

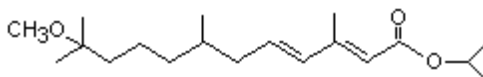
Environmental Fate of Methoprene

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This document summarizes the environmental fate and the effects of methoprene, with a emphasis on its extensive use against Dipteran pests. Methoprene is an insect growth regulator that acts as a juvenile growth hormone, which interferes with the insects' life cycle and disrupts normal development of insects. Methoprene was first registered as a biological pesticide by the EPA in 1975 and later re-classified by the EPA as a biochemical pesticide.

Chemical (IUPAC) name: isopropyl (E,E)-(RS)-11-methoxy-3,7,11-trimethyldodeca-2,4-dienoate. **CAS number:** 40596-69-8. Molecular formula: C₁₉H₃₄O₃ and structural formula of methoprene:



General Information and Mode of Action

Methoprene is a long chain hydrocarbon ester, characterized as an amber or pale yellow liquid with a faint fruity odor (Farm Chemicals Handbook, 1997). It is classified as an insect growth regulator and selective larvicide. Methoprene is used principally against mosquitoes, but is effective against a range of insects, including the orders Diptera, Lepidoptera and Coleoptera (Glare and O'Callaghan 1999).

Common trade names of methoprene include Altosid®, Apex®, Diacon®, Dianex®, Kabat®, Minex®, Pharoid®, Precor®, and Z-515® (Glare and O'Callaghan 1999). The available forms of methoprene are solid (sustained release pellets, boluses and briquettes), liquid, and aerosol. Methoprene is commonly applied directly to water for the control of mosquitoes.

Methoprene is an insect growth regulator that interferes with the normal maturation process of insects, preventing them from completing their life cycle and reaching adulthood, thus ultimately preventing them from reproduction. Reported sublethal effects from methoprene usage include abnormal morphology and development, reduced fertility, alterations in pheromone production, and altered behavior patterns (Glare and O'Callaghan 1999). Morphogenetic abnormalities of insects are normally irreversible and it is the most readily observed effect of methoprene.

These insect growth regulators are found in high concentrations in the hemolymph of particular stages of larval insects, where their function is to maintain the larval stage or prevent metamorphosis (Glare and O'Callaghan 1999). The character and magnitude of the response differs among insects, but generally it is the last instar of larvae or nymph, or pupal stages, which are most affected by methoprene (Staal 1975).

The exact mode of methoprene's action is not completely understood. In mosquitoes, methoprene was reported to interrupt the lysis and re-absorption of old endocuticle, thus halted the synthesis and deposition of new, complex procuticle by the epidermal cells. Cocke, et al. (1979) concluded that the tissues examined were suggestive of possible changes in membrane permeability and selectivity due to disrupted mitochondria and other vesicles.

Molecular Structure

Table 1. Physiochemical Characteristics of Methoprene

Molecular weight _b	310.48 g/mole
Water solubility _b	1.4 mg/L (at 25° C)
Solubility in other solvents _b	Miscible in organic solvents
Boiling point _a	100° C at 0.05 mm Hg
Vapor pressure _d	2.36x10 ⁻⁵ mm Hg (at 25° C)
Henry's law constant _a	6.9x10 ⁻⁶ atm m ³ /mole
Octanol-water partition coefficient _c	log Kow 5.50
Flash point _a	96 ° C (closed up)
Specific gravity _a	09261 g/ml (at 20° C)
K _{OC} (estimated) _e	23,000

^a Farm Chemicals Handbook, 1997

^b Kidd and James, 1991

^c Hansch, et al., 1995

^d Tomlin, 1997

^e Toxnet, 2003

Toxicological properties of methoprene

<i>Daphnia magna</i> ^a	LC ₅₀	900 µg/L
<i>Mysidopsis bahia</i> ^a	LOEC	2 µg/L
<i>Hyallela azteca</i> ^a	LC ₅₀	1250 µg/L
Rat ^b	Acute oral LC ₅₀	> 34,600 mg/kg
Dog ^b	Acute oral LC ₅₀	> 5000 mg/kg
Rabbit ^b	Acute dermal LC ₅₀	> 3500 mg/kg
Chicken ^b	LC ₅₀	> 4640mg/kg
Bluegill sunfish ^b	LC ₅₀	4.6 mg/L (96 hour)
Trout ^b	LC ₅₀	4.4 mg/L (96 hour)
Channel catfish ^b	LC ₅₀	> 100 mg/L (96 hour)

a – Siemering 2004, b - Glare and O'Callaghan 1999

Environmental Fate and Toxicity

Air: Methoprene has a moderate Henry's law constant and vapor pressure (Table 1). Consequently methoprene has the potential to volatilize from water or moist soil. However volatilization is mitigated by the affinity of methoprene for soils and sediment as indicated by its moderately high K_{OC} (Table 1).

Vapor phase methoprene may be degraded by reaction with photochemically produced hydroxyl radicals and ozone in the atmosphere. The half-lives for these reactions are calculated to be 1.5 hours (hydroxyl radicals) and 48 minutes (ozone) (Toxnet, 2003). The photodegradation of methoprene is expected to be very rapid due to its absorbance in the environmental spectrum ($\lambda > 290$ nm) (Toxnet, 2003).

Water: When methoprene is released into water, it is expected to adsorb to suspended solids and sediments based on its estimated K_{oc} value of 23,000 (Toxnet, 2003). Methoprene showed rapid degradation in both sterile and nonsterile pond water exposed to sunlight, more than 80% of applied methoprene was degraded within 13 days (U.S. EPA, 1982).

