● HERBICIDE FACTSHEET

IMAZAPYR

Imazapyr is a broad-spectrum herbicide in the imidazolinone family. Its primary uses in the U.S. are for vegetation control in forests and rights-of-way.

Imazapyr is corrosive to eyes and can cause irreversible damage. Imazapyr-containing herbicides are irritating to both eyes and skin.

Adverse effects found in laboratory animals after chronic exposure to imazapyr include the following: fluid accumulation in the lungs of female mice, kidney cysts in male mice, abnormal blood formation in the spleen of female rats, an increase in the number of brain and thyroid cancers in male rats, and an increase in the number of tumors and cancers of the adrenal gland in female rats.

Imazapyr can persist in soil for over a year. Persistence studies suggest that imazapyr residues damage plants at concentrations that are not detectable by laboratory analysis.

Imazapyr moves readily in soil. It has contaminated surface and ground water following aerial and ground forestry applications.

Small amounts of imazapyr (as little as 1/50 of a typical application rate) can damage crop plants. Imazapyr exposure also has the potential to seriously impact rare plant species. The U.S. Fish and Wildlife Service has identified 100 counties in 24 states east of the Mississippi River where endangered species may be jeopardized by use of imazapyr.

Over a half-dozen weedy plant species have developed resistance to imazapyr.

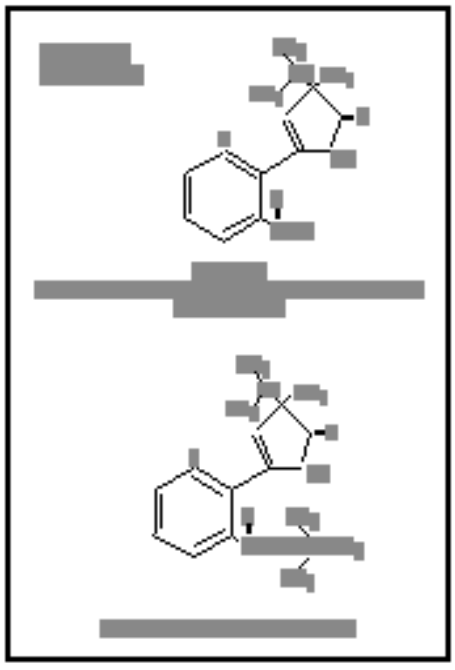
BY CAROLINE COX

Imazapyr (see Figure 1) is a broad-spectrum imidazolinone herbicide used to kill unwanted plants in industrial sites, coniferous forests, railroad rights-of-way, rubber plantations, oil palm plantations, and sugarcane.[1] Commercial products use the isopropylamine salt of imazapyr.[2]

Imazapyr is manufactured by American Cyanamid Co. and sold under the trade names Arsenal, Chopper, and Assault. It was first registered in the United States in 1984.[1]

Mode of Action

Like all members of the imidazolinone family of herbicides, imazapyr kills plants by inhibiting the first enzyme used when plants synthesize branched chain amino acids (valine, leucine, and isoleucine). The name of this enzyme is acetohydroxyacid synthase.[1] (This enzyme is also known as acetolactase synthase.) Amino acids are the building blocks from which living organisms make proteins. The enzymes needed to synthesize the branched chain amino acids are not present in animals, who must obtain these amino acids by eating them.[3] Another class of herbicides, the sulfonylureas, has a similar mode of action.



Within a few hours after treatment with imazapyr, synthesis of DNA (genetic material)[4] and cell division stops. Next plant growth stops, first in the roots and then in growing portions of the above ground plant. This is presumably because of the lack of necessary amino acids.[1] Complete death of the plant occurs slowly, taking as long as a month after treatment.[1]

Acute Toxicity

The amount of imazapyr required to kill mammals by oral ingestion, exposure through the skin, or inhalation is relatively large. In most of the laboratory studies submitted to the U.S. Environmental Protection Agency (EPA) in support of imazapyr's registration, few or no deaths occurred even

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at maximum doses.[5] However, effects other than death have been observed in tests of imazapyr's acute toxicity. Bleeding and congested lungs were observed in rabbits dermally exposed to imazapyr and in rats inhaling Arsenal Railroad Applicators Concentrate or Arsenal Herbicide Applicators Concentrate.[6,7,8] Congestion of the kidney, liver, and intestine was also observed in laboratory tests.[8]

