PONTIFICIA
ACADEMIA
SCIENTIARVM

COMMENTARII

VOL. III N. 19

# NATURAL PRODUCTS AND THE PROTECTION OF PLANTS

## SUMMARY

OF THE STUDY WEEK HELD

October 18-23, 1976

EX AEDIBVS ACADEMICIS IN CIVITATE VATICANA

PONTIFICIA
ACADEMIA
SCIENTIARVM

*COMMENTARII*
*Vol. III* - *N.* 19
pag. 1-48

# FOREWORD

The papers and discussions constituting the Proceedings of the Study Week on *Natural products and the protection of plants* of the Pontifical Academy of Sciences, held in the Vatican City on October 18-23 1976, have now been published in a coedition by the Academia Pontificia Scientiarum and Elsevier North-Holland.

Nevertheless, owing to the importance of the topics, we considered it useful in order to reach a larger audience to give with this publication a brief account of the scope, contents and results of this meeting.

January 1978

G. B. Marini-Bettòlo
*Chairman of the Study Week*

# MODERN TRENDS IN THE USE OF NATURAL PRODUCTS FOR CONTROLLING PESTS AND PLANT DISEASES

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## *Introduction*

Man's survival depends on the availability of food, and plants, directly or indirectly, supply that food. To ensure adequate food production man must fight daily against pests, such as insects, fungi molds, rodents and nematodes which would otherwise destroy the greater part of his crops.

In spite of the use of all available means for plant protection about one-third of the yearly harvest of the world (worth about 75 billion dollars) is destroyed by these pests [1].

In addition to the food plants like cereals, fruits and legumes other plants of commercial and industrial importance such as cotton, coffee, sugar cane, sugar beet, hemp and the trees which provide timber and cellulose are also at risk.

Tropical countries, because of their temperature and their particular environments suffer the most severe losses from pests. These losses may lead to serious famine in large areas of the world, many of which are densely populated.

Until 1945 the weapons used against the pests were mainly based on metallic salts (frequently copper salts), a few synthetic substances, and a limited number of natural products like nicotine, rotenone, rianodine, quassin and the pyrethrins.

Not all these substances were particularly efficient in protecting cultivated plants from the attack of insects and fungi however.

Therefore the finding in the early 1940's of the extraordinary properties of such substances as DDT and later BHC (Benzenhexachloride) and the subsequent development of the chlorinated cyclodienes, of organophosphates and of carbamates marked a major advance in the field of plant protection [2].

The use of these substances in the last twenty-five years has contributed greatly to the increase of food production but it has also raised a number of ecological and medical problems. In addition the repeated and continuous use of chemicals, some of which are very persistent, has led to the development of resistant strains which are unaffected by compounds that were previously very efficient in controlling these particular pests. The phenomenon of resistance is rather complex and generally is based on an induced biochemical modification which allows the pest to metabolize the pesticide. As a consequence, in the past, higher and higher quantities of the pesticide were frequently used, and ultimately new and more powerful pesticides had to be introduced for the treatment of the plants. It must also be remembered that insects very often develop a resistance not merely to a single compound but rather to a group of related compounds [3].

The use of insecticides may also lead to ecological imbalance, the destruction of species which prey upon the harmful insects as well as the harmful insects themselves and the destruction also of pollinating insects.

Some of the pesticides, e.g. organochlorine derivatives, are degraded very slowly by atmospheric and biological factors and thus they may last in the environment for years. This fact leads to the development of resistant strains among the pests on the one hand and to the contamination of the environment and the food chain on the other.

Considerable effort has been made all over the world to study the fate of the persistent organochlorine pesticides which accumulate





in human and animal bodies and now pollute the food chain even in remote areas like the arctic region.

The presence of organochlorine in the human bodies and the associated danger of long-term toxicity has resulted in national and international legislation to limit and even to ban the use of some compounds of this group. High toxicity is also a problem with some organophosphate compounds as well, and this problem taken together with the development of resistant pest strains makes the ongoing search for control agents which are less toxic to man and more readily degradable a matter of urgency [4].

The search for such compounds is based both on the random screening of as great a range of known organic products as possible and on the testing of new synthetic compounds which have been "tailor made" according to the general rules which relate structure to biological activity. By these means a number of new products come into use every year and help in the struggle to keep losses due to pests within limits [5].

In addition to the efforts of the chemists, biologists have developed biological weapons for pest control. Such methods of biological control are mostly in the early stages of development however.

Clearly an integrated approach using biological and chemical means separately or together as is most appropriate must be the ultimate objective. A number of examples of this approach such as the work at the Cañete Valley in Peru have shown how efficient it can be, even in very difficult conditions [6].

Basic research over more than thirty years on the biology and biochemistry of insects and plants has made it possible to envisage not only how new pesticides may be synthesised but also a completely new approach for the protection of plants using secondary plant products which may be toxic to a specific pest species yet harmless to man.

I should like to emphasize at this meeting that even though fundamental research is considered by many people and even by some administrators and governments as an academic exercise and even a luxury, it is only the results of many years of fundamental research which allow new practical solutions for extremely difficult problems to be reached. This is particularly true of plant protection where the new solutions envisaged are based on the combined knowledge arising from fundamental research in biology, biochemistry, chemistry, plant and insect physiology.

The purpose of this Study Week is to examine the present state of the basic research on natural products which may afford protection to plants and assess their possible use in agriculture.

In considering natural products we shall also consider those which can be more readily synthesised than extracted and also close synthetic analogues which are likely to be readily biodegradable like the natural products themselves.

In this meeting natural products which are not only those extracted from plants or insects but also their synthetic analogues provide the common denominator for our work. We shall consider and examine not only their application in the control of insects, using our knowledge of insect secretions, such as pheromones, molting hormones, repellents, attractants, antifeeding compounds, etc. but also our knowledge of other natural substances such as those obtained from plants, bacteria and the viruses.

A second matter that we shall consider is the biochemical basis of plant resistance. The finding of particular substances only in resistant plants, and the recognition that other substances may be formed under the stimulating action of insects or molds, illustrates how fundamental research is bringing us to a better understanding of plant resistance. We shall consider how this knowledge may be applied in the near future to the practical problems of crop protection.

* * *

In introducing this meeting I do not intend to summarize the results so far obtained in the two main areas described as we have here some of the most distinguished researchers in these fields. These researchers themselves will present up-to-date critical reports of the present knowledge in these different areas and these reports will form the basis of our discussions. My task will therefore be limited to tracing the guidelines for the discussions and outlining the aims and the spirit of the present "Study Week".





*Biochemistry of insects*

Early research on the biochemistry and physiology of insects led to the discovery not only of insect hormones but also of a number of other substances which condition insect behaviour. Knowledge of compounds like pheromones, repellents, attractants and antifeeding substances have been integrated by recent research which has led to the isolation and identification of a great number of natural products from insects which show interesting biological properties [7]. For example, more than 400 repellant substances have been isolated and characterised from 700 species of arthropods, and we have structural information on compounds affecting the physiology or behaviour of a number of different insects [8].

