chemicalWATCH Factsheet

SYNTHETIC PYRETHROIDS

Pesticide products containing pyrethroids are often described by pest control operators and community mosquito management bureaus as "safe as chrysanthemum flowers." While pyrethroids are a synthetic version of an extract from the chyrsanthemum, they were chemically designed to be more toxic with longer breakdown times, and are often formulated with synergists, increasing potency and compromising the human body's ability to detoxify the pesticide.

What are Synthetic Pyrethroids?

Synthetic pyrethroids are synthesized derivatives of naturally occurring pyrethrins, which are taken from pyrethrum, the oleoresin extract of dried chrysanthemum flowers. The insecticidal properties of pyrethrins are derived from ketoalcoholic esters of chrysanthemic and pyrethroic acids. These acids are strongly lipophilic and rapidly penetrate many insects and paralyze their nervous system (Reigart et al., 1999). Both pyrethrins and synthetic pyrethroids are sold as commercial pesticides used to control pest insects in agriculture, homes, communities, restaurants, hospitals, schools, and as a topical head lice treatment. Various formulations of these pesticides are often combined with other chemicals, known as synergists, to increase potency and persistence in the environment.

While chemically and toxicologically similar, pyrethrins are extremely sensitive to light, heat and moisture. In direct sunlight, half-lives that can be measured in hours. However, the pyrethroids, the synthetic analogues of naturally occurring pesticides, were developed to capture the effective insecticidal activity of this botanical insecticide, with increased stability in light, yielding longer residence times (Gosselin et al., 1984).

Pyrethroids and Health Effects

Pyrethroids have irritant and/or sensitizing properties. They are not easily absorbed through the skin, but are absorbed through the gut and pulmonary membrane. Tests of some pyrethroids on laboratory animals reveal striking neurotoxicity when administered by injection or orally. Systemic toxicity by inhalation and dermal absorption is low. The acute toxicity, calculated by LD_{50}'s, ranges from low to high, depending on the specific formulation. Low toxicity is attributed to two factors: limited absorption of some pyrethroids, and rapid biodegradation by mammalian liver enzymes (ester hydrolysis and oxidation). Insects, without this liver function, exhibit greater susceptibility to the chemicals (Reigart et al., 1999).

Pyrethroids interfere with the ionic conductance of nerve membranes by prolonging the sodium current. This stimulates nerves to discharge repeatedly causing hyper-excitability in poisoned animals. The World Health Organization explains that synthetic pyrethroids are neuropoisons acting on the axons in the peripheral and central nervous systems by interacting with sodium channels in mammals and/or insects. The main systems for metabolism include breakage of the ester bond by esterase action and oxidation at various parts of the molecule. Induction of liver microsomal enzymes has also been observed (WHO, 1999).

Signs and symptoms of poisoning by pyrethroids may take several forms. Because of the similarities to crude pyrethrum, pyrethroids may act as dermal and respiratory allergens. Exposure to pyrethroids has resulted in contact dermatitis and asthma-like reactions. Persons, especially children, with a history of allergies or asthma are particularly sensitive, and a strong cross-reactivity with ragweed pollen has been recognized. Severe anaphylactic (allergic) reactions with peripheral vascular collapse and respiratory difficulty are rare. Other symptoms of acute toxicity due to inhalation include sneezing, nasal stuffiness, headache, nausea, incoordination, tremors, convulsions, facial flushing and swelling, and burning and itching sensations. The most severe poisonings have been reported in infants, who are not able to efficiently break down pyrethroids (ETN, Pyrethroids, 1994). With orally ingested doses, nervous symptoms may occur, which include excitation and convulsions leading to paralysis, accompanied by muscular fibrillation and diarrhea (ETN, Pyrethroids, 1994). Death in these cases is due to respiratory failure. Symptoms of acute exposure last about 2 days.

