FENITROTHION

A monograph compiled by

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1.0 Introduction

This monograph has been prepared by the Chemical Control Research Institute, Forestry Service, Department of the Environment, Canada, for the Subcommittee on Pesticides and Related Compounds formed under the direction of the National Research Council of Canada, Associate Committee on Scientific Criteria for Environmental Quality.

The Subcommittee has commissioned at least twelve monographs on pesticides and related compounds including DDT, P.C.B.'s, organophosphorus and carbamate compounds, particularly those pesticides having a wide-scale distribution throughout the environment and either a direct or indirect impact, beneficial or otherwise, with the ecology of Canadian flora and fauna.

This report is further intended to give a comprehensive view of fenitrothion use throughout the world and the author has therefore incorporated a large body of data published by the Food and Agriculture Organization of the United Nations World Health Organization, 1970 in their "1969 Evaluations of Some Pesticide Residues in Food".

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1.1.0 Identity

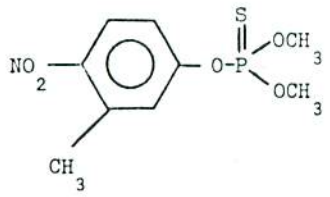
1.1.1 Common Name

Fenitrothion, is recommended by the International Organization of Standardization (ISO).

1.1.2 Chemical Name

O,O-dimethyl *O*-(4-nitro-*m*-tolyl) phosphorothioate

1.1.3 Structural Formula



$C_9H_{12}NO_5PS$

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1.1.4 Alternative Names

O,O-dimethyl *O*-(3-methyl-4-nitrophenyl) phosphorothioate;
Sumithion® (Sumitomo Chemical Co.); S-1102A;
Folithion® (Farbenfabriken Bayer AG); Bayer 41831;
Accothion® (American Cyanamid); Agrothion®; Novathion®; Nuvanol®;
Metathion® (Czechoslovakia);
methylnitrophos (countries in eastern Europe);
Danathion® (Denmark).

1.1.5 History

Introduced in 1959 as an experimental insecticide by the Sumitomo Chemical Co., Japan and independently by Farbenfabriken Bayer AG; described by Nishizawa, Y. 1960, 1961 (a) and protected by Belgian Patents 596,091 (Farbenfabriken Bayer AG), 594,669 (Sumitomo Chemical Co.).

1.1.6 Manufacture

By the reaction of *O,O*-dimethyl phosphorochloridothioate with an alkaline metal salt of 3-methyl-4-nitrophenol (Nishizawa, Y. *et al.* 1961 (b)).

1.1.7 Physical Properties

A yellowish-brown liquid, b.p. 140-145°C at 0.1 mm Hg (decomp.); v.p. 6 x 10^{-6} mm Hg at 20°C; d_4^{25} 1.3227; n_D^{25} 1.5528; soluble in most organic solvents but of low solubility in aliphatic hydrocarbons; insoluble in water, (Spencer 1968).

1.1.8 Chemical Properties

Hydrolised by alkali: half-life in 0.01N NaOH at 30°C, 272 mins. (cf. methyl parathion, 210 mins.). Readily isomerizes on distillation, (Spencer 1968).

1.1.9 Biological Properties

An effective contact insecticide particularly against rice stem borer, *Chilo suppressalis* and spruce budworm, *Choristoneura fumiferana* Clem.; a selective acaricide but of low ovicidal properties. Of low mammalian toxicity; acute oral LD_{50} of technical product for mice, 870 mg/kg; for rats, 250 mg/kg (Schrader, G., 1961); dermal LD_{50} for mice, over 3000 mg/kg; as toxic as parathion to fish, LC_{50} 48 hrs. ca. 2 ppm, (Nishizawa, Y. *loc. cit.*). The lowering of mammalian toxicity by the introduction of methyl group in the *o*-position to the nitro- (and methylthio-) group is discussed with several examples by Schrader (*loc. cit.*), and also by Drabek and Pelikan 1956.

Rats 500 ppm significant inhibition of growth and various cholinergic signs for 2 or 3 weeks. Misu, Y. *et al.* 1966. Decomposed rapidly in tissues to desmethylsumithion, dimethylphosphorothioic acid and phosphorothionic acid. The presence of Sumithion and metabolites in rice is within the permissible limit. Miyamoto, J. *et al.*, 1965.

1.2.0 Formulations

80%, 50%, 10% emulsifiable concentrates; 40% wettable powders; 1.5%, 2%, 3% dusts; and granular formulations.

1.3.0 Analysis

(a) Using method of Averell, D.R. and Norris M.V., 1948, which involves reduction of nitro group to a primary amine, diazotisation and coupling with N-(1-naphthyl)ethylenediamine giving an azo dye which can be determined spectrophotometrically. Dawson, J.A. *et al.*, 1964.

1.3.0 Analysis (Cont'd)

(b) Chromatograph over silica gel using methylene chloride as eluting agent. Evaporate and dissolve residue in carbon disulphide. Measure at 3 absorptions peaks in conjunction with relation minima. Delves, R.B. *et al.*, 1966.

1.3.1 Residue Analysis

Metabolic studies on plants and mammals indicate that residues of fenitrooxon and aminofenitrooxon, when they do form, occur in small amount and are degraded or excreted more rapidly than the parent compound. Once pilot experiments establish that no more than traces of these compounds form on a given crop, there does not seem to be any need to analyse for these compounds on that crop in commerce. (For purposes of this discussion, a trace shall be considered less than 10% of the tolerance level of the parent compound).

Analyses for the *p*-nitrocresol have been made and measurable amounts of the compound are found following good agricultural practice. A determination of the cresol is sometimes reported. However, if a pilot experiment on a given crop shows no excessive amount of the cresol to be present at harvest, there does not appear to be any need for its analysis on that crop in commerce. Other metabolites are generally rather polar and do not tend to be stored.

In essence then, the analyst will be concerned with residues of fenitrothion itself unless pilot treatments indicate that other metabolites should be taken into account. This same view is expressed by Frehse and Mollhoff in a IUPAC report by Egan (1969).

Fenitrothion is so similar to parathion and methyl parathion that analytical methods used for them may be used for fenitrothion. However, many of the earlier methods lack specificity. Numerous procedures for a wide variety of harvest products are based on thin-layer chromatography, spectroscopy and gas chromatography. Information relating to these analyses follow. No reference to inter-laboratory collaborative studies on analytical procedures was found.

1.3.1.1 Extraction and Partitioning

It is not sufficient simply to wash the analytical samples since small amounts of the active ingredient penetrate into the plant. It is therefore important that complete extraction of the insecticide and metabolites (e.g. by exhaustive Soxhlet extraction) be compared against the extraction method used. Harvest products with a high content of water have been macerated with acetone (Horler, 1966; Mollhoff, 1967, 1968), acetonitrile (Coffin and Savary, 1964; Thier and Bergner, 1966), or ethanol (Fischer, 1968). Very good recoveries were obtained by Soxhlet extraction with chloroform-methanol (9:1 v/v) (Bowman and Beroza, 1969). For milk, a combination of polar and nonpolar extractants is required, e.g. acetone-methylene chloride (Bowman and Beroza, 1969), ethanol-hexane (Franz and Kovac, 1965). Extraction with methanol-acetonitrile also proved suitable for milk samples (Miyamoto *et al.*, 1967). For oil-containing harvest products with a low water content, use is made of benzene (Dawson *et al.*, 1964; Horler, 1966), petroleum ether (Kovac and Sohler, 1965), hexane (Horler, 1966), or chloroform (Yuen, 1966). On account of the favourable partition coefficients (Bowman and Beroza, 1965; Kovac, 1963), fats and waxes are best removed by partitioning between hexane and acetonitrile (Franz and Kovac, 1965; Miyamoto *et al.*, 1967; Mollhoff, 1967; Bowman and Beroza, 1969).

1.3.1.2 Qualitative Analysis

Although no reports of fenitrothion being separated from similar residues by column chromatography have been noted, separation is possible with thin-layer or gas chromatography. Interfering active ingredients are parathion, parathion-methyl, malathion, and fenthion and the resolution is just sufficient for distinguishing fenitrothion from these active ingredients (see e.g. Mollhoff, 1968). By comparing gas chromatograms recorded with a phosphorus detector and an electron capture detector, fenitrothion can often be clearly differentiated from malathion and fenthion owing to differences in sensitivity.

1.3.1.3 Colorimetry

Colorimetric determinations are carried out by the method of Averell and Norris (1948), or by determination of the cresol after

1.3.1.3 Colorimetry (Cont'd)

saponification of the active ingredient with alkali. The limits of determination are about 0.05 ppm.

