NEW INSECTICIDE CHEMISTRY FOR COTTON IPM

J.W. Holloway and N.W. Forrester
Australian Cotton Research Institute
Narrabri, NSW, Australia
B.R. Leonard
Louisiana State University
Winnsboro, LA

Introduction

New insecticide technology is needed in the cotton production system to reduce reliance on old chemical groups and to maintain profitability. Conventional insecticides provide us with the backbone of insect control in cotton and will remain as integral and necessary tool for incorporation into integrated pest management (IPM) programs in the future.

The aim of this paper is to introduce some of the new insect control measures destined for use in cotton in the near future. It is limited to an introduction of novel conventional insecticides (rather than biological insecticides) with new modes of action (rather than additional members of existing chemical groups) that are intended as stand-alone products.

One of the most important forces in the search for new insecticides has been the development of resistance to 'old' chemical groups. Despite the fact that a wide variety of insecticides have been registered for the control of insect pests of cotton, current insect management is dependent on insecticides from only five classes - single representatives from the organochlorine (endosulfan) and formamidine (arnitraz) classes; and several from the carbamate, organophosphate and pyrethroid classes.

Existing Modes of Action

All of these are nerve poisons whose mode of action depends on binding at one of only four target sties in the insect's nervous system: endosulfan at the gamma-aminobutyric acid (GABA) gated chloride channel, amitraz at the octopamine receptor, organophosphates and carbamates at the acetylcholinesterase receptor and the pyrethroids at the voltage gated sodium channel. Heavy selection pressure on these relatively few target sites has contributed to problems of insecticides resistance.

Nowhere is the resistance problem more acute than in efforts to control *Helicoverpa* spp. in cotton. With the exception of formamidines, field populations of *H. virescens* and *H. armigera* have developed resistance to all of the above chemical groups (McCaffery 1998).

Reprinted from the *Proceedings of the Beltwide Cotton Conference*
Volume 2:1086-1089 (1999)
National Cotton Council, Memphis TN

Research and development have resulted in tremendous advances in both conventional and biological insecticides. Perhaps most publicised in recent years have been the results of genetic engineering and the arrival of transgenic cotton expressing the *Bacillus thuringiensis* Cry 1Ac delta endotoxin, with insecticidal efficacy against *Helicoverpa* spp. However, the robustness of this technology and our current limited understanding of how to exploit this technology to its full potential against insect pest species under both US and Australian growing conditions, means that additional, novel foliar insecticides for control of Lepidopteran pests are needed.

Cost-effective control of target pests has to be the number one desirable criterion for any of the new technologies. Additional desirable characteristics include the need for additional early season products that are less disruptive to beneficial insects and therefore more compatible with IPM, and insecticides that will complement existing and new technologies including transgenic Bt cotton.

The following products are the first members of new classes of insecticides such as neonicotinoids (imidacloprid, thiomethoxam and acetamidaprid), phenylpyrazoles (fipronil), avermectins (abamectin and emamectin benzoate), spinosyns (spinosad), pyrroles (chlorfenapyr), oxadiazines (indoxacarb), and diacylhydrazines (RH 2485). Just as early members of the pyrethroid group were superseded by more effective second or third generation compounds, so additional members of these new groups may well be developed in the future.

New Modes of Action

These new classes of insecticides have novel modes of action to which target species (particularly *H. virescens* and *H. armigera*) are not yet resistant. The majority of the new insecticides classes (for example neonicotinois, phenylpyrazoles, avermectins, spinosyns and oxadiazines) are nerve poisons acting at new or established target sites in the insect nervous system. The nervous system of insects has provided most of the target sites for insecticides to date because it is highly specialised and very sensitive, with numerous potential sites for insecticide action.

Disruption at any one of these sites can lead to knock-on effects in other parts of the nervous system, magnifying the effect of the toxin. Nerve poisons produce rapid symptoms of intoxication, lack of coordination, paralysis and death. Although there are resistance problems at a number of existing nerve sites, there are many other sites and new ways of attacking existing sites. So nerve poisons continue to make up the majority of new insecticides.

Where new compounds share a common target-site with a previously commonly used insecticides class (for example, DDT and pyrethroids with indoxacarb or endosulfan with the phenylpyrazoles) the potential for the build up of cross resistance in populations of target pests should be thoroughly investigated before widespread use of the new chemical group.

