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AC 64,475 - A NEW SYSTEMIC NEMATICIDE AND INSECTICIDE

W. K. Whitney

Plant Products R&D, International Divisions, American Cyanamid Company
P.O. Box 400, Princeton, New Jersey 08540 USA

John L. Aston

Plant Products, Cyanamid International Corporation
P.O. Box 832, 8021 Zurich, Switzerland

Summary AC 64,475, cyclic methylene(diethoxyphosphinyl)dithioimino-carbonate, of American Cyanamid Company is a highly active, broad-spectrum nematicide and insecticide. Against nematodes in tobacco fields, the compound is 3-5 times more effective than similar quantities of most of the currently available commercial materials of this type. Although there are some phytotoxicity problems, it appears that they can be resolved by use of correct dosage rates and appropriate methods and timing of application. AC 64,475 is in full-scale development.

INTRODUCTION

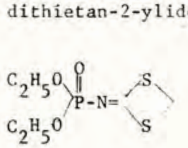
AC 64,475, a broad-spectrum systemic organophosphate nematicide and insecticide, was discovered by American Cyanamid Company at its Agricultural Research Center, Princeton, New Jersey. Five years of field trials have shown a high level of activity against a wide range of economically important plant nematodes and insects following soil applications.

CHEMICAL AND PHYSICAL PROPERTIES

Chemical name and structure:

Cyclic methylene(diethoxyphosphinyl)dithioiminocarbonate (Chemical Abstracts)

Also known as 2-(diethoxyphosphinylimino)-1,3-dithietane; or as diethyl 1,3-dithietan-2-ylidenephosphoramidate (IUPAC)



$C_6H_{12}NO_3S_2$

Other designations: CL 64,475; ENT 27,873

Molecular weight: 241.3

Physical state: Technical product is a yellow liquid with a mercaptan-like odour

Purity: Not less than 85%

Solubility: Soluble in acetone, chloroform, methanol and toluene. 5% in water at 25°C

Formulations: Granular products containing 5%-15% a.i. and a water-soluble liquid concentrate containing 250 g a.i./l.

TOXICOLOGY, METABOLISM AND RESIDUES

The acute mammalian toxicity of technical and formulated AC 64,475 is shown in Table 1.

Table 1

Acute toxicity (LD_{50} in mg/kg b.w.) of AC 64,475 by oral and dermal administration

Product type	Rat, oral	Mouse, oral	Rabbit, dermal[a/]
Technical	5	18	40-50
250 g/l.s.c.	-	-	377
15% granule	46	108	340
10% granule	48	141	766
5% granule	109	281	3124

[a/] 24-hour contact. Granular formulations moistened with water.

Tests with bacteria have shown that AC 64,475 is nonmutagenic.

Complete subacute and chronic toxicological, teratological, reproduction and environmental studies as required for product registration in various countries are in progress.

Metabolism and environmental degradation studies are also in progress. Results to date indicate a fairly rapid breakdown of AC 64,475 with the thiocyanate ion being the principal terminal product.

Analytical methods are available for residue analyses. No residue problems are anticipated. For example, no residues (i.e. < 0.05 mg/kg) are found in cured tobacco leaves from plants grown in soil treated with 4.5 kg a.i./ha (3x the effective rate).

BIOLOGICAL PERFORMANCE

Pesticidal activity:

AC 64,475 is highly nematicidal. For example in U.S. and Australian tobacco fields, it is three to five times more active than most of the currently available commercial materials of this type. The compound also has good activity against subterranean and above-ground insects on plants grown in soil treated for nematode control.

Results of a few representative field trials presented in Tables 2-8 show that AC 64,475 gives good to excellent control of Meloidogyne spp., Ditylenchus spp. and Heterodera spp. in a variety of situations. Other trials have shown similar results against Belonolaimus spp., Criconema spp., Criconemoide spp., Hoplolaimus spp., Longidorus spp., Pratylenchus spp., Trichodorus spp., Tylenchorhynchus spp. and Xiphinema spp.

AC 64,475 when applied to soil for nematode control, is also active against certain insects. Examples of this are shown in Tables 6 and 7 where 53% to 85% control of Leptinotarsa decemlineata was obtained on potatoes grown in nematicide plots. Other arthropods contolled on plants grown in trials where AC 64,475 was applied to the soil include Agriotes spp. and other wireworms, Agrotis ipsilon, Chilo spp., Diabrotica spp., Empoasca spp., Elasmopalpus lignosellus, Epitrix spp., Heliothis spp., Hydrellia spp., Hylemya spp., Lygus lineolaris, Nephotettix spp., Nilaparvata lugens, Ostrinia nubilalis, Pegomya betae, Rhopalosiphum maidis, Schizaphis graminum, Scutigerella immaculata, Sesamia spp., Spodoptera spp., Tetanops myopaeformis, Thysanoptera and Tryporyza spp.

Table 2

Effects of AC 64,475 on Meloidogyne spp. and tobacco plant growth (var. Bright; Verona, Italy - SIAPA CER, 1972)

Treatment[a/]		Nema larvae/100 g soil		Gall index[c/]	Plant growth
Product	kg a.i./ha	28 DAT[b/]	143 DAT	143 DAT	60 DAT
AC 64,475	1.0	45	135	1.07	excellent
AC 64,475	2.0	35	125	1.57	good
Thionazin	2.0	40	185	1.28	good
Aldicarb	1.0	20	150	1.53	good
Untreated	-	80	1,450	1.98	good

a/ Applied as 10% a.i. granules on May 2, localized distribution, pre-transplanting.

b/ DAT = days after treatment.

c/ Rating scale 0-4, where 0 = no galling and 4 = severe galling.

Table 3

Activity of AC 64,475 against *Meloidogyne* spp. and effects on melons (Igea Marina, Italy - SIAPA CER, 1974)

Factor \ Treatment[a] kg a.i./ha	AC 64,475 5% granules 2.5	AC 64,475 5% granules 3.75	Thionazin 10% granules 5.0	Untreated check
Nema larvae/100 g soil				
46 DAT	10	0	20	65
140 DAT	390	170	1220	1575
Gall index[b]				
46 DAT	0.07	0.00	1.22	1.70
140 DAT	0.52	0.52	3.10	3.70
Crop growth[c]	7.23	7.90	7.07	6.57
% Fruits ripe at 120 DAT	25	54	40	21

[a] 80-cm band incorporated 15 cm deep in row at seeding on 25 April.

[b] Rating scale 0-4, where 0 = no galling and 4 = severe galling.

[c] 0-9 scale, where 9 = maximum growth; mean of evaluations made at 46, 83 and 120 days after treatment (DAT). No phytotoxicity.

Table 4

Percent control of nematodes associated with strawberries (var. Poca-Hontas, Ferrara, Italy - SIAPA CER, 1972-73)

Criterion \ Treatment[a] Rate/ha	AC 64,475 1 + 1 kg a.i.[a]	Thionazin 1 + 1 kg a.i.[a]	Dichloropropane-dichloropropene mix, 400 l. formulation[b]	Untreated check
% control of *Ditylenchus dipsaci*				
19 Oct. 72 in soil[c]	57	71	57	(35)
28 Mar. 73 in soil	100	100	71	(35)
11 Apr. 73 in leaves[d]	51	32	19	(185)
18 June 73 in soil	100	100	100	(5)
% control of *Aphenlenchoides* spp. *Pratylenchus* spp.				
19 Oct. 72 in soil	55	50	70	(100)
28 Mar. 73 in soil	0	8	60	(125)
18 June 73 in soil	66	63	31	(160)
Yield (kg/ha)[e]	2600	2500	2900	2000

[a] Granules (10% a.i.) distributed over row and incorporated 10-12 cm deep on 17 July 72 just before planting and on both sides of rows on 28 Mar. 73 and covered by earthing up.

[b] Broadcast and incorporated on 4 July 72 before planting.

[c] Percent control based on nematode counts; Numbers of nematodes per 100 g soil shown in parentheses.

[d] Percent control based on nematode counts; Number of nematodes per 10 g leaves shown in parentheses.

[e] Total of 8 pickings (22 May - 18 June, 73). No phytotoxicity.

Table 5

Potato (var. Primura) yield increases associated with various soil applications of AC 64,475 for control of Heterodera rostochiensis[a/] (Bellaria, Italy - SIAPA CER, 1972)

Product	Rate and timing[b/] kg a.i./ha	Yield as % of untreated[c/]	Phytotoxicity (leaf yellowing)
AC 64,475	6B	138	intense
"	2F	134	slight
"	2F + 1R	133	"
"	2F + 2R	151	"
Thionazin	2F + 2R	135	"

[a/] Nematode and cyst counts not recorded.

[b/] All applied as 10% granules.

B = Broadcast and incorporated just before seeding.

F = Applied in furrow at seeding.

R = Applied over row 48 days after seeding.

[c/] Average yield in untreated plots = 25.6 t/ha.

Table 6

Control of Heterodera rostochiensis and Leptinotarsa decemlineata and yield increases of Primura potatoes by in-furrow soil treatment with AC 64,475 (Bellaria, Italy - SIAPA CER, 1973

Treatment		% control of		Yield
Product	kg a.i./ha	H.r.	L.d.	t/ha
AC 64,475 5% granule	1.0	70	53	15.6
Thionazin 10% granule	2.0	33	0	10.0
Untreated check	-	(15,655)[a/]	(136)[b/]	9.9

[a/] H. rostochiensis cysts/200 g soil at harvest time (4 July).

[b/] L. decemlineata larvae/plot at 2 months after seeding and treatment.

Table 7

Effects of AC 64,475 on populations of Heterodera rostochiensis and Leptinotarsa decemlineata and on potato (var. Bea-Area) growth and yields (Igea Marina, Italy - SIAPA CER, 1974)

Criterion \ Treatment[a] method kg a.i./ha	AC 64,475 5% granules Broadcast 5.0	AC 64,475 5% granules Furrow 1.75	Thionazin 10% granules Broadcast 5.0	Untreated check -
Nematode cysts/200 g soil				
9 May	12.0	19.0	14.0	13.0
16 July	5.0	19.0	19.0	14.0
Nematode eggs + larvae/cyst				
9 May	0.0	14.2	8.6	23.7
16 July	0.0	190.2	104.2	179.2
Free-living nematode larvae/100 g soil				
9 May	0.0	55.0	35.0	35.0
16 July	10.0	10.0	15.0	110.0
Leptinotarsa decemlineata				
% control 29 May	85	74	0	423/plot
Yield (t/ha)	51.7	40.4	45.8	49.7

[a]At seeding 29 March 1974.

Table 8

Control of Heterodera schachtii in sugar beets (Min. of Agric., Valldolid, Spain - 1974)

Treatment[a] Product	Treatment[a] kg a.i./ha	Cysts No./sample	Cysts % Viability	Yield as % of untreated Beets	Yield as % of untreated Sugar
AC 64,475 10% granules	1.75	20.6	21.6	160	150
Fenamiphos 5% granules	10.00	17.3	22.3	119	125
Ethoprophos 10% granules	7.00	16.0	16.6	118	117
Untreated	-	29.0	37.6	(61.5)	(10.6)[b]

[a]Broadcast and incorporated 10 days before seeding.

[b]t/ha shown in parentheses.

Phytotoxicity:

The method and timing of soil treatment appear to be important, especially for certain direct-seeded crops. In general AC 64,475 should not be applied in direct contact with seeds.

Application of AC 64,475 in seed rows may result in plant stand reduction, burning of early leaf margins and temporary plant stunting.

At 1.5 a.i./ha granules incorporated in a band over seed rows of peanuts and soybeans may produce transient, early-season phytotoxic symptoms, but affected plants soon outgrow the injury.

Cabbage and tobacco plants show no significant adverse reactions when transplanted into soil pretreated with AC 64,475 granules. Likewise, application of granules at 0.5-1.0 kg a.i./ha to rice fields after transplanting results in no significant plant injury.

DISCUSSION AND CONCLUSIONS

The high level and broad spectrum of nematicidal and insecticidal activity of AC 64,475 warrant full evaluation and development of the compound. Current and future field work will concentrate on performance aspects in various soil types and on resolving the remaining problems of phytotoxicity by determining the optimum methods and timing of application. Toxicological, metabolism, residue and environmental impact studies are in progress for support of product registration in various countries.

Acknowledgements

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AC 85,258 - A NOVEL ACARICIDE AND APHICIDE

W. Keith Whitney

Plant Products R&D, International Divisions, American Cyanamid Company
P.O. Box 400, Princeton, New Jersey 08540 USA

John L. Aston

Plant Products, Cyanamid International Corporation
P.O. Box 832, 8021 Zurich, Switzerland

Summary AC 85,258, dichloro [4,4-dimethyl-5-[[[(methylamino) carbonyl]oxy]imino]pentanenitrile] zinc, is a highly active experimental acaricide and aphicide with useful activity against several species of associated pests. The compound is effective against strains of mites and aphids which have developed resistance to organophosphates and other pesticides. Full-scale toxicological, metabolism and residue work are under way to support worldwide development of the product.

INTRODUCTION

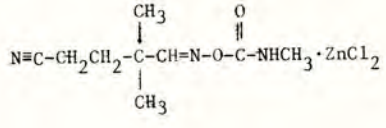
AC 85,258 is an experimental carbamate acaricide and insecticide discovered by American Cyanamid Company at its Agricultural Research Center in Princeton, New Jersey. This compound has demonstrated a high degree of activity against mites and aphids in numerous laboratory, glasshouse and field trials. AC 85,258 is in full-scale, worldwide development.

CHEMICAL AND PHYSICAL PROPERTIES

Chemical names: dichloro[4,4-dimethyl-5-[[[(methylamino)carbonyl]oxy]imino] pentanenitrile]zinc (Chemical Abstracts)

also known as 4,4-dimethylglutaraldehydonitrile O-(methylcarbamoyl)oxime compound with zinc chloride (1:1); or as 4,4-dimethyl-5-(methylcarbamoyloxyimino)pentanenitrile, compound with zinc chloride (1:1) (IUPAC).

Structural formula:



Molecular formula: $C_9H_{15}N_3O_2 \cdot ZnCl_2$

Molecular weight: 333.51

State and colour: Odourless, off-white powder with bulk density of 0.5 g/cm^3

Purity: 90% minimum

Melting point: 120-125°C

Solubility:

Good solubility in acetone, acetonitrile, alcohols and water. Slightly soluble in chloroform. Practically insoluble in benzene, diethyl ether, hexane, toluene and xylene.

Stability:

AC 85,258 is very hygroscopic and must be kept in tightly closed containers except when in use. When stored in the original closed containers at 25°C or below, the product is stable for about one year.

FORMULATION

AC 85,258 25-WP, a 25% a.i. w/w wettable powder, is available for trials.

TOXICOLOGY, METABOLISM AND RESIDUES

Complete toxicological, metabolism and residue studies are in progress.

Both the technical material and the 25% w.p. are highly toxic by single oral doses but only moderately toxic by dermal exposure (Table 1).

Table 1

Acute LD_{50} values (mg/kg body wt) for laboratory animals

	Acute oral		Acute dermal
AC 85,258	Rat	Mouse	Rabbit
Technical	9	18	857
25% w.p.	14	-	2267

Rats were unaffected by a one-hour exposure to a water aerosol which provided a concentration of 131 mg a.i./l. of air.

Studies with rats demonstrated that atropine is an effective antidote.

Laboratory tests with honey bees at the University of California, Riverside placed AC 85,258 in Group III (relatively nontoxic) with an LD_{50} similar to that of trichlorphon.

Tests with bacteria showed that AC 85,258 is nonmutagenic.

Aqueous solutions containing 1% a.i. were not irritating to rabbit eyes or skin; however, undiluted technical material and the 25% w.p. did cause eye and skin inflammation.

There were no instances of human skin contact sensitization in tests conducted on 100 healthy adult volunteers.

Subacute and long-term toxicological studies are under way on rats, mice and dogs. Preliminary results show that the compound is tolerated at much higher levels in continuous dietary administration than would be predicted from the single-dose acute oral LD_{50} values.

PESTICIDAL PERFORMANCE

AC 85,258 has been widely tested in more than 20 countries. The compound is highly active against a wide range of phytophagous mites and aphids and has useful activity against several other groups of insects (Table 2). The spectrum of its pesticidal activity is currently being determined. AC 85,258 is effective against populations of mites and aphids which have developed resistance to other pesticides.

Table 2

Some mites and insects controlled by AC 85,258

Mites	Aphids	Other insects
Aculus schlechtendali	Aphis gossypii	Agonoscena targionii[a/]
Brevipalpus spp.	Aphis pomi	Bemisia spp.
Eotetranychus carpini	Capitophorus braggi	Empoasca fabae[a/]
Oligonychus mexicanus	Eriosoma lanigerum	Empoasca lybica
Panonychus citri	Hyalopterus pruni	Enneothrips flavens
Panonychus ulmi	Macrosiphum euphorbiae	Hydrellia philippina[a/]
Phyllocoptes spp.	Myzus persicae	Hypera postica[a/]
Phyllocoptruta oleivora	Phorodon humuli	Leptinotarsa decemlineata
Tetranychus cinnabarinus		Leucoptera scitella[a/]
Tetranychus evansi		Lithocolletis blancardella[a/]
Tetranychus mcdanieli		Psylla pyricola[a/]
Tetranychus pacificus		
Tetranychus urticae		

[a/] Useful level of control at acaricidal/aphicidal rates but not equal to best standards. All others listed are well controlled with 250-750 mg a.i./l.

The compound usually kills mites and aphids within a few hours after treatment and has local foliar systemic activity, e.g. leaves treated on the upper surfaces are protected against mites feeding on the undersides.

Acaricidal activity:

AC 85,258 has good residual pesticidal activity. This is illustrated in Table 3, which presents the results of laboratory and greenhouse experiments, and has been verified in field trials (Tables 5-11).

Table 3

Foliar residual activity of AC 85,258 against two-spotted spider mites, Tetranychus urticae, in laboratory and greenhouse tests*

Compound	Spray mg a.i./l.	Percent kill of mites at interval shown before infesting									
		0 Day		4 Days		7 Days		14 Days		21 Days	
		Lab.**	G.H.	Lab.	G.H.	Lab.	G.H.	Lab.	G.H.	Lab.	G.H.
AC 85,258	1000	100	100	100	100	100	100	100	100	100	83
50% w.p.	100	100	100	100	100	100	90	51	14	0	0
	10	40	90	0	0	2	0	-	-	-	-
Dicofol	1000	100	100	100	100	100	100	98	89	86	(L.P.)+
18% w.p.	100	100	100	100	100	65	42	32	16	34	0
	10	0	0	0	0	0	0	-	-	-	-
Cyhexatin	1000	100	100	100	100	100	100	77	82	83	85
50% w.p.	100	100	37	97	54	88	85	33	0	37	64
	10	38	3	24	23	52	3	0	0	0	0

*Young primary leaves of bean plants were sprayed to runoff. The plants were air dried and then aged at 27°C (laboratory or greenhouse).

At the intervals shown, the treated leaves were infested with mites. Mortality counts were made 48 hours later.

None of the treatments controlled mites on new growth, indicating that there was little or no systemic movement of the toxicants from treated to untreated leaves.

**Lab. = laboratory; G.H. = Greenhouse.

+L.P. = Lost plant.

\- = Not tested.

Excellent activity against organophosphorus-resistant mites was shown in laboratory tests (Table 4).

Although a large number of field evaluations have been conducted around the world, only a few representative examples with emphasis on European results are presented here for the sake of brevity. These miticidal field studies are summarized in Tables 5-11.

Table 4

Laboratory tests[a] against normal and organophosphorus-resistant Tetranychus urticae on leaves of bean plants

	% Mortality					
	Normal Strain			O-P Resistant Strain		
Compound	100	10	1 mg a.i./l.	100	10	1 mg a.i./l.
AC 85,258	100	100	0	100	100	0
Dimethoate	100	100	33	0	0	0
Parathion	100	90	0	10	0	0

[a] See Table 3 for description of test method.

Table 5

Control of Eotetranychus carpini on grape vines by one spray of 2.5 l./plant on 8 August 1974 (SIAPA, Italy)

Product	Rate mg a.i./l.	% Control at 5 DAT[a]	14 DAT	21 DAT
AC 85,258 25% w.p.	375	99.7	99.7	99.7
AC 85,258 25% w.p.	750	99.4	100	99.6
Cyhexatin 25% w.p.	300	95.8	99.7	96.6
Amitraz 20% e.c.	400	83.3	55.4	49.3
Untreated	-	(308)[b]	(385)	(305)

[a] DAT - days after treatment.

