● HERBICIDE FACTSHEET

DICHLOBENIL

The herbicide dichlobenil is used to kill unwanted weeds in shrub beds, orchards, and berry fields.

It is "among the most toxic chemicals hitherto reported" to nasal tissue. Damage to this tissue reduces smelling ability and the transport of an important amino acid to the brain.

Dichlobenil affects reproduction in both male and female animals. In male hamsters, long-term feeding studies found that ingestion of dichlobenil decreases the weight of the testes, decreases the number of sperm stored in reproductive organs, and causes degeneration of the prostate gland. In female rabbits, ingestion of dichlobenil resulted in an increase in the number of unsuccessful pregnancies. The frequency of cleft palate, a birth defect, in their offspring was increased.

Dichlobenil has caused cancer in three species of laboratory animals. In rats (both sexes) and male hamsters, long-term feeding of dichlobenil caused an increase in the frequency of liver tumors and cancers. Injection of mice with small amounts of dichlobenil caused an increase in the frequency of lymphoma.

Dichlobenil is "remarkably persistent" in soil and residues have been measured five years after application. It volatilizes (vaporizes) readily so it can contaminate air in areas where it is used.

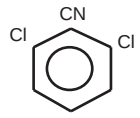
Dichlobenil is acutely toxic to fish, bioconcentrates in fish tissues, and reduces their reproductive success.

Dichlobenil reduces the growth of beneficial mycorrhizal fungi on the roots of apple trees.

BY CAROLINE COX

Dichlobenil (see Figure 1) is an herbicide that has been registered for use in the U.S. since 1964. It is classified in the benzonitrile family of herbicides.[1] Common brand names of dichlobenil-containing herbicides include Casoron, Norosac, and Dyclomec. Major manufacturers include Uniroyal Chemical Company and PBI/Gordon Corporation.[2]

Figure 1
Dichlobenil



Dichlobenil
(2,6-dichlorobenzonitrile)

Use

Dichlobenil is typically used under pavement; in the soil of shrub beds; in orchards, vineyards and berry fields; and as an aquatic herbicide. The U.S. Environmental Protection Agency (EPA) estimates that total annual use in the U.S. is between 150,000 and 225,000 pounds. The largest amounts of dichlobenil are used by homeowners, around ornamental plants, trees, and turf, and in cranberry bogs. (See Figure 2.)

Caroline Cox is JPR's editor.

Mode of Action

Dichlobenil molecules are taken up by roots and transported throughout the plant.[3] Inside the plant, dichlobenil inhibits actively dividing cells by disrupting the formation of the cell plate, a structure which forms during cell division to separate the two new cells.[4] Since germinating seedlings or actively growing plants will have large numbers of dividing cells, they are most affected by dichlobenil.[4]

On a molecular level, dichlobenil is a "potent" inhibitor of cellulose synthetase,[4] the enzyme which produces cellulose from glucose.[5] Cell plate formation is disrupted because cellulose is an important component of the plate.[5]

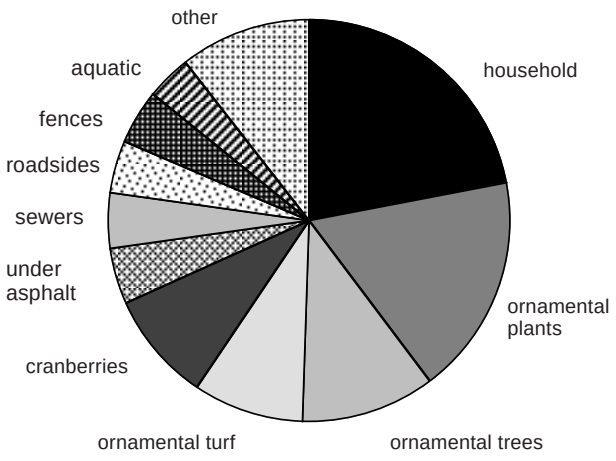
In addition to dichlobenil's inhibition of cellulose synthetase, dichlobenil causes other effects because its breakdown products affect important physiological processes. The two major breakdown products "strongly" inhibit four of the light-based reactions that occur in the chloroplasts during photosynthesis. In mitochondria, (energy-producing structures in the cells of both animals and plants) these breakdown products uncouple reactions that provide the cell with ATP (the molecule that is the cell's basic energy source). Without ATP, cells cannot maintain the structures of their membranes. This explains some of dichlobenil's toxicity to animals.[6]

Acute Toxicity

The amount of dichlobenil that will kill laboratory animals varies widely among species; the oral LD_{50} (median lethal dose, the amount required to kill 50 percent of a population of laboratory animals) is about 500 milligrams per kilogram (mg/kg) of body weight for guinea pigs, about 2000 mg/kg of body weight for mice, and about 4,250 mg/kg of body weight for rats. If humans are as susceptible to dichlobenil

NORTHWEST COALITION FOR ALTERNATIVES TO PESTICIDES/NCAP
P.O. BOX 1393, EUGENE, OREGON 97440 / (541)344-5044

Figure 2
Estimated Use of Dichlobenil in the U.S.

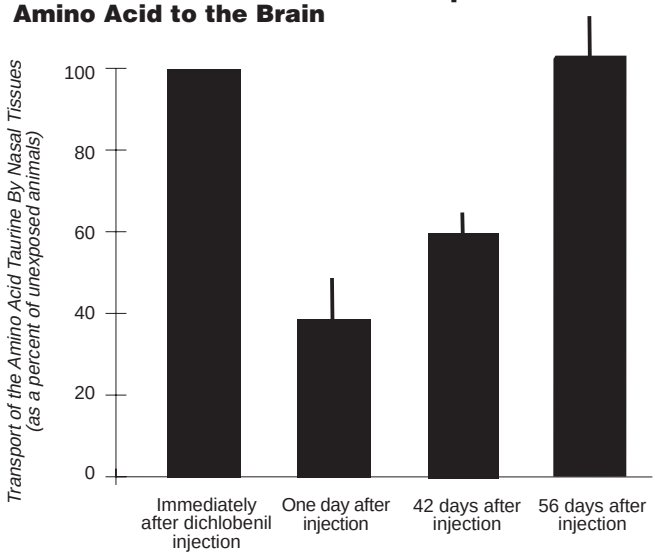


Dichlobenil use totals 227,000 pounds annually.

