● INSECTICIDE FACTSHEET

RESMETHRIN

Resmethrin is a pyrethroid insecticide. Insecticides in this family share some chemical structures and a mode of action with a plant-derived insecticide. However, they generally are more toxic and more persistent than their naturally occurring chemical relatives.

Resmethrin is used to kill a variety of flying and crawling insects, including mosquitoes.

Like all members of its chemical family, resmethrin is a "neuropoison." It kills insects by stimulating discharges from their nerve cells, leading to paralysis and death. It also affects nervous systems in people and other animals. Symptoms of exposure in people include headaches, nausea, rashes, difficulty breathing, and burning eyes.

Resmethrin caused liver cancer and tumors of the uterus in laboratory tests. Although resmethrin has been used as a pesticide since 1967, the U.S. Environmental Protection Agency (EPA) has not yet formally evaluated resmethrin's ability to cause cancer.

Under the Emergency Planning and Community Right to Know Act, EPA listed resmethrin as a toxic chemical in part because of its effects on reproduction. In laboratory tests, exposure during pregnancy caused increases in the frequency of stillbirths, and exposure before birth and during lactation reduced the size of offspring.

Resmethrin is highly toxic to fish. In laboratory tests, fish can be killed by resmethrin concentrations of less than one part per billion. Because it is so lethal to fish, EPA classified resmethrin products used to control mosquitoes and some other outdoor pests as restricted use pesticide products.

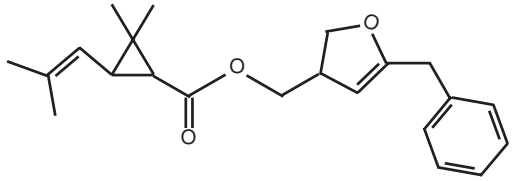
Other kinds of animals can also be killed by tiny amounts of resmethrin. These include water fleas, crawfish, and honey bees.

BY CAROLINE COX

Resmethrin (see Figure 1) is a pyrethroid insecticide. It was one of the first members of this chemical family to be commercially available, and has been used in the U.S. since 1967.[1]

The pyrethroid family of insecticides consists of synthetic molecules that share some chemical structures and a mode of action with the plant-derived insecticides called pyrethrins.[1,2] (See JPR 22(1):14-20 or www.pesticide.org/pyrethrins.pdf.) However, pyrethroids are "often more toxic to insects, as well as to mammals, and last longer in the environment than pyrethrins."[2]

Figure 1
Resmethrin



[5-(phenylmethyl)-3-furanyl] methyl 2,2-dimethyl-3-(methyl-1-propenyl) cyclopropanecarboxylate

Mode of Action

Like all insecticides in the pyrethroid chemical family, resmethrin kills insects by damaging their nervous systems. Pyrethroids cause repetitive electrical discharges from insects' nerve cells, leading to paralysis and death.[3]

Use

According to the U.S. Environmental Protection Agency (EPA), resmethrin's major uses are to kill mosquitoes, insects on ornamental plants, insects on pets and horses, as well as flying and crawling insects in the home, lawn, garden, and industrial sites.[4]

Bioresmethrin

Like many pyrethroids,[2] resmethrin is a mixture of isomers.[5] Isomers are molecules made up of the same atoms, joined together in the same sequence, but with different three-dimensional arrangements.[2] One of the isomers of resmethrin is more insecticidally active than the other three, and this isomer, called bioresmethrin, is used alone as an insecticide.[6]

Piperonyl Butoxide

Several commercial resmethrin-containing insecticides, including some mosquito control products, also contain piperonyl butoxide,[7] a chemical that increases the potency of pyrethroid insecticides.[2] Piperonyl butoxide is classified as a cancer-causing chemical by EPA[8] and also poses a variety of other hazards. For information about

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piperonyl butoxide's health and environmental hazards see JPR 22(2):12-19 or www.pesticide.org/piperonylbutoxide.pdf.

