ENVIRONMENTAL FATE OF PYRIPROXYFEN

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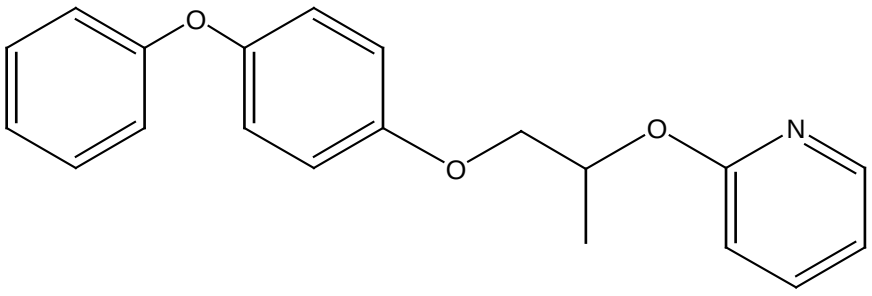
This document reviews the environmental fate and environmental effects for pyriproxyfen 2-[1-methyl-2-(4-phen-oxyphenoxy)ethoxy]pyridine ($C_{20}H_{29}NO_3$). Pyriproxyfen is a juvenile hormone analog and a relatively stable aromatic compound. It functions as an insecticide by overloading the hormonal system of the target insect, ultimately affecting egg production, brood care and other social interactions, and inhibiting growth (Glancey et al., 1990). It is active at 25-100 grams active ingredient per hectare (Hopkins, 1994). Pyriproxyfen works well against public health insects like houseflies and mosquitoes (The British Crop Protection Council 1991). Pyriproxyfen is reported to have 95% inhibition of emergence for mosquito larvae and its effects on mosquito larvae lasted for two months after application (Miyamoto et al. 1993). Currently, pyriproxifen is one of several insecticides used for the control of the Red Imported Fire Ant (*Solenopsis invicta*) in California. For managing fire ant, pyriproxyfen is formulated as bait on small particles such as corncob grits. These particles contain the insecticide plus a food attractant, which is usually soybean oil. The ants are attracted to the bait, and they pick it up and carry it back into the mound. At some point, a toxic dose is reached, and the ants begin to die. Baits are used as mound or broadcast treatments over the infested area. Pyriproxyfen is also effective in controlling other insect pests, such as Green Peach Aphid, Arrowhead scale, Greenhouse whitefly, and Pear psylla.



pyriproxyfen
2-[1-methyl-2-(4-phenoxyphenoxy)ethoxy]pyridine

Physico-Chemical Properties[a] and Environmental Fate

CAS Number:	95737-68-1
Molecular Weight:	321.5
Water Solubility:	0.367 ppm
Melting Point:	45-47º C
Vapor Pressure:	1.0×10^{-7} mm/Hg @ 20º C
Henry's Constant:	1015×10^{-7}
Octanol-water coefficient (Kow):	2.36×10^{5}
Soil Adsorption Coefficient (Kd)	11.7 – 324
Hydrolysis Half-Life[b]	Stable
Photolysis Half-Life (Soil, Artificial Light)[d]	6.8 to 8.5 days
Photolysis Half-Life (Water, Artificial Light)[c]	3.72 to 6.23 days
Field Dissipation Half-life[d]	3.5 to 16.5 days
Aerobic Soil Metabolism (Half-Life)[e]	12.4 days
Aerobic Aquatic Metabolism (Half-Life)[e]	23.1 days
Anaerobic Aquatic Metabolism (Half-Life)[e]	346.5 days

[a] Kollman and Segawa Pest Chem database, DPR 1995
[b] Katagi, T. and N. Takahashi. (1994)
[c] Fathulla (1995)
[d] Tamichi and Wuster (1997)
[e] Fathulla and Ohno (1993)

Toxicity [c]

Acute Ingestion:

Acute Oral LD_{50} (mallard duck):	>2,000 mg/kg
Acute Oral LD_{50} (bobwhite quail):	>2,000 mg/kg
Dietary LD_{50} (mallard duck):	>5,200 ppm
Dietary LD_{50} (bobwhite quail):	>5,200 ppm
Reproductive (mallard duck):	NOEC = 600 ppm
Reproductive (bobwhite quail):	NOEC = 600 ppm

Acute Inhalation LC_{50} (Rat):	>3.48 mg/l air - 4 hours

Ecological Effects [c]:

