PERMETHRIN

The insecticide permethrin (in the synthetic pyrethroid family) is widely used on cotton, wheat, corn, alfalfa, and other crops. In addition, over 100 million applications are made annually in and around U.S. homes.

Permethrin, like all synthetic pyrethroids, is a neurotoxin. Symptoms include tremors, incoordination, elevated body temperature, increased aggressive behavior, and disruption of learning. Laboratory tests suggest that permethrin is more acutely toxic to children than to adults.

The U.S. Environmental Protection Agency has classified permethrin as a carcinogen because it causes lung tumors in female mice and liver tumors in mice of both sexes. Permethrin inhibits the activity of the immune system in laboratory tests, and also binds to the receptors for a male sex hormone. It causes chromosome aberrations in human and hamster cells.

Permethrin is toxic to honey bees and other beneficial insects, fish, aquatic insects, crayfish, and shrimp. For many species, concentrations of less than one part per billion are lethal. Permethrin causes deformities and other developmental problems in tadpoles, and reduces the number of oxygen-carrying cells in the blood of birds.

Permethrin has been found in streams and rivers throughout the United States. It is also routinely found on produce, particularly spinach, tomatoes, celery, lettuce, and peaches.

A wide variety of insects have developed resistance to permethrin. High levels of resistance have been documented in cockroaches, head lice, and tobacco budworm.

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Permethrin is used to kill pest in-sects in agriculture, home pest control, forestry, and in public health programs, including head lice control. It was first marketed in 1973. Worldwide, the dominant use of permethrin is on cotton, accounting for about 60 percent (by weight) of the permethrin used.[1] In the U.S., al-most 70 percent of the permethrin used in agriculture is used on corn, wheat, and alfalfa.[2] Over 100 million applications of permethrin are made each year in U.S. homes, and over 18 million applications are made in yards and gardens.[3]

Permethrin is a synthetic pyrethroid. Like most members of this family of insecticides, it has four isomers, molecules made up of the same atoms with different three-dimensional structures. (See Figure 1)

Mode of Action

Permethrin, like all synthetic pyrethroids, kills insects by strongly exciting their nervous systems. Permethrin makes the nervous system hypersensitive to stimuli from sense organs. Rather than sending a single impulse in response to a stimulus, permethrin-exposed nerves send a train of impulses. This excitation occurs because permethrin blocks the movement of sodium ions from outside to inside of the nerve cells. Permethrin's mode of action is similar to that of the organochlorine insecticide DDT.[5]

Acute Lethal Dose

Permethrin's LD50 (the amount of permethrin that kills 50 percent of a population of test animals) is variable. In a summary of nine oral LD50 tests using rats, the LD50 varied from 430 milligrams per kilogram of body weight (mg/kg) to over 4,000 mg/kg. Some of this variability occurs because the

proportions of isomers in the test materials vary. The cis isomers are about ten times more toxic than the transisomers.[6]

Neurotoxicity

In mammals, permethrin has complex effects on the nervous system. As in insects, it causes repetitive nerve impulses. It also inhibits a variety of nervous system enzymes: ATPase, whose inhibition results in increased release of the neurotransmitter acetylcholine [7]; monoamine oxidase-A, the enzyme which maintains normal levels of three other neurotransmitters [8]; and acetylcholinesterase, the enzyme that breaks down acetylcholine.[9] (Two large families of insecticides, the organophosphates and the carbamates, are acetylcholinesterase inhibitors.) In addition, permethrin inhibits a nervous system receptor, the GABAA receptor, producing excitability and convulsions.[10] Finally, permethrin inhibits respiration (the process by which cells use sugars as an energy source) in a manner similar to other neurotoxic drugs.11 It is therefore not surprising that permethrin causes a wide variety of neurotoxic symptoms.