Source: EPA estimates (unpublished).

The largest single use of dichlobenil is in home yards, but agricultural uses are also significant.

Figure 3
Effect of Dichlobenil on the Transport of an Amino Acid to the Brain



Note: Lines above the bars indicate the amount of variablility between individual animals used in this experment.

Source: Brittebo, E.B. and C. Eriksson. 1995. Taurine in the olfactory system: Effects of the olfactory toxicant dichlobenil. *NeuroToxicology* 16(2):271-280.

Injection of dichlobenil in laboratory animals damages nasal tissue and reduces the transport of an important amino acid to the brain. Normal transport did not resume until eight weeks after dichlobenil treatment.

as guinea pigs, ingestion of just over an ounce would be required to kill a typical adult human (weighing 60 kilograms).[7]

If laboratory animals are exposed to dichlobenil through the skin, or via injection, death occurs at lower exposures (600-1350 mg/kg, depending on species and type of exposure) than when exposure is oral. Concentrations of 0.25 mg/l cause death of rats via inhalation.[7]

Toxicity to the Olfactory System

In the last decade, dichlobenil has been identified as a "potent" olfactory toxicant.[8] Dichlobenil and the related herbicide chlorthiamid are "among the most toxic chemicals hitherto reported"[9] to the lining of the nasal cavity. This lining has a high concentration of enzymes which convert dichlobenil to a toxic form.[9] Injection of a small amount (12 mg/kg) of dichlobenil in mice results in irreversible binding of dichlobenil to the lining of the nasal cavity, followed by severe damage to the tissues.[9] Smelling ability is reduced for four days following exposure,[10] and weeks are required for the damaged tissues to be partially regenerated.[8]

In addition, dichlobenil-damaged nasal lining is unable to transport the amino acid taurine to the brain, as it typically does. In tests using mice, between three and eight weeks were required for taurine transport rates to return to normal. Decreased levels of taurine in the central nervous system have been associated with Alzheimer's disease.[11]

Several studies indicate that olfactory toxicity could be a problem for people who use dichlobenil as an herbicide. Human noses have the enzyme that produces the toxic form of dichlobenil.[12] Also, nasal damage occurred in laboratory mice that were dermally exposed at rates that might be expected in occupationally-exposed humans following a splash from a tank mixture or prolonged contact with a granular product. In addition, researchers observed effects on the central nervous system that are "likely permanent."[13]

Eye Irritation

Tests using rabbits showed that dichlobenil caused corneal lesions, inflammation of the iris, and irritation of the conjunctiva (the white of the eye). The cornea and the iris required 48 hours to return to normal; the conjunctiva required up to 72 hours. If eyes were washed following exposure to dichlobenil, all treated eyes were normal by 48 hours after treatment and no corneal lesions were found.[14]

Four dichlobenil-containing products (Casoron Granules, Norosac 4G, Dyclomec 4G, and Barrier 50W) can cause eye irritation.[15-18]

Skin Irritation

Workers in a plant that formulated dichlobenil granules developed a skin condition called chloracne. Chloracne is a severe acne, characterized by the eruption of several hundred lesions. The physician who treated the workers found that typical acne treatments (drainage, scrubs, ultraviolet light, and an antibiotic) were ineffective in treating the chloracne and that "the only really effective treatment capable of producing lasting results was the removal of the patient from the offending environment."[19] Chloracne is a typical symptom of exposure to the notorious chlorinated compounds called

dioxins.[20]

Four dichlobenil-containing products (Casoron Granules, Norosac 4G, Dyclomec 4G, and Barrier 50W) can cause skin irritation.[15-18]

Other Acute Toxicity

Four dichlobenil-containing products (Casoron Granules, Norosac 4G, Dyclomec 4G, and Barrier 50W) can cause respiratory irritation.[15-19] Three products (Norosac 4G, Dyclomec 4G, and Barrier 50W) can cause intestinal irritation.[16-18]

Subchronic Toxicity

Adverse effects have been seen in five species of laboratory animals exposed to dichlobenil for intermediate lengths of time (generally three months). These effects include the following:

Rats: A study using four dichlobenil doses found that liver and kidney weights increased at all doses tested except the lowest one. Liver degeneration occurred at the two highest doses. At the highest dose tested, liver necrosis (cell death) occurred.[21]

Dogs: A study using three doses of dichlobenil found that lever weights increased at the high and the middle dose used in female dogs.[7]

Mice: A study using four dichlobenil doses found "adverse effects" on the liver in females at the two highest doses tested.[22]

Hamsters: A study using four dichlobenil doses found "adverse effects" on the liver and increased liver weights in females at all but the lowest dose tested. At the two highest doses, increased liver weights in males and swollen liver cells in females were noted. At the highest dose tested, both sexes developed gall bladder stones.[22]

Rabbits: Rabbits dermally exposed to dichlobenil for three weeks lost weight, were inactive, and appeared weak at two of the three doses tested.[7]

