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The Search for Chemical Bait Toxicants

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Control of pest ant species relies characteristically on toxic baits which consist of a toxicant combined with an attractive food material and, if needed, a granular carrier for ease of dispersal in outdoors or large-scale control programs. The effectiveness of this approach depends upon the availability of a delayed-action toxicant so that foraging ants are not killed before they carry it back to the nest and distribute it to all colony members. The ultimate transfer of the toxicant to the queen is of paramount importance since her continued egg production will soon result in colony growth even though 85% or possibly more of the original workers are killed (Williams et al. 1980).

The first studies with bait toxicants for fire ant control were conducted by Travis (1939) against *Solenopsis geminata*. He used thallium sulfate or thallium acetate in syrup baits. The former compound was toxic in cage tests but not in the field while the latter appeared effective in both types of tests. Results in the latter tests were reported to be erratic, probably due to weather conditions. Green (1952) tested a bait containing thallium sulfate against the black imported fire ant, *S. richteri*, and found it effective against captive colonies but ineffective when scattered around mounds in the field.

With the advent of the red and black imported fire ants (IFA), *S. invicta* and *S. richteri*, as major pest species and the promulgation of the Federal-State Imported Fire Ant Control Program in 1957, a concerted drive was made by the United States Department of Agriculture (USDA) to identify effective toxicants and bait formulations. The procedures used to identify toxicants were described first by Stringer et al. (1964). Various modifications of these techniques were made over the next 20 years; the most recent description was published by Williams (1983) who described three steps in the evaluations. These included primary screening tests with individual workers, secondary tests with queen right laboratory colonies, and

field tests with natural infestations.

Basically the primary screening tests involved allowing groups of 20 worker ants in test chambers to feed for 24 hours on soybean oil or sugar-water solutions of the candidate toxicants. After this they were transferred to clean chambers and given neat food; mortality was recorded at regular intervals for 14 days. In the initial tests, field-collected ants were used; however, later, when colony laboratory-rearing procedures were perfected, workers from these colonies were utilized. Any toxic chemicals that produced delayed toxicity (<15% mortality after 24 hours) over a tenfold dosage range were re-evaluated as baits with queen right colonies. In these tests, the chemical was dissolved in soybean oil and fed directly to the ants from micropipettes or following absorption on a granular carrier (corn cob grits or pregel defatted corn grits). Observations of worker and brood mortality and effects on the queen were recorded over a period of one to several months, depending upon the severity of the toxicological response. Toxicants that killed the colonies directly or inhibited development and reproduction were next formulated in soybean oil and a carrier for distribution on small field plots. Effectiveness of the baits was determined by comparing the total number of active nests before and after treatment or by a more complex method that involved rating colony size and presence or absence of brood.

Toxicants that are effective in all of these stages of development are considered candidates for commercial development; however, other factors could influence their successful development. Accordingly, we have determined several characteristics that are essential for a particular chemical to be a suitable ant bait toxicant. The toxicants must:

- a) Be soluble in vegetable oils,
- b) Lack repellency to the ants,
- c) Exhibit delayed toxicity over greater than a tenfold range of concentrations,
- d) Be transferred readily from one ant to another during trophallaxis,
- e) Be rapidly biodegraded,
- f) Exhibit low mammalian toxicity in the formulated bait, and
- g) Be environmentally acceptable.

From 1958 to 1977, over 3200 chemicals were evaluated for activity as bait toxicants (Banks et al. 1977). Only one of these, mirex, was eventually developed commercially as an ant bait. These data vividly illustrate the difficulty in discovering and developing delayed-action toxicants. When mirex registrations were cancelled by the Environmental Protection Agency (EPA) in 1977, we had no suitable alternative so we were faced with the problem of developing a comprehensive program to find other chemicals. In meetings with our own staff and others within USDA, we reviewed all possible

approaches to obtaining delayed-action chemicals or formulations. It was recognized at this point that chemicals other than those that caused direct toxicity needed to be investigated since inhibition of egg production and/or larval development could also cause death of the colony. As a result of our deliberations, the following potential approaches were considered for investigation:

- a) Controlled release technology,
- b) Inhibition of enzymes that detoxify insecticides,
- c) Evaluation of insect growth regulators,
- d) Evaluation of chemicals that inhibit reproduction by the queen,
- e) Synthesis of chemicals with delayed-action, and
- f) Evaluation of conventional chemicals obtained from industry.

All of these approaches have been studied since 1977 through our own research effort and cooperative studies with other USDA laboratories, private research laboratories, university scientists, and private industry. Despite some disappointments, several of the projects were successful and provide us today with an array of potential chemical baits for IFA control. A review of the research on the different projects follows.

