# Xylene

Chemical name: dimethylbenzene. Synonym: xylol. The commercial product is a mixture of three isomers: *ortho* (*o*)-, *meta* (*m*)-, and *para* (*p*)-xylene, where *m*-xylene predominates (75-85%) [1].

CAS: 1330-20-7
MF: $C_8H_{10}$
MW: 106.2
Xylene is a low-viscosity, colorless, flammable liquid.
Solubility: practically insoluble in water, but miscible with many organic solvents such as alcohol and ether [1].

**Major uses**
Xylene is an aromatic hydrocarbon, which is used as a solvent for pesticide formulations, as a raw material for the production of industrial chemicals, and as a cleaning and sterilizing agent [1].

**Human toxicity**
Xylene is irritating to the eyes, skin, and mucous membranes. Acute overexposure to xylene has caused vomiting, diarrhea, renal impairment; liver function disturbances; heart failure; pulmonary edema, and focal alveolar haemorrhage [2]. It can also induce the central nervous system (CNS) depression with ataxia, impaired motor coordination, mental confusion, stupor, and coma [3].

Xylene is considered very toxic by ingestion, with estimated oral lethal doses in adults of 15 to 30 ml, or about 50 mg/kg [2].

Reported concentrations of xylene in human serum or plasma in fatal cases ranged from 3 to 40 mg/l [4].

TLV/TWA*: 100 ppm (430 mg/$m^3$) [2].

*Carcinogenicity*: not classifiable as a human carcinogen [4].

**Kinetic data**
*Absorption*: xylene is rapidly absorbed following ingestion and inhalation. It is less well absorbed through intact skin [2].

*Kinetics* is biphasic, with an early *plasma half-life* of 0.5-1 h and with a terminal half-life of 20-30 h [6].

*Volume of distribution*: unknown. About 10-20% of absorbed xylene is distributed to the adipose tissues of the body [2].

*Peak blood concentrations* occur 1 to 2 h after ingestion [2].

*Plasma-protein binding*: high [7].

*Passage through blood-brain barrier*: free [7].

*Elimination half-life* is 20 to 30 h [6].

**Metabolism and excretion**
The three xylenes are rapidly metabolized by the cytochrome P450 system of the liver and other organs [5], by oxidation of a methyl group to the corresponding *o*-, *m*-, or *p*-toluic acid. These acids are further excreted in the form of a glycine conjugates as *o*-, *m*-, or *p*-methyl hyppuric acid [6].

*Excretion*: approximately 72% to 95% of absorbed xylene is biotransformed and excreted in the urine within 18 h as *o*-, *m*-, or *p*-methyl hippuric acid. About 2% is excreted as xylenols or xylenol conjugates. Less than 0.01% is excreted unchanged in the urine [6]. About 5% of xylene is excreted unchanged via the lungs [7].

**Toxicological mechanisms**
The mechanisms of xylene toxicity are still not very well known; some of them are listed below:
1) Oxygenated intermediates of xylene (see "Metabolism and excretion") may be produced in the lung leading to covalent binding. This covalent binding may be the mechanism that produces pulmonary edema through cellular necrosis [5];
2) Acute CNS toxicity may be associated with xylene vapor ability to paralyze the breathing centers of the brain [7]; xylene is anesthetic in high atmospheric concentrations exceeding 5000 ppm (reviewed in [9]).
3) Heart failure may be possibly due to sensitization of myocardium to endogenous catecholamines [8]. Catecholamines are neurotransmitters in the sympathetic nervous system. High catecholamine levels in blood are associated with stress.

**Target organs**: CNS, heart, lung, liver [8].

**References**
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* Threshold Limit Value / Time Weighted Average. The average concentration under which most people can work consistently for eight hours.

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