Hexachlorobenzene

Synonym: perchlorobenzene

CAS: 118-74-1
MF: C_6Cl_6
MW: 284.8
Solubility in water is limited: 0.005 mg/l; soluble in ethanol, benzene, chloroform, and ether [1].

Major uses
Hexachlorobenzene (HCB) is an aromatic hydrocarbon fungicide/pesticide (known since 1945) used for the protection of cereal grains, such as wheat, barley, oats, and rye, from so called "smut diseases". It was also used to make fireworks, ammunition, and synthetic rubber, and as an organic synthesis reagent [1].
HCB was banned from use in the U.S.A. in 1966.

Human toxicity
The primary toxic effect is cutaneous porphyria*, for the first time described in Turkey (1955), when people consumed bread accidentally contaminated with HCB. Characteristic features of this disease included e.g. hyperpigmentation, photo-sensitivity, permanent loss of hair, cutaneous lysis, weight loss, hepatomegaly (enlarged liver), and arthritis [2]. Other clinical findings were increase in the quantity of smooth endoplasmic reticulum, and in the activities of cytochrome P450-dependent monooxygenases (reviewed in [3]).

The exposure to acute high dose causes abdominal pain, nausea, vomiting, mental confusion, and convulsion (e.g. poisoning by contaminated bread in 1967 in Doha, Saudi Arabia, when 490 persons were admitted to the hospital and 7 persons died ([reviewed in [4]).

Daily intake of 50-200 mg of HCB over several months leads to erythematosus skin lesions, which progress to atrophy, hyperpigmentation, and ulcerations [5].

In New Zealand adults with no known occupational exposure, HCB blood concentrations averaged 0.022 mg/l (0-0.095 mg/l), whereas in a group of occupationally exposed, but asymptomatic subjects, average blood concentration was 0.056 mg/l (0-0.410 mg/l) [6, 7].

In workers occupationally exposed to HCB, a permissible level in blood was estimated to be 0.3 mg/l (reviewed in [8].)

Carcinogenicity: HCB is an animal carcinogen and is considered to be a probable human carcinogen (Group 2B, U.S. Environmental Protection Agency, 2000) [1].

Kinetic data
Very little information regarding kinetic data in humans is available.

Absorption: HCB is easily absorbed through the lymphatic system to accumulate in fat tissues, and persists for many years since it is highly lipophilic and resistant to metabolic conditions [1].

Plasma half-life: 60 days [7].

Metabolism and excretion
The biotransformation of pentachlorophenol in man and animals takes place by conjugation, hydrolytic dechlorination, and reductive dechlorination. Further species dependent reactions are oxidation and methylation. The reaction with glutathione results in the formation of conjugates and cleavage of glycine and glutamate gives cysteine conjugates. Acetylation of the amino group of the cysteinyl moiety in mammals gives mercapturic acids.

In rats, HCB was metabolized by liver microsomal fraction to pentachlorobenzene, pentachlorophenol, tetrachloro-1,2-benzenediol, and tetrachloro-1,4-benzenediol (1:88:2:9) [1].

Excretion: HCB is eliminated from the body predominantly in the feces as a result of intestinal excretion [3].

Toxicological mechanisms
HCB specifically inactivates the enzyme uroporphyrinogen decarboxylase playing an important role in the regulation of heme synthesis, leading to disease cutaneous porphyria.

HCB causes a decrease in the activity of hepatic 3-hydroxysteroid dehydrogenases. Among other effects, a partial uncoupling of oxidative phosphorylation in man, as well as immunosuppression (in rodents) were reported [1, 8].

Target organs: liver, lipid-reach organs (early accumulation), blood.

References
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* Porphyria cutanea tarda (PCT) is a term encompassing a group of disorders in which activity of the heme synthetic enzyme uroporphyrinogen decarboxylase (UROD) is deficient (Medical Dictionary, via Internet)..

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