[b] Number of live mites on 20 leaves per plot shown in parentheses.

Table 6

Activity of AC 85,258 against *Eotetranychus carpini* on grape vines by one spray on 15 July, 1974 (Sandoz, France)

Product	Rate mg a.i./l.	% Control at 2 DAT[a]	7 DAT	14 DAT	28 DAT
AC 85,258	300	96	93	89	74
AC 85,258	600	99	99	95	93
Dicofol	500	76	62	46	65
Untreated	-	(196)[b]	(293)	(126)	(210)

[a] DAT = days after treatment.

[b] Number of live mites on 12 leaves per plot shown in parentheses.

Table 7

Efficacy of AC 85,258 against *Panonychus ulmi* on Stark Delicious apple trees after one spray in July, 1974 (SIAPA CER, Italy)

Product	Rate mg a.i./l.	% Control 2 DAT[a]	7 DAT	15 DAT
AC 85,258	375	94	85	57
AC 85,258	750	97	80	50
Amitraz	400	98	92	68
Cyhexatin	300	96	96	83
Untreated	-	(8.49)[b]	(35.3)	(47.9)

[a] DAT = days after treatment.

[b] Number of live mites per leaf shown in parentheses; evaluations of 50 leaves per plot.

Table 8

Activity of AC 85,258 against Panonychus ulmi on apple trees sprayed on 3 July, 1974 (Sandoz Ltd., France)

Product	Rate mg a.i./l.	% Control at 1 DAT[a]	7 DAT	14 DAT	28 DAT
AC 85,258	300	83	83	91	95
AC 85,258	600	88	96	98	98
Cyhexatin	300	98	95	92	96
Untreated	-	(38)[b]	(71)	(161)	(95)

[a] DAT = days after treatment.

[b] Number of live mites per 25 leaves per plot.

Table 9

Control of Tetranychus urticae on soybeans at 12 days after spraying with 900 l./ha on 14 August, 1974 (Min. of Agric., Spain)

Product	Rate mg a.i./l.	% Efficacy[a]
AC 85,258	375	94
Triazophos	400	100
Methamidophos	400	63
Propargite	570	50

[a] Based on ratios of living and dead mites on 10 leaves per sample in treated versus untreated plots (Abbott's Formula).

Table 10

Control of Tetranychus urticae on cucumbers with one high-volume spray on 16 August, 1974 (Ligtermoet Chemie B.V., Holland)

Product	Rate mg a.i./l.	% Control based on counts of					
		Adults at			Eggs at		
		3 DAT[a]	13 DAT	20 DAT	3 DAT	13 DAT	20 DAT
AC 85,258	250	0	95.2	91.1	0	98.9	90.4
AC 85,258	500	88.4	99.0	94.4	81.4	97.9	93.1
Propargite	300	58.1	87.6	28.9	75.8	88.9	57.4
Untreated	-	(215)[b]	(525)	(450)	(970)	(3105)	(1515)

[a] DAT = days after treatment.

[b] Number of mites or eggs per 3 leaves shown in parentheses.

Table 11

Efficacy of AC 85,258 against Tetranychus urticae on cucumbers with high-volume sprays applied on 12 May and 4 June 1975 (Ligtermoet Chemie B.V., Holland)

Product	Rate mg a.i./l.	Number mites + eggs/10 leaves				
		May 12	May 20	May 30	June 4	June 16
AC 85,258	500	775	145	10	250	5
AC 85,258	250	380	160	30	25	0
Propargite	300	965	765	95	40	20
Untreated	-	10	50	890	1210	30

[a] Untreated check plots sprayed with propargite at 300 g a.i./l. on 4 June 1975.

Excellent control of all mite genera and species listed in Table 2 has been consistently obtained with sprays containing AC 85,258 at 250-750 g a.i./l. Except for Panonychus ulmi which may require 500-750 mg a.i./l. under certain conditions such as cool weather, 250 mg a.i./l. appears to be adequate.

Aphicidal activity:

AC 85,258 is an outstanding aphicide, as illustrated in the representative field test data given in Tables 12-15. Dosage rates of 300 mg a.i./l. or less have consistently given excellent results.

Table 12

Activity of AC 85,258 against *Myzus persicae* on peach trees (SIAPA CER, Italy - 1974)

Product	Applic. dates	Rate mg a.i./l.	% Control on May			
			16th	22nd	24th	31st
AC 85,258	14 & 22 May	375	98.1	96.6	99.8	99.3
AC 85,258	14 May	750	99.9	99.4	99.8	99.7
Pirimicarb	22 May	250	-	-	98.2	99.4
Monocrotophos	14 & 22 May	400	76.5	73.4	79.3	74.5
Untreated	-	-	(117)[a]	(133)	(169)	(243)

[a] Number of live aphids per 15-20 cm long shoot; 15 samples per plot.

Table 13

Activity of AC 85,258 against *Myzus persicae* after spraying peach trees with 650-950 l./ha on 12 June, 1974 (Sandoz, France)

Product	Rate mg a.i./l.	% Control after			
		4 days	1 week	2 weeks	3 weeks
AC 85,258	300	93	96	98	90
AC 85,258	600	98	98	98	92
Pirimicarb	375	98	98	97	77
Untreated	-	(190)[a]	(190)	(190)	(55)

[a] Estimated mean number of aphids per shoot.

Table 14

Control of Aphis pomi on apple trees sprayed with AC 85,258 in 1200 l. water/ha on 12 June, 1974 (Procida, France)

Product	Rate mg a.i./l.	% Control at 2 DAT[a]	9 DAT	21 DAT
AC 85,258	300	100	99	82
AC 85,258	600	100	100	97
Dimethoate	300	36	55	68
Mevinphos	500	12	73	0
Untreated	-	(200)[b]	(218)	(113)

[a]/DAT = days after treatment.

[b]/Mean number of apterous aphids per shoot.

Table 15

Efficacy of AC 85,258 against Aphis pomi on apple trees sprayed 26 August, 1974 (Sandoz, France)

Product	Rate mg a.i./l.	% Efficacy[a] 4 DAT[b]	7 DAT	15 DAT
AC 85,258	300	99.5	99.8	96.8
AC 85,258	600	99.3	99.8	95.8
Azinphos-methyl	500	88.3	95.8	89.5
Untreated	-	(425)[c]	(146)	(43)

[a]/Henderson (1955).

[b]/DAT = days after treatment.

[c]/Number of live aphids per shoot shown in parentheses.

Crop safety:

AC 85,258 is well tolerated by most crops. All main apple, pear, peach and grape varieties in Italy tolerate aqueous sprays containing 500 mg a.i./l. without problem. Isolated cases of foliar yellowing have occurred after spraying with 1000 mg a.i./l., with the apple variety Imperatore showing most susceptibility (Data: SIAPA CER).

Apricots, particularly the variety BULIDA, showed considerable yellowing and leaf loss after spraying with 1000 mg a.i./l. (SIAPA CER data, 1974).

No significant phytotoxicity has been recorded from the 100 or so field efficacy trials carried out in some 10 European countries.

DISCUSSION

A significant amount of data is available concerning the performance of AC 85,258.

The compound has consistently shown a high degree of activity against many phytophagous mite species at rates of 250-500 mg a.i./l.

Panonychus ulmi appears to be a little more difficult to control requiring rates of 500 mg a.i./l. in hot climates and 600-750 mg a.i./l. where temperatures are lower.

AC 85,258 has outstanding activity against aphids at rates of 250-500 mg a.i./l. in a wide range of situations. It is effective against strains of mites and aphids which have developed resistance to organophosphates and other pesticides.

The compound has useful activity against several other pests which are often associated with mites and aphids. For example, good control of the Colorado potato beetle (*Leptinotarsa decemlineata*) has been achieved with two applications of 0.5 kg a.i./ha. The high level of aphid control coupled with the results obtained against this pest indicates that AC 85,258 should find use in situations where both pests are common.

AC 85,258 provides a quick knock-down of pests in most situations, a property that has many advantages.

The compound seems to have a good margin of safety to crops and is only moderately toxic to mammals by dermal exposure.

Work in progress will define the spectrum of pesticidal activity, provide information on the effects of the compound on beneficial parasites and predators, and supply details regarding subacute mammalian toxicity, metabolism, degradation and residues.

Acknowledgements

The authors wish to acknowledge the help of many of their colleagues within American Cyanamid Company and subsidiaries. Particular thanks are also expressed to the following organizations which have carried out most of the trials presented here: SIAPA CER Laboratories, Bologna, Italy; Ligtermoet Chemie B.V., Holland; and the Departamento de Plantas de Gran Cultivo, Crida 05, INIA, Ministry of Agriculture, Spain

Reference

Henderson, C.F. (1955). Tests with acaricides against brown wheat mite, *Journal of Economic Entomology*, 48, 157-161.

Proceedings 8th British Insecticide and Fungicide Conference (1975)

THE HYDANTOIN 26,019 RP, A NEW POLYVALENT FUNGICIDE

L. Burgaud, J. Chevrel, M. Guillot, G. Marechal, and J. Thiolliere
Rhône-Poulenc, Division Phytosanitaire
R.J.Cole
May & Baker Ltd., Ongar Research Station, Ongar, Essex.

Summary: 26,019 RP, a protectant and curative fungicide from the hydantoin group of chemicals, has been field-tested on a wide range of horticultural and agricultural crops from 1972-75. Excellent activity against grey mould (*Botrytis cinerea*) of grapes, soft fruit, vegetables, and glasshouse crops has been demonstrated, and strains of *B.cinerea* tolerant to benzimidazole-related compounds have also been controlled. Other fungi successfully controlled include *Sclerotinia* spp. (vegetables), *Pyrenophora* spp. and *Tilletia caries* (cereals), *Alternaria* spp. (pome fruit and brassicas), *Monilia* spp. (stone fruit), *Rhizoctonia solani* and *Phoma solanicola* (potatoes) and *Pellicularia sasakii* (rice). In most trials, a dose of 750 g a.i./ha gives optimum results equal, or superior, to standard products. No phytotoxicity has been observed on any crop treated. Toxicological and residue studies have given satisfactory results and 26,019 RP is now registered in France for *B.cinerea* control in grapes.

Résumé: Le 26,019 RP fongicide préventif et curatif dérivé de l'hydantoine, a été expérimenté en plein champ sur un grand nombre de cultures de 1972 à 1975. L'excellente efficacité contre la pourriture grise (*Botrytis cinerea*) sur vigne, petits fruits, légumes et cultures sous serre, a été mise en évidence. Les souches de *Botrytis* tolérantes aux dérivés du benzimidazoles sont sensibles au 26,019 RP. Les autres maladies combattues avec succès sont: *Sclerotinia* spp. (légumes), *Helminthosporium* spp. et *Tilletia caries* (céréales), *Alternaria* spp. (fruits à pépins et choux), *Monilia* spp. (fruits à noyau), *Rhizoctonia solani* et *Phoma solanicola* (pomme de terre), et *Pellicularia sasakii* (riz). Dans la majorité des cas la dose de 750 g m.a./ha donne les resultats optimum, équivalents ou supérieurs à ceux obtenus avec les produits de reférénce. Les études toxicologiques et de résidus ont donne les résultats favorables. Le 26,019 RP a été autorisé par les services officiels Français pour la lutte contre le *Botrytis* de la vigne.

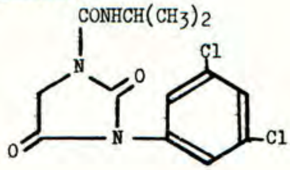
INTRODUCTION

Research carried out over several years by the Société Rhône-Poulenc in the field of plant protection revealed in 1970 a new class of antifungal materials derived from the "hydantoin" group of compounds. The most active compound from this group, which was subsequently selected for commercial development, is 3-(3,5-dichlorophenyl)-1-isopropylcarbamoylhydantoin, or 26,019 RP (proposed trade name 'Rovral'*).

26,019 RP has been tested under several code numbers including NRC-910, LFA 2043, and ROP 500F.

*Registered trade mark of May & Baker Ltd.

(a) Physical and chemical properties:



Molecular weight:	330.17
Melting point:	approx. 136°C
Appearance, etc:	white, odourless, non-hygroscopic crystals.
Solubility at 20°C:	water: approx. 13 mg/l.
	ethanol: slightly soluble
	acetone, benzene, dichloromethane: easily soluble
Volatility:	at 20°C the vapour pressure is negligible.
Stability:	both technical and formulated products are stable under normal storage conditions.
Formulations:	formulations used to date have included wettable powders, flowables, emulsifiable concentrates, seed dressings, and dusts. A 50% w.p. has been selected for commercial development although in some situations, for specific purposes, other formulations are still being evaluated.

(b) Toxicology: Toxicological and pharmacological studies have shown 26,019 RP to be a product of low acute toxicity orally, or by contact with the skin or mucous membranes. The acute oral LD_{50} for rats is 3500 mg/kg, for mice is 4000 mg/kg; the acute intraperitoneal LD_{50} for rats is 1700 mg/kg. It is non-toxic by the percutaneous route in rats and rabbits at doses of 2500 mg/kg and 1000 mg/kg respectively. In long term feeding studies, rats displayed no clinical or toxicological effects at dietary levels of 1000 ppm for 18 months, and on feeding 26,019 RP to dogs at a level of 2400 ppm in the diet for 90 days, no significant effects were displayed. 26,019 RP has been shown to be without teratogenic effect in the rat and rabbit. Of particular note in both the rat and dog studies is the fact that 26,019 RP has not given rise to corneal opacity, which has been observed with certain chloroaniline derivatives.

(c) Residues: 26,019 RP is a non-systemic fungicide. It is not degraded on plant surfaces, although it is slowly absorbed into plant tissues where it is metabolised to non-toxic products. The only residues detected in the crops however are of 26,019 RP. After treatment of tomatoes, grapes, strawberries, raspberries, apples, plums, and peaches with dose rates between 0.5 and 1.0 kg/ha, the residues of 26,019 RP at harvest varied from 0 to 6 mg/kg. The levels of residues of 26,019 RP on grapes and in wine has been extensively studied. Samples of grapes, must, and wine have been taken from various countries after treatment with 3 - 5 sprays (normally 4) at doses ranging from 300 - 1250g a.i./ha (normally 750g a.i./ha). Residues of 26,019 RP recovered from grapes at harvest varied according to the dose and interval between the last treatment and harvest, and, although levels reached up to 10 mg/kg in the extreme, the overall results (drawn from 150 samples) give an average of 3.5 mg/kg. In France the average residue for treatments of 750g a.i./ha is 4.3 mg/kg in grapes. Residues found in musts and wines are always much lower than those present on grapes at harvest. A specific series of trials in France gave residues (from a dose of 750g a.i./ha) ranging from 4.8 - 7.5 mg/kg in grapes, from 2.0 - 4.4 mg/kg in musts and from 0.6 - 1.45 mg/kg in wines. The residues found in wine are composed of 26,019 RP alone, and when the wine is distilled these do not pass into the alcohol distillate.

(d) Environment: 26,019 RP presents little potential pollution hazard in air, water or the soil owing to its low vapour pressure, low water-solubility and to the fact that it is broken down in the soil into non-toxic products.

(e) Spectrum of activity: 26,019 RP has a wide spectrum of activity and is particularly effective against grey mould, Botrytis cinerea; Monilia spp; Sclerotinia spp; white mould, Sclerotium cepivorum; Pyrenophora spp; Alternaria spp; gangrene, Phoma solanicola; bunt, Tilletia caries; stem canker, Rhizoctonia solani; sheath blight, Pellicularia sasakii and other plant pathogens.

METHODS

Where results are presented as 'percent disease control' in the following tables, this has been calculated using the formula:-

$$\frac{\text{untreated infection (\%)} - \text{treatment infection (\%)}}{\text{untreated infection (\%)}} \times 100 = \text{percent disease control for treatment}$$

Spraying regimes and experimental design were generally as follows:-

Vines: Spray application was usually low volume (60 - 200 l/ha) directed into the bunches with timing of sprays as follows:- (i) "petal" fall (ii) tightening of bunches (iii) beginning of ripening (iv) end of ripening.

Plot sizes were usually of at least 5 vines per plot and were replicated up to 6 times.

Soft fruit: High volume sprays (1200 - 2000 l/ha) were used with 3-5 applications being made over the flowering period at 10-14 day intervals.

Other crops: Experimental design has varied depending on the crop and disease under study, but data presented are mainly from small plot replicated trials using standard techniques.

Results have been grouped according to common treatments in Tables 1, 2, 5 and 7.

RESULTS AND DISCUSSION

(a) Grey mould in vines: Grey mould damage in vineyards all over the world is well known for its effect on both quantity and quality of the grape crop, and the methods of chemical control currently available are not wholly satisfactory.

26,019 RP is an important new development in this field. It is noticeably more effective than many of the products already in use, is non-phytotoxic, and, furthermore, is active against certain strains of B.cinerea, tolerant to benzimidazole-related fungicides. The results presented are from trials in which average levels of grey mould on the berries were at least 10%, the majority being 20% and above. The results of trials carried out by Rhône-Poulenc in France are given in Table 1, whilst Table 2 summarises the results of extramural trials carried out by French official co-operators (Institut National de la Recherche Agronomique and Service de la Protection des Vegetaux) and other professional organisations. Table 3 summarises the results of trials conducted outside France by various members of the Rhône-Poulenc Group of companies.

Table 1

Grey mould control in vines (Rhône-Poulenc trials) - France 1972-74

Treatment	Dose g a.i./ha	Mean percent disease control					
26,019 RP	500	53.7	81.0	70.4	58.0	63.8	67.1
26,019 RP	750	-	-	79.6	70.8	74.5	79.7
26,019 RP	1,000	82.8	82.6	86.5	78.0	-	-
Dichlofluanid	2,000	-	-	-	-	-	66.4
Benomyl	500	45.8	-	-	49.4	47.3	-
Mean % infection on untreated		22.7	12.1	26.0	35.0	29.8	29.5
No. of trials		1	1	1	9	8	9

Table 2

Grey mould control in vines (Official trials) - France 1974

Treatment	Dose g a.i./ha	Mean percent disease control	
26,019 RP	750	69.3	84.3
Dichlofluanid	2,000	61.1	78.0
Benzimidazole*	500	43.3	-
Mean % infection on untreated		34.2	44.0
No. of trials		13	4

* benomyl or carbendazim

Table 3

Grey mould control in vines - other countries 1973-74

Treatment	Dose g a.i./ha	Mean percent disease control				
		Spain	Italy	Portugal	Yugoslavia	Switzerland
26,019 RP	500	-	84.7	58.6	63.4	84.7
26,019 RP	750	93.2	91.6	72.8	83.2	81.3
Benomyl	500	71.9	89.9	68.8	-	-
Dichlofluanid	2,000	-	-	-	68.1	-
Mean % infection on untreated		17.1	23.2	22.7	18.6	34.4
No. of trials		3	2	1	2	3

In South Africa, work to-date has been confined to table grapes, and a programme of 3 sprays of 26,019 RP over the 'flowering' period, followed by routine applications of a 5% 26,019 RP dust at 1 kg a.i./ha have given outstanding (>97%) control of B.cinerea infections of the bunches.

In the U.K. 4 sprays of 26,019 RP reduced B.cinerea infection on grapes by over 90% (Hunter 1975) and promising results are also reported from Japan (Yamada 1975). In the USA excellent control of Black rot (Guignardia bidwellii) on grapes has been achieved (Albert 1975).

A rate of 750g a.i./ha has usually given 70-80% B.cinerea control - although in some cases over 90% control has been achieved. In all cases this has been equal, or superior, to existing commercial standards, especially when compared with benzimidazole-related fungicides where presence of tolerant strains has often reduced the effectiveness of the latter.

The excellent control of grey mould of vines achieved with 26,019 RP is because it has both curative and protectant activity. These effects, coupled with the potency of the product against both spores and mycelium, have been reported elsewhere (Lacroix et al 1974). Other favourable properties include - absence of phytotoxicity; no activity against fermentation agents; safety to user and consumer; supplementary activity against powdery mildew of vine, and, finally, good control of secondary rots (Aspergillus niger, Penicillium expansum, Alternaria sp. and Rhizopus sp.). 26,019 RP has recently been registered in France for the control of grey mould in vines.

(b) Grey mould on soft fruit: 26,019 RP has effectively controlled B.cinerea in strawberries, raspberries, blackcurrants, and gooseberries in numerous trials carried out in several countries. Table 4 summarises the main results achieved on strawberries.