At relatively high doses, these neuro-toxic symptoms of permethrin include tremors, incoordination, hyperactivity, paralysis, and an increase in body temperature. These symptoms can persist up to three days.12 Other behavioral effects have been observed at lower doses. For example, sublethal exposure of mice to the permethrin-containing insecticide Ambush increased activities like chewing 13 ; sublethal exposure of rats to permethrin increased aggressive behavior, agitation, and resistance to being captured 14 ; and permethrin disrupted a learned feeding behavior in rats at doses of about 20 percent of the LD50. [15]

Eye and Skin Irritation

Permethrin-containing products can be irritating to both eyes and skin. For example, the agricultural insecticide Pounce 3.2 EC "causes moderate eye irritation."[16] Ortho Total Flea Control 2 and Solaris Flea-B-Gon Total Flea Killer Indoor Fogger both cause "tearing, swelling, and blurred vision."[17,18] They also cause "redness, swelling, and possibly blistering" of the skin.[17,18] Adams 14 Day Flea Dip "causes eye injury"[19] and "may cause al-allergic reactions"[19] on skin.

Effects on the Immune System

Experiments with laboratory animals indicate that the immune system (used by living things to defend themselves from disease) "appears to be a sensitive target for permethrin activity." Ingestion of permethrin reduces the ability of immune system cells called T-lymphocytes to recognize and respond to foreign proteins. Doses equivalent to 1/100 of the LD50 , inhibited T-lymphocytes over 40 percent. Permethrin ingestion also reduced the activity of a second type of immune system cell, natural killer cells, by about 40 percent.[20](See Figure 2.) In tests using mouse cell cultures, permethrin had similar effects on the immune system, inhibition of two kinds of lymphocytes.[21] Researchers concluded that "the immune system is exquisitely sensitive … at exposure levels that cause no overt toxicity."[20]

Effects on Reproduction

Permethrin affects both male and female reproductive systems. It binds to receptors for androgen, a male sex hormone, in skin cells from human males, causing researchers to "advise protection from any form of contact or ingestion of the pyrethroids." [22] Permethrin also binds to a different receptor, called the peripheral benzodiazepine receptor, that stimulates production of the male sex hormone testosterone.[23] In addition, permethrin caused reduced testes weights in a long-term feeding study of mice.24 In females, permethrin exposure has caused embryo loss in pregnant rabbits[24] and in pregnant rats.[25]

Mutagenicity

Permethrin was mutagenic (damaging to genetic material) in three tests with human cell cultures, one with hamster cells, and one with fruit fly larvae. In cultures of human lymphocytes (white blood

cells), permethrin exposure caused an increase in chromosome aberrations, chromosome fragments,26 and DNA lesions.[27] In hamster ovary cell cultures, permethrin exposure caused chromosome aberrations.[28] Exposure to Ambush (a permethrin-containing insecticide) during larval development increased sex-linked lethal mutations in fruit flies.[29]

Carcinogenicity

According to the U.S. Environmental Protection Agency (EPA), permethrin is a possible human carcinogen (chemical that causes cancer).30 EPA found that permethrin increased the frequency of lung tumors in female mice, and increased the frequency of liver tumors in male and female mice.[24] The World Health Organization reports that permethrin increased the frequency of lung tumors in females in two out of the three mouse studies it reviewed. (See Figure 3.) Lung tumors increased with increasing permethrin exposure in the third study, but the increase was not statistically significant.[31]

There are no publicly available studies of the carcinogenicity of permethrin-containing insecticide products.

