

# Efficacy of fluralaner against canine generalized demodicosis

## Eficácia do fluralaner contra demodicose canina generalizada

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### Abstract

Demodicosis is a parasitic dermatopathy, resulting from the excessive proliferation of *Demodex* mites. The rate at which this disease is encountered in the pet clinic is high, despite recent advances in the treatment of the disease. The aim of this study, which was conducted in Brazil, was to analyze the efficacy of fluralaner in the treatment of demodicosis in dogs. Fifteen dogs with generalized demodicosis that were diagnosed with *Demodex* sp. mites from skin scraping were included. All animals were treated with fluralaner at a dose of 25 mg / kg, following the manufacturer's recommendations for the treatment of ectoparasites. The effectiveness of the treatment was evaluated based on clinical improvement of the animals and the time required to obtain two consecutive negative skin scrapes 30 days apart (parasitological cure). The main clinical signs observed were alopecia (100%; 15/15); erythema (86.7%; 10/15); and hypotrichosis, papule, crusts, hyperpigmentation, and hyperkeratosis (26.7%; 4/15). Of the 15 animals evaluated, two of them were excluded for not returning for the second evaluation in 60 days, although they had the first negative skin scrape. After 30 days, six (46.2%) from 13 animals that concluded the study presented the first negative skin scraping. At the end of the study, all dogs presented parasitological cure and clinical improvement, except for three animals. One for developing atopic dermatitis and two that lived in an animal shelter. In conclusion, a single oral dose of fluralaner is effective in the treatment of generalized demodicosis in dogs.

**Keywords:** dogs, acaricidal, isoxazolines.

### Resumo

Demodicose é uma dermatopatia parasitária, decorrente da proliferação excessiva de ácaros do gênero *Demodex*. A doença apresenta alta ocorrência na clínica de animais de companhia, apesar dos recentes avanços no tratamento da doença. O objetivo deste estudo controlado, realizado no Brasil, foi reportar a eficácia do fluralaner, no tratamento da demodicose em cães. Foram incluídos 15 cães apresentando demodicose generalizada, diagnosticados com ácaros do gênero *Demodex*, a partir do raspado cutâneo. Todos os animais foram tratados com fluralaner na dose de 25 mg/kg, seguindo as recomendações do fabricante para o tratamento de ectoparasitos. A eficácia do tratamento foi avaliada pela melhora clínica dos animais e o tempo necessário para a obtenção de dois raspados negativos consecutivos com intervalo de 30 dias (cura parasitológica). Os principais sinais clínicos observados foram alopecia (100%; 15/15); eritema (86,7%; 10/15); e hipotricose, pápulas, crostas, hiperpigmentação e hiperqueratose (26,7%; 4/15). Dos 15 animais avaliados, dois deles foram excluídos do estudo por não retornarem para a segunda avaliação em 60 dias, embora tivessem apresentado um raspado negativo. Após 30 dias, dos 13 animais que concluíram o estudo, (46,2%; 6/13) apresentaram o primeiro raspado negativo. Ao final do período experimental, todos os animais apresentaram cura parasitológica e melhora clínica, exceto em três animais, um por apresentar atopia posteriormente e outros dois casos, cujo animais eram oriundos de abrigo. Conclui-se que que uma única dose oral do fluralaner é efetiva no tratamento da demodicose generalizada em cães.

**Palavras-chave:** cães, acaricida, isoxazolina.



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## Introduction

Demodicosis is considered the most prevalent parasitic skin disease (Delayte, 2016) and is characterized by the presence of larger than normal numbers of demodectic mites diagnosed by deep skin scrapings (Miller et al., 2013).

Treatment of this dermatopathy is multimodal and includes acaricidal therapy, treatment of concurrent bacterial skin infection, internal parasitism and identification of underlying systemic disease (Mueller et al., 2012). The therapeutic end-point is determined by multiple negative skin scrapings, in addition to resolution of clinical signs (Mueller et al., 2012).

Over the years, treatment with topical amitraz (Ghubash, 2006; Kosh et al., 2012) and macrocyclic lactones such as avermectins and milbemycins (Sartor & Santarem, 2006; Singh et al., 2011) have been used as acaricidal therapy. However, the possibility of developing adverse effects, due to its administration, has been described (Sartor e Santarem, 2006; Delayte et al., 2006; Singh et al., 2011). Additionally, macrocyclic lactones are not indicated for use in dogs with a mutation of ABCB1-1 (MDR-1) gene (Ghubash, 2006; Kosh et al., 2012).

