SESSION 1

THE FIFTEENTH BAWDEN LECTURE

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WORLD CROP PROTECTION PROSPECTS : DEMISTING THE CRYSTAL BALL

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INTRODUCTION

Forecasting is rarely straightforward but forecasting in agriculture at a time when it is re-structuring is a particularly precarious pastime. Fortunately, I am not seeking perfection because, inevitably, due to the vast diversity and flexibility of agricultural systems internationally, any predictions I make will be proved to be wrong in many local circumstances. What I do hope to achieve, however, is the identification of those significant factors and trends which will impact generally upon the future.

This paper begins by taking a broad look at international agriculture and crop protection in recent years and uses this information later as the basis for identifying future crop protection prospects. The approach may appear cautious and undramatic; it is, but that is the nature of progress in agriculture. New technology must be integrated painstakingly into existing agricultural systems where its contribution and environmental impact can be assessed; it follows that any new crop protection technology which is destined to have a substantial effect on agricultural productivity by the year 2000 will already exist, at least at the research level.

The agricultural environment

There have been dramatic changes in the international agricultural environment during the last 20 years. The 1970s were characterised by steady growth in agricultural production driven by strong demand, high commodity prices, high economic growth and marked improvements in agricultural productivity.

In the early 1980s, world trade and economic growth slowed and, for the first time, agricultural production exceeded demand in OECD countries. This led to sharp changes in trading patterns: the EEC became a net cereal exporter: Eastern Bloc imports decelerated and the development of agriculture in Lesser Developed Countries (LDCs) accelerated, driven by population growth, self-sufficiency policies and high third world debt.

Consequently the 1980s are characterised by commodity surpluses, low commodity prices, declining farm incomes, increased government subsidy burdens and conflicts between governments over subsidy policies.

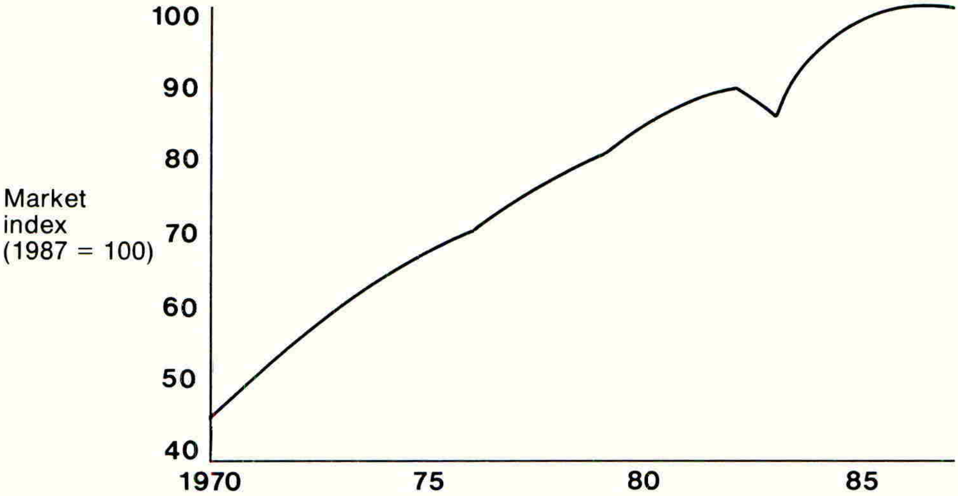
In turn, this has hastened agricultural reform either to reduce planted areas, or to reduce prices, or both. Overall, 17 mn ha were taken out of production worldwide in 1987, of which 8 mn ha were in the USA. In all probability, the drought in parts of the USA in 1988 will cause a temporary reversal to the general trend.

The agrochemical environment

The steady growth of agricultural production in the 1970s fueled high worldwide agrochemical growth, averaging 6.3% per annum in real terms (Fig 1). Growth was interrupted dramatically by the US Payment-In-Kind (PIK) programme in 1983 which led to a 2.9% real decline - the first ever recorded real decline in the agrochemical market.

Fig. 1 World Agrochemical Market Growth

Currency and inflation effects removed



Source: County NatWest WoodMac (formerly Wood Mackenzie & Co Ltd) Selected data

Although growth recovered in 1984, it settled at a lower average rate of 1.1% per annum for the four year period 1984-87. Global sales in 1987 of $20 bn represented a real decline of 1%, the second decline in agrochemical history following only 4 years after the first.

THE PRESENT SITUATION

Market maturation

The agrochemical market overall is now approaching maturity with low growth especially in developed countries. It is generally agreed that there are fewer major unexploited technical opportunities for agrochemicals; technical solutions already exist for most crop protection problems and market penetration is near maximum in most of the major market sectors in developed countries (Table 1).

TABLE 1

Market Penetration in some Major Agrochemical Market Sectors in Developed Countries

Segment	% of total crop area treated
US Soya Herbicides	94
US Maize Herbicides	85
US Rice Herbicides	98
US Cotton Herbicides	90
Japan Rice Insecticides	100
France Vine Fungicides	85

Source: ICI Agrochemicals

Competitive environment

There are a number of factors contributing to a sharp increase in competition between companies. The slower market growth rate has inevitably increased commercial rivalry in the open market. Reduced subsidies and lower farm incomes have also generated strong price pressure on agricultural inputs and farmers have become more cost-conscious then ever before. As a consequence of fewer unexploited technical opportunities remaining, there has been less new product differentiation and increased price competition and, of course, the expiry of patents on major products has resulted in more generic competition. Table 2 shows that all of the top 10 products in USA were introduced before 1976 and 7 of them are now off-patent.

TABLE 2

Patent Status and Launch Dates of Top Ten US Pesticides (1986)

Product	Launch	Patent Expired
Glyphosate	1972	No
Alachlor	1966	Yes
Metribuzin	1971	No
Carbaryl	1956	Yes
Chlorpyrifos	1965	Yes
Carbofuran	1967	Yes
Chlorothalonil	1963	Yes
Trifluralin	1963	Yes
Bentazon	1975	No
Dicamba	1965	Yes

Source: ICI Agrochemicals

The overall effect has been a progressive decline in the profitability of the industry from 11.5% in 1981 to 7.9% in 1986 with US, European and Japanese companies all affected (Table 3).

TABLE 3

Industry Profitability 1981-86
Pretax Profits of Agrochemical Companies (% turnover)

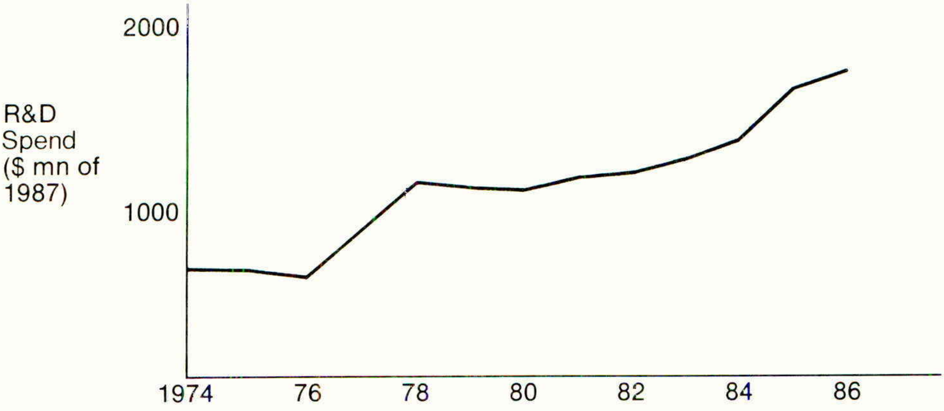
	1981	1986
US companies	15.5	11.0
European companies	9.6	7.2
Japanese companies	8.0	5.6
Average	11.5	7.9

Source: County NatWest WoodMac, Agrochemical Monitor, May 1988

R&D Expenditure

Total R&D expenditure has increased very substantially in recent years (Fig 2), especially the development costs required to satisfy increasing regulatory demands.

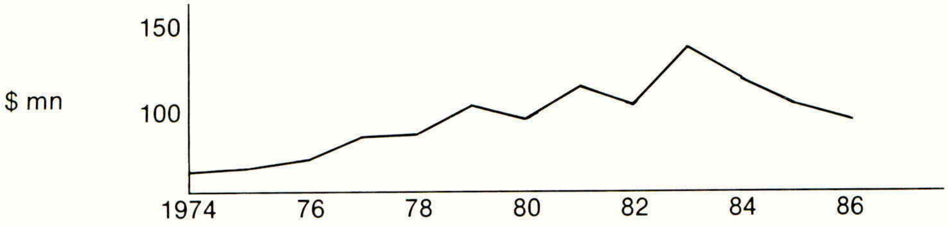
Fig. 2 Agrochemical Research and Development Expenditure



Source: County NatWest WoodMac.

During the early 1970s it became clear that there were fewer technically unsatisfied opportunities for new agrochemicals which would adequately reward the research investment. Random screening, the traditional method of product discovery, was proving conspicuously less effective. As a result, costs of new product generation increased substantially (Fig 3).

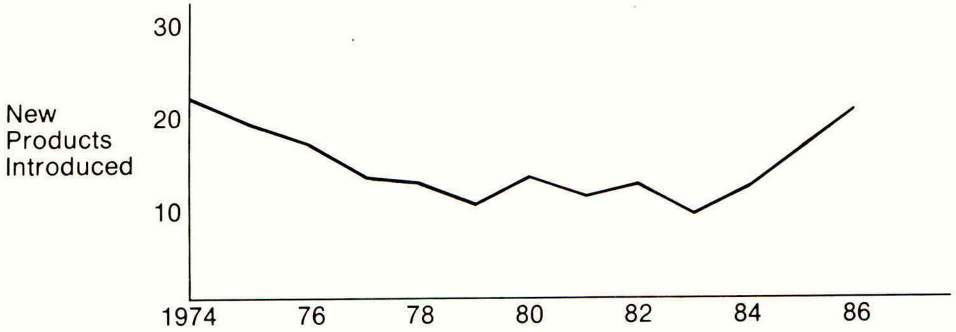
Fig. 3 Industry R&D Spend Per Product Introduced
3 year moving average.



Source: County NatWest WoodMac/ICI Agrochemicals

This trend was reversed by more detailed attention to research targeting and by deploying more inventive resources imitatively in chemical areas with known biological activity; this led to a sharp recovery in the number of products introduced to the market from the early 1980s (Fig 4) and to reduced R&D costs per new product.

Fig. 4 New Product Introductions
3 year moving average



Source: ICI Agrochemicals

A direct consequence of the imitative approach was the clustering of new products around particular areas of chemistry and major market opportunities (Table 4).

TABLE 4

Clustering of New Products in Important Chemical Areas

Triazole fungicides*	Years after launch (in 1976)	0	3	6	9	12
	Number of products	1	2	2	7	14
Synthetic pyrethroid insecticides*	Years after launch (in 1977)	0	3	6	9	12
	Number of products	4	5	7	11	17

* Initially invented by Bayer and NRDC respectively

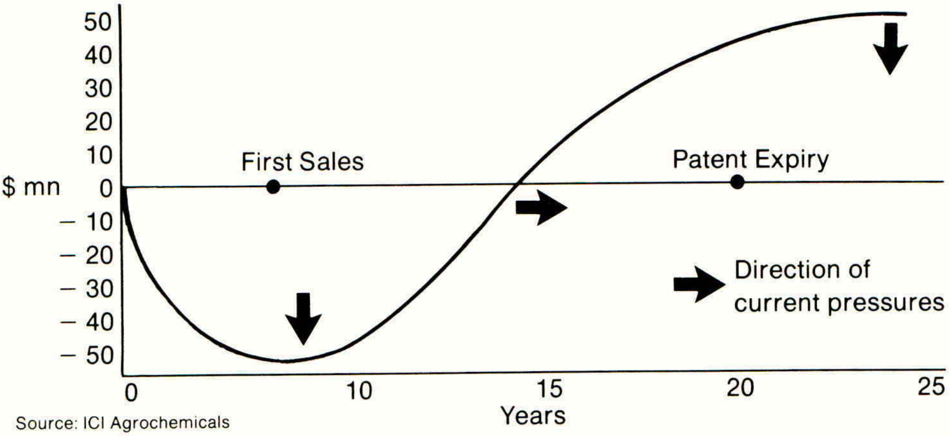
Source: ICI Agrochemicals

Product differentiation was decreased and the potential rewards for new products were reduced due to enhanced price competition early in the product life cycle. New proprietaries were often marketed on economic benefits rather than technical differences compared to competitive technology.

An increasingly strict legislative and environmental climate has substantially increased the costs and the timescale of new product development and registration.

The return on investment has been delayed significantly (Fig 5) raising doubts in some companies about the long-term attractiveness of agrochemical R&D as an investment option.

Fig. 5 Typical Cumulative Discounted Cash Flow for a Successful New Product



Source: ICI Agrochemicals

Other technical costs have also risen sharply, particularly the costs of re-registration and technical stewardship of established products.

Industry consolidation

Consolidation and concentration has accelerated in the last few years with the withdrawal of smaller R&D-based companies and the expansion of larger companies through acquisition in pursuit of economies of scale (Table 5). Significant scope for further rationalisation still remains.

TABLE 5

Major Acquisitions and Mergers 1984-1987

ICI + Stauffer
Rhone Poulenc + Union Carbide
Du Pont + Shell (US)
Shell + Celamerck
Sandoz + Velsicol + SDS Biotech
Sumitomo + Chevron

Consolidation has been accompanied by greater internationalisation. The number of European-based companies in the top 10 in the USA has increased from 2 in 1980 to 5 in 1987; US-based companies have reciprocated by expanding in Europe.

Japanese companies have also striven to internationalise either through joint ventures (e.g. Sumitomo/Chevron in USA) or by jointly developing products with US or European companies. To improve their positions in Japan, the second largest agrochemical market, both US and European companies have increased their efforts there either through joint ventures with Japanese companies (e.g. Sandoz/SDS) and/or by establishing new field stations (e.g. Monsanto, Hoechst, ICI) as a base for new product development.

Changes in the international ranking of agrochemical companies from 1976 to 1987 are shown in Table 6.

TABLE 6

World Ranking of Agrochemical Companies

	1976	1983	1985	1987	
				Rank	(Sales ($ bn)
Ciba Geigy	2	2	2	1	2.0
Bayer *	1	1	1	2	2.0
ICI *	10	5	4	3	1.8
Rhone Poulenc *	4	6	6	4	1.6
Du Pont *	9	8	10	5	1.2
Monsanto	4	3	3	6	1.2
Shell *	3	4	5	7	1.0
BASF	7	9	7	8	1.0
Hoechst	12	7	8	9	0.9
Dow	16	10	9	10	0.8

* Involved in major acquisitions and/or divestments during the period

Source: County NatWest WoodMac.

Distribution

Lower market growth and reduced product differentiation has led to increased distributor rivalry. At the same time, reduced agricultural subsidies and farm incomes have lowered prices with an inevitable knock-on effect on the profitability of distributors.

Consolidation and simplification of distribution through acquisition, mergers, bankruptcies, etc., has led to a general decline in the number of distributors and a reduction in the number of distribution steps.

Farmers

Though not universally appreciative of it, farmers have benefited from industry maturation and consolidation through falls in the real prices of agrochemicals generally (Table 7).

TABLE 7

Trends in Prices of Major US Pesticides (1985-1987)

Product	Price Change (%) 1985-1987	
	Real ($ of 1987)	Nominal ($ of year)
Alachlor	-10.5	- 6.0
Atrazine	+ 2.8	+ 7.8
Butylate	- 7.6	- 2.9
Cyanazine	- 3.3	+ 1.5
Metolachlor	- 5.6	- 1.0
Trifluralin	- 6.7	- 2.0
2,4-D	- 2.4	+ 2.5
Carbaryl	- 3.2	+ 1.6
Carbofuran	-11.4	- 7.0
Chlorpyrifos	- 4.5	+ 0.2

Source: Chemical & Engineering News, Nov 87 and ICI Agrochemicals

At the same time, product safety in use has improved through increased environmental and other regulatory demands and average product applications rates have reduced as newer, more active, products have replaced older ones.

PROSPECTS FOR CROP PROTECTION

Inventions

Chemical

Although biotechnology is making rapid progress and will undoubtedly play a major role in crop protection in the long term, organic chemistry will remain the principal route to new products until at least the year 2000.

Successful new molecules will decrease in frequency, they will be more expensive to develop, and less able to repay the research investment in general. It is likely, therefore, that the total research investment in the industry to generate new chemically-based products will decline, perhaps substantially. There will, of course, be exceptions, especially in areas of chemistry which yield highly cost-effective products e.g. imidazolinone and sulphonyl urea herbicides. Improved understanding of plant biochemistry and of the biochemistry of pests and pathogens will encourage a more rational approach to the invention process and it is probable that industry will cooperate more closely with the public sector to generate this basic, pre-competitive, knowledge.

Although the number of commercially attractive opportunities for new products is decreasing, there is still a requirement for new agrochemical products to satisfy changing technical, environmental, user and economic demands. In general, new products will be: very highly active (with use rates per hectare measured in grams rather than kilograms to enable them to compete with existing, frequently off-patent products): eradicant: broad-spectrum: flexible and convenient in use: compatible with existing products: suitable for use in integrated pest management programmes and with increased margins of safety to the user, the environment and the consumer of treated crops. Examples of opportunities for new active ingredients include: novel insecticidal, fungicidal and acaricidal toxophores to use in programmes to suppress the development of resistance: more cost-effective nematocides, soil fungicides, post-emergence herbicides and plant growth regulators for the major arable crops. There is also an opportunity for new products to replace existing or withdrawn products (e.g. organochlorine insecticides, EDB, cyhexatin, 2,4,5-T) on environmental or safety grounds.

