Lindane

Synonyms: γ-1,2,3,4,5,6-hexachlorocyclohexane, gamma-hexachlorocyclohexane
CAS: 58-89-9
MF: $C_6H_6Cl_6$
MW: 290.85
Log Kow=3.72 to 3.61
Slightly soluble in water (7.3 mg/l, at 25°C); well soluble in the organic solvents, e.g., acetone (>5g/l) and benzene [1].

Major uses

Lindane is an insecticide belonging to the class of organochlorines, primarily used as a scabicide and pediculocide. For treatment of scabies it is used in form of 1% cream or ointment. Lindane may be formulated as an emulsion, solution, aerosol, cream, lotion, or shampoo.

Lindane is used to treat human head and body lice; to control termites, mosquitoes, flies and other insects. It is also used to control pests in animals [2].

EPA has forbidden using lindane on many food crops, as well as in the dairy industry [3].

Human toxicity

Lindane belongs to the toxic organochlorines with the central nervous system (CNS) as a main target organ. At the acute poisoning, among symptoms are CNS excitation and seizures, headache, agitation, tremor and peripheral neuropathy. Other symptoms: ataxia, nausea, vomiting, diarrhea, circular collapse, cardiac arrhythmia, hypotension, hyperthermia, respiratory depression, pulmonary edema, and coma. Poisoning may occur by ingestion, inhalation, or percutaneous absorption [2].

The mean lethal dose of technical grade lindane in humans has been 28 g [4].

The lethal dose of lindane was estimated to be 125 mg/kg [5].

The toxic level of lindane in blood is 0.5 mg/l [5]. The lethal serum concentrations of lindane in two cases were 1.3 mg/l (reviewed in [4]).

Carcinogenicity: not listed (IARC, 2004). However, according ACGIH (2000) it is classified as category A3 – "probably carcinogenic to humans" (confirmed animal carcinogen with unknown relevance to humans). Several cases of acute myeloid leukemia have been reported connected with lindane exposure [2].

Kinetic data

Absorption: Lindane is efficiently absorbed through ingestion, inhalation and by contact with the skin. It is transferred across the human placenta; it was also found in human breast milk [2]. Passage across the blood brain barrier is free [6].

Volume of distribution (V_d) is 300 l/kg, at the acute poisoning with large amount of lindane. Distribution half-life was calculated in the same study to be 15 h [7].

For the overdose situation, kinetic is biphasic [6].

Plasma half-life was calculated to be of 26 h, after infusion in healthy adult. Following dermal application, plasma half-life ranged from 18 to 21 h.[5].

Elimination half-life following en ingestion is generally several days [2].

Metabolism and excretion
Lindane is highly lipid soluble, and it is stored in adipose and other lipophilic tissues. It is metabolized in the liver by the hepatic microsomal oxidase system [8]. Main metabolites are chlorophenols: 2,3,4,6-tetrachlorophenol, 2,4,6-trichlorophenol, 2,3,5-trichlorophenol, 2,4,5-trichlorophenol, 2,4-dichlorophenol, 2,5-dichlorophenol and monochlorophenol [2].

Excretion: metabolites of lindane are excreted in the urine and feces [2].

Toxicological mechanisms
Neurotoxic action of lindane is due to so called "axon poison", affecting primarily the CNS nerve cells. Essentially, the organochlorines interfere with the normal flux of Na^+ and K^+ ions across the axon membrane as nerve impulses pass. This results in irritability and disturbance of mental process, sensory aberrations, and seizures.

In vitro studies suggest that lindane's neurotoxic effects are mediated via blockade of the GABA-receptor coupled sodium channel [2].

The organochlorines do not depress cholinesterase enzymes.

Target organs: CNS, liver, kidney.

References
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Written by Ada Kolman. Stockholm, September-October 2005; revised February 2007
ada.kolman@telia.com