SESSION 1

THE TWENTY-SEVENTH BAWDEN MEMORIAL LECTURE

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New era, new challenges, new solutions

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ABSTRACT

The recent achievements of chemistry-based crop protection will be reviewed and related to the promise of emerging technologies for the future production of food, animal feed and materials.

The arrival of the millennium finds the crop management industry in a phase of unprecedented change. The industry itself is increasingly recognising its role opposite partners in the food provision chain. This has led to wholesale changes in relationships amongst the participants.

However, it is in the technology arena that changes have been most profound and this topic provides focus for this paper. A new paradigm has emerged for the invention of new crop protection chemicals in which several novel technology platforms combine to enable breakthrough innovation. Genetic modification of crops to introduce valuable traits is now firmly established, with remarkably rapid uptake of the technology by growers who seek the commercial and agronomic advantages on offer.

In spite of sustained technical and economic progress, the industry has been less successful in several geographies in achieving the support of the general public for its activities. Compelling strategies for engagement of the public are required to ensure that progress in technology is matched by economic success.

BACKGROUND - WORLD AGRICULTURE IN CONTEXT

The turn of the millennium provides a particularly cogent opportunity to take stock of the remarkable progress made to date by the crop protection industries and to look forward to new challenges. The scope of this paper will include a retrospective view of major progress in the past decade or so, an assessment of the status quo today and a review of the prospects for the future, particularly in terms of the new solutions which science and technology promise. In this light, the scope of the paper will be limited to arable agriculture, with emphasis on both crop protection and crop management. In presenting the 15th Bawden Lecture in 1988, John Finney reminded us that "forecasting is rarely straightforward but forecasting in agriculture at a time when it is restructuring is a particularly precarious pastime" (Finney, 1988). This statement holds perfectly true today, and accordingly the prospects for the use of science and technology-based solutions which I will describe are subject to similar qualification.

At this point, it is useful to remind ourselves that those of us engaged in crop management are making an important contribution to the food provision industry. We are called upon to play a key role in feeding the world safely and sustainably. In pursuing this task, our efforts are focused upon:

- protecting yield - control of weeds, pests and diseases
- increasing yield - agronomic effects (eg. drought and salt tolerance), efficient use of light energy
- improving yield quality - enhanced composition - oils, proteins, vitamins, beneficial dietary components

The first of these endeavours has met with significant success. The organic chemistry-based industry is one half century old and its beneficial output should be a matter for great pride. Regrettably, we have not succeeded in winning public confidence in our activities - in spite of the manifest benefits.

Excellent progress has been made with projects aimed at increasing and improving yield - the promise of biotechnology in these areas suggests an acceleration of achievement in the coming years. We face a severe challenge in feeding a world with increased requirements for quality and variety, in addition to inherent population growth (Pinstrup-Anderson, 1999). Figure 1 analyses increases in population, the area given to arable and permanent crops and the food production index over the period 1985-1995 (FAO, 1996).

Figure 1.

The World 1985-1995

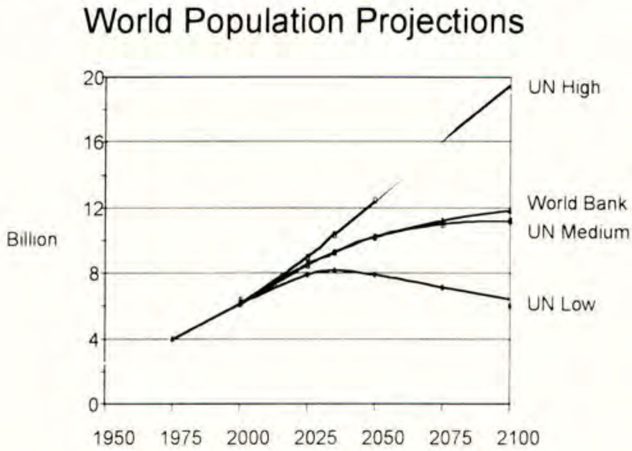
Total land area = 13.0 billion ha

	1985	1990	1995	% Change 1985-1995
Arable and permanent crops (billion ha)	1.44	1.46	1.48	2.8
Population (billion)	4.89	5.28	5.68	16.1
Food production index	90.7	100.8	110.8	22.1

Source : FAO Yearbook, Vol 50, 1996

Whereas the amount of land given to arable agriculture has increased by only 2.8% over the whole period, the population has grown by 16.1% in the same period. Furthermore, the food production index has increased by over 22% in that time. This analysis indicates that intensification of agriculture on a little changed area has met the challenge of feeding the burgeoning and increasingly demanding population. Whether or not this success can be continued will depend on many factors, perhaps the most important of which is the pattern of future world population growth. Figure 2 indicates four estimates which provide significant variation (Avery, 1995).

Figure 2.



However, all four estimates agree that the world population will increase to about eight billion over a quarter of a century. Indeed, world population passed the six billion mark in October, 1999. Thus, the imperative of enhancing food provision remains with us for yet another generation. However, the world is far from homogenous in its requirements. In the developing world, the production of calories (yield) remains the major challenge, but also with increasing requirement for variety and quality. It could be argued that in the Western world, the avoidance of calories appears to be the will of many people. The focus here will certainly be upon variety and quality, with functional foods and contributions to the dietary component of health becoming increasingly important. Notwithstanding these global differences, it is worth noting that economic growth is invariably a driver of crop protection technology usage. A comprehensive review of economic and social trends pertinent to agriculture has recently been published (FAO, 2000).

It is thus fortunate that very significant increases in crops yields have occurred world-wide in the past half century. From the production of corn in the USA through to rice in Indonesia, a relentless gain in crop yields has been evident. In his Bawden Lecture in 1997, Dennis Avery addressed the potential for stabilising world population by provision of food security. He has illustrated that increased food production, for which crop yields are a good proxy, has been a vital element in sharply reducing world birth rates (Avery, 1997). Figure 3 provides some examples of relevant data (Avery, 1995).

Figure 3.

World Population Growth: 1950 - present

Producing more food leads to lower birth rates:

Country	Crop	Yield increase %	Population increase %	Births / Female (1950)	(present)
USA	corn	152	89		2.1
France	wheat	195	38		1.8
Indonesia	rice	160	142	5.5	2.4
Chile	corn	x4	130	4.0	2.1
India	rice	>x2	149	5.8	3.1
China	rice	150	114		1.9

D. T. Avery, 1995

Sustainable development

There are almost as many definitions of sustainability as there are interested parties. Two straightforward and informative statements that I have encountered recently are given below:

"Capacity for continuance into the long term future"
"Development that meets the needs of the present without compromising the ability of future generations to meet their own needs"

With regard to agricultural food provision, sustainability demands that the requirements of several sub-components are satisfied eg.

- agronomy - we must provide effective systems to meet the needs of farmers and growers
- environment - it is essential that we conserve the balance in Nature
- society - our practices must provide nett benefits to the public and communities
- economics - each contributor to the system (in our case the food provision chain) must receive adequate compensation for their efforts.

It is my observation that the latter point is often neglected or disputed in public debate - but unless we expect agriculture to run as a charity, it is as vital a dependency as those mentioned earlier.

THE EVER-PRESENT CHALLENGE - PROMOTION AND MANAGEMENT OF CHANGE

As mentioned earlier, the agri-business world is presently experiencing a time of unprecedented change. Whether making reference to science, technology, economics, politics or public perception, we are currently experiencing a major shift in the paradigm which has hitherto defined crop protection and management. Why do we find ourselves in this situation?

A useful pointer can be found in Richard Beckhard's work on the definition of successful change programmes. In essence:

Successful change is a function of:

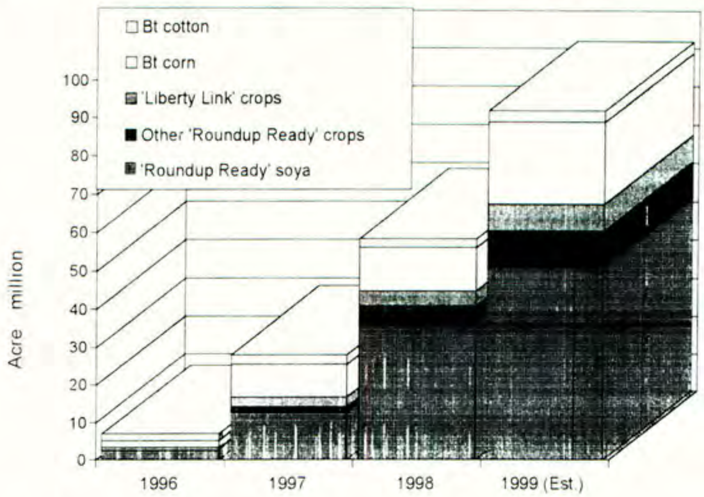
- dissatisfaction with the *status quo*
- vision and desirability of the future end state
- a plan indicating first practical steps

To my mind, dissatisfaction with the current status of agri-business has two seminal components. The first is economics where the situation spans market maturity in crop protection through to weak farm economies which have led to a situation of low industry profitability and, for example, less than satisfactory returns on R&D expenditure. Secondly, and as mentioned above, we have failed to illustrate to the public the benefits of our work (Spedding, 1999). This has led to damaging and often misinformed debates on environmental affairs and food safety. The effects of the latter have been notable with regard to regulatory requirements and political responses. In this context, mention must be made of the current debate on genetic modification in the UK which acts as a potent reminder of the necessity to involve with clarity all stakeholders who are affected by our activities.

In contradistinction to such gloomy dissatisfaction, our vision for the future provides confidence and excitement. As will be explained later, we are now able to apply exquisite technology to solve our problems and to provide superlative offerings to the food provision chain. The power of the current genomics revolution in achieving such objectives is one major contributor to our optimism. There is no doubt in my mind that the progress made in the last decade provides us with a key that unlocks the potential of plant-based economies. In addition to securing future food supplies, we are poised to provide major improvements to the dietary component of health through crop enhancement. Furthermore, new ventures will provide untold opportunities based upon the plant kingdom. The recognition that the energy to fuel these outputs derives from a truly sustainable resource (*viz.* daylight) will surely meet with public and legislative approval. Such advances in technology will be used in conjunction with traditional methods in strategies which provide integrated crop management. We will combine our novel science with advances in hitherto unrelated areas (for example global positioning systems to support precision agriculture) to ensure that the effectiveness of our inputs is maximised.

We are fortunate that the first practical steps towards this vision are already in place. The area planted to genetically modified (GM) crops has increased from less than ten million acres in 1996 to over 80 million acres three years later. For example, there has been unprecedented uptake by farmers and growers of new technologies such as GM crops (Figure 4, James, 1999). Farmers have recognised that they now have available a powerful new methodology for crop production which can be used either as a complement or a supplement to crop protection chemicals. Nevertheless, this rosy picture must be tempered by reference yet again to the public debate on GM crops where the industry, by and large, has to date failed to convince the consumer of the benefits of this approach.

Figure 4. Biotechnology Penetration to Date



Change in context

In order to provide a baseline for future projections, I found it useful to review the Bawden Lectures which have been presented by colleagues over the past two decades or so. Aside from learning many useful lessons, I observed that several contributions were notably prescient in predicting future trends.

In 1984, Mary Dell Chilton in her seminal paper entitled "Genetic Engineering - Prospects for Use in Crop Management" predicted that projects based on genetic engineering would attract added risks due to problems of protectability and regulation, and unpredictable marketability (Chilton, 1984). Nevertheless, she concluded that genetically engineered crops would provide a significant contribution to traditional breeding programmes by the turn of the century - very close to today's situation.

In 1988, John Finney in a paper entitled "World Crop Protection Prospects - De-misting the Crystal Ball" also turned his attention to the rapid advances in biotechnology (Finney, 1988). He predicted that plants modified to be resistant to insects, fungi and herbicides would be attractive to growers but felt it unlikely that in aggregate the new biological products would constitute more than 5% substitution of the total crop protection chemical market by the year 2000 but that rapid progress would quickly follow. Mention was also made of crop protection industry consolidation. In figure 5 I have combined some of the data from the 1988 paper with current information (Shoham, 2000).

Figure 5.

Crop Protection Sales - 1987 and 1999

1987 Sales ($bn)		1999 Sales ($bn)	
Ciba Geigy	2.0	Aventis	4.3
Bayer	2.0	Novartis	3.8
ICI	1.8	Monsanto	3.2
Rhone Poulenc	1.6	Zeneca	2.7
DuPont	1.2	Bayer	2.3
Monsanto	1.2	DuPont	2.1
Shell	1.0	Dow AgroSciences	2.1
BASF	1.0	BASF	1.9
Hoechst	0.9	Cyanamid	1.7
Dow	0.8	Makhteshim-Agan	0.7
(Finney, 1988)		(Wood Mackenzie, 2000)	

It can be seen that the list of players in today's crop protection industry is massively different to the cast in 1987. And, of course, this trend continues unabated today, driven by the imperative of spreading expenses (eg. R&D, sales and marketing) over an additive sales income.

A fuller review of the Bawden lectures indicates that they fall essentially into five recurrent themes, all of significant interest today.

- Environment, conservation and risk assessment
- Science, technology and R&D
- Land use, commercial and legislation
- Food and health
- Public perception

It is noteworthy that the latter two topics were increasingly covered in the later years.

SCIENCE AND TECHNOLOGY FOR THE NEW MILLENNIUM

As stated earlier, the millennium marks a period of rapid change, but the pace of change in science and technology is as profound as it is breathtaking. The focus of the remainder of this paper seeks to highlight the major advances which relate to research into chemical and gene based crop management (Evans D A, 1999). I am conscious that I have been unable to cover current progress in the critical areas of health assessment and environmental safety in this review, aside from scant mention. Excellent reviews of current trends are available (Brooks, 1999).

Chemical crop protection beyond 2000

There is no doubt that chemical pesticides will remain a vital component of crop protection in the new millennium. Firstly, there is no real alternative to herbicides, although there will be continued shift to the use of post-emergence non-selective herbicides used in transgenic resistance strategies. The development of resistance particularly by pests and diseases to current treatments will mean that new toxophores will be highly prized and will be characterised by rapid adoption (as in the recent cases of imidacloprid, fipronil and azoxystrobin). It can be speculated in this context that new toxophores coupled with resistance-breaking strategies will become even more important because today's targeted discovery approaches tend to provide compounds with single sites of action, with consequent concerns over resistance development.

Furthermore, chemists are resourceful and can be relied upon to invent superlative molecules which taken together with careful and novel application regimes will provide sustainable methods into the future. It is paradoxical that there are many who believe that the death knell has been already sounded for chemistry by the emergence of gene-based strategies. However, consider the case of a broad spectrum molecule such as azoxystrobin which is used in over 50 countries on over 50 crops and countless crop varieties. The amount of genetic modification which would be required to replace this molecule would be truly awesome. The use of a safe, flexible and effective molecule will always find utility in such circumstances.

NEW MOLECULE INVENTION

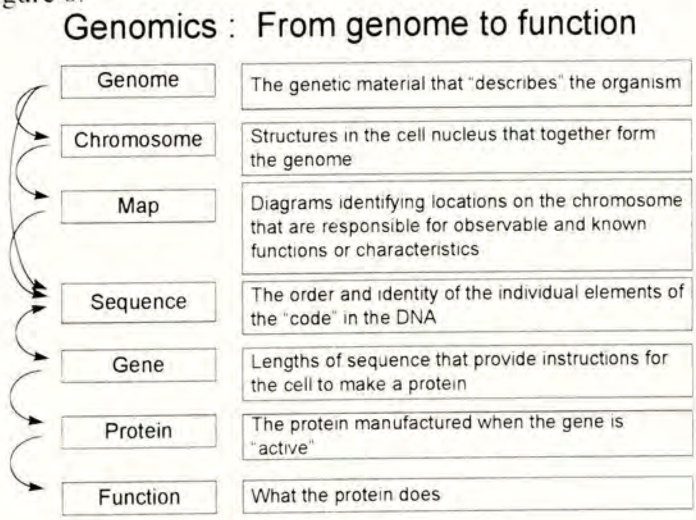
Whereas regulatory requirements and market maturity have rendered the invention of market-leading new molecules an unenviably difficult task, there is an abundance of new technology available to assist the process. Indeed, the chemistry and biology invention laboratories of the year 2000 are almost unrecognisable from those in existence a decade ago. Substantial investment has provided the capability to address a new paradigm for crop protection chemical invention, and this cost burden will need to be sustained and remunerated to be successful (Avery, 2000).