Recently, it was discovered that oral administration of isoxazolines, a class of drugs that act as potent blockers of the GABA gated chloride channel (Lahm et al., 2013), has a remarkable effect on fleas and ticks (Mctier et al., 2016). Fluralaner belongs to this new class and has prolonged activity against fleas and ticks after a single oral dose (Kilp et al., 2014) of 25 mg/kg, with no adverse effects observed during a safety trial, even at higher doses (Walther et al., 2014). No side effects were observed by the authors of previous studies either (Taenzler et al., 2014; Wengenmayer et al., 2014; Fourie et al., 2015). However, one study reported inappetence, vomiting, and diarrhea (Rohdich et al., 2014). The bioavailability of fluralaner was increased when administered with food (Walther et al., 2014).

This compound was successfully used in parasitic skin diseases as miticidal therapy for sarcoptic mange (Romero et al., 2016) and demodicosis (Fourie et al., 2015; Duangkaew et al., 2018). Against generalized demodicosis, its administration resulted in 99.8% reduction of the mean mite observed by skin scrapings 28 days after treatment, while a 100% reduction was observed in 56 days after treatment (Fourie et al., 2015). In comparison, treatment with ivermectin can take up to 90 days to obtain the first negative skin scraping (Delayte et al., 2006). Arias & Cordero (2016) reported fluralaner efficacy with its administration at 2-month intervals to treat this skin disease. Recently, in Brazil, there is a report on the efficacy in two generalized demodicosis cases treated with fluralaner (Bezerra et al., 2017).

As fluralaner is a new medication, there are only few publications that employ different treatment protocols. However, the aim of the current study was to assess the efficacy of oral fluralaner administration against 15 cases of generalized demodicosis.

## Material and methods

The present study was a multicenter retrospective study involving two clinics (The Dermatology Service at the Universidade Federal Rural do Rio de Janeiro Veterinary Hospital and the Dermatology Service at the Universidade Severino Sombra Veterinary Clinic) and two dog shelters in Brazil. This study was submitted and approved by the Veterinary institute Ethics Committee (CEUA-4851170317 and CEUA 040/2018).

Fifteen dogs diagnosed with demodicosis by deep skin scrapings that were positive for *Demodex* mites (immature or adult) were included in the present study. Five dogs were from a dog shelter. All of them presented with the clinical signs of generalized demodicosis, showing lesions such as alopecia, hypotrichosis, erythema, comedones, scale, and crusts involving an entire body region, pododemodicosis, or at least five localized lesions. Breed, sex, and age were recorded. Dogs that were receiving immunosuppressive drugs or those treated with acaricidal therapy within 60 days were not included.

Fluralaner was orally administered with food, at a dose of 25 mg/kg, following the manufacturer's recommendation. Fourteen dogs were bathed with benzoyl peroxide 2.5% shampoo and one dog was bathed with chlorhexidine 3% shampoo every 7 days. Dogs with superficial or deep pyoderma received systemic antimicrobial therapy.

Deep skin scrapings were performed in all dogs on day 0 and every 30 days, until the occurrence of two consecutive negative scrapings. Parasitological cure was considered if two deep skin scrapings were negative at 1-month interval. Samples were collected from five lesion areas, approximately 1 cm<sup>2</sup> each, using a scalpel blade. The skin was squeezed during the scrapping and examined using a microscope under 40x or 100x magnification to observe immature or adult *Demodex* mites, in order to classify as positive or negative. The clinical signs and dermatological lesions were evaluated and recorded on day 0 and on the same day of skin scrapings.

For statistical analysis, Fischer's exact test was used to compare deep skin scrapings (negative or positive) before and after treatment and the presence of skin lesions before and after treatments, with P values  $\leq 0.05$  were considered significant.

## Results

Fifteen dogs were included in the present study. Data on animals, such as sex, age, classification of lesions, and follow-up of animals after treatment are described in Table 1. The age ranged from 6 months to 7 years, with 14 (93.33%) dogs aging up to 1 year old and only one (6.66%) being 7 years old. Seven were female (47%) and 8 were male (53%).

Breeds included were American Bully (2), beagle (1), Teckel (1), Frenchie bulldog (1), Pinscher (1), Pit bull (2), Pug (1), Shih-tzu (1) and mixed breed dog (5). Dogs living in a dog shelter corresponded to 33% (5/15), while 67% (10/15) were household. The most frequent skin lesion observed were alopecia 100% (15/15), followed by erythema 86.7% (13/15) and hypotrichosis, papule, crusts, hyperpigmentation, and hyperkeratosis 26.7% (4/15). Other lesions observed were scale and pustule (20%; 3/15) and comedo, ulcer, and collarette (6.7%; 1/15). Two dogs that already had negative skin scrapings as of 30 days after medication were lost to follow-up; thus, they were excluded from the study.

All patients (100%) showed negative skin scrapings after the treatment, with 46.15% (6/13) obtaining their first negative skin scraping after 30 days, and second scraping on day +60, as described in Table 1. On day 30, it was observed that two dogs had full recovery of skin lesions (13.33%). All dogs showed clinical improvement on day 30, and 69.23% (9/13) showed clinical cure.

