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Effects of orally administered spinosad (Comfortis®) in dogs on adult and immature stages of the cat flea (*Ctenocephalides felis*)

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ABSTRACT

The efficacy of spinosad against adult fleas (*Ctenocephalides felis*) on dogs was evaluated in three controlled, blinded studies. One study was conducted to determine speed of kill on experimentally infested dogs. Two additional studies were designed to assess the efficacy of spinosad in preventing environmental contamination with flea eggs (USA study and EU study). An additional objective of the USA study was to assess the effects of skin and hair-coat debris from spinosad-treated dogs on eggs and larvae of *C. felis*. Dogs were randomly allocated to treatment with beef-flavored spinosad tablets, administered orally at a minimum dosage of 30 mg/kg, or placebo. In the first study, speed of kill was determined by flea comb counts performed at 0.5, 1, 2, 4, 8, 12, 24 and 48 h after spinosad treatment. Reductions in geometric mean flea counts for spinosad-treated dogs, compared to placebo were 53.7% at 0.5 h, 64.2% at 1 h, 85.8% at 2 h and 100% at 4 through 48 h post-treatment ($p < 0.05$ at 1 h and beyond). In the 2 flea egg production studies, dogs were treated (spinosad or placebo) once on day 0, infested with 600 fleas approximately 3 h post-treatment and reinfested with approximately 600 fleas at intervals over 1 month. Flea eggs were collected starting at approximately 72 h after each infestation. Eggs were examined for any effects of spinosad on egg viability. Efficacy of spinosad was also evaluated against environmental eggs and larvae exposed to canine hair-coat debris collected on days 3, 7, 14, 21, and 30. Spinosad was highly effective in reducing flea egg production (>99.8% across the entire study period) compared to control dogs in both egg collection studies. Insufficient numbers of eggs were recovered from spinosad-treated dogs to determine the viability of those eggs. There was no evidence of any effect on environmental flea stages, indicating that spinosad was not present in the skin debris of spinosad-treated dogs. The capability of spinosad to quickly kill adult fleas, and to greatly reduce egg production following challenge with high numbers of adult fleas is important in breaking the flea life cycle and preventing the introduction and establishment of new flea infestations in the household.

1. Introduction

The goal of a successful pet flea control program is to eliminate adult fleas prior to feeding and egg production (Carlotti and Jacobs, 2000). Over time, this will also result in successful elimination of fleas from the pet's environment.

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Until recently there existed no orally administered products that could quickly kill adult fleas and also provide a high level of efficacy for 1 month. Early testing of an experimental formulation of the tetracyclic macrolide spinosad indicated that it could kill adult cat fleas (*Ctenocephalides felis*) for 1 month when administered orally to dogs at a minimum dose of 30 mg/kg (Snyder et al., 2007). Spinosad is now registered in the United States for the treatment of flea infestations on dogs.[1] More recently it has been demonstrated that the commercial formulation of spinosad can also kill adult dog fleas (*Ctenocephalides canis*) for 1 month when administered orally to dogs at a minimum dose of 30 mg/kg (Franc and Bouhsira, 2009). The potential for spinosad to provide household flea control was also demonstrated in client-owned dogs in a field study conducted in the United States (Robertson-Plouch et al., 2008). Monthly administration of a beef-flavored chewable tablet at a dose of 30–60 mg/kg for 3 consecutive months resulted in reduction of adult flea counts of 99.9%.

We herein provide additional data on the efficacy of spinosad against *C. felis*. One study was conducted to determine speed of kill of adult fleas on experimentally infested dogs. Two additional studies were designed to assess the efficacy of spinosad in preventing environmental contamination with flea eggs (USA study and EU study). An additional objective of the USA study was to assess the effects of skin and hair-coat debris from spinosad-treated dogs on eggs and larvae of *C. felis*.

2. Materials and methods

2.1. Overview

The studies summarized in this report were performed at three separate laboratories in accordance with Good Clinical Practices as described in VICH guideline GL9, Good Clinical Practice (EMEA, 2000). All protocols were reviewed and approved by the respective Institutional Animal Care and Use Committee (USA) or Charles River Biolabs Ethics Committee (EU). All studies utilized a randomized block, blinded, parallel-arm, negative control design. Individual dogs were considered the experimental unit.

2.2. Dogs

A total of 100 purebred and mixed-breed dogs (49 males, 51 females), at least 7.5 months old and weighing between 6.0 and 29.5 kg were used in these studies. The dogs were either owned by the trial facility, or were obtained from a licensed vendor. Dogs were uniquely identified by ear tattoo or by a subcutaneous microchip. Water was provided ad libitum. Dry dog ration was provided once daily, except on treatment days and on days immediately prior to treatment, when a canned ration was used.

In the speed of kill study, dogs were housed in individual outdoor, sheltered, chain-link runs (kennels). In the USA and EU flea egg/debris studies, housing was either in cages of appropriate size or in internal/external runs that conformed to accepted guidelines for animal welfare. During collection days in the USA study, dogs were housed in stainless steel cages designed for collection of flea eggs and skin debris (skin scales, flea feces, and hair). Each cage contained a perforated floor, beneath which was placed an egg/debris collection board. In the EU study, dogs were housed individually in pens lined with timber, measuring approximately 1.0 m × 2.0 m. During flea egg collections, pen size was reduced to approximately 1.0 m × 1.0 m.

At the time of selection for the respective studies, all dogs were in good health, and had acceptable dispositions and appropriate hair coats for accurate comb counts. Exclusion criteria included pregnancy, lactation or intention to breed, a history or evidence of flea allergy dermatitis, treatment with an insecticide, insect growth regulator or endectocide within at least 45 days prior to acclimation, or inability to retain an acceptable flea burden.

2.3. Flea infestations

For the speed of kill study, unfed adult *C. felis* were obtained from a resident colony at Young Veterinary Research Services in California, USA. For the egg and pre-adult flea stage studies, fleas were obtained either from the resident colony at Auburn University, Auburn, AL, USA, or Charles River Laboratories in Ireland. Flea infestations were performed by placing approximately equal numbers of male and female adult fleas along the dorsum or the dorso-sacral area of each dog.

Dogs in the speed of kill study were infested on day −1 with approximately 100 adult fleas. To determine flea retention rates, dogs were infested with approximately 100 (USA) or 200 (EU) unfed adult fleas on study day −9 or −10. In the USA egg collection study, 600 fleas were applied to all dogs on day 0 approximately 3 h after treatment. In this and the EU study, 600 fleas were additionally applied to each dog on five occasions during the month after treatment. In the USA study, infestations were completed on post-treatment days 0 (3 ± 1 h), 4, 11, 18, and 27 and in the EU study on days 3, 10, 17, 24, and 28.

2.4. Treatments

In all studies, spinosad was administered orally on day 0. Dogs were fed a canned ration immediately before and after treatment. Spinosad was administered as a beef-flavored chewable tablet based on established dose bands. The target dose range in the speed of kill and USA egg collection studies was 30–90 mg/kg. The target dose range in the EU study was 30–60 mg/kg. Dose rates for individual dogs were based on body weights obtained between days −1 and −3. After completion of the speed of kill and USA egg collection studies, a label dose of 30–60 mg/kg was established for spinosad. Therefore, dogs that were treated within this dose range were the focus of the analyses as reported herein. For the speed of kill study, placebo tablets were identical to spinosad tablets except for active ingredient.

[1] Comfortis® (spinosad) Elanco Companion Animal Health, Greenfield, IN, USA.