1.3.1.4 Thin-layer Chromatography

Thin-layer chromatography has been used for clean-up of the extracts with final determination by colorimetry after deleting the appropriate spot from the plate, or for direct determination on the plate after spraying. Quantitative evaluation is possible in the first instance; in the second, the evaluation is semi-quantitative and more suitable for confirming identity. About 0.1 ppm of fenitrothion can be determined in most harvested products. Determination of lesser amounts is possible with procedures utilizing cholinesterase inhibition (Ackermann, 1966; Mendoza *et al.*, 1968; Schutzmann and Barthel, 1969; Winterlin *et al.*, 1968).

1.3.1.5 Column Chromatography

For extract clean-up or separation of metabolites, columns are suitable, especially those packed with deactivated silica gel (Bowman and Beroza, 1969); deactivated Florisil (Mollhoff, 1967, 1968), or deactivated acid aluminum oxide (Horler, 1966). Columns packed with active Florisil (Beckman and Garber, 1969), magnesium oxide (Coffin and Savary, 1964), polyethylene-impregnated aluminum oxide (Coffin and Savary, 1964), and Sephadex LH_{20} (Horler, 1968; Ruzicka *et al.*, 1968) have also been used.

1.3.1.6 Gas Chromatography

The most reliable and highly sensitive methods for fenitrothion utilize gas chromatography with either the flame-photometric (Bowman and Beroza, 1969) or the thermionic detector (Miyamoto *et al.*, 1967, Sato *et al.*, 1968). These detectors respond to the phosphorus in the molecule with very high specificity. No clean-up is usually required with the flame-photometric detector when analysing for either fenitrothion or its oxygen analogue unless a fatty food is being analysed. In this case a simple hexane-acetonitrile partition is used. A clean-up was used with the thermionic detector but it may often be omitted. Limit of determination is usually 0.01-0.001 ppm.

1.3.1.6 Gas Chromatography (Cont'd)

In the analysis for fenitrooxon a separation from fenitrothion on silica gel is used. The compound is then determined by gas chromatography (Bowman and Beroza, 1969) of enzymatically (Miyamoto *et al.*, 1967). The cresol is determined by electron-capture gas chromatography (Bowman and Beroza, 1969) or colorimetrically (Miyamoto *et al.*, 1967) after column separation. Analysis of fenitrothion, fenitrooxon, and the cresol by electron-capture gas chromatography is possible (Bowman and Beroza, 1969; Dawson *et al.*, 1964; Horler, 1966; Mollhoff, 1967) but less specific; sensitivity, about 0.1 ppm, can be improved with a suitable clean-up.

1.3.1.7 Determination of Metabolites

Gas chromatographic methods have been described for the simultaneous determination of fenitrothion, fenitrooxon (Bowman and Beroza, 1969; Mollhoff, 1968), 3-methyl-4-nitrophenol (Bowman and Beroza, 1969; Miyamoto *et al.*, 1967) and the amino compound of fenitrothion (Miyamoto *et al.*, 1967). As noted, for market controls determination of fenitrothion is generally sufficient (Mollhoff, 1968).

2.0 Uses

2.1.0 World-wide Registrations

(Listed in tabular format on the following pages as reported by Sumitomo Co.).

EUROPE

Country	Target	Insect		Registration	Dosage & Effectiveness	With-holding Period	Brand Name
		English Name	Scientific Name				
Spain	vegetable	aphids	*Aphis*	registered	0.05-0.1% a.i.	3 weeks	SUMIKANE
		miner caterpillar		"	"		SUMIFENE
							SMT-ZELTIA
	citrus	aphids	*Aphis*	registered	0.05-0.1% a.i.	3 weeks	NILARON
		mealybugs	*Pseudococcus*	"	"		SUMITHION
		purplescale	*Lepidosaphes-beckii*	"	"		
	fruit	mealybugs	*Pseudococcus*	registered	0.05-0.1% a.i.	3 weeks	
		aphids	*Aphis*	"	"		
		red louse		"	"		
		purplescale	*Lepidosaphes-beckii*	"	"		
		minor caterpillar		"	"		
	rice	rice stem borer	*Chilo suppressalis*	procedures for registration: being proceeded	effective at 0.05-0.1% a.i.		
Portugal	vegetable	aphids	*Aphis*	registered	0.05-0.1% a.i.	3 weeks	SUMITIAO
		miner caterpillar		"	"		SUMITHION
	citrus	aphids	*Aphis*	registered	0.05-0.1% a.i.	3 weeks	
		mealybugs	*Pseudococcus*	"	"		
		purplescale	*Lepidosaphes beckii*	"	"		
	fruit	mealybugs	*Pseudococcus*	registered	0.05-0.1% a.i.	3 weeks	
		aphids	*Aphis*	"	"		
		red louse		"	"		
		miner caterpillar		"	"		

	cotton	aphids	*Aphis*	registered		3 weeks	
	cocoa		*Coccus viridis*	registered		3 weeks	
	coffee		*Saissetia coffeae*	registered		3 weeks	
			Diarthro thrips coffeae	"			
			Thliptoceras octoguttale	"			
		coffee leaf miner	*Leucoptera caffeina*	registered			
	pasture			registered		10 days	
France	public health	houseflies		registered	0.6-1.2g a.i./m^2		SUMIFENE
		mosquitoes		"	1g a.i./m^2		
	fruit tree	aphids	*Aphis*	registered	0.05% a.i.	15 days	
	vegetable	aphids	*Aphis*	registered	0.05% a.i.	15 days	
	horticultural crop	aphids	*Aphis*	registered	0.05% a.i.		
Holland	cereals	wheat stem gall midge	*Haplodiplosis equestria*	registered	500g a.i./ha	(tolerance) 0.5 ppm	FENICID AAFFENITON TOKIFOS
	orchard	leaf miners	*Lithocolletis ringoniella*	registered	0.05% a.i.	(tolerance) 0.5 ppm	
		caterpillars		"	"		
		aphids	*Aphis pomi*	"	"		
		sawflies	*Hoplocampa testudinea*	"	"		
Denmark	beets		*Pegomyia hyoscyami*	registered	1.5ℓ of Sumithion 50% EC/hectare	2 weeks	SUMITHION
			Aphis fabae	"	"		
	rape		*Meligethes aeneus*	registered	1.5ℓ of Sumithion 50% EC/hectare	2 weeks	
			Ceutorrhynchus assimilis	"	"		

	clover		*Apion spp.*	registered	1.5ℓ of Sumithion 50% EC/hectare	2 weeks	
	apple	apple aphid	*Aphis pomi*	Practically being used	0.1-0.15% a.i.		
		codling moth	*Carpocapsa pomonella*	"	"		
			Hoplocarpa testudinea	"	"		
			Orchestes fage	"	"		
			Ametastegia glabrata	"	"		
			Anthonomus pomorum	"	"		
	peas		*Aphis*	registered	0.1-0.15% a.i.	2 weeks	
			Physopus robusta	"	"		
Sweden	peas		*Physopus robusta*	registered	1ℓ of Sumithion 50% EC/hectare	10 days	SUMITHION
			Macrosiphum pisi	"	"		
			Grapholitta nigricana	"	"		
			Sitona lineata	"	"		
	rape		*Thrips angusticeps*	registered	1ℓ of Sumithion 50% EC/hectare	10 days	
			Ottalia spinarum	"			
			Meligethes aeneus	"	"		
			Eurydema oleracea	"	"		

	wheat barley horticultu- ral crop	aphids weevils thrips	*Hoplodiplosis equestris*	registered Practically being used	1ℓ of Sumithion 50% EC/hectare	10 days

AFRICA

Country	Target	Insect		Registration	Dosage & Effectiveness	With-holding Period	Brand Name
		English Name	Scientific Name				
S. Africa	public health	bed bugs		registered			RESKOL
E. Africa	coffee	coffee leaf miner	*Leucoptera coffeella*	registered	1.5 pints in 100 gallons water/acre	no stipulated period	SUMITHION
		antestia bug	*Antestiopsis lineaticollis*	"	1 pint in 100 gallons water/acre		
		lace bug		"	"		
	mango	red banded thrips		registered	0.5 pint in 40 gallons water/acre	one week	
	cereals	aphids		registered	0.5 pint in at least 20 gallons water/acre		
	public health	bed bugs		registered	1 oz/5gln water		
		cockroaches		"	5 oz/ " "		
		flies		"	5 oz/ " "		
		mosquitoes		"	1 oz/ " "		
W. Africa	cocoa	cocoa mirid	*Sahlbergella singularis*	registered	2 ozs in 5 gallon/100 trees		
			Distantiella theobroma	"	500 trees/acre		
Egypt	cotton	Egyptian cottonworm	*Prodenia litura*	registered	2 kg a.i./acre		SUMITHION

AMERICA

Country	Target	Insect		Registration	Dosage & Effectiveness	With-holding Period	Brand Name
		English Name	Scientific Name				
Canada	forest	spruce bud-worm	*Choristoneura fumiferana*	large scale test:executed	4-6 a.i. oz./acre		ACCOTHION SUMITHION
Central America	coffee	coffee leaf miner	*Leucoptera coffeella*	registered			SUMITHION
Argentina	pasture	tucura (wingless grasshopper)	*Dichroplus sp.*	registered	125g a.i./ha		SUMITHION
	peach	codling moth	*Carpocapsa pomonella*	registered	0.065% a.i.		
		green peach aphid	*Myzus persicae*	"	0.05-0.055% a.i.		
	pear	codling moth	*Carpocapsa pomonella*	registered	0.065% a.i.		
			Chermes pyricola	"	0.05% a.i.		
	citrus	greenhouse thrips	*Heliothrips haemorrhoidalis*	registered	0.05% a.i.		
	onion	thrips	*Thrips tabaci*	registered	0.04-0.05% a.i.		
	bean	thrips	*Hercothrips fasciatus*	registered	0.04-0.05% a.i.		
	tomato	thrips	*Frankliniella paucispinosa*	registered	0.04-0.05% a.i.		
	gladiolus	thrips	*Taeniothrips simplex*	registered	0.04-0.05% a.i.		
Brazil	chicken	poultry mite		registered	0.05-0.1% a.i.		SUMITHION
	vegetable	aphids		registered			
		thrips		"			

fruit	fruit flies		registered	
rice	rice stink bug		registered	
cotton	cotton aphids	*Aphis*	registered	0.01-0.015% a.i.
	cotton bug	*Dysdercus*	"	0.01-0.15% a.i.

