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THE FUTURE OF INSECT GROWTH REGULATORS IN VECTOR CONTROL

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ABSTRACT. Insect growth regulators (IGRs) are diverse groups of chemical compounds that are highly active against larvae of mosquitoes and other insects. The IGRs in general have a good margin of safety to most nontarget biota including invertebrates, fish, birds, and other wildlife. They are also relatively safe to man and domestic animals. The IGR compounds do not induce quick mortality in the preimaginal stages treated. Mortality occurs many days later after treatment. This is indeed a desirable feature of a control agent because larvae of mosquitoes and other vectors are an important source of food for fish and wildlife. On account of these advantages of IGRs and the high level of activity against target species, it is likely that IGRs will play an important role in vector control programs in the future.

INTRODUCTION

The group of pesticides known as insect growth regulators (IGRs) or insect developmental inhibitors (IDIs) are potent insecticides. Several classes of chemicals contain compounds that possess growth-retarding and -inhibiting properties (Mulder and Gijswijt 1973, Post et al. 1974, Slama et al. 1974, Quraishi 1977, Grosscurt and Tipker 1980, Itoh 1981, Worthing and Walker 1987, Mulla 1991). Some of the earlier compounds investigated were chemically related to the natural juvenile hormones (JHs) of insects and these were therefore designated as JH analogues or mimics, commonly known as juvenoids (Slama et al. 1974). There are other compounds that are not chemically related to insect juvenile hormones but produce similar effects by inhibiting cuticle formation (Mulder and Gijswijt 1973, Wellinga et al. 1973, Post et al. 1974, Van Eck 1979, Grosscurt and Tipker 1980, Itoh 1981, Mulla 1991). These compounds are also designated as IGRs. Compounds having insect growth regulating properties are found in the classes of terpenoids, benzamides, carbamates, triazines, benzoylureas, and other classes of chemicals.

BIOLOGICAL ACTIVITY AND POTENCY

Most IGRs have high potency against mosquitoes and other pest and vector species. In laboratory evaluations their activities against mosquitoes range from 0.3 to 50 ppb (= 0.0003 to 0.050 mg/liter, Table 1). Pyriproxyfen is one of the most effective juvenoid compounds, having an LC_{90} of less than 1 ppb (Estrada and Mulla 1986, Mulla 1991). This level of activity is higher than that of some of the most active organophosphate larvicides. The chitin synthesis inhibitors also show high levels of activity, being effective in the range of 2–10 ppb (= 0.002–0.010 mg/liter, Table 1). These as well as other IGRs have been extensively studied against a variety of vectors and human pests.

FIELD EFFICACY

Several studies on laboratory activity and field efficacy of IGRs against mosquitoes have been conducted (Chang 1979, Sharma et al. 1979, Itoh 1981, El Safi and Haridi 1986, Estrada and Mulla 1986, Ali and Nayar 1987, Mulla and Darwazeh 1988, Amalraj and Velayudhan 1989, Mulla et al. 1989). The various IGRs showed different levels of efficacy against various test species (Table 2). In general, the juvenoid compounds acting during a narrow window of susceptibility are less active against asynchronous larval populations. On the other hand, the chitin synthesis inhibitors acting during ecdysal changes are equally effective against synchronous and asynchronous populations. To make the juvenoid compounds more effective and long lasting for the control of asynchronous larvae, they are formulated in a variety of controlled-release formulations that release minute but adequate quantities of the active ingredients into the water where mosquito larvae thrive, thus yielding long-lasting control with one treatment. The relatively high cost of materials to be applied at high rates is more than offset by the savings accrued by the application of fewer treatments.

Water quality and other habitat parameters also influence the field efficacy of IGRs (Table 3). In polluted water, the dosage required for effective control would be higher for the same species than in a clear water situation. Similarly, deeper bodies of water, habitats with vegetation (emergent and submergent), and flowing water will require high dosages.

Table 1. Relative activity of some insect growth regulators against 4th-instar larvae of *Culex quinquefasciatus* (Say) in the laboratory.

IGR	Supplier	LC_{90} (mg/liter)
S-31183 (pyriproxyfen)[2]	Sumitomo	0.0003
S-21149[2]	Sumitomo	0.0015
Diflubenzuron[1]	Philip Duphar	0.002
BAY SIR 8514[1]	Mobay	0.007
EL-1215[1]	Eli-Lilly	0.008
Fenoxycarb[2]	Maag	0.02
Methoprene[2]	Zoecon	0.05

[1] Chitin synthesis inhibitor.
[2] Juvenoid.