Amongst the new technologies on offer are:

Target identification - applications of genomics

As a supplement to the traditional methods for identifying biological targets, current advances in genomics are demonstrating powerful new approaches. It is now possible to observe the effect of a chemical on tens of thousands of genes unique to a particular organism by constructing an array of such genes on a small test plate. Thus, we can move from the "one chemical, one organism" paradigm to what can be described as massively-parallel biology. Thus, up-regulation or down-regulation of specific genes or sets of genes can be followed in response to chemical challenge. Effective mechanisms of control of the biochemistry of the organism can thus be deconvoluted, and next elaborated as the basis of high throughput indicator screens. Some of the customary disadvantages of *in vitro* screening are obviated here since gene expression can be cross-correlated to the phenotype and also to the function of the protein for which the gene codes. Figure 6 illustrates the progression from genomic data to provision of information on protein function.

Figure 6.



High-throughput automated screening - lead detection

The changes evident in screening methodology for crop protection chemicals are quite remarkable. Traditionally, crop protection companies typically obtained ca. 10,000 compounds per annum in half gram amounts, largely from in-house synthesis. These compounds were screened in glasshouses or constant environment rooms against indicator plants, insects and fungi, grown in soil in plant pots or trays. Today's miniaturised screens can handle several hundred thousand screening units, frequently conducted *in vivo* as well as *in vitro*. The secret of this throughput (typically only milligrams of test compound are required) is the adoption of the standard 96 well micro titre plate as the basic test module. Automated handling devices for these plates are commercially available. Kit for dispensing samples, serial dilution and assessment of outcome are also commonly available. Thus, it is not difficult to arrange the broadscale screening of several hundred thousand compounds per annum with automation being employed from sample retrieval right through to assessment of effect. Such methodology has been adapted for *in vivo* insecticidal and fungicidal activity and for weed control. Furthermore, the technology is equally applicable to small molecule or protein screening.

Combinatorial chemistry to feed screens and optimise leads

The next step is to feed the high throughput screens with a diverse range of chemical candidates. Locating hundreds of thousands of novel chemical entities per annum is a challenge but happily a variety of approaches is available - several on offer from boutiques and commercial concerns. The following methods have found favour:

- In-house synthesis, often employing multiparallel automation of repetitive or routine steps
- Compound exchange with third parties or external collaborators (eg. pharmaceutical companies)
- Compound libraries and combinatorial chemistry (both internally - and externally - sourced)

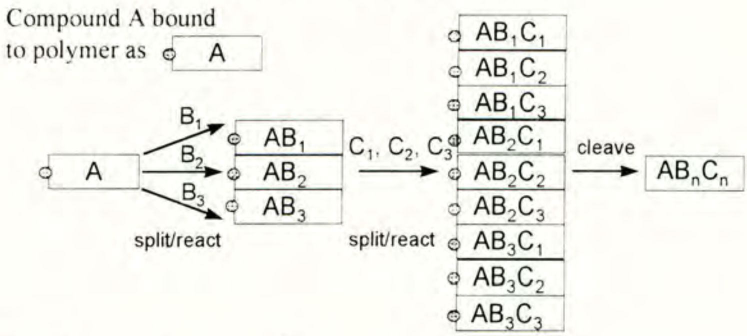
- Robotic synthesis of designed libraries
- Natural product extracts (eg. broths, plants) - an unending source of novelty

Many commercial organisations have been established to supply combinatorial libraries in the 96 well format or more recently 384 well format (commonly used for *in vitro* high throughput screening).

The principle of combinatorial chemistry is illustrated in figure 7. Starting material A is chemically bound to polymer beads. These are divided portionwise and separately reacted with several different B reagents. This process is repeated, followed by cleavage from the polymer support to provide a library of individual compounds.

Figure 7.

Combinatorial libraries



3 split	1	3	9
10 split	1	10	100
20 split	1	20	400

In spite of the inherent simplicity of the generation of a combinatorial library, the defining skill for success is the design of the output (Petsko, 1999). The inventing chemist must ensure that the library design reflects all of the characteristics required in a successful product, whilst ensuring sufficient diversity. Conversely, it is pointless to provide libraries where the compounds produced would be precluded from reaching the intended target site *in vivo* because of inappropriate translocation properties. This requires a detailed understanding *inter alia* of plant physiology, physico-chemical parameters and computational chemistry in addition to a sound knowledge of synthetic organic chemistry. It is by no means the mindless pursuit often suggested by its detractors.

The work of the organic chemist has been much enhanced in recent years by the availability of a number of items of laboratory automation. Robots are now ubiquitous in laboratories and lead optimisation is now commonly conducted robotically. In this context, it is helpful to distinguish lead generation programmes where appropriate diversity is the key, from lead optimisation work where careful trade off of molecular parameters is required to optimise the various properties required in the final product.

Virtual screening

It was mentioned earlier that ensuring diversity of chemical inputs is a major objective. As an alternative to synthesising a vast array of compounds to test the boundaries of activity, it is now possible to employ computational chemistry to select a representative subset of a library. For example, algorithms are available to select a subset of 25 diverse members of a, say, 500 compound set. Synthesis and screening of the 25 molecules in the subset is then completed, the remaining 475 having been deemed to have been "virtually" screened.

Expression analysis for mode of action

It was stated earlier that novel modes of action for molecules are highly prized. Due to the inherent complexity of the process to establish mode of action for a new molecule by conventional biochemical methods, it is paradoxical that this information has often become available at a late stage of the invention process. The gene expression technology described above is proving useful for this task. Thus, the gene set of a test organism (eg. plant, insect, fungus) can be arrayed and challenged for changes in expression by a chemical entity known to exhibit effective *in vivo* biological activity. Analysis of the sets of genes which are significantly up- or down-regulated, followed by identification of the proteins coded, provides an elegant route to mode of action.

Toxicogenomics

Toxicogenomics provides a further application of genomic science to crop protection research and development. Whereas this technology is in its infancy, it holds great promise for providing early alerts for toxicity. In the many cases where toxicity is known to be related to effects upon certain proteins and/or genes, a toxicogenomics-based test (in practice a DNA chip) can be included in early high throughput screens. It must be emphasised here that the technology will only provide early alerts *in vitro* and that many types of toxicity are not amenable to this approach. Nevertheless, this work provides yet another navigation device to take research chemistry into benign areas.

THE IMPACT OF BIOTECHNOLOGY ON AGRICULTURE - NEW VARIETIES

In addition to new avenues for crop protection discovery described above, biotechnology will enjoy its greatest use in agricultural research for:

- Generation of crop varieties with increased pest and disease resistance (self protection) and of varieties resistant to chemical herbicides
- Manipulation of crop quality/crop enhancement
- Smart breeding (marker-assisted breeding)

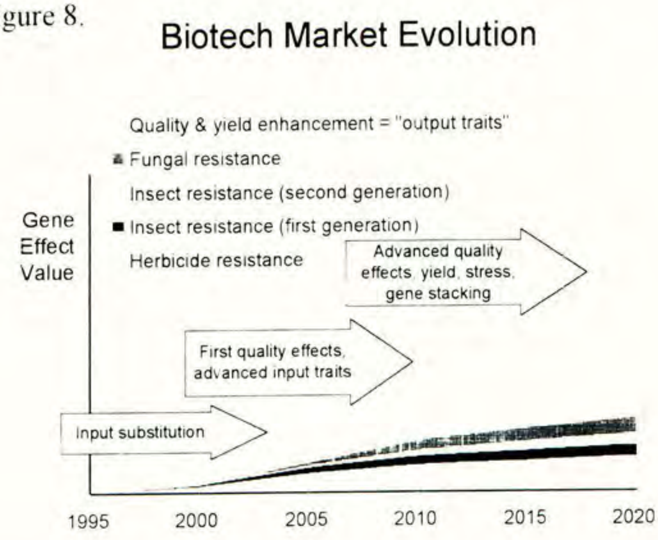
A detailed description of the delivery of crop protection effects through recombinant plants is outside the scope of this review. However, several excellent contributions on this topic are accessible in the current literature (Hammock, 1999).

Crop enhancement

Perhaps the most important contribution that biotechnology will make to agriculture in the next two decades will be in the area of improvement in crop quality ie. enhanced composition of nutrients, oils, proteins etc. There are already successfully demonstrated examples of crop varieties characterised by high oil, modified starch and high protein production either in the commercial launch phase or at an advanced stage in research and development. It has been shown, for example, that both flavour and sweetness of crop plants can be successfully modified. Furthermore, there is great potential for the introduction of agronomic effects (eg. cold tolerance, drought tolerance) so that crops may be raised in environments which hitherto were too hostile. Post-harvest benefits such as anti-sprouting and anti-bruising will be advantageous to producers and food processors alike. There is significant interest in the production of new plant varieties which enhance the dietary component of health (Christou, 1999).

The combined potential of the crop enhancement benefits described above is considered to comprise a market which is several times greater than the current crop protection chemical market of ca. $30 billion per annum. In addition to this, there are possible outlets for biotechnology-based agriculture outside food, animal feed and fibre which significantly expand these markets (Evans J, 2000). In Figure 8, indicative contributions to the total market are estimated.

Figure 8.



It must be pointed out that the route to market from effect gene to remuneration is long and complex. For a transgenic crop strategy, the time span required is almost always likely to exceed ten years and will face a number of hurdles. Once access has been obtained to appropriate effect genes and associated enabling technologies (promoters, markers) freedom to operate through the likely intellectual property maze must be secured. The effect cassette must be introduced into elite germplasm - a superlative effect in an outclassed seed background is doomed to failure. Finally, the challenge of recouping reward from what is likely to be a convoluted chain from grower through processor to retail cannot be lightly dismissed.

In spite of these constraints, the adoption of gene-based technologies by farmers and growers has been remarkably positive. Figure 4 again demonstrates this enthusiastic uptake.

Contribution of genomics to crop enhancement research

Whereas we have only begun to scratch the surface of the benefits provided by the genomics revolution, the potential is already well recognised.

As an example, it is interesting to examine the development by plant breeding of today's corn varieties derived from Teosinte grasses grown in Mexico over several millennia ago. Genomic analysis has shown that essentially five morphological differences between the two plants can be mapped to five regions of the genome, each on a different chromosome. A detailed understanding of such genetic changes provides us with massive benefits which will accelerate the breeding process in the future. Thus, it is not too fanciful to imagine the evolution of future elite corn varieties in years rather than millennia.

Forward genetics

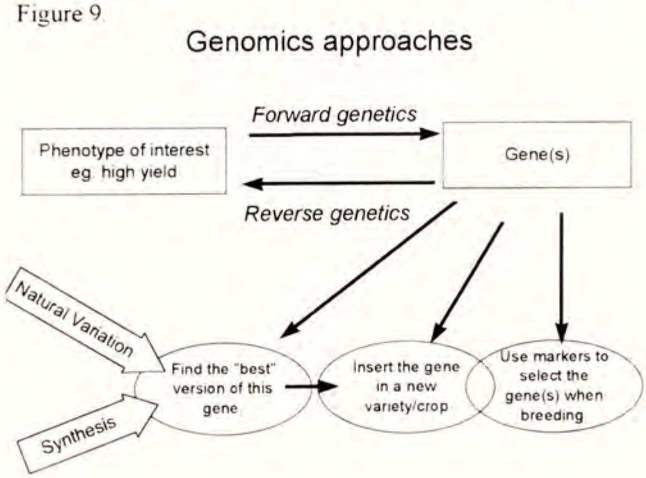
As an example of this approach, consider a crop plant phenotype which is known to be high-yielding. It is now possible to analyse the crop genetic map and to determine which parts of the gene sequences are associated with high yield. This information can be used either to assist traditional breeding by following a marker gene or to transfer the high yield gene into a new crop variety.

Reverse genetics

Here, a total genome surrogate of the crop plant is presented as an expression array as indicated above. Fluorescent DNA probes made from high yielding and "normal" varieties are then used to challenge the array. The differences in expression (differential fluorescence) illustrated by the array helps to pinpoint the genes which are associated with the high yield.

In practice, both approaches are used in concert as illustrated in Figure 9.

Figure 9.



Genetically modified food - information, benefits and choice

As stated earlier, the public reaction to the introduction of produce based upon genetic modification has been mixed around the world. Particularly in parts of Europe, the reaction has been extremely hostile culminating in instances of direct action and sustained press campaigns which have been aggressively negative. Speculation on the causes which underlie the current situation is outside the scope of this paper, but there are one or two simple lessons which are relevant (Sagar, 2000; Taverne, 1999).

Firstly, we scientists must recognise that part of the responsibility for the current furore lies with ourselves. Exaggerated claims, confusing oppositions, premature publication and vocal rancour amongst scientific opponents serve only to confuse and alienate the public. Science itself is the real loser in these battles. Scientific method demands that we do not peddle our beliefs as facts. Regrettably, current reading reveals that there have been many unwise departures from scientific rigour. The situation has been exacerbated by unwarranted scaremongering and exaggeration by pressure groups. In turn, the industry has not sufficiently involved its various stakeholders in its strategies, or the risk assessments which are attached to them (Barnes, 2000).

My observations to date suggest that the projects which have met with reasoned public and media response are those in which there has been clarity of information, statements of benefits to stakeholders and the provision of choice. The example of the tomato puree produced by Zeneca and its partners for sale in two UK supermarkets is suffering from overexposure, but the lessons learned remain pertinent. Clear statements of benefits to the grower, processor and consumer have been supported by information packs. The launch in the UK of tomato puree clearly labelled as being made with genetic modified tomatoes in 1996 met at the time with positive media and public reception. The perception climate in the UK has changed markedly since that time and one can only speculate as to the reaction to such a launch at this time.

Precision agriculture

Much of the foregoing discussion has concentrated on the facilitation by new technology of the invention process for new chemical entities. However, the application and presentation of those molecules is an equally exciting topic (Ganzelmeier, 1999). New formulation technologies such as timed-release preparations based on microencapsulation provide significant advantages such as increased persistence of effect, reduced toxicity and improvement in efficacy. Microencapsulated formulations are often aqueous-based with consequent reduction in volatility and flammability.

Nevertheless, it remains the case that very much of the applied crop protection chemical does not reach its target site or in many cases is provided as under- or overdose (Stafford, 2000). The application of global positioning systems and geographic information systems to the application of chemical treatments to crops has been characterised by remarkable progress in recent years. Using such technology, irregularities across terrain (eg. percentage organic matter, nutrients, pH) can be accurately mapped to within a few metres. This information then feeds decisions on applications both in terms of timing and quantum. Furthermore, boom sprayers with adjustable outputs are being developed to deliver an optimal but varied dose across the crop/field matrix. Research effort is presently being employed into detecting "signatures" for various diseases and pests which infest arable crops. Thus, it is presently possible to provide satellite-generated readings of the emergence of disease pressure in a field. These data can then be correlated to yield following harvest. This enables the building up of a full picture of the economic benefit gained by use of pesticides under a variety of circumstances.

Methodology for formulation and applications holds a special place in the industry because it is here that the physical manifestation of our research and development work comes into contact with our grower customers. Thus it is vital that we provide flexible and safe methods which empower our customers to farm at optimal efficiency.

CONCLUSION

As we take stock of progress in crop management at the turn of the millennium, contributors from the agribusiness sector can feel justifiably proud of their achievements in securing global food supplies. The co-operative work of public and commercial interests has combined to provide farmers and growers with highly effective technology and agronomic solutions.

