Evaluation of the tolerance of a dinotefuran–pyriproxyfen combination (Vectra Felis) after 7 repeated overdosed topical administration at 2 week intervals on kittens

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INTRODUCTION

The safety of ectoparasiticides in companion animals must be assessed on the target animal species and specifically on the most sensitive population (i.e. puppies, kittens, etc...). Overdoses and increased frequency of administrations are challenging situations that allow evaluating the tolerance of a product. This study was designed to assess the tolerance of a topical combination of dinotefuran- pyriproxyfen (Vectra®Felis, DP) when administered on kittens at up to 5 times the maximal recommended dose every two weeks for 12 consecutive weeks.

METHODS

This study was performed according to the principles of Good

Laboratory Practices. After at least 6 days of acclimatization, 40 purpose-bred kittens (7–8 weeks old, 590–1095 g BW at first application) were allocated to five groups (C, E, DP1, DP3, DP5). Kittens were administered DP excipient (4.5 mL, E) or DP at the maximal recommended dose (0.9 mL, DP1), 3 times the maximal dose (2.7 mL, DP3) or 5 times the maximal dose (4.5 mL, DP5). Treatments were applied topically, between the shoulders every 2 weeks for 12 consecutive weeks (D1, D15, D29, D43, D57, D71, D85). Kittens in the control group were untreated. Animals were subjected to a health assessment/ detailed clinical examination prior to administration and every week post-treatment. This protocol has been previously approved by an ethical committee.

RESULTS

Only one female reacted to administration of excipient alone. Specifically transient observations (salivation, excessive licking and vocalization, increased activity level and/or excessive scratching) were observed shortly after administration (D29, 43, 57 and 71). All these findings were transient and of short duration. As compared to untreated animals and animals treated with excipient alone, no significant findings were observed at any of the tested dose-levels. The results of this study show that 7 repeated dermal administrations of DP, once every 2 weeks over 85 days, on the back of kittens was well tolerated both locally and systemically at 1X, 3X and 5X the highest recommended dose. Vectra Felis can be therefore safely applied on cats including kittens.

Number of reactions (nb of animals)	Untreated (C)	Excipient (E)	Vectra Felis 1x (DP1)	Vectra Felis 3x (DP3)	Vectra Felis 5x (DP5)
Dry skin (application rate)	2 (2)	46 (8)	33 (8)	47 (8)	45 (8)
Soft feces	0 (0)	7 (5)	4 (2)	7 (7)	7 (2)
Loose feces	21 (8)	7 (4)	7 (6)	7 (2)	27 (8)
Liquid feces	24 (6)	2 (2)	15 (8)	6 (5)	29 (6)
Decreased fecal output or absence of feces	8 (6)	12 (6)	11 (7)	10 (6)	17 (7)

Cross-reactivity between *Dermatophagoides farinae*, *Tyrophagus putrescentiae* and *Acarus siro* in dogs from UK with Canine Atopic Dermatitis

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INTRODUCTION

Mite allergens are highly related to Canine Atopic Dermatitis

(CAD). The most relevant species are *Dermatophagoides farinae* (House Dust Mite) and *Tyrophagus putrescentiae* and *Acarus siro* (Storage Mites). We have observed that more than 65% of our positive tested animals were positive to these three species simultaneously. The aim of this study was to investigate a possible cross-reactivity among these three species in dogs from UK with CAD.

METHODS

A positive serum pool against the three species was obtained by mixing sera from dogs with CAD that had high levels of specific-IgE against all these 3 mite extracts (Optical Density>0.800) determined by PET-ELISA® (Alergovet, Madrid, Spain). Inhibition-ELISA for each species was carried out by coating wells with 1 µg of protein and starting all inhibition

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curves at 0.1 µg/µl (10-fold the amount coated). *Alternaria alternata* extract was included in each Inhibition-ELISA assay as a non-inhibitory, negative control. The extract amount (µg) required to reach 50% of inhibition (i50) was calculated in each case in order to compare their inhibitory capacity. Inhibition-Immunoblottings were also performed. Briefly, proteins were immobilized in PVDF membranes and were incubated with pool previously co-incubated with three different concentrations of the same immobilized and the other two extracts. Concentrations ranged from the same strip-fixed amount to 100-fold less.

RESULTS

Inhibition-ELISA assays showed a high inhibitory capacity of the three extracts regardless the one coated. Maximum inhibition percentages of the three species were between 60 and 90%. When *D. farinae* was used in the solid phase, it yielded

the lowest i50 (0.049 µg) as inhibitor, which means the highest inhibitory capacity. When *A. siro* was coated it also showed the highest inhibitory capacity with the lowest i50 (0.411 µg). On the contrary, when *T. putrescentiae* was coated, *D. farinae* showed the lowest i50 (0.185 µg) whereas *T. putrescentiae* presented the highest i50 (0.344 µg). *A. alternata* had no inhibitory effect on any of the tested mite extracts. Inhibition-Immunoblotting showed a signal reduction at high concentration of inhibitor with the three mites, but with slight differences depending on the immobilized extract.

CONCLUSIONS

Using this positive serum pool we have observed a high cross-reactivity among these three mite species, although with slight differences, that could explain the high observed positivity concordance. Further studies with additional sera would be necessary to confirm these results.

Distribution and persistency of dinotefuran and pyriproxyfen in the hairs of cats topically treated with Vectra Felis

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INTRODUCTION

The efficacy and performances of topical ectoparasiticides are linked to the ability of the active ingredients to distribute onto the animal body and to persist in hairs. After administration on the skin in one single location of the body, the actives must move and provide a rapid protection to the whole body surface. These ingredients are also expected to persist in the animals hairs until the next administration. This study was designed to assess the kinetics of distribution and persistency in the hairs of the active ingredients from a topical combination of dinotefuran- pyriproxyfen (Vectra®Felis, DP) on cats.

METHODS

This study was performed according the principles of Good Laboratory Practices. After at least 6 days of acclimatization, adult cats were allocated to 2 groups: a control group (n=2, 3.6±0.5 kg BW) and a DP treated group (n=6, 4.3±0.6 kg BW). Cats in the treated group were administered 0.9 mL of DP while cats in the control group were administered 0.9 mL of a placebo on day 0. Hair samples were collected from cats with electric clippers in 5 body areas: the neck (excluding administration site), the middle of the back, the right and left sides of the thorax and the lumbar area. Sampling was performed at 7 time-points: before treatment, 1, 3, 7, 14, 21 and

30 days post-treatment. Dinotefuran and pyriproxyfen concentrations were measured in each sample using a validated HPLC/MSMS method. Results were considered only if in the analytical sequence results of calibration curves and QCs were within the accepted criteria. Cats were under general health observation for the duration of the study. This protocol has been previously approved by an ethical committee.

RESULTS

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