OCEANIA

Country	Target	Insect		Registration	Dosage & Effectiveness	With-holding Period	Brand Name
		English Name	Scientific Name				
Australia	pasture	grass grub	*Oxycænus fuscomaculatus*	registered	18 oz a.i./acre		
		sitona weevil	*Sitona humeralis*		1/2 lb a.i./ acre		
		corbie	*Oncopera intricata*		1-1.25 pints of 50 EC/acre		
	clover	clover seed moth	*Coleophora alcyonipennella*	registered	2-3 sprays commencing at flowering at 6 oz a.i./acre		
	fruit	fruit fly		registered			
New Zealand	pasture	porima moth	*Wiseana cervinata*	registered	0.5-1 lb a.i./ acre	2 weeks (for EC formula-tions) 1 week (for 5% granules	FENITE

ASIA

Country	Target	Insect		Registration	Dosage & Effectiveness	With-holding Period	Brand Name
		English Name	Scientific Name				
Japan	rice	rice stem borer	*Chilo suppressalis*	registered	0.025-0.06% a.i.		SUMITHION
		paddy borer	*Tryporyza incertulas*	"	0.05-0.06% a.i.		
		green rice leafhopper	*Nephotettix cincticeps*	"	0.05% a.i.		
		smaller brown planthopper	*Laodelphax striatellus*	"	"		
		southern green stink bug	*Nezara viridula*	"	"		
		smaller rice leaf miner	*Hydrellia griseola*	"	0.02% a.i.		
		rice green caterpillar	*Naranga aenescens*	"	0.0125-0.02% a.i.		
	bean	soy bean pod borer	*Grapholitha glycinivorella*	registered	0.033-0.05% a.i.		
	vegetable	aphids	*Aphis*	registered	0.025-0.05% a.i.		
		thrips		"	0.05-0.055% a.i.		
		large 28-spotted lady beetle	*Epilachna vigintio-ctomaculata*	"	0.025-0.05% a.i.		
	fruit	aphids	*Aphis*	registered	0.025-0.05% a.i.		
		peach leaf miner	*Lyonetia clerkella*	"	"		

		oriental fruit moth	*Grapholitha molesta*	registered	0.05% a.i.	
		peach fruit moth	*Carposina niponensis*	"	"	
		comstock mealybug	*Pseudococcus comstocki*	"	"	
		Japanese pear lace bug	*Stephanitis nashi*	"	"	
		aster leafhopper	*Macrosteles fascifrons*	"	0.025-0.05% a.i.	
	grape	grape clearwing moth	*Paranthrene regale*	registered	0.025-0.05% a.i.	
		small grape plume moth	*Stenoptilia vitis*	"	"	
	tea	smaller tea tortrix	*Adoxophyes orana*	registered	0.05-0.07% a.i.	
		tea leaf miner	*Melanagromyza theae*	"	"	
Ryukyu	sugarcane	oriental chinch bug	*Canelerius saccharivorus*	registered	0.05-0.1% a.i.	SUMITHION
		sugarcane cottony aphid	*Ceratovacuna lanigera*	"	"	
		sugarcane shoot borer	*Eucosma schistaceana*	"	0.1% a.i.	
		pink borer (purplish stem borer)	*Sesamia inferens*	"	"	
	rice	rice stem borer (asiatic rice borer)	*Chilo suppressalis*	registered	0.05-0.1% a.i.	
		green rice leafhopper	*Nephotettix cincticeps*	"	0.05% a.i.	

		yellow rice borer (paddy borer)	*Tryporyza incertulas*	registered	0.1-9.125% a.i.	
		southern green stink bug	*Nezara viridula*	"	0.1% a.i.	
		rice leaf roller	*Susumia exigua*	"	0.1-0.125% a.i.	
	fruit	citrus leaf miner	*Phyllocnistis citrella*	registered	0.066-0.1% a.i.	
		arrowhead scale	*Unaspis yanonensis*	"	0.1% a.i.	
	pineapple	pineapple mealybug	*Dysmicoccus brevipes*	registered	0.1% a.i.	
	sweet potato	black marmorated leafhopper	*Nesophrosyne ryukyuensis*	registered	0.1% a.i.	
	tobacco	tobacco cutworm	*Prodenia litura*	registered	0.1% a.i.	
	vegetable	common white (common cabbageworm)	*Pieris rapae crucivora*	registered	0.1% a.i.	
		tobacco cutworm	*Prodenia litura*	"	"	
		diamond-black moth	*Plutell macutipennis*	"	"	
	pig (parasite)	intestinal thread worm	*Strongyloides ransomi*	registered	120mg a.i./m^2	
Korea	rice	rice stem borer	*Chilo suppressalis*	registered	0.05-0.025%	SUMITHION
		smaller brown planthopper	*Delphacodes striatella*	"	"	

		green rice leafhopper	*Nephotettix cincticeps*	registered	0.05-0.025%		
	fruit	peach fruit moth	*Carposina niponensis*	registered	0.05-0.025%		
		apple leaf roller	*Cacoecia xylosteana*	"	"		
		woolly apple aphid	*Eriosoma lanigerum*	"	"		
	vegetable	aphids	*Aphis*	registered	0.05-0.025%		
		diamond-black moth	*Plutella maculipennis*	"	"		
		cabbage armyworm	*Barathra brassicae*	"	"		
	forest	pine caterpillar	*Dendrolimus spectabilis*	registered	0.05-0.025%		
		pine leaf gall midge	*Thecodiplosis pinicols*	"	"		
	domestic animals	ticks			0.05-0.25% a.i. 50-100ml/m^2		
		places infested with maggots			0.025-0.0125% a.i. 1-2l/m^2		
		places where flies and mosquitoes breed			0.5% a.i. 25-50l/m^2		
Formosa	rice	yellow rice borer	*Schoenobius incertulas*	registered	0.8-1.5ℓ (50 EC)/ha 0.05% a.i.	3 weeks	SUMITHION
		rice stem borer	*Chilo suppressalis*	"	1.2-1.5ℓ (50 EC)/ha 0.05% a.i.		
	soy bean	soy bean pod borer	*Naruca testulalis*	registered	0.6-1.2ℓ (50 EC)/ha 0.025-0.05% a.i.		

		southern green stink bug	*Nezara viridula L.*	registered	1.2ℓ (50 EC)/ ha		
	vegetable	southern green stink bug	*Nezara viridula L.*	registered	0.05% a.i.	10 days	
	sugarcane	sugarcane shoot borer	*Eucosma schistaceana*	registered	0.05% a.i.		
		pink borer	*Sesamia inferens*	"	"		
	banana	banana mealy-bug	*Dysmicoccus brevipes*	registered	0.05% a.i.		
	litchi	fruit worm	*Acrocercops cramerella*	registered	0.05% a.i.	10 days	
		lac insect	*Laccifer lacca*	"	"	2 weeks	
	tobacco	green peach aphid	*Myzus persicae*	registered	0.05% a.i.		
C. China	rice	rice stem borer	*Chilo suppressalis*	practically being used			SUMITHION
S. Vietnam	rice			practically being used			SUMITHION
Indonesia	rice			practically being used			SUMITHION
Thailand	cotton			practically being used			SUPRATHION
Pakistan	cotton	bollworm		standardized	0.15-0.2% a.i.		SUMITHION
		jassids		"	0.05-0.1% a.i.		
		white flies		"	"		
	rice	leaf rollers		standardized	0.05-0.1% a.i.		
		paddy borer		"	1.5 lb a.i./acre		
	sugarcane	aphids					
		top borers		standardized	0.1-0.15% a.i.		
		stem borers		"	"		
		leafhopper		"	"		
		jassid		"	"		
		pyrilla		"	"		

	jute	hairy caterpillar		standardized	0.1-0.15% a.i.	
		weevils		"	"	
		semi-looper		"	"	
		apion		"	"	
	orchard	mango hopper		standardized	8 ozs a.i./acre	
		mealy bugs		"	"	
		hairy caterpillar		"	"	
		scales		"	16-20 ozs a.i./acre	
		aphids				
Ceylon	rice	thrips	*Thrips oryzae*	registered	12 ozs a.i./acre	
		leafhopper	*Nephotettix bipunctatus*	"	30 fl. ozs (50 EC) in a suitable quantity of water per acre	
			Hydrellia	"		
	pineapple	mealybug	*Pseudococcus brevipes*	registered	1 fl. oz. (50 EC) in 5 glns. of water sprayed at high volume	
India	rice	paddy jassids	*Nephotettix spp.*	registered	0.05% a.i.	SUMITHION
		paddy stem borer		"	"	
	gram	gram podborer	*Heliothis sp.*	registered		
	livestock	poulty lice		registered		
		cattle ticks		"		