CONTROLLED RELEASE FORMULATIONS PROLONG EFFICACY

As mentioned above, mosquito larvae exhibit a narrow window of susceptibility to juvenoid compounds. This window of susceptibility usually occurs during the late 4th-instar larvae. To effectively control asynchronous larvae, the active entity needs to be present during the susceptibility period of larvae progressing to becoming 4th instars. For example, because *Culex* mosquito larvae develop asynchronously, and because the window of susceptibility in their life cycle is narrow, emulsiable concentrate formulations of methoprene are required at higher dosages for the control of *Culex* mosquitoes. Because of the instability of this compound, only short-term control (3–7 days) is obtained with these types of formulations. However, controlled-release formulations of methoprene, such as pellets, can yield excellent control of asynchronous broods of *Culex* mosquitoes (Table 4). Most of the mortality, as expected, is in the pupal and adult stage. One treatment of pellets can yield long-lasting control of *Culex* mosquitoes for over a month in a duck-pond marsh ecosystem.

ACTIVITY AGAINST INSECTS OTHER THAN MOSQUITOES

In addition to exhibiting a high level of activity against mosquitoes, most IGRs also have high levels of activity against other vectors and human pests (Lacey and Mulla 1977, 1979; Quraishi 1977; Ali and Lord 1980; Schmidt and Dorntlein 1980; Mohsen and Mulla 1982; Takahashi et al. 1985; Ali and Nayar 1987). The literature is replete with reports dealing with the activity and efficacy of IGRs against many groups of insects of medical and public health importance.

COMMON IGRS FOR MOSQUITO CONTROL

Among the juvenoids or JH analogues and mimics, several compounds have been evaluated in vector control programs. The well-known JH analogue methoprene was registered in 1974 and its use in the earlier years was geared primarily to control *Aedes* larvae. Due to its low stability in aquatic habitats, its use against *Culex* and *Anopheles* species was minimal. However, recent developments in formulation technology have resulted in the availability of slow- or controlled-release formulations that can significantly increase its persistence at the low lethal concentrations required for the control of asynchronous larvae.

Other compounds that have been extensively

Table 2. Field efficacy of some insect growth regulators against various species of mosquitoes. Control of 90% or better obtained at field rates shown.

Material	Formulation	Approximate field rate (lb/acre AI)		
		Culex[1]	*Aedes*[2]	*Psorophora*[3]
Pyriproxyfen[5]	0.5% granular (G)	0.005	0.005	0.005
Fenoxycarb[5]	1.0 G	0.10	0.005	0.005
Diflubenzuron[5]	25 wettable powder (WP)	0.025	0.01	0.01
BAY SIR 8514[4]	25 WP	0.05	0.01	0.01
Methoprene[5]	SR10	0.1	0.025	0.025

[1] *Cx. stigmatosoma* Dyar and *Cx. tarsalis* Coquillett.
[2] *Ae. nigromaculis* Ludlow and *Ae. melanimon* Dyar.
[3] *Ps. columbiae* Dyar & Knab.
[4] Chitin synthesis inhibitor.
[5] Juvenoid.

Table 3. Field efficacy of some insect growth regulating compounds against mosquitoes breeding in clean and polluted waters. Control of 90% or better obtained at field rates shown.

Material	Formulation	Approximate field rate (lb/acre AI)		
		Flood water[1]	Clean water[2]	Polluted water[3]
Pyriproxyfen	0.5% granular	0.005	0.005	0.10
AC-291898	5% emulsifiable concentrate (EC)	0.010	0.010	0.05
XRD-473	5% EC	–	0.010	0.05
Fenoxycarb	12% EC	0.05	0.1	>0.25
Methoprene	4% pellets	0.05	0.25	>0.25

[1] *Psorophora columbiae.*
[2] *Culex tarsalis.*
[3] *Culex quinquefasciatus* Say and *Cx. stigmatosoma.*

studied are fenoxycarb and pyriproxyfen. The former compound is quite unstable in water, whereas the latter exhibits some degree of persistence. Fenoxycarb is now used for the control of some household insect pests. Large-scale field trials are planned for pyriproxyfen against mosquitoes once an Experimental Use Permit is issued by the U.S. Environmental Protection Agency.

