

● INSECTICIDE FACTSHEET

SUMITHRIN (D-PHENOTHRIN)

The synthetic pyrethroid insecticide sumithrin is commonly used to kill household insects and mosquitoes. The U.S. Environmental Protection Agency (EPA) estimates that about 100 million applications of sumithrin are made annually in U.S. homes, yards, and gardens.

Sumithrin is a neuropoison. Symptoms of exposure include dizziness, headache, fatigue and diarrhea.

In laboratory tests, sumithrin has damaged the liver and the kidneys. It has also caused anemia and increased the incidence of liver cancer.

In breast cancer cells, sumithrin increases the expression of a gene that is involved with proliferation of cells in the mammary gland. Sumithrin can also mimic certain activities of the sex hormone estrogen and keep another sex hormone from binding to its normal receptors.

Thousands of cat poisonings and some dog poisonings have been reported following the use of some sumithrin-containing flea control products.

Low concentrations of sumithrin (as low as one part per billion) kill fish and other aquatic animals. Sumithrin is also highly toxic to bees.

BY CAROLINE COX

Sumithrin (see Figure 1) is an insecticide in the synthetic pyrethroid pesticide family. It is also called d-phenothrin. Marketed as an insecticide since 1977,¹ it is sold by many pesticide companies using a variety of brand names, including Raid, Enforcer, Ortho, and Anvil.² There are about 250 sumithrin-containing pesticide products registered for sale in the U.S.²

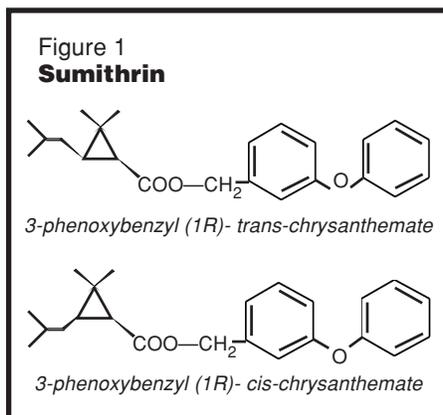
Pyrethroid insecticides are related chemically to the insecticidally active compounds called pyrethrins extracted from chrysanthemum flowers. Chemists have designed the structure of synthetic pyrethroids to make them both potent and stable in sunlight.³

Like most synthetic pyrethroid insecticides, sumithrin exists as a mixture of stereoisomers,¹ molecules that have the same atoms linked in the same order, but differ in their spatial arrangement.⁴ Sumithrin is a mixture of 2 stereoisomers which are both insecticidally active.¹ (See Figure 1.)

Synthetic pyrethroid insecticides,



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including sumithrin, “are widely perceived as being safe”⁵ according to one neurotoxicologist. However, sumithrin poses a variety of hazards for human and environmental health, and those are the focus of this article.

Use

Sumithrin is primarily used to kill household insects, insects which pose public health problems (mosquitoes, for example), insects in stored grains, and lice.¹ The International Programme on Chemical Safety estimated in 1989 that worldwide use was about 70 to 80 tons per year;¹ more recent estimates are not publicly available. A U.S.

Environmental Protection Agency (EPA) survey estimated in 1992 that almost 100 million applications of sumithrin were made annually in U.S. homes, yards, and gardens. About 2/3 of these applications occurred indoors.⁶

How Does Sumithrin Kill Insects?

Sumithrin kills insects by disrupting the transmission of nerve impulses along axons, the elongated parts of nerve cells. Synthetic pyrethroids allow excessive amounts of sodium atoms to enter nerve cells, stimulating the nerve cells and eventually causing paralysis. This mode of action is similar to that of the organochlorine insecticide DDT.³

Pyrethroids' effects on human nerves are similar to their effects on insect nerves.⁵ However, human nerves are generally less susceptible to pyrethroid poisoning. This is because human nerves are intrinsically less sensitive, pyrethroids are less potent at the higher body temperatures in humans, and human nerves recover more quickly from poisoning.⁷

Synergists

About a dozen sumithrin products,

including the Anvil products used to kill mosquitoes, contain piperonyl butoxide.⁸ This chemical is used to synergize (to make more toxic) sumithrin and other insecticides. Piperonyl butoxide is classified as a carcinogen by EPA, causes atrophied testes, and reduces the activity of important immune system components. For detailed information about the hazards of piperonyl butoxide see JPR 22(2):12-20 or www.pesticide.org.

