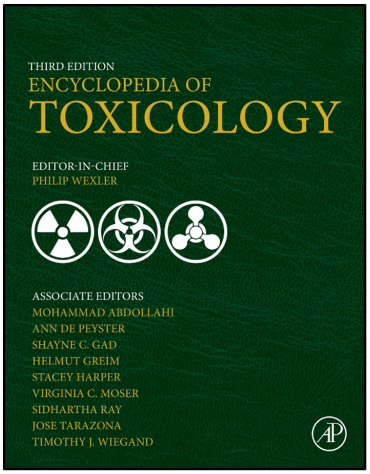

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Sulfuryl Fluoride (Vikane)

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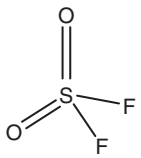
- Name: Sulfuryl fluoride (Vikane)
- Chemical Abstracts Service Registry Number: 002699-79-8
- Synonyms: Sulfonyl fluoride, Sulfur dioxide difluoride, Sulfuryl difluoride, Sulfuric oxyfluoride, Vikane
- Chemical/Pharmaceutical/Other Class: Inorganic fumigant
- Molecular Formula: SO_2F_2
- Molecular Mass: 102.06 g mol^{-1}
- Chemical Structure:



Background

Sulfuryl fluoride (Vikane) is an odorless gas and was first registered as insecticide and rodenticide in 1959. It was developed by Dow Chemical in the 1950s to control drywood termites typically found in warm climates. The chemical is in a gas state at atmospheric pressure; however, it is sold as a pressurized liquefied gas. For dispersal into a room or chamber, the liquid is released through an application hose toward a distribution fan, where volatilization occurs rapidly after its release.

It has a low solubility in water, and hydrolyzes slowly in it but rapidly in basic solution. Upon contact with water, it hydrolyzes to fluorosulfonic and fluoride ions, and further to sulfuric acid and hydrogen fluoride, according to the reaction:

$$SO_2F_2 + 2OH^- \rightarrow SO_3F^- + F^- + H_2O$$

Sulfuryl fluoride is nonflammable, nonexplodable, and stable to store in steel cylinder for up to 6 years. However, it decomposes when exposed to high temperature (>400 °C) to form a toxic, reactive gas consisting of hydrofluoric acid and sulfur dioxide.

A registration standard for sulfuryl fluoride was issued by the US Environmental Protection Agency (EPA) in June 1985 to ensure that proper use of the pesticide poses no unreasonable effect to human health and the environment.

Occurrence

Sulfuryl fluoride is prepared by direct reaction of fluorine gas (F_2) with sulfur dioxide gas (SO_2). It is primarily prepared by Dow as a fumigant, and, thus, the primary source of Vikane® in the environment. It does not remain inside the room after fumigation and completely dissipates without leaving any surface residues.

Uses

Sulfuryl fluoride is introduced into structures as a gas intended to fill all air spaces in the enclosed area and penetrate cracks, crevices, and pores in the wood. It penetrates materials quickly and rapidly dissipates during the ventilation process. It has been widely used as a fumigant to kill both the eggs and the adults of insects such as cockroaches, termites, beetles, moths, and flies after exposure of 16–22 h with the concentration ranged from 0.5 to 3.5 and 5–77 g m^{-3} for LD_{95} for adults and eggs, respectively. It also has been successfully used on post-embryonic forms of fleas, rodents, ants, bees, wasps, spiders, millipedes, bedbugs, silverfish, springtails, earwigs, fire- brats, book lice, and brown dog ticks. To be effective, sulfuryl fluoride must be contained for a sufficient period of time; therefore, workers usually place a tent around the structure during the fumigation.

