Preliminary Toxicology Profile Malathion

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(Cythion, Emmatos, Emmatos Extra, Fyfanon, Karbofos, Kop-Thion, Kypfos, Malaspray, Malamar, MLT, Zithio, Mercaptothion, Carbofos, Maldison)

Summary of Use Profile:

1 • SEP 1978

Regulatory Status - No ongoing review of regulatory status (July, 1978)

Chemistry

Malathion is an organophosphate efficacious as a nonsystemic insecticide and acaricide.

Physical Characteristics: clear liquid which may be colorless, yellow, amber or brown. Technical material is at least 95% pure
m.p. = 2.85 C
b.p. = 156 - 157 C
v.p. = 0.00004 mm Hg at 30 C
solubility - 145 ppm in water at 25 C, completely soluble in most alcohols, esters, high aromatic solvents, ketones and vegetable oils. Poor solubility in aliphatic hydrocarbons.

Impurities in technical grade: methyl mercaptan (_ 30 ppm) and iron (_ 10 pp and organophosphates listed below.

		%Concentration	LD_{50}
TES	$(MeO)_2P(S)(SMe)$	1	450
OTE	$(MeO)_2P(O)(SMe)$	0.1	47
ITE	$(MeS)_2P(O)()Me)$	0.02	96

These organophosphate impurities greatly increase the toxicity of technical malathion compared to pure malathion. The marked increase in the LD_{50} of technical malathion (98% compared to less pure technical malathion(95% is due to the potentiation effect of these impurities. Studies by Pellegrini and Santi (1972) show the potentiation of these impurities separately.

Major Formulation: The major formulations are dusts (concentrated and dilut dusts and wettable powders) liquid formulations (emulsifiable liquids as solubilized formulations and oil - based formulations) and other special preparations.

Chemical Properties: Hydrolysis is the most prevalent decomposition reactio It can be degraded by ultraviolet light, but is reasonabley stable at modera temperatures.

Toxicology Summary

Acceptable Daily Intake: The FAO/WHO established A.D.I is 0.02 mg/kg as set in 1966.

The U.S. has established tolerances on many raw agricultural commodities.

Metabolism: Malathion is rapidly absorbed from the gut via passive transpor not related to its oil/water coefficient. Greatest absorption is greatest i the colon and least in the small intestine.

Malathion does not accumulate in body tissues. Small amounts can be detecte in the liver and milk of animals after exposure, but the decreases to zero within several days after cessation of exposure.

Malathion is efficiently excreted via urine principally as desmethyl malathi and mon-and di-acids, or in the feces as dimethyl phosphate, malathion and malaoxon.

Activation of malathion is necessary for inhibition of acethlcholinesterase activity viadesulfuration to malaoxon. Activation occurs in the liver microsomes, possible via a peroxide intermediate.

Detoxification occurs in the mouse liver via the carboxylesterase pathway an via vigorous hydrolysis in liver, kidney and lung (principally by phosphatas the mouse detoxifies 70-80% of malathion within one half hour.

Potentiation of malathion effects have been demonstrated by EPN Administrati The action has been shown to be reduction of activity of malathion's detoxification enzymes by EPN, resulting in a 50-fold increase in malathion toxicit

TOTP (tri-o-tolyo phosphate) increased malathion toxicity almost 100 fold.

Potentiation of malathion by chlordane plus parathion has been reported. Antagonism seems to exist between malathion and aldrin or DDT.