Most of the natural substances obtained from insects have rather simple structures like Juvenile Hormones (JH), which are alicyclic terpenes with several functional groups. Owing to the extremely low concentration of these substances in the insects, however, the isolation work constitutes one of the most interesting features of the chemistry of natural products [9]. More complicated structures have been found in the Molting Hormones (MH), like the ecdysones, and in some particular substances like pederin and dendrolasin. The fact however that the majority of these substances possess simple molecular structures allows their synthesis and the synthesis of analogues for biological assay. Some compounds like the ecdysones are not available in large quantities and this makes a practical application more difficult although new important sources of these hormones have been found in plants [10].

According to the phytotherapeutical rules slight modification of the structure of the natural product may modify or enhance its activity. Such modification may affect the absorption of the substance and also render it more resistant to degradation by light, atmospheric oxidation or geochemical agents. Industry has supported much work in this area recently, both in the laboratory and in the field.

In the last year a discovery of particular importance was the finding of precocenes in plants. These substances of rather simple structure belonging to the chromene group, are able to modify the role of juvenile hormones and under their influence dwarf insects are produced [11]. The use of precocenes thus opens another avenue to the chemical control of insects.

These findings of insect biochemistry have permitted field experiments to be carried out both in temperate and in tropical areas. When the results of these experiments have been fully assessed it may be possible to see more clearly how such products can be used most effectively in the future. Their evaluation should not be limited to their efficacy in controlling plant pests however, but must take into account their impact on the environment and their eventual toxicity to man even over very prolonged periods. Their cost and the difficulties of producing them on an industrial scale must also be considered.

All these points which will be decisive in determining whether a natural product will find a practical use in agriculture should be thoroughly discussed in order to establish if we can seriously consider such a substance as providing a new approach to the chemical control of pests.

*Insecticides from plants, bacteria and viruses*

We have considered the products which constitute the chemical agents of biochemical regulation and behaviour in insects. We have now to examine another application of natural products chemistry, that is the use of products obtained from plants, bacteria and viruses, as new weapons against insects.

Rotenone, ryanodine and, to a large extent, nicotine, have been abandoned for major field use for several reasons; the pyrethrins, obtained from *Chrysanthemum cinerafolium* are still widely used and the plant is cultivated over large areas in the highlands of Africa and South America. At present the main use of pyrethrin is for domestic insecticides because it is non-toxic in man and mammals and is highly sensitive to light.

Much work has been carried out on the synthesis and biological evaluation of pyrethrin analogues and these have given encouraging results in field trials.





Bacterial toxins have also been shown to be effective weapons against many insects, but only toxins of *Bacillus thuringiensis* have given positive results in the field against lepidoptera. It is certain that the use of toxins specific for certain insects could, with the help of modern microbiological fermentation techniques, be of great importance in the future strategy of plant protection [12].

The use of viruses for the control of insects and disease vectors has been studied in the last years and much information has been obtained in the use of some specific viruses, like those of the nuclear polyhedrosis. These methods could represent a new important approach in integrated pest control although the risks will have to be carefully evaluated before introducing them in agriculture [13].

*Plant resistance*

The second approach to the protection of plants from attack by insects or fungi, is through the biochemistry of plant resistance.

The introduction of resistant strains of plants after severe outbreaks of disease, for example of maize, have solved some extremely difficult situations in the past few years. It will also be remembered that in the last century European vineyards were saved by using American vines resistant to *Phyloxera.*

Resistant varieties are not always of good quality nor give high yields. Nevertheless plant geneticists have a very important responsibility to identify resistant varieties of the most important industrial and economically valuable annual plants in order that modified strains may be available in case of need.

Work carried out over many years primarily in the United Kingdom has given us much information on the chemical basis of plant resistance. On the one hand resistance may be due to the presence of some particular substance or substances which are accumulated in all plants of the resistant strain, on the other hand the substances that confer resistance may only be produced by the plants under attack by the insect or the molds; these are the so-called "stress products". Many of these substances have been isolated and their structure determined. They are generally substances of particular structures like the phytoalexins derived from furans or from pterocarpans [14].

There are also some rather uncommon stress substances formed in the plant under the stimulus of mold attack like the mansonones in elms infected by *Ceratostomella ulmi*, or lubimin and related germacrolides which are synthesised by *Datura stramonium* when infected by *Monilina fructicola*. Recent literature reports a number of these substances with unfamiliar structures and much work on their biological activity remains to be done [15]. The mechanism which induces the formation of the substances which protect the plants against further attack is also far from being understood. The first recognised example of this type of protection was provided by *Quercus* (oak) which produces gallotanic acid in response to the attack of the insect *Cynips*. The function of special substances present in the pest which induce resistance may give a reply to this point.

In a recent report it was stated that fungi like *Phytophtora megasperma* produce polyglucans, called *elicitors* which have the property of inducing the formation of defence products in plants. This finding may give a new lead to the control of pests especially if it can be confirmed that elicitors can be produced also from simple fungi like common yeasts (*Saccharomyces cerevisiae*) and that the eliciting action is due not to the whole molecule of polyglucan but to a low molecular product with 6 glycoside residues, easily soluble in water and thus absorbed by the plant [16].

Another approach to the problem is the study of the mechanism of action of pathogenic fungi on plants.

It has been known for many years that some strains of pathogenic fungi produce metabolites of low molecular weight which are apparently the chemical agents of the plant diseases. These substances which belong to several chemical groups were named *phytotoxins*: one of the first of these to be studied was lycomarasmin which causes the wilt of Tomato [17].

Recent research on the role of phytotoxins in plant diseases has provided results which make it possible to consider new means for the protection of plants [18].





* * *

I must apologize if, even though very rapidly, I have summarised facts that you all know well, but the aim of this meeting is not only to review critically all the chemical and biological data we have on the issue of this pressing problem, but also to try to foresee ways in which natural products may be used to protect plants and thus crops, thereby increasing the availability of food for the growing world population, which is largely concentrated in tropical areas and in the developing countries where for climatical conditions pests are much more diffuse [19].

The presence here at this Study Week of scientists from all over the world representing different fields of Science, together with the representatives of the Food and Agriculture Organisation of the United Nations and the researchers from agriculture and from industry, provides a unique opportunity to consider ways to establish new practical and economical systems for the defence of crops and for the protection of the natural environment. Such ways could be a great contribution to the wealth and health of mankind.

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# SUMMARY OF THE COMMUNICATIONS

## I

## PRODUCTS ACTIVE ON PLANT PESTS

P. KARLSON - Institutsgruppe Lahnberge der Medizinischen Fakultät der Philipps-Universität, Institut für Physiologische Chemie, Marburg (Lahn), Germany.

*Chemistry and Physiology of Insect Hormones and Insect Pheromones.*

Among the hormones in insects, only those regulating the post-embryonic development need to be discussed in context with the topic of this Study Week. Three hormones are involved: the brain hormone that stimulates the activity of the prothoracic gland, the ecdysteroids, products of the prothoracic gland that induce molting and metamorphosis, and the juvenile hormone, a product of Corpora allata, that modulates the effect of ecdysteroids and stimulates yolk production in the adult female. Chemically, the brain hormone is a peptide, ecdysone belongs to the steroids, and juvenile hormone is related to the isoprenoids. Juvenile hormone and its analogs can be synthesized comparatively easily, and studies for their use in insect control are under way.

