ChemicalWatch Factsheet

A Beyond Pesticides/ NCAMP Factsheet

Fipronil

Fipronil, 5-amino-1-(2,6-dichloro-4-(trifluoromethyl) phenyl)-4-((1,R,S)-trifluoromethyl)sulfinyl)-1-H-pyrazole-3-carbonitrile, is a phenyl pyrazole, broad-spectrum insecticide, first introduced to the U.S. in 1996 for commercial turf and indoor pest control. It is particularly effective by way of ingestion and causes neural excitation and convulsions in insects, resulting in death.[1,2] It is used to control ants, beetles, cockroaches, fleas, ticks, termites, mole crickets, thrips, rootworms, weevils, and other insects.[3]

Common products containing fipronil are Chipco Brand, Frontline®, TopChoice, Regent, Termidor, Combat®, and MaxForce®.[4] Concerns about human exposure to Frontline spray treatment were raised in 1996, leading to a denial of registration for the spray product.[5]

A U.S. EPA study conducted between 2005-2006 found fipronil residues (on floor wipes) in approximately 40% of homes studied.[6] Fipronil is not easily absorbed dermally, but human exposure can occur through hand-to-mouth transfer after petting treated animals.[7] One study detected fipronil residues on gloves worn while petting treated dogs for 5 minutes, with the highest concentration of 589.3 ppm (± 205.7ppm) detected 24 hours after application.[8] A 2009 U.S. Geological Survey (USGS) study found that residences with a pet on which a flea-control product containing fipronil was used were among homes with elevated fipronil concentrations, and concentrations 15 times higher indoors than those found outdoors.[9] Occupational exposure to fipronil may occur through inhalation of dust and dermal contact with this compound at workplaces where fipronil is produced or used.[10]

Mode of Action

Fipronil is part of a new generation of insecticides that possesses greater affinity at GABA receptors in insects. Fipronil acts by preventing the passage of chloride ions through γ-aminobutyric acid (GABA) -gated chloride channels.[11] It is considered a selective GABA antagonist because it shows a greater binding affinity to insect than to mammal GABA receptor chloride channels. It induces accumulation of the receptors in a novel, long-lived blocked state.[12]

chemicalWATCH* Stats*:

CAS Registry Number: 120068-37-3
Chemical Class: phenyl pyrazole
Use: Broad-spectrum insecticide mostly used for structural pest control
Toxicity Rating: Toxic
Signal Words: Caution, Warning
Health Effects: Endocrine disruption, possible carcinogen, neurotoxic and reproductive effects
Environmental Effects: Toxic to fish, aquatic invertebrates and other non target organisms such as bees.

Acute Toxicity

The technical form of fipronil has the signal word "Warning," implying moderate toxicity, while all formulated or end-use products in the U.S. carry the signal word "Caution," indicating low toxicity.

Symptoms of exposure to fipronil include headache, nausea, dizziness, and weakness -symptoms typically associated with the antagonism of GABA receptors in the brain.[13] In pets, poisoning symptoms include irritation, lethargy, incoordination, and convulsions.[14] It may cause mild irritation of the eyes and slight skin irritation, but is not a skin sensitizer.[15] Adverse effects in short-term studies have been observed in the central nervous system for all test species used, and in the liver and thyroid for the rat.[16] It has moderate acute toxicity by oral and inhalation routes in rats. It is of moderate dermal toxicity to rabbits, and is less toxic to mammals than to fish, some birds, and invertebrates. Severe skin reactions to Frontline Topspot for cats and Topspot for dogs have occurred, with skin irritation and hair loss at the site of application.

Once absorbed, fipronil is rapidly metabolized and residues widely distributed in tissues where significant amounts of residues remain, particularly in fat and fatty tissues. Levels of residues in fat and other tissues are greater with repeated exposures to low doses or a single high dose exposure than with a single low dose. The long half-life (150-245

hr in some cases) of fipronil in blood may reflect slow release of residues from fat and might suggest potential bioaccumulation of metabolic products of fipronil.[17]

Chronic Toxicity

Neurotoxicity

Fipronil has demonstrated neurotoxicity in the acute and subchronic rat neurotoxicity studies, as well as in the rat chronic/oncogenicity and chronic dog studies. Behavioral changes and decreased absolute brain weights were seen only at levels where there was maternal toxicity (decreased body weight, body-weight gain and food consumption).[18] The NOEL was 0.5 mg/kg for males and females rats. The LOEL was 5.0 mg/kg for males and females based on decreased hind-leg splay at the 7 hour post-treatment.[19]

A study by Lassiter et al. found that fipronil inhibited DNA and protein synthesis in undifferentiated neuronotypic PC12 cells and evoked oxidative stress, resulting in reduced cell numbers even though cell viability was maintained.[20] These researchers also found fipronil is inherently a more potent disruptor of neuronal cell development than chlorpyrifos.

