APPOINTMENTS

Asa S. Knowles, president, Northeastern University, to chancellor at the university. . . . **James Frank**, vice president for academic affairs, Medgar Evers College, City University of New York, to president, Lincoln University. . . . **Thomas E. Broce**, executive assistant to the president, University of Oklahoma, to president, Phillips University. . . . **Thomas R. Fitzgerald**, academic vice president, Georgetown University, to president, Fairfield University. . . . **Archie R. Dykes**, chancellor, University of Tennessee, Knoxville, to chancellor, University of Kansas. . . . **F. Carter Pannill**, founding dean, University of Texas Medical School, San Antonio, to vice president for health sciences, State University of New York, Buffalo. . . . **Philip D. Vairo**, dean, College of Professional Studies, University of Tennessee, Chattanooga, to dean, School of Education, California State University, Los Angeles. . . . **Warren S. Wooster**, professor of oceanography, Scripps Institution of Oceanography, to dean, Rosentiel School of Marine and Atmospheric Science, University of Miami. . . . **Ernest S. Kuh**, chairman, electrical engineering and computer sciences department, University of California, Berkeley, to dean, College of Engineering at the university. . . . **Max L. Williams, Jr.**, dean, College of Engineering, University of Utah, to dean, School of Engineering, University of Pittsburgh. . . . **Herman Feshbach**, director, Center for Theoretical Physics, Massachusetts Institute of Technology, to head, physics department at M.I.T. . . . **Paul S. Lykoudis**, director, Aerospace Sciences Laboratory, Purdue University, to head, nuclear engineering department at the university.

(Continued on page 880)

RESEARCH NEWS

Insect Control (II): Hormones and Viruses

Insect pests are man's major competitors for food, fiber, and forest. Because control of these pests is essential, entomologists are seeking alternatives to the broad-spectrum chemical insecticides now used almost exclusively. Although these have been effective, they can also cause problems. Such insecticides are not very selective—they kill helpful as well as harmful insects and may also be toxic to birds and mammals. Of special concern is the fact that their use has resulted in the emergence of resistant insect strains that are no longer killed by the chemicals.

Thus, investigators are trying to develop more specific techniques based on inherent physiological and behavioral regulatory mechanisms of insects. The application of pheromones to insect control was discussed in a previous article (*Science*, 24 August 1973). This article is concerned with examples of the use of hormones in insect management programs and also with efforts to curb insect populations by infecting them with viruses.

Juvenile hormones (JH) and molting hormones (MH) or ecdysones are two of the major types of hormones regulating insect growth and maturation. In order to grow, insect larvae must molt —that is, they must shed their rigid cuticles and replace them with new ones. Both JH and MH are required for larval molting. However, JH secretion must cease in order to allow the larvae to develop into sexually mature adults.

Since larvae die as a result of the abnormal development that occurs when JH is present at the "wrong" time, Carroll Williams of Harvard University, Cambridge, Massachusetts, suggested in 1956 that JH and analogs of JH could be used as insecticides. One such compound, Altosid SR-10, a product of the Zoecon Corporation, Palo Alto, California, has now been registered for experimental use by the Environmental Protection Agency (EPA). According to John Siddall, Zoecon's vice president for research, Altosid SR-10 is effective against several species of flies and mosquitoes; however, its registration is for control of floodwater mosquitoes.

At present, JH insecticides can be applied only in somewhat restricted circumstances. This is because such compounds interfere with development only at specific stages of the insect's life. An insect species undergoes a characteristic number of molts as it grows; the periods between molts are called instars. At the end of the last larval instar, an insect that has a complete metamorphosis molts first to the pupa and the pupa then molts to the adult form. Insects with incomplete metamorphoses molt from the sexually immature nymph to the adult. Only these molts are disrupted by JH and JH analogs, usually with the production of intermediate forms that have both immature and mature characteristics.