Environmental Fate and Behavior

Sulfuryl fluoride is slowly hydrolyzed in water under neutral conditions. However, under alkaline conditions, it undergoes rapid hydrolysis. There are no available data addressing the fate of sulfuryl fluoride in soil and biota. The data were not required for reregistration due its chemical properties and strict indoor uses. Sulfuryl fluoride is dissipated into the atmosphere in the gaseous state following application and aeration of treated structures. Once present, it may be transformed and then removed through photolysis and/or reactions with atmospheric radicals ($\cdot OH$ and NO_3) or ozone (O_3). Researchers believed that the atmospheric lifetime of sulfuryl fluoride is 30–40 years. Further, it has significant potential contribution to global warming even though its potential extent is uncertain. There would only be little likelihood that residues would leach to groundwater due to its volatility, thus, making groundwater contamination unlikely. In summary, little or no data on sulfuryl fluoride's environmental and atmospheric loss processes are available.

Toxicokinetics

The toxicokinetics of human sulfuryl fluoride poisoning have not been well described. However, it was found out that sulfuryl fluoride breaks down to fluoride and sulfate inside the insect's body. Fluoride, the primary toxin, interferes with the metabolism of stored fats and carbohydrates that the insect needs to maintain a sufficient source of energy by disrupting glycolysis and citric acid cycle. The insect then uses protein

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and amino acids as alternative sources of energy; however, the metabolic rate fails to increase sufficiently, and consequently the insect dies. Mortality may not occur for several days. Moreover, termites exposed to nonlethal dose of sulfuryl fluoride excrete inorganic sulfate, suggesting release of fluoride.

Mechanism of Toxicity

Sulfuryl fluoride has a complex mode of action even though the mechanism of toxicity is not understood. It is thought to be toxic primarily through the action of the fluoride ion, which it contains. It inhibits oxygen uptake, disturbs the normal phosphate balance, and inhibits hydrolysis of fatty acids. The fluoride ion in sulfuryl fluoride is thought to bind to calcium as well as potassium and magnesium (leading to spasms and seizures). Sulfuryl fluoride is also known to inhibit enzymes such as enolases and ATPase, which require a magnesium ion for their normal function, thus preventing stored fats from being utilized and insufficient energy for survival.

Acute and Short-Term Toxicity or Exposure

Animal

Sulfuryl fluoride gas administered via inhalation in rats and mice was found to have low to moderate toxicity. The 4 h LC_{50} was calculated to be about 500 ppm. In 14 day studies of exposure by inhalation, the lowest no observed adverse effect concentration (NOAEC) was 30 ppm in mice based on brain vacuolation, while the NOAEC in dogs was 100 ppm based on tremors and tetany. In 90 day studies in mice and in rabbits, the NOAEC was found to be 30 ppm and the lowest observed adverse effect concentration was 100 ppm on the basis of vacuolation in the brain. Sulfuryl fluoride was found to be moderately acutely toxic when administered by the oral route. Whole-body (excluding head) exposure has not been indicated with any significant toxicity after exposure via the dermal route. In a 1 year study of dogs exposed by inhalation, the NOAEC was 80 ppm on the basis of deaths and general toxicity (including brain vacuolation) at 150 ppm. Principal effects of long-term exposure in both sexes of rats by inhalation were reduced survival, brain vacuolation, chronic progressive glomerular nephrosis, and associated lesions such as fibrous osteodystrophy exposed at 80 ppm.

Human

There were no tests reported for skin and eye irritation nor studies of skin sensitization conducted. Mechanistic studies on 'time to acute incapacitation' have revealed an approximately linear relationship between concentration and duration of exposure. Upon inhalation of sulfuryl fluoride vapor, humans have developed pulmonary edema of delayed onset. Fatalities were reported during the fumigation process, or when sulfuryl fluoride was not dissipated to appropriate levels prior to reentry.

Chronic Toxicity or Exposure

Animal

In subchronic inhalation studies, rats and rabbits exposed to sulfuryl fluoride for 6 h a day for 90 days at concentrations of 0, 30, 100, or 300 ppm showed decreased body weights, mottled teeth, and injuries to the brain, nervous system, liver, kidneys, lungs, and nasal tissues at 100 and 300 ppm of sulfuryl fluoride.