For the past half century, we have placed a strong reliance upon remarkable progress largely with organic chemicals to provide effective crop protection. With the recent arrival of biotechnology-based solutions, growers now enjoy the complementary benefits of crops which are self-protected from attack by insects and diseases, and which tolerate specific herbicides. Biotechnology also holds great promise for increasing harvested yield and for beneficial enhancement of the constituents of crops.

The genomics revolution which underpins these advances is the key which unlocks the future potential of plants for production of useful materials, ranging from plastics to pharmaceuticals. As such, we have in our grasp the possibility of an alternate plant-based economy, complementary to fossil fuels, based upon a truly sustainable resource - daylight!

ACKNOWLEDGEMENTS

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SESSION 2A

NEW COMPOUNDS AND USES FOR PEST MANAGEMENT

Chairman: Dr G le Patourel
Imperial College, Ascot, UK

Session Organiser: Dr R Bateman
CABI Bioscience, Ascot, UK

Papers: 2A-1 to 2A-7

Thiacloprid[1], a novel neonicotinoid insecticide for foliar application

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ABSTRACT

Thiacloprid, (2*Z*)-3-[(6-chloro-3-pyridinyl)methyl]-1,3-thiazolidin-2-ylidenecyan-amide is a highly active novel insect control agent with broad spectrum efficacy against sucking and biting insects at 48-180 g a.i./ha depending on crop, pest and application type. Five years of field studies have revealed excellent control of important pests in pome fruit, cotton, vegetables, and potatoes. Besides aphids and whiteflies it is also active against various species of beetles (e.g. *Leptinotarsa decemlineata, Anthonomus pomorum, Lissorhoptrus oryzophilus*) and Lepidoptera such as leaf miners and *Cydia pomonella* in apples and shows good plant compatibility in all relevant crops.

Like imidacloprid thiacloprid acts agonistically on the nicotinic acetylcholine receptor. As a result there is no cross-resistance to conventional insecticides such as pyrethroids, organophosphates, and carbamates and consequently it will fit well into resistance management strategies. Thiacloprid is an acute contact and stomach poison with systemic properties.

Thiacloprid has a favourable environmental profile with a short half-life in soil, and good margins of safety for birds, fish species and many beneficial arthropods. Its bee safety also allows the application during the blossom period of bee-attractive crops. Due to its low acute toxicity to mammals the product is safe for operators and consumers.

INTRODUCTION

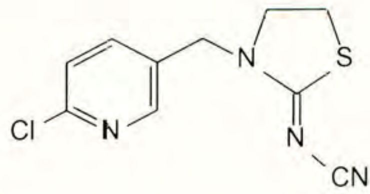
The chloronicotinyl or neonicotinoid insecticide imidacloprid represents the most successful active ingredient to be marketed in the last decade for the control of sucking and some chewing pests in agriculture. As a consequence, an extensive research and development program performed by Bayer AG, Germany jointly with Nihon Bayer Agrochem, Japan and Bayer Corporation, USA led to the discovery of a second insecticide from this chemical class: thiacloprid.

The physico-chemical properties, toxicological and environmental behaviour of the new active ingredient are presented. The biological profile, elaborated in laboratory, greenhouse and field studies will be demonstrated. The product will be registered world wide under the trade name Calypso®[1], the basic formulation is a 480 SC. Market introduction is expected for Brazil, Europe, Japan and US between the years 2000 and 2003.

[1]proposed common/trade name

CHEMICAL AND PHYSICAL PROPERTIES

Structural Formula:



Common Name:	Thiacloprid
Chemical Name, IUPAC:	(2Z)-3-[(6-chloro-3-pyridinyl)methyl]-1,3-thiazolidin-2-ylidenecyanamide
CAS RN:	111988-49-9
Empirical Formula:	$C_{10}H_9ClN_4S$
Molecular Weight:	252.8 g/mol
Appearance:	yellowish powder
Vapour pressure:	3×10^{-10} Pa at 20°C
Solubility in water:	185 mg/litre at 20°C

FORMULATIONS

480 SC, 36 WG. Good compatibility with conventional crop protection products.

HUMAN SAFETY

Acute oral LD_{50} rat (males):	836 mg/kg body weight
(females):	444 mg/kg body weight
Acute dermal LD_{50} (24h) rat (males, females):	> 2000 mg/kg body weight
Acute inhalation LC_{50} (4 h, aerosol) rat (males):	> 2535 mg/m^3 air
(females):	~ 1223 mg/m3 air
Skin irritation (4 hours) rabbit:	no irritation
Eye irritation (24 hours) rabbit:	no irritation
Skin sensitation guinea pig:	no skin sensitation
Chronic toxicity/carcinogenicity rats:	no primary carcinogenic potential
Developmental toxicity:	no primary developmental toxicity in rats and rabbits
Genotoxicity:	no evidence of a genotoxic or mutagenic potential

ENVIRONMENTAL SAFETY

Rainbow trout, acute toxicity LC_{50} (96 h),	30.5 mg/litre
Daphnia magna EC_{50} (symptoms 48 h at 20°C):	≥85.1 mg/litre
Algae EC_{50} (growth rate 72 h at 20°C)	
Scenedesmus subspicatus	97 mg/litre
Bobwhite quail, acute toxicity LD_{50},	2716 mg/kg

Earthworms (mg/kg dry weight substrate)

Eisenia fetida LC_{50} (14-day at 20° C)	105 mg/kg
Honey bee, LD_{50} oral and contact	5.3 and 24.2 µg/bee

ENVIRONMENTAL FATE

Soil half-life (6 soils)	7 - 21 days
Soil mobility (6 soils)	low to medium

METHODS AND MATERIALS

Table 1. Details of field trials

Table/ Figure	Insect	Application rate (litre/ha)	No. of treatments	Evaluation based on	Evaluation days after last treatment
Table 3	*C. pomonella*	2000-3000	8	larvae/200 fruits	14-17
	A. pomorum	300	3	adults/600 flowers	15
Table 4	Leafminers	1000-1500	2	mines/100 leaves	38-62
Table 5	Aphids	1000-2000	1-2	larvae/10 leaves	3-13
Table 6	Sucking pests	300-1000	1-2	larvae/10 leaves	5-14
Table 7	*L. decemlineata*	100-800	1	larvae/40 plants	14-22
Figure 2	Honeybees	360	1	bees on 5 m^2	see figure

BIOLOGICAL PROFILE

Laboratory studies

The spectrum of activity of thiacloprid against important agricultural pests is summarised in Table 2.

Table 2. Activity of thiacloprid against important agricultural pests after leaf-dip application in comparison to standard products

Species	Thiacloprid		Standard		
	LC_{50}, mg a.i./litre	CL95%		LC_{50}, mg a.i./litre	CL95%
Myzus persicae, mp	1.5	1.4 - 1.7	methamidophos	10.1	9.0 - 11.4
Aphis fabae, mp	0.8	0.7 - 0.9	methamidophos	10.5	9.3 - 12.0
Aphis fabae, mp*	≤ 0.6	-	carbofuran	0.3	-
Aphis gossypii, mp	0.8	0.7 - 0.9	methamidophos	19.5	17.1 - 22.2
Bemisia tabaci, mp	1.1	0.3 - 2.4	imidacloprid	3.8	1.7 - 6.8
Nephotettix cincticeps, L2	0.6	0.5 - 0.7	fenobucarb	15.6	13.7 - 18.0
Cydia pomonella L2,3	1.1	0.8 - 1.4	azinphos-methyl	0.6	0.2 - 1.9
Phaedon cochleariae, L2	18.5	15.9 -21.6	imidacloprid	19.8	17.0 - 22.8
Lissorhoptrus oryzophilus, ad	1.8	1.2 - 2.7	imidacloprid	19.1	14.3 - 25.0

*soil application, LD_{50}, mp: mixed population, L: larval stage, ad: adult, CL95%: confidence limit

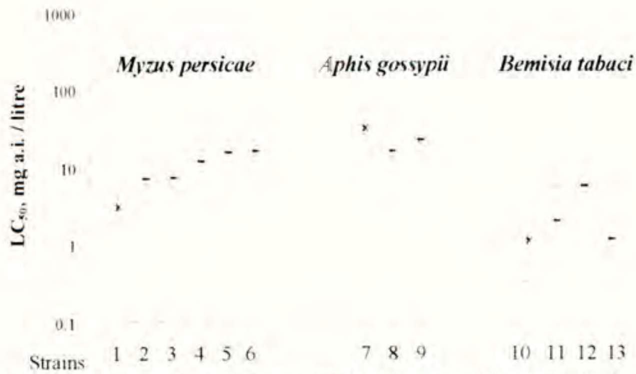


Figure 1. Efficacy of thiacloprid against susceptible (x) and resistant (-) aphids and whiteflies

The response of susceptible laboratory strains of *M. persicae*, *A. gossypii* and *B. tabaci* (Figure 1, strains 1, 7, 10) was measured in comparison to a range of field strains (2-6, 8, 9, 11-13) which exhibited resistance to organophosphates, carbamates and in some cases to pyrethroids and endosulfan. Apart from a natural variability no difference between susceptible and field populations of the three species was detected. Resistance management for thiacloprid will be handled according to the guidelines published for imidacloprid (Elbert *et al.*, 1996).

Sprayed on cabbage at 50 mg a.i./litre, thiacloprid 480 SC showed a complete residual activity against *M. persicae* under greenhouse conditions for at least 18 days. A good plant compatibility in tomato, French bean, cucumber and soy bean was found up to a spray concentration of 1000 mg a.i./litre.

Field studies

Table 3. Control (% Abbott) of *Cydia pomonella* and *Anthonomus pomorum* in apple and pear tree

Treatment	Rate % a.i.	*Cydia pomonella* South Africa 1998, 1999				*Anthonomus pomorum* Belgium, 1996
thiacloprid	0.0048	87	90	–	98	–
thiacloprid	0.0072	89	92	96	99	–
thiacloprid	0.0096	96	97	97	100	93
azinphos-methyl	0.0175	92	93	94	97	–
carbaryl	0.025	-	-	-	-	83
untreated		(39)	(49)	(13)	(28)	(61)

Table 4. Control (% Abbott) of lepidopteran leaf miners in apple 1995, 1996

Treatment	Rate % a.i.	*Lithocolletis blancardella* Italy I	*Lithocolletis blancardella* Italy II	*Lithocolletis coryfoliella* Italy	*Lyonetia clerkella* Germany
thiacloprid	0.0096	90	100	94	100
flufenoxuron	0.0075	24	47	90	-
triflumuron	0.02	-	-	-	100
untreated		(253)	(19)	(78)	(24)

Table 5 Control (% Abbott) of aphids in apple 1995, 1996

Treatment	Rate % a.i.	*Aphis pomi* Spain I	*Aphis pomi* Spain II	*Aphis pomi* Germany	*Dysaphis plantaginea* Spain	*Dysaphis plantaginea* France	*Dysaphis plantaginea* Germany
thiacloprid	0.0072	99	98	100	100	99	100
thiacloprid	0.0096	99	95	100	100	97	100
pymetrozine	0.03	70	84	90	46	42	77
untreated		(27)	(37)	(66)	(25)	(100)	(18)

Table 6. Control (% Abbott) of sucking insects in cotton and vegetables

Treatment	Rate g a.i./ha	*Aphis gossypii* Cotton USA 1995	*Aphis gossypii* Cotton Brazil 1996	*Bemisia argentifolii* Cucumber USA 1999	*Bemisia tabaci* Pepper Spain 1996
thiacloprid	25	89	94	95	-
thiacloprid	50	94	93	100	-
thiacloprid	144	-	-	-	100
methamidophos	560	19	38	-	-
pymetrozine	96	-	-	53	-
methomyl +pyriproxifen	400 +50	-	-	-	95
untreated		(1350)	(190)	(55)	(56)

Table 7. Control (% Abbott) of *Leptinotarsa decemlineata* in potato

Treatment	Rate g a.i./ha	U.S.A. 1999		Portugal 1997	
thiacloprid	28	99	99	—	—
thiacloprid	48	—	—	100	99
thiacloprid	56	100	99	—	—
thiacloprid	72	—	—	100	99
fipronil	28	92	92	—	—
cyfluthrin	49	80	92	96	—
lambda-cyhalothrin	15	—	—	—	55
untreated		(68)	(38)	(146)	(381)

Tables 3-7 demonstrate the excellent activity of thiacloprid against key pests in pome fruit, cotton, vegetables and potato under field conditions.

Due to its bee safety, thiacloprid can even be used during flowering in pome fruit. In a field trial with *Phacelia* using a plot size of 5000 m^2 no effect on foraging bees was found (Figure 2). Hive weight and food stores increased during the study as in untreated controls. The brood was not affected.

The effect of thiacloprid on honeybees was also examined in combination with fungicides which may simultaneously be used as a tank-mix for the treatment of pome fruit. Laboratory studies showed only a moderate synergistic effect of azole fungicides which is not considered relevant under field conditions. The potential effects under field conditions are under further investigation.

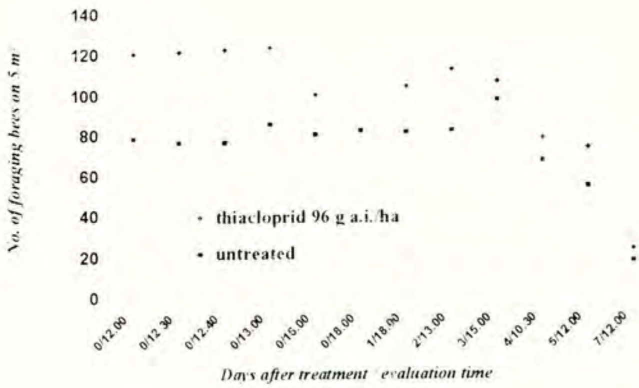


Figure 2 Influence of thiacloprid on foraging activity of honeybees in a *Phacelia* field trial, Germany 1995

CONCLUSION

World-wide field tests of the new neonicotinoid insecticide thiacloprid have shown outstanding control in the range of 48-180 g a.i./ha depending on pest and crop following foliar application. Honey- and bumblebee safety allow a flexible use of the product in pome fruit and vegetables even during flowering. Due to its fast degradation in the environment and its safety to operators and consumers thiacloprid can be regarded as a valuable tool in modern crop protection systems.

ACKNOWLEDGEMENTS

We would like to express our gratitude to all our colleagues involved in the development of thiacloprid. We thank Prof. A. L. Devonshire, IACR Rothamsted for the resistance studies performed with thiacloprid on *M. persicae* and *A. gossypii*.

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ANS-118: A Novel Insecticide

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ABSTRACT

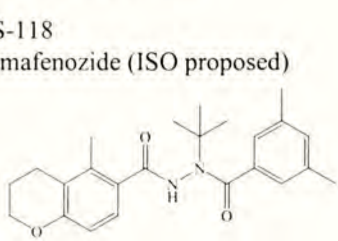
ANS-118 [2'-*tert*-butyl-5-methyl-2'-(3,5-xyloyl) chromane-6-carbohydrazide] is a novel diacylhydrazine insecticide characterized by a methyl-chromane moiety in its structure. Results of greenhouse and field trials have shown this chemical to be effective in controlling various lepidopterous pests (i.e. Tortricidae, Pyralidae, Noctuidae, etc.) on vegetables, tea, fruits, rice, ornamentals, trees and other crops at application rate ranging from 5 to 200 grams active ingredient per hectare. Immediately after treated with ANS-118, lepidopterous larvae stop feeding. This phenomenon can be explained by rapid induction of ecdysis. No phytotoxicity caused by this insecticide has been reported. ANS-118, a novel ecdysone agonist, has large margins of safety to mammalian, avian and aquatic organisms, and has no adverse effects toward non-target arthropods. These properties as well as the high specificity to target insect pests make ANS-118 a suitable tool for the integrated pest management (IPM).

INTRODUCTION

ANS-118 was discovered and developed in a collaboration between Nippon Kayaku Co., Ltd. and Sankyo Co., Ltd. The insecticidal effect of ANS-118 is highly specific to lepidopterous larvae. Products containing ANS-118 are now under world-wide development. This paper reports the chemical and biological properties of ANS-118.