Toxicity

Acute Toxicity

	Route	LD_{50} (mg/kg) Male	Female
rats	oral	1,375-1,845	1000
rats	i.p.	750	
rats	i.v.	50	50
rats	subcutaneous	1,000	
rats	dermal	74,444	74,444
rats	inhalation	LC_{50} mg/l (1hr) 60	

mice	oral	(mixed) 720-3,321	
mice	i.p.	(mixed) 420-815	
mice	inhalation	LC_{50} mg/l (8hr)	15mg/l
guinea pig	Oral	(mixed) 570	
guinea pig	dermal	(mixed) 712,300	
guinea pig	i.p.	(mixed) 500	
dogs	oral	143.5	
rabbits	oral	900	
sheep	oral	150	
(minimum toxic dose = 100 mg/kg)			
dairy cows	oral		560
cattle	oral	200	
dairy calves			80
(minimum toxic dose to calves is 10-20 mg/kg)			

Acute toxicity to chickens is uncertain and appears to vary with age - adults 800 mg/kg; 1 yr. olds: 150-200 mg/kg; 2 to 3 weeks old: 370 mg/kg.

Subacute and Chronic Toxicity

Rats have been fed 5,000 ppm (250 mg/kg) of malathion for 33 days without lethality or any other sign indicating gross toxicity, although blood cholinesterase was depressed. Red blood cell cholinesterase was depressed when 1000 ppm (50 mg/kg) were fed to rats for 6 months. Other signs of toxic were not observed.

Rats have been fed 100,1000 and 5000 ppm (5,50,250 mg/kg) of 65% malathion a 25% wettable powder for 2 years. There was no mortality at any level.

Body weight gain was reduced at 5,000 ppm and blood cholinesterase was reduc at 1000 and 5000 ppm levels.

In another study 500,1000,5000 and 20,000 ppm (25,50,250,1000 mg/kg) of tech 99% malathion as a 25% wettable powder was fed to rats for 2 years. There w marked effects on ChE, growth and food intake at the highest level.

A no-effect level of 100 ppm has been established for rats.

There was significant ChE depression when mice were exposed to 5 ppm (.25 mg for 8 hr/day, five days a week for four weeks in an inhalation chamber.

RBC and plasma ChE activity was depressed when dogs were exposed to aeresol concentrations of 5 ppm daily for 4 weeks.

Malathion levels of 250 and 2,500 ppm have been fed to chickens for 2 years no effect on chicken or eggs. At doses of 5000 ppm for 12 weeks, some letha was observed.

Reproductive Effects

The daily intake of 240 mg/kg of malathion in rats reduced the number of newborn at 7 days of age by 50%. Survivors had decreased body weights and retardation (significant to p .01).

The sperm of swine in the presence of malathion does exhibit reduced mortali with no change in respiration or glycolysis.

Teratogenic Effects
The injection of 900 mg/kg of malathion into pregnant rats on the 11th day d not produce malformation in the yound.

Mutagenic and Oncogenic Effects
No information available.

Effects on Humans
Toxic symptoms have been reported at doses of 71 mg/kg. Survival of doses a high as 1,000 mg/kg are reported when fast thereapeutic action was taken.

Sixteen mg administered for 47 days had no measurable effect. After 56 days of administering 25 mg, blood ChE was decreased by 25%.

Dermal application of 1,5 or 10% dust five times per week for 8 to 16 weeds not decrease blood ChE.

Application of 0.1,1.0 and 10% solutions retained by a dressing for 2 days y sensitization with the highest dose.

In extensive Army tests no effects were noted after 2 weeks of exposure to 1 10% malathion dust.

No toxic manifestations occurred when subjects were exposed 84 times in 42 c secutive days to concentrations of aerosols ranging from 0.15mg to 2.4 gm of actual malathion per 1,000 cubic feet.

Records of occupational exposures suggest no hazard to spray operators or ne residents. The TLV set by the American Conference of Government and Industr Hygienists is 10 mg/m^3. Exposure estimates in spray operations is less than 0.01% the toxic dose.

General Characteristics of Poisoning
The general sequence of poisoning events is characteristic of most organopho phorus compounds-malaise, anoroxia, headache, weakness anxiet, nausea, vomit abdominal pains, wheezing, bradycardia, visual difficulties. In the highly progressive state, bronchoconstriction, pulmonary edema, cyanosis, convulsic prostration and coma occur.

General Reference:

"Initial Scientific and Minieconomic Review of Malathion", March 1975 Substi Chemical Program, OPP/EPA.