In another study, the inhalation toxicity of sulfuryl fluoride was evaluated in rats and rabbits. In 2 week exposure preliminary studies conducted for 6 h day^{-1}, 5 days $week^{-1}$, at 0–600 ppm of sulfuryl fluoride, death of rats was observed at 600 ppm. All rats exposed at 600 ppm had extensive kidney lesions and those exposed at 300 ppm had minimal renal changes. Rabbits exposed at 300 or 600 ppm for 2 weeks resulted in vacuolation and/or malacia in the cerebrum with moderate inflammation of nasal tissues. Both rats and rabbits exposed at 0–300 ppm for 13 weeks also had vacuolation and/or malacia while rats exposed at 300 ppm had mottled incisor teeth, minimal renal effects, pulmonary histiocytosis, inflammation of nasal tissues, and cerebral vacuolation. Repeated exposure of rats and rabbits at 100–600 ppm resulted in the toxicity of the kidneys (rats only), brain, and respiratory system; no effects were detected in animals exposed at 30 ppm for 13 weeks.

Dogs exposed to sulfuryl fluoride for 6 h a day for 90 days with concentrations of 0, 30, 100, or 200 ppm resulted in a no observable effect level of 100 ppm. At 200 ppm (5.0 mg kg^{-1} day^{-1}), dogs have decreased body weight and body weight gain.

Human

Whole-body exposures and experience in humans over a period of 40 years of use indicated that sulfuryl fluoride is not a significant irritant, nor a skin sensitizer. Symptoms of sulfuryl fluoride poisoning include nose, eye, throat, and respiratory irritation, shortness of breath, numbness, weakness, nausea, abdominal pain, and slowed speech or movements. Sulfuryl fluoride is also identified as a central nervous system depressant, and repeated exposures to high concentrations of sulfuryl fluoride was found to cause lung and kidney damage.

In Vitro Toxicity Data

The effects of sulfuryl fluoride exposure in a 10-day-old *Ceratocystis fagacearum* at concentrations of 16, 40, 60, 80, and 120 g m^{-3} were investigated for 24 and 48 h. Cultures exposed to 80 g m^{-3} for 48 h and 120 g m^{-3} for 24 h were unable to grow, and staining confirmed that both mycelia and conidia were nonviable.

Reproductive and Developmental Toxicity

In a two-generation reproductive study on rats, sulfuryl fluoride administered through inhalation had no effect on reproductive

parameters when inhaled at concentrations of up to 150 ppm for 6 h day^{-1}, 5–7 days a week for up to 20 consecutive weeks. Based on an increased incidence of aggregates of alveolar macrophages in adult rats, the parental no observed adverse effect levels (NOAELs) for males and females were 5 and 20 ppm, respectively. In offspring, the NOAEL was 20 ppm based on reduced growth during lactation at 150 ppm. Study confirmed that there were no adverse effects on offspring at concentrations of up to and including 225 ppm of sulfuryl fluoride. The developmental NOAEL in rabbits was 75 ppm based on reduced body weights of offspring at 225 ppm.

In another study, pregnant rats on gestation days 6–15 exposed to air concentrations of 0, 25, 75, or 225 ppm (0, 27, 81, or 244 mg kg^{-1} day^{-1}) for 6 h a day did not show any developmental or maternal toxicity. On the other hand, pregnant rabbits had shown reduced fetal body weights and crown rump length when exposed to 0, 10, 28, or 85 mg kg^{-1} day^{-1} for 6 h a day. Sulfuryl fluoride was found to be neither teratogenic in rats nor rabbits.

No human development and reproductive toxicity data were available regarding sulfuryl fluoride. There were also no work-related exposures, accidental poisonings, or other human studies to indicate whether sulfuryl fluoride is likely to cause reproductive or developmental effects in humans.

