



## BIOOTHERAPY EFFECTIVENESS IN THE TREATMENT AGAINST TICKS IN DOMESTIC DOGS

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Recebido em: 15/08/2022 – Aprovado em: 15/09/2022 – Publicado em: 30/09/2022  
DOI: 10.18677/EnciBio\_2022C10

### ABSTRACT

Ticks are ectoparasites that can infest various domestic animals. There is concern about the side effects that chemical antiparasitics cause in animals, despite these drugs being approved by regulatory bodies and considered safe by health professionals. Biotherapeutics have been presented as a safe and effective alternative for treating ticks. This retrospective study evaluated the efficacy of biotherapeutic use against ticks in naturally-infested domestic dogs. Sixty-four *Canis familiaris* animals were divided into the test group (biotherapy) and the control group (fipronil). The evaluation followed the criteria: initial and final degree of parasitism, presence or absence. The intensity of the following signs was evaluated in the presence of ectoparasites: pruritus, respiratory distress, alopecia, vomiting, and diarrhea; as well as the way and the difficulty in administration. At the end of the study, it can be concluded that the test product (biotherapy) was more effective in the treatment against ticks with a reduction in the level of parasitism of 84.7% against 70.8% of the control group.

**KEYWORDS:** Biotherapy; Canine; Ectoparasitosis.

### INTRODUCTION

Dogs are the pets most adapted to human habitation worldwide and have contributed to the physical, social and emotional well-being of their owners, being associated with the highest level of self-esteem. However, some animal ectoparasites can infest humans and lead to the development of dermatitis or other diseases (KRISHNA MURTHY et al., 2017).

Ticks are ectoparasites that can infest various domestic and wild animals and even humans and are a public health concern due to the high risk of transmitting diseases such as spotted fever, babesiosis and others (BOOZER; MACINTIRE, 2005; MADISON-ANTENUCCI et al. 2020). Several species of ticks can parasitize domestic animals, specifically dogs and cats (BOOZER; MACINTIRE, 2005; MADISON-ANTENUCCI et al. 2020).

*Rhipicephalus sanguineus* is the most prevalent tick species on domestic dogs in different Brazilian states (RIBEIRO et al., 1997; SANTOS et al., 2022). Tick control is carried out using conventional chemical acaricides, which have the disadvantage of toxic effects (FIGUEIREDO et al., 2018).

The indiscriminate use of parasiticides and their probable relationship with resistant tick populations has caused concern, since it results in greater complications in the fight against these parasites (SANTOS et al., 2018). In 2015, a study looked at how regularly and at what intervals antiparasitic drugs were being used to control ectoparasitosis, as well as which types of drugs were used most frequently for dogs and cats. The study showed that of the 92.2% of dogs being treated, 50.5% were treated at monthly intervals (all year round or seasonally), with imidacloprid with permethrin being the predominant combination used (89%). Only 28.4% of dogs were protected uninterruptedly throughout the year against fleas, ticks, sandflies, and mosquitoes. Only 63.6% of cats were treated with ectoparasitic drugs, 44.4% of which were treated with imidacloprid (MATOS et al., 2015).

Researchers have also demonstrated the high risks of developing side effects in animals when administering anti-parasitic drugs such as 1% injectable moxidectin. An evaluation carried out on dogs and rabbits showed that 14% of animals had to stop treatment due to side effects (WAGNER; WENDELBERGER, 2000). Important cholinergic side effects have been caused by antiparasitic drugs for the treatment of canine babesiosis, such as: diminazene, azithromycin, imidocarb, atovaquone and trypan blue. There is also a list of side effects caused by diminazene: anaphylaxis, convulsions, vomiting, pain and salivation, although in most cases the parasites have not been completely eliminated (BOOZER; MACINTIRE, 2005).

A survey aimed at assessing how pet owners choose to treat their pets with antiparasitic drugs showed concern about the side effects that chemical antiparasitic drugs cause in animals, despite these drugs being approved by regulatory bodies and considered safe by professionals in the field (BEBRYSZ et al., 2021). The great challenge for the pharmaceutical industry is to discover molecules with the ability to eliminate parasites, but not harm or affect the hosts, especially using the fewest doses and with ease of application. However, it is recognized that this is not always possible with the chemical antiparasitic drugs traditionally used (WOODS; KNAUER, 2010).

