Veterinary Parasitology 202 (2014) 54–58

Contents lists available at ScienceDirect

Veterinary Parasitology

journal homepage: www.elsevier.com/locate/vetpar

Efficacy of a novel topical combination of fipronil, (S)-methoprene, eprinomectin and praziquantel against adult and immature stages of the cat flea (*Ctenocephalides felis*) on cats

Christine Baker[a,*], Eric Tielemans[b], Joseph B. Prullage[c], S. Theodore Chester[c], Martin Knaus[d], Steffen Rehbein[d], Josephus J. Fourie[e], David R. Young[f], William R. Everett[g], Joseph K. Rosentel[c]

[a] *Merial Limited, 115 Transtech Drive, Athens, GA, USA*
[b] *Merial S.A.S., CRSV, 1 allée des Cyprès, 01150 St Vulbas, France*
[c] *Merial Limited, 3239 Satellite Boulevard, Duluth, GA 30096, USA*
[d] *Merial GmbH, Kathrinenhof Research Center, Walchenseestr. 8-12, 83101 Rohrdorf, Germany*
[e] *ClinVet International (Pty) Ltd., Uitsig Road, Bainsvlei, 9321 Bloemfontein, South Africa*
[f] *Young Veterinary Research, 7243 East Avenue, Turlock, CA 95380-9124, USA*
[g] *BerTek, Inc., 104 Wilson Bottoms Road, Greenbrier, AR 72058, USA*

ARTICLE INFO

Keywords:
Ctenocephalides felis
Fleas
Eggs
Topical
Fipronil
(S)-methoprene
Eprinomectin
Efficacy

ABSTRACT

The efficacy of a novel topical combination of fipronil 8.3% (w/v), (S)-methoprene 10% (w/v), eprinomectin 0.4% (w/v) and praziquantel 8.3% (w/v) (BROADLINE®) was tested against adult and immature stages of *Ctenocephalides felis* fleas in six studies. For that purpose, fleas from different colonies from North America, Germany and South Africa were used to induce infestations in cats under laboratory conditions. In each study, between 12 and 16 cats were allocated randomly to 2 groups. Cats in Group 1 were not treated and served as controls. Cats in Group 2 were treated once on Day 0 with BROADLINE® at the minimum recommended dosage of 0.12 mg/kg body weight. In 4 studies, all animals were infested experimentally with unfed *C. felis* (100 ± 5) on Days 2 (or 1), 7, 14, 21, 28 and 35. Live fleas were counted 24 h post-treatment or infestation. In 2 additional studies, animals were infested at the same frequency with gravid *C. felis* fleas (100 ± 5) that were fed previously on an untreated host. Forty-eight hours post-infestation, flea eggs were collected, counted and incubated for the evaluation of the reduction of emergence of adults. The combined curative efficacy against adult fleas at 24 h after treatment was 94.3% and the combined preventive efficacy values remained greater than 95.9% at 24 h after 5 subsequent weekly infestations. In addition, the product reduced dramatically the emergence of new adult fleas for at least 5 weeks (>98.1% for one month and 93.2% at 5 weeks after infestation), demonstrating its efficiency in preventing environmental contamination by immature stages.

1. Introduction

The cat flea, *Ctenocephalides felis*, is the most common ectoparasite found on cats and many other animal species worldwide (Rust and Dryden, 1997). In addition to

* Corresponding author. Tel.: +1 706 552 2445; fax: +1 706 552 2451.
E-mail address: christine.baker@merial.com (C. Baker).

http://dx.doi.org/10.1016/j.vetpar.2014.02.040

causing annoyance and discomfort to pets and their owners, cat fleas are associated with several diseases. *C. felis* is primarily responsible for flea bite allergy dermatitis (FAD) in dogs and cats (Dryden and Blakemore, 1989; Plant, 1991; Carlotti and Costargent, 1994) as a result of hypersensitivity to components of flea saliva (Dryden and Rust, 1994; Stopler, 1994). The cat flea is also the primary intermediate host of the tapeworm *Dipylidium caninum*, the common intestinal cestode of dogs and cats (Dunn, 1978; Pugh, 1987). In addition, *C. felis* can transmit the agent of flea-borne spotted fever, *Rickettsia felis*, and it has been implicated in the transmission of some *Bartonella* species, such as *B. henselae*, the agent of Cat Scratch Disease (Azad et al., 1997; Orloski and Lathrop, 2003; Just et al., 2008; Dryden and Hodgkins, 2010).