There will be advances in associated technologies to ensure that agrochemicals are applied optimally using the minimum effective rate. Application rates will trend towards lower volumes thereby improving timeliness; improved pest and disease monitoring systems will be developed and improved computer data-bases will improve the quality of information available to farmers.

Biological

Rapid advances in biotechnology will lead to novel microbial products and crop varieties which will become important crop protection agents and increasingly supplement or supplant the effects provided by agrochemicals. It is difficult to generalise about the rate of progress and degree of substitution; in my view, however, it is unlikely that, in aggregate, the new biological products will constitute more than 5% of the total crop protection market by the year 2000, though more rapid progress can be anticipated early in the 21st century.

Plant breeding will dominate in importance. Crop resistance to insect pests and fungal pathogens will rapidly replace some insecticide and fungicide usage. Initially resistance will be limited to individual pests or pathogens and it will be decades before pest and disease complexes will be controlled exclusively by this technology without the complementary use of agrochemicals.

The development of herbicide resistance in crop plants, which has been demonstrated for a range of toxophores in recent years, will also be important; interestingly, it will probably lead to a global increase in herbicide use, though changing the spectrum towards non-selective, post-emergence products. The rate of uptake of the new technology will probably be limited at least as much by economics when compared to modern, selective herbicides, as it will by the time taken to develop the technology.

Biotechnology may also provide approaches to some technical targets which have proved elusive to traditional chemical control (e.g. the development of virus-resistant crop plants) and via highly specific assays for candidate agrochemicals.

The development of novel microbial products will have an earlier impact than new crop varieties but on a much smaller scale. Recombinant microbes have the potential to overcome some of the problems associated with existing microbial products such as, poor spectrum, slow action and high cost, but regulatory concerns are likely to increase the time-scale and cost of development.

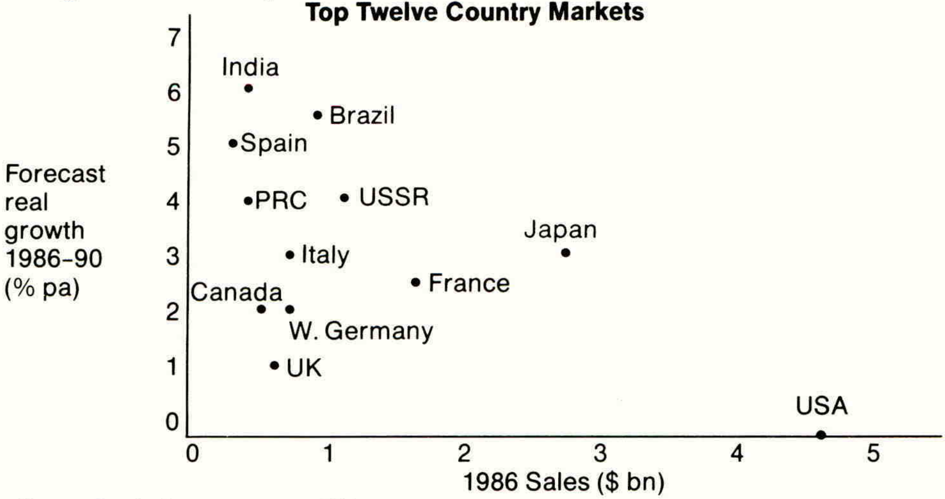
In summary, biotechnology offers the promise of industry revival, but it will be accompanied by a demanding legislative framework which will constrain the rate of commercial exploitation.

Prospects for the crop protection industry

Growth

Long term growth will be at a lower rate overall (2% p.a. in real terms) though with a higher rate in LDCs (5% p.a.) where the itensification of agriculture will continue to be driven by high population growth (Fig 6).

Fig. 6 Relationships Between Market Size and Forecast Growth Rate for Top Twelve Country Markets



Source: County NatWest WoodMac, 1986

Growth in herbicides is expected to be particularly rapid in LDC's as labour costs rise with population drift away from rural areas.

The quality of the growth in the LDC agrochemical market will be affected *inter alia* by the availability of foreign currency, import controls, price controls and the local business culture; as a result, the investment risk will often be higher.

Very low growth of agrochemicals will continue in developed countries as a result of agricultural reform to control surpluses, Japanese agricultural import liberalisation and further subsidy reduction worldwide.

Intermediate growth will occur in Centrally Planned Economies where opportunities for collaboration with the Western world will improve.

As product differentiation between active ingredients declines further, the emphasis on product differentiation through formulation novelty and application technology will increase.

Competition between companies will increase in intensity and substantial further rationalisation will occur through acquisitions and mergers. The most successful companies will be those who are strong internationally, who have effective R&D aimed at generating both chemical and biological products and who give high priority to ensuring that their products, when used as directed, are safe to the user, the environment and the consumer of treated crops.

Acknowledgements

I would like to acknowledge the contribution from many colleagues within ICI but most particularly Mr C S Major, Mr M K Reeves and Mrs U M Stewart.

SESSION 2

NEW COMPOUNDS, FORMULATIONS AND USES

CHAIRMAN PROFESSOR P. T. HASKELL

SESSION ORGANISERS DR A. R. THOMPSON
DR P. GLADDERS

RESEARCH REPORTS 2-1 to 2-8

STOP PRESS

BSI Common Names for Pesticides

Because the camera-ready copy is required relatively early, in order that the *Proceedings* can be printed in time for the Conference, it sometimes happens that BSI names are adopted *after* the final copy was received and so are not mentioned in the text. Names recently adopted by BSI include:

Paper	*Firm's code no.*	*BIS common name*
2-2	CGA 106630	diafenthiuron
2-7	CGA 142705	fenpiclonil
5-1	LS 840606	furconazole-cis
5-8	PH 70-23	flucycloxuron
4B-1	PP321	lambda-cyhalothrin
	WL 85 871	alpha-cypermethrin

DIMETHOMORPH (CME 151), A NOVEL CURATIVE FUNGICIDE

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ABSTRACT

Dimethomorph, a cinnamic acid derivative is a new systemic Oomycete fungicide. It shows specific activity against members of the family Peronosporaceae and the genus Phytophthora. Important diseases controlled are Plasmopara viticola on vines and Phytophthora infestans on tomatoes and potatoes. Dimethomorph shows translaminar activity following foliar application and exhibits systemic uptake via the roots following soil drench. In addition to long residual activity dimethomorph has good protectant, curative and excellent antisporulant activity. Studies indicate a novel mode of action and no cross-resistance to phenylamide-fungicides has been observed. Field trials have demonstrated the excellent activity of dimethomorph especially in mixtures with contact fungicides. Dimethomorph causes no phytotoxicity or crop effects at dose rates well in excess of those required for effective disease control.

INTRODUCTION

The control of plant diseases caused by Oomycetes has become more difficult in recent years with the appearance of pathogens resistant to systemic fungicides (Decker 1982). Attempts have been made to solve this problem by using mixtures of fungicides or by alternating applications of compounds without cross resistance (Gisi & Wiedmer 1983; Levy, Y., Levi, R. & Cohen 1983; Samoucha, Hugelshofer & Gisi 1987; Samoucha & Gisi 1987; Staub & Sozzi 1983). One aim of research is to discover compounds which have no cross resistance to known groups of compounds.

Dimethomorph, developed by Shell Forschung GmbH is an Oomycete fungicide acting against members of the family Peronosporaceae and the genus Phytophthora but not Pythium. It belongs to a new chemical group (Nickl, Piper, Curtze, Drandarevski & Lust 1984) which is of special interest for markets in which resistance problems are already occuring. Dimethomorph is being developed for use in mixtures with contact fungicides. The properties of dimethomorph determined in laboratory, glasshouse and field trials are described below.

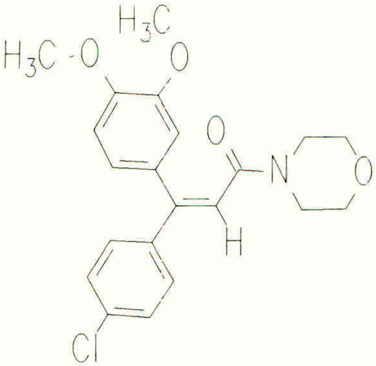
TECHNICAL DETAILS

Chemical name :	(E,Z) 4-[3-(4-chlorophenyl)-3-(3,4-dimethoxyphenyl)-acryloyl]-morpholine (IUPAC)
Common name (BSI) :	dimethomorph
Code number :	CME 151
Molecular Formula :	$C_{21}H_{22}ClNO_4$

2—1

Molecular Weight:	387.9
Structural Formula:	

Dimethomorph is a mixture of E and Z isomers (typically 50 : 50).


Z-isomer


E-isomer

Appearance :	colourless, odourless, crystalline solid
Melting Point :	127 - 148 °C
Solubilities (g/l) at 25 °C:	water < 0.05, acetone 50, toluene 20, methanol 20, dichloromethane 500.
Stability :	Dimethomorph is hydrolytically, photolytically and thermally stable under practical conditions.
Formulations :	WP 500 g/kg, EC 100 g/l

TOXICOLOGY

Acute toxicity (technical material):

Acute oral LD 50 to mouse :	Male	> 5000 mg/kg	body weight
	Female	3700 mg/kg	body weight
Acute oral LD 50 to rats:		3900 mg/kg	body weight
Acute percutaneous LD 50 to rats:		> 5000 mg/kg	body weight
Acute intraperitoneal LD 50 to rats:		312 mg/kg	body weight

Acute inhalative LD 50 to rats:	> 4240 mg/m^3
Skin sensitation to guinea pigs:	negative
Skin irritancy to rabbits:	non-irritating
Eye irritancy to rabbits:	non-irritating

EQUIPMENT AND METHODS

Glasshouse trials

Plants used were vines (cultivars Müller-Thurgau and Cabernet Sauvignon) cut back to four equal-sized leaves prior to treatment and tomato (cultivar Professor Rudloff) at the two-leaf stage. A minimum of 4 test plants per concentration were sprayed to run-off. After inoculation with aqueous spore suspensions (density of 3×10^6 /ml), the plants were incubated at 20 °C for 48 hours at high humidity in the dark. The vines were then moved into a glasshouse at 100 % RH, 3000 Lux, daytime temperature 23 °C, night temperature 18 °C. The tomatoes were moved for a few hours prior to evaluation to a dry atmosphere (50 % r.h.) in the light. Fungicidal activity was calculated as:

$$\%\text{efficacy} = 100 - \frac{\%\text{ infected leaf area in treated}}{\%\text{ infected leaf area in untreated}} \quad \times 100$$

Systemicity was examined following application to the soil and to the foliage. In the former, the fungicide was applied at different concentrations and the vine and potato plants were then inoculated at different stages. Thus, vine cuttings were cut back to three leaves and sprayed with the fungicide. Ten to fourteen days later the whole plant was inoculated with P. viticola and when the symptoms appeared, the infection on the old and new leaves was assessed.

Activity against metalaxyl-resistant P. viticola strains was investigated on Müller-Thurgau vine cuttings in a two day curative trial.

Field trials

Potato trials were designed as a randomized block with 4 replications with plots of 25-50 m^2. The trials in vines were conducted on cultivars Müller-Thurgau and Faber with 4 replications of 5 vines per treatment, in a randomized block design. Dimethomorph was used in tank mixtures with mancozeb. Applications to both crops were made using motorized portable sprayers (Solo F 320) equipped with flat fan or swirl nozzles respectively (pressure 3.5 resp. 4 bar). Spraying intervals were selected according to local commercial practice. Plants were sprayed to run-off to give complete cover. The results were recorded as % infection.

RESULTS

Mode of action

The precise mode of action of CME 151 has not been identified. Preliminary tests (Buchenauer 1987; Davidse et al 1987; Kuhn - personal communication) have shown that DNA synthesis, RNA synthesis, protein synthesis, energy production, cell wall synthesis and lipid synthesis are not directly affected. It was also observed that the morphological changes provoked by dimethomorph in the mycelium of P. infestans in liquid culture differ from those provoked by cymoxanil or phenylamides. These observations imply a novel mode of action.

Activity of isomers

In vitro tests on P. infestans have shown that, with the light excluded, only the Z isomer is fungitoxic. The results from field trials using WP formulations with different E : Z ratios at 150 mg/l are shown in Table 1.

TABLE 1

Influence of the isomer ratio of dimethomorph (50 % WP) on the activity against Plasmopara viticola under field conditions.

Ratio of Isomers E : Z	Site Number 1	 2	 3	 Mean
	% activity			
0 : 100	85	80	81	82
50 : 50	83	86	90	86
70 : 30	73	84	84	80

The results show that in light, all ratios were equally effective. Under field conditions fungicidal activity does not depend on the isomer ratio because fast equilibration to a Z : E ratio of about 80:20 occurs.

Fungicidal activity

The residual activity of dimethomorph is shown in Table 2. Applications were made 10 days before infection and disease control assessed 6 days after infection.

TABLE 2

Residual activity of dimethomorph and standard fungicides against Plasmopara viticola in outdoor pot grown vines (100 % attack in untreated plants).

Active ingredient	Formulation (% a.i.)	Concentration (mg/l) 100	 25	 6.3
		% efficacy		
Dimethomorph	10 EC	100	98	86
Cymoxanil	50 WP	32	0	0
Mancozeb	80 WP	70	61	32

At all concentrations dimethomorph gave longer lasting protection against infection than the standards.

Curative activity is shown in Table 3 when applications of 100 mg/l were made 2 or 5 days after infection.

TABLE 3

Curative activity of dimethomorph and standard fungicides applied at 100 mg/l in aqueous acetone against Plasmopara viticola when applied to infected vine cuttings (c.v. Cabernet Sauvignon) in the glasshouse.

Compound	Age of infection 2 days	 5 days
	% efficacy	
Dimethomorph	100	100
Metalaxyl	100	99
Cymoxanil	100	9

It can be seen that the curative activity of dimethomorph on longer-established lesions is greater than that of cymoxanil.

The antisporulant activity of dimethomorph can be seen afterapplication to a non-sporulating lesion at the visible "oil" spot stage. Under field conditions, application in the evening results in no sporulation with dimethomorph in comparison to some sporulation with cymoxanil or metalaxyl and extensive sporulation in untreated plots.

The activity of dimethomorph against P. viticola and P. infestans was confirmed in field trials. Tables 4 and 5 show the typical activity of mixtures with mancozeb in comparison to the control achieved by commercial standards.

TABLE 4

Control of Plasmopara viticola on vines following prophylactic treatment on a 10 day spray interval.

Treatment	Dose (g a.i./ha)	% disease control
Dimethomorph + mancozeb	200 + 1200	96
Mancozeb	1200	87
Metalaxyl + mancozeb	200 + 1200	98

Dimethomorph as the EC 10 % formulation.

TABLE 5

Control of Phytophthora infestans on potatoes following application on a nominal 14 day spray interval.

Treatment	Dose% (g a.i./ha)	efficacy	Yield as % of control
Dimethomorph + mancozeb	180 + 1200	93	143
Metalaxyl + mancozeb	200 + 1200	93	145
Dimethomorph + mancozeb	180 + 1200	99	135
Oxadixyl + mancozeb	200 + 1120	99	132
Dimethomorph + mancozeb	180 + 1200	89	146
Cymoxanil + mancozeb	120 + 1120	80	121

Dimethomorph as the WP 50 % formulation

Resistance

Tests on phenylamide-resistant and susceptible strains of P. viticola on vine are shown in Table 6. Applications of 100 mg/l were made 2 days after infection.

TABLE 6

Action of dimethomorph and metalaxyl applied in aqueous acetone against phenylamide resistant and susceptible strains of Plasmopara viticola in the glasshouse.

Compound	Susceptible	Resistant
	% efficacy	
Dimethomorph	99	99
Metalaxyl	100	62
% infection of control plants	87	41

The results show that there is no cross-resistance between dimethomorph and phenylamides. A similar result was obtained with P. infestans. No mutants naturally resistant to dimethomorph have as yet been found. Resistance-monitoring tests have been in progress since 1987.

Systemic properties

The systemic movement of dimethomorph from root to shoot is shown in Table 7. In this test tomatoes were inoculated 5 days after soil treatment and control assessed 2 days after inoculation; vines were inoculated 7 days after soil treatment and assessed 6 days after inoculation.

TABLE 7

Dimethomorph activity after soil application at 25, 100 and 400 mg/l to vine cuttings infected with Plasmopara viticola and tomatoes infected with Phytophthora infestans.

Compound	Formulation	% efficacy against					
		Phytophthora infestans			Plasmopara viticola		
		400	100	25	400	100	25
Dimethomorph	aq. acetone	100	100	99	100	100	40
Cymoxanil	aqueous	100	65	21	0	0	0
Metalaxyl	aq.acetone	100	100	100	100	100	100

The results indicate that dimethomorph can affect foliar disease control apoplastically via the roots of potatoes and vines. New growth of vines was not protected by foliar applications.

Crop tolerance

Dimethomorph in both EC and WP formulations is well tolerated by vines, potatoes and tomatoes. Phytotoxicity has never been seen on these crops. Tests carried out using recommended protocols (Biologische Bundesanstalt für Land- und Forstwirtschaft) show that both the fermentation of grapes and the taste of the wine are not affected when dimethomorph is used under typical commercial practice.

DISCUSSION

The results from a series of glasshouse and field trials show that dimethomorph has good fungicidal activity against Peronosporaceae and Phytophthora spp. This activity embraces residual, curative and antisporulant activity. The value of dimethomorph for plant protection has been established in field trials in vines and potatoes. The antisporulant activity is of particular practical significance in the control of P. viticola in vines such that infection pressure can be reduced considerably. No phytotoxicity nor other crop effects have been observed at dose rates well in excess of those required for effective disease control.

Although the precise mechanism of action is as yet unknown, results to date imply a novel mode of action for dimethomorph. No cross-resistance to phenylamides is observed. Dimethomorph will provide a valuable addition to the current range of Oomycete fungicides in giving disease control within a resistance strategy programme.