There are two molecular mechanisms which could explain permethrin's carcinogenicity. First, permethrin reduces the activity of an enzyme involved in the breakdown of the amino acid tryptophan. This can lead to the buildup of carcinogenic tryptophan breakdown products.[32] Second, permethrin inhibits what is called "gap junctional intercellular communication" (GJIC), chemical communication between cells. GJIC plays an important role in the growth of cells, and some cancer promoting chemicals inhibit GJIC.[33]

Other Chronic Effects

The liver is a sensitive target for permethrin effects. When EPA summarized 17 medium- and long-term laboratory studies that exposed rats, mice, and dogs to permethrin, effects on the liver were noted at the "lowest effect level" in all of them.[24] Other chronic effects in laboratory tests include enlarged adrenal glands at all doses tested in a rabbit feeding study, and increased kidney weights at all doses tested in a rat feeding study.[24]

Synergy

Synergy occurs between two or more chemicals when their combined exposure causes more adverse effects than the sum of their individual effects. A possible cause of the health problems reported by 30,000 veterans who served in the Persian Gulf War is exposure to a combination of chemicals, including permethrin. The combination of permethrin, the anti-nerve gas drug pyridostigmine bromide, and the insect repellent DEET has been tested in laboratory animals. Neurotoxic symptoms, including decreased activity, diarrhea, shortness of breath, tremors, inability to walk, and damage to nerves, were observed in hens exposed to all three chemicals, but not in hens exposed to permethrin alone. Permethrin with just pyridostigmine bromide or just DEET also caused tremors and inability to walk, but symptoms were not as severe.[35]

Other pesticides interact synergistically with permethrin with in other species. Permethrin and the herbicide atrazine synergistically induce growth of the soil fungus *Pythium ultimum*, 36 and permethrin and the insecticide amitraz are synergistically toxic to the bollworm.[37]

Individual Susceptibility

Individuals vary in their susceptibility to permethrin, as has been illustrated by the following research:

- Based on tests with laboratory animals, it appears children may be more sensitive to permethrin than adults. Permethrin is almost 5 times more acutely toxic to 8-day-old rats than it is to adult rats.[38](See Figure 4.)
- Since sulfates are involved in one of the major pathways by which permethrin is broken down in humans, individuals with defects in sulfate-related enzymes may be unable to easily break down permethrin, leading to increased susceptibility to motor neuron disease.[39,40]

- Individuals with genetic variants of the enzyme pseudocholinesterase that have reduced activity are at higher risk of adverse effects from exposure to certain chemicals, including the permethrin combination implicated in symptoms seen in Gulf War veterans.[35]

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Effects on Nontarget Animals

Beneficial Arthropods: As a broad spectrum insecticide, it is not surprising that permethrin impacts beneficial arthropods, those that are useful in agriculture. Examples include the following:

- Permethrin is acutely toxic to honey bees; the median lethal dose is 0.008 micrograms per bee.[41] Sublethal exposures cause increased abnormal behavior (trembling, etc.), decreased foraging,[42] and impairment of bees' learning.[43]
- The International Organization for Biological Control tested the acute toxicity of permethrin to 13 species of beneficial arthropods and found that permethrin caused 99 percent mortality of 12 of the species, and over 80 percent mortality of the other. Effects were persistent, lasting over 30 days.[44] Sublethal doses also impact beneficial arthropods: permethrin inhibited the emergence of a parasitoid wasp from eggs of the rice moth Corcyra cephalonica [45] and disrupted the foraging pattern of another parasitoid wasp as it searched for its aphid prey.[46] (Parasitoids are insects that lay their eggs in, on, or near their prey. The eggs hatch and the larvae consume the prey as they develop. They often keep populations of agricultural pests at low levels.)

Aquatic Insects: Because it is a broad spectrum insecticide, permethrin has severe impacts on aquatic insects. Permethrin applications to forest streams caused "a major increase in the density of drifting invertebrates" described as "catastrophic." (Drifting animals are those that are sufficiently poisoned by the insecticide that they are washed down-stream.) Most applications were also followed by "rapid depletion of bottom fauna," insects that live in the stream bed. Recovery required between 1 and 18 months.[47] Mayflies and damselflies are the most sensitive species.[49] Permethrin also bioconcentrates in aquatic insects; bioconcentration factors in stoneflies ranged from 43 to 570. [49]