Endocrine Disruption and Breast Cancer

Many pyrethroids have also been linked to disruption of the endocrine system, which can adversely affect reproduction and sexual development, interfere with the immune system and increase chances of breast cancer. Pyrethroids contain human-made, or xenoestrogens, which can increase the amount of estrogen in the body (Garey et al., 1998). When tested, certain pyrethroids demonstrate significant estrogenicity and increase the levels of estrogen in breast cancer cells (Go et al., 1999). Because increased cell division enhances the chances for the formation of a malignant tumor in the breast, artificial hormones, like those found in pyrethroids, may increase breast cancer risk (PCBR, 1996). Some pyrethroids are classified by EPA as possible human carcinogens.

Pyrethroids and the Environment

While the development of the synthetic pyrethroids was heralded with claims of selective toxicity to insects, both pyrethroids and pyrethrins are extremely toxic to aquatic or- ganisms, including fish such as the bluegill and lake trout, with LC_{50} values less than 1.0 parts per billion. These levels are similar to those for mosquito, blackfly and tsetse fly larvae, often the actual target of the pyre- throid application. Lobster, shrimp, mayfly nymphs and zooplankton are the most

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susceptible non-target aquatic organisms (Mueller-Beilschmidt, 1990). The nonlethal effects of pyrethroids on fish include damage to the gills and behavioral changes.

Pyrethroids are moderately toxic to birds, with most LD_{50} values greater than 1000 mg/kg. Birds can also be indirectly affected by pyrethroids, because of the threat to their food supply. Waterfowl and small insectivorous birds are the most susceptible (Mueller-Beilschmidt, 1990). Because pyrethroids are toxic to all insects, both beneficial insects and pests are affected by pyrethroid applications. In some cases, predator insects may be susceptible to a lower dose than the pest, disrupting the predator-prey relationship.

Pyrethroids Residues / Persistence

As mentioned before, pyrethroids are designed to breakdown more slowly than the naturally occurring pyrethrins. While pyrethrins, extremely sensitive to light, heat and moisture, break down in a few hours, the synthetic pyrethroids are stable and persist in the environment much longer. As a general rule, pyrethroids break down most quickly in direct sunlight, usually just a few days after application, with a few exceptions. However, in areas with limited sunlight, such as grain silos and subway tunnels, pyrethroids can persist for months. For more specific breakdown times see the sections below on resmethrin, permethrin and sumithrin.

Synergists

Both pyrethroids and pyrethrins are often formulated with oils or petroleum distillates and packaged in combination with synergists, such as piperonyl butoxide (PBO) and n-octyl bicycloheptene dicarboximide (Gosselin et al., 1984). Synergists are added to increase the potency of the pesticide. A range of products from repellants to foggers to pediculicides (lice killers) to garden sprays contain synergists. Many formulations of permethrin, resmethrin and sumithrin, including Scourge™ and Anvil™, used along the East Coast for mosquito control to combat the West Nile Virus, contain the synergist PBO.

PBO inhibits important liver enzymes responsible for breakdown of some toxins, including the active ingredients of pesticides. Specifically, it has been shown to inhibit hepatic microsomal oxidase enzymes in laboratory rodents and interfere in humans. Because these enzymes act to detoxify many drugs and other chemicals, a heavy exposure to an insecticidal synergist may make a person temporarily vulnerable to a variety of toxic insults that would normally be easily tolerated. Symptoms of PBO poisoning include anorexia, vomiting, diarrhea, intestinal inflammation, pulmonary hemorrhage and perhaps mild central nervous system depression. Repeated contact may cause slight skin irritation. Chronic toxicity studies have shown increased liver weights, even at the lowest doses, 30 mg/kg/day. While not considered a carcinogen by EPA, animal studies have shown hepatocellular carcinomas, even treatments as low as 1.2% (Takahashi et al., 1994).