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CGA 106630 - A NEW TYPE OF ACARICIDE/INSECTICIDE FOR THE CONTROL OF THE SUCKING PEST COMPLEX IN COTTON AND OTHER CROPS

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ABSTRACT

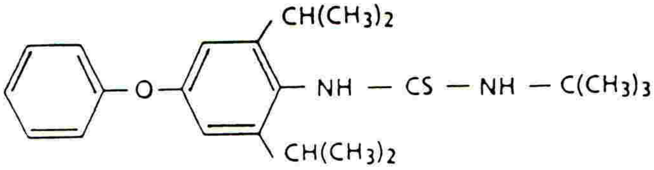
CGA 106630 is a new type of thiourea derivative having promising acaricidal and insecticidal activity. It gives good control of phytophagous mites as well as whiteflies, aphids and jassids in cotton, vegetables and ornamentals. Furthermore, the favourable acute mammalian toxicity coupled with its good selectivity on beneficial insects and predatory mites indicate that CGA 106630 will be an outstanding compound for future use. Laboratory and field experiments are discussed.

INTRODUCTION

The intensive use of synthetic pyrethroids against chewing insects in cotton has caused increasing problems with spider mites and sucking insects in a number of countries. Mites and sucking pests have also developed resistance to organophosphorus and carbamate insecticides. In order to solve these pest problems there is particular interest in the development of chemicals with novel modes of action. Ciba-Geigy has been intensively involved in such development culminating in the discovery of a novel type of compound with the code number CGA 106630. This paper reports the technical properties of CGA 106630 and its efficacy against a wide range of pests.

CHEMICAL AND PHYSICAL PROPERTIES

Chemical name	1-tert-butyl-3-(2,6-di-isopropyl-4-phenoxyphenyl) thiourea
Molecular formula	$C_{23}H_{32}N_2OS$
Structural formula	



Molecular weight	384.59	
Melting point	149.6°C	
Physical state	colourless crystals	
Vapour pressure at 20°C	1.8×10^{-8} PA (1.4×10^{-10} Torr)	
Solubility (g/100 ml solvent at 20°C)	water	0.00005
	cyclohexanone	38
	xylene	21
	hexane	0.8

FORMULATION

The activity of CGA 106630 correlates inversely with the particle size in the formulation. The smaller the particles in the formulation the better is the biological activity.

Formulations available:	500 SC	containing 500 g a.i./litre, mean particle size of 3.5 μ
	50 WP	containing 500 g a.i./kg, mean particle size of 4.0 μ

TOXICOLOGY AND ENVIRONMENTAL PROPERTIES

Based on acute toxicity data, CGA 106630 and its formulations are slightly hazardous to mammals (WHO class III) (Table 1).

TABLE 1

Acute toxicity of technical CGA 106630 to rats.

Acute oral LD_{50}		2068 mg/kg
Acute dermal LD_{50} (24h)	>	2000 mg/kg
Acute inhalation LC_{50} (14h)		558 mg/m^3
Eye irritation		none
Skin irritation		none

The technical CGA 106630 was practically non toxic in acute oral and 8-day feeding tests to Bobwhite quails and Mallard duck (LD_{50} and LC_{50} >1500 mg/kg).

Technical CGA 106630 was highly toxic to carp (Cyprinus carpio) , rainbow trout (Salmo gairdneri), and bluegill (Lepomis macrochirus) after 96h exposure (LC_{50} < 0.5 mg/l).

The compound was also toxic to the water flea Daphnia magna (LC_{50}, 48h: < 0.5 mg/l) but it did not harm the alga Scenedesmus subspicatus (EC_{50}, 72 h: > 50 mg/l).

Technical CGA 106630 was non-toxic to the earthworm Eisenia foetida (LD_{50}, 14d: > 2000 mg/kg). It was toxic to bees (Apis mellifera) by oral (LD_{50}, 48h: 2.1 μg/bee) and topical (LD_{50}, 48h: 1.5 μg/bee) application.

BIOLOGICAL PERFORMANCE

Acaricidal activity

Laboratory tests

The sensitivity of eggs and the developmental stages of Tetranychus urticae was studied using the leaf dip test (Puppin et al., 1983). CGA 106630 killed larvae, nymphs and adults and it also showed some ovicidal activity (Table 2).

TABLE 2

Corrected percent mortality data (Abbott, 1925) for developmental stages of Tetranychus urticae 4 days after dipping in aqueous solutions of a 50 % SC formulation of CGA 106630.

Stages	Concentration (mg a.i./litre)	
	200	400
Egg	67	72
Larva	100	100
Protonymph	93	100
Deutochrysalis	95	100
Deutonymph	92	99
Adult female	100	100

An important feature of CGA 106630 is its good translaminar activity on cotton. Pests (e.g. whiteflies, mites) located on the underside of leaves not directly hit by the spray are controlled, as demonstrated in tests with the carmine mite, Tetranychus cinnabarinus (Table 3). In this test, cotton plants were infested with all mobile stages of T. cinnabarinus. In the first series, plants were totally sprayed with volumes of 360 l/ha. In the second series only the upper surfaces of the leaves were treated, as done under practical conditions.

TABLE 3

Number of mobile stages of Tetranychus cinnabarinus per cotton leaf in assessments made with a mite brushing machine 10 days after treatment.

Chemical	Formulation	Concentration (mg a.i./litre)	Application method	
			Total plant	upper side of leaves
CGA 106630	50 % SC	300	0.5	23
Propargite	57 % EC	300	9.0	175
Untreated	-	-	282.0	282

Field trials

CGA 106630 has been evaluated extensively in the field against the most important mite species in different crops throughout the world. CGA 106630 provided good spider mite control for a period of at least 21 days. Typical results are shown in Tables 4 and 5.

TABLE 4

Control of Tetranychus cinnabarinus on cotton, South Africa (1985).

Chemical	Formulation	Dose 1) (g a.i./ha)	Mean % efficacy in 4 trials 2)		
			2 DAT	14 DAT	21 DAT
CGA 106630	50 % SC	400	95	98	93
CGA 106630	50 % SC	300	92	90	89
Profenofos	50 % EC	750	94	89	78
Triazophos	42 % EC	500	96	84	77
Untreated 3)	-	-	(52)	(65)	(47)

1) Low volume spray (150 l/ha) with a horizontal spray bar
2) Efficacy values were corrected according to Henderson and Tilton (1955)
3) Mean nos. mites/10 leaves

TABLE 5

Percent control of Polyphagotarsonemus latus on cotton, Brazil (1987).

Chemical	Formulation	Dose 1) (g a.i./ha)	DAT 2)		
			7	14	21
CGA 106630	50 % SC	400	98 a	96 a	91 a
CGA 106630	50 % SC	300	91 a	90 b	76 a
Bifenthrin	10 % EC	50	13 bc	23 bc	11 bc
Profenofos	50 % EC	500	91 a	58 b	35 b
Untreated 3)	-	-	(70) c	(114) c	(192) c

1) Low volume spray (150 l/ha) with a horizontal spray bar
2) Treatments with common suffices are not statistically different ($P = 0.05$)
3) Mean nos. mites/10 leaves

Insecticidal activity

Cotton

The cotton whitefly, Bemisia tabaci, is a major pest of cotton in many countries and has developed resistance to a wide range of insecticides.

CGA 106630 has provided excellent whitefly control under high infestation pressure in cotton in spray programmes carried out in Guatemala, Sudan and Turkey. CGA 106630 controlled nymphs as well as adults of B. tabaci and provided good yield results (Table 6).

TABLE 6

Control of B. tabaci in a cotton spray programme, Guatemala (1986).

Compound	Formulation	Dose [1] (g a.i./ha)	Mean nos. whiteflies on 20 leaves nymphs	Mean nos. whiteflies on 20 leaves adults	Yield of seed cotton (kg/ha)
CGA 106630	50 % SC	300	64	185	2364
CGA 106630	50 % SC	150	158	290	2136
Methamidophos	60 % EC	860	239	356	1727

1) The compounds were applied in 6 sprays by aerial application (25 l/ha) at intervals of 10 days

The cotton aphid (Aphis gossypii) is also becoming increasingly important in different cotton growing countries. Very good control was achieved in field trials in Turkey (Table 7). Slow initial response to CGA 106630 but excellent residual effectiveness were apparent.

TABLE 7

Control of A. gossypii on cotton, Turkey (1985).

Chemical	Formulation	Dose [1] (g a.i./ha)	Mean nos. aphids/10 leaves 1 DAT	Mean nos. aphids/10 leaves 7 DAT	Mean nos. aphids/10 leaves 14 DAT
CGA 106630	50 % WP	500	74 a [2]	6 a	2 a
CGA 106630	50 % WP	250	104 a	7 a	5 a
Phosphamidon	50 % SCW	750	31 a	43 a	25 a
Fenpropathrin	20 % EC	300	208 b	106 b	198 b
Untreated	-	-	661 c	1166 c	655 c

1) Applied with a mistblower using 400 litres spray/ha
2) Treatments with common suffices are not statistically different (P = 0.05)

CGA 106630 is generally effective in controlling aphids on vegetables at doses of 30-40 g a.i./100 l. Four tests in Italy against the green peach aphid (*Myzus persicae*) on tomato showed that CGA 106630 compared favourably with pirimicarb (Table 8).

TABLE 8

Control of green peach aphid (*M. persicae*) on tomato in Italy (1987).

Chemical	Formulation	Dose [1] (g a.i./ha)	Mean % control [1] in 4 trials 7 DAT	 16 DAT	 21 DAT
CGA 106630	50 % SC	40	97	99	92
Pirimicarb	25 % WP	40	97	99	87
Untreated[2]	-	-	600	1510	1620

[1] Corrected using Henderson-Tilton (1955) formula
[2] Mean nos. aphids/20 plants

Persistent control of *Aphis fabae* on broad bean and of *Macrosiphum euphorbiae* on potato has been achieved in Italy using 40 g a.i./100 l (Table 9). CGA 106630 50 % SC provided excellent control for 3-4 weeks.

TABLE 9

Control of *Macrosiphum euphorbiae* on potato and *Aphis fabae* on broad bean, Italy (1987).

Chemical	Formulation	Dose (g a.i./ha)	Mean % efficacy[2] *M. euphorbiae* 5 DAT	 27 DAT	 *A. fabae* 6 DAT	 22 DAT
CGA 106630	50 % SC	40	95 a	97 a	96 a	95 a
Pirimicarb	25 % WP	40	94 a	74 a		
Dimethoate	20 % EC	40			99 a	99 a
Untreated[1]	-	-	1676 b	7800 b	2919 b	4773 b

[1] Mean nos. aphids/10 leaves
[2] Treatments with common suffices are not statistically different (*P* = 0.05)

Good results have also been obtained against *Trialeurodes vaporariorum* in glasshouses following two sprays after a 7 day interval with CGA 106630 at 30 g a.i./100 l. Results from Switzerland are presented in Table 10.

TABLE 10

Performance of CGA 106630 50 % SC against T. vaporariorum on eggplant in a glasshouse test, Switzerland (1987).

Chemical	Formulation	Dose (g a.i./100 l)	Mean nos. adults/shoot[1) 3 DAT]	7 DAT	14 DAT
CGA 106630	50 % WP	30	23 a	26 a	33 a
Cypermethrin	10 % EC	4	36 a	45 a	73 a
Untreated[2)]	-	-	340 b	260 b	290 b

1) Treatments with common suffices are not statistically different (P = 0.05)

The diamond-back moth (Plutella xylostella) is a widespread pest of many vegetables, especially cabbage, and development of resistance of this pest to conventional insecticides has become a serious problem in South East Asia. Table 11 shows the control of P. xylostella given by CGA 106630 in a spray programme on cabbage in Thailand. CGA 106630 was very effective against P. xylostella and exhibited better activity than teflubenzuron and cypermethrin.

TABLE 11

Control of the diamond-back moth on cabbage, Thailand (1987).

Chemical	Formulation	Dose 1) (g a.i./ha)	% control 6/6	% control 13/6	% control 19/6	% damage 27/6
CGA 106630	50 % SC	50	72	78	82	18
Teflubenzuron	50 % EC	5	32	34	0	30
Cypermethrin	20 % EC	110	35	16	0	42
Untreated[2)]	-	-	(16)	(74)	(61)	54

1) Application dates: 30/5, 6/6, 13/6, 19/6, 27/6/87 using 1000 litres/ha, applied with the spray boom

2) Mean nos. larvae and pupae/10 plants

TOXICITY TO BENEFICIAL ARTHROPODS

In laboratory tests with the predatory mite Amblyseius fallacis (Streibert 1981) CGA 106630 reduced the population following a direct spray. However a four day old spray deposit had practically no effect on the predatory mite (Table 12).

TABLE 12

Toxicity of CGA 106630 to the predatory mite, A. fallacis.

Chemical	Formulation	Concentration (mg a.i./litre)	Mean % reduction of the population	
			direct spray	residual effect 4 DAT
CGA 106630	50 % SC	400	86	57
CGA 106630	50 % SC	200	77	20
Cyhexatin	50 % SC	400	83	82
Untreated1)	-	-	(68)	(80)

1) Mean nos. of adults, larvae, and eggs of A. fallacis/leaf

DISCUSSION

It can be concluded that CGA 106630 is a promising new acaricide/insecticide. It has outstanding strengths in the control of the sucking pest complex in cotton. CGA 106630 can replace conventional insecticides and acaricides in short interval spray programmes; alternatively the longer residual performance may be exploited to reduce the number of sprays per season. Because of its novel chemistry and mode of action CGA 106630 controls insects and mites resistant to other insecticides and acaricides. Since sucking pests in cotton develop resistance rapidly, alternating applications with other suitable products are recommended.

CGA 106630 also provides a solution for the control of several vegetable pests including mites, aphids, whiteflies, and diamond-back moth. First field trials have indicated that CGA 106630 may also be effective against the citrus rust mite (Phyllocoptrula oleivosa), citrus red mite (Panonychus citri), fruit tree red spider mite (Panonychus ulmi), hop aphid (Phorodon humuli), cotton leafhoppers (Empoasca spp.), citrus snow scale (Unaspis citri), white peach scale (Pseudolaucaspis pentagona), but not against thrips.

CGA 106630 did not show adverse effects against beneficial insects. Temporary reductions of populations of juvenile stages of heteropterous predators (Anthocoridae, Miridae) were observed in field trials, but recovery took place within 10 days. Adults of Hetoptera, Coccinella and Chrysopa were not affected.

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BRIGHTON CROP PROTECTION CONFERENCE—Pests and Diseases—1988

2—3

RH 7592, A NEW TRIAZOLE FUNGICIDE WITH HIGH SPECIFIC ACTIVITY ON CEREALS AND OTHER CROPS

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ABSTRACT

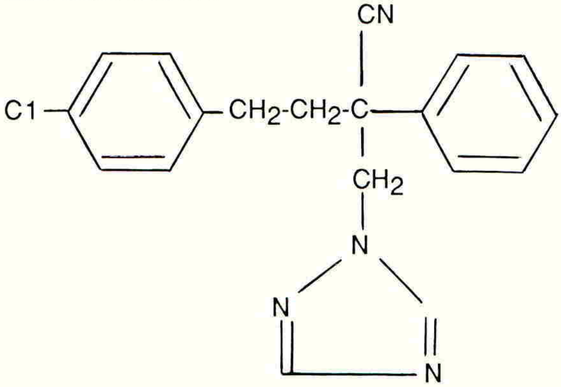
RH 7592, (R,S)-4-(4-chlorophenyl)-2-phenyl-2-(1H-1,2,4-triazol-1-yl methyl) butyronitrile, is a new broad spectrum fungicide giving excellent control of *Septoria tritici*, *Septoria nodorum, Puccinia recondita* , *Puccinia striiformis,* and good activity against *Rhynchosporium secalis* in cereals. It has a strong protectant and good residual activity. RH 7592 is also effective against the following crop disease complexes: *Venturia inaequalis* in apples, *Monilinia spp.* in stone fruit, *Uncinula necator, Guignardia bidwellii, Botrytis cinerea* in vine, and *Cercospora beticola* in sugar beet. It shows minimal phytotoxycity and growth regulatory effects. RH-7592 has undergone several years of laboratory tests and field trials.

INTRODUCTION

RH 7592 is a new triazole fungicide with systemic properties which was synthesized by Rohm and Haas scientists. This paper describes its chemical properties and its fungidical performances on cereals and other crops.

TECHNICAL DATA

Structural formula



2—3

Molecular formula : $C_{19}H_{17}ClN_4$

Code number : RH 7592

Systemic chemical name : (R,S)-4-(4-chlorophenyl)-2-phenyl-2-(1H-1,2,4-triazol-1-ylmethyl)butyronitrile

Appearance : White crystalline solid

Melting point : 124 -126 ° C.

Solubility : 0.2 ppm 25°C in water; soluble in common organic solvent such as ketones, esters, alcohols, aromatic hydrocarbons, etc. Insoluble aliphatic hydrocarbon solvents.

Stability : Stable under normal storage conditions.

Vapour pressure : 0.37×10^{-7} torr.

TOXICOLOGY

Acute Oral LD_{50} : Rat (male) > 2000 mg/kg
Acute Dermal LD_{50} : Rat > 5000 mg/kg
Skin irritation (rabbit) : Practically non irritating
Eye irritation (rabbit) : Inconsequential
Mutagenicity : Negative

BIOLOGICAL PROPERTIES

RH 7592 is chemically related to the ergosterol biosynthesis inhibitor (EBI) family of fungicides. RH 7592 is a broad spectrum, systemic fungicide possessing protectant, curative and eradicant properties against a wide range of diseases attacking cereals, fruits, vine, vegetables and ornamentals. The disease spectrum includes rusts and smuts, powdery mildew, diseases incited by *Helminthosporium, Septoria, Cercospora* and other Ascomycetes, Deuteromycetes and Basidiomycetes. The primary means of effectiveness is achieved by foliar applications, but seed treatments and post harvest applications are also being evaluated.

