Formaldehyde

Synonyms: formalin, methyl aldehyde, methylene oxide
CAS: 50-00-0
MF: HCHO
MW: 30.03
Solubility: very soluble in water; soluble in ethanol, ether, and acetone [1].

Major uses

Formaldehyde has wide commercial and medical applications. It is used as disinfectant, tissue preservative, and feedstock for synthetic chemical processes. Industrial uses include e.g. the manufacture of urea formaldehyde foam, paint pigment, and plastic molding [2]. Formaldehyde is also used as an ingredient in fertilizers, biocides, antimicrobial hair shampoos and conditioners, industrial and soil sterilants etc. [3].

Commercially available formalin is a 37 to 50% aqueous solution of formaldehyde that contains up to 15% methanol to inhibit polymerization [2].

Formaldehyde is a major oxidation byproduct of combustion processes, including tobacco smoking [2].

Human toxicity

Formaldehyde is a highly reactive substance; it may be irritating to the eyes, skin, and mucous membranes. Ingestion may cause corrosive injury to the gastrointestinal mucosa and the mucous membranes of the respiratory tract.

Some clinical effects of acute poisoning are summarized here: a) cardiovascular: hypotension and cardiovascular collapse may occur with severe ingestion; b) respiratory: inhalation of formaldehyde vapors at elevated concentrations may result in upper respiratory tract irritation and coughing. Bronchitis, pulmonary edema, or pneumonia were described at severe exposure; ARDS (adult respiratory distress syndrome); c) neurologic: lethargy and coma may occur following large ingestions or marked inhalation exposure; d) gastrointestinal: nausea, vomiting, and severe abdominal pain; corrosive gastritis, edema, ulceration, and even perforation of the esophagus may occur; e) hepatotoxicity.

Workers exposed to formaldehyde at a concentration of 7 mg/m3 developed blood levels of 0.6-4.0 mg/l (reviewed in [4]).

The ingestion of formalin has caused several deaths, preceded by severe corrosive damage to the stomach and small intestine, circulatory collapse and kidney damage [5].

A 41-year-old woman ingested 120 ml of 37% formaldehyde solution (containing 12.5% methanol); her initial formaldehyde blood concentration was 4.8 mg/ml, but dropped rapidly and remained within a range of 1-2 mg/ml over the next 15 hours, however, she suffered of hypotension, apnea and acidosis and died. Her blood formic acid concentrations rose and fell within a range of 250-500 mg/ml (the case reviewed in [4]).

Ingestion of as little as 30 ml of 37% (approximately 2 tablespoons) formaldehyde solution (formalin) has been reported to cause death in an adult [3].

The minimum lethal exposure in man is 477 mg/kg, in woman – 108 mg/kg [6].

At the fatal poisoning cases concentrations of formaldehyde in blood may vary between 4 to 11 mg/l (reviewed in [4]).

Time-weighted average (TWA): 0.016 ppm [3].
Threshold limit value (TLV): 0.3 ppm in air (0.4 mg/m^3), which is below the odor threshold for formaldehyde [4].

Carcinogenicity. EPA classification: B1 (probable human carcinogen – based on limited evidence of carcinogenicity in humans) [3].

Kinetic data
Absorption: when formaldehyde is orally ingested, absorption is usually rapid from gastrointestinal tract..
Very little formaldehyde is absorbed via the dermal route. In all cases, absorption appears to be limited to cell layers immediately adjacent to the point of contact [3].

Kinetics: order is unknown.

Volume of distribution: unknown.

Distribution: systemic distribution to all organs in the body.

Passage of blood brain barrier: free.

Plasma half-life: unknown.

Time to peak blood concentration: uncertain. In one fatal poisoning case, when a 57 year old male ingested 120 ml of formalin, peak serum formaldehyde and formic acid levels of 11 and 1360 mg/l, respectively, were observed at 5.5 hours post ingestion, with death occurring at 12 hours [7].

Plasma protein binding: unknown.

Elimination half-life: 80 to 90 min [3].

Metabolism and excretion
Formaldehyde is readily combined with cellular constituents in all exposed tissues. It is rapidly oxidized to formic acid largely in the liver by the catalytic action of alcohol dehydrogenase, and to a lesser extent in erythrocytes, brain, kidney, and muscle. Formic acid is further oxidized to carbon dioxide and water via a folate-dependent enzymatic pathway. The conversion of formaldehyde to formic acid is very rapid: the estimated half-life is 1.5 min [3].

Excretion: formaldehyde is normally converted and excreted as carbon dioxide in the air, and as formic acid in the urine. Concentration of formic acid in the urine of normal unexposed subjects averages 17-19 mg/l. In 11 persons believed to be exposed to formaldehyde, urine formic acid concentrations averaged 101 mg/l (range, 33-384 mg/l) (reviewed in [4]). Because of rapid absorption by both the oral and inhalation route and the rapid metabolism of formaldehyde, little or no formaldehyde is excreted in the urine.

Toxicological mechanisms

Formaldehyde reacts rapidly with DNA, RNA, and proteins in biologic systems. When cells are exposed to high concentrations, cellular functions cease and necrosis is rapid.

Formaldehyde may affect neural functions by condensing nonenzymatically with neuroamines, catecholamines, and indolamines to form tetrahydroisoquinolines and tetrahydrobetacarbolines, respectively [3].

Target organs: CNS, GI, liver, and all other organs (systemic toxicity).

References

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Written by Ada Kolman, March 2006, revised November 2006
ada.kolman@telia.com