

Evaluation of K9 Advantix Versus Frontline Plus Topical Treatments to Repel Brown Dog Ticks (*Rhipicephalus sanguineus*) on Dogs

David R. Young, DVM, PhD^a

Wendell Davis, DVM^b

Robert G. Arther, PhD^b

Terry Settje, BA^b

^aYoung Veterinary Research Services
Turlock, California

^bBayer HealthCare, LLC, Animal Health Division
Shawnee, Kansas

The ability of pesticides to repel or kill ticks before they attach to a host and feed is important for the prevention of transmission of tick-borne pathogens. A study design to compare the repellency/acaricidal properties of topically applied products against European deer ticks (*Ixodes ricinus*), the primary vector of Lyme disease in Europe, following exposure to treated dogs has been previously reported.^{1,2} A similar study design was reported to demonstrate repellency and acaricidal properties of Advantage (9.1% imidacloprid, Bayer Animal Health) used concurrently with Kiltix (45% permethrin, Bayer Animal Health) against American dog ticks (*Dermacentor variabilis*), the primary vector of *Rickettsia rickettsii*, the causative organism of Rocky Mountain spotted fever in dogs.³ The present study was conducted to compare the tick repellency/acaricidal properties of K9 Advantix (8.8% imidacloprid + 44% permethrin, Bayer Animal Health) with Frontline Plus (9.8% fipronil + 8.8% S-methoprene, Merial) against brown dog ticks (*Rhipicephalus sanguineus*), the vector of *Ehrlichia canis* in dogs.

MATERIALS AND METHODS

A total of 18 healthy, conditioned laboratory dogs (9 males and 9 females) ranging in size from 15.1 to 54.6 pounds with the ability to harbor tick infestations were included in the study. The dogs had not been treated with any type of tick-control product within 60 to 90 days of study initiation. Physical examinations were performed on each dog during acclimation to verify their health.

- On test day -12 all dogs were bathed with a mild, nonmedicated shampoo. The dogs were housed in individual runs during the study when not exposed to ticks as described below.
- The dogs were fed a commercially available balanced dry dog food (United Kennel Meat-Based Dog Food). Water was available ad libitum from automatic waterers.
- All dogs were vaccinated prior to the start of the study. No

medications or therapy, other than the test products, were administered during the trial.

- Unfed adult ticks (*R. sanguineus*), obtained from EL Ward II Labs (Soquel, CA), were used for the experimental infestations during the study.

This study design evaluated the transfer and attachment of ticks from the environment to dogs. Individual heavy-gauge plastic pet transport carriers (27" × 30" × 40" in size) were used for tick challenges. Each carrier contained a light-colored nylon carpet with a nap of 12 to 15 mm to cover 50% to 60% of the floor area. For each tick challenge, 50 adult *R. sanguineus* ticks (approximate male/female sex ratio of 1:1) were placed on the carpet. Air vents in the carriers were covered with a fine-mesh screen to prevent ticks from escaping. The carpet was sprayed lightly with water prior to placement with the ticks. After a 15-minute acclimation period, dogs were placed in the carriers for a 2-hour period to expose them to the live ticks. The dogs were then removed, examined visually, and combed for ticks. The number of live ticks (attached and unattached) and dead ticks on the dogs were counted and removed. Live and dead ticks remaining on the carpet and in the carriers were counted. Carriers were thoroughly washed and carpets were discarded after each use.

On test day -3 each dog was exposed to ticks as described above. Pretreatment live tick counts (attached and unattached on each dog) were recorded. The dogs were then ranked by the total number of live ticks and were blocked into groups of three. Within each block the dogs were randomized to one of the three treatment groups:

- K9 Advantix (8.8% w/w imidacloprid + 44.0% w/w permethrin)
- Frontline Plus (9.8% w/w fipronil + 8.8% w/w S-methoprene)
- Control (untreated)

The dogs were also weighed on test day -3. On test day 0 the dogs

were treated following the labeled dosages and application directions for each product.

