Glyphosate

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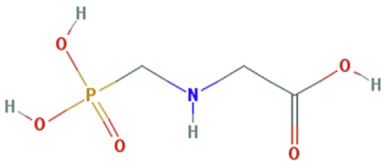
- Name: Glyphosate
- Chemical Abstracts Service Registry Number: 1071-83-6
- IUPAC Name: *N*-(Phosphonomethyl)glycine
- Synonyms: Glifonox, Glycel, Glycine, *N*-phosphonomethyl
- Chemical Formula: $C_3H_8NO_5P$
- Chemical Structure:



Background (Significance/History)

Glyphosate (*N*-(phosphonomethyl)glycine; 1071-83-6) is the active ingredient in several commercial herbicides for nonselective weed control. Glyphosate herbicides are among the world's most widely used herbicides. Roundup®, containing the active ingredient glyphosate, was developed and introduced by Monsanto Company in 1974. Other formulations include WeatherMax, UltraMAX, Buccaneer, Razor Pro, Rodeo, and AquaMaster®. Some crops such as soybeans and cotton have been genetically engineered to be resistant to glyphosate (Roundup Ready), allowing farmers to use glyphosate as a postemergence herbicide. The United States Environmental Protection Agency (EPA) considers glyphosate to be relatively low in toxicity compared to organochlorine and organophosphate pesticides.

Uses

Glyphosate is the active ingredient in several commercial herbicides. It is a broad-spectrum systemic herbicide for various types of weeds, grasses (Poaceae), and woody plants.

Environmental Fate and Behavior

Routes and Pathways

Glyphosate enters the environment through agricultural applications and in residential settings as a broad-spectrum nonspecific herbicide. Volatilization is not expected to be important.

Relevant Physicochemical Properties

- Physical state: colorless crystal at 20 °C
- Odor: odorless
- Density: 1.705 g ml^{-1} at 20 °C
- Water solubility = 10.5 g l^{-1} at 20 °C and 1.9 pH, 12 g l^{-1} at 25 °C
- Insoluble in acetone, ethanol, and xylene
- Dissociation constants: $pK_{a1} = 2.3$ (20 °C – phosphate acid), $pK_{a2} = 5.7$ (20 °C – secondary amine), and $pK_{a3} = 10.2$ (25 °C – carboxylic acid)
- Vapor pressure: negligible
- Henry's law constant: 2.1×10^{-12} atm-m^3 mol^{-1} at 25 °C
- Melting point: 184.5 °C
- Boiling point: ~100 °C; decomposes at 187 °C.

Partition Behavior in Water, Sediment, and Soil

- Partition coefficient: −3.2218 to −2.7696
- Adsorption coefficient: 6920–24 000.

Environmental Persistency (Degradation/Speciation)

Persistence in soil is extremely variable and can range from days to months. The degradation times (DT_{50}) range from 3 to 174 days, but are less persistent in water ($DT_{50} < 14$ days). The average half-life is 47 days. Biodegradation is the major route of environmental degradation. Glyphosate half-lives for aerobic degradation in Ray, Drummer, and Norfolk soils were 3, 27, and 130 days, respectively. Anaerobic degradation in silty clay loam was 8.1 days. No degradation of glyphosate has been noted in sterilized soil. Photodegradation and volatilization are thought to be not significant. Due to strong adsorption, glyphosate is not expected to be present in runoff at amounts greater than 2% of total applied.

Long-Range Transport

Glyphosate is strongly bound to clay particles and is considered moderately persistent in soil. Glyphosate has very little leaching capacity and therefore has a low potential to contaminate groundwater. Glyphosate is not expected to volatilize from soil or water and therefore has little potential for long-range transport.

Bioaccumulation and Biomagnification

Bioconcentration is considered to be low. For example, bioconcentration factor values in bluegill were 0.63 (viscera), 0.38 (edible), and 0.52 (whole body).

Exposure and Exposure Monitoring

Routes and Pathways (Including Environmental Release)

Glyphosate is released *via* production in waste streams and agricultural use. The compound exists solely as a particulate in air.

Human Exposure

Industrial workers and homeowners may be exposed to glyphosate by inhalation and dermal contact during spraying, mixing, and cleanup. In addition, exposures may occur by contact with soil and plants to which glyphosate was applied. Dermal exposure may also occur during glyphosate's manufacture, transport, storage, and disposal.