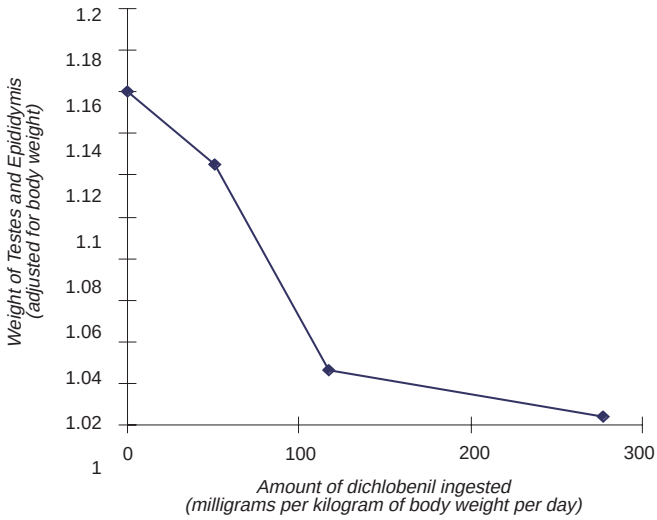
Chronic Effects

Long-term feeding of dichlobenil to laboratory animals has shown adverse effects in three species. These effects include the following:

Rats: In a study using three doses of dichlobenil, decreased weight gain, decreased food consumption, and increased liver and kidney weights were found at the middle and high dose in both sexes.[21] Kidney degeneration, increased kidney weight, and excessive growth of cells in the parathyroid were found in males fed both the middle and high dose. At the same two doses, abnormalities of liver cells and increased liver weight were found in females. At the highest dose tested, death of liver cells, liver nodules, and kidney stones were found in both sexes.[22]

Dogs: A two-year feeding study found increases in liver and thyroid weights, as well as degeneration around the central veins of the liver in both males and females. These effects were seen at the highest dose tested, although this was a relatively low dose (8.8 mg/kg of body weight per day).[7]

Figure 4
Effect of Dichlobenil on Male Hamster Reproductive Organs



Source: U.S. EPA. Office of Pesticide Programs. 1992. Data evaluation report: Dichlobenil chronic oncogenicity study. Potential tumorigenic effects in prolonged dietary administration to hamsters. Prepared by Clement International Corp. (Sept.)

Feeding of dichlobenil reduces testes size in hamsters.

Hamsters: Two separate long-term feeding studies have been conducted with hamsters, The first study used doses of dichlobenil that were about one-sixth of the doses used in the second study. Except for excessive growth of cells in the stomach lining, the first study found effects only at the highest dose tested. These effects included excessive growth cells in the pancreas in males; inflammation of the abdominal cavity in females; enlargement of liver cells in females; excessive growth of cells in the intestine, bone marrow, skin and adrenal glands in females; and decreased weight gain in both sexes. The second, higher dose, study found decreased weight gain in both sexes, decreased food consumption in males, enlargement of liver cells in males, and increased liver weights in females at all doses tested. At both the middle and high dose hepatitis and pale adrenal glands were found in females, while pale livers and increased liver weight were found in males. Effects seen at the highest dose tested were enlargement of liver cells in females, hepatitis in males, inflammation of stomach and intestine in females, pituitary cysts in females, excessive growth of bladder cells in females, enlarged livers in males and females, distended bladders in males, and pale spleens in males.[22]

Chronic inhalation of the dichlobenil-containing product Casoron 50W can cause lung damage.[23]

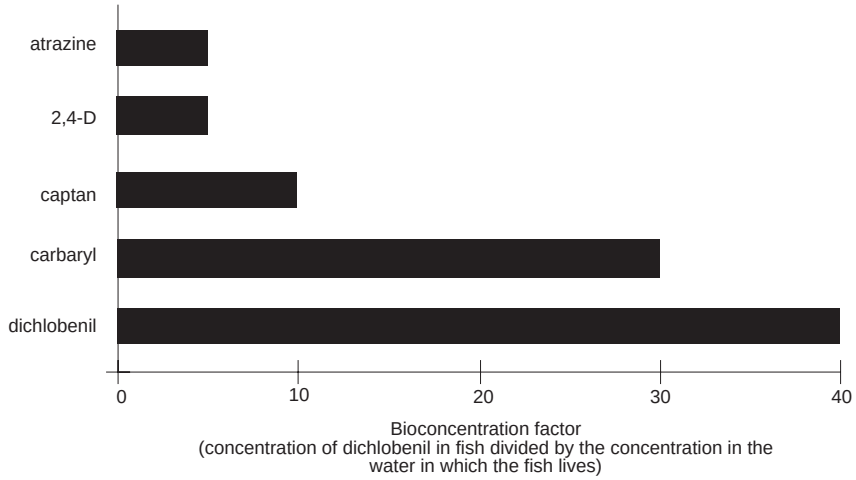
Effects on Reproduction

Exposure to dichlobenil affects successful reproduction in both male and female laboratory animals. These effects include the following:

Males: In hamsters, the testes are "target organs" of dichlobenil toxicity according to EPA. Effects on testes included reduced production of seminal fluid by the seminal vesicles, decreased weight of the testes and epididymis, decreased seminal vesicle weight, tubular degeneration in the testes, a decreased number of sperm in the epididymis (a sperm-storage structure on the surface of the testes), and dilation of the sperm-producing tubules in the testes. The last four effects were found only at the highest dose tested. In addition, long or medium term feeding of dichlobenil caused reduced production of seminal fluid by the prostate gland, decreased prostate weight, degeneration of the prostate, and increased incidence of a protruding penis. All of these effects occurred at two or three doses.[22]

Females: In rabbits, feeding of dichlobenil during pregnancy caused decreased food con-

Figure 5
Bioconcentration of Dichlobenil in Fish



Source: Freitag, D. et al. 1985. Environmental hazard profile of organic chemicals. *Chemosphere* 14(10):1589-1616.