Inert Ingredients

Like most pesticides, commercial resmethrin insecticides contain ingredients which, according to U.S. pesticide law, are called "inert."[9]

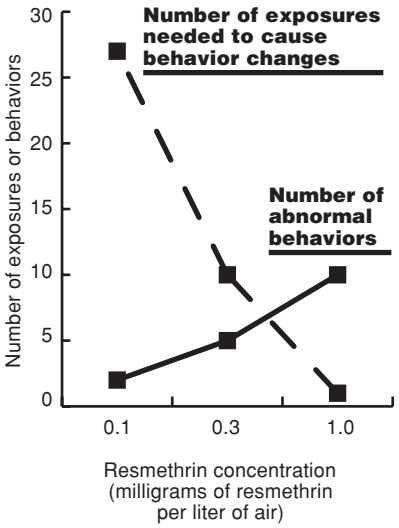
There is little publicly available information about the identity of ingredients in resmethrin products. The laboratory studies summarized in the rest of this article mostly concern resmethrin alone, not resmethrin in combination with inert ingredients.

For information about the hazards of some of the inert ingredients in commercial resmethrin products, see "Inert Ingredients," right.

Symptoms of Exposure

Exposure to pyrethroids can cause tingling and burning of the skin, as well as dizziness, salivation, headache, fatigue, vomiting, and diarrhea.[10]

Figure 2
Effects on Behavior



U.S. EPA. Office of Pesticides and Toxic Substances. 1986. EPA Reg. No.: 432-487. Resmethrin: review of a 90-day subchronic inhalation study conducted by the Huntingdon Research Centre, England and dated June 26, 1985. Washington, D.C., Aug. 3. See attached Data Evaluation Record for MRID No.158476.

Symptoms of resmethrin exposure are similar to those of exposure to other pyrethroids. Symptoms reported to California's Pesticide Illness Surveillance Program between 1999 and 2002 include headaches, nausea, vomiting, upset stomach, rashes, difficulty breathing, sweating, burning eyes, sore or burning throat, sleepiness, dizziness, and nasal congestion.[11]

Effects on the Nervous System

According to the World Health Organization, all insecticides in the pyrethroid family are "neuropoisons."[12] Laboratory tests have demonstrated that resmethrin is no exception.[13]

One way to test for effects on the nervous system is to study changes in behavior caused by exposure. In one study sponsored by a resmethrin manufacturer, breathing resmethrin caused behavioral changes (agitated grooming, for example) in rats at all dose levels tested.[14] At the higher exposure levels in this experiment, behavioral effects occurred after fewer exposures and more unusual behaviors were observed. (See Figure 2.)

"INERT" INGREDIENTS

Examples of the hazards of the inert ingredients in commercial resmethrin insecticide products include the following:

- **Trimethyl benzene (mixed isomers)** (Chemical Abstract Services number 25551-13-7)[1] is a solvent that is a mixture of three forms of trimethyl benzene.[2] All three forms, according to the National Institute for Occupational Safety and Health (NIOSH), cause genetic damage in a variety of laboratory tests.[3-5]
- **Butylated hydroxytoluene**[1] caused genetic damage and a variety of reproductive effects in laboratory tests, according to NIOSH. According to criteria used by NIOSH's Registry of Toxic Effects of Chemical Substances, it has also caused several types of cancer in laboratory tests.[6]
- **Propane**[1] is used as a propellant in aerosol resmethrin products. It is extremely flammable and easily ignited by heat, sparks, or flame according to the U.S. Department of Transportation. Its vapors can cause dizziness or asphyxiation without warning.[7]
- **Naphthalene**[8,9] caused genetic damage and reproductive effects, including reduced numbers and survival of offspring, in laboratory tests according to NIOSH. According to criteria used by NIOSH's Registry of Toxic Effects of Chemical Substances, it has also caused lung tumors in laboratory tests.[10]