MATERIALS AND METHODS

RH 7592 has been tested alone and in tank mixtures with several other fungicides against a wide range of pathogens throughout Europe. On cereals all treatments in trials were replicated 4 times and arranged in randomised block designs. Plot sizes were 20-100 m^2. Applications of fungicides were made using a knapsack sprayer in water volumes of 200-400 l/ha. Assessment methods for efficacy and crop tolerance were based on nationally accepted guidelines and usually involved counting the infected leaves or ears and estimating disease or damage relative to either an untreated or standard treatment. Spray application schedules were initiated either at the outset of disease incidence or were based on plant development according to local recommendations. The results presented are representative of a large number of trials throughout Europe. The selected trials had uniform and heavy disease pressure. All treatments in trials on apple were replicated 3-4 times and arranged in randomised block designs. The plot size was 3-4 trees. Water volume of 1500-2000 l/ha were used.

RESULTS AND DISCUSSION

RH 7592 has been tested at 75 g a.i./ha against *Septoria tritici* and *Septoria nodorum* at 2 growth stages : GS 39 or GS55. The assessments were effected the same day i.e. 36 DAT for the GS39 application and 24 DAT for the GS55 application.

TABLE 1

Control of *S.tritici* on winter wheat (mean of 18 sites in France, U.K., Italy 1986-87-88)

Treatment	Dose (g a.i./ha)	Mean % leaf area affected	
		application at GS 39	application at GS 55
RH 7592	75	11	18
Propiconazole	125	14	17
Untreated		54	54

TABLE 2

Control of *Septoria nodorum* on winter wheat (mean of 11 sites in France, U.K., Germany 1987-88)

Treatment	Dose (g a.i./ha)	Mean % leaf area infected	
		application at GS 39	application at GS 55
RH7592	75	11	8
Propiconazole	125	15	10
Untreated		37	37

RH 7592 was more effective when applied as a preventative treatment but also showed eradicant activity particularly when used before symptoms appeared. As a systemic fungicide, RH 7592 was more readily translocated upward in the plant than in the basipetal direction. Preliminary evidence suggests than RH 7592 possesses a relatively high level of residual activity. RH 7592 gave yield increases in winter wheat when applied at GS 38/55 (Table 3).

TABLE 3

Yields corresponding to the *Septoria spp.* trials (mean of 19 sites in France, U.K., Germany and Italy 1986-87-88)

Treatment	Dose (g a.i./ha)	Yields (t/ha)	
		application at GS 39	application at GS 55
RH 7592	75	7.45	6.90
Propiconazole	125	7.00	6.55
Untreated		5.65	5.65

Two types of applications were evaluated against *Puccinia recondita* one early in season (GS 38-45) prior to infection and a second when the first pustules appeared. Assessments were made between 29 to 34 DAT for the preventive application and 17 to 22 DAT for the eradicant application. The results hereunder confirm the excellent preventative efficacy and the long residual control of RH 7592.

TABLE 4

Control of *Puccinia recondita* on winter wheat (mean of 17 sites in France, Italy, Spain 1986-87-88).

Treatment	Dose (g a.i./ha)	Mean % leaf area affected			
		Leaf 2		Flag leaf	
		P	E	P	E
RH 7592	75	3	7	1	3
Triadimenol	125	7	13	4	8
Untreated		42	42	17	17

P : Preventative E : Eradicant

RH 7592 has been tested at doses of 2.0-3.5 g a.i./hl for the control of apple scab (*V. inaequalis*) . Excellent control of fruit and leaf infections has been achieved with RH 7592 at 2.0 g a.i./hl in trials throughout Europe. Nine sprays were applied on 6-10 day preventative schedule.

TABLE 5

Control of *Ventura inaequalis* on apples (cv Double red), at Lavezzola (RA), Italy, in 1988.

Treatment	Dose (g a.i./hl)	% Control	
		Leaves	Fruit
RH 7592	2.0	97	85
RH 7592	3.0	99	91
Flusilazole	2.0	97	81
Untreated*		(100)	(96)

* : % infected leaves and fruit

TABLE 6

Control of *Venturia inaequalis* on apples (cv Dallago) at Albaredo (VR), Italy, in 1988 with 7 sprays on a 7-14 day curative schedule.

Treatment	Dose (g a.i./hl)	% Control	
		Leaves	Fruit
RH 7592	2.0	84	95
RH 7592	3.5	93	96
Flusilazole	2.0	77	89
Untreated*		(100)	(83)

* : % infected leaves and fruit

OTHER CROPS

RH 7592 was also effective against the range of major diseases shown in Table 7: (Neither the crop nor the disease list is considered to be exhaustive).

TABLE 7

Crop	Pathogen	Effective Dose (g a.i.)
Cereals	*Tilletia spp.* *Ustilago spp.*	10 -20/100 kg seed
Barley	*Helminthosporium spp.* *Puccinia spp.* *Rhynchosporium secalis*	65/ha
Beans (Phaseolus)	*Uromyces phaseoli*	65-280/ha
Sugar beet	*Cercospora beticola*	65-280/ha
Stone fruit	*Monilinia laxa* *Sphaerotheca pannosa* *Tranzschelia pruni-spinosae*	18-70/ha
Pome fruit	*Venturia pirina* *Gymnosporangium spp.* *Podosphaera leucotricha*	18-70/ha
Vine	*Uncinula necator* *Guignardia bidwellii* *Botrytis cinerea*	30-180/ha
Vegetable	*Cercospora spp.* *Puccinia spp.* *Septoria apiicola* *Erysiphe cichoracearum* *Leveillula taurica*	65-280/ha

CONCLUSIONS

In greenhouse screens and field trials throughout Europe, RH-7592 was identified as a broad spectrum fungicide for use on a number of important crops. Disease control was achieved at low doses in a wide range of climatic conditions without crop phytotoxicity of growth regulator effects. On cereals, excellent control of *Septoria spp.* and *Puccinia spp.* was obtained at 75 g a.i./ha.

Strong preventative activity linked to a good residual was demonstrated. RH-7592 is not effective on *Erysiphe graminis* and must be mixed with a partner in some areas. On pome fruit, RH-7592 has shown excellent efficacy at 2.0 g a.i./hl against scab in preventative and curative applications.

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NC-129 - A NEW ACARICIDE

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ABSTRACT

NC-129 is a new acaricide which provides excellent control of mites and some insects including whiteflies, aphids and thrips. NC-129 is highly active to all developing stages of mites. It has rapid knockdown activity, long residual activity and stable activity under wide temperature conditions. NC-129 possesses a novel chemical structure and mode of action. It is very effective against acaricide-resistant mites.

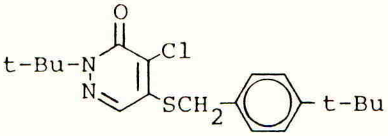
INTRODUCTION

In research into pyridazinone derivatives, a new class of acaricidal compound was discovered by Nissan Chemical Industries, Ltd.

NC-129 was selected as the most active compound among many derivatives. NC-129 is now being developed worldwide as a promising acaricide for crops including citrus, top fruit, grape, vegetables, tea and ornamentals.

CHEMICAL AND PHYSICAL PROPERTIES

Chemical name	:	2-*tert*-butyl-5-(4-*tert*-butylbenzylthio)-4-chloropyridazin-3(2*H*)-one
Code number	:	NC-129, NCI-129
Structural formula	:	



Molecular formula; molecular weight : $C_{19}H_{25}ClN_2OS$; 364.9

Physical appearance : white crystalline solid

Odour : odourless

Melting point : 111 - 112 °C

Specific gravity : d^{20}_{4} : 1.2

Vapour pressure : 1.9×10^{-6} mmHg at 20 °C

Solubility (g/100 ml solvent at 20 °C):

acetone	46	benzene	11
corn oil	4.2	cyclohexane	32
ethanol	5.7	hexane	1.0
methyl cellosolve	11	n-octanol	6.3
xylene	39	water	1.2×10^{-6}

Stability :	in water	stable at pH 4, 7 and 9
	to heat	no decomposition at 50 °C for 3 months
	to light	relatively unstable but NC-129 EC is stable for at least two years under normal storage conditions
	in organic solvents	stable in most organic solvents

TOXICOLOGY

Acute oral LD_{50} (14 days) :	Rat (male)	435 mg/kg
	(female)	358 mg/kg
	Bobwhite quail	> 2,250 mg/kg
	Mallard duck	> 2,500 mg/kg
Acute dermal LD_{50} (14 days) :	Rabbit (male)	> 2,000 mg/kg
	(female)	> 2,000 mg/kg
Eye irritation :	Rabbit	non-irritant
Dermal irritation :	Rabbit	non-irritant
Dermal sensitization:	Guinea pig	negative
Mutagenicity :	Ames	negative
	DNA repair	negative
	in vitro chromosomal aberration (Chinese hamster lung cells)	negative
	Micronucleus-mouse	negative

LABORATORY EVALUATION

Acaricidal activity

NC-129 has excellent activity against spider mites, tarsonemid mites and eriophyid mites. NC-129 is about 10 times more active than cyhexatin against larvae of *Tetranychus* spp. and *Panonychus* spp. (Table 1).

TABLE 1

Larvicidal activity of NC-129 and cyhexatin against *Tetranychus* spp.* and *Panonychus* spp.*, using leaf-disc sprays.

Compoud	LC_{50} (mg a.i./1)				
	T.u.	T.k.	T.c.	P.c.	P.u.
NC-129	0.20	0.44	0.40	0.23	0.43
Cyhexatin	3.5	4.0	3.0	5.5	6.3

* T.u. : *T. urticae*
T.k. : *T. kanzawai*
T.c. : *T. cinnabarinus*
P.c. : *P. citri*
P.u. : *P. ulmi*

NC-129 has high activity against all developing stages of mites: egg, larva, nymph and adult. Table 2 shows the high activity of NC-129 on all developing stages of *P. citri*.

On *T. urticae*, NC-129 is highly active on larva and nymph and moderate active on egg and adult.

TABLE 2

Miticidal activity of NC-129 against different stages of mites, using leaf-disc sprays.

Species	LC_{50} (mg a.i./1)			
	Eggs	Larvae	Protonymphs	Adults
Panonychus citri	7.2	0.09	0.17	0.42
Tetranychus urticae	30	0.10	0.18	15

The ovicidal activity of NC-129 is evident against eggs of most ages and NC-129 is more active than hexythiazox against eggs (Figure 1).

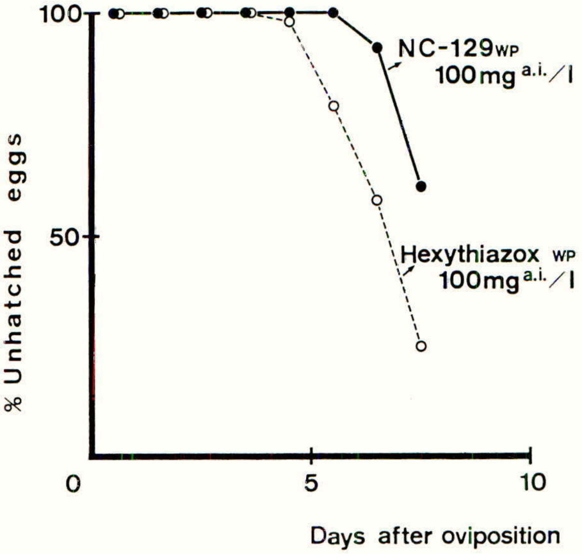


Figure 1 Ovicidal activity of NC-129 and hexythiazox against P. citri, using leaf-disc sprays.

NC-129 shows very rapid knockdown. It acts within one hour at 10 mg a.i./l against more than 90 % of adult females of T. urticae (Figure 2).

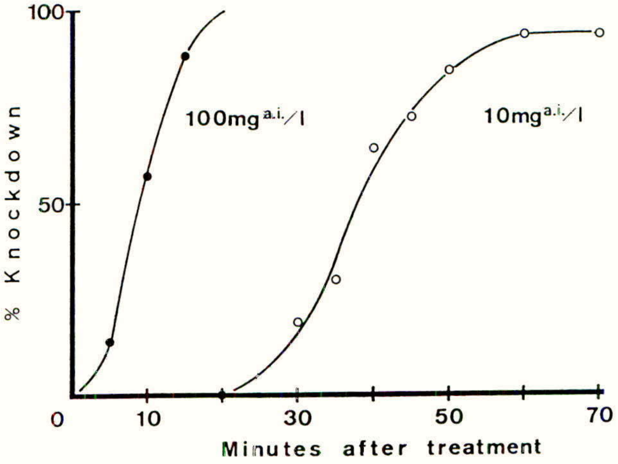


Figure 2 Knockdown time of NC-129 (EC) against adult females of T. urticae, using leaf-disc sprays.

NC-129 has long residual activity against all stages of Panonychus spp. and larvae of Tetranychus spp. Figure 3 shows the long residual activity of NC-129 at 100 mg a.i./l in comparison with cyhexatin at 125 mg a.i./l against adults of P. citri.

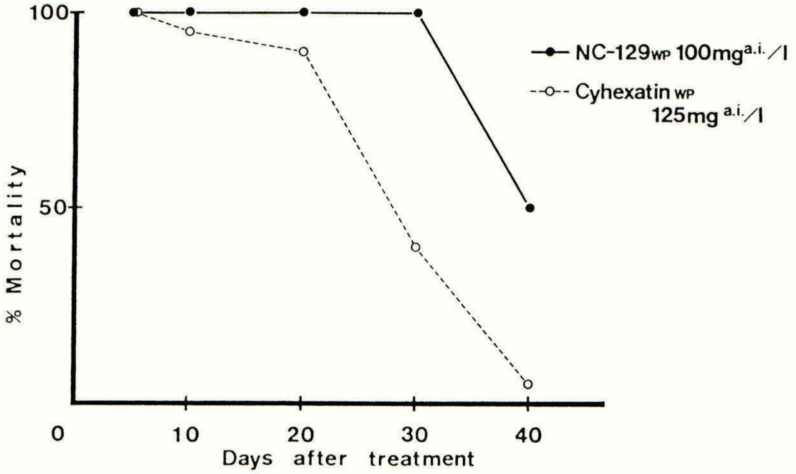


Figure 3 Residual activity of NC-129 and cyhexatin against adults of P. citri, using glasshouse pot tests.

Influence of temperature on the activity of NC-129 against eggs of P. citri was assessed. The results indicate that NC-129 has stable activity under various temperature conditions (Table 3).

TABLE 3

Ovicidal activity of NC-129 against P. citri under various temperature conditions, using leaf-disc sprays.

Compound	LC_{50} (mg a.i./l)		
	20 °C	25 °C	30 °C
NC-129	7.0	6.4	5.0

Recently, resistance to hexythiazox was reported in Japan (Kobayashi & Nonoshita, 1988). Table 4 shows that NC-129 has high activity against strains of P. citri resistant to fenbutatin-oxide and hexythiazox.

TABLE 4

Larvicidal activity against two resistant strains of P. citri, using leaf-disc sprays.

Compound	LC50 (mg a.i./l)		
	Susceptible strain (*)	Resistant strain (**)	
		A	B
NC-129	0.095	0.090	0.15
Fenbutatin-oxide	9.3	460	-
Hexythiazox	0.18	-	> 50

(*) : Saitama Shiraoka strain
(**) : A : Wakayama Kokawa-cho strain
B : Saga Taira-cho strain

Insecticidal activity

NC-129 has specific insecticidal activity, including high activity against some species of hemipterous and thysanopterous insects.

NC-129 shows excellent activity against all developing stages of *Trialeurodes vaporariorum* and is more active than methidathion (Figure 4).

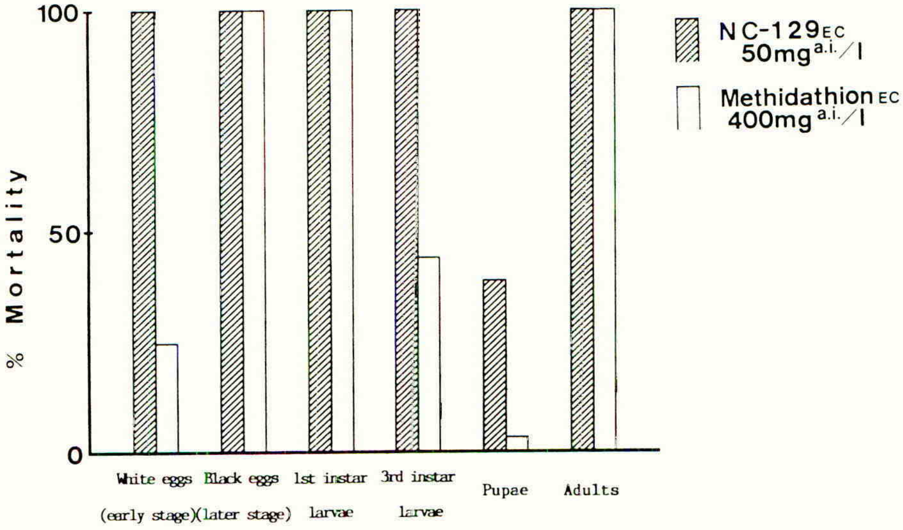


Figure 4 Activity against different stages of *T. vaporariorum*, using leaf-disc sprays

NC-129 is less active against lepidopterous, coleopterous and dipterous insects. It is supposed that the impact of NC-129 on beneficial insects and natural enemies is minimal in fields.

FIELD EVALUATION

NC-129 is being evaluated in many areas and many crops such as citrus, top fruit, grape, vegetables, cotton, tea and ornamentals.