Dichlobenil bioconcentrates in fish more than several other common pesticides.

sumption and decreased weight gain in mothers. These mothers also had an increased number of unsuccessful pregnancies (resorptions and fetal losses). Among their offspring, increases in cleft palate, missing fingers or toes, abnormal eyes, and skeletal defects were found.[7] In rats, exposure to dichlobenil during pregnancy caused decreased body weight gain, and decreased food consumption for mothers.[7,24] These effects were found at both the high and the middle dose tested.[24] In their offspring, decreased birth weight[7] and an increase in the incidence of extra thoracic ribs was found.[24] Extra thoracic ribs were found at the highest dose tested,[24] while effects on weight were found at both the middle and the high dose tested.[7] In a multi-generation study, feeding of dichlobenil caused decreased offspring survival in the first generation and decreased fertility in the second generation.[7] These effects were seen at the highest dose tested, although it was a relatively low dose (5 mg/kg of body weight per day).

There are no publicly available tests of the effects of dichlobenil-containing products on reproductive success.

Carcinogenicity

EPA classifies dichlobenil as a possible human carcinogen.[25] In laboratory studies, dichlobenil has caused increases in the incidence of cancer in three species of animals:

Rats: In a two-year feeding study, dichlobenil caused a dose-related increase in liver tumors and cancers (singly or combined) in both males and females. EPA's classification as a possible human carcinogen is based on these results.[22]

Hamsters: Two two-year feeding studies have been completed with hamsters. The first study used doses of dichlobenil that were about one-sixth of the doses used in the second study. The first study found an increase in tumors of the islet cells of the pancreas at the highest dose tested in females. In males, excessive growth of pancreas islet cells, but not tumors, was found. In the second study, a dose related increase in liver tumors and combined tumors and cancers was found in males.[22]

Mice: A study using mice injected with very small doses of dichlobenil (.0065 mg over a 40-day period) found increases in four types of cancer: lymphoma, lung cancer, liver cancer, and mesothelioma. Based on the relatively small numbers of animals used in this study, only the increase in lymphoma was statistically significant. Both abdominal and subcutaneous injections caused an increase in cancer incidence. The physicians who authored the study stated that dichlobenil injected into the abdomen passes through the liver in the same way that ingested substances do, and that the subcutaneous injections were similar to skin absorption, the major source of human exposure. They therefore believe that the study provides good "evidence of a tumorigenic potential" for dichlobenil.[26]

There are no publicly available tests of the ability of dichlobenil-containing products to cause cancer.

Residues on Food

Little data is publicly available about dichlobenil residues on food. Monitoring by the U.S. Food and Drug Administration has found dichlobenil residues on food in 5 of the 6 years from 1990 and 1995.[27-32] In addition, experiments have shown that currants from plants treated with dichlobenil contain residues.[33]

Persistence in Soil

Dichlobenil has been called "remarkably persistent" in soil.[34] In a field in Great Britain, amounts sufficient to damage carrots persisted for two to five years after application, depending on the initial application rate. Laboratory analysis of the same soil found dichlobenil residues on the last date samples were tested, five years after treatment.[35] Two studies in orchards found dichlobenil residues one and two years after treatment[36] and a study in a cranberry bog found dichlobenil persisted for a similar length of time.[35] Another study found that 99 percent of the original dichlobenil applied could be recovered 105 days after treatment.[37]

Persistence in Water

Dichlobenil is also persistent in water. Four studies of ponds treated with dichlobenil found that persistence varies from 63 to 189 days, with an average of 130 days.[38-40]

In the muddy sediments at the bottom of ponds, persistence is longer, 126-312 days.[38-40]

Persistence in groundwater is even longer. Dichlobenil was found in groundwater for three years under an industrial site in Ireland that had been treated with dichlobenil over an 18 month period. The water sample analyzed from the last collection date contained dichlobenil, so three years is a minimum estimate of its persistence.[41]

Water Contamination

According to EPA, dichlobenil "has the potential to reach ground water resources based on its chemical structure, water solubility and use patterns."[21] As a result, EPA requires a warning

about this problem on labels of dichlobenil-containing products. Manufacturers of dichlobenil herbicides also have found that water contamination, and subsequent movement of the herbicide, is a problem. For example, the label for Casoron 2G states, "Do not apply to sloping areas as runoff may occur and result in damage to lawns and other plants in adjacent areas."[42]

Although no systematic monitoring for dichlobenil contamination has been done, it has been found in three creeks in western Washington,[43] a creek in Oregon's Willamette Valley,[44] and in the groundwater below a public garden in the Netherlands.[45] Dichlobenil was also the most commonly detected herbicide in monitoring of rainwater in Italy.[46]

Air Contamination

Dichlobenil volatilizes (vaporizes into the air) readily. When applied to soil, volatilization is dichlobenil's "primary fate" and is an important fate following an aquatic application.[47] One study found that 75 percent of the dichlobenil applied to an aquatic system volatilized.[48] More volatilization occurs when temperatures are high, when soils are wet, or when sprays instead of granules are used.[49] Covering a dichlobenil application with a layer of soil reduces its volatility, but only to about 50 percent of its original value if soils are wet.[49]

Dichlobenil also volatilizes from leaf surfaces once it is taken up by a plant. In an experiment with bean seedlings, for example, about 90 percent of the dichlobenil translocated to the leaves volatilized and thus ended up in the air. (This represented almost half of the dichlobenil taken up by the plant.)[50]

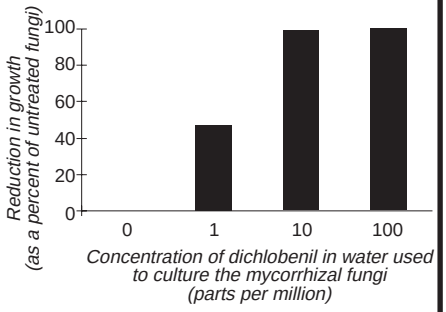
Effects on Animals

As an herbicide, the effects of dichlobenil are targeted at plants. However, adverse impacts occur when wild and domestic animals are exposed to dichlobenil. Examples include the following:

Fish: The acute toxicity of dichlobenil to fish under laboratory conditions varies depending on species and the length of exposure. If exposed for a ten day period, concentrations less than 2 parts per million (ppm) kill fish. Rainbow trout are a particularly sensitive species; the median lethal concentration (LC_{50}: the amount required to kill half of a population of test animals) was less than 5 ppm for a four-day exposure. LC_{50}s for other fish species range from 6 to 16 ppm.[36]

A field study of fish in small ponds treated with three concentrations of dichlobenil found no immediate mortality except at the highest concentration tested (40 ppm), but mortality over a 3-month period was strongly affected by treatment at all three concentrations. Dichlobenil residues were found in fish for as long as analysis was done (up to 189 days after treatment). Fish in the treated ponds had lower hematocrit values (a measure of the number of red blood cells in the blood) than did fish from the untreated pond. In addition, fish from treated ponds developed liver tumors. In bluegills from the pond treated with the highest concentration of dichlobenil, inflamed nodules were found in the kidneys. Dichlobenil also appeared to affect bluegill reproduction; "the greater the amount of dichlobenil added in April, before spawning, the smaller the number of offspring seen in September."[51]

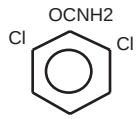
Figure 5
Effect of Dichlobenil on the Growth of a Mycorrhizal Fungi Found on Apple Trees



Source: Hamel, C. 1994. Mycorrhizal colonization increases herbicide toxicity in apple. *J. Amer. Soc. Hort. Sci.* 119(6):1255-1260.

Dichlobenil reduces the growth of beneficial mycorrhizal fungi at concentrations as low as one part per million.

Figure 7
Dichlobenil's Major Metabolite



2,6-dichlorobenzamide

Dichlobenil bioconcentrates in fish by a factor of 40, meaning that the concentration in fish tissue is forty times the concentration in the water in which the fish live.[52]

Farm animals: Tests using dichlobenil-containing products showed that they are acutely toxic to domestic animals. Cattle were poisoned after a single dose equivalent to 50 mg/kg of body weight of dichlobenil, and died after two doses. Sheep were poisoned after 10 drenches with 25 mg/kg of body weight of dichlobenil, lost weight, and died 20 days after the last dose. Chickens died or lost weight after 10 doses of 100 mg/kg.[53]

Effects on domestic animals have also been found in tests using dichlobenil alone. A six-month feeding study with pigs found increased liver weights at a dose of 4 mg/kg of body weight.[35] Similar increases in liver weight were found at all doses tested in a feeding study with chicks, as well as an increase in kidney weights.[54]

Frogs: The nasal lining in frogs is damaged by dichlobenil. Injections of dichlobenil in laboratory frogs resulted in "extensive damage" and a reduction in the frogs' response to odors. The nasal lining recovered three months after treatment, and responses to odors returned.[55]

Aquatic invertebrates: Dichlobenil's acute toxicity to aquatic invertebrates varies widely among species. Sand fleas, water fleas, and stonefly nymphs are particularly susceptible, with LC_{50}s of 1.5 ppm, 3.7 ppm, and 4.4 ppm respectively.[36] Other invertebrates with LC_{50}s of less than 20 ppm include a second species of water flea,[36] a mayfly, an amphipod crustacean, a caddisfly, a midge,[56] seed shrimp, and glass shrimp.[57]

Sublethal effects also occur in aquatic invertebrates. These include a "narcotizing" effect on many invertebrate species, gill irritation in damselflies, immobilization of caddisflies, who also left their nymphal protective cases,[56] and a loss of pigmentation in water boatmen (potentially increasing their risk of predation).[58]

Aquatic invertebrates can also be affected indirectly by dichlobenil. For example, in California, Big Bear Lake's "normally diverse" community of mud-dwelling invertebrates changed following dichlobenil treatment to one that was entirely segmented worms. Researchers suggested that this could have resulted because dichlobenil treatment killed all of the aquatic plants in the area. The invertebrates then had no place to

hide, and were "easy prey for fish."[59] In an experiment in Great Britain, populations of a water flea that clung to aquatic vegetation while feeding declined after dichlobenil treatment. The likely cause was the disappearance of the vegetation; a related species that fed in clear water increased in population.[60]

Effects on Plants

Dichlobenil-containing herbicides are designed to kill plants, and will kill most plants exposed to this herbicide. In addition, there are more complex interactions between desirable plants and dichlobenil. Examples include impacts on mycorrhizal fungi, soil nitrification, and soil microorganisms.

Mycorrhizal fungi: Mycorrhizal fungi are symbiotic fungi that live in or around the roots of higher plants. In apple trees, as with many other plants, mycorrhizal fungi increase the trees' uptake of nutrients, improve their resistance to drought, strengthen their resistance to disease, and increase their growth rate. Recent research shows that mycorrhizal fungi also increase apple trees' susceptibility to dichlobenil. When soil around greenhouse apple trees was treated with 25 ppm of dichlobenil, 20 percent of trees without mycorrhizae died, while all trees with mycorrhizal died. Similar results were found at other herbicide concentrations. In addition, dichlobenil reduces growth of mycorrhizal fungi. Soil concentrations of just 1 ppm reduced growth by almost 50 percent.[61]

Soil nitrification: Nitrogen is an important plant nutrient which must be converted to ammonia and nitrates before it is available for use by plants. The process of creating nitrates is called nitrification and is carried out by a number of soil bacteria.[62] In laboratory tests, dichlobenil inhibits these soil bacteria; reductions in nitrate production from 50 to 85 percent (depending on soil type) were measured when relatively high concentrations of dichlobenil (80-100 ppm) were used.[63,64]

Other soil microorganisms: "Microorganisms are of primary importance in the soil environment in the recycling of key elements essential for biological processes and thus for the maintenance of soil fertility."[63] Therefore, impacts on the populations of these organisms are likely to impact the growth of plants. In laboratory tests, dichlobenil reduced populations of soil bacteria between 22 and 33 percent and populations of soil fungi between 60 and 85 percent (depending on soil type). Dichlobenil was more toxic to soil microorganisms than ten of the eleven other herbicides tested.[63]