Eye irritation

Imazapyr is "corrosive" to the eyes and "causes irreversible eye damage."[8] Imazapyr-containing products are also irritating to the eyes: Arsenal Herbicide Railroad Applicators Concentrate caused eye irritation which subsided by 24 hours post-treatment,[9] and Arsenal caused eye irritation which subsided by 72 hours post-treatment.[8]

Skin irritation

Arsenal caused reddening, scaling, and crusting of treated skin at all doses tested in rabbits dermally exposed over a 21 day period.[10] With a single exposure, Arsenal and Arsenal Herbicide Railroad Applicators Concentrate caused swelling and redness, or just redness depending on whether or not the skin was abraded.[6,8]

Subchronic Toxicity

Oral administration of imazapyr to female rabbits over a 12 day period caused stomach ulcers and intestinal lesions at most doses tested.[10]

Chronic Toxicity

Laboratory studies in which mice were fed imazapyr for two years found the following chronic effects: fluid accumulation in the air sacs of the lungs in females; an increased incidence of congestion of the brain in females; and an increased incidence of kidney cysts in males.[11] In a two year feeding study with female rats, different symptoms were observed: an increase in abnormal blood formation in the spleen; an increase of blood pooling in the liver; an increase in thyroid cysts;[12] and a decrease in food efficiency (the ability to transform ingested food into body weight gain).[13] Most of these effects were not considered significant by EPA.[5]

There are no publicly available data concerning chronic effects of imazapyr-containing products.

Reproductive Effects

In a review of imazapyr toxicity concluded in 1992, the U.S. Forest Service and two other federal agencies concluded that "the potential for causing adverse effects on fertility or reproduction has not been determined at this time."[14] This is the most recent publicly available information. There are no publicly available data regarding the reproductive hazards posed by imazapyr-containing products.

Carcinogenicity

EPA has evaluated the potential of imazapyr to cause cancer and placed it in Class E, "evidence of noncarcinogenicity."[15] However, it is important to look at the data produced by the two-year feeding studies of both rats and mice on which this evaluation was based. The study using rats indicated the following carcinogenicity concerns: an increase in the number of brain tumors in male rats, an increase in the number of thyroid tumors and cancers in male rats, and an increase in the number of tumors and cancers of the adrenal glands in female rats.[12] EPA found that the frequency of thyroid and adrenal gland tumors and cancers did not increase above the levels found in other studies done by the same laboratory.[12] With respect to the brain tumors, American Cyanamid reanalyzed tissues from the original study. They discovered an additional tumor in the high-dose group, as well as an additional tumor in the untreated (control) group. EPA found that with the addition of the new data the increased incidence of brain tumors was no longer statistically significant.[5]

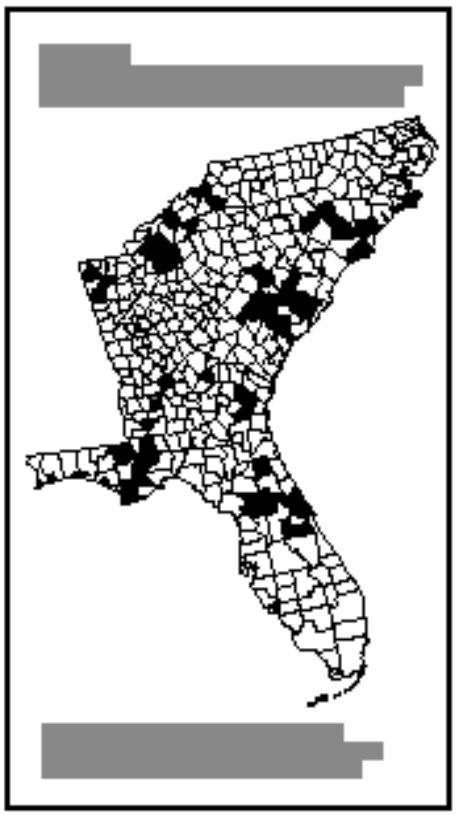
There is no publicly available data considering the carcinogenicity of imazapyr-containing products.