Pheromones are substances allowing communication between individuals of the same species by chemical means. Virtually all pheromones are perceived by chemoreception. Among insects, the sexual attractants are the most important group. Their chemical structure is in many cases rather simple: they are straight-chain mono- or poly-unsaturated alcohols or esters (acetates). It is often observed that rather definite mixtures of two components are the active substance(s) of a given species, and related species use different mixtures of the same substances.

In contrast to insect hormones, the pheromones are species-specific. They would therefore, in principle, be the ideal tool for the control of insect pests, not affecting harmless or useful insects. However, their practical use meets with many difficulties.

J. B. SIDDALL - Zoecon Corporation, Palo Alto, California, U.S.A.

*Juvenile Hormones and their Analogs.*

Rapid progress has been made in the control of insect populations by the use of insect growth regulator chemicals, which behave as mimics of insect juvenile hormones. Such chemicals appear to have significant but limited applications. These are discussed with reference to hormone mimics which illustrate this concept. Inherent limitations to their utility can be anticipated if the insect's pestiferous life stage already contains significant amounts of endogenous natural hormone. This is the case with young larvae of moths and beetles, which comprise the major economic pest insects. The results of research on the chemical nature and internal concentrations of natural hormones in larvae suggest a very complex system of three hormones competing for three or more binding or receptor proteins, in the presence of esterolytic and epoxide-hydrating enzymes, to provide a stabilized effective level of hormones. The progress since 1966 in insect juvenile hormone research, development and practical application to pest control, as a basis for an attempt to explore the near future of insect hormone research, is reviewed.

H. SCHILDKNECHT - Organisch-Chemisches Institut der Universität, Heidelberg, Germany.

*Protective substances of Arthropods and Plants.*

Where life forms have arisen, they have had to defend themselves, even on the lowest levels, against their own kind. This struggle for existence can be carried on chemically with compounds of widely differing classes. Examples of defensive substances found





are hot quinones in bombardier beetles, and weak and strong carboxylic acids, phenols, terpenoids, steroids and alkaloids in other arthropods. An interesting parallelism can be drawn to the repellents of insects, regarding the irritant principle of Primulaceae, Urticaceae and Euphorbiaceae. The question arises if the chemical compounds found in the glandular or stinging hairs have the same biological function in higher plants as in insects, a question which might be answered by comparing the insect repellents with the plant chemicals.

C. CARDANI - Politecnico di Milano, Istituto di Chimica, Milano, Italy.

*Some Insect Metabolites and their Biological Significance.*

In recent years chemists, biologists and ecologists have devoted most of their interest to substances produced by insects and acting by chemical stimuli on their social behavior, growth and life itself. Some of these substances, owing to their exceptional properties, have already found an appropriate use in harmful insect control, either as they are or modified, both to facilitate their synthesis and to improve their properties; e.g., Juvenile Hormones, Molting Hormones and Sexual Attractants.

Many other substances, though they have not awakened such wide interest, have properties that indicate important possibilities for practical use. Examples of these are the Trail, Identification, Defensive and Offensive Substances.

From the chemical point of view, these substances are very different. Sometimes they are a single compound, sometimes they are complex mixtures of different compounds. Small differences in their quantitative composition may cause large differences in their biological properties.

The function of some substances produced by insects has not yet been defined, but biological activity — of tremendous intensity sometimes — and the relatively large quantity of substances contained in a single insect are a true indication that they perform a specific vital or social function. In these cases the insufficiency of our knowledge must be a stimulus for the entomologist to study further the behavior and the role of the insects themselves also in connection with their habitat.

In the study of the substances produced by insects, the interest of the chemist goes far beyond the definition of the structure, which often presents considerable difficulty, due mostly to the extremely small quantity of the substance available and the difficulties in isolating it. The supplying of the active substances by extracting them from the insects being impossible, the possibility of their use is strictly connected with the realization of suitable synthesis.

Chemists must also carefully examine the conditions of use to ascertain the possibility of degrading the substance in order to avoid dangerous concentrations in the field, and they must study the nature of the degradation products and their influence on the ecosystem.

W. S. BOWERS - New York State Agricultural Experiment Station, Cornell University, Department of Entomology, Geneva, N. Y. 14456, U.S.A.

*Anti-juvenile Hormones from Plants: Chemistry and Biological Activity.*

Juvenile hormone analogs are effective in insect control primarily by interfering with adult development during the ultimate stages of metamorphosis, when the natural juvenile hormones must be absent. During the immature and adult stages, however, natural juvenile hormones are continuously secreted and therefore these stages can not be controlled by treatment with juvenile hormone analogs. Since juvenile hormones are necessary during these stages, the most effective endocrinologic method of insect control would be through the use of anti-juvenile hormones or juvenile hormone antagonists.

We have isolated and identified two naturally occurring anti-juvenile hormones from the common bedding plant *Ageratum houstonianum*. These are the first anti-juvenile hormones discovered. We have also developed an inexpensive, high yield synthesis for these compounds, and have prepared several analogs with increased biological activity.





By contact and fumigation the anti-juvenile hormones induce certain immature insects to halt their immature development and undergo precocious metamorphosis into tiny sterile adults. Because of this action, we have named the natural compounds "precocenes".

Adult insects treated with the precocenes are sterilized. Contact or fumigation of eggs results in embryocidal effects or precocious metamorphosis of surviving nymphs. Certain adult insects which normally diapause due to the natural lack of juvenile hormones are induced to go into diapause following treatment with the precocenes.

All of the physiological actions of the precocenes duplicate the effects of surgical ablation of the Corpora allata which are the natural source of the juvenile hormones. Further, each of the anti-juvenile hormone actions of the precocenes can be prevented or reversed by the treatment with exogenous juvenile hormones.

In certain insects the precocenes interfere with all stages of insect life and therefore represent potentially important candidates for the development of a new class of safe and selective insecticides.

M. ELLIOTT - Rothamsted Experimental Station, Harpenden, Herts., England.

*Synthetic Insecticides Designed from Natural Pyrethrins.*

In many respects the natural pyrethrins are ideal insecticides, because they act rapidly against a wide range of insect species, do not harm mammals under normal conditions, and, being quickly rearranged or decomposed in air and light to inactive products, do not leave persistent residues. The structural features associated with these properties are discussed to indicate how synthetic compounds with greater insecticidal activity, lower mammalian toxicity and considerably increased stability in light have been developed.

K. NAKANISHI - Department of Chemistry, Columbia University, New York.

*Insect Growth Regulators from Plants.*

Some plants have given compounds having strong antifeedant activity against certain insects. The structural types of these compounds do not necessarily belong to one group. These aspects will be discussed together with other plant products which affect insects, like azadirachtin, warburganal and others.

L. CANONICA - Istituto di Chimica Organica dell'Università di Milano, Italy.

*Phytoecdysones: Environmental Degradation.*

The presence of ecdysones in many plants and their possible application as biological insecticides draw attention to their bio- and photodegradation processes and to the products formed by this degradation.

The microbiological oxidation of crustecdysone, makisterone A, muristerone A and α-ecdysone has been investigated using microorganisms which hydroxylate the 11-position of pregnane derivatives.