Bifenthrin (Talstar™, Brigade™, Capture™)

Bifenthrin is an off-white to pale tan waxy solid, characterized by its slightly sweet smell. As a Restricted Use Pesticide, bifenthrin may only be purchased or applied by certified applicators or persons under the direct supervision of a certified applicator. EPA has registered bifenthrin for use on greenhouse ornamentals and cotton. Studies show bifenthrin to be relatively insoluble in water. Its half-life in soil can range anywhere from 7 days to 8 months depending on the soil type and the amount of air in the soil (ETN, Bifenthrin, 1995). Bifenthrin is one of a few synthetic pyrethroids that are relatively stable in direct sunlight. EPA has classified products containing bienthrin as toxicity class II (I = most toxic, IV = least toxic), and the word WARNING must appear on all product labels.

Bifenthrin is moderately toxic to mammals when ingested (oral rat LD50 = 54 to 70 mg/kg), and like all pyrethroids affects the central nervous system. Symptoms of poisoning include incoordination, tremor, salivation, vomiting, diarrhea, and irritability to sound and touch (ETN Bifenthrin, 1995). Although bifenthrin does not cause inflammation or irritation on human skin, it can cause a tingling sensation, lasting about 12 hours. A study on laboratory mice shows that bifenthrin causes gene mutation in white blood cells (ETN, Bifenthrin, 1995). EPA classifies bifenthrin as a Class C (possible human) carcinogen (EPA, 1997). Of concern in the environment, bifenthrin is very highly toxic to fish, crustaceans, other aquatic animals and bees, and is moderately toxic to birds. Scientists are particularly concerned about possible bioaccumulation in birds.

Cypermethrin (Ammo™, Cymbush™, Demon™)

Cypermethrin, one of a handful of light-stable synthetic pyrethroids, is registered to control cockroaches, fleas and other indoor pests in homes, restaurants, hospitals, schools and food processing plants, and also in agriculture to control pests on cotton, fruits and vegetables. About 90% of the cypermthrin manufactured worldwide is used to combat pests feeding on cotton crops (WHO, 1989). Depending on the specific product formulation, EPA classifies pesticides containing cypermethrin as toxicity class II or III (I = most toxic, IV = least toxic) and must display the word WARNING or CAUTION on the labels. Compared to other pyrethroids, cypermethrin is relatively stable, with a half-life of 8 - 16 days in direct sunlight. In soil, studies have shown the half-life to be as long as 8 weeks, and in water as long as 100 days (ETN, Cypermethrin, 1996). After treatments in the home, cypermethrin persists for about three months (Wright et al., 1993).

Cypermethrin is considered to be moderately toxic (oral male rat LD50 = 187 to 326 mg/kg, dermal rat LD50 = 1600 mg/kg) and like all pyrethroids, affects the central nervous system (ETN, Cypermethrin, 1996). Symptoms of cypermethrin poisoning in humans include numbness, burning, loss of bladder control, vomiting, incoordination, seizures, coma and death. In California, cypermethrin is the fourth most common cause of pesticide-related illness in pest control operators. EPA classifies cypermethrin as a class C (possible human) carcinogen (EPA, 1997). Studies in laboratory animals have shown exposure to cypermethrin to cause reproductive

effects, including abnormal sperm and disruption of sex hormones (Cox, 1996). Cypermethrin should not be applied near water, because it is very toxic to fish and other aquatic organisms.

Deltamethrin (Butoflin™, Butoss™, Crackdown™)

Deltamethrin is pyrethroid insecticide that kills insects on contact and through digestion. It works by paralyzing the insects' nervous system and therefore giving a quick knock-down effect. It is used commonly to control caterpillars on apples, pears and hops, and for the control of aphids, mealy bugs, scale insects, and whiteflies on glasshouse cucumbers, tomatoes, peppers, potted plants, and ornamentals (ETN, Deltamethrin, 1995). It is also registered for use on livestock and for public health uses. Depending on the product formulation, deltamethrin pesticides may range in toxicity from EPA toxicity class I to class III (I = most toxic, IV = least toxic), bearing the words DANGER-POISON, WARNING or CAUTION on the label (PANNA, 2000). Deltamethrin products may be general or Restricted Use Pesticides. Most deltamethrin products persist from one to two weeks in the environment, with shorter times in direct sunlight (ETN, Deltamethrin, 1995).