Table 4

Grey mould control in strawberries 1973-75

Treatment	Dose g a.i./ha	Mean percent disease control					
		France	Spain	Italy	Belgium	Canada	U.K.
26,019 RP	500	55.2	-	49.7	-	62.6	76.9
26,019 RP	750	69.5	45.8	55.2	58.5	53.7	60.8
26,019 RP	1,000	76.6	54.9	71.2	74.2	54.8	57.3
Benomyl	500	62.3	43.3	71.5	-	63.2	49.0
Mean % infection on untreated		15.4	14.2	20.2	28.9	19.0	14.3
No. of trials		5	1	2	3	3	3*

* Grown under low-level polythene tunnels

These results show that 26,019 RP gives good protection of strawberries at a dose rate of 750-1000 g a.i./ha, and yield increases of up to 50% have been recorded over untreated areas . No off-flavours or taints have been observed on fruit treated at 2 kg a.i./ha and subsequently processed by canning, freezing or pulping for jam or juice.

(c) Disease control in vegetables: Results of trials carried out in France and Spain on field-grown autumn and winter lettuce, treated 4-6 times with 26,019 RP, are summarised in Table 5:-

Table 5

Disease control in field lettuce - France and Spain 1974-75

Treatment	Dose g a.i./ha	Mean percent disease control			
		S.sclerotiorum		B.cinerea	
26,019 RP	500	69.4	54.3	68.2	68.3
26,019 RP	750	80.6	-	76.9	-
26,019 RP	1,000	-	70.3	-	65.8
Benomyl	500	58.9	48.7	49.3	65.8
Mean % disease on untreated		14.0	25.3	59.1	48.0
No. of sites		7	3	5	4

In the U.K. on vegetables, excellent results have been reported on the control of dark leaf spot (Alternaria brassicicola) on cabbage by seed treatments at 1.25 g a.i./kg seed (Maude, 1975). On onions, control of white rot (Sclerotium cepivorum) was obtained at 50 g a.i./kg seed (Entwistle and Munasinghe 1975) and of neck rot (B.allii) by foliar sprays.

In Japan control of Sclerotinia spp, has been achieved on cucumber, lettuce, cabbage, bean and onion, equal or better to that given by reference compounds (Kishi 1975).

(d) Glasshouse crops: Work in the U.K. on tomatoes, lettuce and ornamentals under glass has shown that where strains of B.cinerea tolerant to benzimidazole-related products occur, 26,019 RP effectively controls these as well as sensitive strains. Routine spray applications at 14-21 day intervals, using 0.5-1.0 g a.i./l. (HV), gives optimum control without sign of phytotoxicity. Besides cyclamen (Table 6) over 20 other species of ornamental pot plants have been treated safely with the wettable powder formulation.

Table 6

Grey mould control in glasshouse crops

Treatment	Dose g a.i./l.	Mean percent disease control		
		Lettuce	Tomato	Cyclamen
26,019 RP	0.25	82.3	55.8	81.2
26,019 RP	0.50	91.2	60.2	92.5
26,019 RP	1.0	92.9	83.3	98.7
Thiophanate-methyl≠	1.0	24.8	36.7	42.0
Dichlofluanid	0.50	-	53.1	-
Mean % disease on untreated		11.3	90.0*	60.0
No. of trials		2	2	2

* Mean No. B.cinerea lesions per treatment
≠ Strains of B.cinerea with known tolerance to benzimidazole-related fungicides present in trials.

(e) Top fruit:

(i) Stone fruit: In France, the U.S.A., Canada and New Zealand sprays of 1 kg a.i./ha 26,019 RP have given good control of Monilia spp. on both blossom (blossom wilt) and fruits (brown rot). Used as a dip at a rate of 0.5-0.75 g a.i./l., good post-harvest control of brown rot on peaches has been obtained in South Africa and Canada. In South Africa rates of 1 g/l have also controlled Rhizopus, and similar results on this disease have been obtained on stone fruit in the U.S.A. using foliar sprays of 26,019 RP at 1.1 kg a.i./ha. (Szkolnik et al 1975)

In Japan 26,019 RP (as NRC 910) gave superior control of brown rot of cherries (Sclerotinia cinerea) when compared with thiophanate-methyl (Yamada 1975).

(ii) Pome fruit: In Japan, promising results have been obtained on blossom blight (Sclerotinia mali), leaf spot (Alternaria mali) and rust (Gymnosporangium yamadae) on apples. On Japanese pear, 26,019 RP (as NRC 910) gave good control of black spot (Alternaria kikuchiana) (Yamada 1975).

In the U.K. brown rot (Sclerotinia laxa) on apples has been controlled using 3 late season sprays of 26,019 RP, and approximately 70% control of bitter rot (Gloeosporium spp.) has been achieved using either pre-harvest sprays or post-harvest dips.

(f) Control of cereal diseases:

(i) Seed treatment: 26,019 RP shows promising activity against various seed and soil-borne pathogens of cereals. Results of several trials on bunt (Tilletia caries) and leaf stripe (Pyrenophora graminea) are summarised in the following table:-

Table 7

Control of bunt and leaf stripe on cereals

Treatment	Dose g a.i./100 kg seed	% infection Bunt		% infection Leaf Stripe	
26,019 RP	90 - 100	1.2	0.9	0.1	1.7
Mercury	3	-	1.6	-	2.6
Carboxin + oxine-copper	100 + 30	-	-	1.4	-
Untreated	-	16.4	23.5	31.4	14.8
No. of trials		3	3	4	2

In addition to showing good activity against these two cereal pathogens, 26,019 RP also has some activity against Septoria nodorum and Fusarium spp. The incorporation of 26,019 RP in a dressing with other fungicides, e.g. thiophanate-methyl, will extend the spectrum of activity to cover all the major seed and soil-borne diseases of cereals.

(ii) Rice: Very encouraging results have been obtained in Japan on sheath blight of rice (Pellicularia sasakii) with a 2% dust formulation of 26,019 RP.

(g) Disease control in potatoes: Control of stem canker (Rhizoctonia solani) and gangrene (Phoma solanicola) by tuber dipping (3-5 minutes) prior to planting has been obtained as shown in the following table:-

Table 8

Control of stem canker and gangrene on potatoes

Treatment	Dose g a.i./l.	Stem canker* % healthy shoots	Gangrene≠ % infected tubers after: 39 days	59 days	99 days
26,019 RP	2.0	71.0	0.0	1.5	10.0
26,019 RP	4.0	76.7	1.5	9.0	15.0
Mercury	0.045	79.6	-	-	-
Untreated		14.3	45.5	58.0	86.5
No. of trials		2		1	

* Natural infection ≠ Artificial infection

(h) Turf: In the U.S.A. and Canada, good results have been obtained against Dollar spot (Sclerotinia homoeocarpa), Fusarium spp. and Helminthosporium spp. at rates of 0.3 - 1.2 g a.i./m^2. In the U.K., similar doses have given excellent control of Sclerotinia homoeocarpa (Woolhouse, 1974) under code number LFA 2043.

CONCLUSIONS

26,019 RP is a fungicide having a wide spectrum of activity against many diseases which are not adequately controlled by fungicides in current use. This, coupled with its activity on strains of fungi showing tolerance to other products, represents an advance in the realms of plant disease control.

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SULPHENYLATED FORMAMIDINES AS INSECTICIDES AND ACARICIDES

P.H. Parham, E.G. Gemrich II and T.E. Weddon

The Upjohn Company, Kalamazoo, Michigan, U.S.A.

Summary A group of sulphenylated formamidines were examined to determine the structure-activity relationship against ova and imagoes of three acarine species, and ova and first-instar larvae of three lepidopterous insects.

Excellent ovicidal and larvicidal activity is associated with $\underline{N}^2$-(4-chloro-2-methylphenyl)-substituted formamidines while the $\underline{N}^2$-(2,4-dimethylphenyl)-analogues were usually more effective against adult acarines and aphids.

INTRODUCTION

A group of compounds belonging to the general class of chemicals known as formamidines has proven to be effective for the control of certain insects and acarines (McGarr 1973, Harding 1973, Westigard *et al.* 1972, Boling 1972, Cowan and Davis, 1972, Batiste *et al.* 1970, Asquit 1973, Harding 1971, Wood 1973, Carlson 1971). Two types of formamidines, chlordimeform and amitraz, have demonstrated commercial utility. The former is an ovicide with selected acaricidal and insecticidal properties while the latter is a more effective acaricide with selected insecticidal properties (Weighton *et al.* 1973).

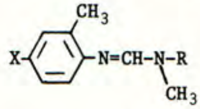
A few years ago we began investigating the bioactivity of several classes of formamidines in an attempt to find a compound with high ovicidal, insecticidal and acaricidal properties. While we have not been completely successful in discovering a single compound which offers obvious advantages over both chlordimeform and amitraz, we were successful in finding several compounds which have essentially the same ovicidal activity as chlordimeform yet possess greater acaricidal activity and insect larvicidal activity. The most outstanding members being from $\underline{N}^2$-aryl-$\underline{N}^1$-benzenesulphenyl-$\underline{N}^1$-methylformamidine and $\underline{N}^1$-alkanesulphenyl-$\underline{N}^2$-aryl-$\underline{N}^1$-methylformamidine groups.

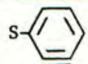
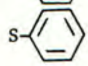
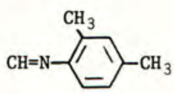
CHEMICAL AND TOXICOLOGICAL PROPERTIES

Structural formulas and toxicology discussed in this paper are presented in Table 1.

Table 1

Structural formulae and acute toxicology data



X	R	Compound	AO Rat LD_{50}
Cl		U-42558	132 mg/kg
CH_3		U-42564	113 mg/kg
Cl	$S-CCl_3$	U-42662	1000 mg/kg
CH_3	$S-CCl_3$	U-42660	297 mg/kg
Cl	CH_3	chlordimeform	170-369 mg/kg
CH_3		amitraz	938 mg/kg

MATERIALS AND METHODS

The chemicals used in this investigation (Table 1) were analytically pure and were formulated as 10% w/w emulsifiable concentrates for suspension in water. Cultures of the two-spotted spider mite (*Tetranychus urticae*), carmine spider mite (*T. cinnabarinus*), citrus red mite (*Panonychus citri*), green peach aphid (*Myzus persicae*), southern armyworm (*Spodoptera eridania*), cabbage looper (*Trichoplusia ni*), and cotton bollworm (*Heliothis zea*) were reared and tested according to standard practices. All data discussed are the results of replicated treatments.

BIOLOGICAL ACTIVITY

These sulphenylated formamidines have been tested in the laboratory and small plot trials against a range of acarine and insect species. As seen in Tables 2 and 3, the compounds are very active against several acarine and lepidopteran species.

In Table 2 these data show that the $\underline{N}^2$-(2,4-dimethylphenyl) substituted formamidines are more efficaceous against mobile and adult forms than their corresponding $\underline{N}^2$-(4-chloro-2-methylphenyl) analogues (compare U-42564 vs. U-42558; U-42660 vs. U-42662). In contrast, acarine ova were considerably more susceptible to the action of the $\underline{N}^2$-(4-chloro-2-methylphenyl) substituted formamidines (*e.g.* U-42558 and U-42662). The green peach aphid susceptibility seems to parallel that of the adult acarine rather than their ova.

Table 2

Acaricidal and aphicidal activity

		Average corrected mortality (%) to					
		Spider mites					Aphids
		Two spotted		Carmine		Citrus red	Green peach
Chemical	Conc.	Ova	Adult	Ova	Adult	Adult	Mobile
42558	A	67	51	51	33	49	84
	B	68	81	58	91	73	98
	C	72	99	86	100	100	100
42564	A	0	81	6	51	82	100
	B	2	100	29	100	100	99
	C	7	100	28	100	100	100
42662	A	34	11	10	28	21	-
	B	41	43	10	41	56	-
	C	86	37	40	65	89	-
42660	A	7	23	0	17	35	-
	B	11	54	0	57	42	-
	C	40	82	2	93	96	-
chlordimeform	A	12	7	48	8	21	38
	B	52	39	65	6	38	88
	C	82	78	94	64	50	96
amitraz	A	73	72	66	84	91	-
	B	96	83	81	95	100	-
	C	100	97	98	97	100	-
Concentration mg/1	A	3.3	25	3.3	25	11	20
	B	10	75	10	75	33	50
	C	30	225	30	225	100	125

As seen in Table 3, the $\underline{N}^2$-(4-chloro-2-methylphenyl) substituent is important in imparting maximum toxicity to lepidopterous ova and first-instar larvae--compare U-42558 with U-42564; and U-42662 with U-42660. In general the cotton bollworm is considerably more susceptible to the formamidines than either the cabbage looper or southern armyworm. Ova of the cabbage looper were very tolerant to the action of chlordimeform whereas the larvae were susceptible. As chlordimeform is reportedly effective as an ovicide against several lepidopterous species, including cabbage looper, these experiments were repeated several times, always with similar results. Ova of the cabbage looper are very susceptible to the action of U-42558, the sulphenylated 4-chloro-2-methylphenyl formamidine.

As noted in these tests and as reported by Gemrich (1975), all the formamidines examined permit the lepidopterous embryo to develop to the "black head" stage before they are killed by the chemical treatment. Larvae in untreated ova chew through the egg and eclose within a matter of hours, whereas larvae in treated ova fail to eclose. At times they are successful in chewing a hole in the chorion. Thus, although several formamidines are considered to be ovicides, they might better be classed as early instar larvicides.

Two of the sulphenylated formamidines and chlordimeform were tested to determine their translaminar activity against the two-spotted spider mite and the cabbage looper, Table 4. Both U-42558 and U-42564 produced a high degree of translaminar miticidal activity while chlordimeform produced significant ovicidal activity, probably because of its potent vapour action. The translaminar activity of the $\underline{N}^2$-4-chloro-2-methylphenyl formamidine and the $\underline{N}^2$-(2,4-dimethylphenyl) compound was similar to that obtained in the tests reported in Table 2. Namely, the $\underline{N}^2$-(4-chloro-2-methylphenyl) was more ovicidal and the $\underline{N}^2$-(2,4-dimethylphenyl) was better against mobile acarines. The translaminar control of cabbage looper with U-42558 suggests that thorough coverage might be less important with the sulphenyl formamidines than with insecticides that do not have translaminar activity. These data also demonstrate that localized systemic and larvicidal rather than ovicidal activity of formamidines in providing effective field control are worthy of further study.

Table 3

Toxicity of several formamidines to Lepidoptera

		Average corrected mortality (%) to					
		Bollworm		Cabbage Looper		Southern Armyworm	
Chemical	Conc.	Ova	Larvae	Ova	Larvae	Ova	Larvae
42558	A	86	46	44	37	2	80
	B	90	80	94	79	94	85
	C	97	74	100	84	98	100
42564	A	—	11	6	—	0	15
	B	66	31	38	5	0	30
	C	100	54	36	11	0	30
42662	A	69	28	6	41	0	39
	B	79	24	13	41	29	93
	C	92	55	31	68	47	86
	D	98	64	84	100	97	100
42660	A	24	0	26	0	0	0
	B	14	0	25	0	0	18
	C	27	0	55	0	0	18
	D	68	0	93	0	0	18
chlordimeform	A	96	51	0	5	43	65
	B	100	46	7	53	72	80
	C	100	74	19	89	94	95
amitraz	A	9	0	7	0	0	4
	B	22	7	8	0	0	22
	C	45	12	58	18	17	39
	D	60	19	87	55	33	22
Concentration mg/l	A	1	1	4	1	1.25	3.3
	B	4	5	16	4	5	10
	C	16	25	64	16	20	30
	D	64	64	256	64	64	90

Table 4

Translaminar activity of three formamidines

	g a.i./ha	Two-spotted mite % Mortality Ova	nymph	Cabbage Looper % ova hatched*	% larvae alive*
U-42564	280	5 a	77 c		
	420	8 a	90 c		
	560	2 a	97 c		
U-42558	140	-	-	91 a	0 a
	280	8 a	82 c	84 a	0 a
	420	13 a	78 c	72 a	0 a
	560	88 d	N.R.		
chlordimeform	280	45 bc	0 a		
	420	62 c	35 b		
	560	82 d	N.R.		
Control	—	2 a	0 a	91 a	74 b

*Analysis of variance using Duncan's Multiple Range Test. Treatments not differing at the 0.05 level of significance have a common suffix.

In summary, high adult acaricidal and aphicidal activity are associated with formamidines of the $\underline{N}^2$-(2,4-dimethylphenyl) substituted type. The most pronounced acarine and lepidopterous ovicidal activity are associated with the $\underline{N}^2$-(4-chloro-2-methylphenyl) substituted formamidines.

Only U-42662 and possibly U-42660 will be available for testing in 1976.

Acknowledgements

The authors are grateful for the assistance of V.L. Rizzo in the preparation of the sulphenyl formamidines and to their many co-workers in the Insecticides Research Unit of The Upjohn Company.

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PROFENOFOS - A NEW INSECTICIDE FOR THE CONTROL OF COTTON AND VEGETABLE PESTS

F. Buholzer

CIBA-GEIGY Ltd., Agrochemicals Division, CH-4002 Basle, Switzerland

Summary Chemical, physical and toxicological properties of profenofos (CGA 15324 = CURACRON®), an organophosphate insecticide, are described. Results are presented from field trials against important cotton and vegetable pests. Profenofos is very active against chewing and sucking insects and also against mites, it is equal in performance to the best standard compounds.

INTRODUCTION

Profenofos is an organophosphate insecticide discovered by CIBA-GEIGY Ltd. This compound has given consistent economic control of important cotton pests in various countries. It is of moderate to slight acute mammalian toxicity and of medium persistence, properties which make it also suitable for use in vegetables.

MATERIALS

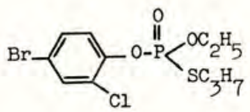
Description of profenofos (CGA 15324, CURACRON®)

BSI and proposed ISO common name : profenofos

Systematic chemical name : O-(4-bromo-2-chlorophenyl) O-ethyl S-propyl phosphorothioate

Molecular formula : $C_{11}H_{15}BrClO_3PS$

Structural formula



Molecular weight : 373.64

Solubility at 20°C	: water 20 ppm; miscible with methanol, dichloromethane benzene and hexane
Appearance	: slightly yellowish liquid
Density	: 1.455 g/cm^3 at 20°C
Boiling point	: 110°C at 0.001 mm Hg
Vapour pressure	: approx. 10^{-5} mm Hg at 20°C

Formulations : EC 500, EC 400, EC 200 are emulsifiable concentrates containing indicated grams a.i. per litre. In the trials described the EC 500 was used, except in the USA where the formulation was 4 E, i.e. 4 lb a.i./US gal. Granules containing 5% a.i. Ultra-low-volume formulation containing 250 g a.i. litre.

Toxicology

Acute studies	Profenofos (technical a.i.)	EC 500	G 5
Oral, rat, LD_{50}(mg/kg)	358-400	613	>7700
Dermal, rat, LD_{50}(mg/kg)	approx. 3300	3100	>3100
4 hours inhalation, rat, LC_{50}(mg/m^3)	approx. 3000	approx. 3700	-

Technical profenofos has a moderate toxicity to mammals. The EC formulations are only slightly toxic and the 5G formulation is practically non-toxic.

Standard commercial chemicals

The following locally available formulations of commercial products were used as standards : chlordimeform, 50% e.c.; chlorpyrifos, e.c. containing 4 lb/US gal; diazinon, 25% e.c., USA 4 E = e.c. containing 4 lb/US gal; dimethoate, 40% e.c.; dicofol, 18.5% e.c.; dioxacarb, 50% w.p.; DDT 50% w.p.; leptophos, 30% e.c.; methomyl, 90% s.p.; monocrotophos, 40 or 60% s.c.; parathion-methyl, 60% e.c.; phosfolan, 25% e.c.; pirimicarb, 50% w.p.

METHODS

The mode of application in cotton was a low volume spray, using 100-200 l/ha. In vegetables high volume sprays were used, with the addition of a wetting agent for brassica crops and onions. All rates are given in terms of the active ingredient.

Trial layout : Small plots 10-200 m^2, larger for aerial application. Randomized complete block design with 4 replicates.

Statistical analysis was on data transformed to log (x + 1). Significance is calculated at the 5% level, using Tukey's test. In the tables, treatment means followed by the same letter are not significantly different at this level.

RESULTS

Trials on cotton

Table 1 summarizes results of single applications on Heliothis virescens in Brazil. Application was on 1st-2nd (rarely up to 3rd) - instar larvae. Counts were 2-4 days after application.

