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Assessment of the anti-feeding and insecticidal effects of the combination of dinotefuran, permethrin and pyriproxyfen (Vectra® 3D) against *Triatoma infestans* on rats

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Abstract. This study, based on the rat model, was designed to explore the anti-feeding and insecticidal efficacy of a topical ectoparasiticide, dinotefuran–permethrin–pyriproxyfen (DPP), against *Triatoma infestans* (Hemiptera: Reduviidae), a vector of *Trypanosoma cruzi* (Trypanosomatida: Trypanosomatidae), for which dogs are domestic reservoir hosts. Twenty rats were divided into two equal groups: untreated and treated. Each rat was exposed under sedation to 16 *T. infestans* of mixed life stages for 1 h on days 1, 7, 14, 21 and 28 post-treatment. The anti-feeding and insecticidal effects of DPP were estimated after 1 h of exposure. Insecticidal efficacy was also assessed after incubation of the insects for 24 h post-exposure. Anti-feeding efficacy was 96.7, 84.7, 80.5, 81.5 and 42.6% on days 1, 7, 14, 21 and 28, respectively. Insecticidal efficacy evaluated at 1 and 24 h after exposure on days 1, 7, 14, 21 and 28 was 100, 91.2, 82.5, 80.0 and 29.1, and 100, 100, 100, 96.0 and 49.9%, respectively. This study demonstrates that a single administration of DPP spot-on treatment at a dose equivalent to the minimal recommended dose in rats has a powerful effect against *T. infestans* starting from day 1 that lasts for at least 3 weeks.

Key words. *Triatoma infestans*, *Trypanosoma cruzi*, ectoparasiticide, efficacy, rat model.

Introduction

Chagas' disease, also known as American trypanosomiasis, is a tropical parasitic disease caused by the protozoan *Trypanosoma cruzi*. An estimated 6 million people infected with *T. cruzi* currently reside in the endemic regions of Latin America [World Health Organization (WHO), 2015]. The protozoan parasite *T. cruzi* is mainly transmitted through the faeces or urine of infected blood-sucking insects of the family Reduviidae, subfamily Triatominae (WHO, 2016). Triatomine bugs, especially *Triatoma infestans* and *Rhodnius prolixus* (Hemiptera:

Reduviidae), are considered to be the most relevant vectors of *T. cruzi* because of their anthropophily, high density in peridomestic areas, good adaptation to human dwellings and *T. cruzi* vectorial capacity (Noireau *et al.*, 2009), as well as for their wide geographic distribution, principally in Latin America (Noireau, 2009). It is important to stress that the vector elimination programme started in 1991 that aimed to eradicate Chagas' disease in Southern Cone countries such as Argentina, Bolivia, Brazil, Chile, Paraguay and Uruguay produced good results in terms of the elimination of *T. infestans* in some South American countries. For example, the greatest successes were obtained

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by Uruguay in 1997, Chile in 1999 and Brazil in 2006, all of which were certified by the Pan American Health Organization (PAHO)/WHO as free from *T. infestans* (Dias, 2009; Abad-Franch *et al.*, 2013). However, it is important that these countries remain vigilant if they are to avoid the reintroduction of *T. infestans*, which still exists in Argentina, Bolivia, Paraguay and Peru, and of other species that have not been eliminated (Abad-Franch *et al.*, 2013).

Triatoma infestans prefers to feed on humans and domestic animals in homes. It derives its bloodmeals from four main sources: humans, chickens, dogs and cats (Gürtler *et al.*, 2014; Provecho *et al.*, 2014; Coura, 2015; Cecere *et al.*, 2016). *Triatoma infestans* nests in thatched or straw roofs, in the crevices of mud walls, and in cement and brick. Other than vector control with insecticides, there is no way to control Chagas' disease, no vaccine and no effective treatment for chronic forms (WHO, 2006). Because triatomines can live in homes, prevention includes cleaning, the use of mosquito nets and insecticidal treatment of the premises. This prophylaxis gives results, but resistance to mono-insecticides has been detected (Gomez *et al.*, 2015; Mougabure-Cueto & Picollo, 2015) and some insecticides, such as spinosad and indoxacarb, are not effective against triatomine bugs (Carvajal *et al.*, 2012). In the last decade, field and laboratory studies have reported high levels of resistance to deltamethrin in *T. infestans* in Argentina and Bolivia (Picollo *et al.*, 2005; Toloza *et al.*, 2008). Indeed, pyrethroids are the insecticides most commonly used for the chemical control of the vector (WHO, 2006).

