Ethanol

CAS: *64-17-5*
MF: C_2H_5OH
MW: 46.07
log Kow= -0.31
Solubility: Miscible in water, ether, acetone, benzene and some other solvents.

Major use
Ethanol is mostly used as a component of alcoholic beverages. Other uses are as solvent in laboratory and industry (paint and lacquer), in the manufacture of denatured alcohol, pharmaceuticals (rubbing compounds, solvents, lotions, tonics, colognes), in perfumery, in organic synthesis etc. [1].

Human toxicity
Ethanol is toxic by oral, inhalation, subcutaneous, intravenous, intra-arterial, intraperitoneal, and dermal routes [2].

Dose-related central nervous system (CNS) depression occurs, ranging from inebriation to anesthesia, narcosis, coma, respiratory failure, and death in significant exposures. Other effects include hypothermia, hypoglycemia (especially in infants and children), acidosis, electrolyte imbalances, and gastrointestinal (GI) upset and bleeding. Ethanol vapors can produce CNS depression, eye and upper respiratory tract irritation [2].

Examples of chronic effects include physical dependence, malnutrition, neurological effects (e.g., amnesia, dementia, and somnolence), cardiac myopathy, hepatotoxicity, GI bleeding, esophageal varices and pancreatitis. Repeated dermal exposure can result in drying of skin. Combined exposure to ethanol and certain other chemicals may result in increased toxic effects [2].

Lethal symptoms: CNS depression (main cause of death) and cardiovascular failure [3].

Minimal lethal doses in non-tolerant adult are 5 to 6 g/kg of body weight via oral route [3].

Lethal blood concentration: concentrations of ethanol in blood from 4500 mg/l (the minimum lethal serum concentration) and over may lead to coma and death, except in tolerant individuals [3, 4]. The average ethanol blood concentration in 10 acute fatal cases were 7400 mg/l (range 4200-17700) (reviewed in [4]).

Working place limits: TLV-TWA: 1000 ppm [2].

Kinetic data
Absorption of ethanol in the gut is good [3]. Eighty to 90% is rapidly absorbed from the stomach and small intestine within about 30 to 60 minutes under optimal conditions [2]. Food, GI disease, other drugs, high ethanol concentration, and decreased GI motility can delay absorption 2 to 6 h [2].

Kinetics is zero-order [3]. There is some evidence that kinetics may vary, depending on the dose (reviewed in [4]).

Volume of distribution – 0.47 to 0.6 L/kg [2, 3].

Distribution:
Ethanol distributes rapidly throughout the body water [2] and passes freely over the blood-brain barrier [3]. It does not accumulate in specific organs [3].

The plasma half-life: The elimination of ethanol is generally considered to follow Michaelis-Menten kinetics, and thus half-life determination is not meaningful. At overdoses, 4 h have been reported [3].
Time to peak: 0.5-> 3 hours [3]. The time to peak levels is delayed > 2 hours after larger doses.
Protein binding: None [2, 3].

Metabolism and excretion
Ethanol is mainly metabolized in the liver (about 95%) by alcohol dehydrogenase to acetaldehyde and then to acetic acid. A small amount is metabolized through the hepatic microsomal ethanol-oxidizing system (MEOS) and a hepatic peroxidase-catalase system. The MEOS system may be involved to a larger degree in biotransformation under conditions of chronic ethanol use. The remainder of ethanol (about 5% to 10%) is excreted unchanged in the breath, urine, feces, and sweat [5].

Mean rate of clearance was 20.43 +/- 6.86 mg/dl/h (study based on 103 intoxicated patients) and was not found to be correlated with race, sex, age, or time of day [2].

Excretion: about 95% of a dose undergoes metabolism and the remainder is excreted unchanged in the breath, urine, sweat and feces [4].

Metabolites more toxic than ethanol: acetaldehyde [3].

Toxicological mechanisms
Hypothetical: Interfere with cell membrane fluidity, perturbing proteins such as ion channels [3].
Ethanol is the CNS depressant that causes stupor, coma and eventually death if ingested in excessive quantities [2].
Ethanol-induced ketoacidosis requires a relative fasting state. In the absence of dietary and hepatic sources of glucose, free fatty acids are mobilized from adipose tissue. As the only available source of glucose and as a result of an increase in the NADH/NAD ratio from ethanol oxidation, fatty acids are oxidized to acetoacetate and beta-hydroxybutyrate (ketogenesis). Ketogenesis coupled with volume depletion, decreased ketone elimination, and lactic acid production leads to acidosis [3].
Based on animal studies, it has been postulated that cardiac dysfunction from ethanol abuse may be due to depressed myocardial protein synthesis, secondary to disturbed intracellular calcium homeostasis etc [3].
Ethanol ingestion produces hepatic lipid accumulation ("fatty liver"). The following mechanisms contribute to this: 1. Decreased lipid oxidation by the liver, 2. Decreased hepatic clearance of lipoprotein, 3. Enhanced hepatic lipogenesis, 4. Enhanced uptake

of circulating lipids and 5. Increased mobilization of peripheral fat. Ethanol is hepatotoxic due to NADH production in its alcohol dehydrogenase pathway [3].

Target organs*:* CNS and cardiovascular system [3].

References

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2. Poisindex, Thomson Micromedex (2005).
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