Although the use of highly effective and practical insecticides such as fipronil, imidacloprid or selamectin have revolutionized flea control, treatment and prevention of cat flea infestations remain a major concern for pet owners and veterinarians (Rust, 2005; Dryden and Hodgkins, 2010; Beugnet and Franc, 2012; Siak and Burrows, 2013). The most difficult component of flea control is related to an aspect that the majority of pet owners are unaware of, namely controlling the pre-existing environmental infestation by immature stages (Rust, 2005; Beugnet and Franc 2012; Beugnet and Fourie, 2013). As a result, pet owners only treat their animals once when they see fleas, an approach that allows for continuous re-infestations by new emerging fleas. In order to improve owner compliance, there is a need for efficient and easy to administrate solutions allowing integrated control.

Broadline® (Merial) is a new topical combination of fipronil, (S)-methoprene, eprinomectin and praziquantel developed for cats with the aim to offer a wide spectrum of antiparasitic activity. The association of the phenylpyrazole fipronil with the insect growth regulator, (S)-methoprene is well known for its efficacy against adult and immature flea stages and for its ability to break the flea life cycle on treated animals and in their environment (Ritzhaupt et al., 2000; Young et al., 2004; Franc and Yao, 2007; Bonneau et al., 2010; Cadiergues et al., 2011; Everett et al., 2011). The objective of the studies presented in this paper was to examine the efficacy of Broadline® against adult and immature stages of several strains of *C. felis* fleas. For this six controlled, blinded and randomized laboratory studies were conducted in four different laboratories located in Germany, South Africa, and the United States.

2. Materials and methods

2.1. Animals

All animals were healthy, purpose-bred laboratory short hair cats. Each study was conducted under a controlled and blinded design, with cats randomly allocated to two groups (treated and control), each with eight (studies 1–5), or six cats (Study 6). Before treatment, the good health of each cat was confirmed by a physical examination conducted by a veterinarian, and by daily health observations by trained personnel. The protocol of the studies was reviewed and approved by the Merial Institutional Animal Care and Use Committee. Cats were handled with due regard for their welfare. To detect the presence or absence of any treatment-related or unrelated health abnormality or adverse event, health observations were conducted at hourly intervals for four hours after treatment and daily thereafter throughout all studies.

2.2. Study design

The studies were designed in accordance with the "World Association for the Advancement of Veterinary Parasitology (W.A.A.V.P.) guidelines for evaluating the efficacy of parasiticides for the treatment, prevention and control of flea and tick infestation on dogs and cats" (Marchiondo et al., 2007), and were conducted in accordance with Good Clinical Practices as described in International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) guideline GL9 (EMEA, 2000). All animals were managed similarly, with due regard for their well-being and in compliance with Merial Ethics Committee, other local applicable regulations and requirements, and International laws and ethics.

2.3. Flea strains

The six studies were conducted by four different investigators in four different laboratories. Each study used a distinct flea colony for infestations, sourced from North America, Germany, or from Germany and South Africa. All fleas were laboratory-maintained *C. felis*.

2.4. Treatment

Cats assigned to the control groups were not treated. On Study Day 0, each cat in the treated groups received a topical application of BROADLINE® at the minimum recommended dose of 0.12 mL/kg body weight (bw), delivering 10 mg/kg bw fipronil, 12 mg/kg bw (S)-methoprene, 0.5 mg/kg bw eprinomectin and 10 mg/kg bw praziquantel. The treatments were applied directly onto the skin, after parting the hair, in one spot on the midline of the neck between the base of the skull and the shoulder blades.

2.5. Flea infestations and adult flea counts

Each cat was infested with 100 (±5) unfed adult fleas on Days 2, 7, 14, 21 and 28. An additional flea infestation was performed on Day 35 for 2 studies. All live fleas remaining on the cats were removed and counted via thorough combing of all body areas with a fine-tooth flea comb on Day 1 at 24 h after treatment (72 h after pre-treatment infestation), and at 24 h after each of the subsequent weekly flea infestations.

2.6. Evaluation of the adult emergence from flea eggs

The adult emergence after incubation of the flea eggs collected during the month after treatment was evaluated in two studies using the study design described by Franc et al. (2007). Briefly, each cat was infested with