Efficacy and Longevity of Nitenpyram Against Adult Cat Fleas (Siphonaptera: Pulicidae)

M. K. RUST,[1] M. M. WAGGONER,[1] N. C. HINKLE,[1, 2] D. STANSFIELD,[3] AND S. BARNETT[3]

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ABSTRACT Nitenpyram (Capstar) is a fast acting, orally administered flea treatment that is absorbed into the blood of the host animal and is readily available for uptake by feeding fleas. We examined the efficacy of a single dose of nitenpyram against adult cat fleas, *Ctenocephalides felis* (Bouché), over several days. We recorded adult flea mortality and flea egg production on treated and untreated cats. Nitenpyram provided 100% kill of all fleas on the host at the time of treatment and for up to 24 h after treatment. Between 24 and 48 h after treatment, there was a 98.6% reduction in adult flea numbers. From 48 to 72 h, there was a 5% reduction in adult fleas. There was a 97% reduction and 95.2% reduction in the number of flea eggs collected from treated versus untreated animals during the first 48 h and from 48 to 72 h, respectively. In addition, we quantified three distinct behavioral responses of infested adult cats treated with nitenpyram to determine the extent of any immediate, overt behavioral responses in treated animals. A significant increase in scratching, biting, licking, and twitching occurred for 5 h. The biting and licking continued for 7 h after treatment. Administration of nitenpyram provides an effective mechanism to eliminate adult fleas from hosts for up to 48 h after treatment.

KEY WORDS nitenpyram, cat flea, *Ctenocephalides felis*, Capstar, behavioral observations

THE CAT FLEA, *Ctenocephalides felis* (Bouché), is one of the most common ectoparasites of domestic cats and dogs worldwide. The use of systemic and topical insect growth regulators (IGRs) and spot-on treatments has revolutionized flea control on pets (Rust and Dryden 1997, Dryden 1999, Dryden et al. 1998). Generally, topical application of imidacloprid (Advantage) and fipronil (Frontline) provides residual activity against adult cat fleas for up to 30 d (Dryden et al. 1998) and 90 d (Dryden et al. 2000), respectively. Orally administered lufenuron (Program) acts primarily against eggs (Hink et al. 1991), but Dean et al. (1999) found significant adult flea mortality with in vitro studies, death being attributed to abnormal endocuticle production, the maximum effect occurring between 7 and 10 d after treatment. Monthly treatments of fipronil or imidacloprid provided complete protection of cats in simulated home environments (Jacobs et al. 2001). Cadiergues et al. (1999) found that two doses of nitenpyram weekly or in combination with a single dose of lufenuron provided >94% reduction in adult cat fleas for at least 63 d. The combination treatment provided significant reductions for at least 112 d. Similarly, Miller et al. (2001) found 90–100% reductions with the combination treatment for at least 40 wk.

Nitenpyram binds to nicotinic acetylcholine receptors, interfering with normal nerve transmission (Nagata et al. 1999, Chatellier 2001). It has low mammalian toxicity (acute oral rat, LD_{50} = 1,575 mg/kg; acute dermal rat, LD_{50} > 2,000 mg/kg) and high toxicity to insect pest species, including fleas (Kashiwada 1996). Nitenpyram is readily absorbed from the gastrointestinal tract, and peak plasma levels appear within 30 min (Miller et al. 2001). The reported half-life of nitenpyram is ≈8 h (Chatellier 2001). Engorged fleas became excited, as evidenced by trembling of the legs and an inability to remain attached to the host's fur. Fleas began dislodging from the host within 15–30 min of treatment (Mahoney et al. 2001), and ≈85.9% of the fleas were off the hosts at 6 h (Dobson et al. 2000).