Deltamethrin produces different signs of poisoning than other pyrethroids. When exposed to deltamethrin, mammals exhibit typical type II motor symptoms, which include a writhing syndrome in rodents, as well as copious salivation. The acute oral LD_{50} in male rats has been reported as low as 128 mg/kg to greater than 5,000 mg/kg depending on the carrier and conditions of the study (ETN, Deltamethrin, 1995). Some studies have shown deltamethrin to cause skin irritation. Especially characteristic of deltamethrin poisoning is rolling convulsions. The sequence of the signs of poisoning is clearly defined, progressing from chewing, salivation, and pawing to rolling convulsions, tonic seizures, and death (ETN, Deltamethrin, 1995). In humans, symptoms of poisoning include ataxia, convulsions leading to muscle fibrillation and paralysis, dermatitis, edema, diarrhea, dyspnea, headache, hepatic microsomal enzyme induction, irritability, peripheral vascular collapse, rhinorrhea, serum alkaline phosphatase elevation, tremors, vomiting and death due to respiratory failure. Deltamethrin is a suspected endocrine disruptor. Deltamethrin is also toxic to fish, aquatic organisms, amphibians and bees.

Fenvalerate (Esfenvalerate, Sumifly™, Sumiflower™)

Fenvalerate is registered for use on a wide array of crops including cotton, soybeans, corn, vegetables, apples, peaches, pears and nuts, as well as a termiticide and insect repellent. Fenvalerate was first formulated for agricultural use in 1974, but was approved as a termiticide in 1987, as an alternative to the voluntarily cancelled cyclodiene termiticides. During the late 1980's, fenvalerate received national press coverage due to over 200 dog and cat poisonings, including 26 deaths, following the use of Blockade**TM**, a product containing fenvalerate in combination with DEET, a common insect repellant. EPA classifies fenvalerate products as toxicity class II (I = most toxic, IV = least toxic), and include the word WARNING on all product labels. Some formulations are Restricted Use Pesticides, and may only be purchased or applied by certified applicators or persons under the direct supervision of a certified applicator. The half-life of fenvalerate ranges from 15 days to 3 months in soil, 21 days in water and 2-4 weeks on vegetation. Fenvalerate is considered to be moderately toxic (oral rat LD50 = 486 mg/kg). Symptoms of poisoning through direct contact include dizziness, burning and itching (which is worsened by sweating and washing), blurred vision, tightness in the chest, and convulsions. When ingested by laboratory animals, symptoms of poisoning include muscle incoordination, tremors, convulsions, nerve damage, and weight loss. Fenvalerate is a strong eye irritant and a suspected endocrine disruptor (PANNA, 2000). Sweden has banned the chemical for use in forestry following health related complaints from workers.

Studies have found that immediate application of vitamin E to exposed areas can lessen the painful effects. Fenvalerate is extremely toxic to bees and fish, and is slightly toxic to birds.

Permethrin (Pounce™, Torpedo™, Dragnet™)

Prior to 1978, permethrin was registered for use on cotton crops only. During the early 1980's registration was expanded to include use on livestock and poultry, eggs, vegetables and fruit. Today uses also include lice treatments and urban/suburban pest control. Permethrin resembles pyrethrins chemically, but is chlorinated to increase its stability. There are four isomeric forms, two cis and two trans of technical permethrin. Although the acute toxicity of the mixture (oral rat LD50 > 5000 mg/kg, oral mouse LD50 = 500) is less than that of natural pyrethrins, the cis-isomer is considerably more toxic (oral mouse LD50 = 100), and in rats, the metabolites of the cis-isomer are more persistent biologically. (The cis and trans isomers differ in the spatial arrangement of the atoms.) Product formulations of permethrin can vary greatly in isomeric content. Compared to other pyrethroids, permethrin is very stable, even when exposed to ultraviolet light. Permethrin is strongly absorbed to soil and other organic particles, with half-lives in soil of up to 43 days. When used as a termiticide, permethrin can persist up to 5 years.