Ecosystem Effects

The impacts of dichlobenil in a natural ecosystem are not confined to a single species. Instead, a complex web or interactions ripples through the ecosystem. A good example comes from a British pond treated with dichlobenil. The dominant plant species were killed, and an algae bloom followed. A variety of impacts on insect and other invertebrate populations followed. Populations of a midge declined, mayfly populations were reduced, damselflies became rare, some water beetles disappeared, water boatmen were unaffected, backswimmers increased, and caddisflies became rare.[60]

A pond near Pensacola, Florida showed different, but similar effects. An algae bloom followed dichlobenil treatment, and at least four algae species increased in number. In addition, a copepod and several rotifers increased, but Volvox (a colonial algae) was eliminated.[65]

Breakdown Products

Dichlobenil's major breakdown product in soil is 2,6-dichlorobenzamide. (See Figure 6.) It is highly persistent in soil. In a laboratory test, 90 percent of the 2,6-dichlorobenzamide applied to soil was unchanged six months after application.[66] Similar results have been found in field studies: "toxic quantities" remained in the soil of an apple orchard two years after the last application of dichlobenil,[67] and contamination with 2,6-dichlorobenzamide was measured for five years after a dichlobenil application to an agricultural field.[37] It is "very water-soluble and weakly adsorbed by the soil."[68]

In plants, 2,6-dichlorobenzamide causes chlorosis (yellowing) of leaves, a symptom not caused by dichlobenil.[68] It decreases both the survival and growth of rainbow trout larvae at concentrations above 18 ppm and causes a "clear delay" in one of their developmental stages, resorption of the yolk.[69]

In laboratory rats, feeding 2,6-dichlorobenzamide for 3 months caused a decrease in weight gain and a decreased efficiency of food utilization.[21] Other laboratory studies have shown that it causes rats to lose muscle tone.[36] Like dichlobenil, it damages the lining of the nasal cavity.[70]

"Inert" Ingredients

Like all pesticide products, dichlobenil herbicides contain ingredients that are typically claimed as trade secret by pesticide manufacturers. These ingredients are legally called "inert" ingredients, although they are neither chemically, biologically, or toxicologically inert. Limited information about "inerts" in Casoron products is publicly available. Identified "inert" ingredients include the following:[71,72]

Crystalline silica is a mineral dust found in Casoron 50W, 4G, 2G, and 10G. The International Agency for Research on Cancer (IARC) has classified evidence about silica's ability to cause cancer as "sufficient" in animals and "limited" in humans. In laboratory animals, inhalation of crystalline silica induced significant increases in the incidence of lung cancer. Injections induced lymphomas in the thorax and abdomen. In humans, a number of studies have shown that lung cancer occurs more frequently in workers who are exposed to silica.[73]

Polyvinyl alcohol is a polymer found in Casoron G-4. When injected into rats, it produces tumors in cells that store the polymer, mostly white blood cells involved with gathering up foreign materials.[74] IARC has classified evidence about polyvinyl alcohol's ability to cause cancer as "limited" in animals.[75] Injection in rats also causes hypertension, anemia, kidney hemorrhages, coma, and lesions in various other organs.[76] Inhalation of polyvinyl alcohol dust can cause respiratory tract irritation, and eye irritation can occur if it contacts eyes.[77]

References

1. U.S. EPA. Office of Pesticide Programs. 1987. Pesticide fact sheet: Dichlobenil. Washington, D.C. (Mar. 23.)
2. *Farm Chemicals Handbook '95.* 1995. Willoughby, OH: Meister Publishing Co.
3. Kirkwood, R.C. 1983. The relationship of metabolism studies to the modes of action of herbicides. *Pestic. Sci.* 14: 453-460.
4. Vaughan, M.A. and K.C. Vaughn. 1988. Mitotic disrupters from higher plants and their potential uses as herbicides. *Weed Technol.* 2:533-539.
5. Cremlyn, R.J. 1991. *Agrochemicals: Preparation and mode of action.* Chichester, UK: John Wiley & Sons.
6. Moreland, D.E., G.G. Hussey, and F.S. Farmer.