U.S.S.R. & EAST EUROPE

Country	Target	Insect		Registration	Dosage & Effectiveness	With-holding Period	Brand Name
		English Name	Scientific Name				
U.S.S.R.	fruit	codling moth	*Carpocapsa pomonella*	registered			SUMITHION
		aphids	*Aphis sp.*	"			
		San Jose scale	*Aspidiotus pernyciosus*	"			
	wheat	wheat bug	*Eurigaster integriceps*	large scale test: being executed			
Poland	apple	small moth	*Cacoesina rosana*	registered			OWADOFOS
	pear	codling moth	*Carpocapsa pomonella*	registered			
		pear fruit sawfly	*Hoplocampa pyricola*	"			
		aphids	*Aphis sp.*	"			
		apple blossom weevil	*Anthonomus pomorum*	"			
	cherry	cherry fruit fly	*Rhogoletis pomonella*	registered			
	plum	codling moth	*Carpocapsa pomonella*				
		aphids	*Aphis sp.*	registered			
		red plum maggot	*Laspeyresia juvebrana*	"			
	vegetables	cabbage caterpillar	*Pieris brassicae*	registered	50% E.C. 20 kg/ha		
		thrips	*Thrips sp.*	"	"		
		aphids	*Aphis sp.*	"	"		

	beans	pea moth	*Laspeyresia nigricana*	registered		
	clover	weevils	*Apion sp.*	registered		
		aphids	*Aphis sp.*	"		
	beet	spinach leaf miner	*Pegomya hyoscyami*	registered		
	red radish	"	"	registered		
Hungary	fruit	codling moth	*Carpocapsa pomonella*	procedures for registration: being proceeded		SUMITHION
	vegetables	Colorado potato beetle	*Leptinetarsa decemlineata*	"		
Rumania	fruit	hemp moth	*Grapholitha delineania*	registered	0.04% a.i.	SUMITHION
		aphids	*Aphis sp.*	"	"	
	vegetable horticultural crop	aphids	*Aphis sp.*	registered	0.04% a.i.	
		aphids	*Aphis sp.*	registered	0.04% a.i.	

2.1.1 Use Pattern

Fenitrothion is a broad-spectrum insecticide having a much lower acute mammalian toxicity than many similar organophosphorus insecticides. Its action is by direct contact or as a stomach poison. It can be applied as an emulsifiable concentrate, wettable powder, granular formulation or dust on agricultural crops.

It is toxic to bees having an LD_{50} of 0.383 µg/Bee (Atkins *et al.*, 1970) and should not be sprayed on flowering crops.

Fenitrothion can be combined with all conventional insecticides and fungicides except those having an alkaline reaction.

The insecticide has been used throughout Europe, East Pakistan, East Africa, United Arab Republic, Japan, Republic of China, New Zealand, Brazil and in Canada against forest insect pests. It is not registered for use in the United States.

2.1.2 Pre-harvest Treatments

Fenitrothion is used on a wide variety of crops including fruits, field crops, vegetables, rice, cotton, cereals, cocoa, tea, and coffee for control of stem borers, hoppers, leaf miners, leaf rollers, whiteflies, fruit flies, mealybugs, mirids and bugs, thrips, aphids, mites, lady beetles, caterpillars, and soft scale insects.

The recommended concentrations and rates of application vary for the different crops and pest species to be controlled. Concentrations of sprays range from 0.05 to 0.1% active ingredient (a.i.) and rates of application from 0.5 to 2.0 kg a.i./hectare. The chemical is generally tolerated by most crops although high dosages may injure cotton, and phytotoxicity on Brassica crops and orchard fruits has been encountered.

Safety intervals prior to harvest range from 10 to 21 days and differ depending on the country and the crop. Pre-harvest treatments are not required in forestry uses for defoliator pests.

2.1.3 Post-harvest Treatments

No post-harvest treatments are made in Europe. Admixture of 1 to 5 ppm of fenitrothion has been recommended to protect grains such as rice, wheat, and barley for months against various weevils and beetles.

2.1.3 Post-harvest Treatments (Cont'd)

Bag treatment is acceptable in Brazil for protecting stored grains and post-harvest treatments are under development in various countries.

2.1.4 Other Uses

Fenitrothion is used to control grasshoppers, locusts, and caterpillars on pastures and defoliators in forests. It also provides control of household and other pests, such as mosquitoes and their larvae, houseflies, cockroaches, lice, bedbugs, and poultry mites. Its action is rapid, and its residual activity is good.

2.2.0 Registered Uses in Canada

Fenitrothion has been used since 1969 in place of DDT for operational control of lepidopterous defoliators in Canadian forests. Fenitrothion will control, spruce budworm (*Choristoneura fumiferana* Clem.) at an economic dosage of 2 - 4 ounces/acre applied by aircraft, without causing any gross damage to forest plants, mammals, birds or fish (Fettes, 1968).

The pesticide is registered for forest use only, against spruce budworm, hemlock looper (*Lambdina fiscellaria* Guenée) and sawfly species and may only be used following consultation with regional forestry officials. The applied dosage may not exceed 6 ounces/acre of active ingredient in total (Canada Department of Agriculture, 1968). Appropriate use directions, dosage rates, and timing of applications vary, depending upon location, size of control program, degree of infestation and proximity of fish-bearing streams, as well as wildlife populations.

In 1970, approximately 5 million acres of forest lands were sprayed to control the spruce budworm, the primary insect pest of Canadian eastern forests (Canada Department of Agriculture, 1971). In 1971, the total area sprayed amounted to some 7.2 million acres.

There are currently (1972) five registrations for fenitrothion in Canada to several companies, e.g. Cyanamid of Canada Limited, Chemagro Limited, Sumitomo Chemical Co. Limited and Ciba-Geigy Limited.

3.0 Movement Within the Environment

3.1.0 Atmosphere

3.1.1 Effect of Method of Application

All forest spraying is done by aerial application due to the vast regions involved. The safe application of pesticides in the forest environment calls for minimum dosage of chemicals combined with appropriate timing of the pest population. This optimum dosage has proven to be 2 - 4 ounces/acre distributed by aircraft equipped with Tee-jet nozzles and affording a droplet size of 100μ for fenitrothion, Randall 1970.

3.1.2 Effect of Environmental Conditions on Drift and Deposit

Workers of the Agricultural College at Davis, California have studied the drift and deposit of insecticides and herbicides applied aerially to agricultural lands. They have shown that the deposit of a cloud of insecticide is affected most by the strength of the temperature inversion and that there is a relationship between the strength of the inversion and the proportion of insecticide which falls to the ground. The drift of the insecticide cloud from the target area is also affected by the strength of the temperature inversion and also by the amount of cross-wind at the time of application.

Field studies (Armstrong and Randall, 1969) carried out by members of the Chemical Control Research Institute have shown that the same correlation exists between the strength of inversion over a forested area and the proportion of fenitrothion which reaches the forest floor. These studies have shown that it is the degree of inversion in the zone above the trees which is the major factor in affecting the amount of insecticide which falls to the ground. Field observations of spray schemes in which fenitrothion was applied using aircraft have shown that anywhere from 15 - 75% of the insecticide emitted from the aircraft will reach the target when applied under an inversion condition. With insecticide applied under unstable or lapse conditions the amount of material which reaches the target may be reduced to as little as 1.4% of the emitted material.

3.1.3 Water and Terrestial Movement

The use of fenitrothion in the operational spraying of Canadian forests has not been in progress long enough to adequately evaluate the distribution of residues in forest soils and watersheds. Nevertheless monitory studies on sprayed foliage have shown that the pesticide has a half-life of about 4 - 5 days, and a maximum persistence in the soil of 64 days, Yule 1971.