These compounds are not affected by the whole cells of the tested microorganisms, but, with the only exception of ecdysone, they are oxidized by the lysed cells. Moreover, instead of the 11-hydroxylation, the microbiological oxidation leads to the 20-ketosteroid posterone through side chain cleavage between C-20 and C-22. Post-sterone is in turn degraded to the 17-ketoderivative rubrosterone.

An analogous cleavage of ecdysones takes place in plant tissues, in insects and in other microorganisms; considering the degradation pathway of cholesterol to sex and adrenal hormones in the mammals, it appears of general significance for living matter. Ecdysones are sensitive to sunlight. Their photochemical transformation through Pyrex filter is strongly influenced by the nature of the solvent.





B. GILBERT - Centro de Pesquisas de Produtos Naturais, Universidade Federal do Rio de Janeiro, Brazil.

*Natural Product Derivatives in Tropical Insect and Parasite Control.*

Some JH analogues of types first developed by Beltsville workers may be obtained by very simple synthetic processes from a natural starting material, and they should compete favorably with insecticides. Laboratory experiments are described with Brazilian insect pests, particularly cereal feeders of the Lepidoptera and Coleoptera. The susceptibility of these families is compared to that of *Reduvii haematophagous* insects. The combined use of insecticides and JHAs is described and their possible antagonism commented.

Testing of numerous unmodified natural products has revealed activity against nematode larvae, which may be applicable to plant protection. Brief comments are made on other pests, particularly Attine ants and aquatic snails, where the use of natural products in control could supplant synthetic materials in certain cases.

H. J. SOMERVILLE - Woodstock Laboratory, Sittingbourne Research Centre, Sittingbourne, Kent, England.

*The insecticidal Endotoxin of Bacillus Thuringiensis.*

*Bacillus thuringiensis* produces several toxins which have activity against insects. However, the successful use of formulated preparations of the bacterium depends on the δ-endotoxin. This endotoxin is associated with a remarkable inclusion body which is formed during sporulation, and some spore fractions have recently been shown to have endotoxin activity. The endotoxin is specific in that it is toxic only to larvae of lepidopterous insects.

The inclusion bodies are insoluble at normal pH and the endotoxin is apparently activated by dissolution in the alkaline gut-juice of susceptible insects. Although conflicting reports exist on the molecular nature of the toxin, recent evidence indicates a single polypeptide of molecular weight 70,000 daltons. The toxin apparently acts by disruption of the mid-gut epithelium; however, there is no clear evidence on the initial site of action.

The molecular nature of the toxin, possible modes of action, and its physiological significance to the parent bacterium are discussed.

A. M. HEIMPEL - Plant Protection Institute, U. S. Department of Agriculture, Beltsville, Maryland, U.S.A.

*The Use of Viruses in Plant Protection.*

Insects are affected by most of the types of viruses that infect other animals and plants. Of these types the Baculoviruses have been selected by insect pathologists as the most promising for insect control. There are several requirements to consider when selecting a virus for development. The virus must be safe for other living forms, have a long storage life, be easily and inexpensively produced and must be effective in controlling insects in the field. The Baculoviruses fulfill these prerequisites better than any of the other virus types, with the possible exception of the cytoplasmic viruses and the entomopox viruses.

The parameters affecting the efficacy and survival of viruses in the field are discussed in detail. These include temperature, radiation, humidity, the speed of growth of the plant and the pH of the leaf surface.

The cost of producing virus is higher than the cost of producing a chemical pesticide and the cost of application is higher due to the number of treatments necessary. Nevertheless, the latter is amenable to research, and new formulations designed to protect these living organisms are now being developed.

The Baculoviruses have been tested in many countries throughout the world, and in most cases the viruses were indigenous. In most cases the viruses used cause natural epizootics in insect population, but unfortunately too late in larval development to protect the plant from damage. Proper timing of virus application is essential to kill the larvae when very young.





## II

## ARTHROPOD CONTROL THROUGH NATURAL PRODUCTS

V. B. WIGGLESWORTH - University of Cambridge, Department of Zoology, Cambridge, England.

*The Juvenile Hormone as an Agent for Pest Control.*

The function of juvenile hormone in the control of metamorphosis, in reproduction, in adult diapause, and in polymorphism is summarized. The theoretical possibilities of using the juvenile hormone for pest control are critically examined. This leads to the consideration of toxic effects and other abnormal effects of juvenile hormone and JH-mimics in embryonic development and subsequent growth. The future potential of such materials for insect control is discussed.

C. M. WILLIAMS - The Biological Laboratories, Harvard University, Cambridge, Mass., U.S.A.

*Anti-juvenile Hormone Effects of a Diffusible Agent that Inhibits the Corpora allata.*

Everything we learn about the insect endocrine system has the potentiality of being, not only of theoretical interest, but also of practical concern. Thus the isolation and characterization of the JH of the Cecropia silkmoth culminated in the theory and practice of the "third generation pesticides", in which synthetic JH analogs are used to block metamorphosis. Agents of this sort are most promising in the case of species whose deleterious effects are limited to the adult stage. This happens to be so in the case of most, but not all, species that transmit human and animal diseases. For example, a mosquito or tsetse fly possesses no problem until it comes to be an adult.

The situation is quite otherwise in the case of the major insect consumers of man's food and fiber, where the larval stages do most

damage. Clearly, the need is for new strategies in the control of larval insects.

There are ample theoretical grounds for believing that anti-hormones will provide at least part of the answer. Thus, an anti-ecdysone would block larval molting as well as metamorphosis and thereby enforce a developmental standstill reminiscent of diapause. An anti-JH would oppose the production or action of endogenous JH and provoke a precocious, lethal metamorphosis of immature larvae; moreover, in species requiring JH for egg maturation, an anti-JH might sterilize females that had already attained the adult condition.

The search for anti-insect-hormones has mainly been preoccupied with the screening of competitive inhibitors bearing a chemical resemblance to ecdysone or JH. Now as we learn more about the mechanisms by which the brain, prothoracic glands, and CA are turned off and on, a theoretical basis is thereby established for the discovery of agents that upset the normal controls.

One such agent is described which acts via the brain to shut off JH secretion by the Corpora allata. Thus indirectly it functions as an anti-JH.

G. B. Staal - Zoecon Corporation, Palo Alto, California, U.S.A.

*Differences between Natural JH and JH Analogs Elucidated by Use of a Substitution Assay.*

Most assay systems for juvenile hormone (JH) activity utilize intact insect specimens at a stage characterized by a low endogenous JH titer. However, such specimens may retain low amounts of residual JH and their Corpora allata may still be somewhat active and able to respond to xenobiotics. The positive results obtained by use of such test systems include abnormal juvenilizing effects, which are often difficult to evaluate quantitatively or even qualitatively. These systems are therefore not particularly suitable for providing data on the biological adequacy of compounds which mimic JH.

A more relevant test system uses IIIrd instar larvae of *Manduca sexta* surgically deprived of their Corpora allata and subsequently reared through two full larval instars into the Vth instar on food media containing precise concentrations of the test compound. In this system, the retention of normal morphology and pigmentation can be quantitated more precisely. The test system has revealed that essential, quantitative differences in the dose/response curves exist between natural JHs and JH analogs. Moreover, several analogs ultimately appear to be less than adequate substitutes for endogenous JH.