Effects on Nontarget Plants

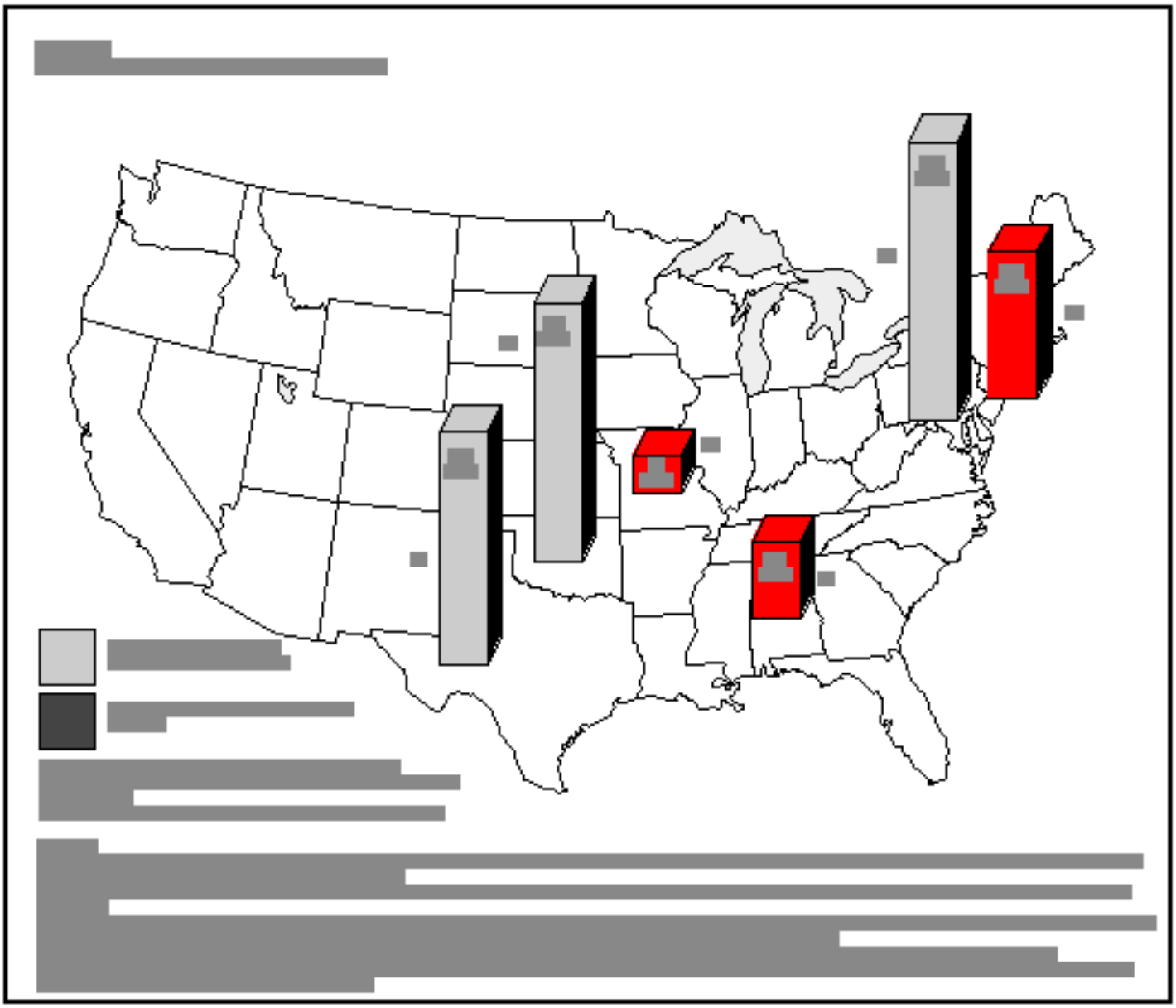
Like all broad spectrum herbicides, imazapyr efficiently kills most plants with which it comes in contact, even those not intended as targets of the herbicide. In addition to this acute toxicity to plants, a variety of other impacts have been reported in nontarget plants exposed to imazapyr. These include hazards to endangered species, increased susceptibility to disease, and disruption of nutrient cycling in soil.

Endangered species: Rare plants are particularly at risk from herbicide exposure because the loss of a few individuals can have significant consequences for a small population. EPA states that "a number of terrestrial and aquatic plant species are listed as being at jeopardy from the use of herbicides and that "jeopardy will also occur from the used of Arsenal."[16] The Fish and Wildlife Service has identified 100 counties in 24 states where endangered species could be at risk from forestry use of Arsenal. (See Figure 2 for a map of these counties in the southeastern U.S.) No such analysis for western states is publicly available.