CONTROLLED RELEASE TECHNOLOGY

Vander Meer et al. (1980) suggested four possible controlled release techniques: A) matrix-bound toxicants, B) microencapsulation, C) modification of toxicant structure (protoxicants), and D) attachment of insecticides to polymers (pendent toxicants). Methods A and B proved impractical for two reasons. All of the formulations tested leaked toxicant, thus, the food attractant always became contaminated. The second problem involved the unique structure of the pharynx of IFA workers that filters out solid particles. The filtration mechanism involves a series of ridges and hairs at the entrance to and in the buccal tube. During feeding, food is taken into the infrabuccal pocket and compressed. The liquid is forced through the pharynx while the particles are retained by the filtering hairs and expelled with the infrabuccal pellet. Tests conducted with fluorescent latex particles revealed almost all particles 0.88 microns in diameter were retained in the infrabuccal pocket (Glancey et al. 1981). This diameter was well below practical technology for microencapsulation at that time.

Method C listed above is defined as the chemical alteration of a known toxicant to a relatively nontoxic material that is structured so that the toxicant can be released in the ant by an enzymatic or hydrolytic mechanism. This technique is used in the pharmaceutical industry. One of the major problems with this technique for ant toxicants is the lack of toxicants with functional groups available

for modification. Research on this method was conducted in collaboration with the USDA Insect Physiology Laboratory, Beltsville, Maryland, who prepared modified structures of trichlorfon and sodium fluoroacetate. Results of these tests (Kochansky et al. 1979) showed some delay in toxicity with caprate and sterol esters, but the range of dosages over which delay occurred was very narrow.

A study of the pendent toxicant method (D) was conducted with the Southern Research Institute at Birmingham, Alabama. With this method, numerous molecules of the toxicant are attached to a polymer backbone. It differs from the protoxicant approach in that the high-molecular weight pendent toxicants do not pass through membranes, and thus, are less readily metabolized. Two toxicants were utilized in the study, trichlorfon and 1H,1H-pentadecafluoro-octanol-1-ol. Pendent toxicant formulations of both compounds were prepared; however, the materials were not soluble in soybean oil. Various methods (sonication, surfactants) were used to suspend the materials so that they would be ingested by the ants, but no increased delay in toxicity was noted in the bioassays. Fortunately, it was the use of the fluorinated surfactants in these studies that led to the discovery that some fluoroaliphatic sulfones were good delayed-action toxicants (see section on Delayed-Action Toxicants). Further studies with protoxicants and pendent toxicants seem warranted but the research is expensive and time-consuming.

ENZYME INHIBITION

SKF-525A is an inhibitor of mixed-function oxidases that are involved in the conversion of the sulfur analogues of some fast-acting organophosphate insecticides to the oxygen analogue (e.g., malathion). The inhibitor was combined at a 10:1 ratio with five different organophosphates and tested in our primary screening test. In every case, the SKF-525A reduced the toxic action of the insecticides to an unacceptable level. No further research was conducted with this approach.

INSECT GROWTH REGULATORS

Since the effects of insect growth regulators (IGRs) are exhibited on caste and larval development rather than direct toxicity (Vinson and Robeau 1974), good colony rearing techniques (Banks et al. 1981b) and the availability of large numbers of colonies is imperative. All active IGRs cause a surge in the development of sexual forms within 2 to 4 weeks after the colony is exposed. A small amount of brood may appear in later months but the colony eventually dies from lack of adult workers. Less active compounds may produce similar temporary effects but the colony almost always recovers. Sterility of queens from exposure to methoprene as

reported for the Pharaoh ant, Monomorium pharaonis, has not been observed (Edwards 1975).

Banks et al. (1978) described laboratory tests with 26 juvenile hormone mimics against queen right colonies and found that AI3-36206 (1-(8-methoxy-4,8-dimethylnonyl)-4-(1-methylethyl)benzene) was the most effective. Since then, better activity has been obtained with several other IGRs (see Banks, Chapter 32). The most active of these compounds (fenoxycarb) gives good control of ants in the field; however, the slow death of the colonies may cause concern because it appears as though the colonies will recover and incipient colonies may appear before all the older colonies die. Repeated treatments every 6 to 12 months and an educational program for the users may be the best answer to this problem. Development of a commercial bait formulation (Logic[®]) is in progress, and a request for registration from EPA has been submitted by the developer, Maag Agro-Chemicals, Vero Beach, Florida. (Registration was granted in late 1985.)

Chitin inhibitors which are also classified as IGRs have been tested; but the best compounds, such as dimilin, are extremely insoluble and, thus, a fair evaluation on their effectiveness has never been obtained.