Table 1 Single applications of profenofos against Heliothis virescens on cotton - Brazil

Date of treatment		1974					1975	
		18.I.	19.I.	4.II.	19.I.	16.I.	17.I.	21.I.
Date of assessment		21.I.	23.I.	6.II.	22.I.	18.I.	20.I.	24.I.
Product	g/ha	Larvae/200 squares						
Profenofos	500	3.75a	8.50a					9.75a
	750	3.75a	5.00a	2.50a	2.50a	4.25a	7.00a	7.50a
Monocro-tophos	750	5.00a	6.00a	3.25a	1.75a	4.00a	6.75a	7.00a
Methomyl	500	4.00a	6.75a	5.00a			5.25a	8.75a
Parathion-methyl	750	7.50ab	8.50a	7.00ab			9.00a	
	1500							9.00a
DDT	1500						9.75a	19.00ab
Untreated		18.2b	23.0a	18.2a	19.5b	15.5b	30.0b	30.2b

Table 2 Repeated applications of profenofos against Heliothis virescens on cotton - Brazil   Dates of treatment : 17.I. + 28.I.1975

Counting date		20.I.	23.I.	31.I.	3.II.
Product	g/ha	Larvae/ 800 squares	% attacked squares	Larvae/ 800 squares	% squares shed*)
Profenofos	750	28a	5.1a	21a	22a
Monocrotophos	750	27a	3.7a	22a	21a
Methomyl	500	21a	6.2a	41a	26ab
Untreated	-	103b	28.7b	111b	58b

*) Part of the shedding was caused by natural abortion and by attack from before the first treatment.

Table 3 Application of profenofos against Heliothis zea on cotton - USA

Dates of treatment : 16. VIII + 21. VIII 1974

Counting date		19. VIII 1974	23. VIII 1974
Product	g/ha	Larvae/25 terminals	% damaged squares
Profenofos	280	2.8a	6
	560	1.3a	7
	840	0.8a	2
Methomyl	560	1.3a	3
Untreated	-	9.8b	20

Table 4 Application of profenofos against *Heliothis virescens* on tobacco - USA

Dates of treatment : 23. V. + 28.V. + 31.V. + 4.VI. 1974

High volume application with 900 l/ha

Damage rating 0-10, 10 for complete defoliation

Product	g/ha	Rating 10.VI. 1974
Profenofos	280	4.5bc
	560	2.5ab
	840	1.5a
Methomyl	560	2.8ab
Untreated	-	8.0bc

Table 5 Application of profenofos against *Spodoptera littoralis* on cotton

Country		Egypt 1972		Egypt 1974		Spain 1974	
Date of treatment		12.VII		15.VII	15.VII	4.X	29.IX
Date of counting		14.VII	18.VII	18.VII	19.VII	8.X	1.X
Product	g/ha	Larvae/m row					
Profenofos	750			0.44a	0.54a	1.3a	1.4a
	1000			0.11a	0.18a	1.4a	0.5a
	1250				0.17a		
	1500	0.12a	0.26a				
Chlorpyrifos	1000	0.14a	0.18a	0.53a	0.18a	4.5a	1.2a
Phosfolan	1000	0.02a	0.17a	0.34a	0.02a		
Leptophos	1500	0.78a	0.28a				
Monocrotophos	1000					3.1a	1.5a
Untreated		43.8b	4.55b	8.30b	3.16b	24.2b	36.8b

Table 6 Aerial application of profenofos against *Spodoptera littoralis* on cotton

Country : Egypt Date of treatment : 4.VII 1974

	Number of larvae/100 labelled plants			
Larvae:	Small	Medium	Large	Total
Before spraying	5357	1589	229	7175
After 2 days	0	64	30	94
" 3 "	0	6	9	15
" 5 "	0	12	0	12

Table 7 Application of profenofos against mites on cotton

Country		Brazil		Brazil	Spain		Brazil	
Species		Tetranychus urticae			T.cinnabarinus		Hemitarsonemus latus	
Date(s) of treatment		7.+14.II 1974		7.+13.II 1974	23.VIII 1974		26.+ 28.II 1975	
Date of counting		12.II	20.II	20.II	25.VIII	3.IX	3.III	7.III
Product	g/ha	Mites/20 leaves						
Profenofos	300				104	284abc		
	400						0.8a	1.8a
	500				70	143ab		
	600	63.5a	20.3ab	70.3a			0.8a	0.6a
	1000	54.0	12.8a	51.5a				
Monocrotophos	500				277	448bc		
	600	105.5ab	60.0bc	61.3a				
Dicofol	600	56.0a	16.5a	47.0a				
	1000				105	90a	6.6b	1.2a
Untreated		193b	167c	249b	516	942c	91c	158b

Table 8 Application of profenofos against Aphis gossypii and Thrips tabaci on cotton

Pest		Aphis gossypii	Thrips tabaci
Country		Egypt	Egypt
Date of treatment		14.VII 1974	7.V 1975
Date of counting		16.VII	12.V
Product	g/ha	Aphids/30 leaves	Adults and larvae/20 leaves
Profenofos	150	3.3a	-
	250	2.0a	1.8a
Monocrotophos	150	0.0a	-
	250		1.0a
Dimethoate	150	1.0a	-
	250		7.5b
Untreated		720b	115c

Trials on vegetables

Table 9 Application of profenofos against Lepidoptera on vegetables

Pest		Mamestra brassicae	Trichoplusia ni		Plutella xylostella		
Crop		Brussels sprouts	Cabbage		Cabbage	Broccoli	
Country		Switzerland	USA		Italy	S. Africa	
Dates of treatment and		3.+17.IX 1973	21.+28.VI + 4.+18. +24.VII 1973		15.IX 1973	9.+25.IX 1974	
assessment		23.X	31.VII	1.VIII	17.IX	25.IX	1.X
Product	g/ha	Damage-rating 0-5	Damage-rating 0-10	Larvae/25 leaves	Larvae/10 plants	Larvae/5 plants	
Profenofos	450	0.67a			3.5a	0.0a	0.0a
	560-600	0.60a	2.3b	2.5a	6.0ab	0.0a	0.0a
	1120		1.3ab	1.0a			
Methomyl	450	0.53a			33.5c	8.0b	0.3a
	560-600		2.0b	4.3ab			
Chlordimeform	560		1.0a	0.5a			
Monocrotophos	450-560		2.3b	2.8a	19.0bc		
Untreated		4.95b	4.5c	13.8b	180d	18.8c	24.3b

Table 10 Application of profenofos against aphids and thrips on vegetables

Pest		Myzus persicae			Brevicoryne brassicae	Thrips tabaci
Crop		Pepper			Broccoli	Onion
Country		Italy			USA	Switzerland
Dates of treatment		3.VI 1974			13.VIII 1974	22.+29.VII 1974
Date of counting		4.VI	9.VI	13.VI	22.VIII	6.VIII
Product	g/ha	Aphids/25 leaves			Rating 0-10*	Thrips/5 plants
Profenofos	300					3.8a
	400	0.0a	3.0a	49.8a		5.8a
	560				1.5a	
Monocrotophos	300					4.3a
Pirimicarb	400	0.8a	4.5a	28.5a		
Dimethoate	280				1.8a	
Dioxacarb	500	0.5a	3.5a	55.3a		
Diazinon	560				2.8a	
Untreated	-	48.5b	74.5b	373b	10.0b	79.8b

* 0 = clean, 10 = heavily infested

DISCUSSION

Profenofos gave good control of the cotton bollworms *Heliothis virescens* and *H. zea* on cotton (Tables 1-3) and on tobacco (Table 4). It was superior in all cases to parathion-methyl at the same rate and to DDT at higher rates, it was about equal to monocrotophos and methomyl.

Against the Egyptian cotton leafworm *Spodoptera littoralis* profenofos, chlorpyrifos, phosfolan and leptophos were equal in efficacy (Table 5). The results of the small plot trials were confirmed with an aerial application, where a dense population of small and large larvae was practically eliminated (Table 6). Table 7 shows results against 3 mite species on cotton. Profenofos performed rather better than monocrotophos and was equal to dicofol against the spider mites *Tetranychus urticae* and *T. cinnabarinus*, whilst against the tarsonemid mite *Hemitarsonemus latus* profenofos (600 g/ha) was equal or superior to dicofol (1000 g/ha). As is frequently observed with cotton mites, two applications are often needed to give satisfactory control.

Profenofos was as active as the systemic aphicides dimethoate and monocrotophos against *Aphis gossypii* and *Thrips tabaci* (Table 8). These results were achieved with low volume application, where mainly the upper leaf-surface was treated. This is good evidence for the good translaminar activity of profenofos although it is not truly systemic. Jassids (*Empoasca* sp.) are not well controlled by profenofos.

The good results against lepidopterous pests on cotton were matched with typical representatives of lepidopterous vegetable pests (Table 9). Profenofos was equal to methomyl against *Mamestra brassicae*, but rather superior to methomyl against *Plutella xylostella*. Against the organophosphorus-resistant American cabbage looper *Trichoplusia ni* acceptable control was achieved by profenofos, monocrotophos and methomyl, none of them quite reaching the level of efficacy of the ovicide chlordimeform.

The good activity against aphids and thrips on cotton was also confirmed in trials on vegetables (*Myzus persicae*, *Brevicoryne brassicae*, *Thrips tabaci*) (Table 10). Again profenofos reached the level of efficacy of good standard aphicides (dimethoate, dioxacarb, monocrotophos, pirimicarb).

Overall, profenofos shows a broad spectrum of activity against the main pests in cotton and vegetables. Its high activity, favourable ecological behaviour and low toxicity make it a most valuable tool in plant protection.

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BUPIRIMATE - A NEW FUNGICIDE FOR THE CONTROL OF POWDERY MILDEWS ON APPLES AND OTHER CROPS

J.R. Finney, G.M. Farrell and K.J. Bent

Imperial Chemical Industries Ltd, Plant Protection Division, Jealott's Hill Research Station, Bracknell, Berkshire.

Summary Bupirimate is a pyrimidine fungicide of low mammalian toxicity, discovered at Jealott's Hill Research Station of the Plant Protection Division of ICI in 1972. It has been extensively evaluated in the field and has shown outstanding activity as a spray against powdery mildews on many crops including apples, roses, peaches, currants and cucurbits in a range of environmental conditions. Its effective activity is limited to powdery mildews and, in view of its specificity of action it should prove useful in integrated control programmes.

Bupirimate has both eradicant and protectant properties; it is freely systemic within sprayed leaves and exhibits translaminar and vapour activity.

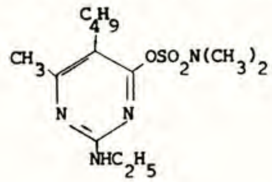
The compound is available as either an emulsifiable concentrate or a dispersible powder and has been introduced commercially in several countries in 1975 under the trade name 'Nimrod'*.

INTRODUCTION

Bupirimate, 5-butyl-2-ethylamino-6-methylpyrimidin-4-yl dimethylsulphamate, is a new pyrimidine fungicide, discovered at Jealott's Hill Research Station of the Plant Protection Division of ICI in 1972. It has been widely tested under the code number PP588, and has been introduced commercially in several countries in 1975, under the trade name 'Nimrod'*.

CHEMICAL AND PHYSICAL PROPERTIES

Structural formula



*'Nimrod' is a registered trade mark of the Plant Protection Division of Imperial Chemical Industries Ltd.

Melting point	50–51°C (pure). Technical material melts at about 40–45°C
Vapour pressure	0.5×10^{-6} torr at 20°C 2.0×10^{-6} torr at 30°C
Appearance	Pale brown, waxy solid
Stability	Unstable on prolonged storage at temperatures above 37°C
Solubility	The solubility in water at room temperature is 22 mg/l. Soluble in most common organic solvents other than paraffin hydrocarbons

FORMULATION

Two formulations are available at present: an emulsifiable concentrate (e.c.) containing 250g a.i./l and a wettable powder (w.p.) containing 250g a.i./kg.

TOXICOLOGY

Bupirimate is of low systemic toxicity

Table 1

Acute toxicity of bupirimate

Route	Test species	LD50 mg/kg	
Acute oral	Rat (female)	ca	4,000
	Mouse (female)	>	4,000
	Guinea pig (male)	ca	4,000
	Rabbit (female)	2,000 -	4,000
	Pigeon	>	2,700
	Quail	>	5,200
Acute intraperitoneal	Rat	2,000 -	4,000

When rats were fed for 90 days on diets containing up to 1,000 ppm bupirimate, no ill effects were detected; in dogs, the no-effect level after 90 days was 15 mg/kg. Longer term feeding tests are in progress.

The 24-hour dermal LD50 of bupirimate for rats is greater than 4000 mg/kg. There were no clinical signs directly related to the compound after 10 daily skin treatments with 500 mg/kg. From such tests and from field experience, it is considered to be neither a skin irritant nor a sensitiser. It caused mild irritation in the rabbit eye.

Bupirimate is not appreciably volatile at ambient temperatures and rats were unaffected when exposed to a saturated atmosphere for six hours/day, five days/week, for three weeks.

It is also of low toxicity to fish and invertebrates. The 96 h T.L.m. for rainbow trout is 1.7 mg/l. No adverse effects have resulted from topical and oral administration to bees at several times the rates recommended for field use. Earthworms and soil micro-arthropods were unaffected after 7 months by 20 kg/ha applied as the e.c. formulation to sandy clay loam and calcareous loam soils.

METABOLISM

The main metabolite of bupirimate found in plant material and in aqueous solutions exposed to sunlight is 5-butyl-2-ethylamino-4-hydroxy-6-methylpyrimidine (ethirimol), a marketed fungicide of low acute and chronic toxicity. Laboratory studies have shown that bupirimate also degrades in soil. Fifteen applications of 2 - 14C - labelled bupirimate were made at 10-11 day intervals to a loamy soil at a rate equivalent to 0.084 kg/ha. One year after the start of the study only 15-25% of recovered radioactivity was parent material. One year after application of bupirimate at 10 or 100 times the above rate 30-40% of recovered radioactivity was bupirimate.

RESIDUES

Apples treated with 11 or 12 HV sprays containing 100-200 mg/l. bupirimate e.c. or w.p. contained 0.04 - 0.12 mg/kg of the parent compound at harvest four weeks after the final spray. Residues of the main breakdown product also occurred, but were usually much lower than those of bupirimate.

SPECTRUM OF ACTIVITY

Bupirimate is highly active against many powdery mildews, but appears to have no useful effect against a wide range of other plant pathogens. Activity against apple powdery mildew (Podosphaera leucotricha) has been investigated in most detail; control of this disease has been generally excellent in field trials in many countries during 1972-75. Good results have also been obtained from field trials against powdery mildews of peach, rose, cucurbits, vine, blackcurrant, apricot, mango, sugar beet, strawberry, chrysanthemum, pea and pepper.

MODE OF ACTION

Only a brief outline of available results can be given here; results will be published in further detail elsewhere. Bupirimate sprays have protectant and curative properties. The compound moves readily from spray deposits into leaves and is translocated towards the leaf margins. Translaminar action is readily achieved, for example on apple leaves from droplets containing less than 1 mg/l. of bupirimate. Uptake occurs from spray deposits on green stems, allowing some movement of bupirimate into young leaves. There is no evidence for phloem mobility, and repeated sprays are usually required for satisfactory protection of new growth. Bupirimate gave relatively poor control of foliar infection when applied to young apple and cucumber plants via the soil.

Bupirimate has activity in the vapour phase at recommended rates of application. In glasshouse bioassays the vapour action of bupirimate against apple powdery mildew is stronger than that of similar concentrations of dinocap, drazoxolon and quinomethionate.

FIELD TRIALS

Apples

Bupirimate has been tested in most of the major apple-growing countries and has given excellent control of both primary and secondary mildew.

The visual effect on primary infections is a suppression of sporulation, usually significantly better at recommended rates of application (75 - 150 mg/l. HV) than that achieved by dinocap (250 - 300 mg/l.), binapacryl (500 mg/l.), sulphur (3,200 mg/l.) or triforine (250 mg/l.) and similar to that achieved by thiophanate-methyl (500 mg/l.), benomyl (250 mg/l.) or ditalimfos (375 mg/l.)

Control of secondary mildew has also been very good, even at low rates of application. Examples are shown in Tables 2 and 3. The e.c. formulation has generally been slightly more active than the w.p.

Table 2

Percent control of secondary mildew in UK trials, 1974

Treatment	Rate mg a.i./l.	Trial 1 Golden Delicious	Trial 2 Cox's Orange Pippin	Trial 3 Cox's Orange Pippin
Dinocap	250	26.6 c	22.3 c	62.2 a
Thiophanate-methyl	500	47.3 ab	38.6 b	73.5 a
Bupirimate w.p.	100	41.9 b	43.0 ab	64.9 a
Bupirimate w.p.	150	55.7 a	47.6 ab	67.8 a
Bupirimate e.c.	100	56.0 a	53.1 a	78.8 a
Bupirimate e.c.	150	57.4 a	48.9 ab	75.5 a

In this and subsequent tables means flanked by a common letter are not statistically different at $\underline{P}$ = 5%. Trials were sprayed HV ar approximately 14 day intervals throughout the season. Secondary mildew was assessed on a 0 - 3 scale on the five youngest expanded leaves on each of 10 extension shoots per tree. On untreated trees 98, 99 and 90% of leaves were infected in Trials 1, 2 and 3 respectively.

Table 3

Percent infection with secondary mildew, Australia 1973/74

Treatment	Rate mg a.i./l.	Trial 1 Jonathan	Trial 2 Jonathan
Bupirimate e.c.	100	24.9 ab	-
Bupirimate e.c.	200	17.2 a	6.7 a
Triforine	250	34.5 bc	15.3 ab
Benomyl	250	43.3 c	19.8 b
Untreated control		97.2 d	66.2 c

Trials were sprayed HV at 14 day intervals, and percent infection was determined on extension shoots. Excellent results have also been reported from many other countries, including New Zealand (O'Connor, 1974), and Israel (Shabi, 1975).

Detailed assessments for phytotoxicity on leaves and fruit have been made on most of the important apple varieties following bupirimate sprays applied high volume as either the e.c. or w.p. formulation at 50 - 400 mg/l. In the vast majority of cases there has been no adverse effect. On the varieties Cox's Orange Pippin, Jonathan and Rome Beauty, HV applications of the e.c. formulation have occasionally induced some premature loss of older leaves, particularly from rosettes (clusters). The effect has occurred mainly under conditions of drought stress, and appears to be an accentuation of the natural loss of leaf which tends to occur when the water supply is restricted. In an extensive series of unreplicated grower trials in the United Kingdom in 1974, covering all the important varieties, neither formulation of bupirimate caused premature defoliation when applied at recommended LV rates (300 - 600 mg/l. in 500 l water/ha applied at 10 - 14 day intervals).

Roses

Bupirimate at 400 mg/l. or above has given excellent control of powdery mildew (Sphaerotheca pannosa) on glasshouse and outdoor roses in several countries. Table 4 gives results from a trial in Holland on the variety Sonia, after seven HV sprays applied at a mean interval of 17 days. A non-ionic wetting agent ('Agral' 90) was included at 0.1% w/v.

Table 4.

Control of powdery mildew on glasshouse roses, Holland 1974.

Treatment	Rate mg a.i./l.	% of leaves infected
Bupirimate e.c.	400	4.7 ab
Bupirimate e.c.	600	1.5 b
Bupirimate e.c.	800	1.7 b
Bupirimate e.c.	1000	0.1 b
Dodemorph	1000	18.0 a

Cucurbits

In trials in Spain, Australia, Hungary and Egypt sprays of bupirimate at 75 - 250 mg/l. were highly effective against powdery mildew (Sphaerotheca fuliginea/Erysiphe cichoracearum) on squash, cucumber and melon. The results in Table 5 were obtained in Australia after two sprays with a 10 day interval.

Table 5

Control of powdery mildew of zucchini squash Australia, 1975

Treatment	Rate mg a.i./l.	Disease grade*
Bupirimate e.c.	150	2.2 cd
Bupirimate e.c.	250	2.0 d
Triforine	250	3.7 b
Benomyl	250	2.5 bd
Dimethirimol	250	2.5 bd
Control	-	7.0 a

* linear scale, 0 = 0 - 10%, 9 = 90 - 100% infection

Peaches

In trials in Europe and S.America excellent control of Sphaerotheca pannosa was achieved with sprays of bupirimate at 50 - 200 mg/l. Results shown in Tables 6 and 7 were obtained on the variety Legrand (a nectarine).