Inert Ingredients

Like most pesticides, sumithrin insecticides contain ingredients in addition to sumithrin. Many of these ingredients, according to U.S. pesticide law, are called "inert."⁹ In general, they have not been publicly identified, and are not included in most of the testing required in order to register these pesticides.¹⁰ "Inert Ingredients" (right) summarizes the hazards of some inert ingredients used in sumithrin products.

Symptoms of Exposure

Sumithrin and other synthetic pyrethroids are "neuropoisons" and symptoms of exposure are related to their

effects on the nervous system.¹¹ According to Medical University of South Carolina physicians, acute (short-term) symptoms of exposure to sumithrin and other synthetic pyrethroids include "dizziness, salivation, headache, fatigue, diarrhea, and irritability to sound and touch."¹²

Effects on the Liver

According to a laboratory study submitted to EPA by a manufacturer as part of the registration process, sumithrin damages the liver. In a long-term (two-year) study in which rats were fed sumithrin, the livers of exposed animals weighed more than those of unexposed animals. In addition,

concentrations of enzymes that are indicators of liver damage increased in exposed animals. These effects occurred at the middle and high dose levels tested in this experiment.¹³

Similar increases in liver weight were found in studies of dogs fed sumithrin and rats breathing sumithrin-contaminated air. Both studies were conducted as part of the registration process.^{14,15}

Effects on the Kidneys

Two laboratory studies submitted as part of the registration process suggest that male kidneys may be particularly susceptible to sumithrin.^{16,17} (See Figure 2.) At all dose levels tested,

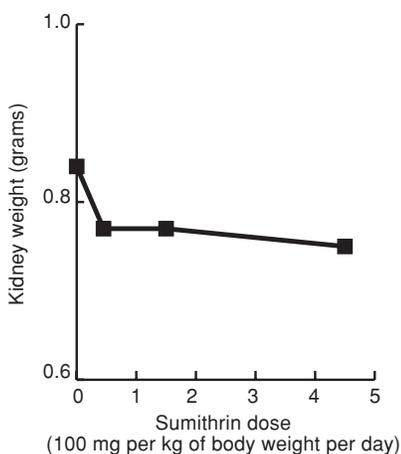
"INERT" INGREDIENTS

Almost 100 sumithrin products contain **petroleum distillates** as inert ingredients.¹ One of these distillates is hydrotreated kerosene (Chemical Abstracts Services (CAS) number 64742-47-8).² According to the International Agency for Research on Cancer (IARC), exposure to hydrotreated kerosene caused skin tumors in a laboratory study.^{3,4} Three other petroleum distillates (with CAS numbers 64742-55-8, 64742-56-9, and 64742-94-5) are used in Anvil mosquito control products.^{5,6} One of these petroleum distillates causes tremors and difficulty breathing,⁷ the second caused skin tumors, according to IARC,^{8,9} and the third contains two hazardous chemicals, naphthalene and trimethyl benzene.¹⁰ Naphthalene exposure has caused lung tumors, cataracts, and anemia¹¹ while trimethyl benzene can depress the central nervous system and cause asthmatic bronchitis.¹²

Many household sumithrin products are sold in aerosol spray cans, and these products often contain "inert" **propellants** that pose a variety of hazards. These propellants include propane and isobutane.² Both of these propellants can cause dizziness when inhaled and are "extremely flammable."^{13,14}

1. Based on a survey of labels of sumithrin insecticide products conducted during May, 2003. Labels were retrieved from: U.S. EPA and Calif. Dept. of Pesticide Regulation. 2003. USEPA/OPP chemical ingredients database. www.cdpr.ca.gov/docs/epa/epachem.htm.
2. U.S. EPA. 2002. Response to Freedom of Information Act request 01245-03.
3. National Institute for Occupational Safety and Health (NIOSH). 1997. Registry of Toxic Effects of Chemical Substances: Kerosene (petroleum), hydrotreated. www.cdc.gov/niosh/rtecs/oa53fc00.html.
4. International Agency for Research on Cancer (IARC). 1989. Occupational exposures in petroleum refining. IARC Monographs 45:39. www-cie.iarc.fr/htdocs/monographs/vol45/45-01.htm.
5. Clarke Mosquito Control Products, Inc. 1999. Material safety data sheet: Anvil 2+2 ULV. Rosedale, IL.
6. Clarke Mosquito Control Products, Inc. 1999. Material safety data sheet: Anvil 10+10 ULV. Rosedale, IL.
7. NIOSH. 2000. Registry of Toxic Effects of Chemical Substances: Mineral oil, petroleum distillates, solvent - dewaxed light paraffinic (mild or no solvent - refining or hydrotreatment). www.cdc.gov/niosh/rtecs/py7aa095.html.
8. NIOSH. 2000. Registry of Toxic Effects of Chemical Substances: Mineral oil, petroleum distillates, hydrotreated (severe) light paraffinic. www.cdc.gov/niosh/rtecs/py7aac4c.html.
9. IARC. 1987. Mineral oils: Untreated and mildly-treated oils; Highly treated oils. IARC Monographs (Suppl. 7):252. www-cie.iarc.fr/htdocs/monographs/suppl7/mineraloils.html.
10. Shell Chemical Co. 2003. Material safety data sheet: Shellisol® A150. www.euapps.shell.com/MSDS/GotoMsds.
11. IARC. 2002. Naphthalene. IARC Monographs 82:367. www-cie.iarc.fr/htdocs/monographs/vol82/82-06.html.
12. Hazardous Substance Data Bank (HSDB). 2002. 1,2,4-trimethylbenzene. <http://toxnet.nlm.nih.gov>.
13. HSDB. 2002. Propane. <http://toxnet.nlm.nih.gov>.
14. HSDB. 2002. Isobutane. <http://toxnet.nlm.nih.gov>.

