

1 **ANTHELMINTIC RESISTANCE IN SMALL RUMINANTS FROM THE SEMIARID**  
2 **OF PARAÍBA STATE, BRAZIL**

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4 **(RESISTÊNCIA ANTI-HELMÍNTICA EM PEQUENOS RUMINANTES DO**  
5 **SEMIÁRIDO DA PARAÍBA, BRASIL)**

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7 **SUMMARY**

8 This study aimed to evaluate the effect of Ivermectine 0.08% and Hydrochloride of  
9 Levamisole 5% in controlling sheep and goat gastrointestinal helminthiasis from Agreste  
10 region of Paraíba State, Northeastern Brazil. The experiment was developed from July 2011  
11 to February 2012. Were used 28 farms, with animals of both sexes and ages between three to  
12 48 months. In each farm were chosen 18 animals without anthelmintic treatments at least  
13 three months. The animals were divided into three groups: group 1, treated with Ivermectine  
14 0.08%, orally, in a single dose of 2.5 mL/ 10 kg l. w.; group 2, treated with Hydrochloride of  
15 Levamisole 5%, orally, in a single dose 1.0 mL/ 10 kg l. w. and group 3, which received no  
16 anthelmintic treatment, serving as a control group. Fecal samples were collected on days zero  
17 and ten days after treatments for fecal analysis. The treatment with Hydrochloride of  
18 Levamisole reduced 86.7% and 93% the parasite load of goats and sheep, respectively.  
19 Although, the treatment with Ivermectine reduced only 30.9% in goats and 24.6% in sheep.  
20 The most prevalent helminth gender was *Haemonchus spp.* The gastrointestinal nematodes of  
21 goats and sheep from Agreste of Paraíba State are highly resistant to Ivermectine.  
22 Hydrochloride of Levamisole is still effective in sheep, but already shows resistance traces in  
23 goats.

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25 **KEY WORDS:** Goats. helminths. ivermectine. levamisole. semiarid. sheep.

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## 30 RESUMO

31 Este estudo objetivou avaliar o efeito da Ivermectina 0,08% e do Cloridrato de Levamisole  
32 5% no controle das helmintoses gastrintestinais de ovinos e caprinos da mesorregião do  
33 Agreste do Estado da Paraíba, Nordeste do Brasil. O experimento foi desenvolvido no período  
34 de julho de 2011 a fevereiro de 2012. Foram utilizadas 28 propriedades, com animais de  
35 ambos os sexos e idades entre três e 48 meses. Em cada propriedade foram escolhidos 18  
36 animais sem tratamento anti-helmíntico a pelo menos três meses. Os animais foram divididos  
37 em três grupos: grupo 1, tratado com Ivermectina 0,08%, via oral, em dose única de 2,5 mL/  
38 10 kg p. v.; grupo 2, tratado com Cloridrato de Levamisole 5%, via oral, em dose única de 1,0  
39 mL / 10 kg p. v. e grupo 3, que não recebeu tratamento anti-helmíntico, servindo como grupo  
40 controle. Amostras fecais foram coletadas nos dias zero e dez dias após os tratamentos para  
41 realização das análises fecais. O tratamento com Cloridrato de Levamisole reduziu 86,7% e  
42 93% a carga parasitária de caprinos e ovinos, respectivamente. Entretanto, o tratamento com  
43 Ivermectina reduziu apenas 30,9% em caprinos e 24,6% em ovinos, O helminto mais  
44 prevalente nas coproculturas foi o *Haemonchus spp.* Os nematódeos gastrintestinais de  
45 caprinos e ovinos do Agreste da Paraíba encontram-se altamente resistentes à Ivermectina. O  
46 Cloridrato de Levamisole ainda é efetivo em ovinos, mas já apresenta traços de resistência em  
47 caprinos.

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49 **PALAVRAS-CHAVE:** Caprinos. helmintos. ivermectina. levamisole. ovinos. semiárido.

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## INTRODUCTION

52 The goat and sheep production occupies a prominent place in the Brazilian Northeastern,  
53 where farmers use their products in food and commerce, resulting in stability and  
54 development. In the Agreste region of Paraíba State, the small ruminant production is a viable  
55 activity, generating a major source of animal protein for human consumption. However, there  
56 are some limiting factors in the productivity of the herds, including the gastrointestinal  
57 helminthiasis, responsible for the decrease in food intake and nutrient absorption, growth  
58 retardation, decrease in the meat and milk production and mortality (LIMA et al. 2010a).

59           The main form of parasite control is done by the use of chemicals with broad spectrum  
60 of activity, most often administered empirically (CEZAR et al. 2010). Among the most  
61 widely used anthelmintics, the Ivermectine stands out, belonging to the macrocyclic lactones  
62 group, which act by opening chloride channels targeted by glutamate causing parasite  
63 neuromuscular paralysis. Another compound widely used is the Hydrochloride of Levamisole,  
64 belonging to the imidazothiazoles group, which has action on acetylcholine receptors, causing  
65 muscle contractions and worm paralysis (COLES et al. 2006).