3.2. Biological Uptake

3.2.1 Animals

3.2.2 Absorption, Distribution and Excretion

Various comprehensive studies in mouse, rat, and guinea-pig have dealt with the pharmacodynamic and biochemical aspects of fenitrothion and its metabolites (Nishizawa *et al.*, 1961; Miyamoto, 1964a, 1964b, 1969; Miyamoto *et al.*, 1963a; Vandanis and Crawford, 1964; Hollingworth *et al.*, 1967; Hladka and Nosal, 1967 and Douch *et al.*, 1968).

Fenitrothion is presumably rapidly absorbed from the marmalian intestinal tract as evidenced by the appearance of radioactivity in blood from guinea-pigs and rats administered phosphorus - labelled fenitrothion orally. The presence of the oxygen analogue was demonstrated in all tissues examined (brain, heart, lung, liver, kidney, spleen and muscle) and it was detectable in blood one minute after an intravenous injection of fenitrothion. This oxygen analogue (II of Fig. 1) is the important metabolite with respect to toxicity. It is formed in the microsomal fraction of the cell, the main organs responsible for the transformation being the liver and kidney. Fenitrooxon is further metabolized as indicated in Fig. 1. The major excretion product found is 3-methyl-4-nitrophenol (VII) which can further be oxidized to 3-carboxy-4-nitrophenol (VIII). Other metabolites are the demethyl-derivatives (V and VI) which, with increasing doses, are excreted in increasing amounts. A total of nine metabolites has been isolated, the majority of which can also be identified. *In vitro* studies showed that formation of the oxygen analogue (II) was dependent on the availability of reduced nicotine adenine dinucleotide phosphate ($NADPH_2$) and oxygen. Liver slices incubated

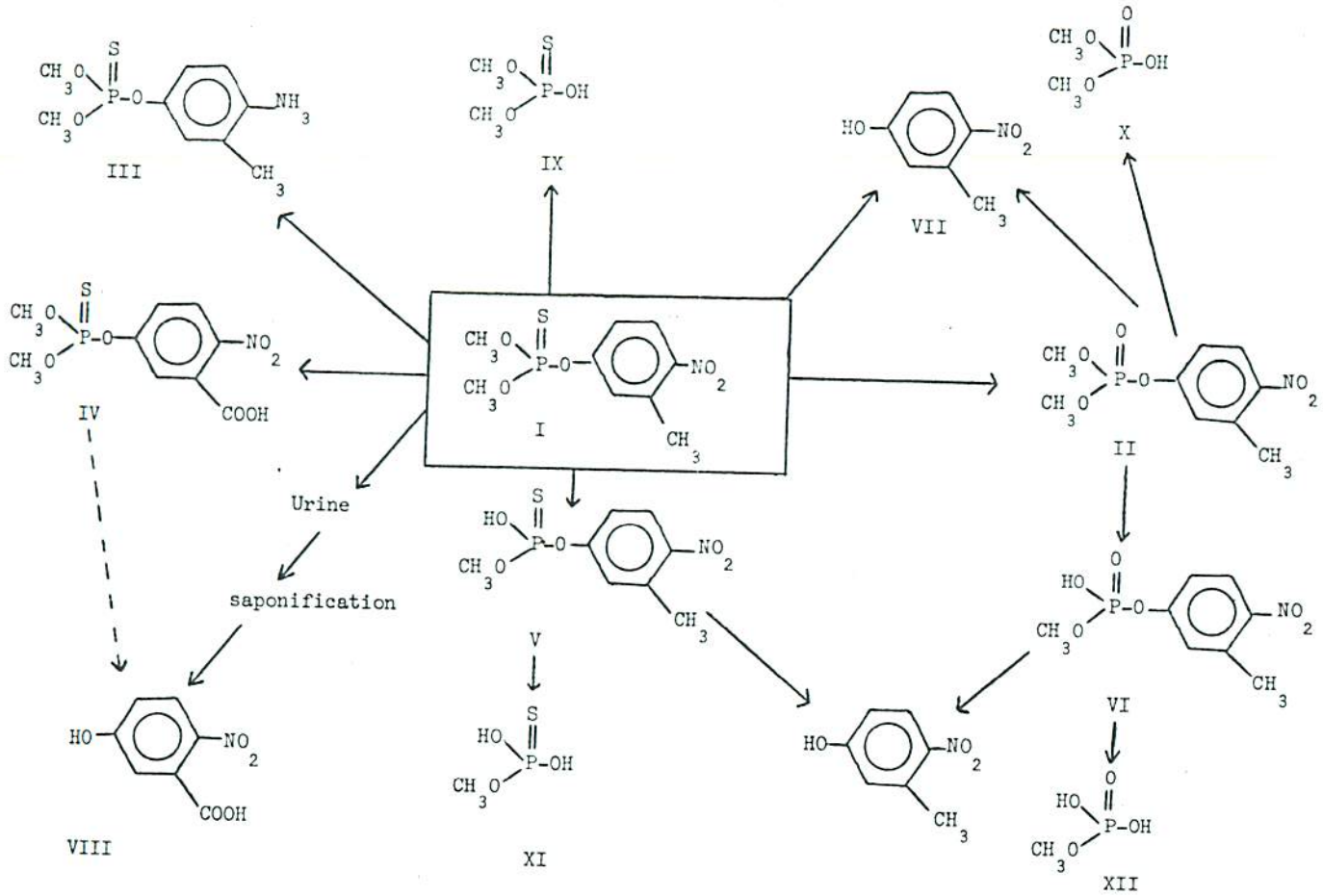

Figure 1.
Metabolism of fenitrothion

3.2.2 Absorption, Distribution and Excretion (Cont'd)

with fenitrothion did not produce measurable amounts of fenitrooxon, while liver homogenates and the supernatant fraction of such homogenates showed appreciable activation of added fenitrothion. No correlation between the toxicity and rate of formation of the oxygen analogue could, however, be demonstrated (Miyamoto *et al.*, 1963a; Miyamoto, 1969).

No observations are available in these studies on the distribution into fatty tissues: however, residue studies on milk, meat and fat from cattle indicate amounts of approximately 0.001 ppm in these samples (Miyamoto and Sato, 1969).

Fenitrothion and its metabolites are excreted mainly in the urine (90 - 95%). Up to 10% was recovered in feces. Within three days nearly complete recovery of an orally administered dose (15 mg/kg) could be obtained. The metabolic pattern of fenitrothion as it appears from these studies is shown in Fig. 1. The ratios between the amounts of metabolites was dependent upon the dose given, as is shown in Table 1, which gives the percentage distribution of metabolites in mouse urine after various doses of fenitrothion (Hollingworth *et al.*, 1967).

3.2.2 Absorption, Distribution and Excretion (Cont'd)

TABLE I

Percentage Distribution of Metabolites of Fenitrothion in Mouse Urine After Administering Various Doses*

Metabolite	Percentage of radioactive metabolite excreted in urine after giving P^{32} - labelled fenitrothion at the indicated dose levels in mg/kg body weight			
	3	17	200	850
Phosphate acid	2.0	2.4	1.9	1.2
Methylphosphoric acid	1.5	2.5	2.4	1.1
Dimethylphosphoric acid	32.2	21.4	5.8	3.0
Dimethylphosphorothioic acid	12.8	20.3	8.7	6.6
Phosphate analogue (II)	2.7	1.6	3.3	2.5
O-demethylphosphate analogue (VI)	26.1	28.4	24.6	17.1
O-demethylphosphorothioate analogue (V)	20.5	20.1	50.9	66.1
Unknown	2.2	2.5	2.4	2.4

* Hollingworth *et al.*, 1967.

3.2.3 Effect on Enzymes and Other Biochemical Parameters

As with other organophosphorus compounds fenitrothion acts in the animal organism as a cholinesterase inhibitor, probably after conversion to the oxygen-analogue. Some evidence presented indicates that the cholinesterase inhibiting effect in brain depends more on the rate of penetration into the brain than on the rate of oxidation and decomposition of fenitrothion (Miyamoto, 1969).

3.2.4 Plants

3.2.5 Residues Resulting from Supervised Trials

Typical maximum residues after treatment of a variety of crops are given in Table II.