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5. National Institute for Occupational Safety and Health. 2002. RTECS: Mesitylene. www.cdc.gov/niosh/rtecs/ox682428.html.
6. National Institute for Occupational Safety and Health. 2004. RTECS: p-Cresol, 2,6-di-tert-butyl. www.cdc.gov/niosh.rtecs/go7829b8.html.
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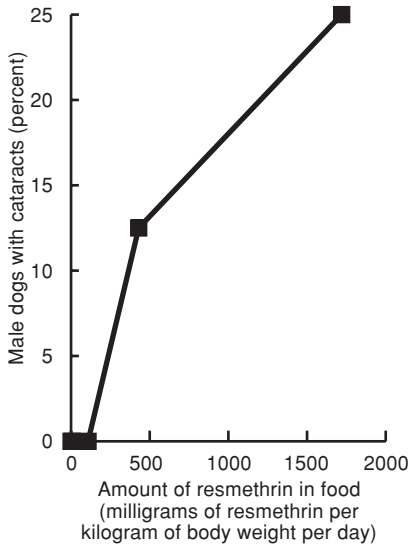
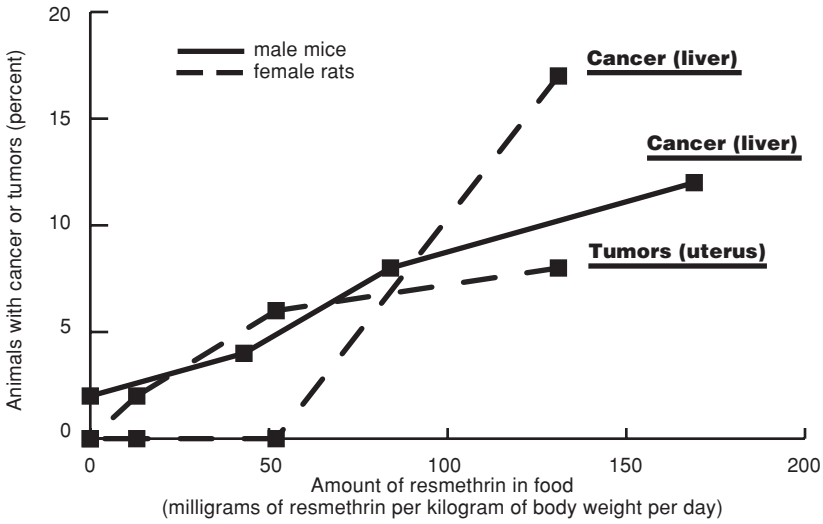
Figure 3
Ability to Cause Cataracts



Source:
U.S. EPA. Office of Prevention, Pesticides, and Toxic Substances. 1994. Rfd/Peer review report of resmethrin . Memo from G.Z. Ghali, Health Effects Div. to M. Johnson, Registration Div. and E. Saito, Special Review and Reregistration Div. Washington, D.C., Nov. 22.

Figure 4
Ability to Cause Cancer and Tumors



Sources:
U.S. EPA. Office of Prevention, Pesticides, and Toxic Substances. 1994. Resmethrin ID#00432-00487. Evaluation of new mouse dietary carcinogenicity study and reevaluation of previously submitted mouse carcinogenicity study on resmethrin (SBP-1382). Memo from G.Z. Ghali, Health Effects Div. to M. Johnson, Registration Div. and E. Saito, Special Review and Reregistration Div. Washington, D.C., Nov. 22.
U.S. EPA. Office of Prevention, Pesticides and Toxic Substances. 1995. 6(a)(2) data: Resmethrin (SBP-1382) ID No. 000432-00487. Review of chronic rat feeding/carcinogenicity study submitted as 6(a)(2) data. Memo from L.J. Hansen, Health Effects Div., to R. Keigwin, Registration Div. Washington, D.C., Aug. 22.

In laboratory tests, resmethrin has caused cataracts, cancer, and tumors.

Based in part on these effects on the nervous system, EPA listed resmethrin as a toxic chemical under the Emergency Planning and Community Right to Know Act. (EPCRA)[13,15]

Cataracts

Resmethrin exposure can increase the risk of developing cataracts.

In a laboratory study sponsored by a resmethrin manufacturer, dogs that had been fed resmethrin developed cataracts more often than did unexposed animals. This increase in the frequency of cataracts occurred at the two highest dose levels of the four tested in this experiment.[16] (See Figure 3.)