Some of these deficient analogs also produce JH antagonistic effects when applied in high doses to intact *Manduca* larvae. This suggests that such analogs compete with endogenous JH for JH receptor sites. Further improvements of this type of JH antagonistic activity may yield compounds useful for insect control.





G. B. Staal - Zoecon Corporation, Palo Alto, California, U.S.A.

*Insect Hormone Analogs for Insect Control.*

Despite very extensive research, none of the thousands of juvenile hormone analogs (JHA) investigated so far have been developed into effective and economical control agents for major insect pests. Among the reasons for this inadequacy are their cost, poor persistence as foliar residues, and above all, their delayed (mode of) action. Furthermore, all target species are sensitive to externally applied JH only during brief periods in their life cycle.

On the positive side, many JH analogs are quite selective and possess only negligible mammalian toxicity. If applied at the right moment, the quantity required to affect insects usually compares very favorably with most insecticides, but due to the usual asynchrony in insect populations this does not automatically translate into low rates for field application.

Successful applications have been developed for special insect pest problems where the disadvantages were less important than the advantages. The JHA kinoprene proved very effective for control of homopterous pests in greenhouses through a combination of high JH activity and an unrelated direct toxicity. The JHA methoprene proved to be extremely potent against larvae of flies and mosquitos. It is registered in the USA for the control of floodwater mosquitos (in a slow release formulation) and for the control of hornfly larvae in manure via oral administration to cattle. Methoprene is also used for increasing the silk production of silkworms in Japan.

Further progress in the development of JH analogs for insect control purposes might be expected with the development of more persistent analogs or formulations and through a redirection of control expectations toward insect population control rather than toward short term effects.

H. H. SHOREY - Department of Entomology, University of California, Riverside, California, U.S.A.

*Current State of the Field Use of Pheromones in Insect Control.*

Some aspects of the behavior of insects appear to be dependent on pheromone communication between the insects. By gaining knowledge concerning these natural uses of pheromones in insect behavior, man might be able to artificially manipulate the pheromone communication systems, leading to the insects not exhibiting the behavior in a proper manner and thus also leading to insect control. Two major strategies for utilizing pheromones in insect control have emerged. In one of these strategies, the pheromone is used as a bait to attract the pests to traps or to other devices, where they are destroyed. The second strategy relies on broad dissemination of a pheromone into the atmosphere, so as to disrupt normal pheromone communication and thus cause insect control. A number of current research programs which are directed toward the development of these strategies for pest control are reviewed and analyzed.

M. JACOBSON - Agricultural Environmental Quality Institute, U. S. Department of Agriculture, Beltsville, Maryland, U.S.A.

*Impact of Natural Plant Protectants on the Environment.*

Naturally occurring insecticides have distinct advantages over most of the synthetic pesticides in that they are *usually* non-toxic





to warm-blooded animals and do not tend to induce resistance in the target organisms. Nevertheless, if natural substances are to be used in a practical way in plant protection, they must first meet stringent specifications to assure that they will have no deleterious effects on vegetation, soil, wildlife, man, and domestic animals. This involves considerable time, effort, and expense in conducting physical, chemical, and toxicological studies in the laboratory and field. Both the known and potential effects of naturally occurring pheromones, repellents, and growth regulators useful in the protection of our food, feed, fiber, and horticultural crops are discussed.

N. ABO-KHATWA - The International Centre of Insect Physiology and Ecology, Nairobi, Kenya.

*Natural Products from Tropical Termite: Macrotermes subhyalinus. Chemical Composition and Function of Fungus Gardens.*

The association between the fungal genus *Termitomyces* and the African termite *Macrotermes subhyalinus* has reached a high degree of specialization.

Chemical analyses were performed on "fungus combs" and on various castes of termites with the ultimate objective of studying the importance of "fungus combs" in the nutrition of termites.

A polyhydroxy sugar was isolated from "fungus combs", and was identified, by spectroscopic and chromatographic methods, as D-Mannitol. Although this sugar was poorly oxidized by extracts of fungus conidia and termite workers, some preliminary results have shown that its presence in the "fungus combs" is important in allowing the growth of monocultures of *Termitomyces* while suppressing the growth of others.

Various other organic constituents (such as lipids, crude fibre, uric acid and several vitamins) plus inorganic constituents (such as Ca, P, Mg and Na) were determined in "fungus combs". These constituents seem to vary according to the various parts of the combs and to the season.

The composition of the lipid fraction was analyzed, by means of a column chromatography, to determine the relationship between lipids of "fungus combs" and those of termites.

## III

## PRODUCTS INVOLVED IN PLANT PARASITE INTERACTION

R. L. WAIN - Agricultural Research Council, University of London, Wye College, Wye, Ashford, Kent, England.

### *The Chemical Basis of Plant Disease Resistance.*

In nature all plants are exposed to many fungi, yet only very few cause disease. Antifungal compounds occurring in plant tissues contribute significantly to this widespread disease resistance.

The isolation and identification of a potent antifungal compound, wyerone, (methyl β-[2-hept-4'-enyl-1'-oxo-2'ynyl-furan-5]-acrylate) from the tissues of healthy broad bean seedlings would appear to be significant in relation to disease resistance, since, although wyerone is active against a range of fungi, it has little effect against the causative agent of Chocolate Spot disease *Botrytis fabae*. The presence of this aggressive pathogen within the leaves of broad bean plants has been found to cause a rapid increase in the quantities of wyerone and its analogues, which, however, do not suppress the invasion as the fungus is able to metabolise them.

The production of phytoalexins in plants infected with microbial pathogens and their importance in relation to disease resistance has been studied intensively at Wye College. A recent development in this work is the discovery that inoculating French beans with the Tobacco Necrosis virus (TNV) promoted the formation of fungitoxic compounds. Four phytoalexins: phaseollin, phaseollidin, phaseollinisoflavan and kievitone, have so far been isolated, the last three being new isoflavanoid compounds.

The production of phytoalexins following virus infection has now been demonstrated with other species of legumes.

An antifungal compound, identified as the diterpene sclareol, has been isolated from the leaves of *Nicotiana glutinosa*, and four more compounds have been shown to be produced in such plants when they are infected with tobacco mosaic virus (TMV). Tobacco plants are not known to be susceptible to rust diseases and it is significant that sclareol, obtained from the tobacco leaf, is capable





of protecting wheat and bean plants against rust diseases when applied to the leaves at concentrations as low as 0.01 per cent.

Chemicals have also been shown to be present in intact living roots which serve to defend them from invasion by micro-organisms present in soil.

From the foregoging it is clear that chemical protection plays an important part in natural resistance shown by plants towards disease. The antifungal chemicals isolated from plants may well prove to have uses in medicine as well as in agriculture.

I.A.M. CRUICKSHANK - Division of Plant Industry, CSIRO, Canberra City, Australia.

### *The Role of Phytoalexins in Disease Resistance Mechanisms.*

Research over the last 20 years on mechanisms of disease reactions in plants supports the concept that disease symptoms are the outward expression of the interrelationships between host, pathogen and environment. The relative resistance or susceptibility of a host plant to a given pathogen appears to depend primarily on the rate of net accumulation of fungal-elicited fungitoxic host-metabolites (phytoalexins) and their selective fungitoxicity.