Plant disease: When used in combination with the herbicide diuron, imazapyr



Counties containing endangered species that could be jeopardized by use of imazapyr. Similar information is available for most states east of the Mississippi River.



imazapyr in soil damaged plants for longer than it is detectable through laboratory analysis. This difference is much greater than geographical differences in persistence.

increased the severity of the fungal leaf disease *Tubakia dryina* on water oak (*Quercus nigra*). The disease resulted in a significant decrease in stem growth when trees were exposed to the herbicides.[17]

Nutrient cycling: Decomposition of plant material (cellulose) is an important component of cycling nutrients through an ecosystem. Imazapyr can disrupt this cycling. In laboratory tests, imazapyr treatment of soil slowed decomposition of cellulose, and decreased the activity of an enzyme used by soil microbes to break down cellulose.[18]

Effects on Animals

According to three federal agencies, imazapyr's acute oral toxicity to birds, fish, and water fleas is low.[14] No studies have been conducted on imazapyr's chronic toxicity to any of these animals,[14] although a related herbicide (imazamethabenz-methyl) has high chronic toxicity to fish, with effects occurring at concentrations of less than 1 part per million.[19] In addition, there are no studies about the chronic toxicity of imazapyr-containing products.[14]

Persistence in Soil

Overall, imazapyr is a persistent herbicide. Persistence in field studies varies from 60[20] to 436 days,[21] with many studies reporting persistence of over a year.[21-23] (See Figure 3.) These are minimum estimates of persistence because imazapyr persisted, in most cases, until the last date tested.

Soil persistence of imazapyr, as with any

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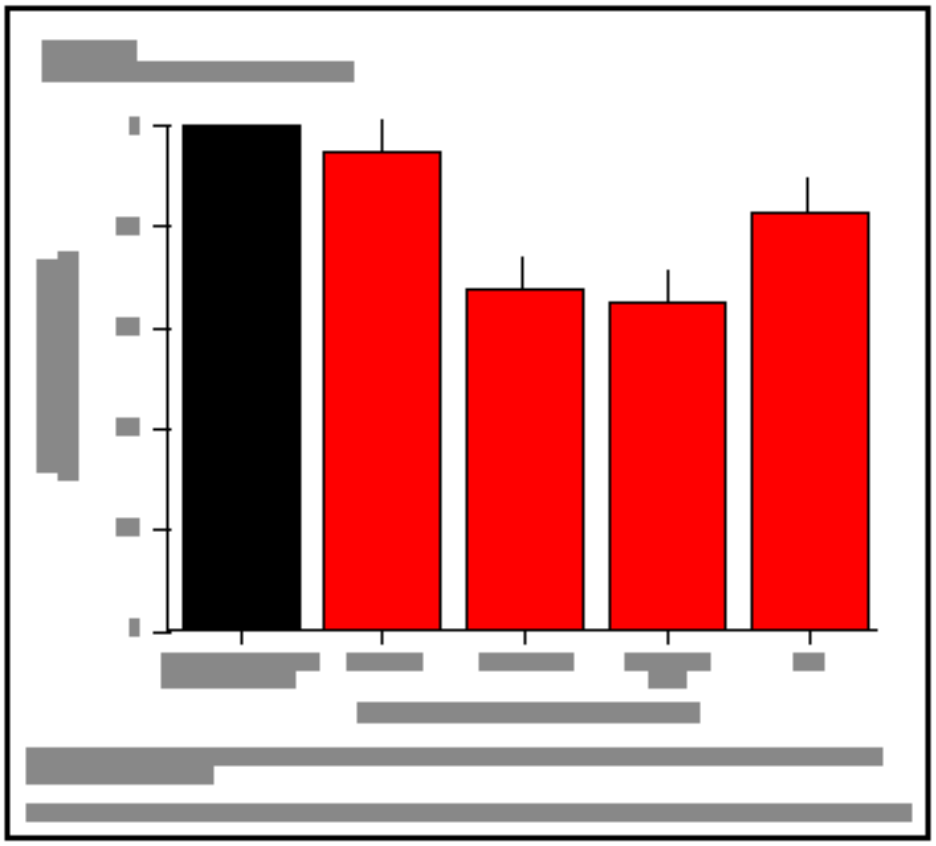

Imazapyr is mobile in most soil types, and almost as mobile as water in clay and clay loam.

pesticide, varies depending on climate, weather, soil type, and other factors. However, in the case of imazapyr, the most important factor appears to be the method used to detect imazapyr. The persistence studies measure the length of time between imazapyr application and the last detection of imazapyr residues by laboratory analysis or the last observation of imazapyr-caused plant injury. All of the studies using plant injury show longer persistence[21-23] than those that depend on laboratory analysis.[21,24,25] This suggests that imazapyr can cause plant damage at levels too low to detect by standard laboratory procedures. This problem has also been observed in another class of herbicides, the sulfonylureas, with the same mode of action as imazapyr.[26]