Historically, the legacy left by Hippocrates was the definition of treatment based on three basic principles: *Natura medicatrix* - nature restoring health; *Contraria Contrariis* - the law of opposites, where symptoms are treated with medicines that fight symptoms in the opposite way to them; and *Similia Similibus* - the law of similars, where a disease should be treated with something similar to it. The medicine of opposites, widely disseminated by Galen, was the one that prevailed for approximately 1,500 years and is still the most commonly applied type of medicine for treating diseases, known generically as allopathy (CHAUÍ, 1994), but not the only one. Paracelsus tended towards treatment by the like-minded as early as the 16th century, and this current has still aroused interest (CORRÊA et al., 1997). The application of the law of similars in the treatment of parasites in animals has been evident for some years. Among the various categories of these medicines, the group of biotherapeutics stands out, medicines that are prepared from the etiological agent itself (SCHIMIDT, 2021).

Treatment with tick biotherapeutics significantly reduced the mass of engorged females and the deposition and hatching rate, consequently resulting in a reduction in the reproductive efficiency of these parasites (GAZIM et al., 2010). Other research

has shown how dynamized drugs, whether biotherapies or other dynamized preparation methods, have treated ticks adequately and efficiently, whether in large or small domestic animals (FIGUEIREDO et al., 2018; PAIXÃO et al., 2021).

The aim of this study was to carry out a retrospective study to evaluate the effectiveness of biotherapeutics for treating ticks in naturally infected dogs.

## MATERIAL AND METHODS

A retrospective study was carried out using a database from 2010 from a veterinary clinic located in the municipality of Niterói- RJ. This study only included records that had complete information on the domestic dogs, the type of treatment used, the presence or absence of environmental treatment, information on the intensity of initial and final parasitism classified according to a scale ranging from nil (-) to very intense (++++); clinical signs of pruritus, difficulty breathing, alopecia, vomiting, diarrhea; as well as data on the form and difficulty of administration.

Information was obtained from 64 records of animals of the *Canis familiaris* species. The records were divided into two groups for comparative analysis, where 32 records were of animals treated with biotherapeutics based on the ticks *Amblyomma cajenense*, *Rhipicephalus sanguineus* sensu lato and *Rhipicephalus (Boophilus) microplus*, for 30 days at a dose of two globules per animal per day, regardless of weight, given directly into the mouth, in the drinking water or together with the feed. Another 32 records were of animals treated with the drug fipronil in a solution ranging from 0.25% to 10% depending on the veterinary prescription.

The data obtained from the animals treated with the biotherapeutic were compared with those obtained from the animals treated with fipronil. The aim was to obtain information on the therapeutic efficacy of the natural product in comparison with the widely used allopathic product.

## RESULTS AND DISCUSSION

Considering the animals included in this study, it was possible to verify that the initial parasitism ranged from intense to very intense in 47.61% of the animals (n=30), in which 53.05% were treated with biotherapeutic and 39.25% were treated with fipronil, thus, it is possible to consider that the group that received biotherapeutic had a greater challenge compared to the fipronil group (Table 1).

**TABLE 1** - Indication of the number of animals treated with biotherapeutics and animals treated with fipronil according to the intensity of initial parasitism.

	BIOTERAPIC		FIPRONIL
	Number of animals	%	Number of animals
(-) null	6	18,7%	4
(+) light	4	12,5%	9
(++) moderate	5	15,6%	6
(+++ ) intense	10	31,3%	8
(++++ ) very intense	7	21,9%	5

