2,4-Dichlorophenoxyacetic acid

CAS: 94-75-7
MF: $C_8H_6Cl_2O_3$
MW: 221.0
pKa=2.64
logKow=2.81
Solubility in water: 900 mg/l, at 25°C; solubility in ethanol and acetone 9.5 g/100 g; in benzene 1.1 g/100 g.

Major uses
2,4-Dichlorophenoxyacetic acid (2,4-D) is a selective systemic hormone type phenoxy herbicide. It is used for weed control in wheat, maize, rice, and similar cereal grass crop. 2,4-D induces several abnormalities in growth and plant structure and finally necrosis of the plants [1].

Human toxicity
The toxic effects in acute cases of ingestion of 2,4-D include burning of oral mucosa, hypersalivation, stomach cramps, vomiting, diarrhea, respiratory failure, pulmonary edema, renal failure. Other reported symptoms were convulsion, cerebral depression, mental confusion and difficulty in speaking, muscular weakness, ataxia, and gradual loss of reflexes. The pulse may be rapid and sometimes irregular with a low blood pressure. Ventricular fibrillation has been reported. In severe cases coma may develop, followed by death.

2,4-D is toxic at the doses of 50 mg/kg. Fatalities have been seen following ingestion of 80 mg/kg [2]. The mean lethal dose of 2,4-D in man was estimated to be 28 g [3].

The toxic and lethal levels of 2,4-D in human blood and tissue are still not well defined. Blood plasma concentrations greater than 100 mg/l have been associated with coma [2]. A woman with reportedly 335 mg/l plasma did not show any signs of poisoning; in general, the acute lethal levels of 2,4-D in blood plasma appear to lie between 447 and 826 mg/l [4]. The mean clinically measured acute lethal serum concentration, based on data from several handbooks, was 510 mg/l [5].

TLV/TWA: 10 mg/m^3 (IARC) [2].

Carcinogenicity: human studies show conflicting results. Twelve out of 20 epidemiological studies concerning development of various cancers in humans, due 2,4-D, revealed that there was association between cancer incidence and exposure, six studies showed that there was no association, and two studies showed a trend of positive association between cancer incidence and 2,4-D human exposure [1].

Kinetic data
Absorption: rapid and almost complete from the gastrointestinal tract. Complete absorption within 24 h [5].

Kinetics: first-order [5].

Distribution: 2,4-D is rapidly carried in the blood to cells and tissues throughout the body; liver and kidney tends to contain the highest concentrations, while brain and

other fatty organs, and muscle including the heart, usually have lower 2,4-D levels (results of post-mortem examination of different organs) [4].

Volume of distribution: 10.2 l/kg at overdose [5].

Passage of blood-brain barrier: restricted [5].

Plasma half-life: 10 to 24 h, rising to 80-120 h after larger doses (pH-dependent) [2]. Other sources: 24 h; in occupationally-exposed people 35-48 h [3]. Plasma half-life may be 58 h at the overdose situation (pH-dependent) [5].

Time to peak blood concentration: 7 to 24 h at overdose situation [5].

Plasma protein binding: high (no data reported) [5].

Metabolism and excretion
2,4-D is not extensively transformed in the liver; no transformation products were found in blood and tissues. 2,4-D is primarily metabolized by acid hydrolysis; a minor amount (up to 27%) is conjugated, however, conjugates were not identified [4].

Excretion: In a study of six human volunteers who were given a dose of 5 mg/kg orally, more than 75% of 2,4-D was excreted unchanged in the urine within 96 h [6].

Toxicological mechanisms
Several hypothetical mechanisms were proposed [2]:
a) Uncoupling of oxidative phosphorylation;
b) Degenerative changes in the brain cells (effect on the CNS);
c) Demyelination of peripheral nerves;
d) Depression of ribonuclease synthesis.

Target organs: histopathological organ lesions in the CNS, liver, and kidney; also heart is a target organ [5].

References
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