Dogs have been shown to be often involved in outbreaks of Chagas' disease (Castillo-Neyra *et al.*, 2015; Gürtler & Cardinal, 2015). The role of the dog in the parasitic cycle is now better understood as a result of molecular biology studies on the blood of dogs (Enriquez *et al.*, 2014; Gürtler & Cardinal, 2015). Mathematical modelling predicts that the elimination of infected dogs from a household with infected people could be sufficient to limit the transmission of *T. cruzi* (Cohen & Gürtler, 2001). This suggests that preventive treatment of dogs using an ectoparasiticide may minimize the risk for transmission of *T. cruzi* to humans. Fipronil-(S)-methoprene spot-on treatment is not recommended in dogs for this purpose because of its limited and transient effect on triatomine bugs (Gürtler *et al.*, 2009) and because of high inter-individual variability (Amelotti *et al.*, 2012). Although the use in dogs of a deltamethrin-based application on collars reduced the survival and fecundity of triatomine bug populations, no difference in insect feeding was noticed between untreated and deltamethrin-treated specimens (Reithinger *et al.*, 2006). Collectively, these data emphasize that currently there are no drug treatments (ectoparasiticides) that effectively prevent triatomine bugs from blood feeding on pets. From the point of view of veterinary medicine, the prevention of triatomine bug bites is essential to the prevention of Chagas' disease in dogs. Infection is more common in puppies than in adult dogs and often presents in the acute form. Symptoms are similar to those in humans and include myocarditis (most commonly), hepatomegaly, splenomegaly, lymphadenopathy, anorexia, weight loss, diarrhoea, hypothermia and dehydration (Snider *et al.*, 1980; Barr *et al.*, 1995; Kjos *et al.*, 2008; Barr, 2009).

Dinotefuran, pyriproxyfen and permethrin (DPP; Vectra® 3D; Ceva Santé Animale SA, Libourne, France) can be combined in a topical ectoparasiticide for dogs. This has been reported to be an efficient repellent and adulticide against ticks, fleas, mosquitoes, stable flies and sandflies for up to 1 month (Coyne, 2009; Franc *et al.*, 2012; Varloud & Hodgkins, 2015; Varloud *et al.*, 2015a) and for up to 2 months against immature stages of fleas (Bouhsira *et al.*, 2012). However, the protective effectiveness of DPP against *T. infestans* in animals has not yet been tested. The aim of the present study was thus to explore the anti-feeding and insecticidal effects of a DPP topical administration in rats against *T. infestans* bugs for up to 4 weeks after administration.

Materials and methods

Animals and ethical approval

Twenty adult (aged 6 weeks) male Sprague–Dawley rats (Charles River Laboratories, Saint-Germain-Nuelles, France), with a mean \pm standard deviation (SD) weight of 160.7 ± 3.6 g, were housed in groups of two individuals per cage ($58 \times 36 \times 20$ cm³) at a temperature of 22 °C under an LD 12 : 12 h cycle. Rats were fed an appropriate maintenance ration of commercial food pellets. Water was available *ad libitum*. The rats were handled according to French rules on the protection of animals used for scientific purposes (decree no. 2013-118; 1 February 2013, Paris) (Legifrance, 2015). The protocol for this study was reviewed and approved by the Ethics Committee for Animal Experimentation at Aix-Marseille University (approval no. 2015090110122337). General health observations were performed at least twice per day from the start of the acclimation period to the end of the study.