CHEMICAL AND PHYSICAL PROPERTIES

Code number: ANS-118
ISO name: chromafenozide (ISO proposed)
Structural formula:



Chemical name: 2'-*tert*-butyl-5-methyl-2'-(3,5-xyloyl) chromane-6-carbohydrazide dibenzoylhydrazine (Wing, 1988; Wing et al., 1988). In a reporter gene assay using luciferase as the reporter gene regulated by ecdysteroid response elements, ANS-118 shows a transcriptional activity in the same manner as the ecdysteroid, ponasterone A (Toya et al., 2000). Based on symptoms of the larvae and luciferase induction activity in cell-based assay, it is considered that ANS-118 acts as an ecdysone agonist and induces transcription of genes that regulate moulting, resulting in disruption of normal moulting process.

Field Evaluation

Table 3. Control of the 2nd generation Grape berry moth (*Lobesia botrana* and *Eupoecilia ambiguella*) on grape (Bad Dürkheim, Germany, 1999)

Test material	Dosage (g a.i./ha)	Spray timing * 1	2	3	Number of larvae / 100 grapes
ANS-118 5SC	120	X	X		12.0
	160	X	X		10.7
Methidathion +	640 +		X		46.7
Parathion microencapsulated	320			X	
Untreated	–				120.0

* Spray timing 1, 4 days before the peak day of moth flight; 2, 10 days after the peak day of moth flight; 3, 17 days after the peak day of moth flight; X, treatment

Table 4. Control of *Cydia pomonella* on apple (St. Patern, France, 1997)

Test material	Dosage	% of damaged fruit by Codling moth		
	(g a.i./ha)	Not marketable	Marketable	Total
ANS-118 5SC	50	1.49	1.76	3.25
	75	0.74	1.40	2.14
	100	0.98	1.00	1.98
Tebufenozide 23SC	144	1.12	1.26	2.38
Untreated	–	20.10	5.84	25.94

Table 5. Control of *Spodoptera littoralis* on cotton (Egypt, 1998)

Test material	Dosage	Number of larvae / plant			
	(g a.i./ha)	Pretreatment	3 DAT *	5 DAT *	7 DAT *
ANS-118 5SC	35.7	12.73	3.93	0.95	0.25
	47.6	15.78	4.70	0.67	0.05
Chlorfluazuron 5EC	47.6	15.28	7.50	2.80	0.75
Untreated	–	14.95	11.45	6.85	2.43

* Days after treatment

Table 6. Control of the 2nd generation *Chilo suppressalis* on rice (Yamagata, Japan, 1994)

Test material	Dosage (g a.i./ha)	Hills % of injured	Stems % of injured
ANS-118 0.3% Dust	120	10.0	0.6
Fenthion 2% Dust	800	23.3	1.6
Untreated	–	50.8	7.5

Table 7. Control of tortoricid moths (*Adoxophyes spp.*) on tea (Kumamoto, Japan, 1997)

Test material	Dosage (g a.i./ha)	Number of rolled leaves / m^2
ANS-118 5SC	100	0.49
Methomyl 45WP	600	0.99
Untreated	–	11.42

Table 8. Control of *Anticarsia gemmatalis* on soybean (Brazil, 1998)

Test material	Dosage (g a.i./ha)	Number of larvae per a plot					
		Small larvae (< 1.5 cm)			Large larvae (> 1.5 cm)		
		4 DAT	7 DAT	11 DAT	4 DAT	7 DAT	11 DAT
ANS-118 5SC	12.5	2.5	1.5	2.0	1.2	0.0	0.7
	25	0.4	0.9	3.2	0.4	0.0	0.2
Lufenuron 5EC	15	2.1	0.2	2.8	3.9	0.7	0.9
Untreated	–	13.9*	5.8*	6.9*	39.4*	23.4*	7.6*

Table 9. Control of *Spodoptera exigua* on shallot (Kanchanaburi, Thailand, 1993)

Test material	Dosage	Number of larvae / 10 plants					
	(g a.i./ha)	25 Nov	2 Dec	9 Dec	16 Dec	23 Dec	30 Dec
ANS-118 5SC	12.5	7	18	18	9	9	3
	25	1	5	10	3	0	1
	50	6	3	11	0	0	0
Chlorfluazuron 5EC	50	9	5	35	60	45	8
Untreated	–	1	64	51	43	66	43

Treatments were applied immediately after each observation day.

CONCLUSION

Results of extensive field tests demonstrate that formulations of ANS-118 are highly effective on lepidopterous insect pests by foliar spray without causing phytotoxicity to any crops. The fact ANS-118 had no adverse effects toward pollinators and other beneficials suggests that it may play an important role in IPM programs throughout the world. In Japan, two formulations of ANS-118 (a 0.3% dust formulation and a 5% suspension concentrate) were registered under a trade name MATRIC® in December 1999.

ACKNOWLEDGEMENTS

We would like to express our thanks to our colleagues who have contributed to our understanding of the value of ANS-118 and to the field evaluations of ANS-118 throughout the world.

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Spinosad, a useful tool for insect control in top fruit

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ABSTRACT

Spinosad is a biological insecticide derived as a fermentation product from the actinomycete *Saccharopolyspora spinosa.* The compound was for the first time in north-western European conditions tested for its possible use in apple and pear. It was extremely efficient on lepidopteran pests as the winter moth, *Operophtera brumata* (L.) and the summer fruit tortrix moth, *Adoxophyes orana* (F.v.R.). On the latter species control strategies are possible on both the hibernated or the summer generations. Besides, good results were obtained using spinosad for the control of the pear sucker, *Psylla pyri* (L.), the most important hemipteran pest in pear culture. Special attention was drawn to the investigation of the stage specificity, persistence, dose rate and rain fastness of the insecticide. Spinosad is selective, and spares the key beneficials in pome fruit i.e. the predatory mite, *Typhlodromus pyri* (Scheuten) and the predatory bugs (Anthocoridae) in pear. Because of its selectivity and its interesting pest spectrum, the compound has generated considerable interest for its development in top fruit in north-western Europe.

INTRODUCTION

Spinsosad is a naturally occurring mixture of two active components, spinosyn A and D, produced by the soil actinomycete *Saccharopolyspora spinosa* (Thompson *et al.*, 1997). This natural compound activates nicotinic acetylcholine receptors by a novel mechanism (Salgado *et al.*, 1997). Spinosad was tested on major pests and key beneficials in pome fruit in nort-western Europe.

METHODS AND MATERIALS

Trials on *A. orana* and *C. pomonella* were executed according to the EPPO guidelines. For *O. brumata* the number of caterpillars was counted at 13 DAT on the total of 5 trees. Trials on *P. pyri* and on beneficials were executed as described (Bylemans, 1997a). Efficacy or side effects of compounds were calculated according to Abbott (1925). After a pre-count for *T. pyri*, heterogeneity was omitted using the adapted Abbott formula (Henderson and Tilton, 1955). For the laboratory trial on *C. pomonella* apples were treated till run off with a diluted solution of the insecticide using a glass atomiser (Vel, Belgium). After drying, the fruits were deposited under a nozzle installation spraying at 25 l/m²/h. After 48, 96 and 144 min fruits were removed to obtain 20, 40 and 60 l/m², respectively. After drying, apples were placed in cages with a high number of moths of *C. pomonella*. Within 2 days enough eggs were deposited and apples were removed from the cages. After one week, the number of penetrations in the fruit was recorded.

The application of the compounds and the calculation of their dose rates was executed according to the leaf wall area (Bylemans, 2000). For reasons of comparison, the amount of active ingredient used is always indicated as was the trial executed in a standard orchard. This is a dwarf tree orchard planted with a single row system, a distance of 3.5 m between the rows and a tree height of 3 m. All compounds (amitraz: Mitac 200 EC, cloropyriphos ethyl: Dursban 480 EC, cyfluthrin: Bayhroid 050 EC, deltamethrin: Decis 025 EC, diflubenzuron: Dimilin 480 SC, fenazaquin: Magister 100 EC, flufenoxuron: Cascade 100 DC, hexythiazox: Nissorun 10 WP, methidathion: Ultracid 400 EC, mineral oil: Oviphyt, parathion ethyl: E605 250 EC, pirimicarb: Pirimor 50 WG, spinosad: Tracer 480 SC, tebufenozide: Mimic 240 SC) were kindly provided by the national services of the producer. If mineral oil (MO) was added, it was used at 1 l/ha.

RESULTS

The control of lepidopteran pests

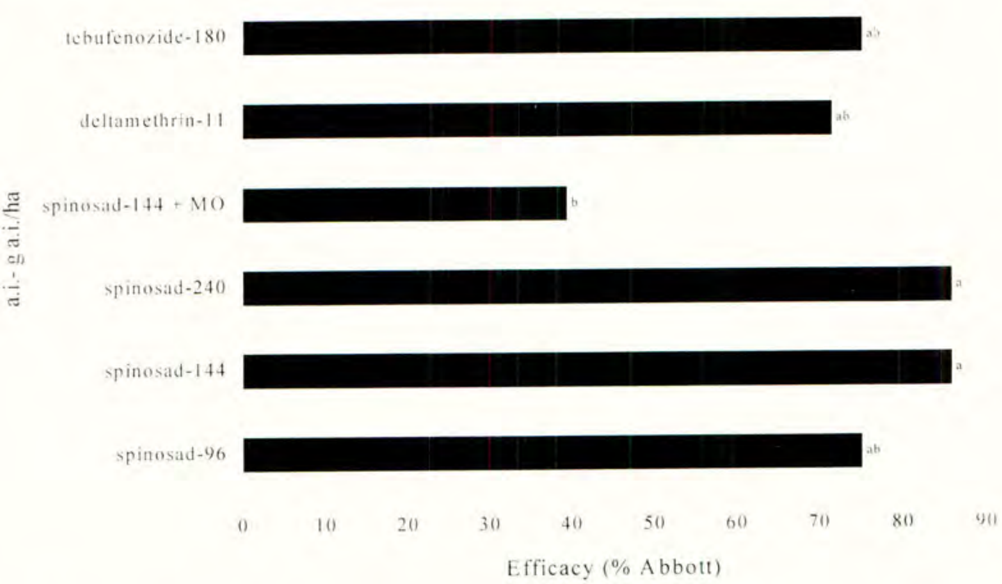

Figure 1. Efficacy after a pre-flowering treatment on hibernated caterpillars of *Adoxophyes orana*. MO: Mineral Oil.

Spinosad was shown to be very efficient for the control of lepidopteran pests. The major pest in Belgian pome fruit is the summer fruit tortrix moth, *Adoxophyes orana* F.v.R. Spinosad was active when it was sprayed on the hibernating generation (Figure 1) as well as on the summer generation (Figure 2). In the trial on hibernated caterpillars, 7 larvae were present on 150 shoots. No statistically significant differences were observed between the dose rates of 96, 144 and 280 g spinosad per ha. The addition of mineral oil caused a reduction of the effect. Spinosad was as effective as the reference compounds deltamethrin and tebufenozide for the control of caterpillars of *A. orana*. If compounds were sprayed when the eggs of the summer generation hatched, spinosad exerted a good control on this major pest. At 20 days after the first treatment, an odd result was monitored. Flufenoxuron, an Insect Growth Regulator and hence the compound with the slowest action, was most effective. However, differences between compounds were not statistically significant. At the second assessment at 14 days after the second treatment, the effect of all compounds had been increased. Spinosad at 144 g a.i./ha was as effective as the reference compounds flufenoxuron and cloropyriphos ethyl. Again, the addition of mineral oil did not improve the result of spinosad. Spinosad was significantly better as parathion ethyl, which might lack the persistence to control this pest sufficiently.

Excellent result was obtained with spinosad for the control of the winter moth, *Operophtera brumata* L., . All caterpillars of this pest were killed by a treatment of flufenoxuron before flowering (Results not shown). No difference could be observed between 108 and 144 g spinosad per ha. In this way, spinosad was superior to diflubenzuron, which killed 92.3 % of larvae of *O. brumata*.

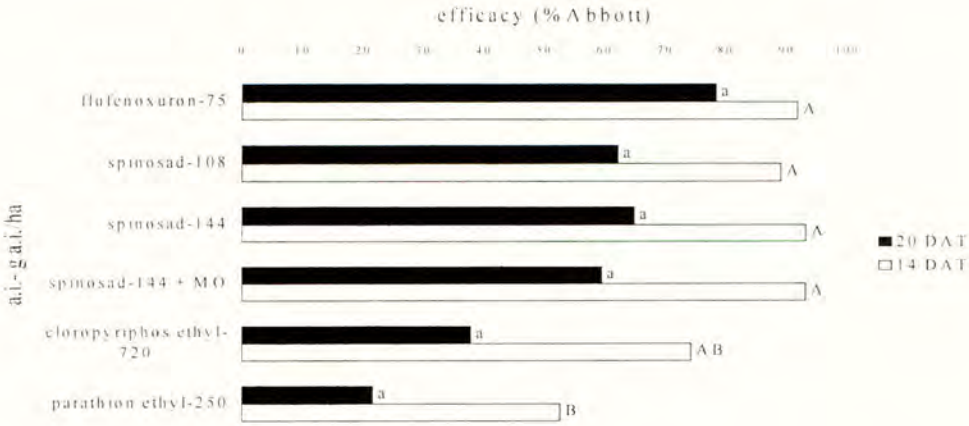

Figure 2. The control of the second summer generation of *Adoxophyes orana* by a repeated treatment of different insecticides. MO: mineral oil.

A laboratory test was executed to check the possibilities for the control of the codling moth, *Cydia pomonella* L. (Figure 3). After 4 days of exposure to adult moths between 17 and 45 eggs were deposited on five apples which were treated with the same compound. In the water treated control, 47.8 % of the eggs were leading to fruit damage at 14 days after egg deposit. This trial indicated good control by spinosad against this major pest, since 91.3 % of the eggs did not result in fruit penetration (if 20 l water per m² was applied). The same trial indicated also the resistance of the spinosad formulation to wash off. Only when 60 litre water per m² was applied, was a slight decrease of mortality observed. After this artificial rain shower 75.2 % of the deposited eggs did not result in fruit damage. This decrease in activity was much more pronounced for tebufenozide at 60 l/m². Diflubenzuron was very resistant for rain fall and did not show a decreased effect till 60 l/m². For unknown reasons, an inferior result of diflubenzuron at 20 l/m² was recorded compared to higher volumes of water.

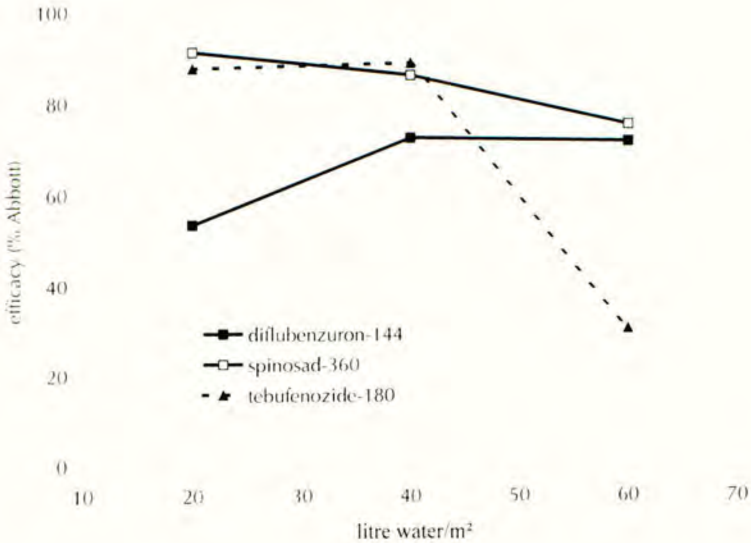

Figure 3. Laboratory test on the efficacy for control of *C. pomonella* after artificial rain fall (l/m²) on treated apples

The control of the pear sucker, *Psylla pyri* L.