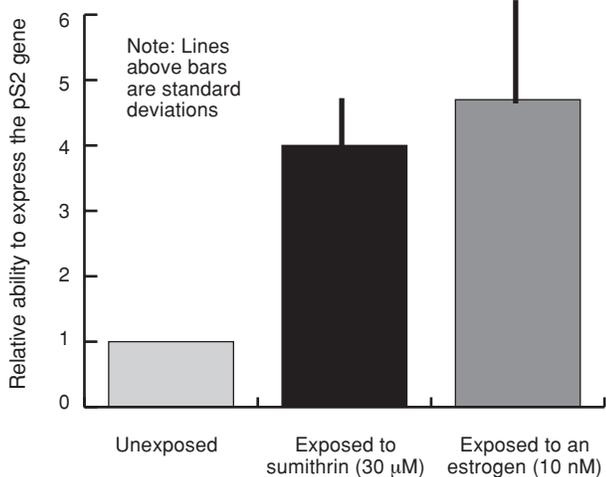
Figure 2
Sumithrin Damages Kidneys



Source: U.S. EPA. Office of Pesticides and Toxic Substances. 1989. Memo from E.R. Budd, Health Effects Div. to J.M. Tavano, Registration Div. Washington, D.C., Mar. 16. See attached Data Evaluation Report for MRID No. 402764-02.

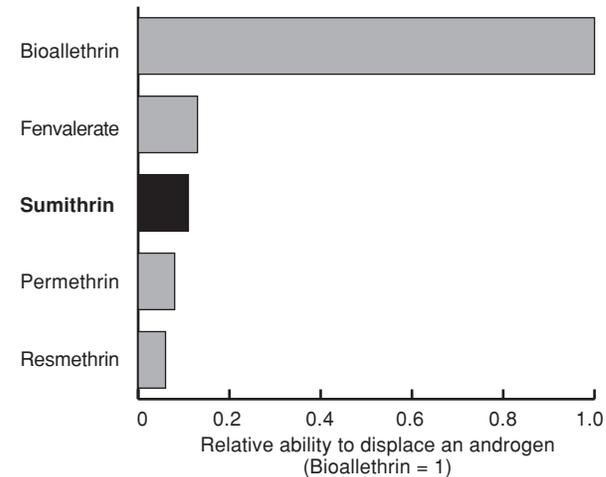
In male mice, sumithrin reduced kidney weight at all dose levels tested.

Figure 3
Sumithrin Mimics the Activity of a Sex Hormone



Source: Go, V. et al. 1999. Estrogenic potential of certain pyrethroid compounds in the MCF-7 human breast carcinoma cell line. *Environ. Health Persp.* 107:173-177.

Figure 4
Sumithrin Displaces a Sex Hormone from its Receptors



Source: Eil, C. and B.C. Nisula. 1990. The binding properties of pyrethroids to human skin fibroblast androgen receptors and to sex hormone binding globulin. *J. Steroid Biochem.* 35:409-414.

In laboratory tests, sumithrin disrupts the normal functioning of hormone systems.