TABLE II

Maximum Residues After Treatment of Crops

Crop	Dosage active ingredient	Pre-harvest interval days	Maximum residues at harvest, ppm respectively	Reference
Rice	1000 g/ha	41	0.005	Sumitomo 1969
Rice	0.07% spray or 5% granules	1-2 months	n.d.	Miyamoto, Sato 1965
Apple	0.05% spray	21	0.05	Sumitomo 1969
Apple	0.2% spray	7 and 14	0.5 and 0.35	Bayer 1969
Apple, Golden	0.15% spray	10 and 15	1.0 and 0.75	Bayer 1969
Cherry	0.2% spray	7 and 14	0.5 and 0.2	Bayer 1969
Grape*	0.05% spray	10	0.50	Sumitomo 1969
Tomato*	0.05% spray	7	0.18	Sumitomo 1969
Cocoa	0.1% spray	14	0.10	Miyamoto *et al.*, 1965b
Red cabbage	0.15%; 1000 l/ha	7	Outside leaves 0.65 Cabbage less outside leaves 0.25	Bayer 1969
Sugar beets	0.15%; 1000 l/ha	8	n.d.	Bayer 1969
Green tea	0.1% spray	14	0.27	Sumitomo 1969
Cauliflower	0.1%; 1000 l/ha	7	n.d.	Bayer 1969
Lettuce	0.1%; 1000 l/ha	7 and 14	1.05 and 0.3	Bayer 1969
Lettuce	0.05%; 600 l/ha	1, 7, and 14	0.65, 0.06, 0.01	Mollhoff 1968
Peas and pods	0.25%; 560 l/ha	0 and 5	0.7 and <0.15	Bayer 1969

* These green-house trials gave residues higher than those of field trials.

3.3.0 Elimination

3.3.1 Metabolism

Fenitrothion may be metabolised as shown in Figure 1. The major route in animals appears to be through splitting of the P-O-aryl bond to give the corresponding dimethyl esters of phosphorothioic and phosphoric acids. Another means of degradation is demethylation of the methoxy group to give desmethyl fenitrothion. Although formation of the oxygen analogue, fenitrooxon, is minor compared to products formed via hydrolysis, fenitrooxon must be taken into account because the mammalian toxicity of oxons is generally much higher than that of parent thiono pesticides. In plants the metabolism of fenitrothion appears to be similar to that in animals.

3.3.2 Excretion

3.3.2.1 Animals

Orally administered ^{32}P-labelled fenitrothion was readily absorbed from the digestive tract of guinea pigs or rats and the major portion of the radioactivity excreted in the urine. Neither fenitrothion nor fenitrooxon was detected and desmethyl fenitrothion, dimethyl phosphorothioic and dimethyl phosphoric acids were identified in the urine (Miyamoto *et al.*, 1963a).

Following intravenous injection of radioactive ^{32}P fenitrothion into guinea pigs and rats, fenitrothion rapidly disappeared from the blood. Fenitrothion and fenitrooxon were found in the tissues, and their amounts decreased rapidly. The desmethyl compound and the dimethyl esters mentioned in the foregoing paragraph were found mostly in the liver and kidneys (Miyamoto, 1964a).

Excretion of metabolic products is rapid and chiefly in the form of 3-methyl-4-nitrophenol (the nitrocresol hydrolysis product) (Hladka and Nosal, 1967; Nosal and Hladka, 1968); the cresol methyl may be oxidized to COOH (Douch *et al.*, 1968). The desmethyl compounds are also excreted (Hollingworth *et al.*, 1967; Miyamoto *et al.*, 1963b). Between 60 and 90% of the insecticide is excreted within two days, chiefly in the afore-mentioned forms. Only up to 10% is excreted

3.3.2.1 Animals (Cont'd)

in the feces. Detoxication via the desmethyl compounds is dose-dependent.

After oral administration of up to 40 grams of fenitrothion per lactating cow, residues in the milk were as high as 0.4 ppm after 6 hours and below the limit of detection after one day (Hais and Franz, 1965). Detoxication in bovine rumens is rapid owing to reduction of fenitrothion to the amino compound (Miyamoto *et al.*, 1967).

Cows fed 3 mg/kg body weight of fenitrothion for seven consecutive days produced milk having up to 0.002 ppm residue of fenitrothion on the second day, and no residue one day after administration was stopped. Less than 0.003 ppm aminofenitrothion and about 0.1 ppm *p*-nitrocresol were detected during treatment, and no fenitrooxon was found (Miyamoto *et al.*, 1967).

Thirty calves (1-1.5 yr. av. wt. 243 kg) confined on a pasture sprayed with 375 g/ha of fenitrothion (11.8 ppm initial residue on grass) were periodically sacrificed and breast muscle and omental fat analyzed. On the first day residues in the meat and fat were about 0.01 ppm. No residue of fenitrothion was found in the meat from the third day on and only 0.004-0.007 ppm was found in the fat on the third day; these amounts decreased almost to control levels by the seventh day (Republic of Argentina, 1968; Miyamoto and Sato, 1969).

Lactating dairy cattle were fed 50 ppm of fenitrothion in the feed (dry basis) for 29 days. No residue of fenitrothion, fenitrooxon, or the cresol appeared in the milk. A maximum of 0.006 ppm of amino-fenitrothion was found (Bowman, 1969).

3.3.2.2 Plants

About 50% of ^{32}P-labelled fenitrothion sprayed on rice plants penetrated into the tissues in 24 hours; at the end of this period only 10% was left, indicating rapid decomposition. Some fenitrooxon formed but it disappeared from the tissues more rapidly than fenitrothion. Rice grains harvested 46 days after treatment contained

3.3.2.2 Plants (Cont'd)

0.0007 ppm fenitrothion and less than 1 ppm of *p*-nitrocresol and dimethyl phosphorothioic acid (Miyamoto and Sato, 1965).

Fenitrothion does not appear to have much systemic action. After treatment of rice plants with fenitrothion, more residue is found in the bran than in the polished grains (Miyamoto and Sato, 1965). Very little active ingredient passed from peel to fruit in stored bananas (Miyamoto *et al.*, 1965a).

The half-life of fenitrothion in green plants ranges between the values established for parathion and parathion-methyl, i.e. between one and two days; the half-life of the oxon is estimated to be only a few hours (Mollhoff, 1968). Yule 1971, has reported the half-life of fenitrothion in forest foliage to be about 4 - 5 days. Salonius 1972, has demonstrated that fenitrothion treatment of forest soils did not alter population numbers or respiration of the forest soil microflora.

Although the oxon may form in plants, it occurs only during the first few days after treatment and in proportions (ca. 1%) smaller than those in animals (Miyamoto *et al.*, 1963; Miyamoto and Sato, 1965; Mollhoff, 1968). Desmethyl compounds occur only in minor amounts in plants.

Phytotoxicity of fenitrothion on cabbage was ascribed to high penetration of the insecticide and accumulation of the cresol hydrolysis product (Tomizawa and Kobayashi, 1964).

3.3.2.3 Soil

The soil bacteria *Bacillus subtilis*, converted more than half of radiolabelled ^{32}P-fenitrothion to the amino analogue under aerobic conditions at 37°C in 24 hours. The desmethyl derivatives of fenitrothion and aminofenitrothion as well as dimethyl phosphorothioic acid formed. None of the oxon or oxons of the degradation products were found (Miyamoto *et al.*, 1966).

3.3.2.3 Soil (Cont'd)

Fenitrothion is gradually inactivated by other bacterial species including gram-positive and gram-negative rods, but not by fungi and yeasts (Yasuno *et al.*, 1965).

Fenitrothion is readily absorbed onto various kinds of soil and decomposed by alkalinity or microorganisms (Muramoto, 1967). Persistence in soil does not appear to be great, Yule 1971.

3.3.2.4 Storage and Processing

Fenitrothion shows promise for control of grain insects in storage. Applied at 2 and 1 ppm to barley, it decreased to 0.4 ppm after 15 weeks storage (Green and Tyler, 1966). On barley in silos the half-life of fenitrothion was about 100 days (Green and Tyler, 1966) and on stored bananas about 15 days (Miyamoto *et al.*, 1965a). Applied to wheat (11% moisture) at rates of 1, 2 and 4 ppm, 0.2, 0.4, and 1.1 ppm of fenitrothion remained, respectively, after 9 months of storage at 25°C and 60% relative humidity (Kane and Green, 1968).

In extensive trials as a wheat protectant, fenitrothion levels steadied below 2 ppm after about 2 months regardless of application rate between 2.5 and 10 ppm. In one trial 6 ppm applied to grain decreased to 2.4, 1.7, and 1.1 ppm, respectively, after 1 1/2, 4, and 6 months. Flour made from the 2.4 ppm sample contained 0.3 ppm fenitrothion, while only traces were found in the flour and bread from the later samples (Cooper Technical Bureau, 1968).

3.3.2.5 Evidence of Residues in Food in Commerce or at Consumption

No report of residues of fenitrothion in food in commerce or at consumption has been found. Reference is made under "Storage and Processing" to the finding of only "traces" of fenitrothion in flour and bread prepared from grain containing 1.7 and 1.1 ppm of the insecticide.

4.0 Toxicity

4.1.0 Insect Pests

4.1.1 Agricultural Insect Pests

These have been enumerated in section 2.1.2 above.

4.1.2 Forest Insect Pests

Fenitrothion has been used extensively in Canadian forests for the control of spruce budworm and other forest insect pests since 1969, when it replaced DDT. Field trials by Randall, 1968, had proven its efficacy against 2nd or 3rd instar larvae of spruce budworm and Nigam, 1972, has reviewed laboratory toxicity studies against 21 species of forest insect pests carried out since 1965. The laboratory results are summarized in Table III.