Source of *T. infestans*

Adult *T. infestans* (CEPEIN susceptible strain) were taken from a laboratory colony initiated in 2009 using adult specimens sourced from Argentina. Since then, this colony has been reared at the laboratory without exposure to any insecticides. All bugs were reared in the laboratory's insectarium at 26 ± 1 °C and $70 \pm 1\%$ relative humidity (RH). The bugs were fed with defibrinated human blood (under an agreement with the Etablissement Français du Sang) using a Hemotek membrane feeding system (Discovery Workshops, Accrington, U.K.). Nymph instars and adults of both sexes were used in the present study. Each rat was exposed to a total of 16 triatomine bugs, including 12 nymph instars (three specimens of each of stages 2, 3, 4 and 5) and four adult triatomines. All bugs were starved for 15 days before they were given access to the rats.

Treatment

The minimum recommended dose in dogs [i.e. 6.4 mg/kg body weight (BW) of dinotefuran, 0.6 mg/kg BW of pyriproxyfen

and 46.6 mg/kg BW of permethrin] was used to determine the dose to be administered to rats with a mean \pm SD weight of 160.7 ± 3.6 g. As the dose per kilogram BW for one species cannot be transposed to another species, it was decided that doses expressed in mg/kg BW for dogs should be converted to equivalent doses based on body surface area in rats and expressed as mg/m² as previously described by Freireich *et al.* (1966). The minimal recommended dose of DPP was therefore estimated to be 0.07 mL per rat. All doses were administered on day 0 and were applied directly to the skin as a line-on treatment along the spine using a micropipette to ensure accurate and complete dosing. Treated rats were observed several times per day for 15 min after treatment for general health status and any adverse events that might be associated with the administration of the agent.

Exposure of rats to *T. infestans*

Before exposure, all rats were anaesthetized with an intraperitoneal injection of a combination of 90 mg/kg ketamine (Imalgene[®] 500; Merial, Lyon, France) and 10 mg/kg xylazine (Rompun[®] 2%; Bayer Santé Animale, Lyon, France). Each rat was placed in a transparent plastic container ($50 \times 20 \times 20$ cm³) in which it was then exposed for 1 h to starved nymph instars ($n = 12$) and male and female adults ($n = 4$) on days 1, 7, 14, 21 and 28 post-treatment. The whole experiment was conducted in a slightly darkened room at a mean \pm SD temperature of 22 ± 1 °C. After the 1-h exposure period, the bugs were categorized and counted as fed or unfed and dead or live. Live bugs from each group were maintained in separate incubators and survival rates at 24 h after the end of the exposure were recorded (Fig. 1).

Statistical analysis

In the present study, each rat represented the experimental unit. The primary endpoints were the fed and live bug counts. The arithmetic mean numbers of engorged bugs and live bugs were calculated at each time-point. Anti-feeding and insecticidal efficacies were calculated using Abbott's formula (Abbott, 1987) as:

$$\text{Anti-feeding efficacy (\%)} = 100 \times \frac{\text{MCe} - \text{MTe}}{\text{MCe}}$$

where MCe represents the mean [geometric mean (GM) or arithmetic mean (AM)] number of fed bugs in the control (untreated) group, and MTe represents the mean (GM or AM) number of fed bugs in the treated group and:

$$\text{Insecticidal efficacy (\%)} = 100 \times \frac{\text{MCi} - \text{MTi}}{\text{MCi}}$$

where MCi represents the mean (GM or AM) number of live bugs in the control (untreated) group, and MTi represents the mean (GM or AM) number of live bugs in the treated group.

Statistical analyses were performed using STATISTICA Version 6.1 (StatSoft, Inc., Tulsa, OK, U.S.A.; www.statsoft.com). At

each time-point, differences between treated and untreated rats were compared using Student's *t*-test. Statistical significance was declared at a two-sided *P*-value of 0.05.