Several of the new inseciicdes act at non-nerve targets including disruption of the insect's respiration (chlorfenapyr), hormone regulation and moulting (methoxyfenozide), mouthparts (pymetrozine) or gut wall (Bt). These targets are not prejudiced by exising cross resistance to nerve poisons and offer great promise for the future of insecticide resistance (IRM) in cotton.

New Insecticides for Sucking Insect Control

Imidacloprid (Gaucho, Provado, Confidor, Admire) - Bayer

Imidacloprid is the first highly successful member of a group of neonicotinoid insecticides with a novel mode of action that is similar to the natural product nicotine. Imidacloprid features low mammalian toxicity (compared to nicotine) and high insecticidal efficacy against a range of target pests. It is particularly active against sucking pests via ingestion, contact and systemic routes - including cotton pests that are resistant to organophosphates and carbamate and pyrethroids (e.g. aphids and whitefly and mirids) (McNally and Mullins, 1996).

No cross resistance has been reported between imidacloprid and other classes of insecticides, although independent selection for resistance has already occurred in some instances. Imidacloprid is currently available for use in cotton as a seed treatment (Gaucho), which provides several weeks of residual pest control, and formulations for use as foliar sprays (Provado and Confidor) are close to registration. Several other neonicotinoid insecticides are also undergoing development for use in cotton, including acetamiprid (NI-25), thiomethoxam (Cruiser), nitenpyram and diacloden.

Fipronil (Regent, Cosmos) - Rhône-Poulenc

Fipronil is the first highly successful member of a new group of insecticides - the phenylpyrazoles. This broad-spectrum insecticide is highly active via ingestion, contact and limited systemic action, and should provide control of insects which are resistant to carbamate, organophosphate and pyrethroid insecticides (Hamon, *et al.* 1996).

Fipronil acts as a GABA receptor in the nervous system at a target site shared with the cyclodienes (for example, dieldrin and endosulfan). Cross resistance between these insecticide groups has been reported in the laboratory and will require careful monitoring before widespread use of phenylpyrazoles against insect species with a history of resistance to these older groups. Phenylpyrazoles have good activity against a wide range of soil insects, foliar-feeding and sucking pests but does not control aphids or whitefly. Fipronil could become available for use in cotton in a number of formulations, including a seed dressing (Cosmos), in-furrow treatments and as a foliar spray (Regent).

Diafenthiuron (Pegasus) - Novartis

Diafenthiuron is a pro-insecticide which is activated by UV light to a stable and highly active carbodiimide derivative which is though to act at the octopamine receptor. This activation process may contribute to the slower speed of kill of diafenthiuron than older insecticide groups. Diafenthiurons active derivative has a strong vapour action and although it is not systemic, has a translaminar insecticidal activity. In cotton this compound has much better insecticidal efficacy following canopy closure. Diafenthiuron provides residual control of a range of sucking pests, chiefly mites, aphids, jassids and whitefly and has recently been released for use in cotton as Pegasus.

Pymetrozine (Chess, Fulfill) - Novartis

This is a novel pyridine insecticide with systemic activity against aphids, whitefly and jassids. The mode of action of pymetrozine is not yet wholly understood, but it is thought to act as a target-site in the nervous system causing paralysis of insect mouth parts which ultimately results in the death of the insect by starvation.

Buprofezin (Applaud) - Nihon Nohyaku

Applaud is a novel chitin disrupting compound which slows promising activity against a range of sucking pests including whiteflies.

Pyriproxyfen (Knack) - Sumitomo

Knack is a new generation insect growth regulator product which is very active against aphids and whiteflies and may find a place in future cotton IRM programs.

New Insecticides for Control of *Helicoverpa* Spp.

Spinosad (Tracer) - DowAgroSciences

The spinosyns are a new class of insecticides derived by fermentation from the metabolites of a new species of Actinomycetes. They have a novel mode of action, acting primarily at the nicotinic acetyl choline receptor in the nerve synapse. Members of this class of compounds are characterised by insecticidal activity, very low mammalian toxicity and a favourable environment profile (Sparks *et al.* 1996).