Briquettes, pellets, granules, and sustained-release methoprene formulations release methoprene slowly into water, resulting in low acute and chronic risk to aquatic non-target organisms such as arthropods as compared to liquid formulations (USEPA 2001 Fact Sheet). Methoprene briquettes have been reported as having relatively long half-lives in water, where mean degradation of the briquettes was 19% by weight after 150 days of submergence, with full degradation estimated after 1.5 years under water (Boxmeyer et al., 1997). The methoprene content of briquettes decreases more rapidly in air as opposed to when immersed in water.

Schooley et al. (1975a) studied the dissipation of methoprene in pond water and sewage at dose rates of 0.001 and 0.01 mg/L, respectively. Methoprene showed a half-life of approximately 30 hours at 0.001mg/L and 40 hours at 0.01 mg/L in pond water, and a 60-70 hour half-life in sewage.

Soil and Groundwater: When applied, methoprene is relatively immobile, tending to reside in the top few centimeters of the soil as expected based on its estimated K_{oc} of 23,000. As a result methoprene is unlikely to leach. Biodegradation of methoprene has been reported to be relatively fast in a variety of soils and environmental conditions. In aerobic sandy loam, radio-labeled methoprene was reported to have a half-life of approximately 10 days after it was applied at a surface treatment rate of 1 kg/ha. Methoprene showed rapid photodegradation on inert surfaces, such as soil, forming methoxycitronellal (Toxnet 2003).

Methoprene degradation has been shown to be much slower on autoclaved soil than untreated soil. Traces of non-polar metabolites were isolated, including the hydroxy ester,

resulting from O-demethylation (0.7% of the applied dose), and more than half of the applied dose was converted to $^{14}\text{CO}_2$ (Schooley et al., 1975b).

Radioactivity from labeled methoprene was conjugated into humic acid, fulvic acid and humin fractions of sandy loam. This data indicate that microbial degradation of methoprene is an important dissipation route in soil.

Biota

Extensive studies have shown that methoprene breaks down rapidly in the environment and displays relatively low risk to non-target organisms (USEPA 1991). Methoprene undergoes demethylation, hydrolysis and oxidative cleavage in microbes, insects and plants and is rapidly metabolized in fish, birds and mammals (Glare and O'Callaghan 1999).

Insects and Aquatic Arthropods: Methoprene has been shown to be toxic to insects closely related to mosquitoes in the order Diptera, as well as those in the orders Lepidoptera and Coleoptera. Methoprene has been studied to undergo ester hydrolysis, O-demethylation and oxidative cleavage at the C-4 double bond in insects. Acute, short-term and subchronic aquatic effect studies have been conducted on non-target adult and immature arthropods, including Crustacea, Insecta, and Mollusca. These studies reported 24 and 48 hours LC_{50} values greater than 900 ppb (Glare and O'Callaghan 1999). Other non-target organisms in early life stages (nymph, larvae) and non-target organisms that are closely related to mosquitoes such as dragonfly (order Odonata or suborder Anisoptera) are not affected by methoprene up to 1,000 ppb (Glare and O'Callaghan 1999). Methoprene are slightly toxic to aquatic macroinvertebrates such as Daphnia, Mysisid and Hyallela (Siemering 2004).

Fish: Methoprene is moderately toxic to cold water and freshwater fish and practically non-toxic to warm water fish. The reported LC_{50} are 4.62 ppm for bluegill, 4.39 ppm for trout, and >100 ppm for channel catfish and largemouth bass. Evidence of methoprene bioaccumulation, was observed in the edible tissues of crayfish and bluegill sunfish (Glare and O'Callaghan 1999).

Mammals: In one study, rats and mice were exposed to methoprene in their daily diet for two years. Methoprene was orally administered to rats at doses up to 34,000 mg/kg of body weight and did not show clinical signs of acute toxicosis (Glare and O'Callaghan 1999). Nagano et al. (1977) concluded that the maximum intake of methoprene that is non-toxic to rats is 400 ppm in their food or 20 mg/kg body weight per day. In dogs studied, methoprene showed very low toxicity with acute oral LD_{50} 's ranging from 5000 to 10,000 mg/kg. A variety of studies indicate that methoprene is not an oncogen, developmental toxicant, or mutagen. Further studies indicate no detectable endocrine effects in mammals (USEPA 2001).

Plants: Studies have been conducted on the metabolic fate of methoprene in rice and alfalfa. When methoprene was applied at a rate of 1,000 g/ha on alfalfa, it showed a half-life of less than two days and less than one day on rice. It was established that

methoprene was metabolized rapidly in both and yielded products that were further metabolized into natural product such as cellulose, chlorophylls and carotenoids (Glare and O'Callaghan 1999).

Conclusion

Methoprene is an insect growth regulator, which controls a variety of insect species including mosquitoes, beetles, horn flies, tobacco moths, and fleas. It is considered a biochemical pesticide, because rather than killing the target species via direct toxicity, methoprene disrupts the insects' metamorphosis and life cycle, thus hindering their ability to reach adulthood and successful reproduction. Special slow-release formulations are commonly used for mosquito control, especially breeding in floodwater sites, rice cultivations, storm drains, ponds and water treatment works.

Based on an estimated Koc value of 23,000, methoprene is expected to be immobile in soil. Methoprene has relatively low persistence in soil, with a reported soil half-life in both sand and silty loam soil of 10 days.

Both the Henry's Law constant and vapor pressure of methoprene are moderate. Consequently methoprene does have some potential to volatilize. Adsorption of methoprene in soil is expected to attenuate volatilization. It has been shown, that methoprene is also rapidly photodegraded in aqueous environments and on inert surfaces such as soil, with one principal degradate being methoxycitronellal.

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