66           The irrational use of anthelmintics has contributed to the resistance to the most available  
67 drugs of the small ruminant gastrointestinal helminthes. Several researches reports the  
68 resistance of these helminthes to Ivermectine and Hydrochloride of Levamisole in Brazil  
69 (CEZAR et al. 2010; MORAES et al. 2010; LIMA et al. 2010b), however no studies of  
70 anthelmintic resistance in the Agreste region of Paraíba State were conducted.

71           Due to lack of studies evaluating the efficacy of anthelmintics in this region, this study  
72 aimed to evaluate the effect of Ivermectine 0.08% and Hydrochloride of Levamisole 5% in  
73 the control of sheep and goats gastrointestinal helminthiasis.

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## **MATERIAL AND METHODS**

76           The experiment was conducted on farms of small ruminant production system in the  
77 Gado Bravo county, Agreste of Paraíba State, during July 2011 to February 2012. The region  
78 has a semi-arid climate, with a rainy season from April to July, which 90% of rainfall occurs  
79 and a dry season. The annual temperature average is 23,5°C (minimum of 18°C and  
80 maximum 29°C), with little variation over the year (VILELA et al. 2008). This region  
81 includes the transition zone between the moist coast and the semiarid backwoods, presenting  
82 vegetation of the Caatinga biome.

83           Were used 28 herds (504 animals), 15 producing goats and 13 sheep (270 and 234  
84 animals, respectively), of both sexes, between three to 48 months-old and without defined  
85 breed. In each herd 18 animals were chosen, they should be without anthelmintic treatment for  
86 at least three months and presenting  $OPG \geq 500$ . Subsequently, animals were individually  
87 identified and randomly assigned into three groups: group 1, treated with Ivermectine 0,08%,  
88 orally, in a single dose of 2,5 mL/ 10 kg l. w.; group 2, treated with Hydrochloride of  
89 Levamisole 5%, orally, in a single dose of 1,0 mL/ 10 kg b. w. and group 3, received no  
90 anthelmintic treatment, serving as a control group.

91           Fecal samples were individually collected on day zero and ten days after treatments and  
92 sent to the Laboratory of Parasitic Diseases of Domestic Animals of the Universidade Federal  
93 de Campina Grande (UFCG), Patos - PB, for fecal examination. Were performed the counting  
94 of Eggs Per Gram of feces (EPG), according to Whitlock & Gordon (1939) and larval culture,  
95 according to Roberts & O'Sullivan (1950).

96           The Fecal Egg Count Reduction test (FECR) was performed according to Coles et al.  
97 (1992). Subsequently, the data were subjected to one-way variance analysis, and followed by  
98 Tukey test at 5% probability. The EPG values were analyzed using logarithmic  
99 transformation  $\log(x + 1)$ , however, are present as arithmetic averages of untransformed  
100 values. The analyses were performed using the BioEstat 5.0 Software. The efficacy of the  
101 drugs was based on Technical Regulation Ordinance N°. 48/1997 of the Ministério da  
102 Agricultura, Pecuária e Abastecimento (MAPA) for chemicals endowed with antiparasitic  
103 activity using the following criteria: is highly effective when it reduces more than 98%; 90-  
104 98% effective, moderately effective 80-89% and insufficiently active <80% (BRASIL, 1997).

105           This research was submitted to the Research Ethics Committee of UFCG and obtained  
106 the protocol number 017/2012.

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## RESULTS

Was observed a statistical difference ( $p < 0,05$ ) between the goat and sheep anthelmintic treatments (Table 1).

Table 1. Values of EPG e FECR of goat and sheep submitted to anthelmintic treatments in the Agreste region of Paraíba State, Brazil.

Groups	Goats			Sheep		
	0	10	FECR	0	10	FECR
Ivermectine 0,08%	5376 <sup>Aa</sup>	4081 <sup>Ab</sup>	30,9%	1800 <sup>Aa</sup>	1255 <sup>Ba</sup>	24,6%
Hyd. of Levamisole 5%	5516 <sup>Aa</sup>	783 <sup>Bc</sup>	86,7%	1521 <sup>Aa</sup>	116 <sup>Bb</sup>	93,0%
Control	5798 <sup>Aa</sup>	5914 <sup>Aa</sup>	-	1682 <sup>Aa</sup>	1665 <sup>Aa</sup>	-

Values followed by the same letters maiuscle in lines and minuscule in columns did not statistically differ ( $p > 0,05$ ) – Tukey's test.

Was observed that the Ivermectine 0,08% EPG did not reduced satisfactorily, especially in sheep, where this was not statistically different ( $p > 0,05$ ) than the control group. Hydrochloride of Levamisole 5% was the best treatment, differing significantly ( $p < 0,05$ ) from the other groups in EPG values post-treatment in both species.

According to Brasil (1997), Ivermectine was insufficiently active in goats (30,9%) and sheep (24,6%). Hydrochloride of Levamisole already appeared moderately effective in goats (86,7%) and effective in sheep (93%).