Spinosad (a mixture of spinosyn A and D) acts mainly via ingestion, but has some secondary contact activity, and has good efficacy against pests that are resistant to organophosphate, carbamate and pyrethroid insecticides. It is very active against a range of agricultural insect pests - particularly against Lepidoptera including *H. virescens, H. zea, H. punctigera* and *H. armigera*. Spinosad poses a moderate risk to thrips and hymenopterans, but is relatively safe to most other beneficial insects including predatory bugs and beetles.

Spinosad has only recently become available for use in cotton as a foliar spray (Tracer). As an 'IPM friendly' larvicide without existing resistance problems, it represents a welcome addition to the Australian IRM strategy. The best fits for Tracer in cotton may be either early in the season to preserve beneficials and/or mid-late season to control *H. virescens* in the US and and *H. armigera* in Australia that are resistant to older chemical groups.

Chlorfenapyr (Intrepid, Pirate) - American Cynamid

Pyrrole insecticides were developed following the discovery of insecticidal properties of a natural product, dioxapyrrolomycin, isolated from a strain of Streptomyces whose mode of action relies on the disruption of mitochondiral respiration. The first commercial product from this class, chlorfenapyr (Intrepid) has recently received an initial registration for use in Australia, and is available on a limited basis (Section 18) as Pirate in some parts of the US. Chlorfenapyr is mainly a stomach poison, but also shows limited contact activity (French *et al.* (1996).

Chlorfenapyr controls adults, nymphs and larvae of over 70 species. Initial studies have shown negative cross-resistance to pyrroles in adult *H. virescens* and the possibility of improved efficacy against some metabolically resistant field populations of *H. armigera* warrants further investigation in Australia. It has excellent miticidal efficacy and promising activity against a broad spectrum of pests including Helicoverpa spp. Intrepid is likely to find a use in mid to late season sprays to control resistant *H. virescens*, *H. armigera* and mites.

Avermectins (Agrimec, Proclaim, Affirm) - Novartis

The avermectins are extremely active insecticides originally derived from a Japanese strain of *Streptomyces avermitilis*. Their primary mode of action appears to be as GABA agonists in the insects nervous system. So far, two memebers of the group have been successfully commercialised; Ivermectin cor control of animal parasites and abamective (Agrimec) as a miticide for use in agriculture (Dunbar *et al.* 1996).

Abamectin is rapidly absorbed into the leaf, delaying it's degradation under field conditions and rendering it safer to beneficial insect species. It is weakly active against most Lepidoptera but shows good activity against *H. puntigera* in Australia, suggesting a promising early season fit for use in cotton.

Emamectin benzoate (Affirm, Proclaim), a synthetic analogue of Abamectin, has far superior efficacy against a range of other Lepidopteran pests including *H. virescens* and *H. armigera* while retaining modest acaricidal activity and is currently undergoing field trials and going through the registration process in Australia.

Indoxacarb (DPX-062, Steward) - Dupont

Indoxacarb is the first of a promising new group of insecticides, the oxadiazines, with a new mode of action caused by binding at a new site in the nervous system. Indoxacarb is a stomach poison which is activated by esterase enzymes inside an insect following ingestion (Wing *et al.* 1998). It has good larvicidal activity at low rates and is reported to be highly selective with little impact on beneficial insects.

No cross-referencing has yet been reported between indoxicarb and existing insecticide groups including the pyrethroids. Indoxacarb is currently undergoing field trials for use in cotton in both Australia and the US. Initial results have confirmed a favourable environmental profile, selectivity towards beneficial insects and high insecticidal efficacy against a range of target pests. As such indoxacarb may provide a valuable tool for the management of insecticide-resistant populations of *H. virescens* in the US and *H. armigera* in Australia.

Methoxyfenozide (RH 2485, Intrepid) - Rohm and Haas/Bayer

This product should not be confused with chlorfenapyr which has the band name Intrepid in Australia. It belongs to a class of chemicals called diacylhydrazines - one of the most promising groups of new generation insect growth regulators. Another product in this group is tebufenozide (Mimic, Confirm) which has high insecticidal efficacy against a number of Lepidopteran species - particularly armyworm.