(45-450 milligrams per kilogram of body weight (mg/kg) per day), male mice exposed to sumithrin in a two-year study developed smaller kidneys than unexposed males.¹⁶ A study in which rats were fed sumithrin for two generations also found small kidneys in the first generation males.¹⁷

Effects on Blood

In the study of dogs mentioned on p. 11, sumithrin exposure also caused anemia. In dogs fed sumithrin for one year, both the number of red blood cells and the amount of hemoglobin (the oxygen-carrying molecule in the blood⁴) were decreased.¹⁴ Anemia occurred at dose levels of 80 mg/kg per day. This was the highest dose tested in this study.¹⁴

Effects on Hormones

The impact of environmental contaminants on the functions of human and animal hormone systems has been a significant concern in the last decade.¹⁸ Hormones are biologically active molecules that control all responses and functions of the body. Dramatic changes in the activity of cells in humans and other animals “are

caused by extremely small amounts” of hormones or other chemicals that disrupt this system.¹⁹

Sumithrin has these kinds of effects on hormones. Researchers at the Mt. Sinai School of Medicine showed that sumithrin can mimic estrogens, sex hormones, in one of their biological activities. The researchers looked at the activity of a gene called pS2 because the expression of pS2 is activated by estrogens. They found that in human cells sumithrin (as well as another synthetic pyrethroid insecticide, fenvalerate) activates the expression in cells of pS2 like estrogens do.²⁰ (See Figure 3.)

Sumithrin also keeps androgens, other sex hormones, from binding to their normal receptors in human tissue. Scientists from Brown University and the National Institutes of Health showed that in genital skin cells sumithrin could displace an androgen from its normal receptors. When compared to other synthetic pyrethroids, sumithrin is intermediate in its displacement potency.²¹ (See Figure 4.)

Effects on Reproduction

Sumithrin has a variety of effects

on reproduction in laboratory studies.

In the two-generation study of rats mentioned in the “Effects on Kidneys” section, the uterus was smaller in female rats exposed to the middle and high doses of sumithrin than in unexposed rats.¹⁷

In a second study of sumithrin’s effects on reproduction submitted during the registration process, pregnant rabbits exposed to sumithrin (at a dose of 500 mg/kg) had more miscarriages than unexposed rabbits. In addition, the sex ratio of the offspring of exposed mothers was different from that of unexposed mothers; more males were born to exposed animals. Also, a brain-related defect occurred in the offspring of rabbits exposed at the dose level of 500 mg/kg. This defect, hydrocephaly, results in an abnormally large amount of fluid around the brain, leading to an enlarged skull and atrophy of the brain.²²

Carcinogenicity (Ability to Cause Cancer)

Sumithrin’s ability to cause cancer has not yet been evaluated by EPA (as of May 2002).²³

However, in two of the laboratory

carcinogenicity studies submitted in support of sumithrin's registration, long-term (two-year) exposure to sumithrin increased the incidence of liver cancer. The studies include one done on mice and another done on rats. In the study with mice, liver cancer was relatively common (it occurred in 18 percent of the unexposed animals tested) and sumithrin exposure caused cancer incidence to increase to almost 25 percent.¹⁶ In the study with rats, liver cancer was relatively rare (no liver cancer was found in unexposed animals) but increased to an incidence of almost 15 percent in exposed animals.¹³ (See Figure 5.)

In addition, a study from the Mt. Sinai School of Medicine links sumithrin with breast cancer. In this study, physicians used a culture of breast cancer cells. They looked at the expression of a gene that is involved in the proliferation of mammary tissue, and therefore in the development of breast cancer. Exposure to sumithrin increased the expression of this gene.²⁴

Synergy

Enzymes called plasma esterases

detoxify pyrethroids in mammals. The activity of these enzymes is inhibited by a common family of insecticides, the organophosphates; this means that "simultaneous exposure to these insecticides will increase the toxicity of pyrethrins and pyrethroids."²⁵

Effects on Pets

Cats, especially young cats, are particularly susceptible to pyrethroid insecticides, possibly because cats' livers are relatively slow in detoxifying pyrethroids.²⁶ Two sumithrin flea control products manufactured by Hartz Mountain Corporation have recently caused a large number of cat poisonings. EPA estimates that there were thousands of incidents, including some deaths, between May 2000 and November 2002. At that time Hartz agreed to relabel the two products to reduce cat exposure.²⁷

Seizures and death have also occurred after use of sumithrin on dogs, but not in as large numbers as the cat incidents.²⁸

Effects on Fish

According to the International

Programme on Chemical Safety, sumithrin is "very toxic to aquatic organisms."²⁹ In tests submitted as part of sumithrin's registration, the most sensitive fish species was the rainbow trout. The LC₅₀ (median lethal concentration; the dose that kills half of a test population) for rainbow trout was 1.4 parts per billion (ppb). All LC₅₀s for fish were less than 100 ppb.³⁰