We initially planned to use nitenpyram to remove adult cat fleas from the cats between rearing studies and to provide the cats relief from adult fleas. When fleas were placed back on treated hosts after 48 h, adult cat flea longevity and egg production dramatically decreased. During the study, it was noticed the cats began intensive grooming shortly after nitenpyram administration. Twitching, scratching, and preening were observed on flea-infested cats treated with nitenpyram. The objective of the study was to determine the longevity of nitenpyram against cat fleas when cats were provided a single dose. In addition, we quantified the preening responses after nitenpyram administration to flea-infested cats.

[1] Department of Entomology, University of California, Riverside, CA 92521.
[2] Department of Entomology, University of Georgia, Athens, GA 30602.
[3] Novartis Animal Health US, Greensboro, NC 27408.

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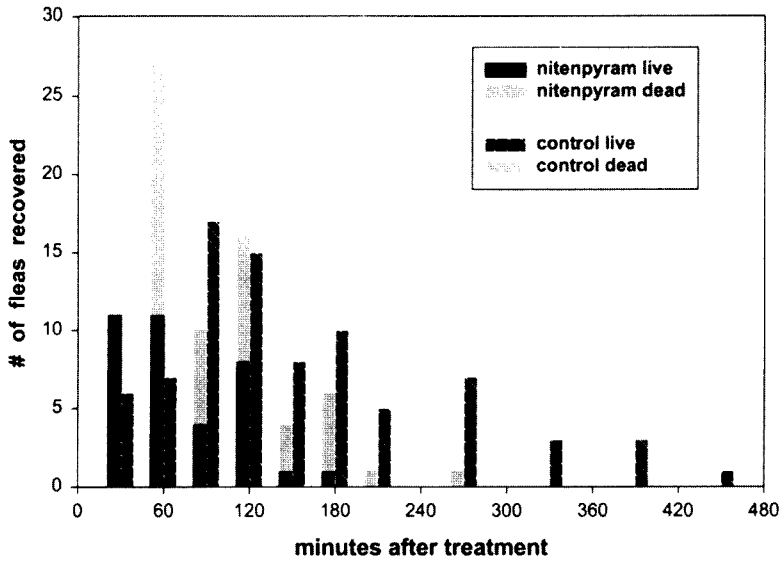

Fig. 1. Numbers of fleas recovered from cats treated with nitenpyram for 6 h after treatment.

Materials and Methods

Insect Rearing. Cat fleas used were a susceptible University of California, UCR laboratory strain, maintained as described by Metzger and Rust (1996). Fleas were selected from groups of adults reared from eggs collected 18–21 d earlier, to ensure both female and male fleas. Adults were anesthetized with CO_2, counted, sexed, and confined in 20-cm-tall test tubes before being placed onto host cats. Six adult cats were infested with 30 pairs of adult male and female cat fleas 3 days before oral treatment with nitenpyram. Four additional adult cats were infested with 30 pairs of adult and female cat fleas ≈30 d after the first series.

Test Article. Nitenpyram (Capstar Novartis Animal Health, Greensboro, NC) was administered orally to half of the flea-infested cats at the recommended dose (11.4 mg tablet for cats between 1 and 11 kg body weight).

Adult Flea Mortality. All treated and untreated adult cats were confined in separate stainless steel cages. Wire mesh cage bottoms allowed debris, cat fleas, and eggs to collect in trays underneath the cages. Numbers of live and dead fleas in the cage trays were counted every 30 min for the first 8 h after treatment. At the same time, cats were lightly groomed by making two long, continuous strokes with a flea comb from the nose to the tail of each animal to dislodge dead fleas while minimizing live flea removal. Fleas dislodged in this way were removed, and numbers were included in the tally.

On days 2–4 after treatment, live and dead fleas were collected from trays beneath the cages, and total number of live and dead fleas was recorded. Each morning, the cats were thoroughly and repeatedly combed (up to 15 min/cat) to remove any live fleas. This procedure was modified from the standard combing technique of 5 min (Kramer and Mencke 2001) to ensure that most of the fleas were removed. After combing, a new aliquot of 30 pairs of fleas was added. On day 4, the final aliquot of adult fleas was placed on each cat. These fleas remained on the cats and were undisturbed for the remainder of the test. This procedure was replicated twice with a total of 10 cats.

