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How Do Flea Control Products Kill Fleas?

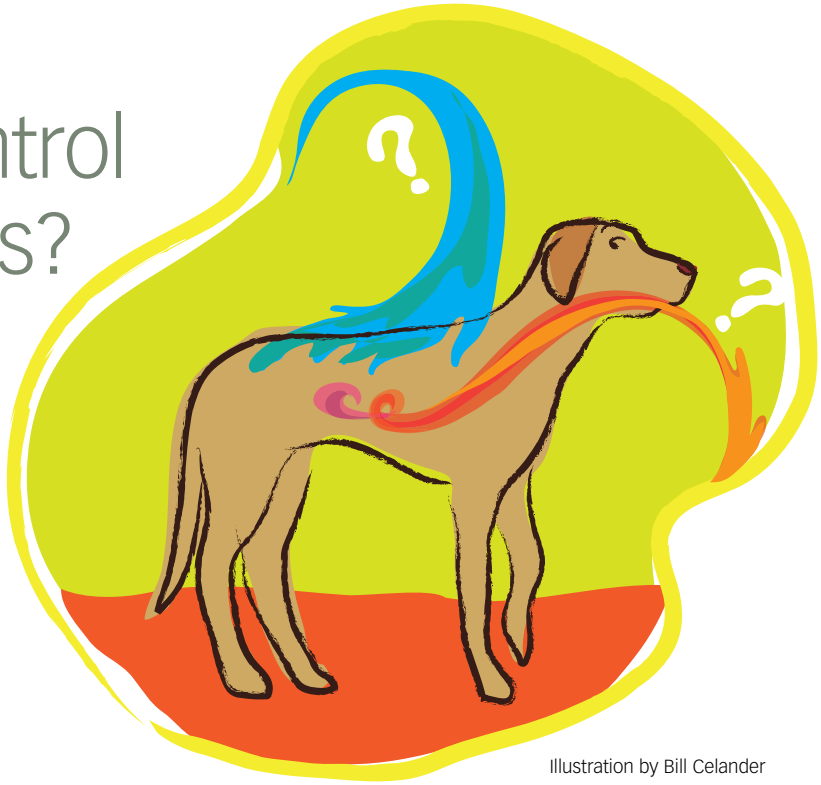

Illustration by Bill Celander

You have asked...

> There are so many products available for flea control; what are the differences between topical and oral therapeutics?

The expert says...

Topical and oral therapeutics have revolutionized flea control for domestic cats and dogs. In many cases, these new products have eliminated the need to treat indoor and outdoor environments; helped manage flea-allergic dermatitis; and controlled other arthropods, such as ticks and mites. This article expands on reviews of topically and orally administered flea products[1–3] (**Table 1**) and discusses whether the active ingredients must be ingested or come into direct contact with fleas.

CONTACT VS INGESTION

More traditional treatments (such as shampoos, dusts, and sprays) contain carbaryl, permethrin, and synergized pyrethrins and insect growth regulators (ie, methoprene and pyriproxyfen) and are designed to work by contact. Some of these treatments are directed at fleas; with others, the fleas contact residual deposits and are killed.

However, in the past 10 years new chemistries have provided the clinician and pet owner with additional choices (**Table 2**). Speed of kill and the inhibition of feeding by adult fleas are especially important as they relate to fast knockdown and prevention of flea feeding. The faster an active ingredient inhibits feeding and kills the fleas, the more likely it will prevent flea-allergic dermatitis.

Although many articles have discussed the efficacy of various products, relatively few have addressed whether these therapies kill fleas through contact (ie, topical activity) or ingestion of the toxicant.

TOPICAL AGENTS

Topical applications of dinotefuran, fipronil, imidacloprid, metaflumizone, and pyriprole spread rapidly over the hair coat within 24 to 48 hours (**Figure 1, page 84**). They are distributed in the skin and stored in the sebaceous glands. The hair coat is toxic to fleas for 30 to 60 days, depending on the active ingredient.