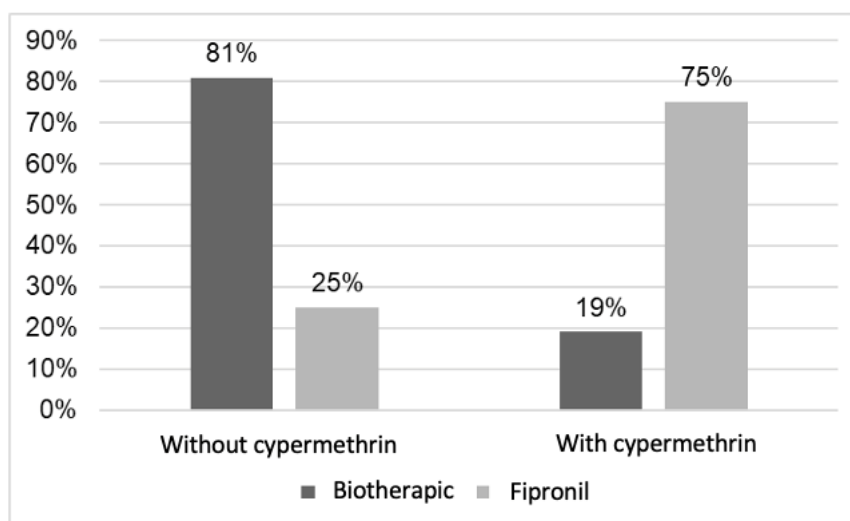
The *Rhipicephalus sanguineus* is the most common species to affect domestic dogs. It is also known as the brown tick and can be found on wild animals and occasionally on humans. This tick can be found on dogs living in urban or rural areas and is adapted to living in homes, being active all year round (DANTAS-TORRES, 2010), living in shelters and remaining in nests waiting for the host (GRAY et al., 2013). The brown tick is known as a vector for pathogens such as *Babesia*

*canis*, *Ehrlichia canis* in dogs and *Rickettsia conorii*, which causes spotted fever in humans (GRAY et al., 2013). Due to their importance in veterinary and human medicine, it is important to control these parasites in animals and the environment.

The database did not contain information on the species of tick present on the animals, but it is known that other species can affect peri-urban or rural dogs in addition to *Rhipicephalus sanguineus*, such as *Amblyomma cajanense* (COSTA et al., 2017) and *Rhipicephalus (Boophilus) microplus* (MISRA et al., 2021). The action of the biotherapies used in this study was produced from nosodes of the ticks *Rhipicephalus sanguineus*, *Amblyomma cajanense* and *Rhipicephalus (Boophilus) microplus*, the action of biotherapies is an approach based on isopathy in which agents that cause a disease or imbalance are used to treat the same disease (SANTOS et al., 2015).

The commonly used animal treatment is fipronil. However, some authors have shown that it can be toxic to mammals (SUZUKI et al., 2021). Thus, the aim of this study was to show that biotherapeutic drugs already on the market can be an effective natural option for treating ticks in various animal species. According to the information obtained, 30 had undergone environmental treatment using cypermethrin. Of these, 19% were being treated with biotherapeutics and 75% with fipronil (Figure 1).

**FIGURE 1** - Graph showing the distribution of cypermethrin use in the environment of animals treated with biotherapeutics or fipronil.



The use of environmental treatment was not an exclusion criterion in this study, since this pesticide is easily obtained by owners from agricultural stores without the need for a prescription. Despite the need for environmental tick control, cypermethrin has a toxic effect on humans and animals and, considering that it has no antidote, toxicity can lead to death (SHARMA et al., 2018).

When analyzing the effectiveness of the treatment after 30 days of drug administration, it was possible to see that the parasites were completely eliminated in 23 animals treated with biotherapeutic (72%) and 16 animals treated with fipronil (50%). The level of parasitism was also assessed in the animals where the ticks were not completely eliminated. The remaining ticks in the animals treated with biotherapeutic ranged from mild (22%) to moderate (6.25%), as in the fipronil group, but these had a higher number of parasitized animals (40.6% and 9.4% respectively).

Table 2 shows the superior effectiveness of the biotherapeutic, as its action was not directly related to the application of cypermethrin in the environment, since only 19% of the owners who were using biotherapeutic treatment on their animals used this product in the environment, while 75% of the owners of animals treated with fipronil chose to use this method as an aid in combating tick infestation in their animals.