One common characteristic of these compounds is that they do not induce rapid mortality in the treated larvae. The active ingredients enter the insect body either through the cuticle or by ingestion or by both modes. Larvae receiving lethal doses do not die outright. With some compounds such as the juvenoids and their analogues, the larvae survive and suffer mortality in the pupal stage or if they do survive, then mortality may occur in the adult stage during eclosion (Table 4). With these types of compounds, the target insects exhibit a narrow window of susceptibility during the molting process. Therefore these compounds have to be present at effective concentrations during the development of asynchronously developing larvae. This is now accomplished by incorporating the active ingredients into a matrix that releases the compound slowly over long periods of time.

Among the chitin synthesis inhibitors, several compounds have been screened and evaluated against mosquitoes and other vectors. Diflubenzuron, hexafluron, and triflumuron are some of these compounds that have been evaluated for the control of mosquitoes and other insects in the USA and abroad. Among these, diflubenzuron is now available commercially for the control of mosquitoes and other insects. These compounds are highly active against mosquitoes and can provide practical control at the rates of less than 1–2 g/h of active ingredient. Treated larvae die during ecdysis; the ecdysing larvae fail to completely shed the old cuticle. Apparently, due to inhibition of chitin deposition, the larvae do not have the rigidity to get out of the old cuticle. They may survive for some period but eventually die.

The mode of action and time of mortality in the urea type of IGRs and related compounds are quite different than that with juvenoids. These compounds interfere with chitin synthesis (Van Eck 1979) and affected larvae die during ecdysis. Those that survive die in the pupal or adult stage. The extent and magnitude of mortality in a given stage or instar is a function of the concentration employed. In each group literally hundreds of compounds have been synthesized and evaluated.

MORPHOGENETIC ABERRATIONS AND EFFECTS ON REPRODUCTION

Some IGRs, in addition to inducing mortality in the subimaginal stages or the imago, can also

Table 4. Extended control of *Culex tarsalis* in duck ponds with controlled release formulation of methoprene (4% pellets) applied at the rate of 0.25 lb/acre of AI.

Post-treatment (days)	% mortality in treatment by stage in larval isolates			% emergence inhibition	
	Larvae	Pupae	Adults	Treatment	Check
14	8	92	0	100	5
21	8	65	27	100	9
28	8	68	24	100	12
35	10	32	32	74	12
42	0	47	21	68	5
49	0	33	13	46	0
56	0	30	3	33	3

induce other effects such as morphogenetic aberrations and reproductive failures. Morphogenetic aberrations induced by IGRs in various stages of mosquitoes, flies, and other insects have been reported in numerous studies (Arias and Mulla 1975a; Awad and Mulla 1984a, 1984b; Saxena and Kaushik 1988). In some studies delayed effects in the imagoes and decline in reproduction and fecundity have been reported (Arias and Mulla 1975b, Lacey and Mulla 1977, Grosscurt and Tipker 1980, Saxena and Kaushik 1986). These are some bonus effects that many IGRs induce later in the life stages of the treated organisms.

SAFETY TO FISH AND WILDLIFE

The IGRs in general have a high margin of safety to fish, birds, other wildlife, and most aquatic nontarget organisms. Some IGRs are safer than others in this regard (Worthing and Walker 1987, Briggs 1992). They also possess extremely low toxicity against humans. However, some of the IGRs, although quite specific, do adversely affect some aquatic crustaceans and species of insects either phylogenetically closely related to mosquitoes or sharing the same habitat (Ali and Mulla 1978, Briggs 1992). In most studies related to impact on nontarget biota, it has been shown that resurgence of affected target and nontarget organisms occurs rather quickly.

On balance, IGRs seem to fit the criteria for safety to the environment, and low risks to nontarget biota, fish, wildlife and humans. They have been successfully and safely used to date without any noticeable impact on nontargets and there are indications that this pattern of use will continue into the future. It is reasonable to assume that IGRs will be employed in mosquito and other vector control programs in the future. New IGRs will be arriving on the scene from time to time but the pace of development for new IGRs will be quite slow, unless widespread and repeated epidemics of vector-borne diseases appear on the horizon.

I do not foresee vector and pest control programs of the future without the inclusion and utilization of safe and environmentally friendly chemicals. As we will need drugs for maintenance of human health, so will we need safe and less hazardous chemicals for the control of vectors and human pests. The IGRs, one of the relatively safe and mostly risk free groups of compounds, will meet the requisites established for the development and use of safe chemical control technology.

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