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Effects of topical application of fipronil spot-on on dogs against the Chagas disease vector *Triatoma infestans*

Ricardo E. Gürtler[a,*], Leonardo A. Ceballos[a], Raúl Stariolo[b], Uriel Kitron[c], Richard Reithinger[d,e]

[a] *Laboratory of Eco-Epidemiology, Department of Ecology, Genetics and Evolution, Universidad de Buenos Aires, 1428 Buenos Aires, Argentina*
[b] *National Vector Control Coordination, Center for Chagas Disease Reservoirs and Vectors, 9 de Julio 356, 5000 Córdoba, Argentina*
[c] *Department of Environmental Studies, Emory University, Atlanta, GA, USA*
[d] *George Washington University School of Medicine and Health Sciences, Washington DC, USA*
[e] *Department of Infectious & Tropical Diseases, London School of Hygiene & Tropical Medicine, London WC1E 7HT, UK*

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Summary We assessed the insecticidal effects of fipronil spot-on applied to experimental dogs on the blood-feeding success and other vital parameters of the *Trypanosoma cruzi* vector *Triatoma infestans*. In the first trial, the cumulative mortality of 30 third or fourth instar nymphs exposed to eight fipronil-treated dogs differed significantly from those exposed to untreated dogs at 1 week post-treatment, but not at baseline or at 2—6 weeks post-treatment. In the second trial, the effects of multiple exposures to fipronil-treated dogs on bug population dynamics were assessed. A population of 80—84 bugs of various life stages were allowed to colonize eight closed experimental huts, and then exposed twice weekly to control or treated dogs over a period of 110 days and censused at monthly intervals. Throughout the trial, multiple exposure to fipronil did not significantly affect bug population size, fecundity, hatching, molting, survival, blood-feeding success and degree of engorgement. Only when engorgement was taken to include only fully fed bugs, did fipronil significantly reduce their degree of engorgement relative to bugs exposed to control dogs. We conclude that at tested dosages fipronil spot-on would have little effect in controlling (peri)domestic *Tri. infestans* or protecting dogs from contact with the bugs.

* Corresponding author. Tel.: +54 11 4576 3318; fax: +54 11 4576 3384.
E-mail address: gurtler@ege.fcen.uba.ar (R.E. Gürtler).

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1. Introduction

Prevention of transmission of *Trypanosoma cruzi*, the causal agent of Chagas disease, has relied on residual spraying of households with insecticides to eliminate triatomine bugs and on screening of blood donors. A series of intergovernmental initiatives dramatically reduced the prevalence and incidence of *Tryp. cruzi* infections in a number of Latin American countries.[1] Nevertheless, some endemic regions (e.g. Gran Chaco, Argentina) are currently experiencing renewed transmission to humans 3—5 years after cessation of control activities as recurrent domestic recolonization by triatomine bugs occurs.[2] For such areas, simple, safe and effective control tools that can be used by the affected communities for the extended surveillance phase, after insecticide spraying campaigns have been completed, are urgently required.[3]

Domestic dogs, cats, goats and chickens play a key role in the eco-epidemiology of Chagas disease as frequent sources of blood meal for triatomine bugs, and dogs and cats are major domestic reservoirs of *Tryp. cruzi*.[2,4,5] Mathematical modeling predicts that elimination of infected dogs from a household with infected people could be sufficient to almost extinguish transmission of *Tryp. cruzi*, barring reintroduction of infected dogs or bugs.[6] For practical reasons and due to lack of adequate tools, Chagas disease control programs have not considered targeting infected domestic animal reservoirs through culling or treatment with the available anti-*Tryp. cruzi* drugs. Yet, treating domestic dogs with deltamethrin-impregnated collars significantly reduced the feeding success of *Triatoma infestans* and eliminated infestations in closed experimental huts.[7,8] The recent emergence of pyrethroid resistance in *Tri. infestans* in northern Argentina and Bolivia,[9] combined with the low effectiveness of residual spraying with pyrethroid insecticides in peridomestic structures,[10] promoted the search for cost-effective alternative tactics. One possible approach is the application of powder or systemic formulations to the domestic animals themselves (xenointoxication), which then would act as baited lethal traps.[11]

