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Preliminary Toxicology Profile Malathion

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

Summary of Use Profile:

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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) ₂ P(S)(SMe)	1	450
OTE	(MeO) ₂ P(O)(SMe)	0.1	47
ITE	(MeS) ₂ P(O)()Me	0.02	96

These organophosphate impurities greatly increase the toxicity of technical malathion compared to pure malathion. The marked increase in the LD₅₀ 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 dilute 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 reaction. It can be degraded by ultraviolet light, but is reasonably stable at moderate 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 transport not related to its oil/water coefficient. Greatest absorption is greatest in the colon and least in the small intestine.

Malathion does not accumulate in body tissues. Small amounts can be detected 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 malathion and mono- and di-acids, or in the feces as dimethyl phosphate, malathion and malaaxon.

Activation of malathion is necessary for inhibition of acetylcholinesterase activity via desulfuration to malaaxon. Activation occurs in the liver microsomes, possible via a peroxide intermediate.

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

Potentiation of malathion effects have been demonstrated by EPN Administration. 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 toxicity.

TOTP (tri-o-tolyl 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

<u>Acute Toxicity</u>		<u>LD₅₀ (mg/kg)</u>	
	<u>Route</u>	<u>Male</u>	<u>Female</u>
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 toxicity were not observed.

Rats have been fed 100,1000 and 5000 ppm (5,50,250 mg/kg) of 65% malathion as 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 reduced at 1000 and 5000 ppm levels.

In another study 500,1000,5000 and 20,000 ppm (25,50,250,1000 mg/kg) of technical 99% malathion as a 25% wettable powder was fed to rats for 2 years. There were 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 aerosol concentrations of 5 ppm daily for 4 weeks.

Malathion levels of 250 and 2,500 ppm have been fed to chickens for 2 years with no effect on chicken or eggs. At doses of 5000 ppm for 12 weeks, some lethality 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 mortality with no change in respiration or glycolysis.

Teratogenic Effects

The injection of 900 mg/kg of malathion into pregnant rats on the 11th day did not produce malformation in the young.

Mutagenic and Oncogenic Effects

No information available.

Effects on Humans

Toxic symptoms have been reported at doses of 71 mg/kg. Survival of doses as high as 1,000 mg/kg are reported when fast therapeutic 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 weeks did not decrease blood ChE.

Application of 0.1, 1.0 and 10% solutions retained by a dressing for 2 days did not sensitize with the highest dose.

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

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

Records of occupational exposures suggest no hazard to spray operators or residents. The TLV set by the American Conference of Government and Industrial Hygienists is 10 mg/m³. 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 organophosphorus compounds-malaise, anorexia, headache, weakness, anxiety, nausea, vomiting, abdominal pains, wheezing, bradycardia, visual difficulties. In the highly progressive state, bronchoconstriction, pulmonary edema, cyanosis, convulsions, prostration and coma occur.

General Reference:

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