Malathion

CAS number: 121-75-5
MF: $C_{10}H_{19}O_6PS_2$
FW: 330.36
Water solubility: 143 mg/l.

Major uses
Malathion is used in agriculture as an insecticide to control insects in a wide range of crops, including cotton, soft and stone fruits, potatoes, rice and vegetables, and for protection of stored grain against insects. It is also used for extermination of mosquitoes, ectoparasites of cattle, poultry, dogs and cats, as well as for treatment of human head and body lice, and household insects [1].

Human toxicity
Ingestion of malathion, the most common rout in fatal cases, causes loss of appetite, nausea, vomiting, abdominal cramps and diarrhea. The symptoms may appear within two hours. Breathing and eye effects are the first to appear after inhalation of malathion. Skin absorption causes sweating and twitching in the area of absorption, usually within 15 min to 4 h. Dizziness, confusion, staggering, slurred speech, generalized sweating, irregular or slow heartbeat, convulsions and coma are additional symptoms that also may occur [2].

Miosis, ocular pain, conjunctival congestion, diminished vision and ciliary spasm are effects occurring in the eye. Respiratory effects consist of rhinorrhea and hyperemia of the upper respiratory tract, bronchoconstriction and increased bronchial secretion [2].

Intoxication by malathion, an anti-cholinesterase agent, is manifested by muscarinic and nicotinic signs as acetylcholine accumulates in CNS. The symptoms are due to the potentiation of responses to acetylcholine released from preganglionic, postganglionic cholinergic, and somatic motor nerve endings whenever nerve volleys reach the periphery [2].

Malathion poisoning may also cause damage to myocardium with dilation of the pericardial blood vessels and marked hemorrhage in the surrounding tissues. Blood pressure may fall to alarmingly low levels.

The cause of death is primarily respiratory failure, usually accompanied by secondary cardiovascular symptoms [2].

The mean fatal dose in man is estimated at 60 g [3]. The minimum oral lethal dose in women was reported to 246 mg/kg and in man 471 mg/kg [2].

Lethal blood concentrations of different cases vary between 0.3 and 7.4 mg/l (average value 0.99 mg/l) [4]. Peak plasma concentration was estimated to be 1.2 mg/l (evaluated from time-related curve for lethal cases, total 23 cases) [4].

TWA: 10 mg/m^3; skin; TWA: 15 mg/m^3 total dust; skin.

Carcinogenicity: not classifiable as a human carcinogen.

Kinetic data

Absorption: malathion is absorbed rapidly and effectively by all routs [2].

Kinetic: multiphasic [5].

Volume of distribution: no data available.

The serum half-life of malathion was approximately 3 h (a case report: 24-year-old man who injected 1.8 g of malathion intravenously into his right forearm, at a suicide attempt). Concentration of malathion in serum ranged from 0.349 mg/l to 0.029 mg/l at 6 and 28 hours post injection, respectively. Km=138 ng/ml; Vmax=125,9 ng/h; and terminal elimination rate constant was 0.24/h determined from three terminal serum concentrations [6].

Time to peak plasma concentration: 1-5 h, for overdose situation [5].

Protein binding: no protein binding has been observed [5].

Passage across blood-brain barrier: free [5].

Metabolism and excretion

In humans, malathion is activated by conversion to the toxic metabolite malaoxon, an oxygen analog of malathion. Both malathion and malaoxon are inactivated by hydrolysis to dimethyldithiophosphoric acid and dimethylthiophosphoric acid, respectively [3].

Malathion is metabolized by hydrolytic cleavage of ethyl groups from the succinic acid moiety of the molecule, by carboxylesterase enzymes and by hydrolysis of the succinate moiety from the dialkyl thiophosphate. It is reported that malathion is less toxic to humans than most anticholinesterase agents because it is metabolized in the liver to an inactive form, moreover, the degradation rate of malaoxon is higher than the rate of its formation [2].

Excretion: There has been reported that 44% of malathion was excreted in urine and 47% still remained in the gastrointestinal tract 8 hours after an oral dose (rat). After 24 hours 83% was excreted in urine, 6% in feces, 3% in expired air and 8% still left in the gastrointestinal tract [2].

Toxicological mechanisms

The toxicity of malathion is probably due to oxidation to malaoxon, which is carried out by the liver microsomal monooxygenase system. Malaoxon is about 1000 times more active as anti-cholinesterase than malathion itself [2].

Malathion and the other organophosphate insecticides are potent cholinesterase enzyme inhibitors that act by interfering with the metabolism of acetylcholine (prevention of hydrolysis). This results in the accumulation of acetylcholine at neuroreceptor transmission sites [2, 5].

Target organs: CNS, muscles, heart [5].

References

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