A common measure of persistence is half-life, the length of time required for half of the amount of a pesticide originally applied to break down or move away. EPA reports that imazapyr's half-life is 17 months in laboratory tests.[27] Half-lives ranging from 21 days to 49 months have been reported in field studies.[20,28] Consistent with the studies measuring persistence, the longest half-lives are reported in the studies that use plant injury to detect imazapyr.[28]

Water Contamination

Several of imazapyr's chemical characteristics mean that it is mobile in soil and thus likely to contaminate water. Researchers in Alabama found that it was more mobile in soil than the widespread water contaminant atrazine.[29] In this study it was nearly as mobile as water in some soil types. (See Fig. 4.) EPA found that it has a "moderate potential for sorption"[30] (ability to attach to the surface of soil particles) but a "high potential for desorption,"[30] when it would then be able to contaminate nearby water. One field study found that between 40 and 70 percent of applied imazapyr leached down to the lowest depth tested (45 cm).[28] Another study found that "significant" residues of imazapyr leached to a depth of between 1.5 and 3 meters (4.9 - 9.9 feet) depending on application rate.[31]

Little monitoring of imazapyr contamination of water has been done. However, the studies that have been conducted show that imazapyr does contaminate water.

In the southeastern U.S., imazapyr was found in surface water following aerial application at both of the two forestry sites for which data are publicly available. Management practices to reduce water contamination were employed at one of the sites.[32] Imazapyr was also found in groundwater following a forestry application using ground equipment in the only published study that tested for groundwater contamination.[33] In the Pacific Northwest, imazapyr was found in surface water in one out of the two sites monitored by the Washington Dept. of Ecology following aerial forestry applications. Again, management practices were used to reduce water contamination.[34]

Ozone degradation, a treatment used to remove pesticides from drinking water is not successful with imazapyr, removing only about half the imazapyr present.[34]

Drift

Imazapyr is a potent herbicide, so it is not surprising that drift of small amounts can severely damage valuable plants. For example, a study of the effect of simulated drift on yield and quality of potatoes found that amounts of imazapyr as small as 1/50 of the normal agricultural rate reduced potato yields to as little as one-third of unexposed plants. Yield of high quality (U.S. #1) potatoes decreased by 99 percent because folded, multiknobbed, and cracked potatoes were common.[36]

There are no publicly available data about the distance that imazapyr can drift.

Resistance

Resistance to imazapyr, the ability to tolerate amounts that typically would be lethal, has developed in a number of weed species from around the world. In general this resistance has not been observed following use of imazapyr. Instead, use of other herbicides with the same mode of action (primarily the sulfonylurea herbicides) has resulted in the development of cross-resistance, when resistance to one herbicide confers resistance to others. Species in which

resistance to imazapyr has been confirmed include rigid ryegrass (*Lolium rigidum*),[37] kochia (*Kochia scoparia*),[38] common chickweed (*Stellaria media*), Russian thistle (*Salsola iberica*), perennial ryegrass (*Lolium perenne*),[39] *Sonchus oleraceus*,[40] and *Arabidopsis thaliana*,[41] In addition, resistance has developed in an algae species, *Chlorella emersonii*.[42]

Plants that are resistant to imazapyr generally have a different form of the enzyme acetolactase synthase than susceptible plants. The resistant form of the enzyme is not as susceptible to inhibition by imazapyr as the susceptible form.[40,43] In at least one case, the resistant form of the enzyme is caused by a single point mutation.[41]

"Inert" Ingredients

Ingredients comprising about 47 percent of Arsenal Applicators Concentrate, the most common imazapyr-containing herbicide, are identified only as "inerts" by Arsenal's manufacturer.[44] There is no publicly available information about the identity of these ingredients. Most of EPA's hazard assessment of Arsenal is based on tests of imazapyr only and not on tests of all the ingredients.

Breakdown Products

There are two primary breakdown products of imazapyr when it is exposed to light.[45] One of them, quinolinic acid, is also a primary breakdown product in soil.[46] It is irritating to eyes, the respiratory system, and skin.[47] It is also a neurotoxin, causing nerve lesions and symptoms similar to Huntington's disease.[48]

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