1974. Comparative effects of dichlobenil and its phenolic alteration products on photo- and oxidative phosphorylation. *Pestic. Biochem. Physiol.* 4:356-364.
7. U.S. EPA. Office of Pesticides. Health Effects Division. TB-1. 1994. Tox oneliners: Dichlobenil. Washington, D.C. June 13.
8. Brandt, I. et al. 1990. Irreversible binding and toxicity of the herbicide dichlobenil (2,6-dichlorobenzonitrile) in the olfactory mucosa of mice. *Toxicol. Appl. Pharm.* 103:491-501.
9. Brittebo, E.B. 1993. Metabolism of xenobiotics in the nasal olfactory mucosa: Implications for local toxicity. *Pharmacol. Toxicol.* 72 (Suppl. 3):50-52.
10. Genter, M.B. et al. 1996. Characterization of olfactory deficits in the rat following administration of 2,6-dichlorobenzonitrile (dichlobenil), 3,3'-iminodipropionitrile or methimazole. *Fund. Appl. Toxicol.* 29:71-77.
11. Brittebo, E.B. and C. Eriksson. 1995. Taurine in the olfactory system: effects of the olfactory toxicant dichlobenil. *NeuroToxicol.* 16(2):271-280.
12. Ding, X. 1996. Metabolic activation of 2,6-dichlorobenzonitrile, an olfactory specific toxicant by rat, rabbit, and human cytochrome P450. *Mol. Pharmacol.* 49:1113-1121.
13. Deamer, N.J., J.P. O'Callahan, and M.B. Genter. 1994. Olfactory toxicity resulting from dermal application of 2,6-dichlorobenzonitrile (dichlobenil) in the C57B1 mouse. *NeuroToxicol.* 15(2):287-294.
14. U.S. EPA. 1986. Data evaluation report: primary eye irritation - rabbits. Dichlobenil. Reviewed by M.P. Copley and J. Harris, Toxicology Branch. Washington, D.C. (May 7.)
15. Chas. H. Lilly Co. 1992. Material safety data sheet: Casoron Granules. Portland, OR. (Oct.).
16. PBI/Gordon Corp. 1996. Material safety data sheet: Norosac 4G. Kansas City, MO. (Sept.)
17. PBI/Gordon Corp. 1993. Material safety data sheet: Dyclomec 4G. Kansas City, MO. (Nov.)
18. PBI/Gordon Corp. 1996. Material safety data sheet: Barrier 50W. Kansas City, MO. (Dec.)
19. Deeken, J.H. 1974. Chloracne induced by 2,6-dichlorobenzonitrile. *Arch. Dermatol.* 109:245-246.
20. U.S. EPA. Office of Research and Development. 1994. Health assessment document for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and related compounds. Vol.1. Review draft. Washington, D.C.
21. U.S. EPA. Office of Pesticides and Toxic Substances. 1987. Guidance for the reregistration of products containing dichlobenil as the active ingredient. Washington, D.C. (March.)
22. U.S. EPA. Office of Prevention, Pesticides and Toxic Substances. 1995. Carcinogenicity peer review meeting on dichlobenil (2nd). Memo from E. Rinde, Health Effects Division. Washington, D.C. (Feb. 21).
23. Uniroyal Chemical Co. 1996. Material safety data sheet: Casoron 50W. Middlebury, CT. (June.)
24. U.S. EPA. 1986. Data evaluation report: teratology (gavage) - rat. Dichlobenil. Reviewed by M.P. Copley and J. Harris, Toxicology Branch. Washington, D.C. (July 23.)
25. U.S. EPA. 1997. Office of Pesticide Programs list of chemicals evaluated for carcinogenic potential. Memo from W.L. Burnam, Health Effects Division. Washington, D.C. (Feb. 19.)
26. Donna, A. et al. 1991. A one-year carcinogenicity study with 2,6-dichlorobenzonitrile (dichlobenil) in male Swiss mice: Preliminary note. *Cancer Det. Prev.* 15(1):41-44.
27. U.S. Food and Drug Administration (FDA). 1991. Residues in foods 1990. *J. Assoc. Off. Anal. Chem.* 74 (Sept./Oct.).
28. U.S. FDA. 1992. Residue monitoring 1991. *J. AOAC Int.* 75 (Sept./Oct.).
29. U.S. FDA. 1993. Residue monitoring 1992. *J. AOAC Int.* 76 (Sept./Oct.).
30. U.S. FDA. 1994. Residue monitoring 1993. *J. AOAC Int.* 77 (Sept./Oct.).
31. U.S. FDA. 1995. Residue monitoring 1994. *J. AOAC Int.* 78 (Sept./Oct.).
32. U.S. FDA. 1996. Residue monitoring 1995. *J. AOAC Int.* 79 (Sept./Oct.).
33. Clay, D.V. and C.E. McKone. 1979. Effects of repeated applications at high rates of chlorthiamid and dichlobenil to blackcurrants. *Pestic. Sci.* 10:429-437.
34. Richards, M. 1968. Dichlobenil and chlorthiamid: A review. *NZ Weed Pest Contr. Conf. Proc.* 21:82-86.
35. Gangstad, E.O. and R.A. Stanley. 1987. Technical review of the factors affecting aquatic use of dichlobenil. Chap. 10. *In* Gangstad, E.O. and R.A. Stanley (eds.) *Environmental management of water projects.* Boca Raton FL: CRC Press. Pp. 117-122.
36. Labat-Anderson, Inc. 1992. Dichlobenil herbicide background statement. Prepared for Bonneville Power Administration. Arlington, VA. (May 15.)
37. Williams, J.H. and D.J. Eagle. 1979. Persistence of dichlobenil in a sandy soil and effects of residues on plant growth. *Weed Res.*19:315-319.
38. Cope, O.B., J.P. McCraren, and L. Eller. 1969. Effects of dichlobenil on two fishpond environments. *Weed Sci.* 17(2):158-165.
39. Ogg, A.G. 1972. Residues in ponds treated with two formulations of dichlobenil. *Pestic. Monitoring J.* 5(4): 356-359.
40. Rice, C.P., H.C. Sikka, and R.S. Lynch. 1974. Persistence of dichlobenil in a farm pond. *J. Agr. Food Chem.* 22(3):533-535.
41. Eades, J.F. 1992. A note on persistence of the herbicide dichlobenil in groundwater. *Irish. J. Agricul. Food Res.* 31:81-83.
42. Uniroyal Chemical Co., Inc. 1996. Casoron 2G label. Middlebury, CT.
43. Davis, D. and A. Johnson. 1994. Washington state pesticide monitoring program: 1993 surface water sampling report. Washington State Dept. of Ecology. Environmental Investigations and Laboratory Services Program. Olympia WA. (Oct.)
