Paraquat dichloride

CAS: 1910-42-5
MF: $C_{12}H_{14}N_2Cl_2N_2 \cdot H_2O$
FW: 257.16
Soluble in water.

Major use
Paraquat dichloride (further only paraquat) is a rapidly-acting herbicide, used both for a domestic and agricultural purposes. Technical products are available as liquids, with concentrations ranging from 10 to 30% for agricultural preparations [1, 2].

Human toxicity
Paraquat causes severe pulmonary fibrosis and death at very low doses. Acute exposure may cause pulmonary edema, heart failure, kidney failure, liver failure, as well as an effect on the central nervous system (CNS): cerebral edema and brain damage [1].

Death may be delayed for a few days to a couple of weeks due to lung, liver, kidney and gastrointestinal damage. [1].

Estimated lethal dose is 10 to 15 ml of the concentrate. The minimum lethal dose is estimated to 30-35 mg per kg body weight [1, 3]. Ingestion of 20-40 mg of paraquat ion per kg body weight results in death in most cases but the death may be delayed for 2 to 3 weeks. Ingestion of less than 20 mg paraquat ion per kg body weight is reported to give no or just gastrointestinal symptoms followed by recovery [1].
The mean lethal dose, based on the values from several handbooks, was 2.5 g [4].

Plasma paraquat concentrations exceeding 0.2 mg/l are usually associated with unfavorable prognosis (reviewed in [5]). However, the data on paraquat toxicity and lethality differ in several handbooks. For example, according to Winek [6], toxic plasma/serum concentration level is 8.5 mg/l, and lethal level is 35 mg/l. Average paraquat blood concentration of 15 mg/l (range from 0 to 63 mg/l) was reported in 9 fatal cases (survival about 1 day; autopsy specimens) [5].

Carcinogenicity: possible human carcinogen (EPA, 2004) [1].

Kinetic data
Absorption: Paraquat is absorbed quickly but not completely after ingestion or inhalation, 5 to 10% is absorbed of an oral dose. Absorption through the skin occurs but there are different opinions of the proportion. A study with human volunteers found out that only 0.3% of paraquat was absorbed through the intact skin after 24 hours of exposure. But if the skin has lesions, chemical or mechanical, paraquat could easily be absorbed [1, 2].

Kinetics is biphasic [4].

Volume of distribution: 1.2-1.6 l/kg [5]. 2.75 l/kg at 39.5 hours following ingestion – case report [1].

Distribution: Paraquat is distributed into all organs in the body, with the highest concentrations found in kidney and lung. It is also accumulated in muscle tissue which may function as storage. That could explain the detection of paraquat in plasma and urine for weeks and months after ingestion [1].

Peak plasma concentration occurs between 0.5 to 2 h following paraquat ingestion [1].

Elimination half-life: from 5 to 84 h [4].

Protein binding: paraquat is not bound to plasma protein [4].

Passage of blood-brain barrier: possibly free? [4].

Metabolism and excretion
Paraquat is a dimethyl substituted dipyridyl, which behaves as a strong cation in aqueous solution. Paraquat is metabolized to highly reactive free radicals in the lung.

Excretion: 80-90% of paraquat is excreted 6 hours after exposure and 100% within 24 hours shown in animal studies. It is thought to be similar in humans mainly through glomerular filtration or active tubular secretion of the parent compound [1].

Toxicological mechanisms
Death is due to asphyxia (inability to breath and suffocation), caused by progressive and generalized proliferation of fibrous connective tissue in the pulmonary alveoli, where paraquat is selectively concentrated. This reaction develops from 3 days to 2 weeks after ingestion and is accelerated by administration of oxygen [1].

On the cellular level, paraquat selectively accumulates in the type I and II pneumocytes. Biotransformation in these cells is believed to result in the generation of the free radicals which may cause lipid peroxidation and cell injury. The injury of the cell membrane causes mononuclear macrophage activation, and eventually, pulmonary fibrosis [1].

Target organs: lung, kidney, liver [6].

References

1. Poisindex, Thomson Micromedex (2005).
2. Swedish Poisons Information Centre (2005).
3. HSDB (2005).
4. Ekwall B., Clemedson C, Crafoord B, Ekwall B, 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
5. Baselt, R.C. & Cravey, R.H. (1995) *Disposition of Toxic Drugs and Chemicals in Man*, 4th edn., pp. 581-583. Chemical Toxicology Institute, Foster City, CA, USA.
6. Winek, C.L. (1994) Drug and chemical blood-level data. *Winek's Toxicological Annual*, Pittsburgh. Allegheny County Department Laboratories.

Written by Erica Toft, September 2005; revised March 2007
erica.toft@expertradet.se