The labels of about 80 sumithrin-containing insecticides contain warning statements about toxicity to fish.⁸

Sumithrin also bioconcentrates in fish. This means that the concentration of sumithrin in fish tissues is greater than the concentration in the water in which the fish lives. According to a study conducted by Sumitomo Chemical Company, bioconcentration factors in carp range from 210 to 730.³¹ (The bioconcentration factor is the ratio between the concentration of a chemical in fish tissues and the concentration in water.³²) When fish were simultaneously exposed to sumithrin and the synergist piperonyl butoxide (as in Anvil insecticide products), the bioconcentration factor of one form of sumithrin increased dramatically. Bioconcentration factors in this experiment varied from 2400 to 3800.³¹

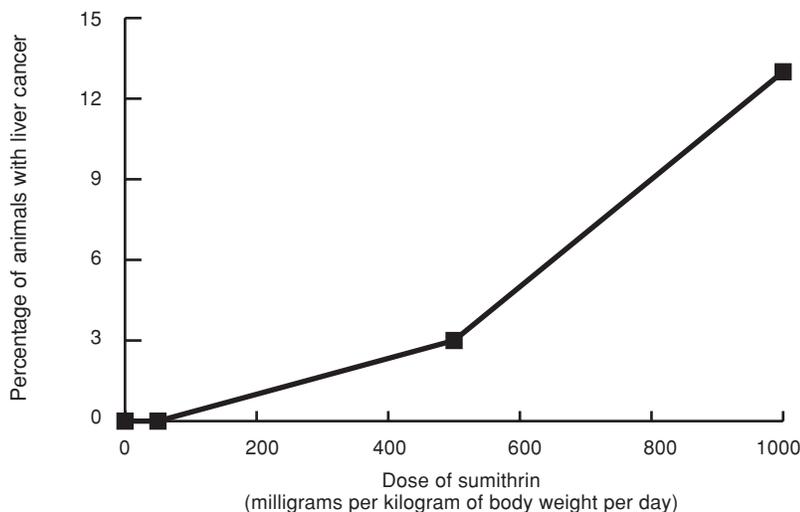
Effects on Other Aquatic Animals

Sumithrin is highly toxic to water fleas, a species that is used in pesticide testing to represent aquatic animals. In a test submitted to EPA for sumithrin's registration, concentrations of less than 1 ppb reduced successful egg hatch in water fleas. A slightly higher concentration (2 ppb) reduced the survival of larval water fleas. Sumithrin is even more toxic to shrimp; concentrations of 0.03 ppb killed mysid shrimp.³⁰

Effects on Bees

Since sumithrin is a broad spectrum insecticide, it is perhaps not surprising that tiny amounts of sumithrin kill bees. In a test submitted to EPA as part of sumithrin's registration, 0.07 micrograms killed honey bees.³⁰ This puts sumithrin into EPA's highest toxicity group for bee toxicity. This toxicity group includes any pesticides that

Figure 5
Ability of Sumithrin to Cause Cancer



Source: Calif. Environmental Protection Agency. Dept. of Pesticide Regulation. Medical Toxicology Branch. 1996. Summary of toxicology data: Phenothrin, June 20. www.cdpr.ca.gov/docs/toxsums/toxsumlist.htm

In a laboratory study of rats, sumithrin increased the incidence of liver cancer.

kill bees in amounts of 2 micrograms per bee or less.³³

Resistance

Insecticide resistance occurs when repeated exposure over generations kills the most susceptible individuals in an insect population. The survivors have genetically determined characteristics that allow them to survive exposures to the insecticide that would usually be lethal.³⁴

Sumithrin resistance has been reported in cockroaches, aphids, mosquitoes and lice.³⁵⁻³⁸ The resistance ratio, the ratio between the amount of sumithrin needed to kill a resistant insect and the amount needed to kill a susceptible one, can be over 50 in both cockroaches and lice.^{36,39,40}

The synergist piperonyl butoxide is sometimes used to "negate" resistance, to kill resistant individuals, but is not always successful.³⁴

Sumithrin resistance can be quite common. French physicians found that 60 percent of the lice populations in the Paris elementary school students they studied were resistant to sumithrin.³⁸ Widespread resistance has also been found in lice in the United Kingdom.⁴¹

Insects resistant to one pyrethroid insecticide are often resistant to many pyrethroids. This means that insects can develop resistance to sumithrin without actually having been exposed to the insecticide.⁴² ♣

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