In order to investigate the stage specificity of an eventual action of spinosad on *P. pyri*, a laboratory trial was executed (Figure 4). Treated shoots contained more than 40 eggs. Differences between timings of application were not statistically significant, but the larvicidal action of spinosad was superior to the ovicidal effect. Nevertheless, the effect of spinosad applied on eggs of not more than 4 days old, was slightly superior to the application on eggs that were ready to hatch (orange coloured and eyes of nymphs visible). The effect of amitraz was, as expected, slightly inferior on eggs compared to nymphs. Eggs close to hatching were more sensitive than newly deposited eggs. Differences between the two compounds or between different timings of a compound were not statistically significant. Because of the unexpected results on eggs, a specific trial was executed in which the number of empty egg scales was counted after application of spinosad on newly deposited eggs (Table 2). A clear ovicidal action was recorded but the effect was slightly inferior to the larvicidal one.

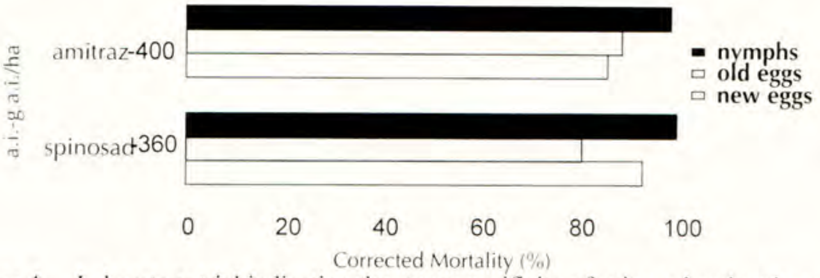

Figure 4. Laboratory trial indicating the stage specificity of spinosad and amitraz for *Psylla pyri*

Different field trials indicate that the effect on *P. pyri* is dose dependent (Figure 5). The results so far suggest that 288 g spinosad per ha controls this pest well if the compound is applied at massive hatching of the eggs of the first summer generation in early June.

Table 2: Percentage egg hatching, % nymphal survival and total effect at 7 DAT after spraying 240 ppm spinosad on shoots with newly deposited eggs of *P. pyri*. Efficacy is indicated between brackets as corrected percentage (Abbott, 1925).

Treatment	% egg hatching	% nymphal survival	Total effect
Water	63.6	100.0	
Spinosad	11.6 (81.7 %)	12.9 (87.1 %)	(97.6 %)

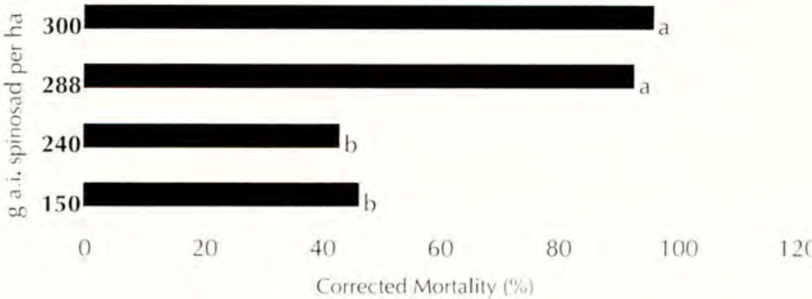

Figure 5. Average mortality of spinosad on *Psylla pyri* in different field trials

Side effects on beneficials

Spinosad was shown to be harmless for the predatory mite, *Typhlodromus pyri* Scheuten. Figure 6 indicates that the compound, applied at 360 g a.i./ha, does not interfere with the biological control of noxious mites by this phytoseiids in apple culture. The Henderson-

Tilton value (not indicated on the graph) was 6.3 % for spinosad whereas it was 78.5 % for the toxic reference compound methidathion at 6 days after treatment. At 21 days after treatment, the population of predatory mites had increased in the spinosad plot in comparison to the water treated control. Methidathion killed at that time 95.4 % of the beneficial mites. The non toxic reference compound pirimicarb was, like spinosad, harmless at both assessments, with a Henderson-Tilton value of 9.8 % and 13.3 %, respectively.

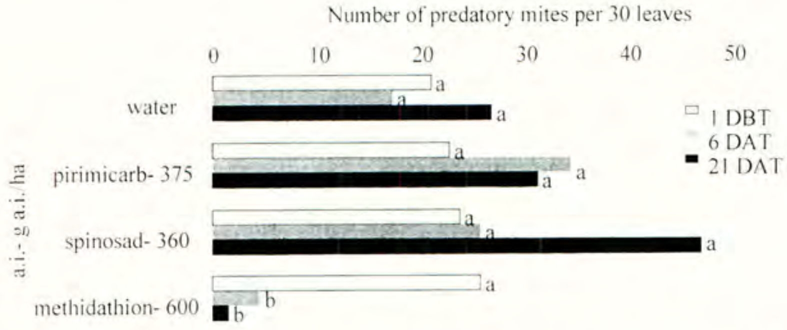

Figure 6. Number of mobile stages of *Typhlodromus pyri* after treatment of different insecticides (DBT: Days Before Treatment, DAT: Days After Treatment).

Spinosad did not influence the population of *Anthocoris* spp., which is a key predator in pear culture. At 6 days after treatment neither the number of nymphs nor the number of adult predatory bugs was reduced (Figure 7) significantly (14.9 % and 20.6 % Abbott on nymphs and adults, respectively). Since the number of nymphs at 21 days after treatment was too low to for statistical analysis, only the number of adults is indicated. A negligible effect of only 2.2 % of spinosad was calculated, indicating that the compound is harmless for predatory bugs. The addition of oil to spinosad did not have any effect on the absence of a side effect at both of the assessment dates. Cyfluthrin, which was used as a toxic reference compound reduced the number of nymphs and adults at the first assessment date with 91.2 % and 68.1 %, respectively. At the second assessment date, more adults were present in the cyfluthrin plot than in the water treated plot, although differences were not statistically significant. The non toxic reference compound, hexythiazox, was shown to be harmless at all assessments.

DISCUSSION

Laboratory and field trials indicated that spinosad might be an useful tool for the control of different important pests of pome fruit. Lepidopteran pests were very sensitive for this natural compound. *A. orana* and *C. pomonella* are most important and necessitate performing anti-resistance strategies (Bylemans, 1997b). The hibernated caterpillars of *A. orana* were very well controlled by spinosad if the number of caterpillars was counted after flowering. Whether this control is sufficient to avoid problems with the succeeding summer generations is still under investigation. Our work demonstrated that for the used reference compounds applied before flowering, differences in population development of this pest might occur if the pest pressure is high (Bylemans, 2000). Therefore large plot trials have to be executed with each compound, even if the result after flowering looks good. The control of the summer generation of *A. orana* by spinosad was excellent by a treatment at the moment of hatching. Using 108 g spinosad per ha, the winter moth was controlled well by a single treatment before flowering.

A laboratory trial on *C. pomonella* indicated that spinosad has a high intrinsic activity on this pest. For the exact determination of the dose rate, the timing and the spray interval further semi-field and field trials are being executed. In contrast to some other natural compounds, spinosad was only slightly affected for high volumes of rain-fall. This might indicate that the spray interval for the control of the codling moth will be comparable to the one of chemical compounds. Nevertheless, UV degradation of natural insecticides might be another import factor of breakdown.

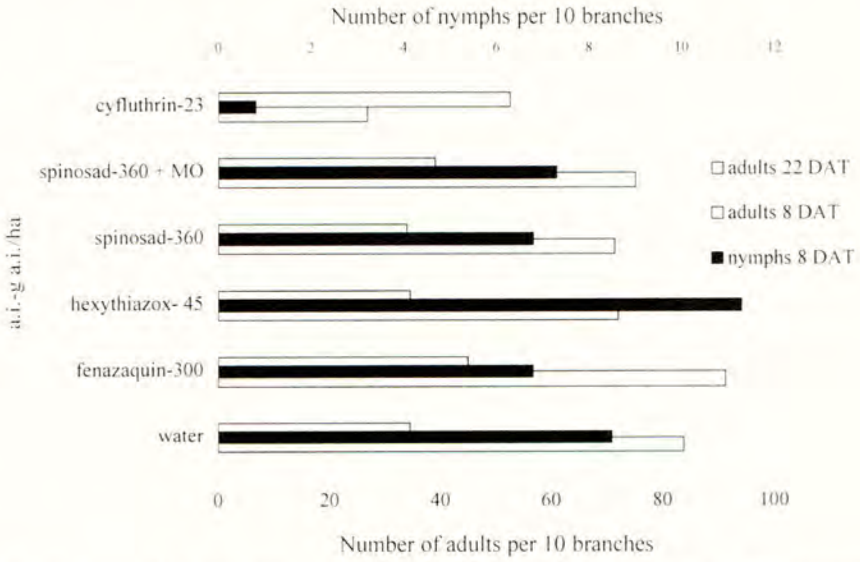

Figure 7. Mobile stages of nymphs and adults of *Anthocoris* spp. after treatment of

Unexpectedly, spinosad had a good activity on a hemipteran pest, *P. pyri*. This sucking insect is still of major importance in pear culture (Bylemans, 1996). Since spinosad has neither systemic nor substantial contact action, the reason for this good control still needs to be investigated. A laboratory trial indicated a higher effect on the nymphs but an ovicidal effect might be present since newly deposited eggs were slightly more sensitive than older eggs. The results on *P. pyri* in field experiments are strongly dose dependent. Good results are obtained from 288 g a.i. per ha onwards.

The addition of mineral oil never increased the results of spinosad in our experiments. According to the IOBC recommendations, spinosad is listed as low risk for the key beneficial insects in pome fruit (Hassan *et al.*, 1994). The use of 360 g spinosad per ha did not reduce the number of predatory mites, *T. pyri*, in apple neither did it have an effect on the number of predatory bugs in pear. These results indicate that the compound can be implemented in Integrated Pest Management, which is essential for both fruit crops. The effect on other beneficials, which are less essential for pome fruit, have to be considered but have to be balanced taking into account anti-resistance strategies (Miles and Dutton, 2000).

Different timing for spinosad treatments are possible for pome fruit. With a pre-flowering treatment, important pests like *A. orana* and *O. brumata* (probably besides many other caterpillar species) can be controlled at once. At the same time, the first nymphs of *P. pyri* are present in pear to reduce their effect on flower and fruit fall and on rusetting. Summer treatments are also likely to be included in the resistance management strategies. In summer, resurging *A. orana* can be controlled together with *C. pomonella*. At the same time in early June, most of the recent years a control of *P. pyri* is necessary (Bylemans, 1996). At none of these timings, were unwanted side effects observed on the key beneficials . Therefore, spinosad might become an interesting addition to the range of selective insecticides used in pome fruit.

ACKNOWLEDGEMENTS

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DBI-3204: A new benzoylphenyl urea insecticide with a particular activity against whitefly

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ABSTRACT

DBI-3204 (Bistrifluron, ISO proposed) is a new IGR insecticide of benzoylphenyl urea class. It is a highly active new insecticide that shows a good controlling effect against whiteflies and lepidopterous insect pests such as *Spodoptera exigua* (Noctuidae), *Plutella xylostella* (Yponomeutidae), *Stathmopoda masinissa* (Stathmopodidae) and *Phyllonorycter ringoniella* (Gracilariidae) at 75-400g a.i./ha. Many field trials show that DBI-3204 is particularly effective against *Trialeurodes vaporariorum* and *Bemisia tabaci*. It has good toxicological, environmental and eco-toxicological profiles. There is no cross-resistance to OP insecticides. Thus DBI-3204 will provide a good resistance management tool for resistant pests. There were no crop injuries to wide range of crops in many field trials. Dongbu Hannong Chemical Co Ltd is to commercialise DBI-3204 and conduct the official field trials to register it for the control of greenhouse whitefly, diamondback moth, beet armyworm and apple leaf miner as a 10% SC formulation in Korea.

INTRODUCTION

Benzoylphenyl urea insecticides have a good reputation for having a low impact on the environment, wild life, beneficial insects and humans. With their unique mode of action, benzoylphenyl urea insecticides act as insect growth regulators (IGR), which lead to insect pest death through the inhibition of chitin synthesis (Nakagawa *et al.*, 1992).

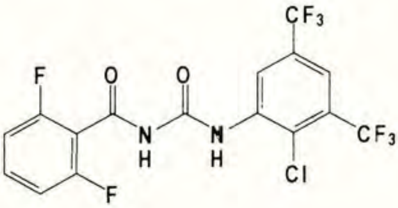
DBI-3204 is a new IGR insecticide of the benzoylphenyl urea class. From synthesis of 2000 derivatives of benzoylphenyl ureas, DBI-3204 was selected as it has good toxicological and biological properties, and interesting efficacy against whiteflies which have become serious pest in greenhouses on many crops.

DBI-3204 is under development by Dongbu Hannong Chemical Co Ltd as 10% SC and 10% EC formulations.

This paper describes the properties and performance of the DBI-3204 under laboratory and field conditions.

CHEMICAL AND PHYSICAL PROPERTIES

Chemical Structure



Code number	DBI-3204
Chemical name	N-(2-Chloro-3,5-bis-(trifluoromethyl)phenyl)-N'-(2,6-difluorobenzoyl) urea
Empirical Formula	$C_{16}H_7ClF_8N_2O_2$
Chemical class	Benzoylphenyl urea
Common name	Bistrifluron (ISO proposed)
Molecular weight	396.68
Colour and state	White powder
Melting point	172-175
Log Kow	5.74
Vapour Pressure	2.7×10^{-8}mbar
Solubility	in water <0.03 mg/litre, 25 acetone >500 mg/litre, 25 dichloromethane 105mg/litre, 25
Stability	stable at room temperature and pH 5 ~ 9

TOXICOLOGY

Acute Oral LD_{50}, Rat	> 5,000mg/kg (male, female)
Acute Dermal LD_{50}, Rat	>2,000mg/kg (male, female)
Subchronic oral (13 weeks), NOEL	60mg/kg (male, female)
Bacterial Reverse Mutation Study (Ames test)	Negative
Chromosomal aberration study	Negative
Micronucleus test	Negative
Teratogenicity (Rat), NOEL	>1,000mg/kg
Cyprinus carpio (carp), LC_{50} (48hr)	>0.5mg/litre
Oryzias latipes (cyprinodont), LC_{50} (48hr)	>10mg/litre
Bee, LD_{50} (48hr)	>100 μg a.i./bee

BIOLOGICAL PROPERTIES

Laboratory evaluation

DBI-3204 has insecticidal activity against various species of lepidopterous insects, stinkbug and beetle under laboratory conditions. The activity of DBI-3204 is presented in Table 3.

Table 3. Activity of DBI-3204

Insect	LC_{50}/LD_{50}	Method
Plutella xyolstella (2nd larva)	0.22 μg/ml	leaf dipping
Spodoptera litura (2nd larva)	0.02 μg/ml	leaf dipping
Spodoptera exigua (2nd larva)	0.07 μg/ml	leaf dipping
Artogeia rapae (2nd larva)	0.37 μg/ml	leaf dipping
Helicoverpa assulta (2nd larva)	0.7 μg/ml	leaf dipping
Hypnatria cunea (2nd larva)	0.82 μg/ml	leaf dipping
Pseudaletia separata (2nd larva)	0.66 μg/ml	leaf dipping
Palpita indica (3rd larva)	<0.01 μg/ml	leaf dipping
Hellula undalis (3rd larva)	3.6 μg/ml	leaf dipping
Adoxophyes orana (larva)	3.5 μg/ml	leaf dipping
Trialeurodes vaporariorum (3rd nymph)	<1 μg/ml	spray
Eurydema rugosa (5th nymph)	13.6 μg/g	topical application - μg/g insect
Corythucha ciliata (3rd larva)	51.1 μg/ml	spray
Riptortus clavatus (5th larva)	0.26 μg/g	topical application - as above
Epilachna vigintioctomaculata (3rd larva)	1.3 μg/ml	leaf dipping
Musca domestica (3rd larva)	38.0 μg/g	artificial diet - μg/g artificial diet
Culex pipiens pallens (3rd larva)	0.07 μg/ml	immersion test
Blattella germanica (2nd larva)	0.25 μg/g	topical application -as above

Efficacy against resistant insects

Table 4. Resistance factors (Rf) of DBI-3204 against OP insecticide resistant strain of *Plutella xylostella*

Compound	LC_{50} of Resistant strain (μg/ml)	LC_{50} of Susceptible strain (μg/ml)	Rf
Prothiofos	99.7	0.89	112.0
DBI-3204	1.20	0.16	7.5

Field evaluation

Many field trials were carried out in vegetable and fruit crops.