These intermediates soon die. However, an insect's susceptible period may be rather brief. Thus, the hormonal insecticides must remain in the environment long enough to ensure that a large percentage of the population is exposed during its sensitive period. This is easily achieved for floodwater mosquitoes. The eggs hatch within minutes of their immersion in water—and the farmer controls the time of irrigation of his fields. This synchronizes the development of the population so that large numbers go through the sensitive period at the same time. Altosid SR-10 formulated in micro capsules retains its efficacy in water for up to 7 days—a period long enough to prevent the emergence of adult mosquito pests.

Siddall pointed out that hormonal insecticides such as Altosid SR-10 are not yet suitable for controlling malarial mosquitoes in undeveloped countries. They do not kill adult mosquitoes, the malaria carriers. Moreover, they cannot compete with DDT on the basis of cost per pound. Thus, the more conventional insecticides will still be needed in such countries, although the problem of resistant insects is of worldwide concern.

Stauffer Chemical Company, of Westport, Connecticut, is also developing JH analogs for pest control. According to Charles O. Persing, director of agricultural chemical research, and

Julius Menn, manager of insecticide research and biochemistry, one compound given the code R-20458 by Stauffer has shown promise in controlling biting insects such as stable flies and mosquitoes. Treating feedlot soil with the chemical prevented the fly larvae (maggots) that live in manure from developing into adults. Since the compound has a half-life of 21 days in the field, Menn said that two to three applications per season should be sufficient for control. Some insecticides that kill the adults but not the larvae need to be sprayed two to three times per day to suppress the adult fly population.

The instability of JH and JH analogs is both an advantage and a problem. Because such compounds usually contain double bonds and epoxide or ester groups, they are readily biodegradable and do not persist in the environment. Frequently their stability must be increased either by modifying the structure of the molecule or by formulating preparations that contain stabilizers. Also advantageous is their low toxicity to mammals. For example, the LD_{50} (the amount required to kill 50 percent of the test animals) of Altosid SR-10 in rats is almost 35 grams per 1000 grams of body weight—a figure much higher than those of conventional insecticides. Most investigators believe that long-term effects, including mutagenicity, will also prove negligible, but these experiments are continuing.

The specificity of JH analogs is less than that of most pheromones but greater than that of conventional insecticides. Some affect members of several insect orders. Investigators at Stauffer, for example, are studying the use of compound R-20458 for control of such diverse pests as cockroaches (order Orthoptera) and the confused flour beetle (order Coleoptera), in addition to flies and mosquitoes (both in the order Diptera).

Other JH analogs are more specific; they are active only on insects that belong to a given order or even to one family. In 1965, Karel Slama, while working in Carroll Williams' laboratory, observed that the European linden bug did not mature when grown on some American paper products (including *Science*). Subsequently, William Bowers and his colleagues at the Insect Physiology Laboratory, Agricultural Research Service (ARS), Beltsville, Maryland, isolated and determined the structure of this "paper factor," now called juvabione. Juvabione, which is found in the wood of the balsam fir, only affects members of one family of "bugs." Structural modification of JH compounds may also lead to greater specificity of action.

A major problem with the use of JH analogs for insect control is their ineffectiveness early in larval life. When the larval form is the pest—the caterpillars of moth species, for example—they may cause substantial damage before they die. Thus, hormonal insecticides are suited for use only against light infestations for which the amount of damage is economically tolerable or against adult pests such as mosquitoes or flies.

This problem could be solved if there were a way to block the action of either JH or MH and prevent molting at all stages of development, even the earliest. Several investigators are looking for compounds that inhibit the synthesis or action of these hormones. William Robbins and his associates at the Insect Physiology Laboratory, ARS, have found some compounds that appear to interfere with ecdysone activity. The ecdysones are steroids. According to Robbins, several azasteroids (steroids containing nitrogen) were shown to disrupt the development of some insect species. The susceptibility of the larvae varied during their life cycles, but the agents were active at all times. The yellow fever mosquito, for example, was most vulnerable during its first two instars. Robbins believes that the azasteroids inhibit either the biosynthesis of ecdysones or their normal breakdown.

Toxicity of Ecdysones

The ecdysones themselves have a toxic effect on insects. They can interfere with cuticle development or produce effects similar to those evoked by JH during the last instars. However, because of their complex steroidal structures, synthesis of compounds with MH activity is difficult and expensive. Robbins hopes that simpler analogs, such as those he has been investigating, may be produced more economically.

