

Acrylamide

CAS: 79-06-1

MF: CH₂CHCONH₂

MW: 71.08

Solubility: soluble in water (215 g in 100 ml); soluble in methanol, ethanol, acetone, ethyl ether, chloroform, and some other organic solvents [1].

Major uses

Acrylamide is a vinyl monomer synthesized from acrylonitrile. It is polymerized to produce flocculants used in waste water treatment, paper strengtheners, grouting agents, and adhesive agents. Acrylamide is widely used in the production of polymers and co-polymers for plastics, making dyes, soil conditioning etc. Acrylamide monomer is used to make *polyacrylamide* and is a component in contact lenses and oil recovery additives. Acrylamide is an ingredient in biotechnical electrophoresis gels (reviewed in [2]).

Human toxicity

Acrylamide is toxic and an irritant. Toxic effects depend on the duration, total dose and rate of exposure. The effects of acute high-dose exposure may be delayed in onset for several hours. Peripheral neuropathy may appear several weeks following significant acute exposure or following significant chronic exposure. Encephalopathy may occur in severe acute poisonings.

Some clinical effects of acrylamide are listed here: a) cardiovascular: hypotension, peripheral cyanosis, cardiovascular collapse; b) neurological: following large exposure, these include somnolence, dizziness, confusion, memory loss, hallucinations, disorientation, tremors, and possibly seizures; c) respiratory: a persistent cough has been reported in sub-acute ingestions, but pulmonary findings were absent; d) gastrointestinal: anorexia and gastrointestinal disturbances; e) hepatic toxicity has been reported [2].

Cases of acrylamide poisoning show signs and symptoms of local effects due to irritation of the skin and mucous membranes and systemic effects due to the involvement of the central, peripheral, and autonomic nervous systems. Local irritation of the skin or mucous membranes is characterized by blistering and desquamation of the skin of the hands (palms) and feet (soles) combined with blueness of the hand and feet [1].

Probable lethal oral dose is 50-500 mg/kg in an adult [2]. A person committed suicide by ingestion 400 mg/kg of acrylamide [3].

Human blood concentrations of acrylamide in the cases of acute poisoning are not available.

TLV-TWA: 0.03 mg/m³ [2].

Carcinogenicity: IARC category 2A (the agent is probably carcinogenic to humans) [2].

Kinetic data

Order: biphasic (see *Elimination*).

Absorption: acrylamide is readily absorbed by ingestion, inhalation and through the skin [1].

Volume of distribution: unknown.

Distribution: acrylamide is distributed rapidly to blood. Large quantities are found in muscle, skin, liver, and small intestine. The nervous system does not concentrate acrylamide despite the prominence of neurological effects. The initial distribution half-life for tissue is approximately 5 h (reviewed in [2]).

Passage of blood brain barrier: limited.

Plasma half-life: 1.7 to 1.9 h (reviewed in [2]).

Time to peak blood concentration: peak whole blood levels occur at 1 h after exposure [2].

Plasma protein binding: approximately 10% binds to erythrocytes.

Elimination: total acrylamide (parent compound plus metabolites) exhibits biphasic elimination with a first component half-life of less than 5 h and a second component half-life of 6 to 8 days (data from animal experiments) (reviewed in [2]).

Metabolism and excretion

The liver and kidney are the primary sites of biotransformation and excretion. Detoxification is by conjugation with glutathione and biotransformation by the liver cytochrome P-450 mixed function oxidase system. Glutathione-S-transferase enzymatically catalyzes conjugation of acrylamide with glutathione, and glutathione depletion enhances the neurotoxic effects. The glutathione conjugate is S-B-propionamide glutathione, which is excreted as mercapturic acid conjugates (reviewed in [2]).

The primary metabolite is S-B-propionamide glutathione, which is transformed to N-acetyl-S-(3-amino-3-oxopropyl)-cysteine. Both metabolites are not toxic (reviewed in [2]).

Among other urinary metabolites in rats and mice are N-acetyl-S-(3-hydroxy-3-oxopropyl)cysteine, N-acetyl-S-(1-carbonyl-2-hydroxy-ethyl)cysteine, glycidamide, and 2,3-dihydroxypropionamide [2].

Excretion: approximately 90 to 95 % is excreted in the urine as N-acetyl-S-(3-amino-3-oxopropyl)cysteine conjugate and less than 2% as parent compound. In rats, 60% of an administered dose appears in the urine within the first 24 h. About 15% of an administered acrylamide dose may appear within 6 h in the bile (reviewed in [2]).

Toxicological mechanisms

Acrylamide causes progressive degeneration of axons in the peripheral and central nervous systems, termed “central-peripheral distal axonopathy” or “dying-back” neuropathy. Degeneration of the axon structures occurs initially at the distal ends of sensory nerves and progresses proximally, with lesser vulnerability of motor neurons.

Degeneration of cerebellar purkinje cells occurs, as well as degeneration of large myelinated fibers in the sympathetic and parasympathetic nervous systems (reviewed in [2]).

The mechanism is thought to be due in part to alterations in the activity of sulfhydryl-dependent glycolytic enzymes, inhibiting axonal energy production. Direct toxicity to neuron cells may also occur by disruption of protein synthesis [4].

Acrylamide also decreases brain dopamine, noradrenaline, and serotonin levels, and may alter responsiveness to dopamine [5].

Target organs: CNS, PNS, liver, kidney, pancreas.

References

1. Hazardous Substances Data Bank, HSDB (2006).
2. Poisindex, Thomson Micromedex (2006).
3. Calleman, C.J. (1996) The metabolism and pharmacokinetics of acrylamide: implications for mechanisms of toxicity and human risk estimation. *Drug Metabolism Reviews* 28, 527-590.
4. LeQuesne, P.M. (1985) Clinical and morphological findings in acrylamide toxicity. *Neurotoxicol* 6, 17-24.
5. Tilson, H.A. (1981) The neurotoxicity of acrylamide: an overview. *Neurobehav Toxicol Teratol* 3, 445-461.

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