DBI-3204 was proven to be highly active against lepidopterous insects (*Spodoptera exigua* (Figure 1) and *Plutella xylostella* (Figure 2) at 75-150g a.i./ha in comparison with other commercial standards. DBI-3204 shows particular activity against *Trialeurodes vaporariorum* at 50-100g a.i./ha (Figure 3).

Chinese cabbage

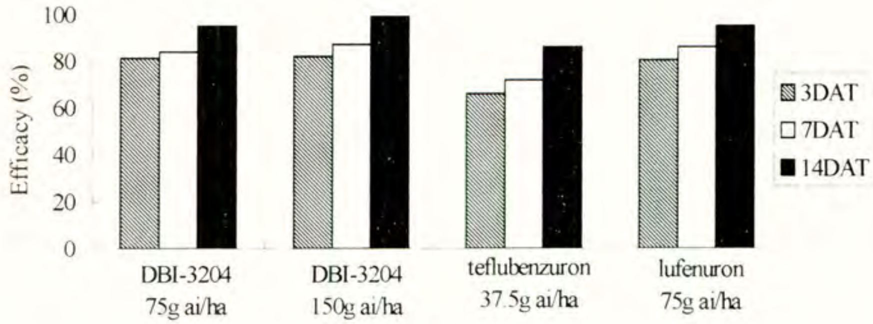


Figure 1. Efficacy of DBI-3204 10% SC against *Spodoptera exigua* on Chinese cabbage by foliar spraying (Korea, 1999)

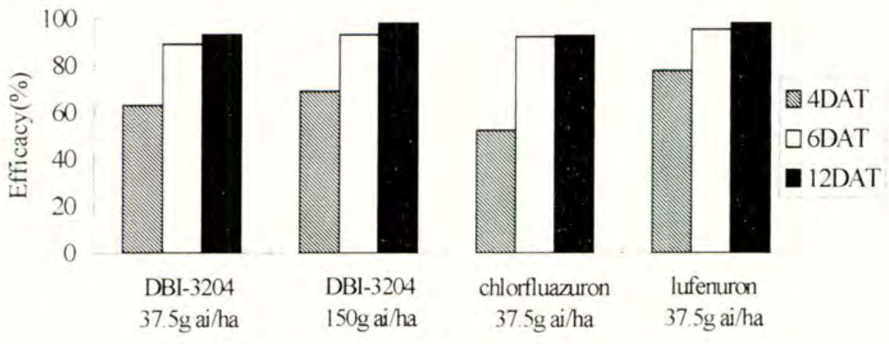


Figure 2. Efficacy of DBI-3204 10% SC against *Plutella xylostella* on Chinese cabbage by foliar spraying (Korea, 1999)

Tomato

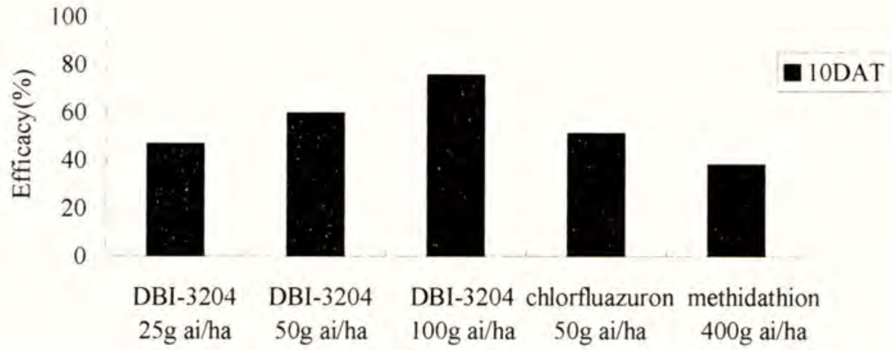


Figure 3. Efficacy of DBI-3204 against *Trialeurodes vaporariorum* in tomato by 2-times foliar spraying at 10-day application intervals (Korea, 1999)

In fruit trees, DBI-3204 showed a good effect on *Phyllonorycter ringoniella* in apple trees at 100-400g a.i./ha (Figure 4), and *Stathmopoda masinissa* in persimmon trees at 200-400g a.i./ha (Figure 5).

Apple

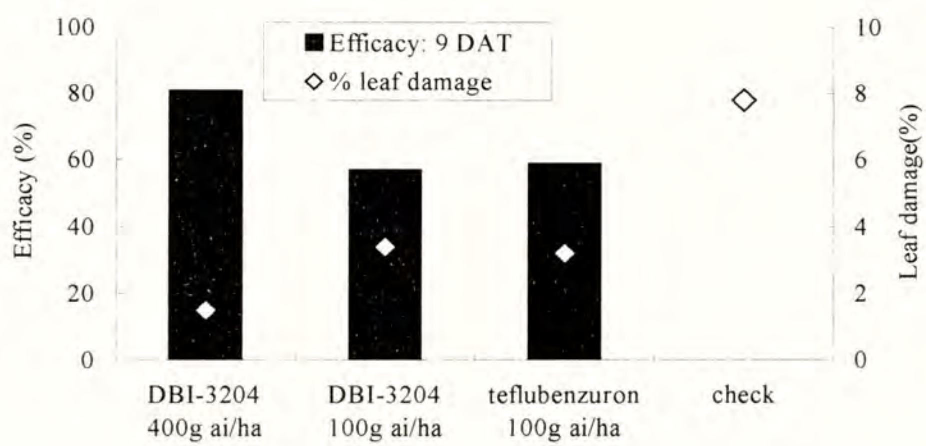


Figure 4. Efficacy of DBI-3204 against *Phyllonorycter ringoniella* in apple by 2-times foliar spraying at 10-day application intervals (Korea, 1998)

Persimmon

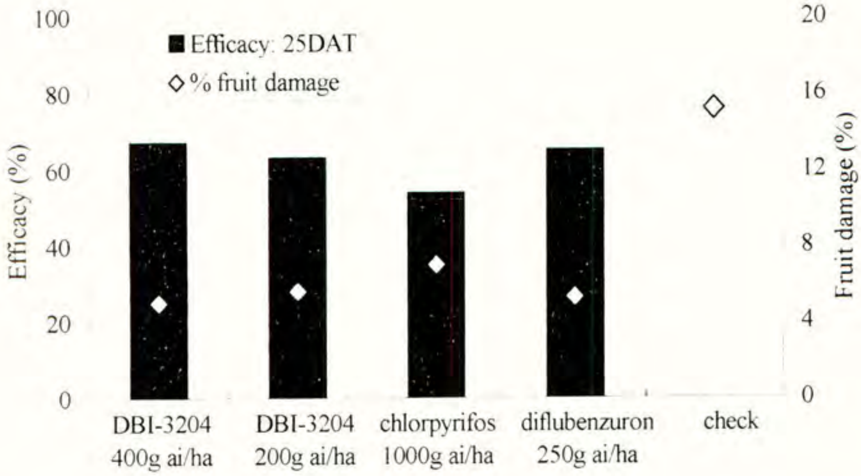


Figure 5. Efficacy of DBI-3204 against *Stathmopoda masinissa* in persimmon by 2-times foliar spraying at 10-day application intervals (Korea, 1999)

DISCUSSION

From laboratory test, DBI-3204 showed good efficacy against a wide spectrum of pest insects. In field trials DBI-3204 is a highly active against lepidopterous insects at 75 - 150g a.i./ha in vegetables, and at 100 - 400g a.i./ha in fruit trees. It also has a good efficacy against whiteflies at 50-100g a.i./ha.

With a good toxicological and ecotoxicological profile, it is suggested that DBI-3204 would be a valuable compound for crop protection.

ACKNOWLEDGEMENTS

The authors thank all of their colleagues who have contributed to research and development of DBI-3204.

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Bacillus firmus formulations for the safe control of root-knot nematodes

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ABSTRACT

Two new bionematicides based on an isolate of the non-pathogenic bacterium *Bacillus firmus* and formulated with non-toxic additives. *In vitro* experiments showed that there is a direct effect of the bacterium on the nematodes. The bionematicides were tested in pot experiments as well as on commercial cucumber and tomato plots infested with root-knot nematodes. One product reduced disease levels from a galling index of 4–5 to less than 2, comparable or better than that observed following an application of cadusafos (Rugby). Its use following an application of dazomet (Basamid) controlled nematodes as effectively as an application of methyl bromide. In trials, a second product, specially formulated for organic farming, was as effective as the first.

INTRODUCTION

Nematodes cause severe damage to a wide range of commercial crops. An estimated $500 million is spent annually on nematode control, with methyl bromide accounting for about half this figure. The root-knot nematodes (*Meloidogyne* spp.) have the widest host range and are responsible for the majority of the crop losses. Spending most of their life cycle within the plant, these nematodes are relatively insensitive to most pesticides. Global concerns about the effects of methyl bromide have led to a forced phase-out by the year 2005 and have heightened the need for environmentally safe alternatives for controlling nematodes (Noling & Becker, 1994). BioNem (for conventional farming) and BioSafe (for organic farming) are two such nematicides based on the bacterium *Bacillus firmus* (DSM Laboratories) which have been shown to be effective in the control of *Meloidogyne* spp. in a variety of commercial crops. They are described below as products A and B, respectively.

MATERIALS AND METHODS

A bacterial isolate (N1) was isolated from cultivated soil in Israel and identified as *Bacillus firmus* based on a biochemical characterisation and by DNA analysis at DSM Laboratories, Braunschweig, Germany.

Both products are biological nematicides manufactured by the Biological Division of Minrav, Ashdod, Israel, and are powder formulations based on the N1 isolate of *B. firmus*.

(a) Efficacy under laboratory conditions: Nematode infested soil (2 juveniles/g soil) was mixed with product A and incubated in closed containers for 20 days. Counts of viable juveniles were made using the Baerman funnel method.

(b) Greenhouse pot experiments: Nematode infested soil (0.7 juveniles/g soil, *Meloidogyne javanica*) was mixed with product A (0.2% w/w). Tomato seedlings were planted in pots (12 cm diameter, 5 replicates) filled with the treated soil. Nematode infection was assessed 30 days following transplanting. Plants were uprooted, washed and assigned a Galling Index (GI) of 0 (= no galls) to 5 (= entire root covered with galls).

(c) Field trials with product A on tomatoes: Trials were carried out over several growing seasons in commercial plots of tomato at sites naturally infested with root-knot nematodes (primarily *Meloidogyne javanica*). A randomised block design was used with 5 replicates, each 7 m long. Product A (a formulation containing 3×10^9 spores per g) was applied to the planting furrow several days prior to planting at 70 g/m furrow (approximately 500 kg/ha, depending on row spacing). The material was incorporated into the soil by rotavation (10–20 cm deep) and activated by irrigation. Tomato seedlings (Hishteel, Israel) were dipped in tolclofos methyl (Rizolex) and propamocarb (Dynone) solution (0.01%) prior to planting. Cadusofos (Rugby) was applied according to manufacturer's instructions. Nematode infestation was assessed at times indicated in the relevant figures. Five plants from each plot were uprooted, washed and assigned a galling index (GI) of 0 (i.e. no galls) to 5 (i.e. entire root covered with galls). A galling index up to 2 is commercially acceptable.

Data analysis: Analysis of variance was used for analysing treatment effect, and was followed by Student's t test, where the ANOVA showed a significant F statistic for treatment. Results followed by the same letter do not differ significantly ($p > 0.05$, Student's t test).

(d) Field trials with product B on tomatoes. Trials were carried out with product B on tomatoes grown on sandy soil under organic farming conditions. Application was as for product A but at 150 g/m of furrow. Counts of viable juveniles in soil samples taken from the field were determined using the Baerman funnel method.

(e) Comparison of efficacy of products A and B in Cucumber field. A trial was conducted in which formulations of both products were applied in a commercial greenhouse. Nematode infection was assessed 50 days after transplanting.

(f) Combined treatment of product A with dazomet. A trial was carried out in a commercial greenhouse (sandy loam soil) in which the soil was either fumigated with methyl bromide according to manufacturer's instructions, treated with dazomet (Basamid) at 45 g/m^2 and incorporated into wet soil by rotavation (about 20 cm deep) three weeks prior to planting, treated with product A alone (as in (c)), or treated with dazomet and then with product A as above. The plots (plot was three rows of plants width) were then planted with cucumber seedlings. Galling index was determined after 75 days, and crop yield was measured over a three-week period.

RESULTS AND DISCUSSION

Biological activity of product A

Treatment of nematode-infested soil under laboratory conditions resulted in a rapid decline in juvenile populations of *Meloidogyne* spp. (Figure 1). Under these conditions there is a gradual loss in juvenile viability in untreated soil.

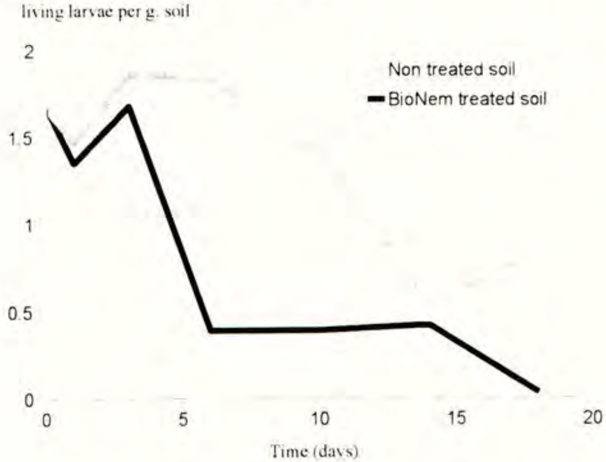

Figure 1. The effect of product A on the viability of root knot nematode

Monitoring of the nematode population in soil taken from a tomato field treated with product B also showed a consistent control of the juvenile population (Figure 2)

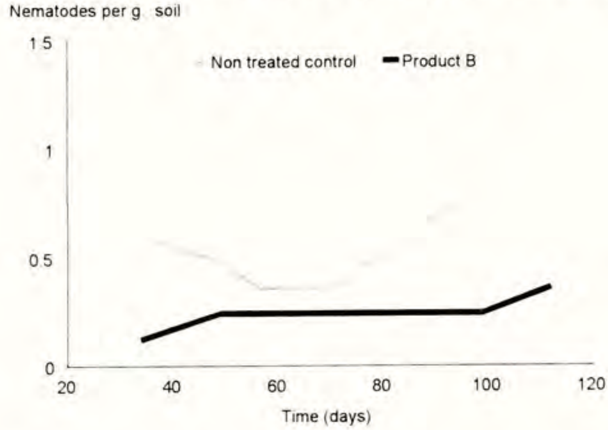

Figure 2. The effect of product B on larval root knot nematodes in a treated tomato field

Microscopic examination of egg sacs isolated from treated tomato roots showed colonisation of the egg sacs by the bacteria and destruction of the eggs (Figure 3).

It is suggested that the observed decline in juvenile viability in soil treated with product A under laboratory conditions is due, at least in part, to the destruction of nematode eggs by the bacteria.