At the metabolic level little is known of the role of the pathogen, although recent data suggest that certain macromolecules formed and secreted during conidial germination and mycelial growth may be important. The chemistry of phytoalexins on the other hand has received extensive study, especially in the Leguminosae and Solanaceae where isoflavonoid and sesquiterpenoid compounds, respectively, have been identified in this role.

The nature of the qualitative and quantitative relationships between fungal elicitor molecules and the initiation and control of the biosynthesis of phytoalexins remains a continuing challenge. A knowledge of the rate-controlling steps in phytoalexin biosynthesis could open the way to the manipulation of plant metabolism through chemotherapy to new and improved methods of disease control through the activation of the plant's own defense system.

E. A. BELL - Plant Sciences Department, University of London King's College, London, England.

*The Possible Significance of Uncommon Amino Acids in Plant-insect, Plant-animal and Plant-plant Relationships.*

Some 25-30 amino acids are commonly found in living organisms, either as protein constituents or as metabolic intermediates, such as ornithine and homoserine. The majority of amino acids (of which over 200 occur in plants) are of more limited distribution.

Many of the "uncommon" amino acids accumulate in high concentration in plants. For example free 5 hydroxy-L-tryptophan may represent as much as 14% of the dry weight of *Griffonia simplicifolia* seeds, and the amino acid azetidine-2-carbocyclic acid as much as 6% of the rhizomes of *Polygonatum multiflorum.*

If a plant diverts a large proportion of its resources, energy and storage capacity to the synthesis and accumulation of an uncommon amino acid which is not required for its primary metabolic processes, then that plant is unlikely to survive in competition with less prodigal neighbours unless the presence of the "uncommon" amino acid confers some selective advantage on the plant which accumulates it.

That some at least of these "uncommon" amino acids have a role in protecting the plants which contain them from predatory animals is suggested by the known toxicity of such compounds as α-amino-β-oxalylaminopropionic acid (the lathyrogen from *Lathyrus sativus*) to man and higher animals, while other "uncommon" amino acids such as L-3,-dihydroxyphenylamine (L-dopa) which is found in *Mucuna* seeds in concentrations of as much as 10%, is repellent and toxic to certain insect larvae.

The observation that some plants which synthesise "uncommon" amino acids can discriminate against them whilst other plants to which these compounds are foreign, incorporate them into their proteins with lethal effect, suggests that an "uncommon" amino acid in one plant species may serve to discourage competition from another.





R. F. CHAPMAN and E. H. BERNAYS - Centre for Overseas Pest Research, College House, Wrights Lane, London, England.

*The Chemical Resistance of Plants to Insect Attack.*

It is known that chemicals contained in plants may confer some degree of resistance to insect attack. Recent work with locusts and grasshoppers emphasizes the wide distribution and variety of such chemicals. There is enormous potential for the development of plant varieties which are resistant to insect attack because plants contain many chemicals which, when present in a sufficiently high concentration, prevent feeding by one or more species of insects. Resistance does not necessarily entail the total prevention of feeding; longer term antibiotic factors may effectively reduce pest population to economically unimportant levels. The significance of these naturally occurring chemicals to the plant must not be overlooked in breeding plant varieties more acceptable for human use.

A. BALLIO - Istituto di Chimica Biologica, Università di Roma, Italy.

*Phytotoxins: Structural Aspects and Biological Properties.*

The term "phytotoxin" is used alternatively, and ambiguously, to indicate either toxic metabolites of plants, or metabolites toxic to plants. Whereas the first class of products are dealt with exhaustively by other lectures in this Study Week, I consider only the second class, further restricting the discussion to phytotoxic compounds produced by phytopathogenic micro-organisms. A definite role of phytotoxins in a wide range of plant diseases is now generally accepted by phytopathologists, and an ever-increasing amount of work is developed to clarify their structure, biosynthesis and mode of action. Results from studies on phytotoxins are relevant not only to a better understanding of pathogenesis, but also to a rational approach to plant protection.

After a selected survey of bacterial and fungal phytotoxins, the results of an interdisciplinary investigation of chemical and biological aspects of the toxic metabolites of *Fusicoccum amygdali* Del., a widespread pathogen of Almond and Peach, is illustrated in detail; they represent a suitable "case history" of this type of study.

A. GRANITI - Istituto Sperimentale per la Patologia Vegetale, Roma.

*New Trends in the Use of Phytotoxins.*

Phytotoxins are metabolites produced by plant pathogenic microorganisms, which in low concentration interfere with or alter the plant cell metabolism, thus resulting in injuries to protoplasts. The presence of phytotoxins is a key factor in pathogenesis of many fungal and bacterial diseases of plants.

Once the chemical structure and the way of action of phytotoxins have been recognized, the possibility exists that these substances can be used for practical purposes.

Resistance of species or varieties of cultivated plants to toxigenic diseases can be tested using toxin assays. Plant breeders developing resistant varieties may select plants which resist diseases by screening them with phytotoxins in place of the pathogens. This is the case of the so-called "host specific" or "host selective" phytotoxins, i.e. toxins exhibiting specificity similar to that of the pathogens that produce them.

When no other means of control are available, reduction of the severity of a disease could be achieved by toxin inactivation or detoxification procedures.

Finally, phytotoxins themselves can be used for practical applications, e.g., as herbicides or plant growth regulators.

## IV

## NATURAL PRODUCTS IN THE PROTECTION OF PLANTS

R. H. GONZALEZ, E. J. BUYCKX, L. BRADER - Plant Production and Protection Division, F.A.O., United Nations, Rome.

*Prospects for New Control Practices of Agricultural Insect Pests in Developing Countries.*

Agricultural pest control strategies in developing countries increasingly require pest control practices alternate to pesticides, in order to reduce the ever-increasing dependence on chemical pesticides and to make better use of the components of the agro-ecosystem.





The need for developing more permanent pest management systems based on technical, ecological, economic and social considerations, is more keenly felt as unilateral approaches to crop protection often prove to be short-lived, apart from having several undesirable side effects. In the continuous struggle against pests, the use of simplistic approaches has resulted in the appearance of new pest problems, in the increase of genetic vulnerability of crops to pest attack, in the appearance and spreading of pesticide-resistant pest species, in toxicity to man, natural enemies of pests and wildlife, and in environmental problems due to extensive use of persistent chemical pesticides.

The Food and Agriculture Organization of the United Nations has been promoting and implementing national and regional crop protection programmes based on integrated pest control measures, including biological control, plant resistant varieties, cultural methods, selective chemical pesticides and where possible, natural substances such as attractants, pheromones and the like. Examples of on going national programs are cited.

Moreover, F.A.O. in collaboration with the United Nations Environment Program is currently undertaking a Cooperative Global Program on the development and application of integrated pest control in agriculture. This program aims to increase in various countries the capability to develop and apply integrated pest control programs. As such, it is meant to create a structure which will allow developing countries to make full use of knowledge acquired in developed countries. The new developments in natural products such as pheromones and selective control means clearly fall into the category of knowledge to be transferred. There is, however, also a strong need to identify the major pest control problems in agriculture in developing countries and to see how they can be tackled with the help of research facilities which have been built up elsewhere.

E. Zanini and F. Frilli - Facoltà di Agraria, Università Cattolica del S. Cuore, Piacenza, Italy.

*Field Use of Natural Products for Pest Control in Relation to Environmental Protection and Productivity.*

Modern agriculture, in order to produce for mankind the food and the raw materials necessary to life, must produce at minimum cost.