Results

No adverse effects of treatment were observed in any of the treated rats. The proportions of fed bugs in the untreated groups ranged from 94.3 to 99.3%, with an average of $97.2 \pm 1.9\%$, throughout the study (Table 1). In both groups, *T. infestans* bugs introduced into the plastic containers holding the rats immediately attacked the rats. Bugs showed conspicuous signs of feeding after 10–20 min of exposure to untreated control rats. Generally, adult bugs fed longer than instar nymphs. It was noted that the bugs always defecated on the rats while feeding. In the treated rats, bugs expressed signs of intoxication such as inconsistent movements, unfolding of the rostrum, swelling of the abdomen and shiny cuticle. It is important to note that no blood was observed when a needle was pressed into the swollen abdomen in such bugs. In treated rats, the proportions of fed bugs were 3.1, 15.0, 19.3, 18.1 and 55.0% on days 1, 7, 14, 21 and 28, respectively (Table 1).

Fed bug counts were significantly lower for DPP-treated rats than for untreated control rats ($P < 0.0001$) at all time-points. The anti-feeding efficacy of DPP was high at 96.7, 84.7, 80.5 and 81.5% on days 1, 7, 14 and 21, respectively, and decreased to 42.6% on day 28 (Table 2). At 1 and 24 h post-exposure, the AMs of live bugs were significantly lower for DPP-treated rats than for untreated control rats ($P < 0.0001$) throughout the study (Table 2). Insecticidal efficacy evaluated at 1 h after exposure ranged between 80.0 and 100% up to day 21 and declined to 29.1% at 28 days after treatment, whereas insecticidal efficacy assessed 24 h after exposure remained above 96.0% until day 21 and declined to 49.9% at 28 days after treatment (Table 3). No difference in treatment sensitivity was observed between adults and instar nymphs.

Discussion

Animal models can provide preliminary and complementary information that is useful in further testing on targeted animals. In the present study, a rat model was selected to explore the anti-feeding and insecticidal efficacy of DPP against *T. infestans*. Previous studies have demonstrated the possibility of extrapolating the results obtained in mice treated with a mosquito repellent to humans (Reifenrath & Rutledge, 1983; Rutledge *et al.*, 1994). Although representativeness can be questioned, the information collected from the models is definitely useful in terms of optimizing the designs of experiments in the target animals.

In the present study, the feeding rate of *T. infestans* on control rats exceeded 94.0% at all five time-points tested (Table 1). This strong feeding rate showed that the population of *T. infestans* used in the experiment was robust and the challenge was reliable. This is consistent with previous observations in experiments conducted in *Triatoma rubrofasciata* fed on Swiss mice (Braga & Lima, 1999) and *T. infestans* fed on Sprague–Dawley rats,

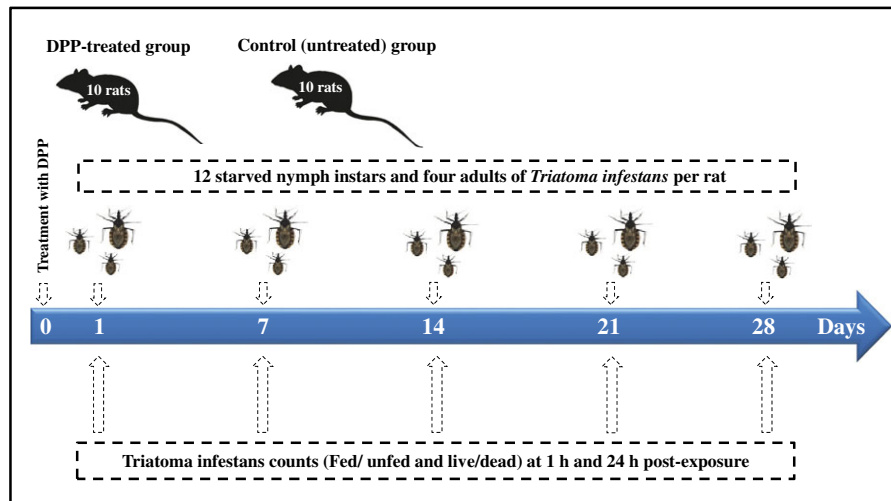


Fig. 1. Schematic representation of the experimental design. DPP, dinotefuran, permethrin and pyriproxyfen. [Colour figure can be viewed at wileyonlinelibrary.com].

