Insect Growth Regulators and Insect Control: A Critical Appraisal

Kumari Sweeti[1], Savita[2] and Rajesh Kumar[3]

Department of Chemistry

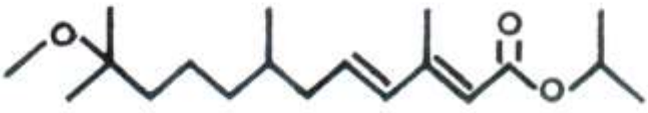
[1 and 2] Ph.D. (Chemistry), B. N. Mandal, University, Madhepura (Bihar)

[3]Assistant Professor, B. P. S. College, Desari (Vaishali)

ABASTRACT: *Insect growth regulators (IGRs) of the juvenile hormone type alter physiological processes essential to insect development and appear to act specifically on insects. Three natural juvenile hormones have been found in insects but not in other organisms. Future use of antagonists or inhibitors of hormone synthesis may be technically possible as an advantageous extension of pest control by IGRs.*

I. Objective

Since the purpose of this conference is to review current knowledge and to anticipate future human health effects of new approaches to insect pest control, it is particularly appropriate to review and discuss insect growth regulators. At this time they represent the newest of all approaches to operational and commercial insect control. Only one insect growth regulator (IGR) has so far achieved the government regulator (IGR) has so far achieved the status of full commercial registration by any government regulatory agency (in this case the Environmental Protection Agency) for its uses, and my discussion will therefore focus on this chemical, common name methoprene, trademark name Altosid IGR, for the main reason that a large body of information and knowledge is available for this substance. However, it is important to note that its first registered use pattern is for the control of flood water mosquitoes, which are among the insect carriers of serious diseases. Thereby its human health effects are directly discernible through the prevention of human diseases, and these effects could even be estimated by NIEHS in terms of cases prevented.



Methoprene

Since the second registered use pattern is the controlled feeding of Altdosid IGR to cattle for the control of manure breeding fillies, which results in increased yields of beef and milk, we may again anticipate beneficial human health effects in the form of greater availability of high value nutrition, the cost of which would be higher without such fly control.

II. Introduction

An IGR may be defined in terms of its mechanism of action, as a substance which accts within an insect to accelerate or inhibit a physiological regulatory process essential to the normal development of the insect or its progeny, in such a way that the action of the substance is necessarily dependent on the life stage of the insect. Although there are numerous other physiological processes which are essential for the survival of an insect, chemical such as organophosphates or carbamates which interfere with these other processes are not to be included, since they interfere with processes which accompany but do not regulate normal development.

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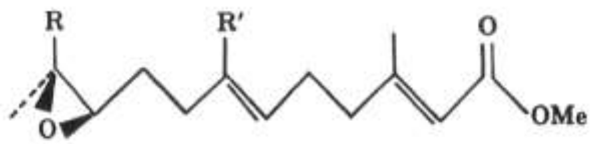
Although numerous natural substances regulate the growth and development of insects, the juvenile hormones (JH) have been singled out for refinement of their biological and chemical properties by synthesis chemical analogs which are insect growth regulators. Historically, the major reasons for the selection of JH as a rational lead for pesticide design were that beliefs that this hormone occurred in insects, that it had a specific function in insects, and that it did not occur in higher animals. The implication was that juvenile hormone would therefore be selectively active in insects. Although current knowledge strongly supports the beliefs, we have no formal proof that JH does not occur outside the class of insects. It may be philosophically impossible to obtain proof since we are only able to say that JH has not yet been identified in other organisms, within the detection limits of our instrumentation. The real problems are that very few species have been extracted and examined in chemical detail, and that numerous plants and animals are already known to contain sesquiterpenelike molecules which possess weak JH activity. To pursue this question, which bears on the environmental impact of JH analogs, new research would have to involve chemical identification rather than rely on bioassay, which formed the basis of reports of JH activity in mammalian tissues in the late 1950's.

At the present time there appear to be only three natural JH molecules, despite the variety of insects which has now been investigated in chemical detail.



JH I: R=R′=Et
JH II: R=Et, R′=Me
JH III: R=R′=Me

From the relatively primitive cockroaches and grasshoppers to the more recently evolved moths, whose metamorphosis is considerably more complicated, the same three hormones appear to be the regulatory molecules.

Table-1.

Properties of methoprene (Altosid IGR), isopropyl (2E, 4E)-11 methoxy-3, 7, 11-trimethyl-2, 4-dodecadienoate.

Property	
Empirical formula	$C_{19}H_{24}O_2$
Molecular weight	310
Physical state	Amber liquid (technical material)
Specific gravity (20°C)	0.9261g/ml
Solubility	
Organic solvents	Soluble
Water	1.39ppm
Vapor pressure	
At 25°C	2.37×10^{-5}mm Hg
At 40°C	1.60×10^{-4}mmHg

This raw material is in turn manufactured form the pinenes present in oil of turpentine. Curiously, 7-methoxy-citronellal, used in the perfumery industry, is one of the earliest metabolites of methoprene in alfalfa.

Biological Properties

IGRs with JH activity have been reviewed in detail from a biological viewpoint. Practical results are covered in this review and laboratory bioassay methods are detailed elsewhere. Perhaps more so than in other fields of pesticide research, large variations in insect biological activity are associated with small changes in chemical structure. High biological activity in one species of insect cannot be extrapolated to related families. This selectivity of action within the insects has been discussed and appears to be a stumbling block to commercial development of IGRs.

Use Patterns

Aspects of the mosquito use pattern have been discussed in detail by Staal, and the selectivity for target versus nontarget species has been reported by Miura and Takahashi to be excellent. Though the effects of methoprene are demonstrable on numerous insect species, the demonstration of such widespread effects requires remarkably high doses relative to the field use rate. Since the field use rate is mainly determined by economic considerations, the selectivity which methoprene exhibits in practical use reflects the fact that the molecule is basically much more active on dipteran insects than on several other orders of insects. At times this selectivity can be unfavorable, for example larvae of *Culex pipiens* are 10 times less sensitive than those of *Aedes aegypti* mosquitoes. This problem, added to the nonsynchronous nature of *Culex* populations, leads to a requirement for higher field use rates and more frequent applications which are economically unacceptable in present day mosquito abatement practice. The greater degree of synchronization in floodwater mosquitoes, their greater sensitivity to methoprene, the absence of larval damage by these species of insects and the urgent need for control of insecticide-resistant floodwater mosquitoes stimulated the selection of this use pattern for early registration, which was completed in 1975.

Toxicology

The toxicological properties of Altosid IGR technical, as summarized by the manufacturer and are discussed in more detail by Wright. Methoprene is a relatively nontoxic substance for which finite residue tolerances have been established.

Other IGRs

From several thousand candidate compounds a small number of IGRs have received considerable attention for possible development toward commercial use. Their field performance problems and prospects in selective insect control have been reviewed recently. Though much has been written, only one IGR has been registered for use as of September 1975.

III. Conclusion

Perhaps the only certain conclusion is that in- sects will continue to be devastating pests, but it is also clear that IGRs have devastating effects on their target insects. In contrast, the approved uses of methoprene appear to be environmentally harmless, and the fact that it is technically feasible to achieve this goal is encouraging.

However, it has been pointed out emphatically that unless major changes occur in regulatory and governmental policy, few if any improvements are likely. The multimillion dollar investment without which the discovery and development of significantly improved pesticides is impossible carries no guarantee of a return. Corbett concluded that "there are no biochemical reasons to suggest that such improvement is impossible," and the ball appears to be in the legislative court.

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