Chloroform

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Chloroform ($CHCl_3$) is a colorless liquid that quickly evaporates into gas. It has a pleasant, nonirritating odor and a slightly sweet taste.

Most of the chloroform found in the environment comes from industry. It will only burn when it reaches very high temperatures. Chloroform was one of the first inhaled anesthetics to be used during surgery, but it is not used for anesthesia today. Nearly all the chloroform made in the United States today is used to make other chemicals [ATSDR]

Usage and exposure

Occupational exposure to chloroform may occur during its production and use as a solvent and chemical intermediate. The general population may be exposed as a result of its presence in chlorinated drinking-water, ambient air and some foods [IARC].

Chloroform is used in many industries. It is released from pulp and paper mills, hazardous waste sites, chlorinated water, and certain landfills.

The level of exposure depends upon the dose, duration, and work being done.

Chloroform is used in some refrigerants, solvents, and chemical manufacturing. Some examples of workers at risk of being exposed to chloroform include the following:

- Workers involved in paper manufacture or recycle industries
- Service employees exposed to some air conditioner refrigerants
- Equipment operators working at sanitary landfills
- Workers who work in water treatment plants [CDC].

Chloroform is used in pesticide formulations, as a solvent and as a chemical intermediate. Its use as an anesthetic and in proprietary medicines is banned in some countries. Chloroform is used as a solvent for fats, oils, rubber, alkaloids, waxes, guttapercha and resins; as a cleansing agent; in fire extinguishers to lower the freezing temperature of carbon tetrachloride; and in the rubber industry. It is used in the manufacture of fluorocarbon plastics, resins, refrigerants and propellants. It has been used as an

analgesic, muscle relaxant, carminative, flavouring agent, preservative, bactericide, heat-transfer medium and as a counter-irritant in liniments [IARC].

Routs of exposure:

Inhalation, skin absorption, ingestion, skin and/or eye contact.

Target organ:

Liver, kidneys, central nervous system, heart, eyes, skin.

Metabolism

Chloroform is readily absorbed from the lungs, gastrointestinal tract and skin. Approximately 60 – 80% of inhaled chloroform is absorbed [Toxicological overview].

Chloroform is metabolized by oxidative and reductive pathways. Under normal conditions, oxidative metabolism is the major pathway, and reductive metabolism does not play a significant role. Oxidative metabolism of chloroform results in the generation of phosgene, which either reacts with water to give carbon dioxide and hydrogen chloride or binds covalently to tissue macromolecules [IARC].

Chloroform is mainly excreted via the lungs unchanged or as the main metabolite carbon dioxide [Toxicological overview].

Health hazards

Chloroform can be toxic if inhaled or swallowed. It can harm the eyes, skin, liver, kidneys, and nervous system [CDC]**.**

Acute inhalation of chloroform can cause systemic effects such as excitement, nausea, vomiting followed by dizziness, ataxia and drowsiness. Convulsions, coma and death may occur following substantial exposures. In severe cases paralysis of the medullary respiratory center may lead to respiratory failure and sudden death**.** Early death following exposure to high levels of chloroform is often due to cardiac arrhythmias. Chloroform may also cause hypotension [Toxicological overview].

Delayed effects of chloroform exposure include renal and hepatic damage (up to 48 hours post exposure) [Toxicological overview].

Following acute ingestion of chloroform, systemic effects as seen following inhalation may occur as well as a burning sensation in the mouth and throat, nausea and vomiting. Hepatic toxicity has been reported following chronic ingestion of chloroform.

Acute ocular exposure to chloroform may cause a stinging sensation and exposure to chloroform liquid can cause irritation of the conjunctival tissue, corneal necrosis and ulcers.

Following acute dermal exposure to chloroform, local effects may include irritation and redness. Prolonged contact may result in systemic toxicity, dermatitis and burns.

Chronic inhalation or ingestion of chloroform may cause hepatic damage.

Local effects are observed following inhalation (irritation of the nose and throat), ingestion (burning sensation of the mouth and throat), ocular (stinging) and dermal exposure (irritation and redness) [Toxicological overview].

Extensive exposure to chloroform is fatal to humans, rapid death being attributed to cardiac arrest and delayed death to liver and kidney damage. The symptoms of exposure to chloroform include respiratory depression, coma, renal damage and liver damage as measured by elevated serum enzyme levels [CDC].

There is a consistent, tissue-, species-, strain- and sex-specific pattern in the rate of metabolism, cytotoxicity and cell proliferation produced by chloroform in rodent liver and kidney. Under the conditions of the high-dose regimens used in cancer bioassays in which tumors are produced, chloroform induced cytotoxicity and regenerative cell proliferation in the target organs for cancer. These findings are consistent with a mode of action for tumorigenesis in the liver and kidney of rodents that involves cytotoxicity [IARC].

There is strong evidence that cytotoxicity is a critical component of the induction of tumors in rodents by chloroform inhalation. Fetal toxicity in the form of growth retardation has been observed in several studies, concurrent with evidence of maternal toxicity. Malformations were observed in one study in rats exposed by inhalation. In a continuous breeding study, no reproductive effects were noted. No data were available on the genetic and related effects of chloroform in humans. There is weak evidence for the genotoxicity of chloroform in experimental systems in vivo and in mammalian cells, fungi and yeast in vitro. It was not mutagenic to bacteria [IARC].

There is inadequate evidence in humans for the carcinogenicity of chloroform. There is sufficient evidence in experimental animals for the carcinogenicity of chloroform. Chloroform is possibly carcinogenic to humans (Group 2B) [IARC].

References:

- ATSDR**.** https://www.atsdr.cdc.gov/phs/phs.asp?id=51&tid=16#bookmark01
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