Acaricidal activities

NC-129 gave excellent control of the following mites: *Polyphagotarsonemus latus*, *Steneotarsonemus pallidus*, *Tarsonemus pallidus*, *Lorryia* sp., *Brevipalpus phoenicis*, *Eotetranychus kankitus*, *E. pomi*, *E. carpini*, *Oligonychus coffeae*, *Panonychus citri*, *P. ulmi*, *Schizotetranychus* sp., *Tetranychus cinnabarinus*, *T. kanzawai*, *T. pacificus*, *T. urticae*, *Aculops pelekassi*, *A. schlechtendali*, *Phyllocoptruta oleivora*, *Rhizoglyphus echinopus*

Table 5 exemplifies the good control of *P. citri* on citrus. In this trial, NC-129 gave rapid action and long residual activity at a dose of 67 mg a.i./l.

TABLE 5

Control of *P. citri* on citrus in Wakayama Prefecture, Japan, after treatment on 4 July, 1986.

Compound	Conc. (mg a.i./l)	Number of adult females/100 leaves				
		Pre-spray	3 DAT	10 DAT	20 DAT	30 DAT
NC-129	67	468	0	0	39	39
Hexythiazox	33	135	15	37	216	1
Untreated	-	135	239	895	2,908	171

Insecticidal activities

NC-129 showed good efficacy against the following insects: Hemiptera; *Arboridia apicalis*, *Empoasca onukii*, *Trialeurodes vaporariorum*; *Aphis gossypii*; Thysanoptera; *Scirtothrips dorsalis*, *Thrips palmi*

NC-129 gave good control of *T. vaporariorum* in Japan (Figure 5).

CONCLUSIONS

NC-129 has excellent acaricidal activity against a wide range of phytophagous species.

NC-129 has good activity on all developing stages of mites.

NC-129 has rapid knockdown activity and long residual activity.

NC-129 has relatively stable activity at various temperature conditions.

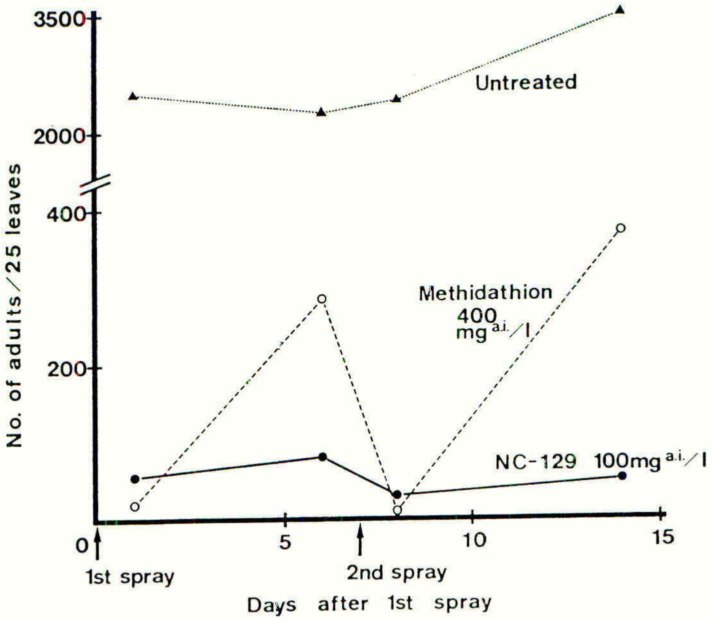


Figure 5 Control of *T. vaporariorum* on tomato in glasshouse test.

It is considered that NC-129 will be used in different conditions and in many countries.

NC-129 is very effective against acaricide-resistant mites because of its novel chemical structure and mode of action. Considering the development of resistance in many countries, NC-129 will be a very promising acaricide in these countries.

NC-129 is specifically effective against some hemipterous and thysanopterous insects.

NC-129 is less effective against lepidopterous, coleopterous and dipterous insects.

It is expected that effects of NC-129 on non-target invertebrates will be relatively slight.

REFERENCES

Kobayashi, M.; Nonoshita, K. (1988) Development of hexythiazox resistance in *Panonychus citri* in citrus glasshouse. *The 13th Annual Meeting of Pesticide Science Society of Japan Abstract*, 74

M 14360, A NEW BROAD-SPECTRUM AND VERSATILE ANTIFUNGAL TRIAZOLE

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ABSTRACT

M 14360, (±)-2-(2,4-dichlorophenyl)-3-(1*H*-1,2,4-triazol-1-yl)-propyl 1,1,2,2-tetrafluoroethyl ether, is a new systemic compound characterised by a broad spectrum of antifungal activity and low risk of phytotoxicity in all crops of agricultural interest. The excellent performance of curative and protective foliar treatments made it possible to control *Erysiphe* spp, at exceptionally low dosages as well as a number of diseases such as *Puccinia* spp, *Podosphaera* spp, *Venturia* spp, *Unicinula* spp, and *Cercospora* spp. Greenhouse fungicidal activity data and biological properties in disease control are presented and discussed. Field results confirm and extend the efficacy of disease control observed in the greenhouse.

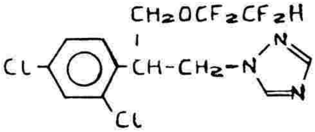
INTRODUCTION

M 14360 is a new, broad-spectrum, triazole fungicide synthesized at the Agrimont Research Centre and patented by Montedison in several countries.

CHEMICAL AND PHYSICAL PROPERTIES

Chemical Name : (±)-2-(2,4-dichlorophenyl)-3-(1*H*-1,2,4-triazol-1-yl)propyl 1,1,2,2-tetrafluoroethyl ether

Structural formula :



Molecular formula : $C_{13}H_{11}F_4Cl_2N_3O$
Molecular weight : 372.1
Common Name : none given yet
Appearance : viscous colourless oil
Vapour pressure at 20°C : 1.2×10^{-5} mmHg
Solubility at 20°C : in water = 150 mg/l; readily soluble in dichloromethane, acetone, methanol
Partition Coefficient : log P = 3.1; between octan-1-ol and water, pH 7
Hydrolytic stability : stable in dilute aqueous solutions at pH 5 to 9
Photostability : stable under sunlight

TOXOLOGY

Acute oral, LD50 : rat, 1150 mg/kg
Mutagenicity, Ames test with & without activation : negative
Subchronic toxicity : 90-day feeding study on rats underway

BIOLOGICAL PROPERTIES

In vitro antifungal activity

M 14360 shows a broad spectrum of fungicidal activity by inhibiting the mycelium growth of a number of Ascomycetes, Basidiomycetes, and Deuterumycetes (Table 1). In order to induce effects that are quantitatively similar to those observed with reference triazoles (penconazole, propiconazole), higher concentrations are needed. However in greenhouse tests M 14360 was consistently more effective against obligate parasites than most standard compounds.

TABLE 1

In vitro fungicidal activity of M 14360 expressed as the concentration producing 50% inhibition of mycelial growth (EC50 value).

Fungus	EC50 (mg/l)
Botrytis cinerea	2.4
Cercospora beticola	0.1
Cladosporium cucumerinum	0.07
Cochliobolus heterostrophus	0.25
Cochliobolus sativus	2.5
Fusarium moniliforme	1.5
Fusarium roseum	5.0
Guignardia bidwellii	0.05
Leptophaeria nodorum	0.13
Pseudocercosporella herpotrichoides	0.35
Pyrenophora graminea	0.9
Pyrenophora teres	0.27
Pyricularia oryzae	1.5
Rhizoctonia solani	3.5
Sclerotium cepivorum	0.2

Disease control under greenhouse conditions

M 14360 has shown strong residual protective and curative action against a broad spectrum of fungal pathogens on all plants tested. On cereals, it controlled Erysiphe graminis at exceptionally low concentrations. Comparison with some of the most effective triazoles, as reported in Table 2, shows the new compound to be the most effective. It effectively control Puccinia graminis at concentrations lower than, or at the most comparable with, those of the best known standards (triadimefon, propiconazole). When applied to leaves of fruit and vegetable crops, in both preventive and curative applications, M 14360 controls various diseases completely. The effective concentrations giving 90% control (EC90 values) are shown in Table 3 for Venturia inaequalis on apples and Sphaerotheca fuliginea on cucumbers. The doses needed to control these pathogens make M 14360 competitive also with those triazoles that are specifically used against fruit and vegetable crop diseases.

Vapour-phase activity was clearly detected when untreated wheat and cucumber plants were infected with P. graminis and S. fuliginea, respectively, and kept in the same plastic bags together with treated plants of wheat for 48 hours (Table 4).

TABLE 2

Action against *E. graminis* on wheat in the greenhouse. Comparative values of residual protective and curative activity of M 14360 and known triazoles, expressed as EC90(mg/l).

Treatment	Residual	protective		Curative
	treated leaves		untreated leaves	inoculated leaves
	1 day*	5 days*	5 days*	1 day**
M 14360	0.22	0.37	1.7	0.064
Penconazole	1.3	20	25	0.094
Propiconazole	4.8	30	30	0.18
Triadimefon	5.4	50	-	0.45
Flusilazol	1.5	17	21	0.09
Flutriafol	5.2	18	18	0.18
Hexaconazole	16.5	64	80	0.25

Interval: * from treatment to inoculation
** from inoculation to treatment.

TABLE 3

Residual protective (P) and curative (C) activity against various diseases in the greenhouse, expressed as EC90 (mg/l)

Treatment	*P. graminis* (wheat)		*V. inaequalis* (apple)		*S. fuliginea* (cucumber)
	P	C	P	C	P
	1 day	1 day	1 day	4 days	1 day
M 14360	70	6	22	40	0.04
Propiconazole	125	17	-	-	1.35
Penconazole	-	-	70	90	0.07
Triadimefon	50	40	-	-	2.80

TABLE 4

Vapour phase activity assessed as the dosage (mg/l) on treated plants giving some disease control on untreated plants (EC90 value)

Treatment	*S. fuliginea* (cucumber)	*P. graminis* (wheat)
M 14360	19	200
Penconazole	68	-
Propiconazole	420	> 500
Triadimefon	190	> 500
Flutriafol	70	320
Flusilazol	320	> 500
Hexaconazole	40	125

Effects on plant physiology

M 14360 was found to be highly compatible with all treated crops in the sense that its use did not lead to any undesirable effect. This aspect was further investigated by applying M 14360 on leaves or roots of peas and beans at rates substantially higher than those usually needed to achieve complete disease control. Very weak growth-retarding effects, fully reversible by application of gibberellic acid, were observed. An example is shown in Table 5 for peas that were treated by soil drench and grown at 20°C under a 16-hour photoperiod. Fungicides and GA were supplied as aqueous solutions during imbibition of pea seeds sown in sand (50 ml solution in 200 ml sand).

TABLE 5

Effects of some triazole fungicides and gibberellic acid (GA_3) at $5x10^{-5}$ on epicotyl length (mm) of two pea cultivars.

Treatment	Concn	Relative length of pea epicotyl			
		cv Alaska		cv Ronda	
	$x10^{-5}$ M	0	GA_3	0	GA_3
Control		100	198	100	342
M 14360	1	95	191	104	352
M 14360	5	83	173	85	349
Penconazole	1	46	169	88	340
Penconazole	5	30	125	46	311
Propiconazole	1	40	127	45	272
Propiconazole	5	25	71	26	105

SE = ± 5% for samples without GA_3 and S ± 10% for GA_3 treated samples;
values are means of ten measurements;
the length of controls after 12 days was 136 mm for cv Alaska and 80 mm for cv Ronda.

FIELD TRIALS RESULTS

Because of its versatility, the new compound has been tested on a large number of crops and diseases. All trials have been carried out by foliar applications according to the guidelines recognised in the various countries. The results represent the overall performance as obtained during 1986 (preliminary) and, more extensively, during 1987.

Cereals

M 14360 was tested on barley and wheat to control the major and some minor diseases. On powdery mildews single applications of 75 - 125 g a.i./ha gave very good control. The performance was in any case better than that of the standard propiconazole at 125 g a.i./ha (Table 6). The effectiveness of M 14360 extended over a period of 6 weeks or more after spraying. However, in order to adequately control a late epidemic, a second application may be useful. Excellent control of rusts, especially brown rust (Puccinia recondita), was also obtained as shown in Table 7. Against other diseases, such as Septoria spp. and Rhynchosporium secalis, M 14360 at 75 125 g a.i./ha gave better control than the standard, propiconazole + carbendazim (125 + 150 g a.i./ha).

TABLE 6

Control of *Erysiphe graminis* on barley and wheat, 1986-1987

Treatment	Dose (g a.i./ha)	Mean % disease control					
		Barley			Winter Wheat		
M14360	75 or 84*	91.5	79.8	89.8*	87.3*	94.4*	56.4
M14360	100	90.1	82.5	-	-	-	80.4
M14360	125	90.6	86.6	90.5	86.4	98.3	-
Propiconazole	125	86.5	55.5	80.0	74.6	91.5	42.5
Number of applications		1	1	1	2	1	1
Title of application		Ie	Se	T	T,A	Ie	Ie
Number of trials		3	8	1	2	7	2
Country		UK	UK	AUS	France	Italy	UK

Ie = inflorescence emerged; Se = stem elongation;
T = tillering; A = anthesis
AUS = Australia

TABLE 7

Control of *Puccinia spp*. on wheat and barley, 1987

Treatment	Dose (g a.i./ha)	Mean % disease control					
		Puccinia recondita			*Puccinia striiformis*		*Puccinia hordei*
M 14360	75 or 84*	97*	85*	97.3	74.1	97.3*	76.2
M 14360	125	97	88.7	98	84.6	97.1	86.2
Propiconazole	125	60.5	56.6	67.7	82.4	96.8	82.6
Number of trials		4	4	1	4	3	7
Country		France	Italy	UK	UK	Italy	UK

Apples

M 14360, at 2-4 g/hl using calendar schedules, gave very good to excellent control of powdery mildew (*Podosphaera leucotricha*), and apple scab (*Venturia inaegalis*) as shown in Tables 8 and 9, respectively. Its long-lasting effect allowed good control of apple scab at 4 g/hl by adopting a 10 and 14 day schedule. Under these conditions M 14360 performed comparably or better than the standard triazoles applied according to a 7 and 10 day schedule. A curative trial showed an outstanding performance of M 14360 as an eradicant by applicants delayed up to 6 days after artificial infection (Table 10).

TABLE 8

Control of *Podosphaera leucotricha* on apple leaves (sprays at 14 day intervals, 1987

Treatment	Dose (g a.i./hl)	Mean % disease control		
M 14360	2	97.7	-	-
M 14360	3	-	96.9	92.5
M 14360	4	99.8	-	-
Penconazole	2	89.2	-	-
Penconazole	3	-		84.8
Penconazole	4	96.2	95.4	-
Triadimefon	2.5	60.1	-	-
Triadimefon	4	-	89.7	-
Triadimefon	5	-	-	56.3
Number of trials		2	1	2
Country		Italy	Italy	France

TABLE 9

Control of *Venturia inaequalis* on apple fruits (F) and leaves (L), 1987.

Treatment	Dose (g a.i./h)	Mean % disease control					
		7&10 days*		10&14 days**		14 days	
		F	L	F	L	F	L
M 14360	2	95.1	84.5	82.2	71.7	93.5	79.2
M 14360	4	96.8	97.3	91.3	92.5	97.8	88.4
Penconazole	4	89.8	93.8	-	-	-	-
Bitertanol	18.75	80.1	66.2	-	-	-	-
Penconazole + captan	2.5+47.5	-	-	-	-	93.5	83.0
Number of trials		1	4	1	4	1	1
Country		Italy	Italy	Italy	Italy	Spain	Spain

* days up to fruit-setting, then 10 days

** 10 days up to fruit-setting, then 14 days

Sugar beet

Cercospora beticola was controlled by two or three applications of M 14360 at 100 g a.i./ha, with results superior to all commercial standards tested as references (Table 11). When applied in mixture with fentin hydroxide (TPTH: 160 g a.i./ha) the dose of M 14360 could be reduced to 40 or 50 g a.i./ha, giving a substantial increase of sugar production over untreated controls in all cases. Excellent control of other diseases was also obtained in applications at 100 g a.i./ha, especially for *Uromyces* and *Erysiphe* spp. (Table 12).

TABLE 10

Control of *Venturia inaequalis* by curative applications at different times after artificial inoculation by conidia, Italy, 1987.

Treatment	Dose (g a.i./ha)	Mean % disease control 72 h	148 h	200 h
M 14360	4	100	93	50
Bitertanol	25	-	12	0

Vegetables

Control of *Leveillula taurica* was excellent (1.5-2.5 g/hl) on artichoke and much higher on pepper and tomato, at 2-4 g/hl, than that shown by penconazole. Control of *Puccinia asparagi*, at 5 g/hl, was better than that obtained by chlorothalonil at 122 g/hl.

TABLE 11

Control of *Cercospora beticola* on beet in Italy and Germany, 1986-1987

Treatment	Dose (g a.i./ha)	Mean % disease control			Relative % sugar production	
M 14360	100	79.9	73.1	93.9**	114.5	-
M 14360+TPTH	50+150	-	72.6	-	116.4	123.5*
Propiconazole	100	37.4	-	-	-	-
Propiconazole +TPTH	125+150	-	-	-	-	113.5
Propiconazole +TPTH	150+216	-	49.1	-	109.4	-
TPTH	300					111.3
Maneb+TPTH	80+270	-	-	88.3***	-	-
Number of trials		3	3	1	3	30
Country		Italy	Italy	Germany	Italy	Italy

* 40+150 g a.i./ha, ** 2 applications, *** 3 applications

Grapes and other crops

M 14360 gave substantially complete control, at 1.5 g/hl, of *Uncinula necator* on grapes (bunches) when applied according to a 14-day schedule in Italy, France and Spain (Table 13). Preliminary indications of activity against *Guignardia bidwellii* need to be confirmed. Good-to-excellent control of *Sphaerotheca pannosa* was achieved on peach, at 2-4 g/hl with a 14 day spraying schedule, and on rose at 1.5-5 g/hl with a 14 day spraying schedule (Table 13). Against gladiolus rust, *Uromyces transversalis*, M 14360 showed good activity at 8-10 g/hl.