Developmental and Reproductive Toxicity

In EPA studies, there was no evidence of developmental toxicity. In a two-generation reproduction study in the rat with fipronil, toxicity to the offspring (clinical signs of toxicity, decreased litter size, decreased body weights, decreased pre- and postnatal survival, and delays in physical development) occurred only at levels where there was maternal toxicity (including maternal mortality). A study by Ohi et al. found that treatment with fipronil altered cyclicity of female wistar rats lengthening the estrous cycle (days) after a single topic administration, reduced the pregnancy index and altered plasma progesterone and estradiol levels, leading the researchers to conclude that fipronil may alter the normal functioning of the endocrine system and cause adverse reproductive effects.[21]

Endocrine Disruption

Fipronil can disrupt thyroid function – responsible for the regulation of cell metabolism- by decreasing plasma concentrations of total thyroxine (T4) likely through increased T4 clearance. However, the mechanism of fipronil action on thyroid function remains unclear.[22] One study concluded that fipronil-induced thyroid disruption results from an increased rate of T4 elimination likely mediated by increased hepatic enzyme activity.[23]

In rats, treatment with fipronil appeared to result in stimulation of the thyroid glands as evidenced by increased accumulation of 125I in the thyroid glands and by increases in the ratios of radioactive distribution between the blood and thyroid.[24] These changes were accompanied by increases in thyroid weight. Relevance of this mechanism for the risk of fipronil for human health is subject to controversy because of the specificities of adult rat for thyroid hormone (TH) plasma binding properties which often lead to the assumption that rats are more sensitive than humans to thyroid disruption. Thus, in a study done with sheep, a species more relevant to human from the standpoint of TH plasma binding, effects were limited to a moderate increase in free T4 clearance.[25]

Carcinogenicity

Fipronil is carcinogenic to rats at doses of 300 ppm, causing thyroid cancer - thyroid follicular cell tumors - related to disruption in the thyroid-pituitary status, and is classified by EPA as a Group C (Possible Human) carcinogen based on the rat carcinogenicity study. EPA concluded, "The thyroid tumors appear to be related to a disruption in the thyroid-pituitary status, and fipronil is not likely to be carcinogenic to humans at doses that do not alter rat thyroid hormone homeostasis."[27]

Metabolites

Fipronil has several break-down products including: fipronil-sulfone (MB46136), fipronil-thioether (MB45950) and fipronil-desulfinyl (MB46513). Fipronil-sulfone, the primary biological metabolite of fipronil, and fipronil-thioether have a similar toxicological profile to fipronil, even though fipronil-sulfone is reportedly six times more potent in blocking vertebrate GABA-gated chloride channels than fipronil. Fipronil-desulfinyl however, appears to be about 10 times more acutely toxic to mammals and more persistent than fipronil itself.[28,29] Fipronil-desulfinyl is not an animal or plant metabolite, rather it is a photodegradate of fipronil - meaning it forms when the parent compound fipronil is exposed to sunlight.[30]

Clinical signs of neurotoxicity in mice and rats fed a diet of fipronil-desulfinyl included excessive jumping, irritability to touch, aggressivity, and increased motor activity. Studies showed that there is potential for bioaccumulation of fipronil-desulfinyl in fatty tissues.[31] In mice, fipronil-sulfone was found in brain, liver, and kidney seven hours after administration.[32]

Effects on Wildlife

Fipronil is highly toxic to fish and aquatic invertebrates, highly toxic to bees, highly toxic to upland game birds, and moderately toxic to waterfowl, but is practically non-toxic to mallard ducks and other bird species. Some fipronil formulations present a risk to endangered bird, fish, and aquatic and marine invertebrates.[33] The metabolite fipronil-sulfone is more toxic to birds, and both fipronil-sulfone and fipronil-thioether are more highly toxic to freshwater invertebrates than fipronil itself.[34] There is evidence

that fipronil and some of its degradates may bioaccumulate, particularly in fish.[35] Stehr et al. discovered that fipronil can also impair the development of spinal locomotor pathways in fish by a mechanism unrelated to its effect on the GABA receptor.[36]

Environmental Fate

Fipronil is stable at normal room temperature for 1 year in the absence of metallic ions. Decomposition of fipronil was less than 0.5% after storage at 100oC for 1 day and 50oC for 7days.[37] It is classified as having an 'extremely low' volatility (2.8x10-9 mmHG), but given new research showing the adverse effects of exposure to extremely low doses, indoor use should be avoided. The half-life of fipronil was found to range from 122-128 days in oxygenated sandy loam soil, 0.7 to 1.7 months on soil surfaces, and 3 to 7.3 months when incorporated in soil.[38] It has low soil mobility and little potential for groundwater contamination, based on an experimental Koc range of 1,086-6,863. The photolytic half-lives for the photodegradation of fipronil in soils range from 147 hours to 217 hours, depending on soil type and concentration of organic matter.[39] Fipronil is not considered to be readily biodegradable.

In water and sediment that lack oxygen, fipronil degrades more slowly, with a half-life of 116-130 days. Adsorption to suspended solids and sediment is expected. Its half-life in basic solutions is 28 days, and it remains stable to breakdown by water at a mildly acidic to neutral pH. An estimated bioconcentration factor (BCF) of 240 suggests the potential for bioconcentration in aquatic organisms is high.[40] When exposed to sunlight, fipronil has a half-life of 3.6 hours in water.[41] The half-life on vegetation is 3-7 months.

Alternatives to Fipronil

Fipronil is used mainly for structural pest control, i.e. control of termites, ants, cockroaches. However there are many alternatives available for the control of structural pests. The recommended method is the implementation of an integrated pest management plan (IPM) that includes one or more pest control methods, including sanitation, structural repairs that prevent insects from entering structures, mechanical controls and other non-chemical methods.

Least-toxic pesticide options include:

-boric acid & disodium octobrate tetrahydrate
-silica gels
-diatomaceous earth
-essential oils

For more information on pest control alternatives, visit Least-toxic Control of Pests Factsheets at http://www.beyondpesticides.org/alternatives/factsheets/index.htm

Fipronil *chemicalWATCH* Factsheet Bibliography

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