Environmental Exposure (Monitoring Data in Air, Water, Sediment, Soil, and Biota)

Glyphosate is rapidly inactivated by strong adsorption to soil particles. The concentrations of glyphosate in barley fields 2, 58, and 210 days posttreatment were 1.6, 0.5, and 0.2 mg kg^{-1}, respectively. Glyphosate levels near the Wuchuan River in China were 0.03–0.73 ng g^{-1} in soil and 0.02–0.12 ng g^{-1} in sediment. Glyphosate is generally not expected to contaminate water supplies, but it has been detected in certain rare cases. Glyphosate was detected in groundwater and water supply monitoring in Texas and in 1 out of 45 surface water samples from golf courses around the United States. It was also detected in one out of six ponds in Ontario, Canada, at a concentration of 42 μg l^{-1}. Glyphosate was detected in runoff from a California highway in concentrations ranging from 1.36 to 9.44 μg l^{-1}.

Toxicokinetics

Glyphosate is not metabolized in mammalian systems to any significant degree. Only one metabolite, aminomethylphosphonic acid (AMPA), has been detected at <0.5% of the original compound. The oral and dermal absorption of glyphosate is low. After oral administration in laboratory animals, >90% is rapidly eliminated unchanged within 72 h; 70% in feces; and the remainder in urine. Evidence from human poisonings suggests an elimination half-life from blood at 2–3 h, assuming normal renal function. Neither glyphosate nor AMPA exhibits any tendency for bioaccumulation.

Mechanism of Toxicity

Glyphosate's herbicidal action works by disrupting 5-enolpyruvylshikimate-3-phosphate (EPSP) synthase, a plant enzyme involved in the production of the amino acids such as phenylalanine, tyrosine, and tryptophan. EPSP synthase is not present in humans or animals and is the reason why glyphosate has relatively low mammalian toxicity. Additional mechanisms of action such as uncoupling of oxidative phosphorylation have been proposed. Glyphosate-based formulations have been shown to disrupt aromatase activity and mRNA levels and interact with the active site of the purified enzyme in human placental cells. As a result, some researchers consider formulations like Roundup® to be a potential endocrine disruptor. Adjuvants present in many commercial preparations may facilitate the observed effect. In contrast to organophosphate insecticides, glyphosate is not an inhibitor of acetylcholinesterase.

Acute and Short-Term Toxicity

Animal

Glyphosate is a compound of low mammalian toxicity. Oral LD_{50} values for laboratory rodents range from 1568 to >5000 mg kg^{-1}. The dermal LD_{50} value in rabbits is ~5 g kg^{-1}. Glyphosate produced moderate to severe ocular irritation in rabbits. There is no evidence of dermal sensitization in guinea pigs. The 4-h LC_{50} rat inhalation value is >4.98 mg l^{-1}.

Human

The acute toxicity of glyphosate is very low. Concentrated glyphosate and glyphosate in formulated products can cause eye and skin irritation. In human exposure studies, no evidence of skin sensitization or potential for photoirritation or photosensitization was observed. In suicide attempts by oral ingestion, the average volume of the concentrate containing glyphosate and a surfactant ingested was 120 ml and toxicity ranged from 104 ml (nonfatal) to 206 ml (fatal). The primary effects following ingestion include mucous membrane irritation, abdominal pain, vomiting, diarrhea, hypotension, oliguria, and anuria. Esophageal and gastric erosions have occurred after ingestion of concentrated solutions (41% glyphosate). In fatal cases, hypovolemic shock, cardiac arrhythmias, metabolic acidosis, and pulmonary edema have been reported. Laboratory studies suggest that other ingredients combined with glyphosate may contribute to the observed toxicity.

Chronic Toxicity

Animal

Glyphosate exhibits little potential for chronic toxicity. Studies of glyphosate lasting up to 2 years have been conducted in rats, dogs, mice, and rabbits, and with few exceptions, no effects were observed.

Human

Dermatitis resembling sunburn has been reported following prolonged skin exposure. No significant chronic toxicity has been reported.