Permethrin receives an EPA toxicity class rating of II or III (I = most toxic, IV = least toxic), and carries either the word WARNING or CAUTION on its label, depending on the formulation. While it is not extremely toxic to humans, there are numerous reports of transient skin, eye and respiratory irritation. Like all pyrethroids, permethrin is a central nervous system poison. Workers and researchers report tingling in face and hands, and some report allergic reactions. Based on studies demonstrating carcinogenicity, EPA ranks permethrin as a class C, or possible human carcinogen (U.S. EPA, 1997). Other studies have shown effects on the immune system, enlarged livers and at high doses, decreased female fertility and endocrine disruption. Permethrin is extremely toxic to aquatic life, bees and other wildlife. It should not be applied in crops or weeds

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where foraging may occur (ETN, Permethrin, 1996).

Resmethrin (Scourge™, Raid Flying Insect Killer™)

Resmethrin is used for control of flying and crawling insects in homes, green- houses, processing plants, commercial kitchens, airplanes and for public mosquito control. Resmethrin is considered slightly toxic to humans and is rated EPA toxicity class III (I = most toxic, IV = least toxic), bearing the word CAUTION on its label.

The oral rat LD50 is about 2500 mg/kg. Although resmethrin has a very short half-life (under an hour in direct sunlight), it persists much longer in soil with a half-life of 30 days (ETN, Resmethrin, 1996). Resmethrin breaks down into a smelly byproduct, phenylacetic acid, which binds strongly to textiles and dissipates slowly, smelling of urine.

Resmethrin is absorbed rapidly and distributed to all tissues including the brain. Skin absorption is low, although it should be noted that some individuals manifest allergic responses including dermatitis, asthma, runny nose and watery eyes after initial contact. In laboratory animals, chronic toxicity studies have shown hypertrophy of the liver, prolifera- tive hyperplasia and benign and cancerous liver tumors. EPA reviewers noted slight, but significant, increases in the number of offspring born dead and decreased viability, which they thought might be secondary to trans placental toxicity. Tests for neurotoxicity have been negative, but it is a suspected endocrine disruptor (PANNA, 2000). Resmethrin is extremely toxic to fish, other aquatic life and bees. The domestic manufacturer of resmethrin, Penick Company, will not identify the inert ingredients in its product, but recommends that it is not sprayed on paint, plastic or varnished surfaces, and that treatment of living areas or areas with large amounts of textiles be avoided.

Sumithrin (Anvil™, d-Phenothrin)

Sumithrin has been registered for use since 1975. It is used to control adult mosquitoes and as an insecticide in transport vehicles, commercial, industrial and institutional non-food areas, in homes, gardens, greenhouses and on pets. Chemically, it is an ester of chrysanthemic acid and alcohol. It is a combination of two cis and two trans isomers. Sumithrin is slightly toxic and is rated EPA toxicity class IV (I = most toxic, IV = least toxic) bearing the word CAUTION on its label. The oral rat LD50 is greater than 5,000 mg/kg, and the LC50 for inhalation is greater than 1210 mg/m3. Sumithrin degrades rapidly, with a half-life of 1-2 days under dry, sunny conditions. Under flooded conditions, the half-life increases to 2-4 weeks for the trans isomer and 1-2 months for the cis isomer. In grain silos, with no sunlight and little air circulation, most of the product still remains after one year (WHO, 1990). Symptoms of acute sumithrin poisoning include hyperexcitability, prostration, slow respiration, salivation, tremor, ataxia and paralysis. Chronic feeding studies resulted in increased liver weights in both males and females. In rat studies, sumithrin was completely excreted in 3-7 days (WHO, 1990). Studies have shown that sumithrin is an endocrine disruptor, demonstrating significant estrogenicity and increases the level of estrogen in breast cancer cell, suggesting that sumithrin may increase the risk of breast cancer (Go et al., 1999).

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