REPRODUCTIVE INHIBITORS

One of our early screening programs involved the evaluation of chemicals that caused sterility in insects. As with the IGRs, it was necessary to conduct primary screening tests with these compounds on queen right colonies. Several hundred materials were tested with little success (Banks, unpublished data). Our one success in this area came from an unexpected source when Merck and Company, Rahway, New Jersey, submitted some novel compounds obtained from the soil microorganism, Streptomyces avermitilis. In the initial primary screening tests, some mortality of workers was noted; but it was not sufficiently delayed to warrant further tests. However, because these compounds were good nematicides and were from a unique source, we also tested one of them, avermectin B₁, against queen right colonies at a concentration of 1%. Limited worker mortality occurred but, much to our surprise, no brood was found in the colonies after 4 weeks, even though the queen was alive. We next tested successively lower concentrations and found that brood production could be stopped at concentrations in soybean oil as low as 0.0025%. In no instance did brood production resume. In field tests, we obtained similar results. Worker brood was found in only 8 of 928 colonies that fed on baits that were applied at rates of AI ranging from 0.0077 to 7.41 g/ha (Lofgren and Williams 1982). As with the IGRs, total colony death was slow since most workers present at the time of exposure died slowly of "natural" causes.

Commercial development of a formulation of avermectin B₁ (Affirm®) containing 0.011% AI is underway. It will be applied at the rate of 1 lb/acre or 120 mg AI/ha.

Toxicological studies of the avermectins indicate that they are gamma aminobutyric acid (GABA) agonists. Glancey et al. (1982) found that avermectin B₁ caused irreversible damage to the ovaries of IFA queens which resulted in complete sterility.

SYNTHESIS OF TOXICANTS

The only synthesis program for IFA toxicants was undertaken by the Chemistry Department of Mississippi State University. Their syntheses were based on data from the USDA screening program. Fisher et al. (1980) reported that alkoxycarbonylphenyl compounds showed promise but the toxic delay was inadequate. In a second study, Fisher et al. (1983) synthesized and tested 21 diethyl aryl phosphorothionates. Compounds with either a bromine or ester substituent were the better toxicants. While their studies were partially successful, they could not be continued because of a lack of funds.

CONVENTIONAL DELAYED-ACTION TOXICANTS

Three new classes of chemicals were discovered that exhibited good delayed toxicity: amidinohydrazones, phenylenediamines, and fluorinated sulfones. Williams et al. (1980) published the results of tests with nine of the amidinohydrazones. The most effective of these compounds was American Cyanamid AC 217,300 (tetrahydro-5,5-dimethyl-2(1H)-pyrimidinone, [3-[4-(trifluoromethyl)phenyl]-1-[2-[4-(trifluoromethyl)phenyl] ethynyl]-2-propenylidene] hydrazone). In preliminary screening tests, the chemical in soybean oil gave delayed kill over more than a tenfold dosage range; however, the compound had low solubility in soybean oil (<1%). This was eventually overcome by using oleic acid as a cosolvent. In secondary tests, concentrations of 2.5 to 10% in the oil gave either complete colony mortality or the queen and most of the workers were killed. Later studies showed queen kill and mortality at concentrations as low as 0.1%. The effects of this compound on the queen are its most striking property. Field studies with baits containing AC 217,300 were effective in field tests (Banks et al. 1981a; Harlan et al. 1981). The most effective concentration in the soybean oil baits was 2.5%. A bait (Amdro) containing AC 217,300 was registered for fire ant control in August 1980.

The second promising toxicant was a phenylenediamine provided by Eli-Lilly and Company, Greenfield, Indiana. This compound, EL-468 (N-[2-amino-3-nitro-5-(trifluoromethyl)phenyl]-2,2,3,3-tetrafluoropropanamide), gave delayed kill at 0.1 and 1.0%

concentrations in primary screening tests; in secondary tests, it killed laboratory colonies at concentrations in soybean oil of 1, 2.5, and 5%. In field tests, baits with 2.5 and 5.0% concentrations in the soybean oil gave 86 to 91% control (Williams and Lofgren 1981). EL-468 was on the verge of commercialization when toxicological studies revealed possible teratogenic effects. It was then withdrawn and no further research or development has taken place.

A third group of new toxicants are the fluoroaliphatic sulfones. These toxicants were discovered serendipitously when they were used as surfactants to suspend pendent toxicant formulations. Over 300 compounds of this type have been screened and many of them have shown excellent delayed toxicity (Vander Meer et al. 1985). The most consistent results in field tests have been obtained with AI3-29757 (N-ethyl heptadecafluorooctyl sulfonamide). This compound is not soluble above 2% and it is somewhat repellent to the ants. Commercial development is being undertaken by Griffin Corporation, Valdosta, Georgia. Little is known at this point about its mammalian toxicology. Biodegradability might be a problem also.

SUMMARY

Delayed-action toxicants are difficult to obtain because this type of toxicity runs counter to standard synthesis programs that seek chemicals that kill very fast. However, the search for delayed toxicants or compounds that affect reproduction over the past 8 years has been rewarding. It is possible that four chemicals will be registered in bait formulations for IFA control by the end of 1986. The leads obtained, especially with IGRs and inhibitors of reproduction, suggest that many other similar compounds await discovery and development. The synthesis program described was very limited in scope and more intensive research in this area should be productive. Finally, the controlled release technique, while unsuccessful, did lead to valuable information on ant morphology and formulation techniques.

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