44. U.S. Dept. of the Interior. U.S. Geological Survey. 1995. Analytical data from phases I and II of the Willamette River Basin water quality study, 1992-1994. Portland, OR.
45. Lagas, P., B. Verdam, and J.P.G. Loch. 1989. Threat to groundwater quality by pesticides in The Netherlands. *In Groundwater management: Quantity and quality* (Proceedings of the Benidorm Symposium, Oct. 1989). IAHS Publ. No. 188.
46. Trevisan, M. et al. 1993. Pesticides in rainfall and air in Italy. *Environ. Pollut.* 80:31-39.
47. Howard, P.H. 1991. *Handbook of environmental fate and exposure data for organic chemicals.* Vol. III. Pesticides. Chelsea MI: Lewis Publishers. Pp.240-245.
48. Miyazaki, S., H.C. Sikka, and R.S. Lynch. 1975. Metabolism of dichlobenil by microorganisms in the aquatic environment. *J. Agric. Food Chem.* 23(3): 365-368.
49. Parochetti, J.V., E.R. Hein, and S.R. Colby. 1971. Volatility of dichlobenil. *Weed Sci.* 19(1):28-31.
50. Verloop, A. and W.B. Nimmo. 1974. Absorption, translocation and metabolism of dichlobenil in bean seedlings. *Weed Res.* 9:375-370.
51. Cope, O.B., J.P. McCraren, and L. Eller. 1969. Effects of dichlobenil on two fishpond environments. *Weed Sci.* 17(2):158-165.
52. Freitag, D. et al. 1985. Environmental hazard profile of organic chemicals. *Chemosphere* 14(10):1589-1616.
53. U.S. Dept. of Agriculture. Agricultural Research Service. 1969. The toxicity of some organic herbicides to cattle, sheep, and chickens. Production Research Report No. 106. Washington, D.C. (May.)
54. Davison, K.L. and J.E. Bakke. 1988. Intermediary metabolism of 2,6-dichlorobenzonitrile (dichlobenil) in chickens and growth of chickens fed dichlobenil. *Xenobiotica* 18(8):941-948.
55. Delaleu, J.-C., and G. Sicard. 1995. Physiological and histological recovery of the olfactory mucosa of the frog after a dichlobenil injection. *Chem. Senses* 20:433-440.
56. Wilson, D.C. 1967. The effects of the herbicides diquat and dichlobenil on pond invertebrates. MS thesis. Corvallis, OR: Oregon State University. (Nov. 27.)
57. Sanders, H.O. 1970. Toxicities of some herbicides to six species of freshwater crustaceans. *J. Water Pollut. Cont. Federation* (Aug., Pt.1):1547.
58. Tooby, T.E. and D.J. Macey. 1977. Absence of pigmentation in corixid bugs (Hemiptera) after the use of the aquatic herbicide dichlobenil. *Freshwater Biol.* 7:519-525.
59. Siegfried, C.A. 1984. The benthos of a eutrophic mountain reservoir: influence of reservoir level on community composition, abundance, and production. *Calif. Fish Game* 70(1):39-52.
60. Newbold, C. 1975. Herbicides in aquatic systems. *Biol. Conserv.* 7:97-118.
61. Hamel, C. et al. 1994. Mycorrhizal colonization increases herbicide toxicity in apple. *J. Amer. Soc. Hort. Sci.* 119(6):1255-1260.
62. Cook, K.A. and M.P. Greaves. 1987. Natural variability in microbial activities. Ch. 2 in Somerville, L. and M.P. Greaves (eds.) *Pesticide effects on soil microflora.* London, UK: Taylor and Francis. Pp.15-43.
63. Bakalivanov, D. and O. Kostov. 1981. Soil microbiological assessment of toxicity of alkanoate, amide and other herbicides. *Acta Microbiol. Acad. Sci. Hung.* 28:141-146.
64. Helweg, A. 1972. I. Persistence of chlorthiamid in soil. II. Influence of chlorthiamid and dichlobenil on CO_2-liberation, ammonification and nitrification in soil. (In German). *Tidsskvifr for Planteavl* 76(2):145-155.
65. Walsh, G.E. and Heitmuller, P.T. 1969. Effects of dichlobenil upon physical, chemical, and biological factors in a freshwater pond. *Abstr. Meet. Weed. Sci. Soc. Am., Weed Abstr.* 20(5):372.
66. Verloop, A. and W.B. Nimmo. 1970. Metabolism of dichlobenil in sandy soil. *Weed Res.* 10:65-70.
67. Khan, S.U. and S.R. Miller. 1982. Effects of repeated application of dichlobenil in a commercial apple orchard. *J. Agric. Food Chem.* 30:1246-1248.
68. Leach, R.W.A. and N.L. Biddington. 1971. A side effect of chlorthiamid and dichlobenil herbicides. *Ann. Appl. Biol.* 67:137-144.
69. Van Leeuwen, C.J. and H. Maas. 1985. The aquatic toxicity of 2,6-dichlorobenzamide (BAM), a degradation product of the herbicide dichlobenil. *Environ. Pollut.* (Ser. A) 37:105-115.
70. Brittebo, E.B. et al. 1991. Toxicity of 2,6-dichlorothiobenzamide (chlorthiamid) and 2,6-dichlorobenzamide in the olfactory nasal mucosa of mice. *Fund. Appl. Toxicol.* 17: 92-102.
71. Letter from Calvin Furlow, U.S. EPA Office of Pesticide Programs, Public Response and Program Resources Branch. Feb. 13, 1997.
72. Letter from Calvin Furlow, U.S. EPA Office of Pesticide Programs, Public Response and Program Resources Branch. Jan. 29, 1997.
73. U.S. Dept. of Health and Human Services. Public Health Service. 1994. *Seventh annual report on carcinogens.* Summary.
74. Hueper, W.C. 1959. Carcinogenic studies on water-soluble and insoluble macromolecules. *A.M.A. Arch. Pathol.* 67:589-617. (Abstract.)
75. NTP Chemical Repository (Radian Corporation, August 29, 1991). Poly (vinyl alcohol). gopher://gopher.chem.utah:70/00/MSDS/P/POLY%28VINYL%20ALCOHOL%29.
76. Hall, C.E. and O. Hall. 1963. Eclampsialike syndrome in rats treated with poly(vinyl alcohol) (PVA). *Texas Rept. Biol. Med.* 21:16-27. (Abstract.)
77. MSDS for poly(vinyl alcohol). http://ntp-db.niehs.nih.gov/NTP_Reports/NTP_Chem_H&S/NTP_Chem9/Radian9002-89-5.txt