At present the above reasons, as well as economic problems, may suggest for the protection of plants not only the use of an increasing quantity of pesticides, but also different cultural methods (i.e. crop rotation, water management, adequate use of fertilizers, use of new genetical resistant strains).

Moreover, natural products and their synthetic analogs may offer a solution to the ecological problem, but so far there are not sufficient data available to assess their economic feasibility.

Therefore it is necessary to adopt agricultural interventions, capable of promoting the formation of natural products useful for the defense of plants, any drastic reduction in the use of persistent pesticides being at present rather difficult.

In the future the strategy of pest control at the level of the single farm should be planned, everywhere in the world, on a highly scientific base in order to obtain a better harvest.

S. H. Risco Briceño and R. Alves de Lima - Universidade Federal de Alagoas, Maceio, Brazil.

*Use of Natural Processes for Control of Insect Pests of Sugar Cane in Northeastern Brazil.*

Among the various insects which infest plantations of sugar cane in Brazil, the mothborer *Diatraea* spp. represents the most disastrous. Owing to the climatic conditions in Northeastern Brazil, which favor proliferation of these insects in their ecological niches, the application of insecticides would cause adverse economic and ecological effects and is not to be recommended.

Focusing on the problem of *Diatraea,* the Federal University of Alagoas and the Sugar Cane Experimental Station have initiated





a research on the use of pheromones to study population trends of *Diatraea,* to interfere favorably on the efficiency of natural predators, both native and imported, to control infestations, and finally, on the direct use of pheromones to reduce *Diatraea* populations.

Preliminary experiments with traps baited with *Diatraea* virgin females have been sufficiently promising to be included as an essential part of the "National Program of Diatraea Control" supported by the Brazilian Government.

M. Quijano Rico - Laboratorio de Investigaciones sobre la Quimica del Café, Federacion Nacional de Cafeteros de Colombia, Colombia.

*New Trends in the Research for the Protection of Coffee Plant against Coffee Rust.*

The problems of the protection of coffee plant against *Hermileia vastatrix,* known as coffee rust are discussed. The new approaches for the researches in this field are considered, mainly the study of resistant varieties and that of the role of microelements in the plant.

E. Knüsli - Ciba-Geigy AG., Basle, Switzerland.

*Industrial Aspects of the Practical Use of Natural Products or Derivatives in the Protection of Crops.*

The chemist searching for biologically active structures will miss an opportunity if he does not give his full attention to the stupendous chemical treasury offered by nature. He may detect there new tools directly suitable for practical application or useful as models for structural variation. In order to reach the level of practical application, however, promising offsprings of such an approach have to satisfy the same requirements as agents conceived and developed in other ways; i.e., to be efficient, to be toxicologically acceptable, to be compatible with the environment, to be economically competitive.

# CONCLUSIONS

The basic aim of the Study Week has been to review and discuss the present position in regard to fundamental research which might lead to more efficient control of plant pests and diseases.

In spite of control measures which are at present available, such as the use of conventional insecticides and fungicides, the world losses of human and animal food due to these causes — especially if both the growth and storage phases are taken into account — are enormous.

The seriousness of the problem of providing the growing needs of the underfed, steadily-increasing world population and the aggressiveness of plant insect pests and disease organisms justify making intensive efforts to combat these enemies. Scientists from all the relevant disciplines must work together towards achieving this objective. The following requirements, however, have to be satisfied before any method or measure can be generally adopted in crop protection:

- it must be efficient;
- it must not be disruptive or harmful to man and his environment;
- it must be economically acceptable.

There are various ways in which pest and disease control can be achieved, for example by:

- adopting proper cultural practices;
- using disease-free seed and planting material;
- breeding and selecting resistant varieties of crop plants;
- utilization of biological control measures and use of chemicals.

Studies on the biochemistry of host plant, pest and pathogen, the recognition of sophisticated chemicals which play a unique part in insect behaviour and other developments of this kind have led to a particularly attractive strategy for pest control which involves the use not only of these naturally occurring molecules but also of some of their structural analogues.

## I. Naturally occurring products

1. We consider that natural materials are one of the best sources for providing agents for pest control or for providing leads to their development. Despite long and extensive studies of natural products their potential use has been largely neglected.

2. The most appropriate natural products to be studied for potential practical use are those containing compounds acting endogenously and/or exogenously.

Endogenous compounds are defined as those which are produced by the particular plant, animal, microorganisms, etc., for the purpose of sustaining its life, either overtly or covertly, e. g., toxins, hormones, pheromones.

Exogenous compounds are defined as those which are produced by the various organisms which seemingly are not involved in life maintenance but, nevertheless, exert physiological activity on other living organisms, e. g., antibiotics, alkaloids, phytoecdysones, and numerous other odd natural products.

3. (*a*) We recommend that collection and extraction of natural products should be oriented towards demonstrated or suspected chemically controlled biological phenomena. In this way such research would develop from the naturally occurring biologically active compounds rather than from a less precise " screening " approach.

(*b*) As a consequence, isolation should be guided by biological activity, rather than by suitability of compounds for chemical investigation.

4. It would be most important to have a list of laboratories willing to perform biological assays, with details of amounts needed, and preliminary information required for testing.





One aspect of this Study wrek program was related to the insect hormones, pheromones and attractants. The natural products belonging to the group which can be used for plant protection may be divided into *two major categories*.

*A*) Natural products used *per se*:

1) ecdysteroids (operational use is pending);

2) pheromones of pests used for *monitoring*, as survey tools. These are used very successfully in numerous countries with great economic benefit;

3) a very limited number (about ten) of pheromones from *key* pests, which are now being explored on a semi operational scale (100 Ha). On the basis of present knowledge pheromones for direct control are only likely to be used operationally for *key pests*. A key pest is here defined as a pest species which if reduced to non economical levels would lessen the need for pest control measures.

The need for a low pest-population density prerequisite for successful pheromonal control imposes obvious limitations; thus, for example, they should operate during the whole season and be applied over wide areas in a co-operative program not involving individual growers.

*B*) Natural products which have provided a lead towards structures for practical use in plant protection.

Some specific examples already developed and used in operational practice are listed below:

| | | |
|---|---|---|
| Nereitoxin | led to the development of | PADAN insecticide |
| Juvenile hormone I | « » | Epofenonane |
| Juvenile hormone II | « » | Methoprene; kinoprene ... |
| Indoleacetic acid | « » | 2,4-D and many analogues |
| Ethylene | « » | Ethephon (an ethylene producing compound) |
| Pyrethrines | « » | Pyrethroids |

In the case of analogues of juvenile hormones only 3 different compounds are in current operational use as insecticides at the present time; these are methoprene, kinoprene and epofenonane.

The total current sales of such analogues are less than 0.25 % of the worldwide insecticide sales which amount to approximately U.S. \$ 1.2 $10^9$ (Farm Chemicals, Sept. 1975, data source for total). The compounds affecting chitin synthesis (diflubenzoron, difluron) were not derived from a natural product and are considered outside the scope of this Study Week.