Carcinogenicity (Ability to Cause Cancer)

Does exposure to resmethrin cause cancer? This question has been the focus of four laboratory studies sponsored by resmethrin's manufacturer. EPA found several problems with the methods used in the older two of these studies (done in 1979 and 1980),[17,18] but found that the newer studies (done in 1992 and 1994) used acceptable methods. Results of these studies included the following:

- In the 1992 study, male mice fed resmethrin developed liver tumors and cancer more often than did unexposed mice.[19,20] (See Figure 4.)
- In the 1994 study, female rats fed resmethrin developed liver cancer more often than did unexposed rats.[20,21] These rats also developed tumors of the uterus more often than did unexposed rats. (See Figure 4.)

Although resmethrin has been registered as a pesticide since 1967,[1] EPA has not completed its evaluation of these laboratory studies. This means that the agency has not yet formally classified resmethrin as to its cancer-causing ability.[8]

There are no publicly available studies of the carcinogenicity of commercial resmethrin-containing insecticide products including the inert ingredients.

Effects on Reproduction

In 1994, when EPA listed resmethrin as a toxic chemical under EPCRA, one of the reasons was its reproductive toxicity. EPA's decision was based on two studies sponsored by resmethrin's manufacturer. In both of these studies, exposure to resmethrin during pregnancy caused an increase in the number of stillbirths at all dose levels tested.[13,15]

The California Environmental Protection Agency lists resmethrin as a chemical "known to the state to cause cancer or reproductive toxicity" based on the same studies.[22]

Resmethrin's manufacturer has also sponsored a newer laboratory study of effects on reproduction. This study was completed after the EPCRA and

the California evaluations were finished.

The new study showed that exposure to resmethrin for two generations caused an increase in the number of offspring that died shortly after birth in both generations. In addition, the surviving offspring of exposed animals weighed less than offspring of unexposed animals. (See Figure 5.) These effects occurred at the highest dose level tested in this experiment.[23]

Resmethrin has also caused reproductive problems in laboratory tests with rabbits. In two studies, both sponsored by resmethrin's manufacturer, rabbits fed resmethrin during pregnancy had more miscarriages than unexposed rabbits. In one study, the increased miscarriages occurred at all dose levels tested; in the second study they occurred at the highest dose level tested.[24]

There are no publicly available studies looking at whether or not commercial resmethrin insecticide products, including the inert ingredients, cause reproductive effects.

Toxicity to Fish

According to the Extension Toxicology Network, "resmethrin is highly toxic to fish."[25] In tests reported to EPA, many species of fish were killed by concentrations of resmethrin less than one part per billion (ppb). These include bluegill sunfish, brown trout, coho salmon, lake trout, rainbow trout, yellow perch,[26] fathead minnow (fingerlings), and largemouth bass.[27]

Because of resmethrin's toxicity to fish, EPA has classified mosquito uses of resmethrin, as well as its uses for "pest control treatments at nonagricultural sites,"[28] as restricted uses.[28] This means that the products must be used "by or under the direct supervision of a certified applicator."[29]

Resmethrin's toxicity to fish can cause problems for mosquito control. Mosquito fish (*Gambusia affinis*), often used to control mosquitoes, are killed by application rates of resmethrin recommended for mosquito control.[30]

Toxicity to Other Aquatic Animals

Resmethrin is toxic to a variety of aquatic animals. Some examples include the following:

- The red swamp crawfish is a commercially important crawfish in Louisiana. Resmethrin (with added piperonyl butoxide) is extremely toxic to crawfish; concentrations as low as 0.8 ppb are lethal. The concentration that kills crawfish is only 7 percent of the concentration that kills mosquitoes,[31] so that resmethrin mosquito spraying is likely to kill crawfish.
- Water fleas are often used as representative aquatic animals in water quality testing.[32] Resmethrin is extremely toxic to water fleas. In one study submitted to EPA as part of the registration process, water fleas were killed by a resmethrin concentration of 0.4 ppb. In another study, in which water fleas were exposed to resmethrin during their entire life cycle, their growth was reduced by a concentration of 0.06 ppb.[33]