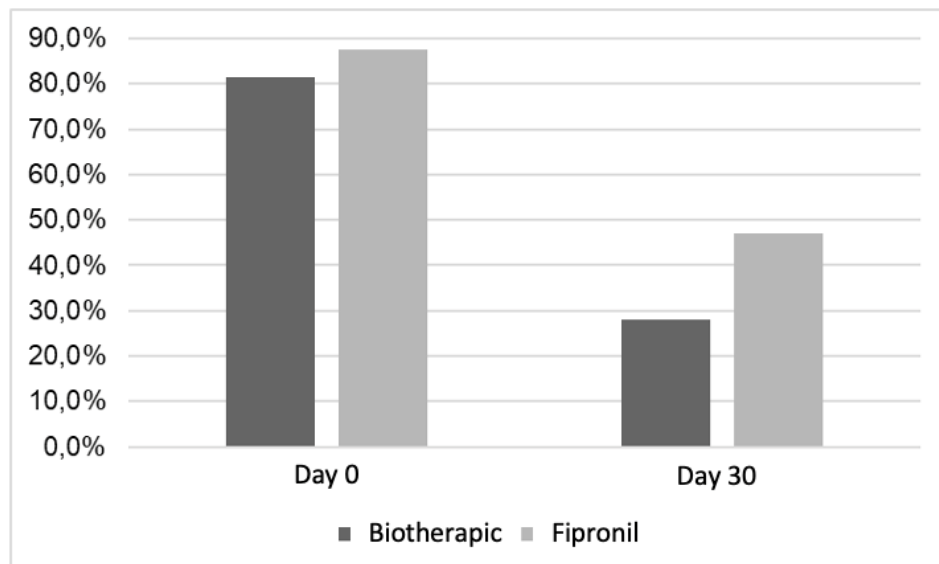
**TABLE 2** - Initial and final parasitism intensity and ratio of application of environmental treatment with cypermethrin obtained from the follow-up forms of animals treated with biotherapeutic or fipronil.

Identification card	BIOTHERAPIC			FIPRONIL		
	Initial parasitism	Final parasitism	Environmental treatment	Initial parasitism	Final parasitism	Environmental treatment
1	++++	+	N	+++	+	Y
2	+++	-	N	++	+	N
3	-	-	N	++	-	Y
4	+	+	N	++++	+	N
5	+++	-	Y	+	-	Y
6	+++	++	N	+	-	Y
7	++++	+	N	-	-	Y
8	-	-	N	+++	+	Y
9	+	-	N	+	-	N
10	+	+	N	+++	++	N
11	+++	-	Y	+++	+	Y
12	+++	-	N	++	+	Y
13	+++	+	N	+	-	Y
14	++++	-	N	-	-	Y
15	++++	-	N	-	+	N
16	+++	-	N	++	-	Y
17	-	-	N	++++	++	N
18	-	-	N	+++	+	Y
19	++++	-	N	+	-	Y
20	+++	-	Y	++++	+	Y
21	++	-	Y	++	-	Y
22	+++	++	N	++	-	Y
23	-	-	Y	+	-	Y
24	++++	-	N	+	-	Y
25	++	+	N	+	-	N
26	++	-	N	+++	+	Y
27	++	-	N	+++	-	Y
28	+	-	N	++++	+	Y
29	-	-	N	-	+	Y
30	++	+	N	+	-	Y
31	++++	-	Y	+++	+	Y
32	+++	-	N	++++	++	N

Where: (-) none; (+) mild; (++) moderate; (+++) intense; (++++) very intense; (Y) yes; (N) no.

The reduction in the level of parasitism of the test group (84.7%) was greater than that of the control group (70.8%) as shown in figure 2. Santos et al. (2015) showed that the use of biotherapeutics was able to reduce the infestation of *R. (B.) microplus* in naturally infested cattle, demonstrating that this is a promising alternative for tick control. Gazim et al. (2010) showed that the use of biotherapeutics reduced the reproductive efficiency of *R.(B.) microplus* ticks when the biotherapeutic treatment was added to mineral salt in naturally infested Dutch cows and Paixão et al. (2021) showed that *R.(B.) microplus* parasitism was controlled in a field test with the use of biotherapeutics, affirming the possibility of establishing this new methodology for controlling tick parasitism in cattle in the field.

**FIGURE 2** - Graph showing the degree of parasitism of animals treated with biotherapeutic or fipronil on day 0 (initial parasitism) and day 30 (after 30 days of treatment).



The use of natural treatments seeks less interference from chemical products, being a less aggressive way and aiming at the well-being and safety of the animals (BRACCINI et al., 2019). Biotherapeutics act on ticks by interrupting the cycle and reducing infestation in the environment. The ticks encounter the blood and consequently with the treatment, causing them to die and then disconnect from the host, falling to the ground (GEMELLI; PEREIRA, 2018).

Tick engorgement occurs during the last 24 hours of feeding, in which the females obtain 2 to 8 times more blood, gain weight, multiply their body mass with lipid-rich protein. Whereas this enables the production of thousands of eggs, it is nevertheless a crucial process for tick survival (KRÖBER; GUERIN, 2007). Since the biotherapeutic acts in the blood sputum phase, it reduces the ticks' reproductive efficiency by simultaneously treating the animal and the environment in a natural way.