When pupae are treated with ecdysones they may molt to form another pupa rather than molt to the adult form. Howard Schneiderman and his colleagues at the University of California, Irvine, have suggested that the insect rapidly secretes a new cuticle in response to the hormone. The response is so fast that the epidermal cells do not have sufficient time to perform the DNA replication necessary for the synthesis of an adult cuticle, and a second pupa is formed.

The effects of ecdysone may be seen in arthropods other than insects. Schneiderman found that one natural ecdysone induced molting in all of the species examined, including the horseshoe crab, spiders, a freshwater crayfish, and a fiddler crab. This lack of specificity may be a disadvantage if the natural ecdysones are applied to insect control.

Although the steroidal nature of the ecdysones might appear to be an impediment to their use as insecticides, especially on crops eaten by man, this is not necessarily the case. Several investigators pointed out that similar materials are already widespread in nature. Many steroids with ecdysone activity, including the two of the four known insect ecdysones, have been isolated from plants. The role of these chemicals is still unclear. Some researchers have proposed that they may protect the plants from predatory insects. Whatever their roles, compounds with JH or MH activity are widely distributed in the plant kingdom.

The emergence of insects resistant to the insecticides formerly used for their control has been a major concern of entomologists. One of the arguments for development of hormonal insecticides is that insects would be less likely to become resistant to their own hormones or to closely related chemicals. Nevertheless, insects are notoriously adaptable. Schneiderman believes that such resistance will indeed be a result of the application of hormonal insecticides.

As he points out, insects must already have mechanisms for inactivating JH so that metamorphosis can occur. There is also great variability in the responses of different species to JH. Since these species differences are undoubtedly genetic, they may also occur among individuals of the same species. Thus, the less susceptible insects will survive treatment with the insecticides, and resistant strains will appear.

In addition, the structures of many analogs differ substantially from those of the naturally occurring hormones. Insects may be able to detoxify such analogs just as they do the more conventional insecticides. However, most investigators believe that development of resistance to hormonal insecticides will be slower than that caused by the older insecticides.

Methods of pest control based on the use of pheromones or hormones differ significantly from control with broad-spectrum insecticides. The former should produce much less environmental deterioration because of their greater selectivity, their low toxicity to vertebrates, and their effectiveness at relatively low doses. Nevertheless, they are still chemical control methods. One strategy that is completely biological is the use of viruses to control pest insects.

Epidemics caused by viruses occur periodically in insect populations and help to check their growth. Entomologists are seeking ways to aid these natural control processes—to infect pest insects before they cause serious damage. The Douglas-fir tussock moth, for example, undergoes population explosions at intervals of approximately 10 years. During these outbreaks, which last up to 3 years, the moth larvae can cause severe damage—usually defoliating and killing trees—in the forests of the western United States. According to Clarence G. Thompson of the Pacific Northwest Forest and Range Experiment Station, U.S. Department of Agriculture (USDA), Portland, Oregon, the eventual collapse of these explosions is largely due to a viral infection.

Until it was banned, DDT helped to keep the tussock moth population in check. Thompson and his colleagues are now attempting to devise ways to terminate the current outbreak of the pest with the virus. A suspension of the tussock moth virus can be sprayed on foliage with the same equipment used for chemical insecticides. When this procedure was tried, according to Thompson, the results looked promising. Treatment did not prevent all of the tree damage, but the pest population declined and fewer trees were actually killed.

The tussock moth virus is an example of a nuclear polyhedrosis virus (NPV). The viral particles—DNA plus protein—are imbedded in a protein matrix. The whole complex, called an inclusion body, is shaped like a polyhedron. The protein matrix apparently protects the virus particles from the harsh field conditions. These viruses spread when larvae eat contaminated foliage. The viruses multiply in the larval cells and eventually cause the larva to literally dissolve. Thus, additional foliage is contaminated. One of the disadvantages of viral control methods is that infected larvae may live—and continue eating—for several days after infection.