Toxicity to Honey Bees

According to the Extension Toxicology Network, "resmethrin is highly toxic to bees."[25] Tiny amounts of resmethrin (0.06 micrograms per bee) are lethal.[34]

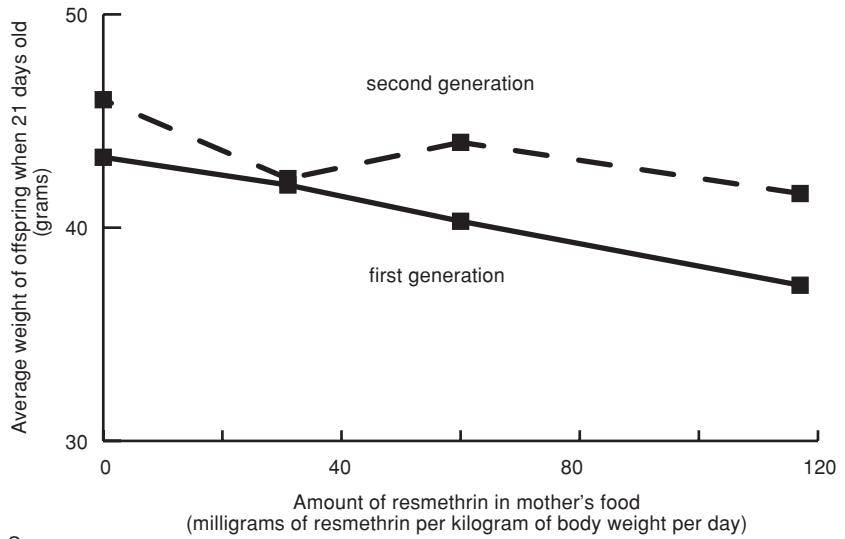
Development of Resistance

Within natural populations of pest insects, there is a range of susceptibility to insecticides. When these chemicals are used, they often kill the most susceptible pest individuals, leaving the insects that have genetic factors that allow them tolerate higher exposures to survive and reproduce.[35] This process is called resistance and is a growing problem with resmethrin.

Resistance to resmethrin was first documented in greenhouse whiteflies in the United Kingdom in 1974,[36] only a few years after commercial use of resmethrin began. Four years later, researchers reported resmethrin resistance in another agricultural pest insect, the diamondback moth.[37]

Since then, two household insects have developed resistance to resmethrin, the house fly and the

Figure 5
Effects of Resmethrin on Size of Offspring



Source:
U.S. EPA. Office of Prevention, Pesticides, and Toxic Substances. 1994. SBP-1382® (Resmethrin technical manufacturing use product.) ID No. 000432-00487. Evaluation of 2-generation reproduction study in rat and reevaluation of the following previously submitted studies: 3-generation reproduction study in rat, six-month dog, rat developmental, and rabbit developmental toxicity studies. Memo from L.J. Hansen, Heath Effects Div. to R. Brennis and A. Layne, Reregistration Div. Washington, D.C., Nov. 17.

Resmethrin has caused a variety of reproductive effects in laboratory tests, including reducing the weight of offspring.

German cockroach.[38,39]

Development of resistance to resmethrin and other pyrethroids in mosquitoes is problematic because resmethrin is widely used in mosquito control programs. Mosquitoes resistant to chemical relatives of resmethrin were first reported in Cuba in 1991.[40] Since then, they have been reported in Africa, the Middle East, and Asia.[41]

Entomologists first reported resmethrin resistance in U.S. mosquitoes in 2003 after studying a population in Marin County, California.[41]

Resmethrin resistance in mosquitoes has also been reported from Huntsville and Mobile, Alabama. Entomologists measured resistance ratios in mosquitoes collected in these urban areas as high as 830. The resistance ratio is the increased amount of resmethrin required to kill resistant mosquitoes.[42]

Soil Persistence

Pyrethroid insecticides are often described as "fairly rapidly degraded in soil."[12] However, resmethrin is surprisingly persistent. The U.S. Department of Agriculture's Agricultural Research Service reports that resmethrin's half-life in soil (the time required for half the applied amount of resmethrin to break down or move away from the application site[20]) is 30 days.[43]

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