During the clinical assessment of the animals after 30 days of treatment, the owners reported mild clinical signs in 6 animals treated with biotherapeutics. In the animals treated with fipronil, 8 animals showed moderate (21.5%) and mild (78.5%) signs, with vomiting and alopecia being the most frequent, which could be related to the toxic effects of topical fipronil (Table 3).

**TABLE 3** - Symptoms reported by guardians after 30 days of treatment with biotherapeutic or fipronil, obtained from the animal monitoring forms.

Identification	BIOTHERAPIC					FIPRONIL				
	P	DB	A	V	D	P	DB	A	V	D
1	-	-	-	-	-	+	-	+	+	-
2	-	-	-	+	-	-	-	-	-	-
3	-	-	-	-	-	-	-	-	-	-
4	-	-	-	-	-	-	-	+	-	-
5	-	-	-	-	-	-	-	-	-	-
6	-	+	-	+	-	-	-	-	-	-
7	-	-	-	-	-	-	-	-	-	-
8	-	-	-	-	-	-	-	-	-	-
9	-	-	-	-	-	-	-	-	-	-
10	-	-	-	-	-	-	-	++	-	-
11	-	-	-	-	-	+	-	-	-	-
12	-	-	-	-	-	-	-	-	-	-
13	-	-	-	-	-	-	-	-	-	-
14	-	-	-	-	-	-	-	-	-	-
15	-	-	-	-	-	-	-	-	-	-
16	-	-	-	-	-	-	-	-	-	-
17	-	-	-	-	-	+	-	-	++	-
18	-	-	-	+	-	-	-	-	-	-
19	+	-	-	-	-	-	-	-	-	-
20	-	-	-	-	-	-	-	-	-	-
21	-	-	-	-	+	-	-	-	-	-
22	-	-	-	+	+	-	-	-	-	-
23	-	-	-	-	-	+	-	-	-	-
24	-	-	-	-	-	-	-	-	-	-
25	-	-	-	-	-	-	-	-	-	-
26	-	-	-	-	-	-	-	-	-	-
27	-	-	-	-	-	-	-	+	-	-
28	-	-	-	-	-	+	+	-	++	+
29	-	-	-	-	-	-	-	-	-	-
30	-	-	-	-	-	-	-	-	-	-
31	-	-	-	-	-	-	-	-	-	-
32	-	-	-	-	-	-	-	-	-	-

Where: (-) nil; (+) mild; (++) moderate; (P) pruritus; (DB) difficulty breathing; (A) alopecia; (V) vomiting; (D) diarrhea.

Fipronil belongs to the group of chemicals based on phenylpyrazole and is responsible for blocking GABA neurotransmitters, eliminating ectoparasites by hyperexcitation without them biting the animal, acting by contact. Due to its toxic effects, some authors recommend that it should not be used on domestic animals where the owners spend a lot of time caring for or handling the treated animals (TINGLE et al., 2003).

It is worth pointing out that owners need guidance on the correct use of the different drugs. For animals treated with the biotherapeutic, it is necessary to inform them that the same care should be taken with the medication as with homeopathic medicines for human use, which is generally to avoid proximity to electro-electronic devices, due to the electromagnetic field generated by these, to avoid proximity to products that give off a strong smell and also, in the case of administration in drinking water, not to place the medication in aluminum or other metal bowls.

Considering that the indiscriminate use of chemical agents affects the environment, animals and people, and following evidence of the positive action of biotherapeutics on ticks (GAZIM et al., 2010; SANTOS et al., 2018; PAIXÃO et al., 2021), they can be considered an alternative medicine for tick control, as they reduce the negative impact of the use of chemical products on human and animal health.

## CONCLUSION

According to the results observed, it was concluded that the biotherapeutic was safe, with similar or better results than the conventional drug, and that it was easy to apply. The biotherapeutic proved to be advantageous in that it made it unnecessary to apply products to the environment as auxiliaries and therefore had zero environmental impact in helping to combat ticks on animals.

## ACKNOWLEDGMENTS

The authors would especially like to thank Multiboi Nutrição Animal (GO) for providing the biotherapeutic samples for the evaluations and the Pet Life clinic (ES) for access to the data already collected.

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