These products disrupt moulting in a range of Lepidopteran pests, including several major pests of cotton. They are stomach poisons and are reported to be highly selective - causing minimal disruption of beneficial insects at moderate rates (Harrison *et al.* 1997). In addition to its novel mode of action, RH2485 may provide us with a much needed 'soft option' for the control of larval Lepidopteran pests in cotton.

Greater Selectivity (Insect and Human)

Increasing environmental concerns are high on the list for insecticide choice, and with existing products such as endosulfan and methyl parathion under review in Australia, the cotton industry has to take the initiative to research and develop alternative insecticides which will become their eventual replacements.

Generally the new chemical groups are more environmentally acceptable than existing insecticide chemistry because they:

- Offer greater specificity to target pests;
- Have greater intrinsic activity;
- Achieve acceptable insect control at low field use rates;

- Degrade more rapidly in the environment to harmless metabolites; and,
- Have lower mammalian and aquatic ecotoxicity.

Several of the new classes of insecticides offer great promise for the future of cotton IPM because their selectivity to target insects should allow more effective preservation of early season beneficial insects in both conventional and transgenic cotton. Further field trials of new insecticides need to be carried out on both conventional and Ingard Bt cotton varieties. Sublethal poisoning by Bt in a transgenic crop may alter the behaviour of target insects (i.e. decreased feeding and/or changes in movement or spatial distribution) and this may affect the performance of a given insecticide compared with its performance in conventional cotton.

Ensuring Effectiveness

Only through the wider use of these products by growers and consultants will we develop a sufficient knowledge base to determine their strengths and weaknesses in cotton. More field trials need to be performed to determine how well these products perform under a variety of cotton-growing conditions.

A barrier for several promising technologies - for example improved strains of foliar Bts and a number of insect baculoviruses - remains their stability in high ambient temperatures, high ultra-violet (UV) light and a rapidly growing cotton plant which causes growth dilution of insecticide deposits, particularly stomach poisons.

The new insecticides are not 'silver bullets'. Ironically, the acceptance of new technologies by the cotton industry may be prejudiced by expectations of insecticide efficacy developed in the early days of the pyrethroids.

The new heliothicides (Tracer, Intrepid, Proclaim, RH2485 and Steward) are predominantly stomach poisons - they need to be ingested by the target insect in order to be effective. Lessons that have been learned about the application, coverage and timing of older stomach poisons such as thiodicarb are equally important for the efficacy of these newer groups. Pirate/Intrepid and Steward have to be bioactivated inside the target insect.

Both stomach activity and bio-activation are positive features for insecticides because they can contribute to greater selectivity to target pests relative to beneficial species. But they may also result in a slower speeds of kills (days rather than hours) compared with contact poisons. Growers and consultants will need to give some of the new products more time to work (up to five days), before deciding that a first time spray of an unfamiliar compound has been unsatisfactory.

Managing Resistance

None of the new insecticides are 'resistance proof'. Adding new insecticides to IRM strategies will help to prevent their over-use and preserve their efficacy for the future. Several new compounds show promising efficacy towards *Heliothis/ Helicoverpa* spp. and should help to alleviate current difficulties in the management of these major pests. They will be most cost-effective and under reduced selection pressure for resistance if they can be launched with proactive 'anti-resistance' guidelines included on the label and targeted against pest populations with a background of susceptibility to existing chemical groups.

As the new insecticdes become available, their novel modes of action will provide the necessary additional tools to allow effective rotation of insecticide groups, essential for successful implementation of IRM programs. So preserving the remaining efficacy of 'old' chemical groups will have as much bearing on the sustainability (and cost) of new technologies as the initial use of the new products themselves.

Where appropriate, these new compounds should provide enough cost-effective alternatives to allow a repositioning of older, overused broad-spectrum insecticide groups to their optimal places in the cotton IRM strategies.

Summary

New (affordable) insecticides should provide alternatives to old chemical groups, reducing reliance on them while maintaining the profitability of cotton production. Several new groups of insecticides offer great promise to cotton IPM because of their new modes of action, greater selectivity and safety to the user and the environment.

The cotton industry is now faced with the challenge of learning how to use these new groups wisely, with realistic expectations. Enthusiasm for any one (or all) of these new technologies must not be allowed to result in their initial over use, so that the early development of resistance by major pests species can be avoided and the new chemistry can provide cost effective insect control for the future.

