

## Benzene

CAS: 71-43-2

MF: C<sub>6</sub>H<sub>6</sub>

MW: 78.1

Miscible in most organic solvents.

### Major use

Manufacturing of industrial chemicals such as polymers, detergents, pesticides pharmaceuticals, dyes, plastics, resins. Solvent for waxes, resins, oils, natural rubber, etc. Gasoline additive. The use as solvent is now discouraged [1].

### Human toxicity

Ingestion of 9 to 12 g of benzene has caused vomiting, tachycardia, staggering gait, somnolence, loss of consciousness and delirium, followed by chemical pneumonitis and collapse, with initial stimulation followed by abrupt CNS depression. At moderate concentrations, pallor, dizziness and excitation, followed by flushing, dyspnea, chest constriction, headache and weakness may occur. Clinical signs from ingestion of higher concentrations may include euphoria and excitation, followed by fatigue, coma and death [2].

The maximum tolerated human exposure to this agent has not been delineated. Oral doses from 9 to 30 grams have proven fatal [1]. It is estimated that the probable human oral lethal dose is 50 to 500 mg/kg [1]. It has been estimated that 10 mL benzene is a lethal dose for humans [2].

Fatal blood concentrations are between 0.9 and 38 mg/l [3].

Working place limits: TLV-TWA: 0.5 ppm and TLV-STEL: 2.5 ppm [2].

*Lethal symptoms:* Exposure to benzene is lethal in humans by means of asphyxiation, respiratory arrest, central nervous system depression or cardiac collapse [2].

### Kinetic data

*Absorption:* In animals nearly 100% of benzene is absorbed orally [2].

*Distribution:* Because of the high lipid solubility of benzene, high levels may be found in the brain and body fat [2].

*Accumulation in vital organs:* liver, heart, and brain.

*The plasma half-life:* The rate of elimination is biphasic, with an initial rapid excretion of most of the unchanged material, followed by a slow elimination of much lower levels. The half-life for the rapid phase is estimated to 1-3 hours and the half-life for the terminal elimination phase to 9 to 24 hours [4].

*Passage of blood-brain barrier:* free.

### Metabolism and excretion

Benzene is converted in the liver by the cytochrome P450 system into water-soluble metabolites which are conjugated and excreted in the urine [4]. The initial metabolite of benzene is benzene oxide. Benzene oxide rearranges spontaneously to form phenol,

which is subsequently hydrolyated to form hydroquinone, catechol, and 1,2,4-benzenetriol [5].

Metabolites include:

Phenol: 23 to 50% detected in urine;

Catechol: 3 to 5% detected in urine;

Hydroquinone: 1 to 5% detected in urine;

Phenylmercapturic acid: 0.5% detected in urine;

Benzene dihydrodiol: 0.3% detected in urine;

Trans, trans-muconic acid: 1.3% detected in urine;

Hydroxyhydroquinone: 0.3% detected in urine.

Other metabolites include quinol and muconaldehyde [7]. Quinol is further oxidized to p-benzoquinone, which binds to vital cellular components or undergoes redox cycling to generate oxygen radicals. Muconaldehyde is toxic through depletion of intracellular glutathione.

*Metabolites more toxic than benzene:*

Phenol, (catechol, hydroquinone, and 1,2,4-trihydroxybenzene) [7].

*Excretion:* following human exposure to benzene, only about 12% of a dose is exhaled unchanged by the lungs and about 0.1% is excreted unchanged in the urine. The remainder is metabolized in the liver to highly toxic oxidation products (see above) [4].

### **Toxicological mechanisms**

The mechanism whereby benzene causes death in acute exposures may be either through its anesthetic properties with resultant respiratory arrest, or through the production of fatal arrhythmia in an adrenalin primed myocardium [8].

Exposure to benzene may also stimulate cytochrome P450, which is responsible for the oxygenation of benzene and has a propensity to generate oxygen radicals. These radicals are a chief cause of benzene toxicity [6].

The mechanism(s) by which benzene can induce leukemia and perhaps other cancers is not known, but may be related to its ability to cause chromosomal aberrations in blood-forming cells. Myelogenous cancer cells often seem to be of common origin, with very high frequencies of abnormal chromosomes [9].

**Target organs:** blood, bone marrow, CNS, and liver.

### **References**

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*Written by Cecilia Clemedson, May 2005, revised February 2007*

*Cecilia@Stifud.se*