TABLE 12

Control of other diseases of beet in various countries, 1987

Treatment	Dose (g a.i./ha)	Mean % disease control Ramularia betae	 Uromyces betae	 Erysiphe betae
M 14360	100	86.7*	94.3	98.6
Maneb+TPTH	80+270	80**	-	-
Triadimefon	250	-	45.3	30.7
Number of trials		1	2	3
Country		Germany	France	Italy, France

* 2 applications, ** 3 applications

TABLE 13

Control of powdery mildew on leaves (L) and fruits (F) of peach, on rose, and on bunches of grapes in various countries, 1987

Treatment	Dose (g a.i./hl)	Mean % disease control Sphaerotheca pannosa peach L	 F	 rose		 Uncinula necator grapes (bunches)
M 14360	1.5	-	-	-	-	99.2
M 14360	2	97.9	99.5	-	-	-
M 14360	2.5	-	-	98.4	87.4	99.4
M 14360	4	99.8	100	-	-	-
M 14360	5	-	-	99.5	91.9	-
Penconazole	2	98.6	95.1	-	-	-
Penconazole	2.5			89.4	33.8	99.4
Penconazole	4	98.7	99.8	-	-	-
Penconazole	5	-	-	97.7	-	-
Number of trials		1	1	2	1	9
Country		Italy	Italy	Italy	Spain	Italy, France, Spain

ACKNOWLEDGEMENTS

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4"-DEOXY-4"-METHYLAMINO-4"-EPIAVERMECTIN B1 HYDROCHLORIDE (MK-243): A NOVEL AVERMECTIN INSECTICIDE FOR CROP PROTECTION

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ABSTRACT

Abamectin, a macrocyclic lactone produced by fermentation of the soil microorganism Streptomyces avermitilis, is currently being developed for control of phytophagous mites and certain insect species on horticultural and agronomic crops. 4"-Deoxy-4"-methylamino-4"-epiavermectin B1 hydrochloride (MK-243), a novel semi-synthetic avermectin derivative, has recently been discovered through chemical modification of abamectin. It has shown high potency against a broad range of economically important lepidopterous larvae, including armyworm species, which have low susceptibility to abamectin. In foliar residue bioassays, LC90 values of 0.002- 0.014 mg a.i./l were obtained with MK-243 against a spectrum of lepidopterous pests. Field trials with MK-243 on vegetables and corn have shown excellent control of larval insect populations and reduction in crop damage at doses of 5.6-22.4 g a.i./ha. MK-243, because of its unique chemistry, mode of action, and pest spectrum, has high potential for applications in crop protection for control of Lepidoptera.

INTRODUCTION

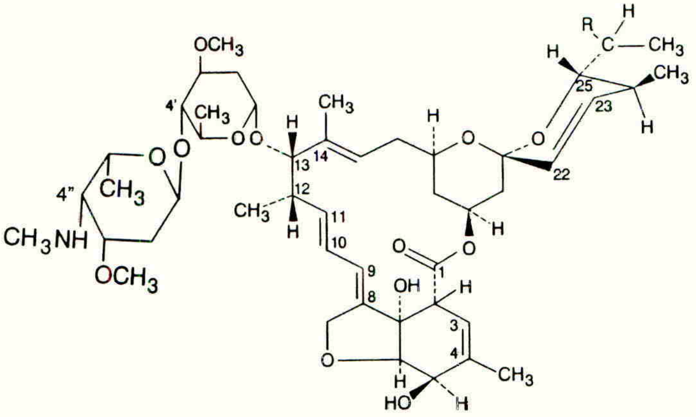
The avermectin family of macrocyclic lactones, fermentation products of the soil microorganism Streptomyces avermitilis, were discovered in the mid-1970's. The major component abamectin (MK-936, avermectin B1) is currently under development worldwide for control of phytophagous mites and certain insect species on horticultural and agronomic crops (Dybas and Green, 1984). Abamectin has a unique mode of action in arthropods. It acts on the chloride ion channel where it functions as an agonist of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) to increase chloride ion entry into the post-synaptic region of GABAergic cells (Mellin *et al*., 1983). Because of its novel mechanism of action, abamectin has been shown to control pests which have become resistant to conventional acaricides and insecticides (Hoy and Conley, 1987; Roush and Wright, 1986).

Abamectin is a potent broad spectrum acaricide but shows high innate toxicity only against specific insect species. Research into avermectin chemistry has led to the discovery of 4"-deoxy-4"-methylamino-4"-epiavermectin B1 hydrochloride with particularly high toxicity against Spodoptera eridania (Mrozik *et al*. 1988). This novel avermectin derivative, code named MK-243, has also shown similar potency against a broad range of economically important lepidopterous larvae, including armyworms, which are difficult to control effectively with abamectin and currently available insecticides (Dybas _et al_., 1988). This paper reports the technical properties of MK-243 and the biological activity of the compound against lepidopterous pests in the laboratory and in replicated field plots on vegetables and sweet corn.

TECHNICAL DATA

Chemical and Physical Properties

Code Number: MK-243
Chemical Name: A mixture containing a minimum of 80% 4"-deoxy-4"-methylamino-4"-epiavermectin B1a hydrochloride and a maximum of 20% 4"-deoxy-4"-methylamino-4"-epiavermectin B1b hydrochloride



a-Component R = $C_2H_5 \geq$ 80%
b-Component R = CH_3 $\leq$ 20%

Molecular Formula: $C_{49}H_{75}NO_{13}\cdot HCl$ B1a $C_{48}H_{73}NO_{13}\cdot HCl$ B1b

Molecular Weight: 922.55 B1a 908.53 B1b
Appearance: White crystaline powder
Melting Point: 167°C
Formulation: 18 EC (18 g a.i./liter)

Mammalian Toxicity

Acute oral LD50: Rat 75 mg a.i./kg
Rat 3,450 mg formulation/kg
Acute dermal LD50: Rabbit > 1,500 mg a.i./kg
Rabbit > 2,000 mg formulation/kg
Irritation: moderate eye and skin irritant
Mutagenicity: Negative in Ames Assay

Aquatic Toxicity

96 h LC50: Bluegill sunfish 240 ug a.i./l
Rainbow trout 670 ug a.i./l
48 h LC50: _Daphnia magna_ 2.9 ug a.i./l

Biological Activity

MK-243 is a novel semi-synthetic macrocyclic lactone insecticide derived from the avermectin family of natural products which has demonstrated high activity against a broad range of lepidopterous larvae. MK-243 acts through ingestion and topical action but ingestion is the most effective route of lethal dose accumulation. The onset of action by MK-243 in insects is rapid. Within a few hours of exposure, larvae become irreversibly paralyzed and stop feeding. Affected larvae usually die within 48-72 h of exposure. Plant damage is minimal since feeding ceases soon after larvae ingest the chemical. MK-243 is non-ovicidal but larvae hatching from treated eggs die shortly after eclosion. MK-243 is non-systemic; however, it penetrates plant cuticle effectively and consequently shows long residual action in target crops.

PERFORMANCE

Laboratory Evaluation

Foliar ingestion and topical application bioassays were conducted with MK-243, abamectin, and standard carbamate and pyrethroid insecticides against a range of economically important insect pests. The LC90 values for MK-243 to *Heliothis zea*, *Heliothis virescens*, and *Spodoptera eridania* first instar larvae are shown in Table 1.

TABLE 1

Comparative foliar ingestion toxicity of MK-243 to *Heliothis virescens* (H.v.), *H. zea* (H.z.) and *Spodoptera eridania* (S.e.) larvae.

	LC90 (mg a.i./l) at 96 h		
Compound	H.v.	H.z.	S.e.
MK-243	0.003	0.002	0.005
Abamectin	0.128	0.21	5.83
Methomyl	10.0	8.1	8.6
Thiodicarb	5.0	6.6	4.42
Cypermethrin	--	0.41	--
Fenvalerate	1.5	--	1.34

MK-243 is highly toxic to the three noctuid species by ingestion, with LC90 values of 0.002-0.005 mg a.i./l. It was found to be 1,166-fold more potent than abamectin against *S. eridania* at the LC90 level, thus exhibiting a significant improvement over the parent molecule in intrinsic activity. Similarly, MK-243 was also more toxic to *S. eridania* larvae than the standard carbamate or pyrethroid insecticides, being 1,720-, 884-, and 268-times more potent than methomyl, thiodicarb, and fenvalerate, respectively. In addition, MK-243 was 105- and 43-fold more toxic to *H. zea* and *H. virescens* larvae compared to abamectin at the LC90 level.

The activity of MK-243 has also been determined against spider mites and insects of several Orders including Coleoptera, Homoptera and other Lepidoptera. The LC90 values are presented in Table 2.

The high susceptibility of lepidopterous larvae to MK-243 was further demonstrated in foliar bioassays with Manduca sexta, Trichoplusia ni, S. exigua and S. frugiperda where LC90 values of 0.003, 0.014, 0.005 and 0.01 mg a.i./l were obtained. MK-243 was also toxic to the two coleopterous species, Leptinotarsa decemlineata and Epilachna varivestis, and the spider mite, Tetranychus urticae, included in the foliar assay. The homopterous insect, Aphis fabae, was the least susceptible among the insects tested and MK-243 was considerably less toxic than abamectin to aphids (Dybas and Green, 1984).

TABLE 2.

Foliar ingestion activity of MK-243 against insect larvae and adult spider mites and aphids.

Species (common name)	LC90 (mg a.i./l) at 96 h
Manduca sexta (L.) (tobacco hornworm)	0.003
Trichoplusia ni (Huebner) (cabbage looper)	0.014
Spodoptera exigua (Huebner) (beet armyworm)	0.005
Spodoptera frugiperda (J. E. Smith) (fall armyworm)	0.01
Leptinotarsa decemlineata (Say) (Colorado potato beetle)	0.032
Epilachna varivestis Mulsant (Mexican bean beetle)	0.20
Tetranychus urticae Koch (twospotted spider mite)	0.29
Aphis fabae Scopoli (bean aphid)	19.9

FIELD EVALUATION

The performance of MK-243 against lepidopterous insects was evaluated in a series of field trials on vegetables such as broccoli, cabbage and lettuce; and sweet corn.

In these trials, an 18 g a.i./l EC formulation of MK-243 was used at application rates ranging from 5.6-22.4 g a.i./ha. Criteria such as a reduction in feeding damage, percent increase in marketable blemish-free crop and reduction in larval numbers were evaluated.

Broccoli

In a season-long study in California against beet armyworm (S. exigua) and cabbage looper (T. ni), four applications were made at approximately weekly intervals. Plots were sampled for larvae seven days after the first spray application (7 DAT1) and at regular intervals following the subsequent treatments. S. exigua and T. ni populations were initially low, but increased rapidly, and were quite large following the third and fourth spray treatments.

Plant injury due to insect larval feeding was assessed 5 days after the fourth treatment (5 DAT4) and also at 14 days (14 DAT4) to measure the residual activity of MK-243. Excellent control of *S. exigua* was obtained at all three doses of MK-243; however, most effective control of *T. ni* was obtained with 11.2 and 22.4 g MK-243/ha (Table 3). Significant reduction in feeding damage was observed with 11.2 and 22.4 g a.i./ha rates at both 5 DAT4 and 14 DAT4; however, the lowest dose (5.6 g a.i./ha) was less persistent and provided effective protection from feeding damage only at 5 DAT4 (Table 3).

TABLE 3

Control of *Spodoptera exigua* on and *Trichoplusia ni* on broccoli

Compound	Dose (g a.i./ha)	Seasonal mean number of larvae per plant S. exigua	Seasonal mean number of larvae per plant T. ni	Percent Damaged Plants 5 DAT4	Percent Damaged Plants 14 DAT4
MK-243	5.6	6.23b	8.05b	8.3	32.5
MK-243	11.2	1.15c	3.60c	1.8	12.5
MK-243	22.4	0.54c	0.88c	1.3	3.5
Permethrin	224.0	8.68ab	5.03bc	4.8	10.5
Untreated	--	33.05a	17.15a	48.8	61.3

*Data analyzed after log transformation. Figures in a column followed by the same letter are not significantly different using a 5% LSD test.

Cabbage

Season-long field trials were conducted in California, Florida, North Carolina, and Texas to evaluate performance against populations of cabbage looper (*T. ni*), diamondback moth (*Plutella xylostella*), imported cabbage worm (*Pieris rapae*) and cabbage webworm (*Hellula rogatalis*). In a trial in Texas, 6 applications were made during the season against a mixed population of *T. ni* and *P. xylostella*. Larval counts were taken at 5-7 day intervals after each application. At 5 days after the last treatment, the marketability of the cabbage heads was evaluated. At all doses (5.6, 11.2 and 22.4 g a.i./ha), MK-243 provided effective control of larval populations and resulted in a high percentage of marketable cabbage heads at harvest (Table 4).

TABLE 4

Control of *Plutella xylostella* and *Trichoplusia ni* on cabbage

Compound	Dose (g a.i./ha)	Seasonal mean larvae/5 plants	Percent Marketable Heads
MK-243	5.6	4.8bc	74b**
MK-243	11.2	3.5bc	88ab
MK-243	22.4	2.7c	98a
Methomyl	560.0	9.3a	37c
Permethrin	112.0	5.5b	84ab
Methomyl + Permethrin	560.0+ 112.0	4.4bc	89ab
Untreated	--	8.7a	15c

**Data analyzed after arcsin transformation. Figures in a column followed by the same letter are not significantly different ($P > 0.05$) (Duncan's New Multiple Range Test).

MK-243 was evaluated in a season-long trial in Florida where 9 weekly applications were applied under *P. xylostella*, *H. rogatalis* and *T. ni* pressure. Feeding damage and percent marketable heads were assessed 8 days after the last treatment (8 DAT9). At all doses, MK-243 effectively controlled larval populations of all 3 lepidopterous pests and reduced foliar feeding significantly, resulting in 95-100% marketable cabbage at harvest (Table 5).

TABLE 5

Control of *Plutella xylostella* (P.x.) and *Hellula rogatalis* (H.r.) and *Tricloplusia ni* (T.n.) on cabbage

Compound	Dose g a.i./ha	Seasonal mean number of larvae per 10 plants			Percent Marketable Heads 8 DAT9
		P.x.	H.r.	T.n.	
MK-243	8.4	0.17	0.0	0.13	95
MK-243	11.2	0.10	0.0	0.03	100
MK-243	16.8	0.03	0.0	0.07	100
Methomyl	504.00	6.03	0.13	0.10	2
Methomyl	1008.0	2.03	0.0	0.03	28
Permethrin	112.0	5.97	0.22	0.13	0
Methomyl+ Permethrin	504.0+ 112.0	2.50	0.0	0.0	18
Dipel	560.0	5.38	1.35	0.40	22
Untreated	--	8.67	5.55	2.38	0

*Rated from 0 = no feeding injury to 10 = all foliage consumed

**Marketability determined by absence of feeding damage on the tight wrapper leaves of the head.

Lettuce

Four applications of MK-243 at 5.6, 11.2 and 22.4 g a.i./ha were made at 5 to 9 day intervals against cabbage looper (*T. ni*) populations on lettuce in California. Populations of *T. ni* were large throughout the trial, resulting in nearly 90% foliar feeding damage in the untreated control at harvest. All doses of MK-243 significantly reduced larval numbers at each evaluation date, and plant feeding damage at harvest (Table 6).

TABLE 6

Control of *Trichoplusia ni* on lettuce

Compound	Dose (g a.i./ha)	Mean number of larvae per plot				Percent Feeding Damage*
		8 DAT1	4 DAT2	6 DAT3	6 DAT4	
MK-243	5.6	5.5a	7.5b	3.75b	3.75b	31.25bc**
MK-243	11.2	2.25a	0.75b	0.0b	2.5b	27.5bc
MK-243	22.4	1.5b	0.0b	0.0b	0.0b	17.5c
Methomyl	1008.0	2.25b	0.75b	3.75b	8.75b	35.0b
Untreated	--	14.25a	39.00a	70.00a	100.00a	88.75a

* Mean percent plants with feeding damage at harvest.
** Means in a column followed by the same letters are not significantly different ($P > 0.05$; Duncan's New Multiple Range Test).

Corn

In a season-long trial in Florida, 8 applications of MK-243 at doses of 5.6 and 11.2 g a.i./ha were made to sweet corn at 2-3 day intervals during the silking period against populations of *H. zea*. The 11.2 g a.i./ha dose of MK-243 was the most effective treatment, resulting in a significant reduction in larval populations and an increase in percent marketable ears (Table 7).

TABLE 7

Control of *Heliothis zea* on sweet corn

Compound	Dose (g a.i./ha)	Larvae*/ 25 ears	% Reduction in larvae	% Marketable ears**
MK-243	5.6	4.6	41	35
MK-243	11.2	1.0	87	62
Permethrin	112.0	2.6	67	42
Methomyl	562.0	3.6	54	54
Untreated	--	7.8	--	6

*Consisting of mid and late instar larvae.
**Marketability: measured as total absence of feeding damage on the ears.

CONCLUSION

4"-Deoxy-4"-methylamino-4"-epiavermectin B1 hydrochloride (MK-243) represents a novel second generation avermectin derivative, with exceptional potency and breadth of spectrum against economically important Lepidoptera. Preliminary field trials have demonstrated excellent control of larval populations and reduction in plant feeding damage at doses of 5.6-22.4 g a.i./ha on vegetables and sweet corn. Because of its novel chemistry, mode of action and pest spectrum, MK-243 has high potential for applications in crop protection worldwide for control of lepidopterous pests.