Freshwater Species:	
Bluegill Sunfish 96-hour LC_{50}:	>270 µg/L
Rainbow Trout 96-hour LC_{50}:	>325 µg/L
Rainbow Trout 21 day LC_{50}:	90 µg/L
Carp 96-hour LC_{50}:	450 µg/L
Killfish 96-hour LC_{50}:	2660 µg/L
Daphnia magna 48-hour EC_{50}:	400 µg/L
Daphnia magna 21 day MATC:	20 ppt
Rainbow Trout 21 day MATC:	5.4 µg/L
Estuarine Species:	
Sheepshead minnow 96-hour LD_{50}:	>1.02 ppm
Mysid Shrimp 96-hour LD_{50}:	>92 µg/L
Oyster Shell Deposition 96-hour EC_{50}:	>92 µg/L
Nontarget Organisms:	
Bee Contact LC_{50}	>100 µg/bee

[c]Toxicity and Ecological Effects Data Obtained From Valent USA Corporation, Post Office Box 8025, 1333 N. California Blvd., Suite 600, Walnut Creek, CA 94596-8025.

Mode of Action of Pyriproxyfen

Two major insect-hormones act to control metamorphosis: the molting hormone and the juvenile hormone (JH). High concentrations of JH and low concentrations of molting hormone cause molting larva to continue growing as larval instars (a stage of an insect or other arthropod between molts). Presence of the molting hormone coupled with the absence of JH in insect circulation results in larvae which change into adults. Insects often go through a number of instars however when the JH secretion stops metamorphosis follows (Staal 1972). JH maintains the "youthful character" of the insect and prevents the insect from becoming an adult before it is fully grown. Abnormal amounts of JH often result in the eventual death of the larva.

The search to apply knowledge of JHs to the development of effective insecticides has since been limited to the area of JH analogs (JHAs) (Matolcsy et al., 1988). JHAs act in the same manner as JHs, but are much more chemically stable.

Pyriproxyfen is a JHA and a fenoxycarb derivative in which part of the aliphatic chain has been replaced by pyridyl oxyethylene. Although these active JHA compounds bear little resemblance to JHs, their high stability allows them to compete for JH binding site receptors (Riddiford 1994). Pyriproxyfen mimics the action of the juvenile hormones on a number of physiological processes, and is a potent inhibitor of embryogenesis, metamorphosis and adult formation (Ishaaya and Horowitz, 1992).

Environmental Fate of Pyriproxyfen

Air: The vapor pressure and Henry's Law constant of pyriproxyfen are moderate which indicates that it may have a tendency to volatilize slightly from aqueous solution into the atmosphere.

Soil: In 1993 and 1994, field studies were conducted in California to evaluate the mobility and persistence of pyriproxyfen when applied to bare ground. A single broadcast application of a 10% w/v active ingredient concentrate (100g/L) of pyriproxyfen was performed at a rate of 715 g active ingredient per hectare. Soil core samples were taken to 36 inches deep at specified intervals immediately before and after application. Core composites were analyzed for pyriproxyfen and two metabolites, 4-(4'-hydroxyphenoxy)phenyl-2-(2-pyridyloxy)-propyl ether (*a.k.a.* 4'-OH-Pyr) and 2-(2-pyridyloxy)propionic acid (PYPAC). Average pyriproxyfen concentrations found in the 0-6 in inch soil layer were 0.34 ppm on day zero and 0.012 ppm on day 181. In the 6-12 inch layer, average residue concentrations were found to be up to 0.027 ppm through day 31, and below the 0.010-ppm level of quantitation thereafter. No pyriproxyfen residues were found above the level of quantitation at any soil depth below 12 inches. The half-life of pyriproxyfen in the 0-6 inch soil layer was 36 days. Average 4'-OH-Pyr concentrations found in the 0-2 inch soil layer reached a maximum of 0.026 ppm on day 23. No 4'-OH-Pyr residues were found below 2 inches or greater than 120 days. The half-life of 4'-OH-Pyr in the 0-2 inch soil layer was 83 days. Average PYPAC concentrations found in the 0-2 inch soil layer reached a maximum of 0.023 ppm on day 7. No PYPAC residues were found below 2 inches or greater than 120 days. The half-life of PYPAC in the 0-2 inch soil layer was 33 days (Jacobson and Gresham, 1995).

The soil metabolism of ^{14}C-Pyriproxyfen (4-phenoxyphenyl-2-(2-pyridyloxy)propyl ether) was studied under aerobic conditions using a California sandy loam soil. Pyriproxyfen was uniformly labeled in the phenyl ring ([Phe-^{14}C]-pyriproxyfen) and at C_2 and C_6 of the pyridyl ring ([Pyr-^{14}C]-pyriproxyfen). Eighty-nine soil samples were prepared in glass containers, forty-four of which were fortified with [Phe-^{14}C]-pyriproxyfen at a concentration of 0.60 µg test material/g soil, and forty-five of which were fortified with [Pyr-^{14}C]-pyriproxyfen at a concentration of 0.61 µg test material/g soil. Samples were incubated in glass chambers maintained in a dark, temperature-controlled room at 25±2 ºC. Humid air was passed through the system continuously to create a humid aerobic environment. Samples were extracted at various times and the radioactivity of each sample was determined by liquid scintillation counting. Pyriproxyfen was

found to degrade via biological catalysis, serving as a carbon source for soil microorganisms. Pyriproxyfen degraded rapidly in soil under aerobic conditions, with a half-life of 6.4 days for [Phe-^{14}C]-pyriproxyfen and 9.0 days for [Pyr-^{14}C]-pyriproxyfen (Fathulla, 1994).