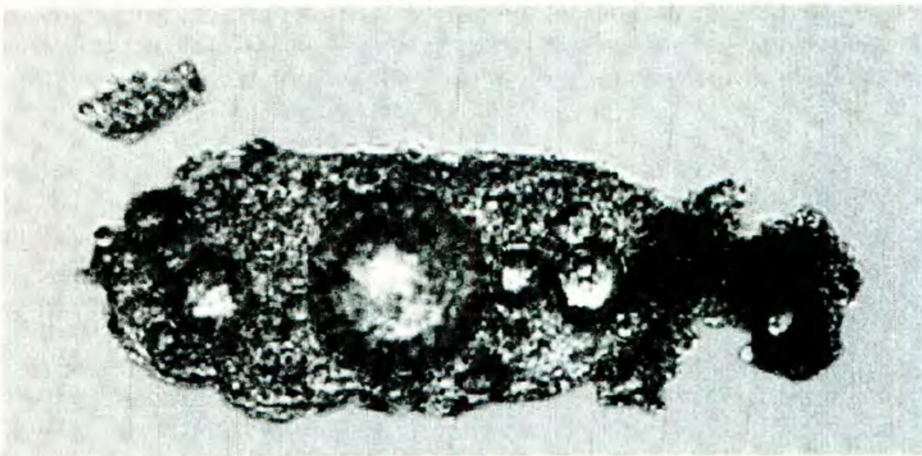

Figure 3. The effect of product A on a nematode egg

Field Performance

The results of field trials with tomatoes growing on sandy loam soil are summarised in Figure 4.

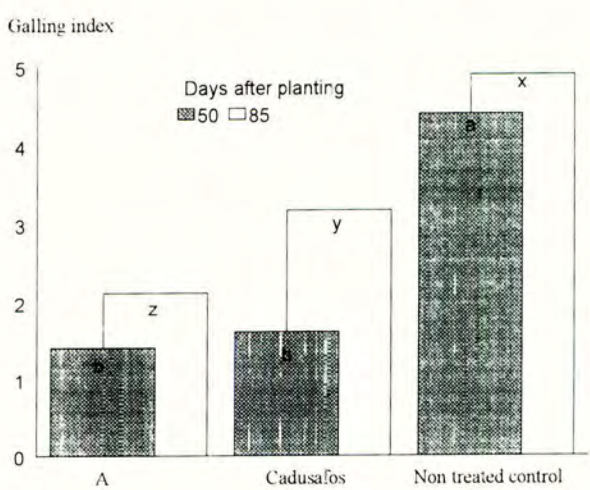

Figure 4 Control of root-knot nematodes in tomatoes using product A.

Galling index assessment 50 days after planting showed that product A and cadusofos protected the tomato plants from nematode infection. A second assessment 85 days after planting indicated that treatment with product A was still effective in reducing galling to below economic threshold. At the same time, low but economically significant infection was observed following the chemical treatment.

A trial using product B, a formulation incorporating the same nematicidal isolate as product A but suitable for use in organic farming, demonstrated that it was as effective as product A in controlling nematodes in cucumbers grown in sandy loam soil in a commercial greenhouse (Figure 5).

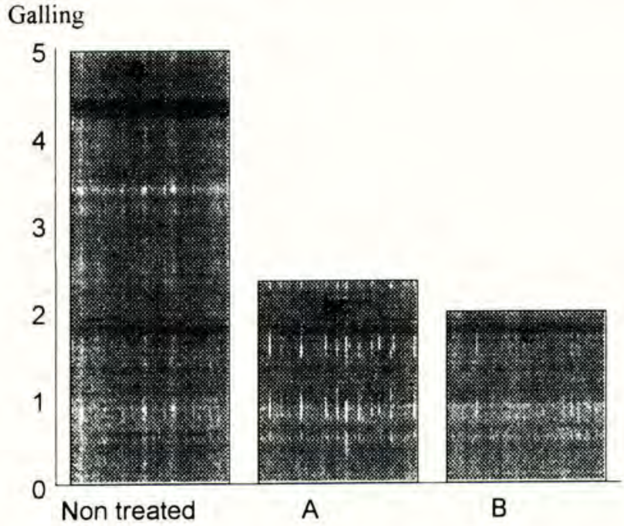

Figure 5 Control of root knot nematodes in cucumbers using products A and B

Incorporation of product A in IPM programmes

In most instances, commercial horticultural plots suffer from fungal root diseases and the common practice of methyl bromide fumigation has provided effective control of these pathogens along with nematode control. Nematode control must be accompanied by fungal disease control to achieve a comprehensive solution to soil-borne diseases (Shephred, 1988). Product A has been shown to be compatible with the use of both propamocarb (Dynone) and tolclofos-methyl (Rizolex) (results not shown) enabling their use for the control of soil pathogens in fields treated with product A. As product A is based on living bacteria it is sensitive to common methods of soil disinfection (heat or fumigation). However, it can be used following such methods. Figure 6 shows a comparison between galling indices and yield of cucumbers obtained following the use of methyl bromide fumigation, dazomet treatment with and without subsequent application of product A, and treatment with product B alone in a commercial greenhouse conditions.

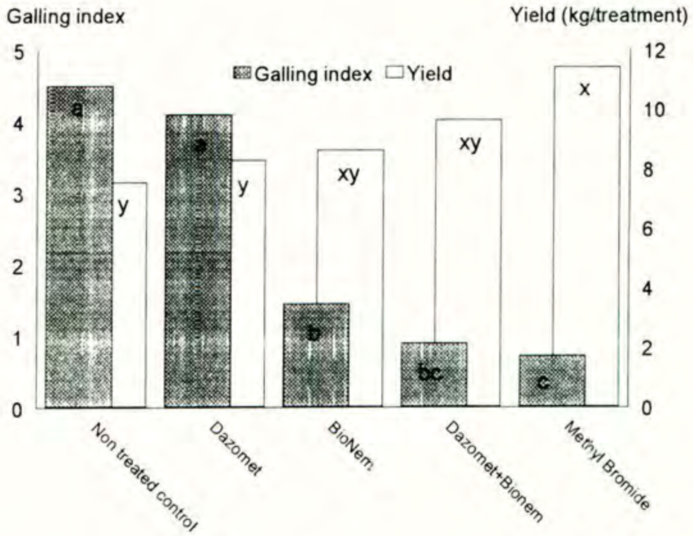

Figure 6. Comparison of treatments for control of root knot nematodes in cucumbers. This trial was performed in cooperation with DSBG, Beer-Sheva, Israel.

Dazomet alone had no noticeable effect on nematode infection. Product A alone lowered the nematode infection to below the economically significant level (Galling Index = 2), but the product A-dazomet combination was somewhat more effective than product A alone. Control level in the combined treatment was comparable to that obtained by methyl bromide fumigation (Figure 6).

CONCLUSIONS

1. Both products are effective pesticides against root-knot nematodes (*Meloidogyne* spp.).
2. Control with product A is probably achieved by affecting egg viability.
3. Product A can be used with dazomet in IPM programmes designed to replace methyl bromide as a soil sterilant.

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BAJ2740, a novel broad spectrum acaricide

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ABSTRACT

BAJ2740 (proposed common name: spirodiclofen) is a novel acaricide from the new chemical class of tetronic acids. The compound provides excellent control of important mite pests such as *Panonychus spp.*, *Phyllocoptruta spp.*, *Brevipalpus spp.*, and *Aculus* and *Tetranychus* species. Use rates range from 50 to 200g a.i./1000 litres. It shows no cross-resistance to currently available acaricides and although the mode of action is still under investigation, there is strong evidence that the compound interferes with the mite development. Therefore the onset of activity of BAJ2740 is somewhat slower compared to that of acutely acting acaricides but significantly faster than that of chitin synthesis inhibitors. The residual efficacy of BAJ2740 is outstanding. The compound has no impact on beneficial insects and is safe or only slightly harmful to beneficial mites depending on the use pattern. BAJ2740 is safe to users and consumers and has a favourable environmental profile. Its broad spectrum of activity, excellent long lasting efficacy, good plant compatibility in all relevant crops and lack of cross-resistance make BAJ2740 an excellent compound for the use in the most important markets for specific acaricides, e.g. citrus, pome fruits, stone fruits, grapes and nuts.

INTRODUCTION

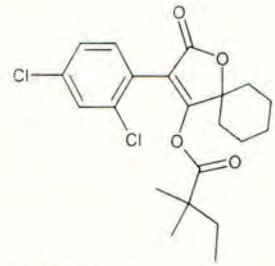
BAJ2740 was selected as the most effective compound from the newly discovered acaricidal group of tetronic acids. It is currently under development as a promising new acaricide for citrus, pome fruits, stone fruits, grapes and nuts. BAJ2740 will be registered world wide under the proposed brand name Envidor® 240SC as the basic formulation. Market introduction is expected for Japan, Europe and the US between the years 2002 and 2004.

In this paper the technical properties and the toxicological and environmental behaviour of BAJ2740 will be presented as well as the miticidal activities under greenhouse and field conditions.

CHEMICAL AND PHYSICAL PROPERTIES

Common name (ISO proposed):	spirodiclofen
Chemical name (IUPAC):	3-(2,4-dichlorophenyl)-2-oxo-1-oxaspiro[4.5] dec-3-en-4-yl 2,2-dimethylbutyrate
CAS RN:	148477-71-8

Structural formula:



Empirical formula:	$C_{21}H_{24}Cl_2O_4$
Molecular weight:	411.3 g/mol
Appearance:	white powder

HUMAN SAFETY

Acute oral LD_{50}, rate:	> 2500 mg/kg b.w. (males/females)
Acute dermal LD_{50} (24h), rat:	> 2000 mg/kg b.w. (males/females)
Acute inhalation LC_{50} (4h), rat:	> 5000 mg/m^3
Skin irritation (4h), rabbit:	non-irritant
Eye irritation (24h), rabbit:	non-irritant
Skin sensitisation, guinea pig:	non-irritant (240SC formulation)
Chronic toxicity (12 months), dogs:	NOAEL 50 ppm
Developmental toxicity:	no teratogenic potential (rats and rabbits), 2-generation rat study revealed no evidence of a primary reprotoxic potential
Genotoxicity:	no evidence of genotoxic or mutagenic potential

ENVIRONMENTAL SAFETY

Fish, LC_{50} (96h):	> 68 mg a.i./l (240SC)
Daphnia magna, EC_{50} (48h):	> 100 mg a.i./l (240SC) at 20°C
Birds, acute toxicity LD50:	> 2000 mg/kg
Earth worms, *Eisenia foetida*:	> 1000 mg/kg of dry weight soil
Honeybee LD50 oral:	non-toxic (>300µg/bee)
contact:	non-toxic (>300µg/bee)
Ladybirds, *Coccinella septempunctata*:	non-toxic at 300g a.i./ha
Predatory mites:	slightly harmful (field conditions, 240SC)

ENVIRONMENTAL FATE

Soil degradation, DT_{50}:	0.5-5.5 days
Soil mobility:	no leaching problems (lysimeter study)

Solubility in water (pH 4):	50µg/L at 20°C
Partition coefficient n-octanol/water (log Pow):	5.8 (pH4) at 20°C
Vapour pressure:	3 x 10^{-7} Pa at 20°C
Microbial mineralisation:	no negative effect

FORMULATIONS

BAJ2740 will be formulated as a 240SC (suspension concentrate). For Japan an additional dust-free 38% water dispersible granule (WG) is under development. The formulations show good compatibility with conventional crop protection products.

BIOLOGICAL PROFILE

Acaricidal spectrum

BAJ2740 shows high activity on phytophagous mites, such as *Panonychus*, *Tetranychus*, *Phyllocoptruta*, *Brevipalpus* and *Aculus* species. The compound is particularly active against eggs, larvae, nymphs and quiescent stages, but slightly less active against adults (Nauen & Stumpf & Elbert, 2000).

Activity under greenhouse conditions

The response of BAJ2740 to larvae of *Tetranychus urticae* was measured in comparison to different commercial acaricides. All acaricides used were of technical grade of the highest purity available with the exception of abamectin which was used as an EC-formulated material (Vertimec®). When applied to leaves infested with *T. urticae* larvae BAJ2740 sprayed to run-off on French beans showed excellent activity with an LC50 value of 0.1ppm (Figure 1).

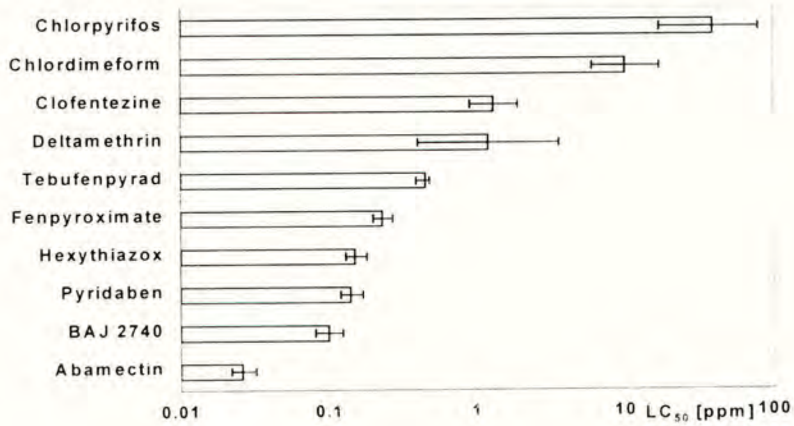


Figure 1. Comparative activity of BAJ2740 and commercial acaricides as contact treatment to *T. urticae* larvae 7 days after treatment.

Field performance

The biological activity of BAJ2740 240SC against phytophagous mites in economically important crops was evaluated in field tests in different countries under varying local spray regimes and under different climatic conditions.

Table 1. Efficacy (%) of BAJ2740 against *Tetranychus urticae* in apples (5 field trials; Japan 1996-1999)

	Application rate g a.i./1000L	Days after treatment 3-4	10-12	19-20	29-32	49-50	57-60
untreated	-	(7)	(15)	(15)	(22)	(15)	(6)
etoxazole	50	1	79	93	94	72	2
acequinocyl	150	84	96	91	76	38	0
BAJ2740	200	45	90	95	93	84	50

Untreated = number of mites/leaf

Table 2. Efficacy (%) of BAJ2740 against *Aculus schlechtendali* in apples (4 field trials; US 1994-1996)

	Application rate g a.i./1000L	Days after treatment 7	14	21	28	35	42
untreated	-	(18)	(30)	(32)	(25)	(21)	(37)
propargite	500	92	93	96	96	82	63
BAJ2740	50	95	94	96	98	87	98

Untreated = number of mites/leaf

Table 3. Efficacy (%) of BAJ2740 against *Brevipalpus phoenicis* in citrus (8 field trials; Brazil 1995-1998)

	Application rate g a.i./1000L	Days after treatment 6-8	14-16	30-44	59-72	91-112	128-132
untreated	-	(11)	(8)	(10)	(12)	(22)	(33)
hexythiazox	15	68	84	95	95	99	98
BAJ2740	48	93	98	96	92	99	100
BAJ2740	96	95	100	98	96	99	100

Untreated = number of mites/fruit

Table 4. Efficacy (%) of BAJ2740 against *Panonychus citri* in citrus (4 field trials; Japan 1996-1997)

	Application rate g a.i./1000L	Days after treatment 3-4	7	14	21	27-31	38-42	49
untreated	-	(10)	(32)	(162)	(114)	(113)	(5)	(57)
pyridaben	100	99	99	99	99	98	88	75
BAJ2740	75	88	98	100	99	99	99	99

Untreated = number of mites/leaf

Table 5. Efficacy (%) of BAJ2740 against *Panonychus ulmi* in grapes (3field trials: Germany, Italy 1994-1996)

	Application rate g a.i./1000L	Days after treatment 5-7	15-18	23-25	36	44-49
untreated	-	(16)	(45)	(70)	(38)	(44)
hexythiazox	50	89	86	98	90	91
BAJ2740	72	99	96	98	96	92

Untreated = number of mites/leaf

Tables 1-5 demonstrate the excellent efficacy of BAJ2740 against *Tetranychus urticae*, *Aculus schlechtendali*, *Brevipalpus phoenicis* and *Panonychus citri* and *ulmi* in pome fruit, citrus and grapes. The initial activity of BAJ2740 is slightly weaker compared to fast acting acaricides like acequinocyl (AKD2023) or pyridaben but significantly faster than that of hexythiazox or etoxazole. The residual efficacy in all trials was outstanding (6 weeks and more) combined with a very good plant compatibility.

