

Hexachlorophene

Chemical name: 2,2'-methylenebis(3,4,6-trichlorophenol)

CAS: 70-30-4

MF: C₁₃H₆Cl₆O₂

MW: 406.9

pKa=7.54

Solubility: practically insoluble in water; soluble in ethanol, acetone, ether and chloroform.

Major uses

Hexachlorophene is a topical antiseptic agent (synthesized 1939) with a bacteriostatic action against staphylococci and other gram-positive bacteria. It is used as antibacterial component for soaps and cosmetics, in cleaning emulsions, and as preoperative surgical scrub. Hexachlorophene is also used in agriculture as a fungicide, plant bactericide and soil fungicide [1, 2]. Its use has been constrained after the 1970's due to accidental poisoning of babies in France, by the talcum powder containing hexachlorophene [3].

Human toxicity

Hexachlorophene is a highly toxic compound because its proven neurotoxicity. The main symptoms following acute ingestion of large amounts of hexachlorophene are: a) neurologic: lethargy, irritability, weakness, intracranial hypertension, seizures, paralysis, and coma, leading in some cases to death; b) cardiovascular: hypotension, bradycardia, and cardiac arrest; c) respiratory: lung edema, and respiration arrest; d) gastrointestinal: nausea, vomiting, anorexia, abdominal pain, and diarrhea; e) dermatological: allergic contact dermatitis [1].

The estimated lethal dose in adult is 2 to 10 g. The minimum lethal dose is not well established.

The data concerning lethal blood concentrations in adults after acute poisoning are found very rare; sometimes the concentrations in poisoned children are available. In one fatal poisoning case in an adult (ingestion of 200 ml of 3% hexachlorophene solution), concentration of hexachlorophene in the blood serum at autopsy was 35 mg/l [4]. The lethal plasma/serum level of 35 mg/l was also reported by Winek [5]. However, survival was occurred in adults with levels between 23 and 74 mg/l [6].

Carcinogenicity: Rating 3 (IARC, 2004). The evidence of carcinogenicity is inadequate in humans and inadequate or limited in experimental animals [1].

Kinetic data

Absorption: following ingestion, hexachlorophene is rapidly and effectively absorbed by the gastrointestinal tract. It is also well absorbed by dermal exposure [1].

Kinetics: apparently first-order kinetics? [7].

Distribution: hexachlorophene is highly lipophilic compound, which is rapidly redistributed into lipid tissues, and also in the CNS. Myelin preferentially binds hexachlorophene [1]. Hexachlorophene accumulates in the liver and kidney [7].

Volume of distribution: not known.

Passage of blood-brain barrier: restricted [7].

Blood protein binding: 92% (at the overdose situation) [7].

Time to peak blood concentration: apparently 3-6 h? [7].

Mean elimination half-life: 24 h (at the overdose situation) [1, 7].

Metabolism and excretion

Hexachlorophene is a chlorophenol compound (see also **Pentachlorophenol** in AcuBase), which is metabolized in the liver. It is conjugated to the glucuronide and excreted into bile.

Hexachlorophene is resistant to biotransformation and tends to persist in the environment and bioaccumulates in food chains [8].

Excretion: orally ingested hexachlorophene is excreted primarily in the feces, and only a small amount is excreted slowly in the urine [1].

Toxicological mechanisms

Hexachlorophene is a potent uncoupler of oxidative phosphorylation in liver mitochondria. It was shown that hexachlorophene strongly binds to proteins of mitochondrial and plasma membranes, which may partly explain its toxic effects.

Hexachlorophene is neurotoxic, causing paralysis of the CNS, associated with edema and spongiform degeneration of cerebral white matter (spongiform encephalopathy) [1].

Experimentally it has been shown that synthesis of myelin is inhibited in hexachlorophene-treated animals, possibly as a result of inhibition of oxidative phosphorylation. Since many axons in the CNS and peripheral nervous system are myelinated, agents that selectively damage the myelin-forming cells may cause the CNS damage [8].

Target organs: CNS, skin, gastrointestinal tract [1].

References

1. Poisindex, Thomson Micromedex (2005).
2. Wikipedia, The Free Encyclopedia (Google, via internet).
3. Haddad, L.M. & Winchester, J.F. (1990) *Clinical Management of Poisoning and Drug Overdose*. 2nd ed., pp. 357-358. W.B. Saunders Company.
4. DiMaio, V.J.M., Mullick, F.G., Henry, L.D. (1973) Hexachlorophene poisoning. *J Forensic Sci* 18, 303-308.
5. Winek, C.L. (1994) Drug and chemical blood-level data. *Winek's Toxicological Annual*, Pittsburgh. Allegheny County Department Laboratories.
6. Ellenhorn, M.J. & Barceloux, D.G. (1988) *Medical Toxicology: Diagnosis and Treatment of Human Poisoning*, pp. 979-981. New York: Elsevier.
7. Ekwall, B., Clemenson, C., Crafoord, B., Ekwall, Ba., Hallander, S., Walum, E., Bondesson, I. (1998) MEIC evaluation of acute systemic toxicity. Part V. Rodent and human toxicity data for the 50 reference chemicals. *ATLA* 26, 571-616.

8. *Casarett and Doull's Toxicology (The Basis Science of Poisons)* (1986) Klaassen, C.D., Amdur, M.O., Doull, J., eds., p. 373, p. 840, Macmillan Publishing Company.

Written by Ada Kolman, January 2006; revised March 2007
ada.kolman@telia.com