**Table 1.** Clinical presentation of dogs diagnosed with demodicosis evaluated until parasitological cure.

Animal	Breed	Age	Sex	Clinical finding	Scrap days		
					Day +30	Day +60	Day +90
1	SRD	3y	M	Alopecia, ulcer, crusts	-	-*	-
2	SRD	3y	M	Alopecia, erythema, hyperkeratosis	-	-*	-
3	SRD	1y	M	Erythema, papules, pustule, alopecia	-	-*	-
4	SRD	1y	F	Descamation, erythema, alopecia, hyperkeratosis	+	-	-*
5	Beagle	7y	M	Alopecia, erythema, hyperpigmentation	-	-*	-
6	SRD	1y	F	Descamação, erythema, alopecia, hyperkeratosis	+	-	-*
7*	Teckel	6m	M	Papule, hypotrichosis, erythema, alopecia	-	Exc	Exc
8	Frenchie bulldog	8m	M	Pustule, papule, erythema, alopecia	-	-*	-
9	Pinscher	2y	M	Hypotrichosis, alopecia, pustule, erythema, hyperpigmentation, hyperkeratosis	+	-	-*
10*	Pit bull	7m	F	Alopecia, erythema, hypotrichosis, comedos	-	Exc	Exc
11	Pit bull	6m	F	Alopecia, erythema, Crusts	+	-	-*
12	Pug	7m	F	pustule, alopecia, erythema	+	-	-*
13	Shih tzu	7y	M	Alopecia, crusts, hyperpigmentation, descamation	+	-	-*
14	American bully	6m	F	papules, pustule, alopecia, erythema, hypotrichosis	+	-	-*
15	American bully	4m	F	crusts, descamation, erythema, alopecia	-	-*	-

Age: (m) months; (y) years; Sex: (M) male; (F) female; (Exc) animal excluded; (\*) Parasitological cure.

For 53.8% (7/13) of the animals, the first negative scraping was observed in the second clinical examination, on day +60. These animals had a second negative scrape on day +90, including the six animals that had already showed two consecutive negative scrapes on day +60. All animals followed up until the end showed parasitological cure on day +90, a date that is recommended by manufacturer for another drug administration. For 23.1% (3/13), even after presenting their third negative skin scraping after 90 days still presented with skin lesions. However, one was later diagnosed with atopic dermatitis and the other two showed some significant improvement. No adverse effects were observed throughout the treatment.

## Discussion

Generalized demodicosis usually starts in dogs aged 3 to 18 months (Miller et al., 2013), as in this study, with most of the dogs aging up to 1 year old. As observed in this study, erythema, alopecia, papules, and crusts are described as clinical signs of canine demodicosis (Mueller et al., 2012; Miller et al., 2013).

The efficacy of the treatment of demodicosis with isoxazolines has been described (Six et al., 2016; Snyder et al., 2017; Lebon et al., 2018). The oral treatment of this disease with fluralaner was effective as observed by other authors (Fourie et al., 2015; Bezerra et al., 2017; Duangkaew et al., 2018) with a single-dose administration. All the dogs obtained negative deep skin scrapings.

In most of the dogs (60%) after 30 days of treatment, it was not observed no *Demodex* mite and after 60 days, all the patients had negative skin scrapings. Bezerra et al. (2017) reported negative deep skin scraping after 75 days, although it was not tested after 30 days of In one study, reduction in mean mite number was observed in 99.8% of treatment. cases after 28 days of treatment and in 100% after 56 days of treatment (Fourie et al., 2015); this finding is in line with the observation that on day 60, there was no positive deep skin scraping. One limitation of this study was the lack of mean mite numbers obtained in each evaluation. Ivermectin is one of the drugs commonly used to treat this disease and it was observed that the first skin scraping took 90 days to turn negative (Delayte et al., 2006), unlike the results observed with fluralaner.

The good clinical response in most of the patients also corroborates the efficacy of the treatment, which has been reported by other authors as well (Fourie et al., 2015; Bezerra et al., 2017). The fact that one of the dogs did not show a full recovery may be explained by the diagnosis of atopic dermatitis at a later stage, which had erythema and alopecia among the skin lesions commonly observed (Salzo, 2016). The two other cases were from a dog shelter, which favors stress situation and may explain the delay in improvement.

As observed by other authors (Taenzler et al., 2014; Wengenmayer et al., 2014; Fourie et al. 2015), no side effects were observed in the current study. The drugs normally used to treat generalized demodicosis may have some side effects (Sartor e Santarem, 2006; Singh et al., 2011, Delayte et al., 2006); however, fluralaner treatment was both effective and safe.

## Conclusion

In conclusion, a single oral dose of fluralaner may be effective in treating canine generalized demodicosis.

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