Table 1. Feeding and mortality rates in *Triatoma infestans* (12 nymph instars and four adults per rat) on rats untreated (control group; $n = 10$) and treated ($n = 10$) with a combination of dinotefuran, permethrin and pyriproxyfen.

Exposure day	Feeding rate, % (n)		Mortality rate, % (n)			
	Untreated group	Treated group	1 h		24 h	
			Untreated group	Treated group	Untreated group	Treated group
1	96.2% (154)	3.1% (5)	0	100% (160)	1.8% (3)	100% (160)
7	98.1% (157)	15.0% (24)	0	91.2% (146)	3.1% (5)	100% (160)
14	99.3% (159)	19.3% (31)	0	82.5% (132)	5.6% (9)	100% (160)
21	98.1% (157)	18.1% (29)	0	79.3% (127)	4.3% (7)	96.2% (154)
28	94.3% (151)	55.0% (88)	0	28.1% (45)	3.1% (5)	50.6% (81)

Table 2. Anti-feeding efficacy against *Triatoma infestans* (12 nymph instars and four adults per rat) on rats untreated (control group; $n = 10$) and treated ($n = 10$) with a combination of dinotefuran, permethrin and pyriproxyfen.

Exposure day	<i>T. infestans</i> feeding, AM \pm SD		Repellency efficacy, %
	Untreated group	Treated group	
1	15.4 \pm 0.8	0.5 \pm 0.7	96.7%*
7	15.6 \pm 0.6	2.4 \pm 0.9	84.7%*
14	15.8 \pm 0.3	3.1 \pm 1.2	80.5%*
21	15.7 \pm 0.4	2.9 \pm 1.6	81.5%*
28	15.1 \pm 1.1	8.8 \pm 1.5	42.6%*

*Significant difference between the treated and untreated (control) groups ($P < 0.0001$).

AM, arithmetic mean; SD, standard deviation.

in which more than 86% of bugs were seen to bite the host (Canals *et al.*, 1999). The single topical treatment of DPP had an immediate effect after administration, as demonstrated by the high anti-feeding efficacy (> 80%) that started at day 1 and lasted until day 21 after treatment. The anti-feeding effect decreased to 42.6% at 28 days after treatment (Table 2). If such a decrease in efficacy were to be confirmed in dogs

at the appropriate dose, DPP could be safely reapplied at 3-week intervals (Coussanes *et al.*, 2015). This anti-feeding performance were not observed in previous studies assessing the effects of deltamethrin-based collars (Reithinger *et al.*, 2005, 2009) or fipronil-(S)-methoprene spot-on treatment (Gürtler *et al.*, 2009) on dogs or with imidacloprid spot-on applied to pigeons (Carvajal *et al.*, 2014). This high level of anti-feeding efficacy of DPP can be explained by the synergistic action of dinotefuran and permethrin against insects at the tested ratio (Varloud *et al.*, 2015a, 2015b). The administration of DPP will prevent bugs from taking bloodmeals from treated animals (dogs) and is expected to reduce the transmission of *T. cruzi* to and from dogs, which are considered to represent the pathogen's main domestic reservoir (Reithinger *et al.*, 2005, 2006; Amelotti *et al.*, 2012).

The feeding rates of *T. infestans* on DPP-treated rats at days 1, 7, 14, 21 and 28 were 3.1, 15.0, 19.3, 18.1 and 55.0%, respectively. These were lower than that reported in a previous dog study in which another insecticide (deltamethrin) of the second-generation pyrethroids was tested on dogs against *T. infestans* bugs using deltamethrin-impregnated dog collars (Reithinger *et al.*, 2005). The earlier results showed feeding rates of 97, 93, 91, 93 and 85% in dogs wearing deltamethrin-impregnated collars, and 99, 100, 97, 91 and 90%

Table 3. Insecticidal efficacy against *Triatoma infestans* (12 nymph instars and four adults per rat) on rats untreated (control group; $n = 10$) and treated ($n = 10$) with a combination of dinotefuran, permethrin and pyriproxyfen at 1 and 24 h post-exposure.