The limitations which operate with chemicals possessing juvenile hormone activity are:

*1)* high selectivity for insect species which give a low economic return on the high industrial investment made (this is also true of other selective insecticides);

*2)* useful selective activity on insects which represent only minor markets;

*3)* activity exerted on major pests is not high enough.

*Prospects for using antijuvenile hormone agents in crop protection* are so far limited by the fact that they act, with two exceptions only, against non economic insects.

Internal homeostatic mechanisms for control of natural hormone levels within insects are both very efficient and virtually unexplored. The lack of knowledge is greatly hindering the possible use of anti-JH chemicals in crop protection.

The *prospects for using juvenile hormone analogues in plant protection* are also limited. Only a few areas in plant protection appear to be suited for control by morphogenetic agents (juvenile hormone analogues). This is primarily because of lack of economic return on grower's investment arising from lack of immediate control of young larvae, the necessity for critical timing of application and the fact that re-invasion can occur.

*Recommendations for future research* may be focused on two points:

*1)* intensive research on the natural mechanism of control of endocrine organs of arthropods is needed so as to provide an understanding and a rational basis for discovery and design of agents which will control young larvae of insects;

*2)* economic research on the provision of funds for both development and production of selective insecticides which are conventionally described as uneconomical in terms of return on investment.





## II. Biological control agents (living organisms and viruses)

Biological control agents for use in plant protection can be divided into two groups based on application procedures:

*a)* those agents that will be applied in the same way as chemicals;

*b)* those for which specialized knowledge and methods will be required.

There may be a broad parallel between these two groups, respectively, and those which require repeated application and those which are semipermanent in effect.

The future production of biological pesticides will probably be carried out at two levels: production within host species and, for some micro-organisms and viruses, large scale production based on fermentation technology.

In both of these areas research is needed to develop inexpensive and effective methods of production. The latter approach shows more immediate promise for new biological control agents. However, it is important that adequate safety checks be carried out on each production batch of material and caution should be exerted before the use of any non indigenous control agent.

Biological control agents that have been used successfully include *Bacillus popilliae*, in control of Japanese beetle, *Bacillus thuringiensis*, which is used in the control of many lepidoptera; and virus and nematode preparations which have recently been made available commercially. The following are examples which are in varying stages of research and development.

There are two *Microsporidia*, several species of nematodes and a spore forming bacterium that show promise in controlling populations of insects known to transmit human and animal diseases.

Several protozoa, viruses and fungi are currently being developed to control phytophagous insects harmful to food and fiber crops and several protozoa, viruses and bacteria are available for control of stored product insects.

For the future it is recommended that any observation of epizootics should be processed as follows:

Contact should be made with a competent biologist who should isolate the causative agent and, at least, demonstrate that Koch's postulates are satisfied. The organism or virus responsible should then be deposited in the most accessible culture collection and the observation published.

Further development may depend on strain selection and host spectrum studies and in this connection the international program for *B. thuringiensis*, mentioned elsewhere in this volume, could serve as an example.

It is possible that detailed study of the molecular mechanisms involved in the efficacy of such control agents will reveal new target mechanisms for the biochemist and, when toxic products of micro-organisms can be identified, we believe research should be directed at elucidation of their mode of action.

## III. Disease resistance

Numerous examples are known of plants which are resistant to pathogens and herbivorous animals. This resistance may depend on static mechanism of protection, either chemical or physical, or on dynamic mechanisms, involving the production of specific chemicals in response to attack. The precise mechanism of resistance is known only in a few cases.

A knowledge of these mechanisms is important to enable us to take a rational approach to the development and use of varietal resistance and enable geneticists to take full advantage of the enormous pool of resources available in plants.

[One aspect of the programme was related to the studies on the chemical basis of plant disease resistance.] Recent research has provided information on why all plants growing in nature are completely resistant to most of the fungal diseases to which they are continuously exposed in the field.

There is now much evidence that defensive chemicals present in healthy plants and chemicals produced within them when under stress conditions, operate in natural disease resistance.

Isolation and identification of the chemicals in this group of





natural products have given a new impetus to research on the control of plant diseases. Such research might also be of benefit to medicine. The importance of these developments was recognized and supported. One became well aware of the many problems which are common to both pest and disease control, and the desirability of close collaboration between research workers within these fields was well recognized.

1) It is recommended that emphasis should be placed on studies of the mechanisms of resistance of existing crop plants, and of mechanisms of pathogenicity of plant parasites, in close collaboration with plant breeders so that the most productive effort can be focused on the development of new relevant varieties.

2) Studies should be made of pest/host plant relationships in naturally occurring populations of wild plants and minor crops with the objects of developing potential food crops which are already adapted in other respects to a tropical environment and of establishing the underlying principles involved in pest/host plant relation which can then be applied in agricultural ecosystems.

3) Investigation should be made of the mechanisms and potential of induced resistance to disease, especially as a possible safeguard against the progressive reduction of gene pools which is recognized as having occurred in some of the major food crops.

4) Communication should be improved between scientists of different disciplines who are involved in the study of plants and their pathogens and pests. Only in this way is it possible to achieve maximum utility from the findings in different areas of research.

## IV. Integrated pest control approach

Crop protection should preferably not be based on unilateral approaches and results of research on natural products and their analogues could be used within the framework of integrated pest control.

Integrated pest control has so far been mainly developed and implemented in the industrialized countries and only in a limited number of situations. Its further extension depends on the availability of research facilities and capabilities as well as adoption by the farmer.

If crop protection is to be fully utilized in increasing food and fibre production in developing countries, it is important that these new approaches be made available to rural communities. In spite of the apparent complexity of integrated pest control, it has been demonstrated that the system can be implemented progressively on a step by step basis. This approach therefore offers a unique opportunity for introducing new research findings to improve crop protection.

Integrated pest control requires a certain degree of infrastructure to fully utilize current scientific information and research capabilities and to develop more advanced pest control techniques.

Furthermore, local knowledge in crop protection, for example, the impact of cultural practice, should be studied and considered for inclusion in crop protection programmes.

In order to overcome the present limitations in development and adoption of integrated pest control programmes, more research and extension work is required. This applies particularly to the developing countries where special efforts are needed to strengthen national capabilities.

Emphasis must also be given to training workers for crop protection research and extension; in this connection, close collaboration with the scientific community is needed.

## V. Information and Communication

The importance of sharing knowledge and the need to perform highly specific biological assays were also emphasized.

Suitable media for documentation exist already; they could be used in a more consequential way, in so far as printed information should be considered more than in the past as a bridge to direct personal contact between researchers engaged in related topics.

In order to strengthen the flow of suitable information the FAO and also other appropriate Agencies are suggested to consider possibilities for a coordination of the interchange and for acting as mediators.





## VI. Conclusions

There was general agreement that the new approach indicated in the title of our Study Week, "Natural products and the protection of plants" provides much promise at the present time.

One of our aims — which has been abundantly achieved — has been the stimulation of new ideas, the sharing of knowledge and educating each other in the various aspects of pest control research in fields different from one's own. As a result, many of the participants will return to their laboratories to initiate experiments whose conception arose directly from the intensive discussions carried out in a calm and relaxed atmosphere between scientists from widely different fields.

As a result of our discussions and deliberations, it is hoped that further achievements towards the welfare and benefit of mankind will be realised.

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