Birds: While permethrin's acute toxicity to birds is low,50 it causes other ad-verse effects. Three-week dietary exposure of chickens reduced hemoglobin (oxygen carrying protein) levels, and red blood cell counts, while increasing the number of white blood cells.51 The reduction in hemoglobin occurred at the lowest dose tested, 33 mg/kg.[51] Permethrin also caused decreased immune responses in chicks,[52] and damaged mallard ovaries.[53]

Fish: Permethrin is highly toxic to fish. This toxicity is due, in part, to the sensitivity of their nervous system.[54] Fish also lack the enzymes that break down permethrin in other animals.[55]

The LC_{50} (the concentration that kills 50 percent of a population of test animals) is less than 1 part per million (ppm) for almost all fish species tested, and for some fish is less than 1 part per billion (ppb). Agricultural permethrin products called emulsifiable concentrates are about twice as toxic to fish as permethrin alone. Small fish are less tolerant of permethrin than large fish, and it is more toxic in cold water than in warm water.[56] Fish also have a particular developmental stage when they are most susceptible.[57]

Sublethal effects on fish include abnormal swimming, a reduced startle response, and loss of equilibrium.[58]

Permethrin bioconcentrates in fish, so that concentrations in fish are higher than the concentration in the water in which the fish live. Bioconcentration factors (the ratio between the concentration in the fish and the concentration in the water) up to 113 have been measured in brook trout,[59] up to 613 in

Atlantic salmon,[59] and up to 631 in rainbow trout.[60]

Complex effects of permethrin on fish have been documented by the Canadian Forest Service in field studies. They found that diets of trout and salmon were altered when permethrin killed the insects these fish use as food. In some cases, diets were altered for a year following treatment. Reductions in fish growth rates, and migration to untreated areas followed; recovery required four months. The researchers concluded that permethrin is "not an acceptable treatment for large-scale use in forest areas containing fish-producing
water."[61]

Amphibians: Permethrin disrupts the growth and development of tadpoles. Exposure slowed growth for two to three weeks, and increased the frequency of a tail abnormality. (See Figure 5.) The increase in this deformity occurred at the lowest concentration of permethrin tested, 0.1 ppm. At this concentration tadpoles also responded to prodding in a jerky and disorganized way, making them vulnerable to predation. Tadpoles exposed to an even lower concentration (0.05 ppm) reduced their feeding for several weeks after exposure.[62]

Permethrin also effects brain function in tadpoles. Concentrations of 0.25 ppm decreased the amounts of two specific proteins in the brain, while increasing the total amount of protein. One of the proteins is associated with learning. Activity of several nervous system enzymes, including acetylcholinesterase, decreased.[63]

Other Aquatic Animals: Permethrin is very highly toxic to lobster; the LC_{50} is less than 1 ppb.[64] It is highly toxic to oyster larvae, with an EC_{50} (the concentration causing abnormal development in half of the larvae) of less than 1 ppm.65 Permethrin bioconcentrates in oysters, with a bioconcentration factor of 1900. [66] Water fleas are also very sensitive to permethrin exposure; LC_{50}s of several species are about 1 ppb.[67] Permethrin also caused "severe mortalities" of two kinds of zooplankton, cladocerans and copepods with recovery taking about 3 months.[68]

Mysid shrimp are killed by permethrin at concentrations so low that they cannot be detected in water (the LC 50 is 0.02 ppb). This means that "any detection of these insecticides in estuarine waters would likely be associated with adverse effects."[66] Another animal that is very sensitive to permethrin is crayfish; LC_{50}s for the red swamp crayfish vary from 0.4 to 1.2 ppb. Researchers concluded that "even the lowest operational treatment level used for insect management would seriously impact crayfish populations."[67]

Residues on Food

The Food and Drug Administration's (FDA's) monitoring program routinely finds permethrin on food. In 1996, it was the 13th most commonly detected pesticide.[68] Similar results were found in monitoring of 14 fruits and vegetables by the U.S. Department of Agriculture; permethrin was the 10th most frequently detected pesticide and was often found on spinach (60 percent of the samples tested) and tomatoes (11 percent of the samples tested).[69] Permethrin was also frequently found on celery and lettuce.[70]