Genotoxicity

Sulfuryl fluoride has been investigated *in vitro* for its capability to induce mutations in bacterial and mammalian cells, for clastogenicity and the induction of unscheduled DNA synthesis, and in a study of micronucleus formation *in vivo*. It showed no genotoxic potential in tests *in vitro* for bacterial cell mutation or unscheduled DNA synthesis in mammalian cells. The results of tests for mutagenicity and clastogenicity in mammalian cells *in vitro* (mouse lymphoma *Tk*+/− and rat lymphocytes) were positive, consistent with the database on genotoxicity of the fluoride ion that are considered not to have direct action on DNA. A test for micronucleus formation *in vivo* gave negative results. The overall extent of the genotoxicity database is considered adequate. Sulfuryl fluoride is a highly reactive compound, and dietary exposures would be predominantly due to the fluoride ion. It is generally recognized that fluoride does not represent a genotoxic risk to humans *in vivo*. Therefore, consumption of foodstuffs treated with sulfuryl fluoride would not present a genotoxic risk to humans. No data regarding genotoxicity in humans were recorded.

Carcinogenicity

For animals, based on the current use pattern of sulfuryl fluoride, the US EPA did not require carcinogenicity tests. As such, the US EPA has not classified the potential for sulfuryl fluoride to cause cancer. Researchers often screen potential carcinogens using studies designed to test the chemical's ability to cause mutations. Sulfuryl fluoride was negative in three mutagenicity studies. In a comprehensive carcinogenicity bioassay in which groups of male and female F344/N rats and B6C3F1 mice were administered drinking water containing up to 79 mg fluoride l^{-1} as sodium fluoride for a period of 2 years, there was no statistically significant increase in the incidence of any tumor in any single exposed group. There was a statistically significant trend of an increased incidence of osteosarcomas in male rats with increasing exposure to fluoride. However, the incidence was within the range of historical controls. Another 2 year carcinogenicity bioassay involving Sprague–Dawley rats exposed to up to 11.3 mg kg^{-1} body weight per day in the diet also found no statistically significant increase in the incidence of osteosarcoma or other tumors. Another study, which reported an increased incidence of osteomas in mice receiving up to 11.3 mg kg^{-1} body weight per day, was difficult to interpret, because the animals were infected with Type C retrovirus. For humans, data are not available from work-related exposures, accidental poisonings, or epidemiological studies to indicate whether sulfuryl fluoride is likely to cause cancer. The International Agency for Research on Cancer has not evaluated sulfuryl fluoride for carcinogenicity.

Clinical Management

Sulfuryl fluoride poisoning usually occurs after inhalational exposure. The predominant manifestations of sulfuryl fluoride poisoning are respiratory irritation and neurological symptoms. Effects of acute exposure usually include lacrimation, nose or throat irritation, cough, dyspnea, paresthesias, and seizures. Medical treatment may consist of giving calcium, correcting acidosis with sodium bicarbonate, and hemodialysis. Post treatment as described by Nitschke with phenobarbital was effective in rats. For respiratory protection, atmospheric levels should be maintained below exposure guidelines as described next. When respiratory protection is required, use an approved self-contained breathing apparatus or positive-pressure airline with auxiliary self-contained air supply.

Exposure Standards and Guidelines

The Occupational Safety and Health Administration permissible exposure limit, National Institute of Occupational Safety and Health (NIOSH) recommended exposure limits, and the American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit value is 5 ppm (21 mg m^{-3}) on a time-weighted average (TWA) for a normal 8–10 h workday and a 40 h workweek. ACGIH and NIOSH short–term exposure limit defined as a 15 min TWA exposure that should not be exceeded at any time during the workday is 10 ppm (42 mg m^{-3}). NIOSH immediately dangerous to life and health maximum concentration for which one could escape within 30 min without irreversible health effects is 200 ppm (840 mg m^{-3}). Sulfuryl fluoride is not registered for any food- or feed-related uses. No tolerances or exemptions from the requirement of a tolerance have been established, and no dietary exposure is anticipated.

See also: Federal Insecticide, Fungicide, and Rodenticide Act, US; Pesticides.

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