Water: A hydrolysis study was conducted with pyriproxyfen using a uniformly ^{14}C-labeled preparation ([Phe-^{14}C]-pyriproxyfen) and a preparation labeled separately at C2 and C6 of the pyridyl ring ([Pyr-^{14}C]-pyriproxyfen). Labeled compounds were dissolved in acetate buffer at pH 5.0 and borate buffers at pHs 7.0 and 9.0, and aseptically incubated at 25 C for 30 days in darkness. Aqueous half-lives were determined to be 147.8 – 604.6 days at pH 5.0, 241.2 – 1292.5 days at pH 7, and 161.4 – 511.4 days at pH 9.0. It was thus concluded that pyriproxyfen is hydrologically stable under the conditions tested (Katagi and Takahashi, 1994).

Schaefer et al. (1988) found that when a 37 m^2 pond was treated with 0.04 lb/acre pyriproxyfen, measured residue concentrations declined by 50% in 24 hours. A similar study was performed several years later, and analogous results were observed (Schaefer and Miura, 1990). In highly polluted water, however, pyriproxyfen readily adsorbed onto organic matter and its biological activity persisted for two months after an initial application rate of 0.1 lb/acre. Its persistence in water in the absence of organic matter declined as temperature and sunlight exposure increased (Schaefer et al., 1988).

Fathulla (1993) conducted an aerobic aquatic metabolism study using [Phe-^{14}C]-pyriproxyfen) and ([Pyr-^{14}C]-pyriproxyfen) in lake sediment and water. Twenty-six samples were fortified with [Phe-^{14}C]-pyriproxyfen (0.306 µg/g of soil), and twenty-six samples were fortified with [Pyr-^{14}C]-pyriproxyfen (0.273 µg/g of soil). The radioactivity in the water layers and sediment extracts was quantified by liquid scintillation counting. For [Phe-^{14}C]-pyriproxyfen, the labeled parent compound was found to be the major component in the combined sediment extracts and water layers, ranging from 90.7% (day 0) to 27.3% (day 31). The half-life for [Phe-^{14}C]-pyriproxyfen was 16.2 days. For [Pyr-^{14}C]-pyriproxyfen, the labeled parent compound was found to be the major component in the combined sediment extracts and water layers, ranging from 91.8% (day 1) to 37.4% (day 21). The half-life for [Pyr-^{14}C]-pyriproxyfen was 20.8 days. The formation of bound residues (parent and degradates) and the accompanying formation of $^{14}CO_2$ suggest that the degradation pathway is governed by biological catalysis. Metabolism in aerobic aquatic media proceeds through oxidative cleavage of the ester linkages. Pyriproxyfen degraded quickly under aerobic aquatic conditions (lake sediment and water) to two major metabolites (PYPAC and 4'-OH-Pyr), several minor intermediate metabolites, bound residues, and CO_2.

Fathulla and Ohno (1993) calculated the metabolic half-lives (days) for pyriproxyfen and its two major metabolites, PYPAC and 4'-OH-Pyr, in soil and in water:

	Pyriproxyfen	PYPAC	4'-OH-Pyr
aerobic soil metabolism:	12.4	8.17	0.69
aerobic aquatic metabolism:	23.1	15.80	0.69

anaerobic aquatic metabolism:	346.5	41.25	4.80

Fathulla (1995) investigated the aqueous photolysis of radiolabeled pyriproxyfen under controlled conditions (25°C in pH 7 buffered distilled water) using artificial light. Radiolabeled pyriproxyfen of both labeling positions (Phe-^{14}C and Pyr-^{14}C) degraded rapidly under artificial sunlight in buffered solution. The Phe-^{14}C and Pyr-^{14}C analogues had half-lives of 6.23 and 3.72 days, respectively, with an average half-life of 5.04 days. Photodegradation rates of radiolabeled pyriproxyfenin in soil were, like those in water, also rapid. The Phe-^{14}C and Pyr-^{14}C analogues had soil photolysis half-lives of 6.8 to 8.5 days, respectively (Tamichi and Wuster, 1997)