Ground spray trials reported by DeBoo and Campbell, 1972, have shown excellent results against spruce budworm for fenitrothion when applied by mistblower.

4.1.2 Forest Insect Pests (Cont'd)

TABLE III

Summary of Contact Toxicity of Fenitrothion to Various Forest Insect Pests Tested Under Laboratory Conditions 1966-1972

Insect	Insect Stage	LD_{50} $\mu g/cm^2$ (48 hr)	Fiducial Limits (95%)	Reference
		1966		
Swaine jack-pine sawfly	IV instar	0.026	0.021 - 0.029	Nigam 1970a
Black-headed jack-pine sawfly	IV instar	0.040	0.037 - 0.042	Nigam 1970a
Larch sawfly	IV instar	0.101	0.096 - 0.108	Nigam 1970a
		1967		
Forest tent caterpillar	III instar	0.154	0.128 - 0.183	Nigam 1972b
		1968		
Ambrosia beetle	Adult	0.138	0.119 - 0.160	Nigam 1969b
European pine sawfly	IV instar	0.046	0.036 - 0.056	Nigam 1970b
Spruce budworm	V instar	0.332	0.288 - 0.376	Nigam 1969a
Spruce budworm	VI instar	0.428	0.371 - 0.486	Nigam 1972b
Jack-pine budworm	VI instar	0.401	0.349 - 0.454	Nigam 1970c
		1969		
Sitka spruce weevil	Adult	0.231	0.197 - 0.267	Nigam 1972b
Eastern hemlock looper	III instar	0.249	0.218 - 0.276	Nigam 1972b
Western hemlock looper	III instar	0.220	0.176 - 0.259	Nigam 1972b
Green-striped forest looper*†	III instar	93% Mort. @ 5.605 $\mu g/cm^2$		Nigam 1971b
		1970		
Red-headed pine sawfly	IV instar	0.016	0.012 - 0.019	Nigam 1971a
		1971		
White pine weevil*	Adult	100% Mort. @ 0.673 $\mu g/cm^2$		Nigam 1972b
Native elm bark beetle*	Adult	100% Mort. @ 0.168 $\mu g/cm^2$		Nigam 1972b
Filament bearer looper	III instar	0.481	0.388 - 0.568	Nigam 1972b
White-marked tussock moth	III instar	0.348	0.243 - 0.491	Nigam 1972b
Gypsy moth	III instar	1.179	1.014 - 1.353	Nigam 1972b
		1972		
European snout weevil*†	Adult	100% Mort. @ 0.112 $\mu g/cm^2$		Nigam 1972a
Western false hemlock looper	III instar	0.421	0.377 - 0.477	Nigam 1972b
Spruce budworm*	Adult	100% Mort. @ 0.484 $\mu g/cm^2$		Nigam 1972a

* No LD_{50} available. Figures show maximum mortality for minimum dosage.

† Results shown are for 72 hours.

‡ Insects from area sprayed with Methoxychlor and Malathion.

4.1.3 Special Studies on Neurotoxicity

4.1.3.1 Forest Birds

Pearce 1971, has reported that several years study of aerial spraying in Canada's New Brunswick forests with fenitrothion at the recommended dosage, showed very little impact on forest bird populations, although higher dosages were damaging, (Pearce 1967, 1968, 1969). Peterson 1969, was unable to demonstrate any major detrimental effects on bird populations in Maine forest areas treated with fenitrothion at the maximum rate of 6 ounces/acre.

4.1.3.2 Hen

Three hens protected against acute anti-cholinesterase effects with atropine and pralidoxime were given a single oral dose of 400 mg/kg body-weight of fenitrothion. No symptoms of paralysis occurred during an observation period of 28 days. Histologic examination of spinal cord and sciatic nerves revealed no pathological lesions in two hens and a few scattered degenerated fibres in the spinal cord of the third (Carshalton, 1962).

Seven hens protected in the same way were given an oral dose of 250 mg/kg body-weight of fenitrothion and three other hens were given 500 mg/kg. Two of the 500 mg/kg group died within 1-2 days, while the remaining eight hens did not show any sign of paralysis during an observation period of six weeks (Kimmerle, 1962b).

4.1.3.3 Aquatic Organisms

4.1.3.4 Fish

In New Brunswick population density determinations of Juvenile Atlantic Salmon found in fenitrothion sprayed streams in 1970 and 1971 do not indicate any short term effects of spraying on numbers of juvenile salmon.[1]

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[1] Report of Meeting of the Interdepartmental Committee on Forest Spraying Operations 1971, Canadian Forestry Service, Department of the Environment, G.H. Penney.

New Brunswick streams sprayed incidental to the spraying operation showed an immediate post-spray concentration of 0.06 ppm. Nagahana et alia have shown that concentrations of Sumithion of 15 ppm had no lethal effects on Salmo irideus, the rainbow trout.[2]

4.1.3.5 Insects

Monitoring of the 1969 spray in Newfoundland revealed no noticeable reduction in aquatic insects as a result of spraying. In New Brunswick, results of studies in 1968, 1969 and 1970, on the effects of Fenitrothion spraying at total application rates varying from 3 to 6 ozs/acre on aquatic insects are reasonably consistent and any decrease shown in numbers and biomass of aquatic insects were not significant enough to be definitely attributed to spraying.[3]

4.1.4 Special Studies on Potentiation

4.1.4.1 Rat

Female rats were given intraperitoneal doses of a combination of fenitrothion and the following organophosphorus compounds: parathion, parathion-methyl, demeton, disulfoton, malathion, EPN, azinphos-methyl, carbophenothion, mevinphos, dioxathion, schradan, ethion, diazinon, Folex®, coumaphos, and fenchlorphos as well as the carbamate, carbaryl. No sign of a potentiating effect was demonstrated (DuBois and Kinoshita, 1963).

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[2]Nagahana, M., K. Matsuo, T. Tamaca, and K. Vemoto. Sumithion Data Collection I at p. 38, Sumitomo Chemical Co. Ltd., Osaka, Japan.

[3]Report of Meeting of the Interdepartmental Committee on Forest Spraying Operations 1971, Canadian Forestry Service, Department of the Environment, G.H. Penney.

4.1.4.1 Rat (Cont'd)

When male rats were given acute oral doses of mixtures of fenitrothion and phosphamidon a marked potentiation of toxicity occurred as evidenced by increased mortality. In female rats a potentiation of toxicity occurred as evidenced by increased mortality. In female rats a potentiation occurred only in mixtures containing relatively low concentrations of fenitrothion, the potentiation effect diminishing as the concentration of fenitrothion was increased. It was concluded that potentiation is associated with a non-linear phosphorothioate conversion (Braid and Nix, 1968).

4.1.5 Special Studies on the Metabolite Fenitrooxon

The metabolite fenitrooxon is more toxic than the parent compound (cf. Tables IV and V).

TABLE IV

Acute Toxicity of Fenitrooxon

Animal	Route	Acute LD_{50} mg/kg body-weight	References
Mouse	oral	90	Miyamoto, 1969
Mouse	oral	120	Hollingworth *et al.*, 1967
Rat	oral	24	Miyamoto, 1969
Rat	i.v.	3.3	Miyamoto, 1969
Guinea-pig	oral	221	Miyamoto, 1969
Guinea-pig	i.v.	32	Miyamoto, 1969

4.1.6 Acute Toxicity

The symptoms of acute toxicity are the same as for other organophosphorus compounds, doses close to the LD_{50} producing symptoms which developed more rapidly after intravenous than after oral administration. The compound is considerably less toxic to mammals than its close structural analogue parathion-methyl (Miyamoto *et al.*, 1963b). Table V gives the LD_{50} in several species:

4.1.6 Acute Toxicity (Cont'd)

TABLE V

Animal		Route	Acute LD_{50} mg/kg body-weight	References
Mouse	(M)	oral	1336	Carshalton, 1964
Mouse	(F)	oral	1416	Carshalton, 1964
Mouse	(M)	i.p.	115	DuBois and Puchala, 1960
Mouse	(F)	i.p.	110	DuBois and Puchala, 1960
Mouse		i.v.	220	Miyamoto *et al*, 1963b
Rat	(M)	oral	740	Gaines, 1969
Rat	(F)	oral	570	Gaines, 1969
Rat	(M)	i.p.	135	DuBois and Puchala, 1960
Rat	(F)	i.p.	160	DuBois and Puchala, 1960
Rat		i.v.	33	Miyamoto *et al.*, 1963b
Guinea-pig	(M)	oral	500	DuBois and Puchala, 1960
Guinea-pig		oral	1850	Miyamoto *et al.*, 1963b
Guinea-pig	(M)	i.p.	110	DuBois and Puchala, 1960
Guinea-pig		i.v.	112	Miyamoto *et al.*, 1963b
Cat		oral	142	Nishizawa *et al.*, 1961

4.1.7 Short-term Studies

4.1.7.1 Dog

In what was described as a preliminary test, groups of dogs, each comprising one male and one female animal, were given daily oral doses by capsule of 0, 2, 9 or 40 mg/kg body-weight of fenitrothion for periods up to 98 days. Body-weight, blood biochemistry, cholinesterase levels and haemograms were checked at intervals. At the 2 mg/kg level there was no effect with respect to any other of the parameters mentioned. At 9 mg/kg a slight depression after 60 days and at 40 mg/kg a moderate depression after 29 days occurred in whole blood, plasma and red-cell cholinesterase. At 40 mg/kg there were also marked toxic symptoms typical of cholinergic stimulation, and the dogs in this group were sacrificed before the end of the 98-day period (Cooper, 1966).