The helminths percentages recovered from fecal cultures are described in Table 2.

130 Table 2. Percentages of gastrointestinal helminths recovered from fecal cultures of goat and  
 131 sheep submitted to anthelmintic treatments in the Agreste region of Paraíba State, Brazil.

		Control		Ivermectine 0,08%		Hyd. of Levamisole 5%	
		0	10	0	10	0	10
Goats	H	70	68	78	56	38	42
	T	25	31	20	34	60	51
	S	0	1	2	4	0	2
	O	5	0	0	6	2	5
Sheep	H	40	49	35	53	45	63
	T	55	38	58	34	40	37
	S	2	11	3	10	11	0
	O	3	2	4	3	4	0

132 H: *Haemonchus* spp.; T: *Trichostrongylus* spp.; S: *Strongyloides* spp.; O: *Oesophagostomum*  
 133 spp.

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135 The most prevalent helminth gender in fecal cultures was *Haemonchus* spp., followed  
 136 by *Trichostrongylus* spp., *Strongyloides* spp., and *Oesophagostomum* spp.

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## 138 DISCUSSION

139 It was observed that the Ivermectine 0,08% do not satisfactorily reduced the animals  
 140 worm burden, with reductions of only 30,9% in goats and 24,6% in sheep. High anthelmintic  
 141 resistance was also observed by Lima et al. (2010a), when evaluating the efficacy of  
 142 Ivermectine 0.02% in goat herds from Cariri region of Paraíba State, obtaining reduction of  
 143 50,1%. Pereira et al. (2008), evaluated this anthelmintic in goats and sheep from Rio Grande  
 144 do Norte State, Brazil, showed a reduction of only 14,2% and 20 7% respectively. However,  
 145 George et al. (2011) evaluated the Ivermectine in sheep from Trinidad and Tobago getting 95-  
 146 97% of FECR, showing up effective. Lima et al. (2010b) in Pernambuco State, Brasil,

147 observed that Ivermectine showed an efficacy of 67,33% in goats, indicating resistance,  
148 although in sheep presented 100% of efficacy considering highly effective.

149 Several studies have confirmed the resistance of gastrointestinal helminthes of small  
150 ruminants to Ivermectine worldwide (LIFSCHITZ et al. 2010; LIMA et al. 2010a;  
151 LEATHWICK et al. 2012).

152 The Hydrochloride of Levamisole 5% showed reductions of 86,7% and 93% for sheep  
153 and goats, respectively, similar to which was observed by Rodrigues et al. (2007), when tested  
154 this anthelmintic in goats from the Sertão region of Paraíba, with 93.3% of efficiency. Duarte  
155 et al. (2012), testing this anthelmintic in Northern of Minas Gerais State, Southeastern Brazil,  
156 achieved efficacy ranging from 90% to 100%. However, Leathwick et al. (2012) observed  
157 anthelmintic resistance to this anthelmintic (efficacy<70%) in New Zealand sheep and George  
158 et al. (2011) observed efficacies between 53% to 81% in sheep from Trinidad and Tobago.

159 The resistance traces to Hydrochloride of Levamisole 5% observed in some farms may  
160 be due to its low efficacy against immature stages of nematodes in general (MELO et al.  
161 2003).

162 The most prevalent helminth gerder was *Haemonchus* spp., corroborating with Vilela et  
163 al. (2012). Probably, this worm acquires faster resistance due to its high biotic potential, a  
164 high genetic variability as well as hosting the allele that causes decreased susceptibility to a  
165 drug (BLACKHALL et al. 1998). Besides *Haemonchus* spp. were found *Trichostrongylus*  
166 spp. and *Strongyloides* spp. and, to a lesser extent, *Oesophagostomum* spp. Similar  
167 percentages of these helminths were also observed in other studies conducted in Northeastern  
168 Brazil (LIMA et al. 2010a; COSTA et al. 2011).

169 Several factors contribute to the development of anthelmintic resistance and  
170 consequently inefficiency of antiparasitic drugs. The indiscriminate use of these drugs most  
171 often occurs by the producers lack of knowledge, poor management practices and the ease in

172 acquiring these drugs. According to Vilela et al. (2012), the high resistance to anthelmintics  
173 observed in studies conducted in semi-arids regions of Northeastern Brazil may be occurs due  
174 to the fact that it is a common practice the deworming of all the small ruminant herds four to  
175 six times per year.

176 Must be widespread the idea that the anthelmintic control based only on massive herd  
177 deworming is a wrong practice. The control must be integrated, where alternative forms of  
178 control such as the use of anthelmintic plants, the Famacha<sup>®</sup> method and/ or in the near future,  
179 nematophagous fungi, along with synthetic anthelmintics and also associated with good  
180 practices of herd management are the solution to minimize the effects of gastrointestinal  
181 helminthiasis.

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## CONCLUSION

184 The goats and sheep gastrointestinal nematodes of the Agreste region of Paraíba State  
185 are highly resistant to Ivermectine 0,08%. Resistance traces to Hydrochloride of Levamisole  
186 5% were observed in goats.

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