References

Dunbar, D. M., Brown, R. D., Norton J. A. and Dybas, R. A. (1996) Proclaim: a new insecticide for use on cotton, *In*: Proceedings Beltwide Cotton Conference, 756-758.

French M. II, White C. A and Treacy, K. M. (1996) Pirate insecticide-miticide for control of cotton insects in mid-south cotton, *In*: Proceedings Beltwide Cotton Conference, 865-870.

Hamon, N., Shaw, R. and Yang, H. (1996) Worldwide development of fipronil insecticides, *In*: Proceedings of the Beltwide Cotton Conference, National Cotton Council, Memphis TN. Pp.759-765.

Harrison, W. E., Walton, L. C. and Duttle, A. E. (1997) Control of Lepidopteran pests in cotton with Intrepid experimental insecticide, *In*: Proceedings Beltwide Cotton Conference, 1091-1093.

McCaffery, A. R. (1998) Resistance to Insecticides in Heliothine Lepidoptera: a Global View, *In*: Proceedings of the Royal Society, London.

McNally, P. and Mullins, W. (1996) The role of Provado in western cotton IPM programmes, *In*: Proceedings Beltwide Cotton Conference, 859-863.

Sparks, T. C., Kirst, H. A., Mynderse, J. S., Thompson, G. D., Turner, J. A., Jantz, O. K., Hertlein, M. B., Larson, L. L, Baker, P. J., Broughton, M. C., Busacca, J. D., Creemer, L. C., Huber, M. L., Martin, J. W., Nakatsukasa, W. M., Paschal, J. W. and Worden, T. W. (1996) Chemistry and Biology of the Spinosyns: Components of Spinosad (Tracer), the first entry into Dowelanco's Naturalyte Class of Insect Control Products, *In*: Proceedings Beltwide Cotton Conference, 692-696.

Wing, D., Schnee, M. E., Sacher, M. and Connair, M. (1998) A novel oxadiazine insecticide is bioactivated in Lepidopteran larvae. Arch. Insect. Biochem. Physiol. 37 91-103.

Acknowledgements

Grateful thanks to the CRDC for funding, to the CRC for sustainable cotton for providing assistance to attend the 1998 Beltwide Cotton Conference and to Dr. L. Wilson for his help with this manuscript.

Table 1: New insecticides for cotton IPM

Target Species	Active Ingredient	Trade Names	Company
Sucking Insects	Imidacloprid	Gaucho, Condifor, Provado*	Bayer
Sucking Insects	Thiomethoxan	Cruiser, Actara	Novartis
Sucking Insects	Acetamidaprid	NI-25, Mospilan	Nippon Soda
Sucking Insects	Fipronil	Cosmos, Regent	Rhône-Poulenc
Sucking Insects, mites	Diafenthiuron	Pegasus, Polo	Novartis
Sucking Insects	Pymetrozine	Chess, Fullfill*	Novartis
Sucking Insects	Buprofezin	Applaud	Nihon Nohyaku
Sucking Insects	Pyriproxyfen	Knack, Admiral	Sumitomo
Helicoverpa punctigera, mites	Adamectin	Agrimec	Novartis
Helicoverpa spp. mites	Emamectin Benzoate	Affirm, Proclaim*	Novartis
Helicoverpa spp.	Spinosad	Tracer	DowAgroSciences
Helicoverpa spp. mites	Chorfenapyr	Intrepid, Pirate*	American Cyanamid
Helicoverpa spp., sucking pests	Indoxacarb	DPX062, Steward*	Dupont
Helicoverpa spp.	Methoxyfenozide	RH2485, Intrepid*	Rohm & Haas/Bayer

* US name

Table 2: Ecotoxicity of old and new insecticides

	Oral rat (mg/kg)	Dermal rabbit (mg/kg)	Fish (mg/L)
Methyl parathion	6	45	4.3
Cyhalothrin	79	632	0.002
Imidacloprid	450	>5000	211
Fipronil	100	>2000	150
Spinosad	>5000	>2000	30
Chlorfenapyr	223	>2000	0.5
Abamectin	70	>2000	0.7
Emamectin Benzoate	1500	>2000	0.9
Indoxacarb	>5000	>2000	>1
Methoxyfenozide	>5000	>2000	---

Note: The lower the number, the more toxic the product.