4.1.7.2 Rat

Groups of male rats (16 or 17 in number) were fed 0, 32, 63, 125, 250, and 500 ppm of fenitrothion in the diet for 90 days. Mortality, food intake, growth, general behaviour, urinalysis, average organ-weights and histopathology were comparable to the controls in the groups fed 32, 63, 125, and 250 ppm. All the animals fed 500 ppm showed clinical symptoms of anti-cholinesterase poisoning and there were minimal symptoms in four animals in the 250 ppm group. In the 500 ppm group the average organ-weights of the testes and brain were increased in comparison with those of the control group. After interim sacrifice every month of four rats from each group, measurement of the cholinesterase activity of plasma, red cells, brain cortex, liver and kidney showed a dose-dependent depression, the lowest being in the brain. The cholinesterase activity in the 32 and 63 ppm groups generally increased after 60 days of dosing to a level within the normal limits, the best recovery being in the plasma, kidney and brain, less in the red cells and the liver (Misu *et al.*, 1966).

Two groups, each of 20 male rats, were dosed by stomach tube on six days a week for six months with 10 mg/kg and 11 mg/kg body-weight of fenitrothion, respectively. During the first weeks the rats showed a temporary deterioration of general condition and loss of weight. Haematology and urinalysis during the experiment and gross and microscopic pathology at its termination did not reveal any abnormalities (Klimmer, 1961).

Male rats were given daily oral doses of 13 mg/kg body-weight of fenitrothion for 28 days. Red-cell cholinesterase activity showed severe depression, but there was recovery 30 days after withdrawal of fenitrothion (Kimmerle, 1962a).

Male rats were fed 5, 10, and 20 ppm of fenitrothion in the diet for an unspecified period. Brain and red cell cholinesterase activity was normal in the 5 ppm group, whereas the 10 ppm group showed a slight depression of red cell activity after five weeks with recovery two weeks after withdrawal.

4.1.7.2 Rat (Cont'd)

The 20 ppm group showed some depression of activity both in red cells and in brain and the recovery in the brain remained incomplete two weeks after withdrawal (Carshalton, 1964).

Other reported studies with fenitrothion in the rat lasting 90 days indicate that the levels causing no appreciable effect on the cholinesterase activity of plasma, red cells and whole blood were 20 ppm in the diet and 10 ppm in drinking water. The only exception was a moderate inhibition of the activity in plasma among the male animals when given 10 ppm in drinking water. The above mentioned levels and higher, namely 92.8 ppm in the diet and 46.2 ppm and 215 ppm in drinking water, caused no effect on food or water intake, weight-gain, average organ-weights, haemogram and blood biochemistry. However, 92.8 ppm of fenitrothion in the diet and 46.4 ppm in drinking water had a moderate effect on whole blood and red-cell cholinesterase and a more marked effect on plasma cholinesterase. The cholinesterase activity recovered between 30-40 days after withdrawal of fenitrothion. The levels of 430 ppm in the diet and 1000 ppm in drinking water caused a depression of body-weight gains (Cooper, 1966).

4.1.8 Long-term Studies

4.1.8.1 Rat

An interim report on what appears to be a two-year feeding study in rats is available. Groups of nine or 10 male rats were fed 0, 25, 100 or 400 ppm of fenitrothion in their diet and were sacrificed after feeding these levels for 63 weeks. As a positive control a group was also fed 800 ppm of malathion. At the 400 ppm level of fenitrothion, food intake and body-weight gain was increased and only a few animals survived the 63 week period. At this level there was a 100 per cent depression of red-cell cholinesterase. At the 100 ppm level a slight (10-30 per cent) cholinesterase depression occurred in the brain and a moderate depression (30-65 per cent) in the red blood cells and plasma. At 25 ppm there was no effect on cholinesterase nor was there any effect with regard to any other parameters evaluated (Ueda and Nishimura, 1966).

4.2.0 Observations in Man

In a field spraying operation in Southern Nigeria including a village using a five per cent spray of fenitrothion, examination of 18 villagers one week later did not reveal any clinical symptoms of toxicity or plasma cholinesterase depression. The same was true of the three spraymen examined on the first, second and sixth day after spraying relative to a pre-spraying level (Vandekar, 1965).

In another field spraying trial in Northern Nigeria, 10,000 huts in which about 16,500 people lived were sprayed. Field test cholinesterase determinations on whole blood did not show any appreciable difference in cholinesterase levels of 535 villagers tested before spraying and 299 villagers tested 5-30 days after spraying. After one week of intensive spraying five out of 20 spraymen developed a 50 per cent depression of cholinesterase which returned to a stable level after a period of rest. One sprayman developed symptoms of toxicity which lasted only a few hours and disappeared without treatment (Wilford *et al.*, 1965).

Fenitrothion was given to a total of 24 human subjects in single oral doses of from 2.5 to 20 mg (0.042 to 0.33 mg/kg body-weight for a 60 kg man). The excretion of the metabolite, 3-methyl-4-nitrophenol, in the urine was almost complete within 24 hours, the maximum excretion occurring in the first 12 hours. The percentage of the dose excreted during this time depended to a certain extent upon the size of the dose administered, being about 70 per cent of theoretical after a 0.042 mg/kg dose and about 50 per cent after a 0.33 mg/kg dose. Both plasma and cholinesterase activity were not depressed below normal except possibly in one person given a 0.33 mg/kg dose, where some depression of plasma cholinesterase was apparent after six and 24 hours (about 65 per cent of the pre-test level). When repeated doses of 2.5 or 5 mg (approximately 0.04 to 0.08 mg/kg) were given to five individuals, four times at 24 hour intervals, most of the nitrocresol metabolite appeared in the urine within the interval 0 to 12 hours after administration. After receiving the third and fourth dose there was a trend towards a rise in red cell cholinesterase activity but in no cases was there any evidence of reduction below normal levels of the activity of this enzyme in either plasma or red cells (Nosal and Hladka, 1968).

4.2.0 Observations in Man (Cont'd)

A recent report by McCarthy 1972, has indicated that monitoring studies of pesticide applicators and handlers in New Brunswick during a period of four years has shown no illness that could reasonably be attributed to fenitrothion exposure.

4.2.1 Comment

Adequate information is available on the toxicity, biochemistry and metabolism of fenitrothion, in three species of rodent. Information is also available in man including field spraying studies and a metabolism study. Only an interim report comprising a 63-week study in rats is available and there are no 1-2 year studies in a non-rodent mammalian species. The short-term studies in the rat, using cholinesterase inhibition criteria, provide a no-effect level. No reproduction or teratogenicity studies are available and in view of the similarity in the structure of fenitrothion to parathion-methyl, it is important that such studies be undertaken. For this reason and because no adequate long-term studies are available it was decided to give only a temporary acceptable daily intake to this compound.

4.2.2 Toxicological Evaluation

4.2.3 Level Causing no Toxicological Effect

4.2.3.1 Rat

5 ppm in the diet, equivalent to 0.25 mg/kg body-weight/day.

4.2.3.2 Estimate of Temporary Acceptable Daily Intake for Man

0-0.001 mg/kg body-weight.

5.0 Summary of Environmental Effects

Although several metabolites of fenitrothion are known to form (fenitrooxon, desmethyl fenitrothion, aminofenitrothion, and 3-methyl-4-nitrophenol), they do not accumulate in significant amounts or they appear to be comparatively non-toxic. Unless experimental trials indicate otherwise, fenitrothion appears to be the only toxic residue to be determined in products in commerce.

6.0 Recommendations for Further Research

1. Reproduction and teratogenicity studies in animals preferably in non-human primates.
2. Adequate long-term studies in rodent and non-rodent mammalian species.
3. Data on residue levels in raw agricultural commodities moving in commerce and in total diet residues.
4. Data on disappearance of residues during storage, processing and cooking.
5. Data on rats of residue decline in rice and pre-harvest interval.
6. Before use as a grain protectant, data on persistence of residues in storage of the grains concerned and definitive data on residues in bread are needed.
7. Data on occurrence of 4-nitro-3-methylphenol residues and their significance toxicologically.
8. Information on ingredients in technical products produced by several manufacturers.
9. Observations in man.
10. Evaluation of gas chromatographic methods for regulatory purposes.

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