Typically, there is a group of fleas that are unaccounted for after totaling the number of live fleas removed with the flea comb and the number of dead fleas in the trays. The efficiency of grooming cats with flea combs to remove live fleas depends on the time and experience of the lab technician (Kramer and Mencke 2001). Combing short-haired beagle dogs for 5 min provided ≈81% recovery, and longer periods of combing did not significantly increase the number of fleas recovered (Zakson et al. 1995). Dryden et al. (1994) found that combing techniques could differentiate between low, medium, and high flea infestations on dogs. Both authors suggested that animals with longer coats might take longer to comb. In addition, grooming activities by cats can remove up to 47% of the fleas within 7 d (Wade and Georgi 1988, Rust 1994). The unaccounted for fleas are typically attributed to mortality because of host grooming, especially in cats.

Flea Egg Production. Flea eggs and debris collected in cage trays beneath the animals were brushed with a paint brush into the top of a series of four sieves (10, 16, 20, and 60 mesh). Flea eggs separated from other material were retained on a 60-mesh screen. To facilitate counting, eggs were transferred to a petri dish (100 mm diameter × 15 mm) and placed on top of dark paper (with 10-mm grid markings) for microscopic examination. Egg counts were recorded for the first 4 days after treatment and also from days 7 to 10 after treatment. Days 5 and 6 were not collected because it was the weekend. Egg viability was determined by adding larval rearing media and holding the petri

Table 1. The efficacy and longevity of nitenpyram treatments on cats infested with *Ctenocephalides felis*

Posttreatment (Hours)	% Mortality[a]		% Unaccounted		No. eggs collected[b]	
	Treated	Untreated	Treated	Untreated	Treated	Untreated
24	100	0.3*	59	8	6.2a	206.8d
48	98.6	0.0*	66	21	1.6a	141.4b
72	5.0	0.3	53.6	1.6	4.6a	97.8b
96	0.0	0.0	34	28		
192	—	—	—	—	430.8c	482.8c

[a] Tested paired t-test; *, indicates significantly different at $P < 0.05$.
[b] Two-way ANOVA (Tukey test, $P < 0.05$). Means followed by the same letter are not significantly different at $P < 0.05$.

dishes in an incubator maintained at 26 ± 2° and 80% RH and counting the number of pupae that developed 12 d later.

Behavioral Observations of Treated Cats. To assess the extent and duration of any possible side effects in cats treated with a nitenpyram pill, three treated and three untreated adult cats were observed for 8 h after treatment. Behavioral observations were made at 15-min intervals throughout the day. Observation periods were alternated with equal time blocks during which observations were not recorded. Three distinct categories of behavior (preening, twitching, and scratching) were recorded. Behaviors lasting longer than 10 s were recorded as multiple events. Categorized behaviors are as follows: twitching, a sudden, short jerking or spasmodic movement of the ear, head, or leg; scratching, a mild scrape using the claws to relieve an irritation; preening, biting and licking to clean or bathe the fur.

Statistical Analyses. The number of fleas killed by the nitenpyram was compared with the untreated controls with a *t*-test (Sigma Stat 1997). The number of eggs collected from treated and untreated cats was analyzed with a two-way analysis of variance (ANOVA), and the means separated with Tukey's honestly significant difference (Sigma Stat 1997).

Results

The nitenpyram acted within 30 min of administration (Fig. 1). Initially, fleas were dislodged from the host and recovered in the trays. After 1 h, fleas were found dead in the trays. Within 24 h, 100% of the adult fleas on the cats treated with nitenpyram were killed (Table 1). When new aliquots of fleas were released on the treated cats at 24-h posttreatment, 98.6% were killed within 24 h. Between 48 and 72 h, only 5% of the adult fleas were killed. After 72 h, no adult fleas were collected from the trays beneath the cats.