Exposure day	Live <i>T. infestans</i> , AM \pm SD				Insecticidal efficacy, %	
	1 h		24 h		1 h	24 h
	Untreated group	Treated group	Untreated group	Treated group		
1	16	0	15.7 \pm 0.6	0	100%*	100%*
7	16	1.4 \pm 1.2	15.5 \pm 0.8	0	91.2%*	100%*
14	16	2.8 \pm 1	15.1 \pm 1.1	0	82.5%*	100%*
21	15.8 \pm 0.4	3.3 \pm 0.5	15.3 \pm 0.9	0.6 \pm 0.8	80.0%*	96.0%*
28	16	11.5 \pm 2	15.5 \pm 0.8	7.9 \pm 1.6	29.1%*	49.9%*

*Significant differences between the treated and untreated (control) groups ($P < 0.0001$). AM, arithmetic mean; SD, standard deviation.

in control dogs on days 0, 15, 30, 60 and 90, respectively. However, over the 90-day period, the average engorgement rate on collared dogs remained significantly lower at 30.8% compared with 55.2% on control dogs (Reithinger *et al.*, 2005). Similar results were reported in another study in which the proportion of feeding bugs was significantly lower (92.2%) on collared dogs than on control dogs (95.1%) over the entire 126-day observation period (Reithinger *et al.*, 2006). It is important to stress that the collars (i.e. impregnated with 40 mg/g deltamethrin) are effective for up to 6 months (Reithinger *et al.*, 2006).

Survival rates of *T. infestans* on the untreated control rats were also satisfactory, with over 98 and 93% surviving until 1 and 24 h, respectively, after the end of the exposure period (Table 1). These data validate the level of challenge in the present study. Although the treatment was applied at the lowest recommended dose, DPP exhibited high insecticidal efficacy against the bugs. Efficacy exceeded 80.0 and 96.0% at 1 and 24 h post-exposure from day 1 and over the 21-day period, respectively. It declined to 29.1 and 49.9% at 1 and 24 h post-exposure on day 28, although mortality remained significant.

The combination of dinotefuran with permethrin at the ratio used in the DPP combination led to a synergistic effect, inducing a faster onset and residual killing activity against insects (Varloud *et al.*, 2015b). The percentages of bugs that died at 24 h post-exposure on days 1, 7, 14, 21 and 28 after treatment in the treated group were 100, 100, 100, 96.2 and 50.6%, respectively. These were higher than the rate reported by Reithinger *et al.* (2006), who tested deltamethrin-based collars on dogs against *T. infestans*. Their results showed that 23.9% of bugs died over the entire 126-day observation period. The insecticidal effect of DPP was also higher than that reported for fipronil-(S)-methoprene spot-on for dogs tested against *T. infestans* (Gürtler *et al.*, 2009). These authors' results showed that cumulative mean bug mortality after exposure differed significantly only at 1 week after treatment, when mortality was 18.7% in bugs infesting dogs treated with fipronil-(S)-methoprene and 4.4% in bugs infesting control dogs. Another study conducted in both laboratory and field conditions tested the efficacy of liquid fipronil (1.0%) against *T. infestans* nymphs on dogs, chickens and goats. Its results showed nymphal mortality of 100% after 7 days and 88.8% after 30 days in the laboratory assessments, and a 65.4% decrease in triatomine density after 30 days in field experiments

