Comparative speed of kill between nitenpyram, fipronil, imidacloprid, selamectin and cythioate against adult *Ctenocephalides felis* (Bouché) on cats and dogs

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Abstract

Speed of kill and percentage kill of nitenpyram (CAPSTAR®) was compared to fipronil (Frontline® spot-on), imidacloprid (Bayvantage®/Advantage™), selamectin (Stronghold™/Revolution™) and cythioate (Cyflee®) against adult fleas on cats and dogs 3 and 8 h post-treatment. Selamectin was used on dogs only; cythioate was used on cats only. Groups of eight cats and eight dogs (four males and four females each) were experimentally infested with 100 unfed fleas 1 day prior to treatment with the test products. One group of cats and one group of dogs served as control. Fleas were collected from four cats and four dogs in each group (two males and two females) by combing 3 h after treatment, the remaining four cats or dogs were combed 8 h after treatment. In cats cythioate treatment resulted in a mean efficacy of 62.4 and 97.4% at 3 and 8 h post-treatment, respectively. Imidacloprid efficacy at the same times was 26.9 and 82.8%, whereas fipronil efficacy was 24.3 and 62.6% efficacy, respectively. In dogs mean efficacy 3 and 8 h after treatment with selamectin was 39.7 and 74.4%; with imidacloprid efficacy was 22.2 and 95.7%, respectively and 35.9 and 46.5%, respectively after treatment with fipronil. Nitenpyram was 100% effective in cats and 99.1% effective in dogs within 3 h of treatment and 100% effective in cats and dogs within 8 h.

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Keywords: Nitenpyram; Imidacloprid; Fipronil; Selamectin; Efficacy; *Ctenocephalides felis*; Flea control; Cat; Dog

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1. Introduction

Fleas on pets are generally considered a nuisance, but fleas are also responsible for the transmission of several diseases of humans and their pets (Dryden and Rust, 1994). In addition, fleas produce discomfort in dogs and cats that can lead to severe irritation and possibly allergic dermatitis. A fast acting flea adulticide will provide rapid relief in these cases.

Long-term prevention of flea infestations and flea control can be achieved by treating pets with an Insect Growth Regulator or Insect Development Inhibitor (IGR/IDI) such as lufenuron (Dryden et al., 1998). If a flea infestation is present at the beginning of this treatment, it is advised to also apply a fast acting adulticide such as nitenpyram to complement the IGR treatment.

Nitenpyram, a neonicotinoid, is rapidly and completely absorbed from the gastrointestinal tract in less than 90 min after oral administration to dogs and cats. Efficacious blood levels are reached within minutes (Schenker et al., 2001). The objective of this study was to compare the speed of kill and percentage kill of nitenpyram (CAPSTAR®) with those of the monthly residual topical flea control products imidacloprid (Bayvantage®/Advantage™), fipronil (Frontline® spot-on) and selamectin (Stronghold™/Revolution™) in dogs, and with imidacloprid (Bayvantage®/Advantage™), fipronil (Frontline® spot-on), and cythioate (Cyflee®) tablets.

2. Materials and methods

In the first phase of the study 24 short-haired cats were experimentally infested with 100 unfed fleas, 50 males and 50 females on Day 1 of the study. Elizabethan collars were placed on every cat to prevent grooming during the time of infestation with fleas. The cats and dogs were kept in individual cages allocated to three treatment groups of four male and four female cats each. Group 1 was treated with nitenpyram, Group 2 with cythioate and Group 3 with was left untreated and served as control group.

As nitenpyram is quantitively eliminated in cats as unchanged active ingredient within 3 days (Maurer et al., 1999a,b), the cats of Groups 1 and 2 were reassigned to Groups 4 and 5 for the second phase after a clearing period of 18 days. Cats in Group 4, after treatment with nitenpyram in the first phase, were treated with imidacloprid in the second phase. Cats in Group 5, after treatment with the short acting cythioate in the first phase, were treated with fipronil in the second phase. Group 3 was reassigned to Group 6 and was again left untreated as control group.

Similarly, 32 dogs were allocated to four treatment groups of four male and four female dogs and experimentally infested with 100 fleas each. Dogs in Group 1 were treated with nitenpyram, while dogs in Groups 2–4 were treated with fipronil, imidacloprid and selamectin respectively by spot-on application. As nitenpyram in dogs is quantitively eliminated as unchanged active ingredient within 1 day (Maurer et al., 1999a,b), the same dogs of Group 1 were used in Group 4 after a clearing period of 14 days. Group 5 was left untreated and served as control group.

