According to Lyons *et al.* (1990) the first organophosphate marketed was Triclorfon, with activity on *Gasterophilus* spp., Ascarids and *Oxyuris equi*, but not over Strongylides. Great efforts must be made to preserve the effectiveness of a few drugs that remain effective. Now and in the future, dewormers must be considered as highly valuable and limited resources. The only realistic strategy for a sustainable parasite control is to develop new non-chemical approaches that aim to lessen the

need for treatment and to use anthelmintics in a more rational way (Coles & Molento, 2008). Therefore, the performance of coprological tests is essential for monitoring the effectiveness of active principles in each property, providing a correct and effective approach to parasite control.

CONCLUSION

The observed results indicate that resistance to macrocyclic lactones is usual in equine parasites in this Brazilian region, despite the results with isolated Ivermectin.

ACKNOWLEDGEMENTS

We thank the owners and veterinarians who sent the samples for diagnosis, for the partnership and confidence in our work.

REFERENCES

- BARBOSA, F.C.; OLIVEIRA, W.J.; COSTA, P.C. *et al.* Eficácia anti-helmíntica da ivermectina em equinos: exames coproparasitológicos e hematológicos. *Cienc. Anim. Bras.*, v.9, p.1-12, 2018.
- BEVILAQUA, C.M.L.; RODRIGUES, M.L.; CONCORDET, D. Identification of infective larvae of some common nematode strongylids of horses. *Rev. Méd. Vét.*, v.12, p.989-995, 2000.
- BORGES, F.A.; NAKAMURA, A.Y.; ALMEIDA, G.D. *et al.* Eficácia de formulações anti-helmínticas comerciais em equinos no município de Douradina, Paraná. *Cienc. Anim. Bras.*, v.11, p.618-622, 2010.
- BRASIL., Ministério da Agricultura, Pecuária e Abastecimento - MAPA. Revisão do estudo do complexo do agronegócio do cavalo, 2016. Disponível em: <http://www.agricultura.gov.br/assuntos/camarassetoriaistematicas/documentos/camaras/equideocultura/anteriores/revisaodoestudodocomplexodoagronegocio-docavalo>. Acesso em: 7 jul. 2020.
- CANEVER, R.J. *Diagnóstico da resistência anti-helmíntica em ciatostomíneos de equinos por meio de testes in vivo e in vitro*. 2012. 99f. Dissertação (Mestrado em Ciências Veterinárias) - Universidade Federal do Paraná, PR.