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CGA 142705: A NOVEL FUNGICIDE FOR SEED TREATMENT

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ABSTRACT

CGA 142705 is being developed by CIBA-GEIGY as a fungicide for seed treatment. In cereals, at a rate of 20 g a.i./100 kg seed, it has given control of *Gerlachia nivalis* (*Fusarium nivale*), *Tilletia caries* and seed-borne *Septoria nodorum* which was equivalent to that achieved by the best current standard products. In combination with imazalil (20 g CGA 142705 plus 4 g imazalil per 100 kg seed) excellent control of *Pyrenophora graminea* and also seed-borne *Pyrenophora teres* in barley has been achieved. CGA 142705 also shows considerable promise as a seed treatment for non-cereals for the control of a broad spectrum of fungi among the Ascomycetes, Basidiomycetes and Deuteromycetes.

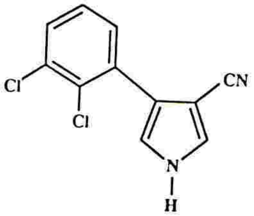
CGA 142705 is the first phenylpyrrole fungicide to be commercially developed. Strains of fungi resistant to products from other chemical classes (e.g. benzimidazoles) show no cross-resistance to CGA 142705. As a cereal seed treatment, this is particularly important for the control of MBC-resistant *G. nivalis*.

Crop tolerance of CGA 142705 is excellent, so that even under the most adverse conditions for emergence it neither reduced stand nor inhibited seedling development, when applied as described in this paper.

INTRODUCTION

A new broad spectrum fungicide with the code number CGA 142705 is being developed by CIBA-GEIGY as a seed treatment and will be marketed under the trade name "Beret"^{R}.

CHEMICAL AND PHYSICAL PROPERTIES

Chemical class:	Phenylpyrrole
Chemical name:	4-(2,3-dichlorophenyl)pyrrole-3-carbonitrile
Structural formula:	
Molecular formula:	$C_{11}H_6Cl_2N_2$
Molecular weight:	237.09
Appearance at 20°C:	colourless, odourless crystals
Melting point:	152.9°C
Solubility in water at 20°C:	2 ppm
Partition coefficient:	log P = 4.3 (n-octanol/water)
Thermal stability:	stable up to 250°C
Hydrolysis:	not hydrolysed after 6h at 100°C between pH 3 and 9

TOXICOLOGY

Acute Toxicity:	oral rat (LD 50)	> 5000 mg/kg
	oral mouse (LD 50)	> 5000 mg/kg
	oral rabbit (LD 50)	> 5000 mg/kg
	dermal rat (LD 50)	> 2000 mg/kg
	inhalation rat (4 h, LC 50)	> 1502 mg/m^3 (highest attainable concentration)
Skin and eye irritation:	non irritant (rabbit)	
Teratogenicity:	no teratogenic potential, no prenatal toxicity	
Mutagenicity:	no mutagenic potential	

FORMULATIONS

CGA 142705 will be available in three formulation-types: powder formulations for dry and wet seed treatment (DS and WS formulations respectively) as well as water-based flowable formulations (FS) either for direct application to seeds or for application after dilution with water. The active ingredient will be formulated alone as well as mixed with imazalil in a ratio of 5:1 by weight . This mixture gives a broader spectrum of activity than does CGA 142705 alone (see the next section for details).

BIOLOGICAL ACTIVITY

Control of common bunt (*Tilletia caries*) on winter wheat

The activity of CGA 142705 against *T. caries* has been evaluated in European field trials over the past four years. These trials were conducted with seed which had been artificially inoculated with 2-5 g *T. caries* spores per kg seed before seed treatment. There were a total of 16 trials, and in all these experiments CGA 142705 at an application rate of 20 g a.i./100 kg seed gave complete disease control. Standard products, which varied from country to country, were also fully effective (Table 1). In two trials in Switzerland 2 g CGA 142705 per 100 kg seed has also given greater than 99.8 % control of *T. caries*.

TABLE 1

Tests of CGA 142705 (20 g a.i./100 kg seed) for the control of *T. caries* on winter wheat

Standard *	Rate (g ai/ 100kg seed)	% incidence in untreated	Year of sowing	Country	No. of trials
Triadimenol, Fuberidazole, Imazalil	37.5, 4.5, 5	10.1 (8.5-11.0)	1985	Great Britain	3
Mercury	3	16.6 (7.9-25.5)	1985	France	2
Methfuroxam, Thiabendazole	30, 5	5.1 (2.0-8.2)	1985	Germany	4
Guazatine, Fenfuram, Imazalil	90, 30, 8	33.7	1985	Switzerland	1
Methfuroxam, Thiabendazole	30, 5	7.7 (4.4-17.9)	1986	Germany	5
Guazatine, Fenfuram, Imazalil	90, 30, 8	27.0	1986	Switzerland	1

* All standards and CGA 142705 gave complete control of *T. caries*.

In 15 trials sown in 1986, the combination of 20 g CGA 142705 plus 4 g imazalil per 100 kg seed has also proved to be fully effective against *T. caries* (Table 2).

TABLE 2

Tests of CGA 142705 plus imazalil (20 + 4 g a.i./100 kg seed) for the control of *T. caries*

Standard *	Rate (g ai/ 100kg seed)	% incidence in untreated	Country	No. of trials
Guazatine, Fenfuram, Imazalil	90, 60, 6	30.0 (1.2-66.1)	Denmark	4
Mercury	3	4.6 (3.3-5.9)	France	2
Methfuroxam, Thiabendazole	30, 5	7.7 (4.4-17.9)	Germany	5
Guazatine, Fenfuram, Imazalil	90, 30, 8	31.0 (22.0-49.6)	Switzerland	4

* All standards and CGA 142705 gave complete control of *T. caries.*

Control of *Septoria nodorum* on winter wheat

Field trials were sown in 1986 and 1987 to evaluate the efficacy of CGA 142705 in the control of seed-borne *S. nodorum.*

Highly infected seed lots were obtained from either naturally infected or artificially inoculated wheat crops. Artificial inoculation was achieved by spraying ears and flag leaves with a spore suspension during ear emergence. Seed infection levels were determined on malt agar after surface sterilisation of the grains and samples with about 50 % of seed infected by *S. nodorum* were selected. Seed samples with a high level of *Gerlachia nivalis* infection were rejected.

In 11 field trials in Switzerland, seed treatment with 20 g CGA 142705 per 100 kg seed gave stand increases similar to the mixture of 90 g guazatine plus 30 g fenfuram per 100 kg seed (Fig. 1). In a total of 8 field trials, the combination of 20 g CGA 142705 plus 4 g imazalil per 100 kg seed tended to give bigger stand increases than this standard product. This is shown in Fig. 2, where the majority of the data-points are above the line indicating the performance of the standard product.

In the laboratory or growth chamber, it can be demonstrated that 20 g CGA 142705 per 100 kg seed does not completely inhibit mycelial development of *S. nodorum.* Thus in fluorescence tests (Kietreiber 1981) CGA 142705 reduced seed infection by 50 % and in seed-tray tests (Holmes and Colhoun 1973) *S. nodorum* still caused coleoptile browning despite seed treatment with CGA 142705 (ca. 75 % efficacy). The mixture of CGA 142705 with imazalil (20 + 4 g a.i./100 kg seed) has given excellent control of *S. nodorum* both in fluorescence and seed-tray tests.

It can be concluded that under field conditions, CGA 142705 alone gives a high level of protection against plant population (stand) reductions caused by *S. nodorum* which is equivalent to current best standards. Performance in the laboratory may be improved by the addition of imazalil.

Fig. 1

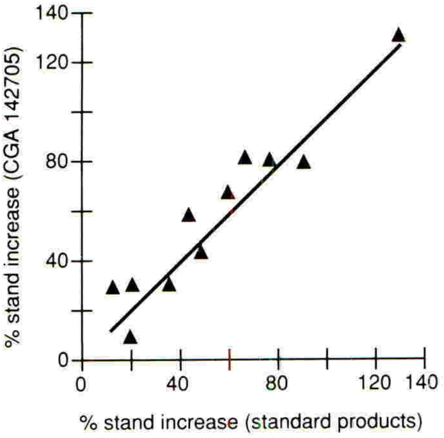
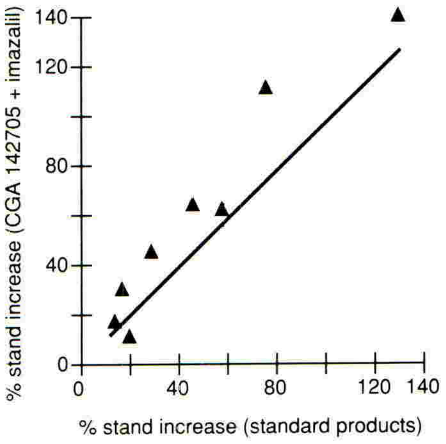


Fig. 2



Figs. 1 & 2: Stand increases at final emergence in CGA 142705 treatments (Fig. 1) or CGA 142705 + imazalil treatments (Fig. 2) plotted against stand increases in the guazatine + fenfuram standard treatments for field tests of *S. nodorum* activity. The solid line shows performance equivalent to the standard and therefore points lying above the line indicate improvement over the standard.

Control of snow mould (*Gerlachia nivalis*) on winter wheat

An extensive field trial programme has been conducted in Switzerland and Germany using heavily infested wheat seed. Infection had occurred either naturally or after ears were artificially inoculated during flowering. Seed infection was confirmed by standard agar-plate assays. In Germany, *G. nivalis* strains were resistant to MBC-fungicides.

In 19 field trials, 20 g CGA 142705 per 100 kg seed gave control of *G. nivalis* which was equivalent to or better than the best current market-product (90 g guazatine plus 30 g fenfuram per 100 kg seed in Switzerland or 60 + 20 g of these a.i.'s in Germany). Stands were assessed in both autumn (GS 11) and in spring (GS 13). The results of the spring evaluations for trials where stand increases exceeded 50 % are shown in Fig. 3. Stand increases of up to 1000 % in comparison to the untreated check were recorded and CGA 142705 gave higher stands than the standards at the highest disease levels (Fig. 3).

The activity of CGA 142705 against MBC-resistant *G. nivalis* has also been demonstrated in a series of growth chamber tests. In these tests, seeds with a high level of natural infection were sown in sterile soil in seed trays (3 x 100 seeds per test). Plants were allowed to emerge under cool conditions (5 - 8°C) and then covered with plastic sheeting to encourage *G. nivalis* development. Numbers of diseased seedlings were recorded up to 9 weeks after sowing.

The results of 3 such tests are shown in table 3. Benomyl gave only partial disease control, as would be expected against MBC-resistant strains of *G. nivalis*. CGA 142705 was extremely effective at a rate of 20 g a.i./100 kg seed. The combination of guazatine plus fenfuram (90+30 g a.i./100 kg seed) was clearly less effective than CGA 142705 in these tests.

TABLE 3

Percent wheat plants affected by *G. nivalis* in three growth chamber tests

Treatment	Rate (g a.i./ 100 kg seed)	Variety Caribo	Kanzler	Mission
CGA 142705	20	2.5	2.0	1.3
Guazatine + fenfuram	90+30	5.7	13.8	5.3
Benomyl	113	36.6	24.0	20.0
Untreated		60.0	31.3	30.0

The combination of 20 g CGA 142705 plus 4 g imazalil per 100 kg seed has also been extensively tested in field and growth chamber tests. Its efficacy was the same as that of CGA 142705 alone (20 g a.i./100 kg seed). The results of field tests are shown in Fig. 4.

Fig. 3

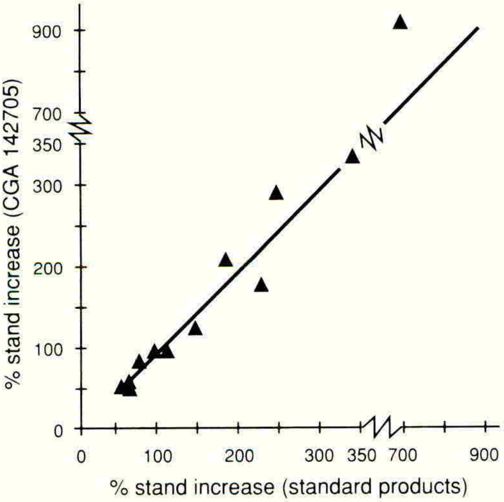
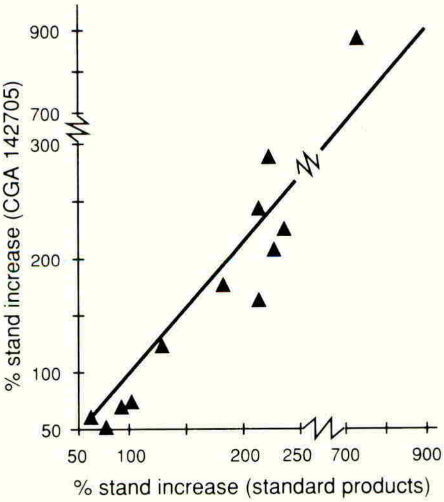


Fig. 4



Figs. 3 & 4: Stand increases in spring in CGA 142705 treatments (Fig. 3) or CGA 142705 + imazalil treatments (Fig. 4) plotted against stand increases in the standard treatments for field tests of *G. nivalis* activity. Standard treatments were 60 + 20 or 90 + 30 g/100 kg seed of guazatine + fenfuram. The solid line indicates performance equivalent to the standards.

Control of snow mould (*G. nivalis*) on rye

CGA 142705 has been tested for the control of seed-borne *G. nivalis* on rye in six field trials in Switzerland. These trials were conducted at high altitude sites (c. 800 m above sea level) where a long lasting snow cover could be guaranteed. Highly infected seed was sown. The percentage leaf area damaged by *G. nivalis* was visually estimated in spring, soon after snow had melted.

In the six trials, damage in untreated plots varied from 43 to 99 % (mean 71 %). In the CGA 142705 treated plots (20 g a.i./100 kg seed), damage ranged from 6.2 to 18 % (mean 10 %) and in the plots treated with a combination of guazatine and fenfuram (90 g and 30 g a.i./100 kg seed), disease severity was in the range 2.1 to 25 % (mean 10 %).

In can be concluded that 20 g CGA 142705/100 kg seed gives excellent control of snow mould on rye caused by *G. nivalis*, even under harsh environmental conditions.

Control of leaf stripe (*Pyrenophora graminea*) on barley

CGA 142705, when applied at a rate of 20 g a.i./100 kg seed provides good control of *P. graminea*. In a series of field trials conducted between 1985 and 1987 throughout Europe, efficacy varied between 80 % and 100 %. The activity of CGA 142705 alone (20 g a.i./100 kg seed) was usually inferior to that of the best commercial products which contain a mixture of active ingredients (Fig. 5). Increasing the rate of CGA 142705 did not increase efficacy, however, a mixture of CGA 142705 and imazalil (20+4 g a.i./100 kg seed respectively) has given excellent control of *P. graminea*. This combination has been tested in a series of 15 field trials in which disease incidence in the untreated plots varied from 1 to 20 %. Disease control by CGA 142705 plus imazalil was always similar to that achieved by the best commercial products (Fig. 6).

Fig. 5

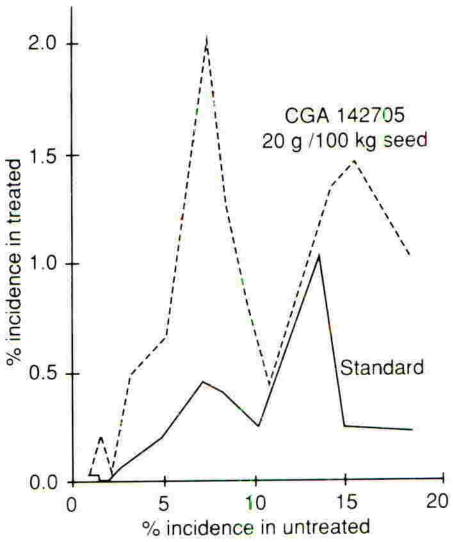
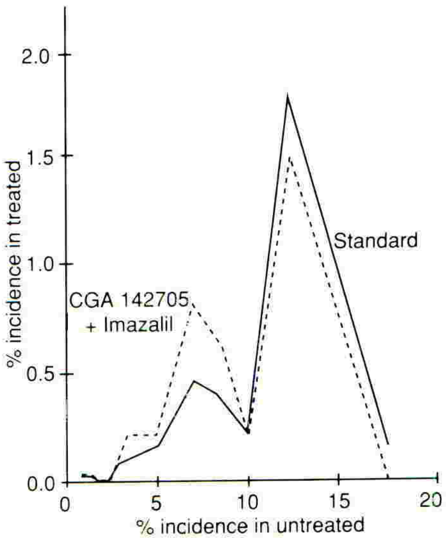


Fig. 6



Figs. 5 & 6: The incidence of leaf stripe symptoms in CGA 142705 treatments (fig. 5.) or CGA 142705 + imazalil treatments (Fig. 6) plotted against disease incidence in untreated plots for a series of 15 international field trials for each product. The solid lines indicate the performance of the standard products which varied between countries (see Table 1 for details).

Control of other seed-borne diseases of cereals

Field trials in Denmark and laboratory tests in Switzerland have shown that CGA 142705 (20 g a.i./100 kg seed) has an efficacy of 80-90 % against seed-borne *P. teres* (net blotch of barley). In combination with imazalil (20 g CGA 142705 plus 4 g imazalil per 100 kg seed), efficacy against this pathogen is consistently geater than 95 %. CGA 142705 (20 g/100 kg seed) was also active against covered smut (*Ustilago hordei*) on barley and in a series of field trials, efficacy varied between 75 and 95 %. CGA 142705 at the above mentioned rate has given complete control of flag smut (*Urocystis occulta*) on rye in Denmark and Sweden. On wheat, in a limited trial programme, CGA 142705 has also shown activity against seed-borne *Fusarium culmorum*.