Each product was applied in accordance with the manufacturers label recommendations.
The products were tested sequentially in pairs of treated group versus untreated control group. The same animals were used as control group throughout. Each group was divided into two subgroups of two male and two female cats or dogs. One of these subgroups was combed for flea count 3 h after treatment, the other subgroup was combed 8 h after treatment.

The number of live, dead and moribund fleas was determined by combing each animal with a fine comb for a minimum of 10 min. If fleas were seen during the last 2 min, combing was continued for another 2 min.

To compare the efficacy of the nitenpyram group to the efficacy of each of the other groups, Analysis of Variance and Dunnett’s tests were applied on individual arcsin square root transformed efficacy percentages.

3. Results

3.1. Cats

Of the original infestation of 100 fleas per cat an average of 67.8 live fleas were recovered after 3 h in the control group for the first phase and an average of 77 live fleas per cat in the control group for the second phase. After 8 h the averages in the two groups were 66.5 and 80.3, respectively.

Cats treated with nitenpyram showed 100% efficacy at the 3 and 8 h counts. Cythioate-treated cats reached 62.4% efficacy at the 3 h count and 97.4% at the 8 h count. Imidacloprid-treated cats showed 26.9% efficacy at 3 h after application, which increased to 82.8% after 8 h. Fipronil-treated cats showed efficacy of 24.3% at the 3 h count and 62.6% at the 8 h count.

Mean number of live fleas and percentage efficacy at 3 and 8 h after treatment of cats are summarized in Table 1. Two-tailed Dunnett’s \( P \)-values are given to compare the efficacy of the nitenpyram group with the efficacy of each of the other treatment groups. Except for the cythioate group at 8 h, the nitenpyram group showed significantly higher efficacy results than the other groups at both time points.

<table>
<thead>
<tr>
<th>Group</th>
<th>3 h post-treatment</th>
<th>8 h post-treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean number of live fleas</td>
<td>S.D.</td>
</tr>
<tr>
<td>1: nitenpyram</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2: cythioate</td>
<td>25.5</td>
<td>7.6</td>
</tr>
<tr>
<td>4: imidacloprid</td>
<td>56.3</td>
<td>9.0</td>
</tr>
<tr>
<td>5: fipronil</td>
<td>58.3</td>
<td>19.5</td>
</tr>
</tbody>
</table>

Two-tailed Dunnett’s \( P \)-values are given for comparison of the efficacy of each group with the nitenpyram group (separately for 3 and 8 h combing times and multiple comparisons with respect to individual efficacy percentages).
Table 2
Mean number of live fleas with standard deviations and efficacy (%) following nitenpyram, selamectin, imidacloprid and fipronil treatment against adult fleas on dogs, 3 and 8 h after administration

<table>
<thead>
<tr>
<th></th>
<th>Mean number of live fleas</th>
<th>S.D.</th>
<th>Efficacy (%)</th>
<th>P-value</th>
<th>Mean number of live fleas</th>
<th>S.D.</th>
<th>Efficacy (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>3 h post-treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1: nitenpyram</td>
<td>0.8</td>
<td>1.5</td>
<td>99.1</td>
<td></td>
<td>0</td>
<td>0</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Group 2: selamectin</td>
<td>55.5</td>
<td>31.4</td>
<td>39.7</td>
<td>0.0011</td>
<td>19.0</td>
<td>13.0</td>
<td>74.4</td>
<td>0.0001</td>
</tr>
<tr>
<td>Group 4: imidacloprid</td>
<td>73.5</td>
<td>17.4</td>
<td>22.2</td>
<td>0.0002</td>
<td>3.5</td>
<td>2.6</td>
<td>95.7</td>
<td>0.3436</td>
</tr>
<tr>
<td>Group 5: fipronil</td>
<td>59.3</td>
<td>11.0</td>
<td>35.9</td>
<td>0.0013</td>
<td>43.5</td>
<td>17.5</td>
<td>46.5</td>
<td>0.0029</td>
</tr>
<tr>
<td><strong>8 h post-treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1: nitenpyram</td>
<td>0.0</td>
<td>0</td>
<td>100</td>
<td></td>
<td>0</td>
<td>0</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Group 2: selamectin</td>
<td>19.0</td>
<td>13.0</td>
<td>74.4</td>
<td>0.0001</td>
<td>19.0</td>
<td>13.0</td>
<td>74.4</td>
<td>0.0001</td>
</tr>
<tr>
<td>Group 4: imidacloprid</td>
<td>3.5</td>
<td>2.6</td>
<td>95.7</td>
<td>0.3436</td>
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<td>17.5</td>
<td>46.5</td>
<td>0.0029</td>
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<td>0.0029</td>
</tr>
</tbody>
</table>

Two-tailed Dunnett’s P-values are given for comparison of the efficacy of each group with the nitenpyram group (separately for 3 and 8 h combing times and multiple comparisons with respect to individual efficacy percentages).