Permethrin has also been found in baby food: FDA's 1996 monitoring found it in 12 percent of the samples tested. The Environmental Working Group found permethrin was the most commonly detected pesticide in peach baby food (44 percent of the samples tested) and was also found in plums (11 percent of the samples tested).[71]

Contamination of Water

Permethrin has been found in ground and surface water. The U.S. Geological Survey has found permethrin in streams and rivers in the Mississippi River Basin, [72] the Central Columbia Plateau (Washington and Idaho),[73] the Georgia-Florida Coastal Plain,[74] the San Joaquin-Tulare Basin (California),[75] and the Ozark Plateau (Arkansas and nearby states).[76] Permethrin has also been found in groundwater in Virginia.[76]

Drift

Drift, pesticide movement during application away from the target area, has been measured for two types of permethrin applications: aerial and back pack mistblower. Aerially applied permethrin drifted 180-240 meters (590- 790 feet) under conditions "highly conducive" to drift.[78] These researchers suggested using buffers of 150 meters (490 feet). Back pack mistblower applications of permethrin drifted 150 meters.[79]

Persistence

According to EPA, permethrin's half-life (the amount of time required for half of the original amount of a chemical to break down or move away from the study site) was 17 days in a North Carolina agricultural soil and 43 days in Illinois.[80] When used as a termiticide, permethrin persists longer; soil concentrations did not decline during the first year.[81] Permethrin also persists longer in tree needles, foliage, and bark, up to 363 days.[82] The ability of permethrin to persist in the environment was graphically illustrated by a study of an application of permethrin ear tags to cattle. Permethrin was found on all surfaces analyzed, not only on the cattle, but also on the bark of trees in their pasture, on a fence pole, and in grass. Some residues were found three months after the ear tags were applied.[83]

Resistance

Resistance (the evolution of a strain of insect that is able to tolerate a particular insecticide) to permethrin has been documented in a wide variety of insects. These species include pear psylla,[84]fall army-worm, [85] German cockroach,[86] spotted tentiform leafminer,[87] diamondback moth,[88] house fly,[89] stable fly,[90] head lice,[91-93] and tobacco budworm.[94] Many of these species are resistant to other synthetic pyrethroids as well as permethrin. The level of resistance is less than tenfold in some of the species but high levels of resistance have been observed in cockroaches (45-fold),[86]lice (up to 385-fold)[91] and budworm (1400-fold).[94]

Inert Ingredients

Like most pesticide products, permethrin insecticides contain ingredients that are typically claimed as trade secrets by pesticide manufacturers. Limited information about "inerts" in permethrin products is available. Examples include:

- Xylenes are in the agricultural insecticides Pounce 3.2 EC,[16] Ambush 2E,[95] and Ambush 50. [96] Xylenes cause eye and skin irritation, headaches, nausea, confusion, tremors, and anxiety in exposed humans. In laboratory tests, xylenes have caused kidney damage, fetal loss, and skeletal anomalies in offspring.[97]
- Methyl paraben is in the head lice cream rinse Nix,[98] regulated as a drug not as a pesticide. Methyl paraben is a skin sensitizer, and causes eye, skin, digestive, and respiratory irritation.[99]
- Dimethyl ether is in the household insecticides Flea-B-Gon Total Flea Killer Indoor Fogger 17 and Ortho Total Flea Control 2. 18 It causes respiratory, skin, and eye irritation and depresses the cen-tral nervous system. It is also a severe fire hazard.100
- Butane is in the household insecticides Raid Yard Guard Outdoor Fogger V and Off Yard and Deck Area Repellant 1. [101,102] It is "extremely flammable" and short-term exposure causes irritation, nausea, drowsiness, convulsions, and coma.[103]

References

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