Table 6

Control of peach powdery mildew, Argentina 1974

Treatment	mg a.i./l.	% Fruits infected with mildew after two applications	% Fruits infected with mildew after three applications
Bupirimate e.c.	50	4.0	7.0
Bupirimate e.c.	100	3.0	4.5
Bupirimate e.c.	200	1.5	2.5
Untreated	-	41.5	42.5

Table 7

Control of peach powdery mildew, Argentina 1974

Treatment	mg a.i./l.	% Fruits infected with mildew 17 days after a single treatment	% Fruits infected with mildew 56 days after a single treatment
Bupirimate e.c.	50	3.0	5.5
Sulphur	10,000	3.5	9.0
Binapacryl	250	9.0	11.5
Dinocap	200	8.0	8.5
Pyrazophos	300	0.0	6.0
Quinomethionate	70	19.5	16.0
Untreated	-	46.5	28.5

Vines

Control of *Uncinula necator* has been achieved with bupirimate at 100 - 200 mg a.i./l in several countries. The results in Table 8 were obtained after six applications at 14 day intervals. Bupirimate was superior to two other systemic fungicides and in contrast to dinocap or sulphur did not cause phytotoxicity.

Table 8

Control of vine powdery mildew, Cyprus 1974

Treatment	mg a.i./l	% leaves infected
Bupirimate e.c.	100	9.8 c
Bupirimate e.c.	200	5.5 c-d
Sulphur	1000	•1.6 d
Benomyl	250	22.8 b
Thiophanate-methyl	250	•20.6 b
Dinocap	125	•3.5 c-d
Control	-	62.3 a

•slight phytoxicity

Mangoes

Good control of Oidium mangiferae was achieved in Egypt. The results in Table 9 were obtained after six applications at 14 day intervals.

Table 9

Control of mango powdery mildew, Egypt 1975

Treatment	mg a.i./l.	Disease index* Trial 1	Disease index* Trial 2
Bupirimate e.c.	100	1.4 b	1.2 b
Dinocap	240	1.8 b	1.2 b
Dinocap	480	1.2 b	1.2 b
Triforine	250	1.4 b	1.2 b
Carbendazim	500	1.8 b	1.2 b
Control	-	4.0 a	3.4 a

*Visual grading, scale 1 (no infection) - 4 (severe infection)

USE IN INTEGRATED CONTROL PROGRAMMES

Evidence from several sources indicates that bupirimate can be used with confidence where lack of activity on insect or mite predators is required. In glasshouse tests at Jealott's Hill Research Station, bupirimate gave no control of various insects, molluscs, acarina or nematodes even when applied at many times the normal field concentrations. In laboratory tests and field trials at the Fruit Research Station, Wilhelminadorp, Holland, no harmful effects were found on populations of Typhlodromus potentillae, an important predator of the fruit tree red spider mite (Panonychus ulmi). Similar results on T.potentillae were recorded at the Orchard for Integrated Pest Control, Lienden, Holland. Another predator, Stethorus punctillum, was unaffected by bupirimate sprays in a field trial in Spain in 1973.

Acknowledgements

The authors are grateful to many colleagues within Imperial Chemical Industries and to collaborators and growers for their kind co-operation. Data on control of powdery mildew on vines and mangoes are quoted by permission of Dr. J.P.Zyngas, Ministry of Agriculture and Natural Resources, Cyprus, and H.Chiati and K.Khatil, ICI PPD Technical Liaison Office, Cairo, respectively.

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Proceedings 8th British Insecticide and Fungicide Conference (1975)

ETRIMFOS - A NEW INSECTICIDE WITH LOW MAMMALIAN TOXICITY

H.J. Knutti and F.W. Reisser
Sandoz Ltd., CH-4002 Basle, Switzerland

Summary Etrimfos (SAN 197 I), O-6-ethoxy-2-ethylpyrimidin-4-yl OO-dimethyl phosphorothioate, is a broad-spectrum, non-systemic contact and stomach insecticide with low toxicity to mammals. The acute oral LD_{50} in male rats is 1800 mg/kg and the dermal LD_{50} is > 2000 mg/kg. It can be formulated as e.c., ULV, granules, microgranules and dusts. It has a residual activity of 7-14 days.

Etrimfos has been field tested up to 3 years in about 30 countries against a wide range of pests, at various dosages, under various climatic conditions. The results revealed good effectiveness against species of Lepidoptera, Coleoptera, Diptera, and, to a variable extent, Hemiptera, mainly on fruits (including grapes), vegetables, paddy, maize and lucerne. The effective rate is 250-750 mg a.i./l. (or 0.25-0.75 kg a.i./ha), depending on species, except for granular application against Pyralidae in paddy, which requires 1-1.5 kg a.i./ha. Etrimfos is well tolerated by the majority of crops.

Résumé Etrimfos (SAN 197 I), O-6-ethoxy-2-ethylpyrimidin-4-yl OO-dimethyl phosphorothioate, est un insecticide de contact et d'ingestion non systémique, à large spectre d'action et de faible toxicité pour les mammifères. Pour le rat mâle, les doses léthales aiguës orale et dermale (LD 50) sont, respectivement, de 1800 > 2000 mg/kg. Il peut être formulé comme e.c., ULV, granulé, microgranulé et poudre pour poudrage. Son activité résiduelle est de 7 à 14 jours.

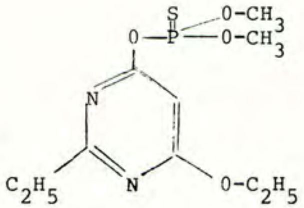
Etrimfos a été testé en plein champ durant 3 ans dans environ 30 pays, contre un grand nombre de ravageurs, à des dosages divers et dans des conditions climatiques variées. Il a fait preuve d'une bonne efficacité contre de nombreuses espèces de l'ordre des Lépidoptères, des Coléoptères, des Diptères, ainsi que contre certaines espèces de l'ordre des Hemiptères, principalement sur fruits (vigne comprise), légumes, riz, maïs et luzerne. La dose active se situe entre 250-750 mg m.a./l. (ou 0.25-0.75 kg m.a./ha), suivant l'espèce, à l'exception de l'application de granulés contre les Pyralides du riz qui se

fait à 1-1.5 kg m.a./ha. Etrimfos est bien toléré par la majorité des cultures.

INTRODUCTION

Etrimfos was developed in 1972 by the Agroresearch Division, Sandoz Ltd., Basle, Switzerland, under the code number SAN 197 I, and found effective against Lepidoptera, Coleoptera and Diptera. Since 1973, it has been tested extensively throughout the world in the majority of economically important crops mainly against pest species of the Orders indicated above.

CHEMICAL AND PHYSICAL PROPERTIES

BSI and proposed ISO common name	etrimfos
Chemical name	O-6-ethoxy-2-ethylpyrimidin-4-yl OO-dimethyl phosphorothioate
Code number	SAN 197 I
Structural formula	
Molecular formula	$C_{10}H_{17}N_2O_4PS$
Molecular weight	292
Colour and physical state	colourless oil
Refractive index n_D^{20}	1.5068
Odour	slight smell, characteristic of thionophosphates
Vapour pressure, at 20°C	6.5×10^{-5} mm Hg
Solubility, at 20°C	in water < 1%; soluble in ethanol, acetone, diethyl ether, xylene, kerosene.
Stability, hydrolytic	measured in an aqueous, buffered solution at 48-50°C, containing 50 mg a.i./l.; the extrapolated half-life periods, at 22-24°C, are 11-16 days, depending on pH in the range of 5-9.
Formulations	50% w/w e.c., 10 and 5% w/w granular. Dust, microgranule, w.p. and ULV formulations are under investigations.

TOXICOLOGY (ACTIVE INGREDIENT)

a. Acute mammalian toxicity

Route	Species		LD_{50} (a.i.)
oral	rat	♂	1800 mg/kg
	mouse	♂	437 mg/kg
dermal	rat	♂	>2000 mg/kg
	rabbit	♂	> 500 mg/kg (higher doses not applicable)

b. Sub-chronic toxicity

In a 26-week feeding study with Beagle dogs, the no-effect level was about 12 ppm; in rats after 3 months, the no-effect level was 9 ppm. Other investigations under way have shown favourable results so far.

c. Acute fish toxicity

For exposure of 48 and 96 hours the concentrations producing 50% kill were 13.6 and 13.3 mg a.i./l., respectively, for carp (*Cyprinus carpio*).

RESIDUES

Residues at harvest, and degradation curves have been determined in certain fruit, vegetable and field crops. Based on this and the chronic toxicological work so far conducted, a waiting period of 1-2 weeks is anticipated.

BIOLOGICAL PROPERTIES

Etrimfos is a non-systemic contact and stomach insecticide with a moderate residual activity, lasting about 7-14 days.

The range of activity of etrimfos covers species of Lepidoptera, Coleoptera, and Diptera, as well as certain specific Hemiptera and Orthoptera (Dictyoptera), mainly in the field of plant protection but also in stored product and hygiene use.

FIELD TRIALS

Although invariably multi-replicate, randomized block designs were used, an analysis of variance could only be conducted on individual trials but seldom on groups of trials even though the same species (as presented here) were involved, because either the number of replicates, methods/dates of evaluation, or sometimes dosages and standards were not identical. All rates are given in active ingredients.

a. Pip fruits

In Europe, etrimfos was found effective against all pre- and post-bloom chewing insect species, and against insect species occurring in summer (Table 1). Usually good suppression was obtained with secondary pests, such as aphids and mites (without affecting certain predators).

In USA spray schedules with 6-7 applications revealed good to excellent control of pest complexes in apples, usually equivalent to azinphos-methyl (Table 2), which has a much higher mammalian toxicity.

The crop safety has been found to be excellent except for certain varieties under specific conditions in USA. This matter is being investigated, and we expect to find a solution.

Table 1

Control of given insects on pip fruits in Switzerland and Italy in 1974

Insect \ Spray mg a.i./l.	Average % control by Etrimfos 50% e.c. 250	Etrimfos 50% e.c. 500	Methidathion 300	Diazinon 300	Phosalone 500	Number of trials
a. Pre-bloom						
Cheimatobia brumata	94	98	97	86	92	4
Spilonota ocellana	78	98	98	92	69	4
Hyponomeuta spp.	100	100	98	98	-	2
b. Post-bloom						
Hyponomeuta spp.	97	100	-	81	96	5
Archips rosanus	88	98	-	-	75	1
Hoplocampa testudinae	97	100	-	99	95	2
c. Summer						
Capua reticulana	93	91	87	78	-	2
Lyonetia clerkella	94	98	96	90	96	1
Laspeyresia pomonella	-	84	-	-	-	4

Table 2

Control of given insects on apples in USA in 1974

Species \ Spray mg a.i./l.	Average % control by Etrimfos 50% e.c. 300	600	Azinphos-methyl 300	Number of trials
Laspeyresia pomonella	90	98	99	5
Other Tortricidae	95	97	98	4
Conotrachelus nenuphar	94	90	91	4
Rhagoletis pomonella	75	81	78	3
Lepidosaphes ulmi	99	99	78	1

b. Grapes

The main investigations concentrated on "cochylis", *Clysia ambiguella*, and the grape berry moth, *Lobesia (Polychrosis) botrana*, in various European countries. Table 3 shows that etrimfos is effective against both species in the 3 countries of investigation, while standards partially failed. No phytotoxicity was reported up to the 1 g/l. applied.

Table 3

Control of Tortricidae on grapes in France, Italy and Switzerland in 1974

Insecticides	mg a.i. g/l.	Average % control of France *Clysia* (3 trials)	France *Lobesia* (1 trial)	Italy (4 trials*)	Switzerland (4 trials**)
Etrimfos (50% e.c.)	250	78	60	77	94
Etrimfos (50% e.c.)	375	74	80	88	93
Etrimfos (50% e.c.)	500	86	93	90	93
Azinphos-methyl	400	64	-	40	84
Parathion	200	79	73	80	86
Trichlorphon	950	-	-	-	73
Methomyl	375	-	-	83	-

* 2 trials against the first generation of *Lobesia* and 2 trials against the second generation of both species.

**2 trials against each species.

c. Vegetables

The spectrum of activity, low mammalian toxicity, general crop safety, lack of unpleasant odour, and the expected short waiting period make etrimfos an ideal product for use in vegetables. In the large number of trials conducted in many countries, etrimfos was found effective mainly against species of the families Plutellidae, Pieridae, Pyralidae, Gelechiidae, Noctuidae (specifically Spodoptera spp.), and Chrysomelidae. Due to the complexity of the results (various crops, many species, different methods and dates of evaluation, and different standards), we refrain from presenting results in detail.

Crop safety was found excellent in all 12 vegetable crops investigated, with the possible exception of tomatoes under certain tropical conditions.

d. Paddy

Due to its low fish toxicity, etrimfos is well suited for use in paddy. Against the paddy stemborer, it is superior to diazinon and equal to quinalphos as a granule, and somewhat inferior as an e.c. (Table 4). Quinalphos was applied as 25% e.c. or 5% granules.

In official trials in Japan, etrimfos at about 1 kg/ha compared favourably to the best standards against rice stemborer, Chilo suppressalis, and certain other paddy pests (Iwata, 1975).

At twice or thrice the rate required for effective control no phytotoxicity problems were encountered.

Table 4

Trials against paddy stemborer, Tryporyza incertulas, in paddy in 1974/75 in India

Insecticides	Granules kg a.i./ha	% control*	e.c. kg a.i./ha	% control**
Etrimfos	1.5	92	0.5	73
10% granules	3.0	90	1.0	87
Diazinon	1.5	75	0.5	72
10% granules	3.0	85	1.0	76
Quinalphos	1.5	90	0.375	81
5% granules	3.0	92	-	-

* Evaluation based on dead heart counts 15 days after first granular application; average of 3 trials.

**Evaluation based on white ear head counts 60 days after the third spray; average 2 trials.

e. Maize

Trials were conducted in field corn with granular formulations against heavy natural infestations of European corn borer, Ostrinia nubilalis in Switzerland/France (in regions with one generation), and mainly against artificial infestations of first and second generations in USA. Table 5 reveals the outstanding performance of etrimfos, being superior to all standards investigated. In addition to the granular formulation the 50% e.c. formulation is being investigated in 1975.

Fall army worm, Spodoptera frugiperda, control was satisfactory to excellent at 500 mg/l. (or 0.5 kg/ha) or at even lower rates in various trials in Florida and Costa Rica.

Maize showed minor susceptibility to higher rates of etrimfos but only in the young crop stage, at a time before insecticide applications are normally made.

Table 5

Control of European corn borer, Ostrinia nubilalis

Insecticides	Granules % a.i.	kg a.i./ha	France* 1973 (%)	Switzerland** 1974 (%)	USA*** 1974 (%)
Etrimfos	10	0.5	-	-	70
Etrimfos	10	0.75	-	88ab	-
Etrimfos	10	1.0	87ab	-	78
Etrimfos	10	1.5	-	93a	-
Etrimfos	10	2.0	91a	-	-
Diazinon	10 or 14	1.0	58c	-	65
Diazinon	10	1.5	-	83b	-
Diazinon	10	2.0	79b	-	-
DDT	5	1.5	63c	84b	-
Carbofuran	10	1.0	-	-	70

* Two trials. Values with common letter suffix do not differ at 5% level by Duncan Multiple Range test.

** Evaluation based on counts in 3 trials of live larvae in 20 completely dissected plants/plot. Values with common letter suffix do not differ at 5% level by Duncan Multiple Range test.

***Evaluation based on counts of cavities in 20 completely dissected plants/plot. 4 trials.

f. Other crops

Etrimfos was tested on many other crops, with the result that it can be regarded as safe in HV-applications, with the exception of cherries in overdosage, and of sorghum at a certain stage of development.

Effective control was achieved against alfalfa weevils, Hypera spp. and pea aphid, Macrosiphum pisi, with etrimfos at 0.25-0.5 kg/ha in alfalfa in USA. Efficacy and possible phytotoxicity against black scale, Saissetia olea, on olives, was evaluated in two trials in Spain in 1975. Etrimfos 50% e.c. was 89, 97 and 95% effective at 250, 500 and 1000 mg a.i./l., respectively, whereas carbaryl at 2100 mg a.i./l gave 87% control and azinphos-methyl at 400 mg a.i./l. gave 93% control.

g. Special studies in plant protection

To investigate the knock-down effect and the persistence of the product under field conditions, a series of trials was conducted, among others, against the Colorado potato beetle, Leptinotarsa decemlineata, in various European countries in 1973.

Table 6 shows that effectiveness is almost complete 1-2 days after application. In fact, in the trials in which counts were made 5 hours after application, control was already at least 85%. At the higher concentrations tested, satisfactory efficacy was recorded up to 16 days (last counts). In these trials, etrimfos was more effective than the standards phosalone and carbaryl at equal a.i. rates.

Table 6

Control of Colorado potato beetle, *Leptinotarsa decemlineata*, with etrimfos 50% e.c. at given application/evaluation intervals in 5 trials

Number of days from application to evaluation	Average % control at 250	500	1000 mg a.i./l.
1- 2	91	98	100
5- 7	93	97	100
8-16	64	79	96

h. Uses other than in plant protection

Etrimfos has been found to be superior to the standard malathion against a number of stored product insects, complete control during 6 months was obtained with the former.

The spectrum of activity and the low toxicity call for certain investigations in the field of hygiene use.

CONCLUSIONS

As a foliar insecticide, mainly against chewing pests or pest complexes on many economically important crops, etrimfos has a remarkable potential for filling a gap in the market for a thoroughly investigated, effective broad-spectrum contact and stomach insecticide, with moderate residual action and of very low toxicity to the user.

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SAN 155 I - A NEW INSECTICIDE OF A NOVEL CLASS OF CHEMICALS

W. Berg and H.J. Knutti
Sandoz Ltd., CH-4002, Basle, Switzerland

Summary SAN 155 I *NN*-dimethyl-1,2,3-trithian-5-ylammonium hydrogen oxalate, is a new insecticide, belonging to a novel class of chemicals. It can be formulated as wettable powder, soluble powder, granular and microgranular formulations, but not as an emulsifiable concentrate. The active ingredient is of moderate mammalian toxicity, the acute oral LD_{50} for male rats being 310 mg/kg.

SAN 155 I is a stomach and contact insecticide with a new mechanism of action, not affecting cholinesterase activity. It has slight systemic action, being acropetally translocated in plants. SAN 155 I is specifically active against a number of economically important lepidopterous and coleopterous pests of different crops. Field trials over 2 - 4 years revealed good efficacy against the larvae of the Colorado potato beetle *(Leptinotarsa decemlineata)*, as well as the rice stem borer *(Chilo suppressalis)* on paddy in Japan, the paddy stem borer *(Tryporyza incertulas)* and the sugarcane borer *(C. infuscatellus)* in India, the European corn borer *(Ostrinia nubilalis)*, the diamondback moth *(Plutella xylostella)* on cabbage, and against various lepidopterous leaf miners in different countries (e.g. *Leucoptera scitella* in Italy, *Lyonetia clerkella* in Switzerland and *Phyllocnistis citrella* in Japan).

Resumé SAN 155 I *NN*-diméthyl-1,2,3-trithiane-5-ylammonium hydrogéno-oxalate, est un insecticide nouveau appartenant à une nouvelle classe de matières actives. La substance peut être formulée en poudre mouillable, en poudre soluble, en granulés, en microgranulés, mais pas en liquide pour pulvérisation (EC). Avec une LD_{50} aiguë par ingestion pour le rat mâle de 310 mg/kg, la matière active peut être considérée comme modérément toxique pour les Mammifères.

SAN 155 I est un insecticide d'ingestion et de contact, modérément endothérapique, ayant un nouveau mécanisme d'action. Le produit n'influence pas l'activité de la cholinestérase. Cet hydrogen oxalate est spécifiquement efficace contre un certain nombre de Lepidoptères et de Coléoptères d'importance économique. Le produit, expérimenté en plein champ pendant 2 à 4 années consécutives, a fait preuve d'une bonne efficacité contre les larves du Doryphore *(Leptinotarsa decemlineata)*, la Pyrale asiatique du Riz *(Chilo suppressalis)* au Japon, les Pyrales du Riz *(Tryporyza in-*

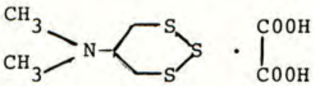
certulas) et de la Canne à Sucre (C. infuscatellus) aux Indes, la Pyrale du Mais (Ostrinia nubilalis), la Teigne des Crucifères (Plutella xylostella) sur Choux, ainsi que diverses chenilles mineuses des feuilles, comme par exemple, Leucoptera scitella en Italie, Lyonetia clerkella en Suisse, et Phyllocnistis citrella au Japon.