As efficacy for each treatment group was based on the control group run in the same phase and at the same combing time of the study, the effect on the results due to variation in flea recovery in the different control groups was calculated. This effect was small, the deviation for imidacloprid was $-10\%$ (3 h) and $-3.5\%$ (8 h), for fipronil $-6.6\%$ (3 h) and $-7.7\%$ (8 h).

3.2. Dogs

Control recovery from the original infestation with 100 fleas in dogs was on average 93 live fleas per dog after 3 h and 82.5 live fleas after 8 h.

The efficacy in dogs treated with nitenpyram reached 99.1% 3 h after treatment and was 100% after 8 h. The efficacy of selamectin was 39.7 and 74.4%, respectively, the efficacy of imidacloprid 22.2 and 95.7%, respectively, and of fipronil 35.9 and 46.5%, respectively.

Mean number of live fleas and percentage efficacy at 3 and 8 h after treatment in dogs are summarized in Table 2. Two-tailed Dunnett’s P-values are given to compare the efficacy of the nitenpyram group with the efficacy of each of the other treatment groups. Except for the imidacloprid group at 8 h, the nitenpyram group showed significantly higher efficacy results than all the other groups at both time points.

Also for dogs efficacy for each treatment group was based on the control group run in the same phase and at the same combing time of the study, and the effect on the results due to variation in flea recovery in the different control groups was calculated too. As for cats, this effect was small, the deviation for imidacloprid was $-0.8\%$ (3 h) and 0.5% (8 h), for fipronil 0.3% (3 h) and 6.5% (8 h) and for selamectin 0.6% (3 h) and 5.0% (8 h).

4. Discussion

Nitenpyram reached 100% efficacy within 3 h in cats, cythioate close to 100% within 8 h. Efficacy was lower for imidacloprid, but the product did obtain 82.8% efficacy 8 h. The slowest onset of activity and lowest overall efficacy was shown in the fipronil-treated group with 62.6% efficacy after 8 h.
Efficacy of nitenpyram in cats was significantly higher at the 3 h combing time than for all other tested compounds. At the 8 h combing time the efficacy of nitenpyram was still significantly higher than fipronil and imidacloprid.

As in cats the efficacy of nitenpyram in dogs was again significantly higher at the 3 h combing time than for all other tested compounds. At the 8 h combing time the efficacy of nitenpyram was still significantly higher than fipronil and selamectin.

The results of this study are consistent with other studies investigating the speed of kill of imidacloprid, fipronil and selamectin in dogs using administrations of the commercial products according to label recommendations and in a practical use pattern, although the time intervals between treatment and flea counts vary from study to study (Cruthers et al., 1999; Dryden et al., 2001; Everett et al., 2000). Faster onset of activity for these compounds has only been shown under specific laboratory conditions when adult fleas were confined under petri dish covers and exposed to imidacloprid, fipronil and selamectin applied directly to the shaved skin of dogs from which the superficial fatty layer had been removed. Under these experimental conditions imidacloprid killed the fleas in the first hour whereas it took at least 12–36 h with fipronil and selamectin (Mehlhorn et al., 2001).

While this study confirmed the high efficacy of nitenpyram at 3 h after treatment, observations from clinical studies suggest that fleas are affected even earlier. Dobson et al. (2000) reported that fleas started to detach from treated animals 30 min after administration of nitenpyram.

**Speed of kill of a flea adulticide is of practical significance in several situations.** When animals harbor a large flea burden a fast acting adulticide gives rapid relief from the irritant effects of the infestation minimizing the exposure to flea bite antigens (Carlotti, 2001). In animals suffering from Flea Allergy Dermatitis (FAD) the initial elimination of fleas is particularly crucial to minimize the number of flea bites on highly sensitive animals.

Nitenpyram has also shown its usefulness in an Integrated Flea Control approach. A field study (Miller et al., 2001) showed that a combination therapy with nitenpyram and the IGR lufenuron, provided superior flea control in terms of both on-animal flea numbers and environmental flea numbers when compared to a topical adulticide used alone. Here nitenpyram provided excellent initial control of the adult flea population.

5. **Conclusion**

Nitenpyram provided rapid relief from fleas for dogs and cats and had the highest overall percent kill when compared to fipronil, imidacloprid, selamectin and cythioate. In a clinical situation this results in fast elimination of exposure to fleas, particularly important for animals suffering from FAD, and in the fast control of adult fleas in an IFC strategy.

**Acknowledgements**

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References