Crop tolerance as a cereal seed treatment

CGA 142705 is well tolerated by wheat, barley and rye when applied at a rate of 20 g a.i./100 kg seed in FS, WS and DS formulations. The combination of 20 g fenpiconil plus 4 g imazalil per 100 kg seed is also well tolerated by these crops.

An advantage of seed treatment with CGA 142705 is that, even under cold conditions, it has not delayed seedling emergence or development. This is in contrast to many seed treatments containing a triazole. Such treatments may delay or reduce emergence under adverse weather or soil conditions (Frohberger 1978, Reinecke et al 1986) . The results of a growth chamber test are shown in Fig. 7. In this test, certified seed of the barley variety Gerbel was sown in sterilised soil and allowed to emerge at 10°C. Seed had been treated with the recommended dosage and also double the recommended dosage of CGA 142705 plus imazalil. These treatments were compared to the combination of triadimenol, fuberidazole and imazalil at both recommended (37.5 + 4.5 + 5.0 g a.i./100 kg seed) and double dosage rates. The CGA 142705 combination gave emergence rates which were very similar to untreated, whereas the triazole-containing mixture reduced emergence rate as well as final plant stand.

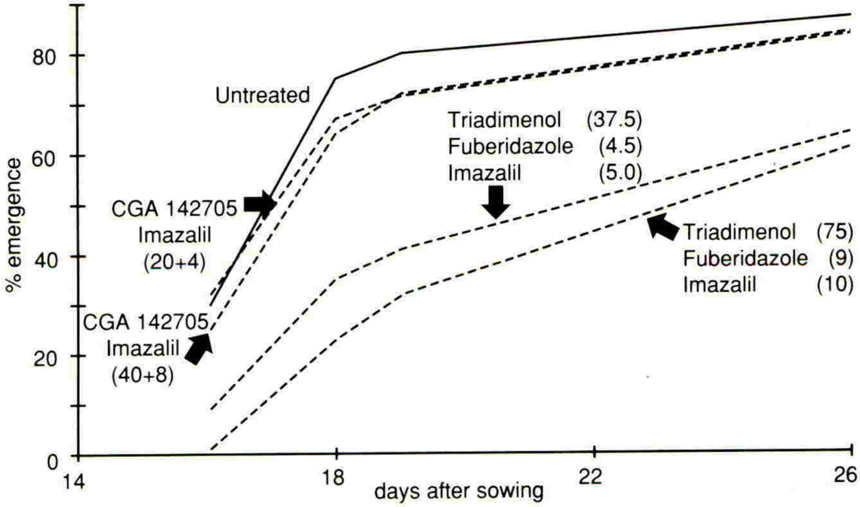


Fig. 7: Emergence of barley seed in a growth chamber test at 10°C. Rates of application of the a.i.'s are shown in brackets (g a.i./100 kg seed).

Control of seed- and soil-borne pathogens of non-cereal crops

CGA 142705 has shown considerable promise as a seed-treatment for several non-cereal crops. A broad-spectrum of fungi is controlled among the Ascomycetes, Basidiomycetes and Deuteromycetes (Table 4).

TABLE 4

Application rates of CGA 142705 as a seed treatment of non-cereal crops.

Crop	Pathogens	Dosage range (g a.i./100 kg seed)	Standard Treatment	Equivalent rate of Standard (g a.i./100 kg seed)
Cotton	*Rhizoctonia solani* *Thielaviopsis basicola* seed rotting fungi	50 - 100	carboxin imazalil captan	170 500 90
Oilseed rape	*Alternaria* spp.	40 - 80	iprodione	250
Peas	*Ascochyta* spp.	20 - 40	thiabendazole	37
Potatoes	*Fusarium* spp. *Helminthosporium solani* (storage rots)	2 - 4	thiabendazole*	3
Potatoes	*R. solani*	5 - 10	pencycuron	25

* CGA 142705 controls strains of *F. sulphureum* and *H. solani* which are resistant to thiabendazole.

CONCLUSIONS

CGA 142705 has shown high-level activity against a broad spectrum of seed-borne pathogens of cereals and is also better tolerated by cereals than current triazole seed treatments. It has demonstrated potential as a fungicide for seed treatment of non-cereals. In this latter case, the spectrum of activity appears complementary to that of metalaxyl and the combination can be expected to give broad-spectrum control of early season fungal pathogens in non-cereal crops.

CGA 142705 is particularly interesting because it is highly active against both MBC-resistant and -susceptible strains of fungi.

ACKNOWLEDGEMENTS

We would like to express our thanks to those many colleagues who have contributed to the international development of CGA 142705.

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RH-7988 : A NEW SELECTIVE SYSTEMIC APHICIDE

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ABSTRACT

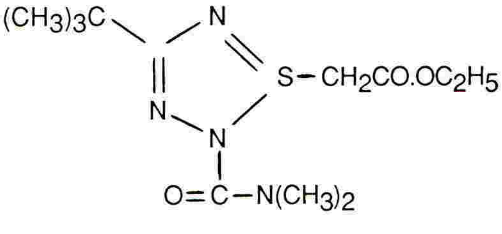
RH-7988 is a potent, highly selective systemic aphicide. It is a fast acting cholinesterase inhibitor, by absorption through the aphid gut wall and contact action. It is efficacious against a broad selection of aphid species on a wide variety of crops. Laboratory and field data suggest that RH-7988 controls resistant strains of Myzus persicae. RH-7988 is highly selective, Diptera and Lepidoptera are not affected by doses that provide aphicidal control. It is safe towards beneficial insects and bees and should be suitable for use in Integrated Pest Management systems. RH-7988 has outstanding systemic properties. Soil applications can control leaf-feeding aphids, whilst foliar applications can control root-feeding aphids. Upward and downward translocation within the plant vascular system occur thus protecting the entire plant. Outstanding levels of initial and residual activity result from foliar and soil applications.

INTRODUCTION

RH-7988, ethyl(3-tert-butyl-1-dimethyl carbamoyl-1H-1,2,4-triazol-5-ylthio) acetate, is a new highly selective fast acting systemic aphicide discovered and patented by Rohm and Haas Company. This paper describes the properties of RH-7988 and its performance against aphid pests in laboratory and field studies.

CHEMICAL AND PHYSICAL PROPERTIES

Structural Formula:



Chemical Name : ethyl (3-tert-butyl-1-dimethyl carbamoyl -1H-1,2,4-triazol-5-ylthio) acetate
Formulations available : 240 g/l EC, 480 g/l EC, 250 g/kg WP
Empirical Formula : $C_{13}H_{22}N_4O_3S$
Appearance : light tan solid
Melting Point : 60°C

Vapour Pressure : 4.8×10^{-6} Torr.
Solubility : technical grade : <1% in water, soluble in methylene chloride and ethyl acetate.

TOXICOLOGY

RH-7988 acts as a non-organophosphorus, non-carbamate cholinesterase inhibitor in insects and mammals. Atropine is antidotal. Acute toxicological data for technical material are shown below:

Acute oral LD$_{50}$: Mouse (14 d) 61 mg/kg, Rat (14 d) 50-200 mg/kg
Acute dermal LD$_{50}$: Rat (14 d) >5000 mg/kg
Eye Irritation : Rabbit inconsequential
Skin Irritation : Rabbit non-irritating
Ames test : negative
Teratology : non-teratogenic

ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY

RH-7988 exhibits little or no toxicity to mites, nematodes, beetles and caterpillars. Toxicological data on other non-target species are shown below:

Mallard dietary LC$_{50}$(8 d) : 368 mg/kg
Quail dietary LC$_{50}$(21 d) : 530 mg/kg
Quail LD$_{50}$ (single dose) : 8 mg/kg
Bluegill LC$_{50}$(96 h) : 1.0 mg/l
Trout LC$_{50}$(96 h) : 0.43 mg/l
Daphnia LC$_{50}$(48 h) : 0.048 mg/l
Honeybee contact LD$_{50}$(24 h) : 27 µg/insect
Soil half-life: sandy loam, 25°C : 1-5 days
Host plant half-life : 5-12 days

BIOLOGICAL PROPERTIES UNDER LABORATORY CONDITIONS

Selectivity

RH-7988 is a highly selective aphicide which does not control dipteran and lepidopteran insect pests at doses recommended for aphid control (Table 1).

TABLE 1

RH-7988 selectivity data from laboratory studies.

Pest	Order	LC$_{50}$ (mg/l)
Myzus persicae (peach potato aphid)	Homoptera	<5
Musca domestica (housefly adult)	Diptera	>25
Epilachna varivestis (Mexican bean beetle larva)	Coleoptera	300
Spodoptera eridania (southern armyworm)	Lepidoptera	600

RH-7988 has been shown to be safe against a wide range of beneficial insects and no adverse effects have been seen in field assays using a specially designed test kit (Table 2). RH-7988 should be suitable for inclusion in Integrated Pest Management systems.

TABLE 2

Relative safety against beneficial insects.

Insecticide	Safety Rating +					
	Apis mellifera	Hippodamia convergens	Stethorus punctum	Uga menoni	Endovum puttleri	Pedobius fovea
RH-7988	**	**	**	**	**	*
Endosulfan	*	**	**	**	o	o
Phosalone	*	o	**	**	**	**
Azinphos-methyl	o	o	*	o	o	o
Dimethoate	o	o	*	o	o	o
Methomyl	o	o	o	o	o	o

+ For A.mellifera from LD_{50}: ** GOOD (>11 µg/bee); * FAIR (2-10 µg); o POOR (<2 µg). For other beneficials from % mortality at 3.82 µg/cm^2 (6-24 hr): ** GOOD (0-30% mortality); * FAIR (31-70% mortality); o POOR (>70% mortality).

Knockdown and Residual Effect

RH-7988 shows fast knockdown activity and excellent residual aphid control following foliar treatment to broccoli (Table 3).

TABLE 3

Knockdown and residual activity of RH-7988 against Myzus persicae on broccoli.

	Mean % mortality (300 mg/l foliar treatment)				
Insecticide	KNOCKDOWN			RESIDUAL	
	1 HAT*	3 HAT	24 HAT	7 DAT	14 DAT
RH-7988	64	82	98	100	91
Fenvalerate	72	86	100	99	45
Pirimicarb	73	82	100	67	21
Acephate	0	39	98	75	0

* HAT = hours after treatment

In laboratory cage experiments against insecticide-resistant strains of Myzus persicae on sugar beet in the UK, RH-7988 has shown excellent knockdown and residual activity (Dewar et al., 1988). These studies have shown that outstanding control of R1 and R2 resistant strains of M.persicae resulted from foliar applications with 70-140 g a.i. RH-7988/ha. This knockdown activity and residual effect was superior to that given by carbamate, organophosphorus and synthetic pyrethroid standards used.

Systemicity

The excellent systemic properties of RH-7988 allow control of leaf-feeding aphids with a soil application (Table 4).

TABLE 4

Mortality of Myzus persicae on tobacco following soil drench treatments with insecticides.

Insecticide	Mean % mortality 3 weeks after treatment		
	0.2 mg/l	0.5 mg/l	1.5 mg/l
RH-7988	82	86	88
Aldicarb	78	80	89

Resistance

Laboratory cage dip studies in the UK (Furk and Murray, 1988) to evaluate the contact activity of RH-7988 and pirimicarb against susceptible (S), moderately resistant (R1) and highly resistant (R2) strains of M.persicae indicated that the contact action of RH-7988 should be able to control field strains of M.persicae resistant to other insecticides. Further laboratory leaf dip studies in Japan showed that RH-7988 controlled susceptible and resistant M.persicae strains equally well (Table 5). In this experiment, pirimicarb and oxydemeton methyl effectively controlled the susceptible strain, but required increased concentrations to control the resistant M.persicae strain.

TABLE 5

Toxicity of insecticides to susceptible and resistant strains of Myzus persicae in leaf-dip assays.

Insecticide	48 h LC_{50} (mg/l a.i.)	
	susceptible strain	resistant strain
RH-7988	<2.0	<2.0
Pirimicarb	<2.0	22.0
Oxydemeton methyl	6.6	210.0

BIOLOGICAL EFFECTS IN THE FIELD

Representative data from trials in Western Europe, the Middle East, South America and the USA between 1986-1988 are given as examples of the field aphicidal activity of RH-7988. In Italy, RH-7988 gave excellent knockdown of Aphis fabae on sugar beet. Results in Table 6 of treatments with 35 g a.i. RH-7988/ha are typical of the control achieved.

TABLE 6

Mortality of Aphis fabae on sugar beet.

Treatment	Dose (g a.i./ha)	% Mortality 2 DAT			
		TEST 1		TEST 2	
Untreated	-	(45.5)	c	(177)	d
RH-7988	35	100	a	100	a
Pirimicarb + Agral	225	94	ab	94	b
Deltamethrin* heptenophos	12*186	61	ab	87	c
Dimethoate	570	52	b	84	c

+ denotes tank mix * denotes formulated mix
Means in each column followed by the same letter are not significantly different at the 0.05 level of probability.

In the UK and France during 1988, 37.5-75 g a.i. RH-7988/ha on sugar beet gave excellent knockdown and residual control of M.persicae after 3 weeks. Results obtained in trials in the UK against Sitobion avenae on wheat indicate that RH-7988 controls cereal ear aphids at 140 g a.i./ha (Table 7).

TABLE 7

Mortality of Sitobion avenae in wheat.

Treatment	Dose (g a.i./ha)	% mortality			
		TRIAL 1		TRIAL 2	
		3 DAT	7 DAT	3 DAT	7DAT
Untreated*	-	(4.4)	(4.3)	(2.9)	(1.3)
RH-7988 + sun oil	140	97	100	97	94
Pirimicarb	140	98	100	100	94
Demeton-S-methyl	244	100	100	100	98

* Numbers of aphids/ear

Numbers of aphids declined rapidly following the 7 DAT assessment. This prevented measurement of the residual activity of RH-7988 on wheat in comparison with standard treatments. In cereals the addition of sun oil to RH-7988 in a tank mix improved aphicidal activity. Table 8 shows the long residual control achieved with RH-7988 against Aphis gossypii in cotton in the USA, up to 18 DAT.

TABLE 8

Mean numbers of *Aphis gossypii*/terminal in cotton plants.

Treatment	Dose (g a.i./ha)	Pre treatment	2 DAT	7 DAT	12 DAT	18 DAT
RH-7988 + sun oil	80	41	0	0	0	0
Untreated	-	40	56	100	86	24

RH-7988 plus sun oil gave excellent knockdown and residual control of *Brevicoryne brassicae* at 140 g a.i./ha in a brussel sprout trial in the UK. In this trial the control achieved with RH-7988 was equal to that with demeton-S-methyl at 325 g a.i./ha and superior to pirimicarb at 210 g a.i./ha.

Doses of 5 g a.i./hl have given effective aphid control in apples. Trials in Italy using covered and uncovered apple shoots during application have demonstrated systemic activity of RH-7988 (Table 9).

TABLE 9

Control of *Dysaphis plantaginea* in apples.

Treatment	Dose (g a.i./hl)	% mortality	
		2DA	7DAT
Untreated *	-	(300)	(641)
RH-7988 (uncovered shoots)	5	100	100
RH-7988 (covered shoots)	5	97	99

* Numbers aphids/shoot

Trials against *Rhopalosiphum rufiabdominalis* on wheat in Brazil demonstrated the excellent downward systemicity action of RH-7988 following foliar application. Control of this root aphid was achieved with 90 g a.i./ha plus rigo oil. The pirimicarb standard failed to give effective control (Table 10).

TABLE 10

Control of Rhopalosiphum rufiabdominalis in wheat

Treatment	Dose (g a.i./ha)	Mean nos. aphids/10 roots				
		Pre treatment	2 DAT	7 DAT	13 DAT	18 DAT
Untreated	-	132a	132a	48a	46a	55a
RH-7988 + rigo oil	60	156a	58b	41a	30ab	39b
RH-7988 + rigo oil	90	126a	44bc	12b	10b	26c
RH-7988 + rigo oil	120	162a	24c	8b	14b	24c
Pirimicarb	250	169a	131a	36a	40a	50a

Means in each column followed by the same letter are not significantly different at the 0.05 level of probability.

Field trials against M.persicae on peach in Italy during 1985-1988 have shown that RH-7988 at 30 g a.i./hl plus crop oil gives effective economic control similar to that achieved with pirimicarb and acephate (Table 11).

In laboratory studies, RH-7988 did not penetrate peach leaves rapidly and was not translocated. The activity shown by RH-7988 on peaches is therefore contact activity alone.

TABLE 11

Control of Myzus persicae on peaches

Treatment	Dose (g a.i./hl)	Mean nos. aphids/shoot		
		2 DAT	7 DAT	14 DAT
Untreated	-	108.7	153.5	- *
RH-7988 + sun oil	30	1.73	4.10	2.75
Pirimicarb	35	4.70	7.20	4.00
Acephate	42.5	10.40	1.35	1.50

* Treated with insecticide 14 DAT

CONCLUSIONS

RH-7988 is an ideal compound for use in Integrated Pest Management programmes because it is safe to beneficial insects. It is highly selective and exhibits fast knockdown and excellent residual activity together with downward and upward systemic properties in many crops.

Laboratory and field data suggest that RH-7988 controls aphids resistant to other groups of insecticides. In field trials, RH-7988 has shown excellent activity against aphid pests on sugar beet at 35-70 g a.i./ha; on other field crops higher doses are required for effective control.

In tree crops RH-7988 is very active against D.plantaginea on apples at 5 g a.i./hl. However, a dose of 30 g a.i./hl is required to control M.persicae on peaches, an indication of lack of systemic action of RH-7988 in this crop. The addition of an oil adjuvent to RH-7988 in the spray tank may increase plant and aphid uptake and hence activity on several crops. RH-7988 is safe to use on a wide range of crops.

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