- CANEVER, R.J.; BRAGA, P.R.; BOECKH, A. *et al.* Lack of Cyathostomin sp. reduction after anthelmintic treatment in horses in Brazil. *Vet. Parasitol.*, v.194, p.35-39, 2013.
- COLES, G.C.; BAUER, C.; BORGSTEEDE, F.H. *et al.* World association for the advancement of veterinary parasitology (WAAVP) methods for the detection of anthelmintic resistance in nematodes of veterinary importance. *Vet. Parasitol.*, v.44, p.35-44, 1992.
- COLES, G.; MOLENTO, M.B. How do we slow the development of ML resistance in cyathostomins? INTERNATIONAL EQUINE PARASITE DRUG RESISTANCE WORKSHOP, 2008, Denmark. *Proceeding...* Denmark: University of Copenhagen, 2008. p.19.
- COSTA, E.; DIEHL, G.N.; SANTOS, D.V. *et al.* Panorama da equinocultura no Rio Grande do Sul. Secretaria Estadual da Agricultura, Pecuária e Abastecimento: Informativo Técnico n.5, 2014. Disponível em: <https://www.agricultura.rs.gov.br/upload/arquivos/201612/02101333-inftec-50-panorama-da-equinocultura-no-rio-grande-do-sul.pdf>. Acessado em: 30 abr. 2020.
- GODESKI, A.; PEDRASSANI, D.; SZCZERBOWSKI, C.E. Eficácia de anti-helmínticos em equinos da raça Crioula no município de Major Vieira/SC. *Rev. Acad. Ciênc. Anim.*, v.15, p.59-66, 2017.
- GORDON, H. MCL.; WHITLOCK, H.V. A new technique four counting nematode eggs in sheep faeces. *J. Counc. Sci. Ind. Res.*, v.12, p.50-52, 1939.
- HOFFMANN, R.P. *Diagnóstico parasitismo veterinário*. Sulina: Porto Alegre, 1987
- KAPLAN, R.M. Anthelmintic resistance in nematodes of horses. *Vet Res.*, v.33, p.491-507, 2002.
- KAPLAN, R.M.; KLEI, T.R.; LYONS, E.T. *et al.* Prevalence of anthelmintic resistant cyathostomes on horse farms. *J. Am. Vet. Med. Assoc.*, v.225, p.903-910, 2004.
- LYONS, E.T.; DRUDGE, J.H.; TOLLIVER, S.C. *et al.* Anthelmintic resistance in equids. RESISTANCE OF PARASITES TO ANTIPARASITIC DRUGS ROUND TABLE CONFERENCE THE INTERNATIONAL CONGRESS PARASITOLOGY, 7., 1990, Paris. *Proceedings...* Paris: [MSD-AGVET], 1990. p.67-80.
- MADEIRA DE CARVALHO, L.M.; GILLESPIE, A.T.; SERRA, P.M. *et al.* Efficacy of the nematofagous fungi *Duddingtonia flagrans* in the biological control of horse strongylosis in the Ribatejo. *Rev. Port. Ciênc. Vet.*, v.102, p.233-247, 2007.
- MATTHEWS, J.B. Anthelmintic resistance in equine nematodes. *Int. J. Parasitol. Drugs Drug Resistance*, v.4, p.310-315, 2014.
- MOLENTO, M.B. Resistência de helmintos em ovinos e caprinos. *Rev. Bras. Parasitol. Vet.*, p.82-87, 2004.
- MOLENTO, M.B. Resistência parasitária em helmintos de equídeos e propostas de manejo. *Ciênc. Rural*, v.35, p.1469-1477, 2005.
- MOLENTO, M.B.; ANTUNES, J.; BENTES, R.N. *et al.* Anthelmintic resistant nematodes in Brazilian horses. *Vet. Rec.*, v.162, p.384-385, 2008.
- PÉREZ, R.; CABEZAS, I.; GODOY, C. *et al.* Pharmacokinetics of Doramectin and Ivermectin After Oral Administration in Horses. *Vet. J.*, v.163, p.161-167, 2002.
- PINK, R.; HUDSON, A.; MOURIÈS, M.A. *et al.* Opportunities and challenges in antiparasitic drug discovery. *Nat. Rev. Drug Discov.*, v.4, p.727-739, 2005.
- REINEMEYER, C.R. Diagnosis and control of anthelmintic-resistant *Parascaris equorum*. *Parasit. Vectors*, v.2, p.1-8, 2008.
- REHBEIN, S.; MARTIN, V.; RENATE, W. Prevalence, intensity and seasonality of gastrointestinal parasites in abattoir horses in Germany. *Parasitol. Res.*, v.112, p.407-413, 2013.

ROBERTS, F.H.Z.; O'SULLIVAN, J.P. Methods for egg counts and larval cultures for strongyles infesting the gastrointestinal tract of cattle. *Aust. J. Agric. Res.*, v.1, p.99-102, 1950.

RODRIGUES, M.; ROSA, G.M.S.; CARVALHO, C.N. *et al.* Diagnóstico de resistência parasitária em equinos da Fazenda Escola Santa Rita, (Urcamp, Alegrete-RS). SALÃO INTERNACIONAL DE ENSINO, PESQUISA E EXTENSÃO, v.1, 2020, Alegrete. *Anais...* Alegrete: UNIPAMPA, 2020.

SANTOS, D.W.; MADEIRA DE CARVALHO, L.M.; MOLENTO, M.B. Identification of third stage larval types of cyathostomins of equids: an improved perspective. *Vet. Parasitol.*, v.260, p.49-52, 2018.

TORRES-ACOSTA, J.F.; MENDOZA-DE-GIVES, P.; AGUILAR-CABALLERO, A.J. *et al.* Anthelmintic resistance in sheep farms: update of the situation in the American continent. *Vet. Parasitol.*, v.189, p.89-96, 2012.

TRAVERSA, D.; SAMSON-HIMMELSTJERNA, G.V.; JANINA, D. *et al.* Anthelmintic resistance in cyathostomin populations from horse yards in Italy, United Kingdom and Germany. *Parasit. Vectors*, v.2, Suppl.2, S2, 2009.

VERA, J.H.S.; FACHIOLLI, D.F.; RAMIRES, L.M. *et al.* Efficacy of ivermectin, moxidectin and febendazole in equine in Brazil. *Vet. Parasitol. Reg. Stud. Rep.*, v.20, 2020.