(Gentile *et al.*, 2004). Even when applied as a spot-on in pigeons at a massive dose (158 mg/kg pigeon), imidacloprid did not provide insecticidal efficacy that lasted over 7 days after administration, although the exposure of bugs to the active ingredient (imidacloprid) was maximized by exposing the insects to the pigeons at the site of administration of the product (Carvajal *et al.*, 2014). Data for the performance of DPP obtained in rats cannot be directly compared with data recorded for fipronil-(S)-methoprene or deltamethrin-based products used in dogs or with data for imidacloprid applied to pigeons. Such differences can be explained by both methodological and product effects. To the present authors' knowledge, this is the first time that a dinotefuran-based combination has been tested against triatomine bugs. Dinotefuran is a furanicotinyl belonging to the third generation of neonicotinoids and is known as a fast-acting insecticide (Wakita *et al.*, 2005). When it is combined with permethrin, the effect of dinotefuran against insects is enhanced at the ganglionic synaptic level, resulting in increases in depolarization and desensitization (Varloud *et al.*, 2015b). When cis-permethrin or deltamethrin were used alone against *T. infestans* nymphs, parasite recovery was observed (Alzogaray & Zerba, 1997). In the present experiments, the bugs did not recover. This lethal effect of DPP is assumed to be linked to the synergistic combination of dinotefuran and permethrin.

Despite the success in eliminating *T. infestans* from Uruguay, Chile and Brazil, triatomine bugs remain widespread and continue to pose serious problems in other countries of the Southern Cone of South America, such as Bolivia, Argentina, Paraguay and Peru. The species is almost exclusively domestic in all of these countries. In outbreaks, particularly in Argentina, where Chagas' disease is transmitted by *T. infestans*, dogs and cats represent domestic reservoirs of *T. cruzi* infection (Cardinal *et al.*, 2007). Levels of canine seroprevalence to *T. cruzi* are high in 15 countries and vary from 8 to 50% across various surveys, which are often conducted using different techniques (Barbabosa-Pliego *et al.*, 2011; Berrizbeitia *et al.*, 2013; Chikweto *et al.*, 2014; Tenney *et al.*, 2014; Alroy *et al.*, 2015; Gürtler & Cardinal, 2015; Saldaña *et al.*, 2015). Dogs should be prevented from becoming infected by restraining their access to ecosystems that feature vector bugs. The protection of dogs using a residual insecticide applied as a spot-on treatment should be strongly recommended in high-risk areas. Studies in Argentina have helped to highlight the correlation between the

number of infected dogs in homes and the number of human cases (Gürtler *et al.*, 2005). Similarly, in Brazil, infection (both acute and chronic) of children is linked to that of dogs (Mott *et al.*, 1978). This is why the prevention of blood feeding on dog hosts is a primary target in the fight against Chagas' disease transmission to humans.

Conclusions

The present study demonstrates that at the dosages tested, DPP has reliable anti-feeding and insecticidal effects against *T. infestans*. Indeed, the anti-feeding effect of DPP against bugs may increase the risk to humans of contracting the parasite because if *T. infestans* is unable to feed on treated dogs, it will bite another host, such as a human. However, the powerful insecticidal efficacy of the product offsets this effect because it will reduce the population of bugs in homes, thus reducing insect bites to humans. On rats, these two efficacy parameters persisted at > 80% for at least 3 weeks after treatment and both actions were detected at significant levels for at least 1 month. Although such results require further investigation in the target species, the tested dose was designed to be representative of the minimal recommended dose in dogs. Consequently, these results are expected to represent a reliable estimate of the anticipated performance of DPP on dogs against triatomine bugs. The preventive treatment of non-infected dogs with DPP may protect them from contact with triatomines and reduce the risk for transmission of certain zoonotic agents to humans.

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DT conceived the study design, performed the experiments, carried out data analysis and interpretation and wrote the first draft of the manuscript. BD participated in the study design, the experiments and in the writing of the manuscript. JMB produced triatomines and participated in the revision of the manuscript. MV was involved in studying designing, interpreting data and revising the manuscript. LA participated in data analysis and revision of the manuscript. DR facilitated the implementation of the work. PP participated in the study design, in data analysis and critically revised the manuscript. All authors have read and approved the final version of the manuscript.

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