Fipronil & Imidacloprid

These insecticides are extremely active against adult fleas; typically < 1 ng is required to kill 50% of adult fleas. Studies with a radiolabeled fipronil

showed that it was found mainly in the sebaceous glands and epithelial layers.[4] Other studies also support the premise that the active ingredient is on the skin and hair. Levels of imidacloprid in serum were below the lowest effective concentration of 0.1 mg/L[5]; analyses of hair and skin showed metaflumizone values 3 orders of magnitude higher than levels in plasma.[6]

Some studies suggest that repeated or long-term exposures to fipronil or imidacloprid may pose health risks to individuals coming into contact with treated pets.[7,8] However, a recent study at the University of California–Riverside showed that fipronil transfer to humans from treated hair coats was undetectable in human urine.[9]

Selamectin

Selamectin is also delivered by topical application, but this novel avermectin is absorbed and found in the plasma. Concentrations peak at a mean (standard deviation) of 12.72 ± 5.13 mcg/mL for male dogs and 0.87 ± 0.85 ng/mL for female dogs in about 5 days.[10] It is also effective in killing the chewing lice *Trichodectus canis* (dogs) and *Felicola subrostratus* (cats), which

Table 1. Active Ingredients, Chemical Classes, & Modes of Action

Active Ingredient	Chemical Class	Mode of Action
Dinotefuran	Neonicotinoid	Inhibits nicotinic acetylcholine receptors
Fipronil	Phenylpyrazole	Blocks GABA-gated chloride channels
Imidacloprid	Neonicotinoid	Inhibits nicotinic acetylcholine receptors
Lufenuron	Chitin synthesis inhibitor	Disrupts chitin development
Nitenpyram	Neonicotinoid	Inhibits nicotinic acetylcholine receptors
Pyriprole	Phenylpyrazole	Blocks GABA-gated chloride channels
Selamectin	Avermectins	Binds to glutamate-gated chloride channels
Spinosad	Natural product: fermentation of an actinomycete *Saccharopolyspora spinosa*	Activates nicotinic acetylcholine receptors; affects GABA receptors

GABA = gamma-aminobutyric acid

Table 2. Active Ingredients & Selected Products Available for Flea Control

Active Ingredient	Product	Application	Route of Toxicity to Fleas	Approval Agency
Dinotefuran	4.95% (w/v), Vectra 3D (summitvetpharm.com)	Topical	Contact	EPA
Fipronil	10% (w/v), Frontline Plus (merial.com)	Topical	Contact	EPA
Imidacloprid	9.1% (w/v), Advantage (bayerah.com)	Topical	Contact	EPA
Lufenuron	90–205 mg/tablet, Program (novartis.com)	Oral	Ingestion	FDA
Nitenpyram	11.4 or 57.0 mg/tablet, Capstar (novartis.com)	Oral	Ingestion	FDA
Pyriprole	12.5% (w/v), Prac-Tic (novartis.com)	Topical	Contact	Not approved for use in U.S. at this time
Selamectin	7.4%–14.2%, Stronghold/Revolution (pfizerah.com)	Topical	Ingestion	FDA
Spinosad	140–1620 mg/tablet, Comfortis (elanco.com)	Oral	Ingestion	FDA