Posttreatment Tick Evaluation

On day 3 the dogs were placed in the pet carriers for 2 hours and exposed to 50 adult *R. sanguineus* ticks as previously described. Following this time interval the dogs were removed. Live and dead ticks observed on the dogs and ticks remaining in the carrier were counted. The 2-hour tick transfer procedures and subsequent tick counts were repeated on test days 7, 14, 21, 28, and 35. Percent efficacy was calculated for the two treatment groups on each evaluation day with the following formula using the geometric mean tick counts:

Percent Efficacy =

$$\frac{\text{Geo Mean No. Live Ticks/Dog (Control)} - \text{Geo Mean No. Live Ticks/Dog (Treated)}}{\text{Geo Mean No. Live Ticks/Dog (Control)}} \times 100$$

Statistical Methodology

Results of this study were evaluated by descriptive and inferential statistical methods. Means, variability parameters, and ranges of values were calculated for tick counts. In addition, repeated measured mixed-model analysis of variance was used on log (count +1) transformed tick counts testing for treatment group differences, using contrast statements to control group comparisons.

RESULTS

The geometric mean number of live ticks/dog (attached and unattached) and percent tick efficacy are displayed in Table 1 and Figures 1 and 2. Pretreatment (test day -3) live tick counts ranged from 27 to 46 (Geo mean = 35.0 ticks/dog) following 2 hours of exposure to ticks in the pet carriers. There were significantly fewer numbers of live ticks on the K9 Advantix-treated dogs than either the Frontline Plus or control dogs for all six posttreatment evaluations ($P < 0.05$). The control dogs had a range of 12.0 to 29.5 live ticks/dog during each of the six posttreatment tick-exposure intervals. A range of 0.4 to 3.6 live ticks/dog was recorded for the K9 Advantix-treated dogs through day 35. The Frontline Plus-treated dogs had a range of 12.8 to 27.4 live ticks/dog through day 35. There were no significant differences between the number of live ticks observed on the control versus Frontline Plus-treated dogs during the posttreatment tick exposure periods for days 3, 14, 21, 28, and 35. On test days 14, 21, 28, and 35 more live ticks were observed on the Frontline Plus-treated dogs than on the control dogs.

The geometric mean number of repelled ticks (dead plus live ticks remaining in the carrier) are displayed in Table 2. There were significantly more ticks repelled on the K9 Advantix-treated group than the control group for all posttreatment evaluations except day 35. There were no differences in the repelled ticks between the Frontline Plus-treated dogs and control dogs for days 3, 14, 21, and 35. Significantly more ticks were repelled on the control dogs than the Frontline Plus-treated dogs on day 28. The repellency values represent 2.3, 1.3, 2.3, 2.0, 3.2, 2.1-fold greater repellency of K9 Advantix versus Frontline Plus for test days 3, 7, 14, 21, 28, and 35, respectively.

TABLE 1
Geometric Mean Number of Live Ticks/
Dog and Percent Efficacy

Test Day	Group 1 K9 Advantix		Group 2 Frontline Plus		Group 3 Control
	Ticks/Dog	% Efficacy	Ticks/Dog	% Efficacy	Ticks/Dog
-3	35.2	—	34.5	—	35.2
3	0.4*	98.5	20.5	25.9	27.6
7	1.3*	95.4	12.8*	56.8	29.5
14	1.8*	90.6	24.0	-28.1	18.8
21	3.6*	84.0	24.1	-7.8	22.4
28	2.7*	89.1	27.4	-11.4	24.6
35	1.7*	85.9	14.6	-21.9	12.0

*Statistically different versus control group ($P < 0.05$).