The percentage of fleas that were unaccounted for remained above 50% for at least 3 d and was significantly higher in nitenpyram treatments than in the untreated control.

The number of eggs laid by the 30 adult flea pairs placed on the treated hosts was significantly lower than numbers from untreated cats. Numbers of eggs produced by adult cat fleas ranged between 97 and 206 eggs/d in the untreated controls. On d 8, the adult cat fleas had been on the treated and untreated cats for 96 h and produced 430–482 eggs/d.

The level of preening events rapidly increased in the nitenpyram-treated cats (Fig. 2). The cats' response levels peaked at 60 min. Increased levels of

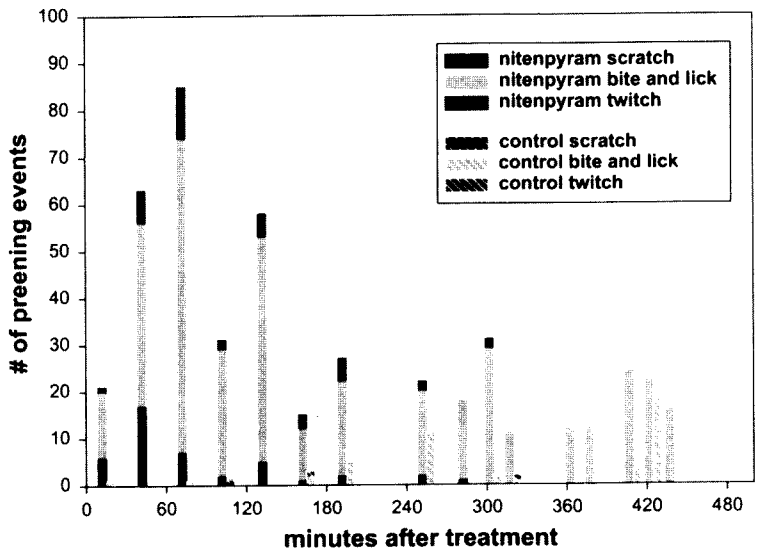

Fig. 2. Grooming behavior after flea-infested cats were treated with nitenpyram.

biting and licking persisted for at least 7 h in cats treated with nitenpyram.

Discussion

The study of Cadiergues et al. (1999) suggests that nitenpyram may have some residual effect on flea populations. They found that single doses of nitenpyram weekly provided >90% flea control on dogs for 14 d in conditions that permitted flea reinfestation. Our results indicate that blood levels of nitenpyram are still lethal to fleas at least 48 h after treatment. By 72 h, levels of nitenpyram in host blood were no longer lethal upon ingestion. However, sublethal effects, the reduction in egg production by female cat fleas, persist for at least another 24 h.

Administration of nitenpyram to flea-infested cats resulted in intense scratching, licking, and biting of the pelage. This intense reaction lasted for ≈2 h. With the removal of fleas from the pelage by host grooming and as fleas were dislodged after ingesting nitenpyram, the amount of grooming decreased dramatically after 2 h, but continued at an elevated level for another 5 h. Mahoney et al. (2001) speculated that the trembling of the fleas may irritate the host, resulting in increased grooming. This seems unlikely because the intense grooming continued for up to 7 h, long after many of the fleas had fallen from the host. There is no real definitive explanation, and additional studies are certainly warranted.

The increased amount of grooming in cats treated with nitenpyram greatly contributes to the percentage of fleas that could not be accounted for at the end of each 24-h test period. Percentages of fleas removed by host grooming were found to be 49.5% (Wade and Georgi 1988) and 8–47% (Rust 1994) in 7 d.

Nitenpyram provides a unique and very useful method of rapidly removing adult fleas from cats and dogs in both clinical and research settings. It certainly would provide animal groomers with an effective means of eliminating adult fleas without bathing the pets. It is a vast improvement from combing or treating with animals with shampoos or dusts to remove fleas. However, in laboratory research settings, the treated animals are unsuitable for reinfestation with fleas for ≈96 h.

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