EPA = Environmental Protection Agency; FDA = Food and Drug Administration

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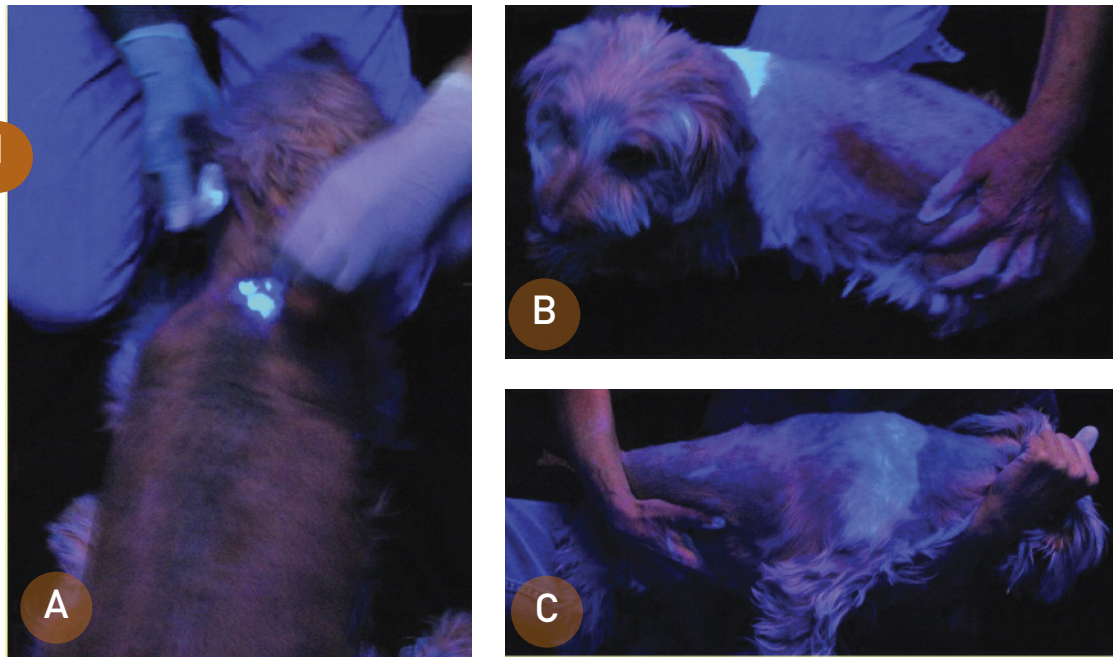

Migration of a fluorescent dye added to fipronil to the neck of a dog: Application (A), 5 hours after application (B), and 24 hours after application (C)

might suggest some activity upon contact. Treated hair is toxic to fleas, albeit very slowly.[11] The agent may be absorbed in the basal layer of the epidermis and released with natural oils onto the skin.

ORAL TREATMENTS

Orally administered treatments include lufenuron (an insect growth regulator), nitenpyram, and spinosad. These agents' modes of action differ considerably.

Lufenuron

Lufenuron is taken up during feeding and disrupts the reproductive capabilities of adult fleas; adult females fail to produce viable eggs. The unabsorbed lufenuron passes through the flea digestive system and is excreted in the fecal blood droplets. This treated fecal material is toxic to developing larvae.

Nitenpyram & Spinosad

In contrast, nitenpyram and spinosad are toxic to adult fleas. Plasma concentrations of the neonicotinoid nitenpyram peak within 30 minutes in cats and dogs.[12] Ingestion produces rapid cessation of feeding and knockdown of fleas. The effects persist for up to 48 hours after treatment. Spinosad, a fermentation product of the actinomycete *Saccharopolyspora spinosa*, contains the active ingredients spinopsyns A and D; unlike nitenpyram, it is effective for 30 days. Topical sprays and pour-on treatments are active against chewing lice on cattle (*Bovicola bovis*), suggesting that there may be some contact activity as well.[13]

THERAPEUTIC MODES OF ACTION

The ability of topical and oral therapies to control fleas depends on their unique properties and modes of action. The mode of action of the active ingredients dictates the speed at which fleas are immobilized and feeding is inhibited, not necessarily the route by which the ingredients are delivered. The wide range of active ingredients in these revolutionary therapies ensures that we will have effective flea control products for years to come.

See Aids & Resources, back page, for references and suggested reading.

Discuss it!

What type of flea control products do you typically recommend for your patients—topical, oral, or a combination of both? Answer our Polling Place question at cliniciansbrief.com.