Biota: Crustaceans and aquatic insect larvae are sensitive to pyriproxyfen. *Daphnia magna* Stras and *Daphnia pulex* Leydig, living in treated water, produced fewer progeny. This effect is, however, reversible. At field rates (6-28 g/ha) pyriproxyfen did not exhibit any marked effect on mayfly, dragonfly, ostracods, cladocerans, copepods, beetles, and other Dytiscidae species. When pyriproxyfen was applied at doubled concentration, minor suppression of the reproductive capacity of cladocerans and copepods was observed (Ishaaya and Degheele, 1998) In a study of the efficacy of pyriproxyfen against mosquito larvae, Schaefer, et al. (1988) found that nontarget aquatic organisms that coexist in mosquito breeding habitats exhibit no significant adverse effects resulting from a 0.01 ppm treatment in aquariums. Brown et al. (1996) chose the estuarine shrimp *Leander tenuicornis* as an indicator species for toxicological studies using several pesticides, including pyriproxyfen. Pyriproxyfen produced LC_{50} values of 0.098 ppm against *L. tenuicornis*, about 12 times the estimated field concentration.

Against non-target terrestrial organisms, pyriproxyfen produced severe deformities at molt of a predatory bug *Podisus maculiventris*, but was harmless to another predatory bug *Orius insidious*. None of the larvae of *Rodolia cardinalis* developed into adults after applications of pyriproxyfen. Pyriproxyfen applied either before or after oviposition on pine needles caused total suppression of egg hatch of *Elatophilus hebraicus*. Treating the black scales of *E. formosa*, 80-88% mortality was found. Pyriproxyfen had marked detrimental effects on the development of the immature stages of *Cryptochetum iceryae* (Ishaaya and Degheele, 1998).

Pyriproxyfen is practically non-toxic to bees. De Wael et al. (1995) found that bumblebee *Bombus terrestris* colonies developed normally after feeding on pyriproxyfen-sucrose solution.

Conclusions

Pyriproxyfen 2-[1-methyl-2-(4-phen-oxyphenoxy)ethoxy]pyridine is a broad spectrum IGR (insect growth regulator). Like fenoxycarb, pyriproxyfen is a relatively stable aromatic compound. Pyriproxyfen is a potent insecticide and works especially well against public health insects like houseflies, mosquito larvae and ants.

Pyriproxyfen is moderately volatile. Pyriproxyfen has low water solubility but does not readily adsorb onto soil surfaces. Measured residue concentrations have been reported to decline by

50% in 24 hours in treated ponds. Pyriproxyfen adsorbs onto suspended organic matter and remains biological activity for up to two months after an initial application. Its persistence in water in the absence of organic matter declines with increasing temperature and sunlight exposure.

Field studies conducted in California to evaluate the mobility and persistence of pyriproxyfen when applied to bare ground showed that both the parent compound and its major degradation metabolites, 4'-OH-Pyr PYPAC, were found to be stable in soil for up to a year. The greatest pyriproxyfen concentrations were found in the 0-6 inch soil-layer. No pyriproxyfen residues were found above the level of quantitation below 12 inches. The half-life of pyriproxyfen in the 0-6 inch soil-layer was 36 days. No 4'-OH-Pyr or PYPAC residues were found below 2 inches or greater than 120 days. The metabolism of ^{14}C-Pyriproxyfen in a California sandy loam soil under aerobic conditions suggests that pyriproxyfen degrades rapidly via biological catalysis, having a half-life of 6.4 to 9.0 days and serving as a carbon source for soil microorganisms.

The aerobic aquatic metabolic half-life of pyriproxyfen was determined to be from 16.2 to 20.8 days. Metabolism in aerobic aquatic media proceeds through oxidative cleavage of the ester linkages. Pyriproxyfen degraded quickly under aerobic aquatic conditions (lake sediment and water) to two major metabolites (PYPAC and 4'-OH-Pyr), several minor intermediate metabolites, bound residues, and CO_2.

Crustaceans and aquatic insect larvae are sensitive to pyriproxyfen, although adverse effects were found to be reversible. Pyriproxyfen did not exhibit any marked effect on mayfly, dragonfly, ostracods, cladocerans, copepods, or beetles. Planktonic organisms showed no significant adverse effects resulting from a 0.01-ppm treatment in aquaria. Pyriproxyfen produced LC_{50} values of 0.098 ppm against the estuarine shrimp *L. tenuicornis*, about 12 times the estimated field concentration. Against non-target terrestrial organisms, pyriproxyfen produced severe deformities at molt of several predatory bugs. Pyriproxyfen is, however, practically non-toxic to bees. Bumblebee colonies were found to develop normally after feeding on pyriproxyfen-sucrose solution.

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