INTRODUCTION

Because of the development of resistance,or even cross-resistance, against different chemical classes of conventional insecticides by many pest species, the need for compounds of novel structure, and with new mechanisms of action, has arisen during the last years.

SAN 155 I was discovered in 1970 by the Agro-research Division, Sandoz Ltd., Basle, Switzerland, and found effective against different economically important lepidopterous and coleopterous pests of different crops. Since 1972, sultamine hydrogen oxalate has been tested extensively in the field in Switzerland, France, Italy, Austria, Spain, USA and India. Preliminary results are also available from Japan.

CHEMICAL AND PHYSICAL PROPERTIES

Proposed BSI and ISO common name	sultamine hydrogen oxalate
Chemical name	NN-dimethyl-1,2,3-trithian-5-ylammonium hydrogen oxalate
Structural formula	
Molecular formula	$C_5H_{11}NS_3 \cdot C_2H_2O_4$
Molecular weight	271·4
Colour and physical state	white crystalline solid
Odour	none
Melting point	the anhydrous solid will melt, with decomposition, between 125 - 128 °C
Solubility, at 20 °C	in water 9·6 %
	ethanol, acetone <1 %
	diethyl ether xylene,
	kerosene insoluble
Thermostability	rather stable
	half-life period at 20 °C $\gg$ 2 years
Stability to hydrolysis	evaluated at 22 - 24 °C in an aqueous, buffered solution con-

taining 40 mg a.i./l. **Under the conditions of such a system the free base is hydrolysed following 1st order kinetics.**

The half-life periods are at:

pH 5 about 41 days

pH 7 about 10 days

pH 9 about 11 days

Formulations

90 % w.s.p. and a 5 % granular. Other granular and wettable powder formulations are possible and were investigated in the field. Emulsifiable concentrates, however, are not possible.

TOXICOLOGY (HYDROGEN OXALATE SALT)

The acute oral LD_{50} is 310 and 273 mg/kg to male rats and mice, respectively. The acute dermal LD_{50} to male rats is 1000 mg/kg. In 4-week studies the no effect level to rats was between 40 and 200 ppm of the diet. Over a 3-month period the no effect level in rats was at a dietary level of 100 ppm and in dogs 75 ppm. Chronic studies in dogs, rats and mice are under way.

The LD_{50} to carp (Cyprinus carpio) after exposure for 48 and 96 hours was 1.12 and 1.03 mg/l., respectively. Preliminary investigations suggest that SAN 155 I is moderately toxic to honeybees (Apis mellifera).

RESIDUES

Degradation curves and residues at harvest have been determined in apples and potatoes, and residues at harvest also in pears. Based on this, and on the subacute toxicological work so far conducted, a waiting period for fruits and vegetables of approximately 2 weeks can be anticipated. For such crops as potatoes and corn, waiting periods, according to good agricultural practice, are no problem.

BIOLOGICAL PROPERTIES

SAN 155 I is a selective stomach and contact insecticide with a moderate residual activity, lasting about 7 to 14 days. It shows a certain degree of systemic activity, being acropetally translocated in the plant. This fact may be useful for the uniform distribution of the compound in treated plants. The mode of action is not by cholinesterase inhibition. Thus, a later occurrence of cross-resistance with conventional insecticides is unlikely.

SAN 155 I has a somewhat specific range of activity against different species of Lepidoptera and Coleoptera, that are commercially important in the field of crop protection.

FIELD TRIALS

Usually randomized block designs with small-medium sized plots and 3 replicates were used. In the following text and Tables, all rates are given in terms of active ingredient (kg/ha or mg/l.). The activity against the various pests is expressed as the range of % effectiveness in the different trials, which was calculated according to the formulae of Abbott or Henderson & Tilton.

(a.) Potatoes

SAN 155 I 90 % w.s.p. was extensively tested against the larvae of the Colorado potato beetle, Leptinotarsa decemlineata, in different countries (Table 1). It proved highly effective at rates as low as 125 mg/l. in 4 trials. Most results were obtained with 250 - 270 mg/l., and they were very consistent, and at least equal to those achieved with normal rates of the phosalone standard. Furthermore, they were equivalent to the results obtained from applications of carbaryl or azinphos-methyl at standard dosages.

As no phytotoxicity could be observed in potatoes at 2000 mg/l. (highest dosage tested), SAN 155 I, at 125-250 mg/l. or 0.125 - 0.25 kg/ha can be regarded as an outstanding product for use against Colorado potato beetle. No residue problems will arise in potatoes according to our findings.

(b.) Maize, rice and sugar cane

SAN 155 I has proven to be highly effective against larvae of different borer species (Lepidoptera, Pyralidae).

In France, satisfactory control of the European corn borer (Ostrinia nubilalis) was achieved by applying 0.75 - 1.5 kg a.i./ha, formulated as 10 % granules (Table 2). Further evaluations of the compound, now formulated as 5 % granules, are under way in different countries. Slight crop phytotoxicity has been found only in exceptional cases.

In India SAN 155 I proved highly efficient against the yellow stem borer (Tryporyza incertulas) on paddy when the usual three applications each of 1 kg a.i./ha were made, the material being applied as 90% w.s.p. (Table 3). For different reasons, the use of a granular formulation, especially for the first application, is desirable; there is then a greater likelihood of more effective distribution of the active substance at the point where it is required with consequent less waste of material. In the case of spray application on small plants, recently transplanted, only a relatively small proportion of the spray liquid will reach the foliage close to the target, whereas material, slowly released from a granular formulation, can gradually be taken up by the plants. Furthermore, in granules there is less likelihood of a quick breakdown of the active material in the water due to hydrolysis etc. Thus, a longer period of activity can be expected. With this in mind, a 10 % granule formulation was tested at the same application rate (1 kg/ha) as the 90 % w.s.p. Results were very good after the first application (Table 2), but erratic after the second and third. Thus, a schedule using granules in the first and 90 % w.s.p. in the subequent applications seems of particular interest and will be tested in future. Generally, SAN 155 I looks very promising against T. incertulas, and no phytotoxicity has been observed in rice up to now.

Efficacy in field trials in Japan was very good at 1.2 kg a.i./ha applied as 4 % microgranules against the Pale-headed striped borer or rice stem borer (Chilo suppressalis) (Table 2).

Trials in India with a 50 % w.p., predecessor of the 90 % w.s.p. formulation, against the sugar cane borer (C. infuscatellus) gave encouraging results at rates of 0.5 kg/ha or concentrations of 500 - 1000 mg/l., equal or superior to those obtained with standard compounds at standard dosages (Table 4). Also no phytotoxicity was observed on sugar cane.

Generally, SAN 155 I, applied as a spray or as granules, can be regarded as very promising for the control of different borers in maize, rice and sugar cane.

(c.) Cabbage

Very good efficacy against diamond back moth (Plutella xylostella) was obtained with concentrations from 250 mg/l. (Table 5). The results were equivalent to those achieved with potent local standard insecticides. Good control was obtained also against cabbage whites (Pieris spp.) (Table 6).

From the residue point of view, and because no phytotoxicity has been recorded on cole crops up to now, the control of the most destructive lepidopterous pests of brassicas using SAN 155 I appears a promising area of application.

(d.) Other insects

Table 6 shows the activity of SAN 155 I on some other interesting pests on vegetable and fruit crops. The special activity of SAN 155 I on larvae of A. lineatella and K. lycopersicella seems to be of particular interest, and the citrus leaf miner (Phyllocnistis citrella) was very effectively controlled in a trial in Japan. Similarly, the leaf miners L. scitella and L. clerkella are effectively controlled, especially the former. This pest is a considerable problem on pear trees in Italy, being difficult to control with conventional insecticides, and which offers itself as a main target for SAN 155 I in fruit crops.

CONCLUSIONS

As a foliar insecticide against certain chewing coleopterous and lepidopterous pests (including borers and leaf miners) on many economically important crops, SAN 155 I has a remarkable potential. This is due to the fact that it belongs to a novel class of chemicals, and that insect strains resistant or cross-resistant to conventional insecticides are susceptible to the compound, which does not itself act by cholinesterase inhibition. The residual action is moderate and, accordingly, the degradation in the plant is relatively quick, allowing its use up to about two weeks before harvest in fruit and vegetable crops.

Acknowledgements

We acknowledge the work of many of our colleagues in the Agro-research Division in Basle, and also the work of the Sandoz Field Testing Groups in Austria, France, India, Italy, Spain, Switzerland and USA. In addition we are indebted to the Agricultural Chemicals Dept. of Sankyo Co. Ltd., Japan, for their developmental work.

Table 1

Results with SAN 155 I 90 %
w.s.p. against larvae of Colorado potato beetle

Country	Days after appl.	Range of effectiveness (%) at stated rate mg/l. and (no. trials)									
		SAN 155 I				Phosalone		Carbaryl		Azinphos-methyl	
		125		250 - 270		500 - 600		1300		400 - 500	
Switzer-land (7 trials)	2-4	-		89-100	(7)	80- 99	(6)	99-100	(2)	-	
	6-7	-		81-100	(5)	69- 97	(4)	99-100	(2)	-	
	9-10	-		99-100	(2)	98-100	(2)	-		-	
	14	-		87- 99	(3)	86	(2)	99	(2)	-	
France (3 trials)	1-2	100	(1)	91-100	(3)	100	(1)	-		99-100	(2)
	6-7	100	(1)	100	(2)	100	(1)	-		100	(1)
Italy (4 trials	1-3	-		95-100	(4)	-		95-99	(2)	91- 99	(2)
	7	-		77-100	(4)	-		80-96	(2)	100	(2)
	14	-		99	(1)	-		-		100	(1)
Austria	7	-		94	(1)	-		100	(1)	-	
Spain (7 trials)	1-3	98-100	(3)	95-100	(7)	98-100	(3)	76-100	(7)	-	
	5-8	80- 96	(3)	90-100	(5)	96-99	(3)	100	(5)	-	
	11	87	(1)	95	(1)	95	(1)	100	(1)	-	
Portugal (1 trial)	2	-		98	(1)	-		-		100	(1)
	7	-		95	(1)	-		-		100	(1)
	14	-		94	(1)	-		-		96	(1)

Table 2

Effect of SAN 155 I granules against Pyralidae larvae

Pest/crop & country	Days after appl.	(No. trials)	SAN 155 I % a.i.	SAN 155 I kg a.i./ha	SAN 155 I % Effectiveness	Diazinon % a.i.	Diazinon kg a.i./ha	Diazinon % Effectiveness
Ostrinia nubilalis maize in France	82-84	(3)	10	0.75	65- 84	10	1.5	74-93
	82-84	(2)	10	1.5	77- 84	10	1.5	74-82
Tryporyza incertulas paddy in India	13-26	(3)	10	1.0	97-100+	5	1.5	98-100+
Chilo suppressalis rice in Japan	20-31	(2)	4*	1.2	100	3	0.9	36-90

* Microgranules. + Based on no. dead hearts.

Table 3

Effect of SAN 155 I 90 % w.s.p. against paddy stem borer in paddy in India

Days after application		SAN 155 I 1.0 kg a.i./ha % Yield*	SAN 155 I 1.0 kg a.i./ha % Effectiveness	Fenitrothion 0.5 kg a.i./ha % Yield*	Fenitrothion 0.5 kg a.i./ha % Effectiveness
18	1st	-	85+	-	76+
57	3rd	115	100‡	106	71‡
11	2nd	-	96+	-	4+
50	3rd	-	77‡	-	52‡
15	2nd	-	85+	-	74+
20	1st	-	96+	-	54+
36	3rd	123	75‡	109	33‡

* Relative to untreated. +Based on no. dead hearts. ‡Based on no. white ear heads.

Table 4

Effect of SAN 155 I 50% w.p.
against sugar cane borer on sugar cane in India

SAN 155 I mg a.i./l.	% Effectiveness	% Effectiveness Endosulfan 400 mg a.i./l.	Phosphamidon 500 mg a.i./l.	Cartap 500 mg a.i./l.
500	68	60	72	-
1000	84			
500	83	84	84	-
1000	85			
500	96	-	-	84
500	81	-	-	61

Table 5

Effect of SAN 155 I
against the larvae of diamond back moth,
Plutella xylostella, on cabbage

Country & formulation	Days after latest applic.		% Effectiveness SAN 155 I mg/l. 250	500	1000	Methomyl 90% w.s.p. 500	1000 mg/l.	Other compounds
U.S.A.	5	2nd	-	96	99	-	100	91*
50% w.p.	6	3rd	-	87	98	-	82	95*
	1	5th	-	92	97	-	98	92*
India	3	1st	-	-	100	-	100	-
90% w.s.p.	10	2nd	-	-	67	-	67	-
	3	1st	100	100	100	50	-	100+
	10	2nd	71	79	79	71	-	79+

*Leptophos (25% e.c.) 1000 mg a.i./l. +Endosulfan (35% e.c.) 700 mg a.i./l.

Table 6

Activity of SAN 155 I against various Lepidoptera and a Coleoptera

Pest/crop & country	% Effectiveness				
	SAN 155 I (normally 90% w.s.p.) at mg a.i./l. 250	500	1000	Standard products at normal rates	No. trials
Epilachna 28-punctata eggplant in India	100*	-	-	100	1
Anarsia lineatella peach in Spain	-	-	84-99	71-98	5
Keiferia lycopersicella tomato in U.S.A.	-	91-100*	100*	31-100	2
Leucoptera scitella pear in Italy	89-100	100	-	46-71	2
Lyonetia clerkella apple in Switzerland**	97-99	-	-	65-96	2
Pieris brassicae cabbage in Switzerland	-	-	93	93-100	1
in Spain	97	100	-	100	1
Pieris rapae cabbage in Switzerland	-	85-98	65-100	15-100	4
Cheimatobia brumata apple in Switzerland	86-94	95-98	-	81-100	5

* 50 % w.p. used. ** 50 % w.p. & 90 % w.s.p. used in one trial each.

EXPERIENCES WITH VINCLOZOLIN IN THE CONTROL OF BOTRYTIS CINEREA IN STRAWBERRIES

C. Hess and F. Löcher

BASF AG, Agricultural Research Station,
Limburgerhof, Federal Republic of Germany

Summary The fungicide 3-(3.5-dichlorophenyl)-5-methyl-5-vinyl-1.3-oxazolidine-2.4-dione (common name: vinclozolin) of the oxazolidine group demonstrated in laboratory and field tests a very specific action against the pathogens *Botrytis cinerea*, *Monilia* spp. and *Sclerotinia sclerotiorum*. Vinclozolin is formulated as 50% and 75% wettable powders under the code numbers BAS 352 00 F and BAS 352 02 F. It is specially developed for use in vines, fruit, hops and ornamentals. For successful control of *B. cinerea* in strawberries three sprays during the period of flowering are necessary. The application rate is 1.0 kg a.i./ha. Both formulations have shown themselves to be non-phytotoxic to strawberries. Work carried out on toxicology indicates that the compound is completely safe for use in agricultural crops.

Résumé Le fongicide 3-(3.5 dichlorophenyl)-5-méthyl-5-vinyl-1.3 oxazolidine-2.4-dione (nom commun: vinclozoline), du groupe des oxazolidines, a fait preuve, lors d'essais de laboratoire et de plein champ, d'une efficacité très spécifique à l'encontre des champignons pathogènes *Botrytis cinerea*, *Monilia spp* et *Sclerotinia sclerotiorum*. La vinclozoline a été formulée sous forme de deux poudres mouillables à 50 et 75% portant les numéros de code: BAS 352 00 F et BAS 352 02 F. La matière active a été spécialement développée pour application en vigne, sur cultures fruitières, houblon et plantes ornementals. Trois traitements pendant la floraison seront nécessaires à l'obtention d'un bon résultat contre le Botrytis du fraisier. La dose est de 1.0 kg de m. a./ha. Aucune des deux formulations n'est phytotoxique. Des études de toxicité ont démontré que ce composé pouvait être utilisé en toute sécurité en cultures vivrières.

INTRODUCTION

For a crop such as strawberries, with a high capital and labour requirement, an attack by grey mould fungus (*Botrytis cinerea*) means considerable yield loss and associated low financial returns. In endangered areas control of *B. cinerea* has become one of the more difficult tasks of the strawberry grower. Following the failure of the very effective benzimidazole related fungicides due to development of tolerance by *B. cinerea*, one of our development aims has been to find a special product for the control of this fungus both in strawberries and other affected plants.

A fungicide in the oxazolidine group, 3-(3.5-dichlorophenyl)-5-methyl-5-vinyl-1.3-oxazolidine-2.4-dione, demonstrated in laboratory tests a very specific action against B. cinerea and some other pathogens such as Monilia spp. and Sclerotinia sclerotiorum. Vinclozolin is the BSI and proposed ISO common name for the active ingredient in this fungicide.

On account of its range of activity, vinclozolin has been specially developed for use in vines, fruit, hops and ornamentals. Initially, it was formulated as a 50% wettable powder under the code number BAS 352 00 F, later as a 75% w.p. code number BAS 352 02 F. Both formulations have been included in biological tests, sometimes in direct comparison. It has not yet been decided which will be developed for use in practice.

TOXICOLOGY

The acute oral LD50 of the technical substance is 10,000 mg/kg in the rat and ca. 8,000 mg/kg in guinea pigs. The acute oral LD50 (rat) of the formulated product BAS 352 00 F is 16,000 mg/kg. Skin irritation, measured on the shaven skin on the back of rabbits, is low, as is the effect on mucous membranes and the inhalation toxicity. 90-day feeding tests have been carried out in rats and dogs, both experiments giving a no effect level of 300 ppm in the diet. A 24 month feeding test on rats, an 18 month feeding test on mice to determine the chronic toxicity, and a 3 generation test on rats are underway.

In special three month experiments carried out to investigate possible effects of the compound on the eyes of rats and dogs no cataract development could be detected. The existence of mutagenic and teratogenic effects could be ruled out on the basis of investigations carried out on warmblooded animals.

In guppies the LC50 of the formulated product (50% w.p.) is 65 mg a.i./l. and for trout 52.5 mg a.i./l. (96 h). Vinclozolin is not dangerous to bees and the application of 100 mg/kg over 4 weeks did not effect earthworms.

On the basis of the available residue analysis results on grapes the German Health Office has set a provisional tolerance of 3 mg/kg for grapes: no results have yet been obtained specifically for strawberries, but a tolerance of 3 mg/kg can also be expected here.

FIELD TRIALS

The successful results obtained using the product in vines, hops, vegetables and ornamentals have already been reported (Pommer and Mangold, 1975; Hess et al., 1975), and the experiments described here deal only with the application of vinclozolin against B. cinerea in strawberries.

Three sprays are necessary in strawberries, one at the beginning of flowering (A), the second in the middle of the flowering period (B), and the third at the end of flowering (C). The spray interval is from 8-14 days according to the influence of climate on the length of the flowering period. An especially high infection pressure and also a long drawn out flowering period can necessitate an additional spray, but in such cases it must be noted that the 4th application should not take place later than the date C. The application rate for the 75% formulation of vinclozolin is 500 mg a.i./l. using 2,000 l. water/ha. Both formulations have shown themselves to be completely non-phytotoxic in all experiments carried out on strawberries.

Table 1

Control of Grey Mould (Botrytis cinerea) in Strawberries in Germany. Three Trials on Variety Senga Sengana 1974

	Untreated	Benomyl	Dichlofluanid	Vinclozolin
Rate kg a.i./ha	-	0.5	2.5	1.0
Concentration mg a.i./l.	-	250	1250	500
Total yield t/ha	9.9	14.7	15.1	16.9
Infected fruits*	43.9	35.5	12.4	7.9
Healthy fruits*	56.1	108.4	137.2	162.0

* as % total untreated yield

Table 2

Control of Grey Mould (Botrytis cinerea) in Strawberries in Germany. Three Trials on Varieties Senga Sengana and Gorella 1975

	Untreated	Dichlofluanid	BAS 352 00 F	BAS 352 02 F
Rate kg a.i./ha	-	2.5	1.0	1.0
Concentration mg a.i./l.	-	1250	500	500
Total yield t/ha	13.7	15.4	16.5	16.8
Infected fruits*	27.6	4.2	1.1	0.7
Healthy fruits*	72.4	112.8	124.4	126.0

* as % total untreated yield

Tables 1 and 2 give the mean figures for three trials in each of 1974 and 1975. Under conditions of medium to severe infection pressure vinclozolin gave both better disease control and a higher yield than the standard dichlofluanid. Dichlofluanid is the more important comparison in the light of the fact that resistance to benomyl and other benzimidazole-related fungicides has led to a decline in their use.