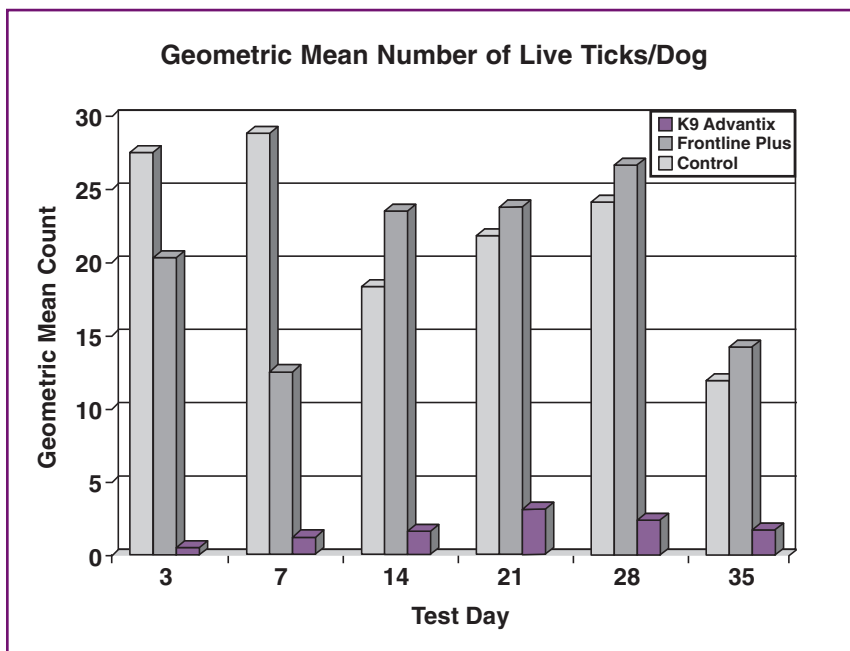


Figure 1—Mean number of live ticks per dog after treatment with K9 Advantix and Frontline Plus.

TABLE 2
Geometric Mean Number
of Repelled Ticks^a/Dog Carrier

Test Day	K9 Advantix	Frontline Plus	Control
	Geo Mean No. Ticks	Geo Mean No. Ticks	Geo Mean No. Ticks
3	40.1*	17.1	12.3
7	37.0*	28.1*	11.7
14	38.5*	17.0	21.0
21	32.3*	16.0	17.3
28	35.2*	10.9*	19.1
35	40.4	19.2	27.2

^aDead and live ticks remaining in the carrier.

*Statistically different versus control group ($P < 0.05$).

two active ingredients are combined.⁸ Fipronil provides little or no repellency activity against ticks. Fipronil does provide a high level of efficacy against ticks; however, data demonstrate that optimal tick control is achieved 24 to 48 hours after ticks have the opportunity to attach and feed.⁹

There are relatively few reports to indicate the duration of blood feeding by ticks to successfully transmit pathogens. Ticks may only require 5 to 20 hours of feeding activity to transmit *R. rickettsii* to dogs.¹⁰ Human and laboratory animal studies indicate *Borrelia burgdorferi* may be transmitted 24 hours after *Ixodes* attach and feed.^{11,12}

The results of the current study are consistent with the results of previous studies and demonstrate that permethrin-containing products offer protection against transmission of tick-borne pathogens by preventing ticks from attaching and feeding.

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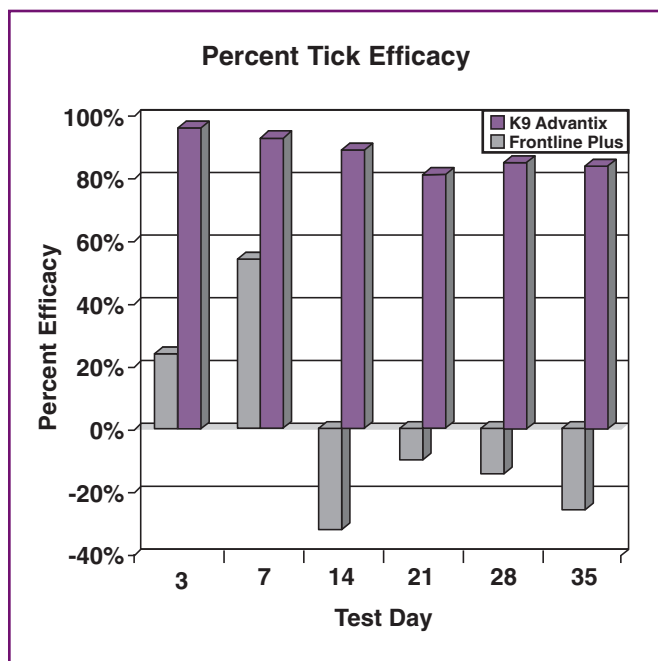


Figure 2—Percent tick efficacy after treatment with K9 Advantix and Frontline Plus.

DISCUSSION

The use of permethrin-containing formulations to repel ticks, including three species of *Ixodes*, *D. variabilis*, and *Amblyomma americanum*, has been previously described.¹⁻⁶ The activity of imidacloprid alone against ticks is inconsistent,⁷ although recent data indicates imidacloprid is able to enhance the activity of permethrin when the