Immunotoxicity

Results from limited animal studies suggest that glyphosate does not produce immunotoxicity. However, several studies indicate that glyphosate may be associated with immunological alterations in plants, fishes, amphibians, arthropods, and snails.

Reproductive Toxicity

Laboratory studies show that glyphosate produces reproductive changes in test animals very rarely and then only at very high doses (over 150 mg kg^{-1} day^{-1}). Glyphosate does not appear to be teratogenic.

Genotoxicity

Glyphosate is negative in well-validated mutagenicity assays.

Carcinogenicity

Glyphosate does not appear to be a carcinogen. The Cancer Classification is Group E: Evidence of Non-Carcinogenicity for Humans.

Clinical Management

There is no specific antidote; symptoms should be treated. Skin contamination should be treated promptly by washing with soap and water. Contamination of the eyes should be treated immediately by prolonged flushing of the eyes with large amounts of clean water. Due to the possibility of esophageal erosion, emesis is not recommended. Activated charcoal and a cathartic should be administered following ingestion of large amounts of glyphosate. Oral irrigation and dilution may be sufficient for smaller ingestions. In severe cases, basic life support, such as fluid replacement for hypovolemic shock, should be provided. Glyphosate is occasionally mistakenly referred to as a cholinesterase inhibitor similar to the organophosphate insecticides. However, atropine or pralidoxime (2-PAM) is not indicated in the treatment of exposure.

Exotoxicology

Freshwater/Sediment Organisms Toxicity

Glyphosate alone is at most moderately toxic to aquatic species. Commercial formulations are generally more toxic due to the presence of surfactants.

- Bluegill 96-h LC_{50}: 120 mg l^{-1}
- Rainbow trout 96-h LC_{50}: 86 mg l^{-1}
- *Daphnia magna* 48-h LC_{50}: 24 mg l^{-1}
- *Rana pipiens* chronic developmental no observed effect concentration: 0.00690 mg l^{-1}
- Some commercial formulations have LC_{50}s around 4–16 mg l^{-1}.

Marine Organisms Toxicity

- Atlantic oysters 96-h LC_{50}: >10 mg l^{-1}
- Fiddler crabs 96-h LC_{50}: 934 mg l^{-1}
- Grass shrimp 96-h LC_{50}: 281 mg l^{-1}.

Terrestrial Organisms Toxicity (Soil Microorganisms, Plants, Terrestrial Invertebrates, and Terrestrial Vertebrates)

- Bobwhite quail acute oral LD_{50}: >2000 mg kg^{-1}
- Mallard duck acute oral LD_{50}: >2251 mg kg^{-1}
- Goat acute LD_{50}: >5000 mg kg^{-1}
- Nontoxic to honey bees and earthworms.

Other Hazards

The use of surfactants to increase herbicide efficacy may be a contributing factor of toxicity to aquatic organisms, especially amphibians. The surfactant polyoxyethyleneamine (POEA) is known to be toxic to tadpoles of the species *Xenopus laevis* at 2.7 mg l^{-1}. Surfactants alone are often more toxic than glyphosate or commercial formulations. POEA contributes to but does not necessarily potentiate glyphosate toxicity. POEA is a severe eye, respiratory, and skin irritant and is also known to be contaminated with dioxanes, which are potential carcinogens.

Exposure Standards and Guidelines

- No occupational exposure limit standards available
- Acceptable daily intake: 0.3 mg kg^{-1} day^{-1}
- EPA Health Advisory: 0.7 mg l^{-1} (lifetime)
- Maximum concentration level (US Drinking Water Standard): 0.7 mg l^{-1}
- Reference dose: 2.0 mg kg^{-1} day^{-1}
- Maximum acceptable concentration (Canada Drinking Water Standard): 0.28 mg l^{-1}.

Miscellaneous

The technical material is a nonirritant in the Draize test but the formulated glyphosate products contain a surfactant that may produce some irritation on direct contact.

See also: Chlorophenoxy Herbicides.

Further Reading

Glyphosate Health Advisory, Office of Drinking Water, US Environmental Protection Agency: 1987, EPA Number 820K88005.

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Relevant Websites

www.monsanto.com/ – Monsanto - home page.
www.extoxnet.orst.edu/pips/ghindex.html – Pesticide Information Profiles.
www.toxnet.nlm.nih.gov/ – Toxicology database.
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