The observed effectiveness of vinclozolin can be reproduced under a variety of conditions, as results from a number of experiments in Germany, Belgium, Holland, France and Italy have shown.

The biological test results together with the toxicological findings indicate that vinclozolin is a fungicide particularly suited, through its long-lasting effect on the one hand, and its sufficiently rapid breakdown on the other, to the important problem of B. cinerea control in strawberries. Registration experiments have been completed in Germany as well as in other European countries.

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HEPTENOPHOS, A NEW SYSTEMIC INSECTICIDE OF SHORT PERSISTENCE

R. T. Hewson

Hoechst UK Ltd., Hoechst House, Salisbury Road, Hounslow, Middlesex

Summary Heptenophos, 7-chlorobicyclo[3,2,0]hepta-2,6-dien-6-yl dimethyl phosphate, is a new systemic insecticide with a 24-hour harvest interval. Extensive tests were conducted in both the U.K. and Germany over the period 1970 - 74, covering a wide range of crops. Applied at 0.038% a.i. in fruit and glasshouse crops, excellent control of all aphis species including *Eriosoma lanigerum* was obtained. In vegetable crops, 0.425 l./ha a.i. gave almost total aphid kill, and had an effective contact action on *Pieris brassicae* larvae. Some control of Dipterous species has also been obtained, but heptenophos was less effective against Acarina and Coleoptera when sprayed onto plants. A rapid effect on aphids was noted, giving a quick clean up of the crop. There was no phytotoxicity on any plant species, even when the material was applied at high rates of use and to ornamentals in flower.

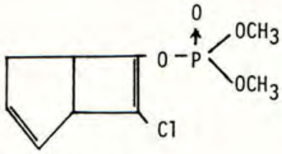
Résumé Heptenophos, 7-chlorobicyclo[3,2,0]hepta-2,6-dien-6-yl dimethyl phosphate, est un nouvel insecticide systémique avec un délai de carence de 24 heures. Une large expérimentation a été réalisée en Angleterre et en Allemagne de 1970 à 74 couvrant un grand nombre de cultures. En appliquant 0.038% m.a. sur arbres fruitiers et cultures de serre, on a obtenu un excellent contrôle sur toutes les espèces de pucerons, *Eriosoma lanigerum* y inclu. En cultures maraichères 0.425 l./ha m.a. a toujours donné un contrôle total des pucerons avec une mortalité effective des larves de *Pieris brassicae*. Un certain contrôle sur diptères a également été atteint, cependant heptenophos appliqué sur les plantes était moins efficace contre acariens et coléoptères. L'effet sur pucerons était rapide en assainissant la culture en 24 heures après le traitement. Une phytotoxicité n'a été observée sur aucune culture, même à hautes doses sur des plantes ornementales en fleur.

INTRODUCTION

For some crops there is often a need to apply an insecticide close to harvest or during the harvest period to control pests which would otherwise reduce the market value. Such a material must have a rapid action, giving a quick clean up of the crop, coupled with short persistence so that residue levels are minimal. Since problems which arise close to harvest commonly involve aphids, a systemic material is preferred. Heptenophos is an ideal material for this use, for it combines a systemic action which gives a rapid control of aphids with a 24-hour harvest interval.

Heptenophos is a phosphoric acid ester with the chemical name 7-chlorobicyclo-[3,2,0]hepta-2,6-dien-6-yl dimethyl phosphate, and is synthesised from dichloro-bicycloketone and trimethyl phosphite in the Perkow reaction. The code number during development was Hoe 2982, and the product is formulated as a 50% emulsifiable concentrate. The trade name is Hostaquick.

Chemical and physical properties

Structural formula	
Empirical formula	$C_9H_{12}Cl\ O_4P$
Molecular weight	250.5
Appearance	Pale brown, oily liquid
Solubility	0.25 g/100 g water at 23°C Soluble in most organic solvents
Boiling point	90 - 91°C at 0.02 mm Hg.
Vapour pressure	7.5×10^{-4} mm Hg. at 20°C
Stability	Unaffected by 3 months storage at 50°C

Acute Toxicity

Fish: Guppy (*Lebistes reticulatus*) LC100 after 24 hours, 10 - 20 ppm.

Birds: Acute oral LD50 Japanese Quail, 55 mg/kg.

Mammals: The following information was obtained from females of the species. The strain of rat was SPF Wistar, rabbit - silver/yellow, and the dogs were beagles.

Route	Preparation	Species	Result
Oral	Active ingredient	rat	LD50: 96 - 117 mg/kg
Oral	50% e.c.	rat	LD50: 143 mg/kg
Oral	50% e.c.	dog	LD50 lies above 500 mg/kg
Dermal (Percutaneous)	50% e.c.	rabbit	125 mg/kg (as 5 x 25 mg), no symptoms observed
Dermal	Active ingredient	rat	LD50 lies above 1000 mg/kg
Intraperitoneal	Active ingredient	rat	LD50: 69 mg/kg
Inhalation (aerosol, 1800 ml over 1 hour)	50% e.c.	rat, dog, rabbit	No symptoms over 14 days

Heptenophos also had no permanent effect on cholinesterase activity in beagle dogs.

Mode of action

Heptenophos has both a contact and systemic action. The latter was demonstrated by Emmel *et al* (1970), who found that when the material was applied by means of a bandage to the lower stem or root of *Vicia faba* there was 50% kill of aphids on the upper parts of the plant within 3 hours, and a complete kill after 6 hours. The same workers also showed that heptenophos has a short residual effect by using radioactive labelled material. In one series of tests using *Vicia faba* only 15% remained

30 hours after application, while in a second test with Phaseolus vulgaris 12% was detected after 24 hours. It was further shown that, after translocation, the compound could be released as vapour without being chemically changed or losing its efficiency.

Emmel et al (1970) also found the material to be very rain-fast. Plants were sprayed with heptenophos (formulated without humectant) and one hour later received artificial rainfall. These plants, together with similar ones which were not watered, were then artificially infested with aphids. Mortality of the insects was found to be as high on those which were watered as on those which were not.

Spectrum of activity

The orders of insects important in crop protection have been divided below according to susceptibility to heptenophos.

Very good control	Some control	Little or no control
Hemiptera	Hymenoptera	Acarina
Thysanoptera	Lepidoptera	Coleoptera
	Diptera	

The range of activity when heptenophos is sprayed onto plants is thus relatively narrow, good control being restricted to sucking species. In the field it was observed that Coccinellidae (ladybirds) which occurred on sprayed plants did not show any ill effects.

Residues

The following information was obtained from U.K. trials. Details of work carried out in Germany was earlier reported by Emmel et al (1970).

Each crop was sampled 24 hours after spraying with a rate of 1.1 litre a.i./ha. The normal rate of application is 0.425 litre a.i./ha.

Crop	Residue (ppm)	Recovery (%)
Brussels sprout	<0.005*	88
Cauliflower	0.018	83
Dwarf French bean	0.07	100
Hop	5.0	99
Lettuce	<0.005*	100
Runner bean	0.076	84

* Limit of detection = 0.005 ppm

Taint

No effects on the flavour or colour of processed samples of peas (seven canned and two quick frozen) or Brussels sprouts (two quick frozen) have been found in tests carried out over the past four years.

METHOD AND MATERIALS

Fruit and hops

In apple experiments, plot size varied from 1 - 6 trees with up to five replicates. Plots of 6 bushes replicated three times were used in bush fruit trials, while plums and cherries were treated commercially on an area of 0.5 - 2.5 ha. In early trials on hops, a plot size of 30 - 50 hills replicated four or five times was adopted; areas of 0.5 - 2.0 ha were later sprayed commercially.

Small-plot trials were sprayed with a motorised knapsack "Stihl" sprayer, and the larger trials with standard air-blast machines. Spray volumes varied from 280 to 1800 l./ha depending on crop type and growth stage, while rates of use varied between 0.025 - 0.075% a.i.

Vegetable crops

Plot size was usually twenty plants with each treatment replicated four times. Applications were made with either a Van der Weij "AZO" or "Kestrel" knapsack-type sprayer, depending on the crop. The water volume was 500 l./ha in aphis trials, and 750 l./ha in those with Brassica caterpillars. Rates of use were from 0.425 to 0.85 l./ha a.i.

Glasshouse trials

Tomato, cucumber and a wide range of ornamental plants were treated with heptenophos at 0.025 - 0.1% a.i. using a pressure-retaining "ASL" sprayer or motorised knapsack sprayer. All plants were sprayed to run off.

In all trials, assessments were made at intervals after spraying of the numbers of insects which survived.

RESULTS

1. U.K. Trials

Fruit and hops

Initial screening of heptenophos on apples in 1970 showed that the product had good aphicidal activity at rates above 0.025% a.i., but a limited acaricidal effect on the organophosphorus-resistant *Panonychus ulmi*, even at 0.1% a.i.

Poor results were obtained against *Phorodon humuli*; 0.1% a.i. being required to give approximately 50% control of summer reproductive stages on hop. Knockdown of alatae was, however, good (>90% control), and excellent control was obtained when heptenophos was mixed with endosulfan.

Against many aphid types on most fruit crops heptenophos at 0.038% a.i. gave excellent results (Table 1). No phytotoxicity was observed with any of the twenty-three plum and eighteen apple and cherry varieties tested at 0.1% a.i. Assessments of *Eriosoma lanigerum* were made 4 days after spraying; all others were after 24 hours. Unlike other aphis species *E. lanigerum* took 2 - 4 days to respond to treatment, even under warm conditions, and it was thought that vapour action was responsible for killing colonies hidden in bark crevices.

Table 1

Percentage kill of aphids in U.K. fruit trials

Crop	Species	Heptenophos (% a.i.)		Standard
		0.025	0.038	
Apple	*Eriosoma lanigerum*	85	100	100*
"	*Aphis pomi*	100	100	-
"	*Rhopalosiphum insertum*	100	100	-
"	*Dysaphis plantaginea*	90	95	-
"	*Dysaphis devecta*	100	100	-
Pear	*Dysaphis pyri*	-	100	-
Blackcurrant and	*Hyperomyzus lactucae*	100	100	100**
Gooseberry	*Nasonovia ribis-nigri*	100	100	100**
Cherry	*Myzus cerasi*	100	100	90***
Strawberry	*Chaetosiphon fragaefolii*	-	100	-

* vamidothion; ** demeton-s-methyl; *** dimethoate

Vegetable crops

Four trials were carried out in 1971 on brassicas for the control of mealy cabbage aphid (*Brevicoryne brassicae*). At two sites, assessments were made 8 hours after spraying, and the mean result is given in Table 2. All rates of heptenophos gave good control which was equivalent to that obtained with dichlorvos.

Table 2

Percentage of plants in each category

Aphids/plant	Heptenophos (l./ha a.i.)			Dichlorvos 0.56 l./ha a.i.	Untreated control
	0.425	0.63	0.85		
0 - 4	81	90	92	87	47
5 - 11	11	7	6	8	31
12 - 33	3	2	1	2	8
34 - 100	5	1	1	3	7
>101	0	0	0	0	7

At a further site assessments were made 24 hours after application. All sprayed treatments gave 100% of the plants with 0 - 4 aphids/plant, whereas the untreated control had 85% in this category, 9% with 5 - 11 aphids/plant, 5% with 12 - 33 and 1% with 34 - 100.

Two trials series were carried out the following year. In one, heptenophos was examined for aphid control on a range of crops viz. cabbage (two trials), pumpkin, cauliflower, lettuce and stick bean, and the mean result of assessments made 24 hours after spraying is given in Table 3.

Table 3

Percentage of plants in each category

Aphids/plant	Heptenophos (l./ha a.i.)		Dichlorvos 0.56 l./ha a.i.	Untreated control
	0.425	0.63		
0	93	93	92	38
1 - 4	7	7	7	27
5 - 11	0	0	1	17
12 - 33	0	0	0	9
34 - 100	0	0	0	4
>101	0	0	0	5

In the second trials series, heptenophos was examined at 1.25 l./ha a.i. on a range of crops for phytotoxicity. No damage was observed on any of the following: broad bean, carrot, cauliflower, celery, courgette, kohlrabi, lettuce, marrow, pea, radish, runner bean, sage, stick bean, sweet-corn and sugar beet.

Five trials were conducted in 1974 to examine heptenophos for control of larvae of the large cabbage white butterfly (Pieris brassicae). On average, 90% control was obtained with a rate of 0.425 l./ha a.i. when the plots were assessed the day after spraying. There appeared to be good control by contact action, and some may have been killed by the chemical acting as a stomach poison. Pests which eat plant tissue shortly after application may thus be controlled.

Glasshouse trials

Tomato: Heptenophos (0.038% a.i.) and dichlorvos (0.05% a.i.) were each applied to approximately two thousand plants of the tomato variety Moneymaker during the harvesting period in June 1974 to control the aphid Aulacorthum solani. Assessments 24 hours after spraying showed 98% of the leaves of plants sprayed with heptenophos to be free of aphids compared with 94% of those tested with dichlorvos. A rate of 0.075% a.i. was applied to plants (varieties Moneymaker, Eurocross BB and Alicante) with three or four true leaves with no adverse effect.

Cucumber: Trials were carried out to study the effect against whitefly (Trialeurodes vaporariorum), but even a rate of 0.1% a.i. failed to give more than 50% control of most stages.

Ornamentals: Heptenophos has been tested on seventy-four varieties of forty-six plant types at rates of 0.025 - 0.1% a.i. No phytotoxicity has been observed on any test plants, even when these were sprayed in flower, and in all trials 0.025% a.i. heptenophos has given 95 - 100% control of aphids, and a complete kill has been obtained with 0.038% a.i. In most cases Myzus persicae was the predominant species. The systemic action of heptenophos was found to be excellent, with pests feeding within curled leaves and crown scales being easily killed.

2. German Trials

A summary of results obtained in German trials is given in Table 4. Much of the work involves aphids, where heptenophos has generally given very good results one day after spraying. Good control of Pegomya betae was also obtained, but Phorbia brassicae, Ceuthorhynchus assimilis and Meligethes aeneus were less susceptible.

In phytotoxicity tests, heptenophos was applied to the following crops at normal and ten-fold rates of application (0.025 and 0.25% a.i.) without adverse effects: apple, carrot, celery, cherry, dwarf French bean, leek, lettuce, pear, spinach and tomato. Assessments were made 3 and 21 days after spraying.

DISCUSSION

The results from these trials show that heptenophos is an insecticide with a very rapid action against aphids; good control being obtained 8 hours after spraying (Table 2), and a complete kill has often been achieved after 24 hours (Tables 1, 3 and 4). The variable results obtained with P. humuli may have been due to organophosphorus-resistant strains, or lack of translocation in dry plant tissue close to harvest as indicated by the high residue level obtained with hop.

The material is systemic and thus gives good control of insects which feed on plant sap. Control of other pests was found to be less, and work with this compound in veterinary medicine (Bonin, 1975) showed that control of parasitic mites required 5 - 10 times higher concentrations than were needed for insects. Nevertheless, some insects are controlled by the contact or stomach poison actions of heptenophos, and work with E. lanigerum indicated the vapour effect may also be important.

Heptenophos is therefore useful where a clean up of aphids and other insects on the crop is needed close to harvest, for the short persistence of the material allows harvesting 24 hours after application. In addition to the insecticidal properties, crop tolerance is outstanding, with no phytotoxicity or taint observed on any plant species tested.

Acknowledgements

I am indebted to Mr. S. J. B. Hay for the fruit work, and Hoechst Aktiengesellschaft for details of trials carried out in Germany.

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Table 4

Percentage control of various insect pests in German trials

Crop	Pest	Heptenophos (% a.i.) 0.025					0.05				
		Assessment (days after application)									
		1	2	3	5	7	1	2	3	5	7
Apple	Psylla mali	-	56	-	-	72	-	74	41	-	82
"	Aphis pomi	94	100	99	99	100	100	-	100	-	-
"	Eriosoma lanigerum	-	28	-	-	83	100	97	100	-	93
Plum	Hyalopterus pruni	90	-	100	100	99	95	-	100	100	100
Cherry	Myzus cerasi	99	-	100	99	90	-	-	100	-	100
Peach	Appelia schwartzi	-	-	100	-	100	-	-	-	-	-
Blackcurrant	Cryptomyzus ribis	100	-	100	-	-	-	-	-	-	-
Hop	Phorodon humuli	88	-	91	-	78	93	100	91	-	90
Spinach	Aphis fabae	-	87	-	-	-	-	97	-	-	-
Lettuce	Aulacorthum scariolae	95	-	-	83	-	98	-	-	96	-
Brassicae	Brevicoryne brassicae	87	-	100	94	100	92	-	100	94	100
"	Phorbia brassicae	-	-	-	-	-	23	-	-	-	-
Bean	Aphis fabae	98	-	92	-	100	100	100	-	-	-
Tomato	Myzus persicae	98	97	97	97	95	100	100	100	100	98
Sugar beet	Pegomya betae	100	100	-	98	-	-	-	-	-	-
"	Aphis fabae	-	-	-	-	71	-	-	-	-	81
Potato	Leptinotarsa decemlineata	-	-	-	-	-	-	-	20	-	-
Rape	Pieris napi	-	-	48	-	-	-	-	100	-	-
"	Ceuthorhynchus assimilis	68	-	-	-	-	-	-	-	-	-
"	Meligethes aeneus	45	-	31	-	4	-	-	-	-	-
"	Athalia colibri	-	-	48	-	-	-	-	100	-	-

Proceedings 8th British Insecticide and Fungicide Conference (1975)

HEPTENOPHOS - A NEW INSECTICIDE FOR THE CONTROL OF ECTOPARASITES

Dr. W. Bonin

Hoechst AG, Department of Veterinary Research, 6230 Frankfurt(M) 80

Summary The testing of the phosphate ester, heptenophos, for its use in veterinary medicine is reported. Tests for efficacy, tolerability and residue revealed that heptenophos is of immediate and short lasting effect against ectoparasites. The broad range of action includes the control of parasitic insects and mites, that of insects requiring a concentration of 50-100 mg/l. and that of mites 500-1000 mg/l. With a therapeutic ratio of 4 in cattle and sheep and of 20-30 in dogs and pigs in whole animal treatment, this tolerance permits the safe use of heptenophos against target species. Heptenophos is rapidly excreted by the organism so that only very low residues were found in sheep and none in pigs.

Résumé Il s'agit d'un rapport sur l'expérimentation d'un ester de l'acide phosphorique, l'heptenophos, pour usage en médecine vétérinaire. Des examens effectués pour étudier l'efficacité, la tolérance et les résidus du produit ont démontré que l'heptenophos était un remède à effet immédiat et brève persévération contre les extoparasites. Son large spectre d'efficacité comprend des insectes et des acares parasites; la concentration nécessaire est de 50-100 mg/l. pour les insectes et de 500-1000 mg/l. pour les acares. La marge de sécurité pour le traitement général des animaux étant de 4 fois la dose thérapeutique chez le Bovin et l'Ovin et de 20 à 30 fois la dose thérapeutique chez le Chien et le Porc, la tolérance du produit permet d'envisager un emploi sans risques contre les parasites. L'heptenophos est éliminé très rapidement par l'organisme, si bien qu'on ne retrouve pas de résidus chez le Porc et très peu chez l'Ovin.

INTRODUCTION

In view of the properties of heptenophos, 7-chlorobicyclo-[3,2,0]hepta-2,6-dien-6-yl dimethyl phosphate, detected in tests as a plant-protective agent (Hewson, 1975) and on account of its low toxicity in warm-blooded animals, testing of the new insecticide for its usefulness in veterinary medicine against ectoparasites suggested itself.

Laboratory tests with bedbugs (Cimex lectularius) and red fowl mites (Dermanyssus gallinae) confirmed the immediate and short lasting effect described by Emmel et al. (1970). The following examinations were aimed at the development of heptenophos against ectoparasites.

METHOD AND MATERIALS

The preparations used in the testing of heptenophos were a 25 % e.c. and a 40 % w.p. The examination of heptenophos included:

Tests for efficacy in animals with a naturally acquired ectoparasite infestation by means of conventional hand spray and dip treatments.