Effect on beneficial organisms

BAJ2740 had no negative effect on beneficial insects but was slightly harmful to predatory mites under field conditions (Figure 2). When sprayed early in the season e.g. against *P. ulmi* in apple at 50% egg hatch BAJ2740 showed little or no impact on predatory mites.

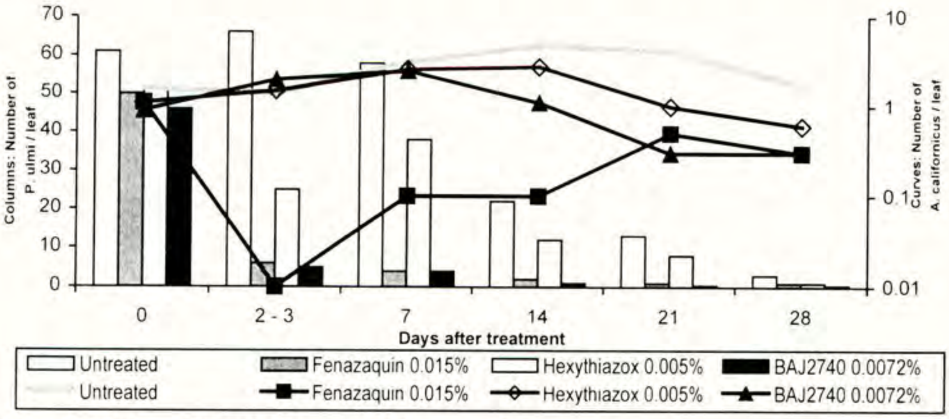


Figure 2. Effect of BAJ2740 on *Amblyseius californicus* and *Panonychus ulmi* on apples (3 field trials, France 1996-1997)

Activity against resistant strains

At present the biochemical mode of action of BAJ2740 is still under investigation, but the compound has no effect on known insecticidal or acaricidal biochemical targets. Many established acaricides encounter resistance problems in several countries (Voss, 1988, Knowles, 1997). BAJ2740 is not cross-resistant to conventional acaricides, such as METI (Mitochondrial Electron Transport Inhibitors) acaricides like pyridaben (Figure 3).

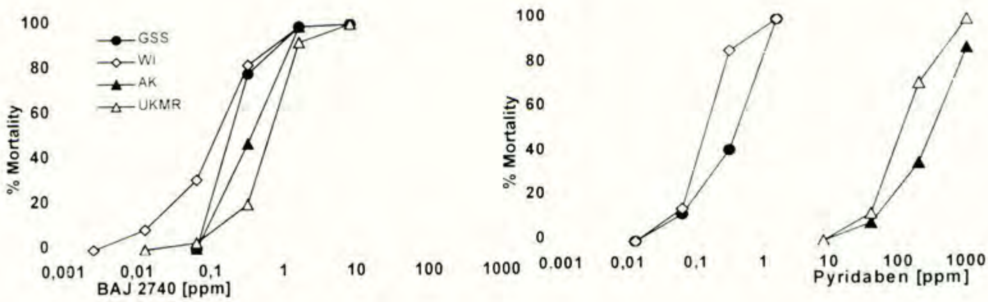


Figure 3. Efficacy of BAJ2740 and pyridaben against 4 different *T. urticae* strains with moderate to strong resistance to METI acaricides (GSS Germany/bean, lab.strain; WI Germany/cucumber, lab.strains susceptible reference; AK Japan/ornamentals, field strain; UKMR UK/hop, field strain)

Its potency against mites resistant to existing acaricides offers a powerful tool for pest management in a variety of crops. Following the IRAC guidelines to avoid development of mite resistance only one application per season is recommended.

CONCLUSIONS

BAJ2740 is a new acaricide which exhibits an excellent activity against a broad range of economically important mite pests combined with a very good plant compatibility. Belonging to a new chemical group it is characterised by a new mode of action and has no cross-resistance to any other commercially available acaricide. This is particularly important in view of the widespread reduced sensitivity of many field populations to existing acaricides. Consequently, BAJ2740 will become a very valuable tool for the use in important markets for specific acaricides.

ACKNOWLEDGEMENTS

The authors would like to thank all colleagues who contributed to the world-wide development of BAJ 2740.

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IKI-220 - A novel systemic aphicide

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ABSTRACT

IKI-220 is a novel selective systemic aphicide discovered and now under world-wide development by Ishihara Sangyo Kaisha, Ltd. This compound is very active against aphids, and also effective against some other species of sucking insects. IKI-220 rapidly inhibits the feeding behaviour of aphids, and provides long lasting aphid control. IKI-220 shows no cross-resistance with conventional insecticides and exhibits excellent systemic and translaminar activity. In field studies, IKI-220 has exhibited excellent performance for the control of various aphid species in fruits, cereals, potatoes, cotton and vegetables at 50-100 g a.i./ha. In trials on a wide variety of crops IKI-220 has shown no phytotoxicity at rates well in excess of the proposed field use rates. IKI-220 has no negative impact on beneficial insects and mites, and therefore it can be recommended for integrated pest management programs. It has a favourable toxicological, environmental and ecotoxicological profile.

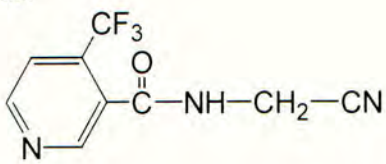
INTRODUCTION

While conducting research on trifluoromethylpyridine derivatives, we discovered that some trifluoromethylnicotinamides were effective in controlling aphids. Out of a large number of synthesised analogues *N*-cyanomethyl-4-trifluoromethylnicotinamide (IKI-220), was selected as a candidate for commercial development, based on its insecticidal activity and its environmental profile. This novel aphicide is being developed as a foliar treatment for use on potatoes, cereals, cotton, pome fruits, stone fruits and vegetables. This is the first report describing the properties and field performance of IKI-220 against some major species of aphid pests.

PHYSICOCHEMICAL PROPERTIES

Code number:	IKI-220
Chemical name (IUPAC):	*N*-cyanomethyl-4-trifluoromethyl-nicotinamide

Structural formula:



Molecular formula:	$C_9H_6F_3N_3O$
Molecular weight:	229.16
Appearance:	White crystalline powder, odourless
Water Solubility:	5.2 g/litre (20°C)
Melting Point:	157.5°C
Vapour pressure:	9.43×10^{-7} Pa (20°C)
Partition coefficient (Log P_{OW}):	0.30
Formulations:	10 WG, 50 WG

PRODUCT SAFETY

Toxicology

Acute oral LD_{50}, Rat male:	884 mg/kg
Rat female:	*1768 mg/kg*
Acute dermal LD_{50}, Rat:	>5000 mg/kg
Acute inhalation LD_{50}, Rat:	>4900 mg/m^3
Eye irritation, Rabbit:	*Non-irritant*
Skin irritation, Rabbit:	Non-irritant
Skin sensitisation, Guinea pig:	*Non-sensitising*
Mutagenicity:	Ames negative

Ecotoxicology

Carp LC_{50} (96hr):	>100 mg/litre
Rainbow trout LC_{50} (96hr):	>91.9 mg/litre
Daphnia magna EC_{50} (48hr):	>100 mg/litre
Algal growth inhibition EC_{50} (72hr):	>91.9 mg/litre

Environmental Fate

Soil degradation DT_{50}:	< 3 days
Predicted ground water concentration:	< 0.1 □g/litre (PELMO modelling)

BIOLOGICAL PROPERTIES

Insecticidal spectrum

IKI-220 is a highly selective aphicide. It does not control coleopteran, lepidopteran, dipteran insects, and mites (Table 1). It is effective against both larval and adult stages of aphids. At the recommended doses under field conditions (50-100 g a.i./ha or 2.5-10 g a.i./100 litres), IKI-220 has been successfully tested against a broad range of aphid species and some other species of sucking insects such as greenhouse whitefly (*Trialeurodes vaporariorum*), yellow tea thrips (*Scirtothrips dorsalis*), tea green leafhopper (*Empoasca onukii*), and brown rice planthopper (*Nilaparvata lugens*).

Mode of action

Table 1. Insecticidal spectrum of IKI-220 under laboratory conditions.

Pest	Stage*	Order	LC_{50} values (mg a.i./litre)
Myzus persicae (green peach aphid)	L2	Homoptera	0.8
Spodoptera litura (common cutworm)	L2	Lepidoptera	>800
Aulacophra femoralis (cucurbit leaf beetle)	A	Coleoptera	>800
Musca domestica (house fly)	L1	Diptera	>800
Tetranychus urticae (two-spotted spider mite)	A	Acarina	>800

* L1, L2: 1st, 2nd larval stage, A: adult stage

The precise biochemical mode of action of IKI-220 is as yet undetermined, but different from any known one. IKI-220 has no action against the classical aphicide targets such as acetylcholine esterase and the nicotinic acetylcholine receptor. Further, spontaneous contractions of the isolated fore-gut of *Locusta migratoria*, enhanced by pymetrozine (Kayser et al., 1994) and a GABA antagonist (personal observation), were unaffected by bath application of IKI-220. From these results, it can be concluded that the target mechanism of IKI-220 is a novel one.

Inhibition of feeding behaviour

A radish leaf infested with first instar larvae of *Myzus persicae* was sprayed with IKI-220 solution. A filter-paper disc stained with a 2 g/litre solution of bromophenol blue in ethanol was placed under the leaf in order to catch the excreted honeydew droplets. Production of honeydew was reduced immediately after treatment. Treated aphids completely stopped feeding within 30 minutes, however they remained on the leaf for 48 hours (Table 2).

Activity against known resistant strains

Leaf dip assays in the laboratory showed that IKI-220 was also highly effective against a field strain of *Aphis gossypii* which had become resistant to organophosphates, carbamates, and pyrethroids (Table 3).

Table 3. Activity of IKI-220 against susceptible and resistant strains of *Aphis gossypii* in leaf-dip assay.

	LC_{90} values (mg a.i./litre)		
Insecticides	Susceptible strain	Resistant strain	TF*
IKI-220	0.8	0.8	1
ethiofencarb	5.0	500	100
oxydeprofos	4.5	450	100
permethrin	1.0	>200	>200

Assessments were made 5 days after treatment.

* Tolerance factor : LC_{90} of resistant strain / LC_{90} of susceptible strain

Systemic and translaminar effect

Solutions of IKI-220 were injected into the soil around eggplant infested with *Myzus persicae*. IKI-220 showed high activity against this species by soil drench treatment (Table 4).

Table 4. Activity of IKI-220 to *Myzus persicae* on eggplant leaf following soil drench treatment.

Insecticide	LD_{90} value (mg a.i./plant)
IKI-220	0.031
pirimicarb	2
triazamate	0.125
imidacloprid	0.031
pymetrozine	0.5

Assessments were made 5 days after treatment.

Solutions of IKI-220 were deposited on the upper leaf surfaces of eggplants. After drying, caged aphids were placed on each side of leaf surface. IKI-220 exhibited a high translaminar effect, comparable or superior to the standards (Table 5).

Table 5. Mortality of *Myzus persicae* on each side of leaf after treatment of upper leaf surface.

Insecticides	Concentration (mg a.i./litre)	% Mortality upperside	underside
IKI-220	100	100	100
pirimicarb	240	92	42
permethrin	100	74	0
imidacloprid	100	100	100
pymetrozine	100	100	82

Assessments were made 5 days after treatment.

Effects on beneficial arthropods

Based on laboratory results to date, IKI-220 has been safe to a wide range of beneficial arthropods such as *Bombyx mori*, *Apis mellifera*, *Harmonia axyridis*, and *Phytoseiulus persiulis*. Also in field tests no adverse effects have been observed on all the tested beneficial insects and mites such as *Harmonia axyridis*, *Typhlodromus pyri*, *Phytoseiulus persimilis*, and *Apis mellifera*.

FIELD STUDIES

The biological performance of IKI-220 against a broad range of aphid species has also been successfully evaluated under field conditions. The following examples demonstrate the aphicidal effectiveness on important crops.

Peach

Table 8. Control of *Myzus persicae* on peach (France, 1998). *

Insecticide	Dose (g a.i./ha)	% Control, DAT 0	7	15	21	28
untreated		(50.8)	(57.1)	(92.8)	(109.7)	(139.4)
IKI-220	60	(38.1)	95.6	99.4	99.8	99.3
acephate	600	(42.5)	85.3	67.6	58.1	70.3
imidacloprid	50	(38.9)	98.4	98.4	98.7	97.1

Figures in parentheses show the No. of aphids/shoot.
* The chemicals were sprayed on March 30 at a spray volume of 1000 litres/ha.

IKI-220 at 60 g a.i./ha gave outstanding control of *Myzus persicae* up to 28 days after treatment (Table 8), and at the same time prevented the rolling of leaves on the tree. In the case of acephate and the untreated control leaf rolling was observed (data not shown). The aphicidal activity was comparable to that of imidacloprid, and superior to that of acephate.

Apple

IKI-220 at 70 g a.i./ha showed good activity against *Dysahis plantaginea* up to 28 days after treatment, which was comparable to imidacloprid at 70 g a.i./ha (Table 9).

Table 9. Control of *Dysaphis plantaginea* on apple (France, 1999). *

Insecticide	Dose (g a.i./ha)	% Control, DAT 0	8	15	21	28
untreated		(32.2)	(40.7)	(53.9)	(72.6)	(73.1)
IKI-220	70	(24.1)	40.5	85.3	96.7	87.9
imidacloprid	70	(29.7)	47.9	70.5	91.8	93.1

Figures in parentheses show the No. of aphids/shoot.
* The chemicals were sprayed on April 8 at a spray volume of 1000 litres/ha.

Winter wheat

IKI-220 at 70-80 g a.i./ha initially exhibited a high activity, and good residual activity against aphids infested on ears of winter wheat. The activity was slightly superior to deltamethrin at 6 g a.i./ha (Table 10).

Table 10. Control of *Sitobion avenae* on winter wheat (France, 1998). *

Insecticide	Dose (g a.i./ha)	% Control, DAT 0	2	7	14	21
untreated		(6.2)	(8.6)	(6.4)	(8.1)	(4.0)
IKI-220	70	(5.4)	95.3	97.8	89.7	78.2
	80	(3.9)	95.7	98.0	89.8	83.2
deltamethrin	6	(5.7)	93.2	91.1	85.8	40.6

Figures in parentheses show the No. of aphids/ear.
* The chemicals were sprayed on July 8 at a spray volume of 300 litres/ha.

Potato

IKI-220 at 80g a.i./ha showed an excellent efficacy against field strain of *Aphis nasturtii*, which was resistant to pirimicarb (Table 11).

Table 11. Control of *Aphis nasturtii* on potatoes (France, 1998). *

Insecticide	Dose (g a.i./ha)	% Control, DAT 0	3	7	14
untreated		(22.8)	(15.6)	(11.0)	(13.7)
IKI-220	80	(22.4)	49.7	90.7	94.8
pirimicarb	250	(24.4)	1.5	24.1	23.3

Figures in parentheses show the No. of aphids/plant

* The chemicals were sprayed on Augest 3 at a spray volume of 300 litres/ha.

Crop safety

There are no phytotoxicity concerns for a wide variety of crops such as peaches, apples, winter wheat, potatoes, cotton and tomatoes even at use rates of up to 400 g a.i./ha.

CONCLUSION

IKI-220 is a representative of a new class of aphid control agent, and possesses excellent systemic and rapid anti-feeding activities. It provides excellent and long-lasting control on a broad range of aphids without any phytotoxicity to all crops tested at use rates of 50-100 g a.i./ha. IKI-220 exhibits no cross resistance to other conventional insecticides, and has a high safety to beneficial insects and mites. It also has a favourable toxicological, environmental, and ecotoxicological profile. These characteristics make IKI-220 well-suited for resistant management strategies and integrated pest management programs.

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