One candidate for xenointoxication is fipronil, a phenylpyrazole insecticide that is highly effective against a broad range of hematophagous arthropods. Fipronil exerts no adverse effects on dogs, cats, goats and people at the recommended low doses, but shows low toxicity to waterfowl and is highly toxic to fish, lizards and gallinaceous birds.[12] Fipronil has a slow lethal activity on triatomine bugs as a spray formulation, and residual effects on mud blocks may persist for up to 3 months post-treatment.[13] A topical formulation of 1% fipronil pour-on in a single dose at 1 mg/kg on a dog, a cat, and a chicken against six third-instar nymphs of *Tri. infestans* exposed to each host was estimated to be 100% and 89% effective at 7 and 30 days post-treatment, respectively.[14] In the same study, a topical application of fipronil pour-on on four dogs, one cat and two chickens residing in an infested rural house was considered to have reduced peridomestic bug densities by 65% (relative to pre-treatment bug densities) at 30 days post-treatment at the end of fall (i.e. June 2003).[14] Both studies have some caveats because they (i) were based on a before-and-after study design, (ii) had a very small sample size, (iii) lacked replicates and (iv) did not include negative controls (i.e. untreated infested compounds). Despite the concerns expressed and limited evidence,[14] provincial vector control programs in Salta and Santiago del Estero (Argentina) started to treat dogs with fipronil pour-on with the expectation of eliminating (peri)domestic bug infestations. In this study we assessed the effects of fipronil spot-on on the vital parameters of *Tri. infestans* when the bugs were exposed once or repeatedly to the dogs.

2. Materials and methods

2.1. Test insecticide

The test insecticide was fipronil spot-on (Frontline Plus, 10% (w/v) fipronil, 9% (*S*)-methopren; Merial Argentina, Martínez, Buenos Aires, Argentina; lot 003/05; manufactured May 2005, expiry date May 2007). Fipronil spot-on for dogs also includes the insect growth regulator methoprene, which interferes with development in insects, including triatomine bugs.[15] According to the manufacturer, a topical application of fipronil is effective against ticks and fleas for up to 1 month post-application. Fipronil was administered with a pipette provided by the manufacturer (up to 10 kg of body weight, pipette size was 0.67 ml; 10—20 kg, 1.34 ml) by parting the dogs' hair on the back midline following manufacturer's instructions.

2.2. Study site and protocol

The trials were carried out in the field station run by the Argentinian National Vector Control Program in Punilla, Province of Córdoba (31°14′S, 64°28′W) between 24 August and 5 December 2006. Study location, design of experimental huts and experimental set-up have been comprehensively described previously.[7,8,16] A total of 25 small experimental huts (80 cm × 80 cm × 80 cm with a 40 cm-wide entrance) simulating typical mud-and-thatch houses are kept for research purposes in a 50 m^2 fenced compound under natural climatic conditions. Hut internal structure is such that bugs cannot escape when released inside the huts. Weather conditions during each bioassay were measured using data loggers (HOBO H08; Onset, Bourne, MA, USA).

Eight adult mongrel dogs (6—18 kg) were used in the trial. All dogs had been exposed to *Tri. infestans* and had worn deltamethrin-impregnated collars for a 3-month period up to September 2005.[8] When *Tri. infestans* bugs were exposed to dogs that previously wore insecticide-impregnated collars in early and mid-2006, they engorged and survived normally, thereby indicating that no insecticide residual effects persisted. Treated and untreated dogs were kept in separate kennels made of chicken wire and a roof, approximately 1 m apart within a fenced compound, and fed twice daily. For the multiple-exposure test (see below), each animal was stationed individually inside a specific experimental hut twice a week, and then released every morning into its specific area within the compound, with no restrictions regarding exposure to rain or movement. The bugs used in this study