The gypsy moth is also susceptible to an NPV. Franklin Lewis and his associates at the Northeastern Forest Experiment Station, USDA, Hamden, Connecticut, in an experiment begun in 1963, found that spraying with gypsy moth NPV reduced both the defoliation and gypsy moth population in a 1-acre test plot. More recently they were able to achieve population reduction but not foliage protection with the virus. Lewis hopes that the NPV, a natural pathogen of the gypsy moth, will remain active in the surviving population. However, epizootics occur naturally only when the insect population is high. By that time the infested forest may have already suffered severe damage.

Specificity of Viruses

Most insect viruses are specific for a few closely related hosts. The gypsy moth NPV infects only the gypsy moth and the nun moth. At least one virus has a much broader specificity. P. V. Vail of the Entomology Research Division, ARS, Phoenix, Arizona, found that the alfalfa looper NPV infects a rather broad series of hosts, including the corn earworm, the cabbage looper, the beet armyworm, and the pink bollworm, in addition to the alfalfa looper.

Cabbage looper and beet armyworm larvae infestations can virtually destroy lettuce fields in the Southwest unless the pests are controlled by frequent and heavy applications of insecticide. Vail found that spraying the fields with either alfalfa looper or cabbage looper NPV could control such lepidopterous pests. Chemical insecticides were still needed for control of other pests, but in greatly reduced quantities.

One reason for using more selective control agents such as viruses is to minimize deleterious effects on pest predators that help check pest population growth. However, Vail found fewer predators in virus-treated fields than in control fields, but the reduction in predators due to the virus was not as severe as that due to chemical pesticides. Vail is now testing the activity of alfalfa looper virus on the pink bollworm and other pests of cotton.

One virus is already being produced commercially (in limited quantities) for control of a major cotton pest, the cotton bollworm. The virus is an NPV that infects both the cotton bollworm and a closely related species, the tobacco budworm. The cotton bollworm is also called the corn earworm and the tomato fruitworm, but the virus is not now licensed for use on food crops. Sandoz-Wander, Incorporated, Homestead, Florida, will market the viral insecticide as Viron/H. (The virus was developed by International Mineral and Chemical Corporation, Libertyville, Illinois, but is now the property of Sandoz-Wander.) The virus preparation of Nutrilite, Incorporated, Buena Park, California, is called Biotrol VHZ.

According to Martin Rogoff of Sandoz-Wander, the performance of the virus in field trials, as measured by cotton yields, was almost equivalent (within 10 percent) to that of the chemical methyl parathion. In his opinion, its performance may be better in the long run because it does not kill parasites and predators as chemicals may. Moreover, it is quite specific for larvae of the moth genus *Heliothis*. Rogoff said that the virus had no harmful effects on a variety of plants and vertebrates.

At present, viruses can reproduce only in living cells. Insect viruses are usually grown in the appropriate hosts. Viron/H, for example, is produced in the bollworm. This means that large quantities of insects or insect larvae must be maintained. It also increases the chance for contamination by unwanted viruses and by bacteria and fungi. Several investigators are trying to develop cell culture systems for propagating insect viruses. One such researcher is W. F. Hink of Ohio State University, Columbus. He has been able to grow alfalfa and cabbage looper viruses in cultured insect cells. Although these systems are theoretically less susceptible to contamination than living insects, he points out that they are expensive. Cultured cells will not be used commercially until they can be grown more simply and cheaply.

Pheromones, hormones, and viruses are three of the weapons now being developed for the insect control arsenal. Entomologists do not think that they will replace more conventional chemical insecticides. Rather, these newer weapons will supplement the older techniques and consequently reduce both our dependence on traditional insecticides and their adverse effects on the environment.

—JEAN L. MARX

Additional Readings

1. R. F. Anderson, T. R. Shieh, H. T. Huang, M. H. Rogoff, *Ferment. Technol. Today* (1972), p. 623.
2. W. E. Robbins, in *Pest Control: Strategies for the Future* (National Academy of Sciences, Washington, D.C., 1972), pp. 172–196.
3. H. A. Schneiderman, in *Insect Juvenile Hormones*, J. J. Menn and M. Beroza, Eds. (Academic Press, New York, 1972), pp. 3–25.