Toxicity tests in target species, including cholinesterase determination in cattle. The concentration that was tolerated without clinical symptoms was considered the upper tolerance limit.

Examination of residues in food producing animals. Sheep and pigs received a 1000 mg/l. dip or spray treatment. One animal of each species was killed 1, 3 and 5 days after the treatment, and liver, kidneys, muscles, fat and subcutaneous fat of the back were examined for heptenophos content by means of gas chromatography.

Excretion with milk, the blood level and the heptenophos content on hair were examined in one cow after a spray treatment with 2.5 l. at 1000 mg/l.

RESULTS

Test for efficacy Concentrations of 50-100 mg/l. were sufficient for the elimination of insect infestation (Table 1). The cure of mite-induced mange, however, required a concentration of 500-1000 mg/l. Heptenophos was not sufficiently effective against soft ticks (Argasidae) and hard ticks (Ixodidae). No animal systemic efficacy was observed.

Table 1

Kinds of ectoparasites and concentrations in which heptenophos proved effective

Ectoparasites	Host	Concentration mg/l.
Ctenocephalides canis (Dog Flea)	Dog	100
Haematopinus suis (Hog Louse)	Pig	50
Haematopinus eurysternus (Short nosed Cattle Louse)	Cattle	100
Damalinia bovis (Cattle Biting Louse)	Cattle	100
Damalinia ovis (Sheep Biting Louse)	Sheep	50
Melophagus ovinus (Sheep Ked)	Sheep	50
Sarcoptes canis (Itch Mites)	Dog	500-1000
Sarcoptes ovis (Itch Mites)	Sheep	500-1000
Sarcoptes suis (Itch Mites)	Pig	500-1000

Ectoparasites		Host	Concentration mg/l.
Psoroptes bovis		Cattle	
Psoroptes ovis	(Scab Mite)	Sheep	1000
Psoroptes cuniculi		Rabbit	
Chorioptes bovis (Chorioptic Mange Mite)		Cattle	1000
Dermanyssus gallinae (Red Fowl Mite)		Poultry	500

Tolerance tests. Taking the tolerance limits listed in Table 2 and a concentration of 500 mg/l. as a basis, the therapeutic ratios also listed in Table 2 were calculated.

Table 2

Tolerance limits and safety factors of heptenophos in several target species

Species	Kind of treatment	Tolerance limit g/l.	Safety factors
Dog	Dipping	10	20 x
Pig	Spraying of whole animal	15	30 x
Cattle	Spraying of whole animal	2	4 x
Sheep	Dipping	2	4 x
Poultry	Spraying of whole animal	10	20 x

After a spraying treatment with a concentration of 1 g/l. the serum and erythrocyte cholinesterase in cattle was reduced by a maximum of 30 %. Within 24 hours the levels returned to the initial values.

Examinations for residues. In a very sensitive method of demonstration no residues were found in pigs (Table 3) - except in porcine subcutaneous adipose tissue, and only very slight residues were found in sheep (Table 3).

Table 3

Residues of heptenophos in sheep and pigs after topical treatment

Days after treatment		Heptenophos mg/kg in				
		Liver	Kidney	Muscle	Fat	Subcut.fat
Sheep	1	n.d.	0.01	0.006	0.05	0.2
	3	n.d.	0.02	0.01	0.03	0.04
	5	n.d.	n.d.	0.002	n.d.	0.07
Untreated		0.002	0.002	0.001	0.003	0.002
Limit of detection		0.009	0.01	0.002	0.01	0.002
% recovery rate		91	86	86	82	86
Pig	1	n.d.	n.d.	n.d.	n.d.	0.03
	3	n.d.	n.d.	n.d.	n.d.	n.d.
	5	n.d.	n.d.	n.d.	n.d.	n.d.
Untreated		0.004	0.003	0.008	0.004	0.003
Limit of detection		0.007	0.002	0.01	0.005	0.003
% recovery rate		94	86	84	95	95

n.d. = not detectable

After topical treatment of a cow, heptenophos passed into blood and milk so rapidly, that only shortly after treatment were slight residues found (Table 4). The amount of heptenophos on hair decreased from 1700 to 9 mg/kg within 9 days.

Table 4

Heptenophos in the milk, blood and on the hair of a cow sprayed with 2.5 l. at 1000 mg/l.

Time after treatment	Heptenophos (mg/kg) in milk	in blood	on hair
15 min	-	n.d.	1700
30 min	-	0.03	-
1 h	0.02	n.d.	1700
4 h	-	n.d.	950
7 h	n.d.	n.d.	589
24 h	n.d.	n.d.	164
48 h	n.d.	n.d.	169
72 h	n.d.	n.d.	74
96 h	n.d.	n.d.	40
9 days	-	n.d.	9
Untreated	0.005	0.005	0.6
Limit of detection	0.02	0.005	-
% recovery rate	90	100	-

n.d. = not detectable

DISCUSSION

Numerous pesticides are used both for plant protection and in veterinary medicine. A reason for the improvement of agents against ectoparasites is to reduce accumulation of residues. Our investigations have shown that heptenophos meets the requirements for a modern and environmentally acceptable insecticide to a large extent. In pigs no residues were observed after topical treatment. Different results were obtained in sheep as the active substance was obviously stored in the wool fat, thus being retardedly absorbed. Very slight residues were found in the organs, except in the liver. After topical treatment the highest residue values in both sheep and pigs were found in the subcutaneous adipose tissue of the back.

An agent against ectoparasites has to have broad range of action in order to affect many pest species. Heptenophos is effective against parasitic insects and mites, the control of mites requiring 5 to 10 times higher concentrations than the control of insects because of the difficult approachability of mites.

A therapeutic ratio of 4 in sheep and cattle and of 20 or 30 in dogs and pigs in the treatment of the entire animal manifests pronounced species-dependent differences in toxicity, yet these results permit the use of heptenophos in cattle and sheep.

According to the reported investigations heptenophos is an insecticide which stands out for its:

- immediate and short lasting effect
- broad range of action
- good tolerance by target animals
- very little residues

Acknowledgement

The examinations of residues were performed by Dr. Gorbach, Hoechst AG.

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CONTROL OF APPLE POWDERY MILDEW BY BUPIRIMATE AND THE INFLUENCE OF ADDED SPREADER-STICKER ON ITS PERFORMANCE*

E. Shabi

Division of Plant Pathology, Agricultural Research Organisation,
The Volcani Center, Bet Dagan, Israel

Summary The efficacy of fungicides for the control of apple powdery mildew was compared in two commercial orchards in Israel. Bupirimate gave excellent control of primary and secondary powdery mildew, performing better than pyrazophos or ditalimfos. The addition of the spreader-sticker Bio-Film to bupirimate resulted in better disease control in one of the two trials.

INTRODUCTION

Powdery mildew, caused by Podosphaera leucotricha is the most serious disease of apples in Israel. The climatic conditions during spring (April, May and June) are favourable for the development of the disease. Moreover, after harvest there is a long period during the autumn when new infections of powdery mildew can occur.

The performance of some fungicides against apple powdery mildew was compared during the spring of 1975 and the effect of adding a spreader-sticker to bupirimate was also studied.

METHODS AND MATERIALS

The fungicides evaluated were : bupirimate (PP 588, 5-butyl-2-ethylamino-6-methylpyrimidin-4-yl dimethylsulphamate), JF 4260, 25% e.c.; ditalimfos, 50% w.p.; guazatine, 60% e.c.; pyrazophos, 30% e.c. The proprietary spreader-sticker, Bio-Film, comprises: alkaryl poly(ethoxy)ethanol, free and combined fatty acids, glycol ethers, dialkyl benzenedicarboxylates and propan-2-ol.

Disease assessment

Primary powdery mildew infection was determined by taking terminal branches, the basal leaves of which were heavily covered with primary infections. All leaves on the terminal branch samples were assessed for mildew severity (%/leaf) according to the following key.

* Contribution No. 211-E (1975 series) from the Agricultural Research Organisation, The Volcani Center, Bet Dagan, Israel.

0 (healthy) = no infection

10 (light) = 1 - 3 powdery mildew spots per leaf

30 (moderate) = 4 - 10 powdery mildew spots per leaf

100 (heavy) = most of the leaf area covered with powdery mildew.

Secondary powdery mildew infection was determined in the Daliya trial by taking at random ten terminal branches from the central tree of each plot. From each terminal branch the five apical unfolded leaves served for disease assessment using the same key. In the 'En Hashofet trial two central trees/plot were assessed in this way.

Trial at Daliya

In the spring of 1975 spray applications were made on 13-year-old Jonathan apple trees in a commercial orchard at Daliya, Israel, which had heavy infections of powdery mildew in previous years. The trees were sprayed to run-off by hand-gun at 20.7 bar (300 lb/in^2). Sprays were applied to three-tree plots, replicated four times, on April 4 (12 mm green), 11, 18, 25, May 4, 14 and 25. Incidence of secondary powdery mildew on leaves of terminal branches was assessed twice: after five sprays on May 11; and after seven sprays on June 3, just after the end of the terminal growth. The effect of the fungicides on terminal branches infected with primary powdery mildew was assessed after five spray applications.

Trial at 'En Hashofet

In the spring of 1975, 18-year-old Jonathan, Golden Delicious, and Grand apple trees in a commercial orchard at 'En Hashofet were sprayed at the rate of 2000 l/ha using an airblast sprayer. Treatments were applied to plots of 30 trees, ten in each of three rows, replicated three times. Sprays were applied, on March 31 (green tip), April 8, 14, 21, 28, May 5, 12, and 19. Disease incidence on leaves of terminal branches was assessed on May 25.

RESULTS

In the trial at Daliya, bupirimate gave excellent control of both primary and secondary infections and was superior to pyrazophos or ditalimfos. Guazatine was much inferior but gave some suppression of powdery mildew as compared with untreated trees. The addition of a sticker-spreader, Bio-Film (0.5 ml/l.), to bupirimate enhanced the performance of the fungicide against both primary and secondary mildew (Tables 1 and 2).

In the trial at 'En Hashofet bupirimate again gave very good control of powdery mildew, compared with pyrazophos or ditalimfos. However, the addition of the sticker-spreader to bupirimate did not add to the efficacy in controlling the disease of any of the three apple varieties (Table 3).

Table 1

Infection of secondary powdery mildew after five and seven sprays - Daliya, 1975

Treatment	Rate (a.i.)	% infection on Jonathan May 11	% infection on Jonathan June 3
Bupirimate	100 mg/l.	1.1	2.7
Bupirimate + Bio-Film	100 mg/l. + 0.5 ml product/l.	0.5	0.8
Ditalimfos	250 mg/l.	5.2	5.9
Guazatine	600 mg/l.	16.4	14.2
Pyrazophos	120 mg/l.	4.1	2.7
Untreated		72.2	70.5

Table 2

Control of primary powdery mildew after five sprays - Daliya, 1975

Treatment	Rate (a.i.)	% Jonathan leaves with infection severity			
		Healthy	Light	Moderate	Heavy
Bupirimate	100 mg/l.	46	2	12	40
Bupirimate + Bio-film	100 mg/l. + 0.5 ml product/l.	59	4	7	30
Ditalimfos	250 mg/l.	31	7	20	42
Guazatine	600 mg/l.	3	4	25	68
Pyrazophos	120 mg/l.	23	3	28	46
Untreated		0	0	0	100

Table 3

Infection of secondary powdery mildew after eight sprays - 'En Hashofet, 1975

Treatment	Rate (a.i.)	% Infection on		
		Jonathan	Grand	Golden Delicious
Bupirimate	100 mg/l.	4.6	5.6	0.6
Bupirimate + Bio-Film	100 mg/l. + 0.5 ml product /l.	4.4	5.2	0.9
Ditalimfos	250 mg/l.	12.4	18.9	1.1
Pyrazophos	120 mg/l.	20.8	18.5	1.3
Untreated		61.2	74.4	10.5

DISCUSSION

In a trial in 1974 (Shabi et al., 1975) secondary powdery mildew on terminal branches was controlled successfully by several fungicides, including bupirimate and pyrazophos. The sticker-spreader Bio-Film when added to pyrazophos improved its performance. In 1975 Bio-Film was added to bupirimate and appeared to enhance control of secondary mildew in one trial where the spray was applied by hand-gun. In a second trial bupirimate alone again gave excellent mildew control on three varieties but Bio-Film did not increase its activity further. It may be significant that the second trial was conducted with a commercial air-blast machine, probably with different deposition characteristics.

Observations of primary mildew in the first trial showed that bupirimate prevented its development, as reported also by Finney et al., (1975). Only a few basal leaves were heavily infected whilst most of the new growth remained clean. Addition of Bio-Film to bupirimate resulted in even better performance of the fungicide, as with secondary mildew in this trial. Ditalimfos and pyrazophos also suppressed primary mildew infection to some extent. On trees left unsprayed, the leaves of terminal branches were heavily infected with primary mildew and the buds on such terminal branches will be a source of powdery mildew infections in subsequent years.

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IPT, A NEW COMPOUND, SHOWING FUNGICIDAL AND INSECTISTATIC ACTIVITY

F. Araki, K. Murata and T. Miyake

Nihon Nohyaku Company Ltd., Division of Research and Development, Tokyo, Japan

Summary The excellent systemic activity of IPT in controlling rice blast has been confirmed through intensive trials during 1968 to 1975 throughout Japan. Although this compound is protective as well as curative in activity, the former is more important when application is into paddy water. During a field trial in 1973, a decrease in the planthopper population was noted in test plots. Through *in vitro* tests it was clarified that first instar larvae treated with IPT died at the third to fifth instar stages and the death frequently occurred at moulting. Such "insectistatic" activity of IPT is quite different from most ordinary insecticides.

INTRODUCTION

Rice production in Japan has long suffered from blast disease caused by *Piricularia oryzae*. In the decade from 1962 to 1972, many fungicides, such as antibiotics, organochlorine and organophosphorus compounds, were evaluated against rice blast. However, on account of their various defects, development of a new compound was required.

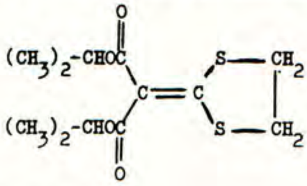
In 1968, we discovered that di-isopropyl 1,3-dithiolan-2-ylidenemalonate (IPT) (Fig. 1) was promising for blast control out of many malonate derivatives tested, and have evaluated IPT especially for its systemic properties. This paper describes the principal biological activities of IPT in controlling rice blast and planthoppers.

GENERAL FEATURES OF IPT

The physical properties of di-isopropyl 1,3-dithiolan-2-ylidenemalonate (Trade name: Fuji-one) are listed in Fig. 1. The acute oral toxicity (LD50) for male rats and mice is 1190 and 1340 mg/kg, respectively. The TL_m (48 h) to carp is 6.7 mg/l. No abnormality has yet been observed in chronic toxicology studies.

Fig. 1

Structure and physical properties of IPT



Molecular weight 290.4

White crystals, melting point 50-54.5°C

Boiling point 167-169°C/0.5 mm Hg

Solubility in water 48 mg/l. at 20°C

BIOLOGICAL PROPERTIES

A. Characteristics as rice blast control agent (Murata, 1975)

1. Effect on the infection behaviour of rice blast fungus (P. oryzae).

Spore suspensions mixed with solutions or suspensions of IPT were sprayed onto barley which is known to be useful in the evaluation of biological effects of blast fungicides (Araki, 1974). Leaves were fixed and observed 48 h after inoculation. IPT affected appressorial formation at 10 mg/l, inhibited almost completely the penetration at 2 mg/l, and suppressed the growth of infection hyphae at 0.5 mg/l. When IPT was applied to the root system, inhibition of infection hyphae was observed at 1 mg/l. In addition, vegetative hyphae and sporulation were inhibited at 40 and 400 mg/l, respectively.

2. Incorporation into rice plant.

IPT is easily translocated from leaf to leaf via the root system. During translocation studies, radioactive IPT, applied to the third leaf, was detected in the root system and whole plant after 6 h and 3 days, respectively. IPT was incorporated into rice plants from both root and leaf sheath applications, which is appropriate for the cultivation of this crop, reaching a maximum after 14 days under favourable conditions.

3. Blast control activity of granular formulation.

IPT is formulated as 12% w/w granules for application in paddy water. When seeking the most appropriate timing of application it is important to determine both the lag time from application to the development of sufficient activity to control the blast and the duration of effectiveness. When IPT was applied at 4.8 kg a.i./ha the concentration in the two uppermost leaves of rice plants increased steadily until 14 days after application, reaching 9.5 mg/kg, then began to decrease to 1.8 mg/kg after 21 days, and remained constant for a further 29 days. According to the correlation between the concentration of IPT in leaf blades and the blast control (Fig. 2), the presence of $>$ 2 mg IPT/kg in the leaf blades is enough to protect rice plants from damage by blast. This was confirmed in the field trials against rice panicle blast by the Plant Protection Society of Japan in 1971-1974 (Fig. 3).

The timing of IPT application recommended for panicle blast control ranged from 10 to 30 days before panicle emergence.

Fig. 2

Correlation between IPT concentration in leaves and rice blast control

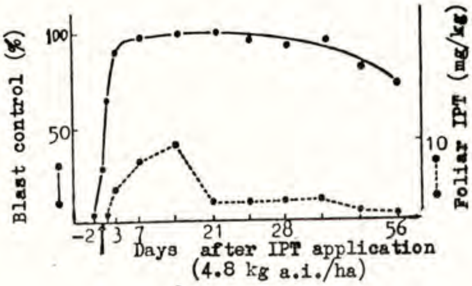
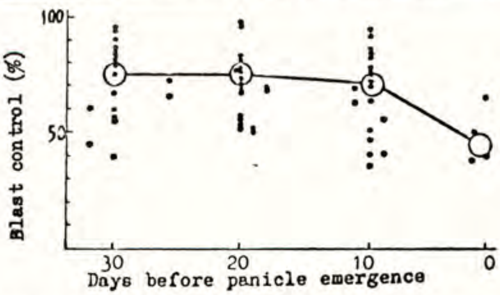


Fig. 3

Effect of IPT on panicle blast at various application times
(From Plant Protection Society of Japan, 1971 - 1974)



B. "Insectistatic" activity (Miyake, 1975)

1. Effect on the life cycle of planthoppers *in vitro*.

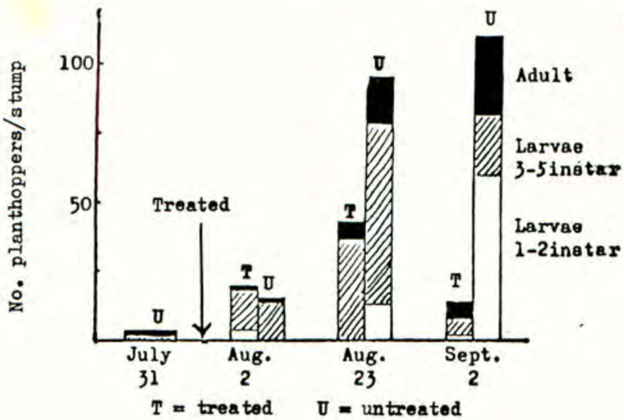
During a field trial in 1973 a marked decrease in planthopper population was observed. Laboratory tests showed that when the first instar larvae of white backed- or brown planthopper were reared on the cut leaf of rice plants previously treated with IPT, the mortality of larvae began to increase at the third instar, reaching almost 100% before adult emergence. Larvae frequently died during moulting. This mortality always occurred if larvae up to the second instar were reared on IPT-treated rice plants for at least 5-6 days. When the third instar larvae were reared on the IPT-treated plants few larvae died, but the longevity of adults and the number of eggs laid a day decreased to half that of leafhoppers reared on untreated plants. Thus the population at the next generation was 28% of that on untreated plants. IPT did not show a direct toxicity such as organophosphorus compounds or carbamates, but affected the growth of larvae, longevity of adult and oviposition, As a consequence, IPT, suppressing growth and reproduction, is what Levinson (1975) classes as an "insectistat".

2. Control of planthopper population in the field.

The characteristic activity of IPT discovered in the laboratory was confirmed in the field trial as shown in Fig. 4. IPT was applied at 3.2 kg a.i./ha on Aug. 1 which is also suitable timing for panicle blast control. The planthopper population in the untreated plots increased considerably up to the end of experiment, but that in the IPT-treated plots slightly increased until Aug. 23 and decreased markedly by Sept. 2, which corresponds to the emergence of the second generation.

Fig. 4

Effect of IPT on the population density of brown planthopper in the field



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