Caffeine: The 'all natural' pesticide

Plants such as coffee, tea, cocoa and kola receive potent benefits from the high levels of caffeine and caffeinelike substances they contain. According to new research, these chemicals serve as natural insecticides. And because they have a known and relatively low degree of human toxicity, it may be possible to use them in developing more potent pesticides that are relatively harmless to people, says James Nathanson, a neurologist with the Harvard Medical School in Boston.

Nathanson began investigating caffeine's pesticide potential by adding finely powdered tea leaves or coffee beans to a food used in raising tobacco hornworm caterpillars in the laboratory. When concentrations in food ranged between 0.3 to 10 percent coffee (by weight) or 0.1 to 3 percent tea, the insects exhibited a dose-dependent decrease in appetite accompanied by hyperactivity, tremors and stunted growth. At higher concentrations of either coffee or tea, the larvae were dead within 24 hours.

Both caffeine and theophylline, found in coffee and tea, are members of a class of chemicals known as methylxanthines. To rule out that something other than these had been at play, Nathanson replaced the coffee and tea in the insects' diet with pure caffeine, the primary methylxanthine that occurs in each. He found that the amount necessary to halve the insects' weight gain "was nearly identical" to the concentration that occurs naturally in the amount of coffee needed to produce a similar effect. Dried tea, which contains two to three times as much caffeine as dried coffee beans, was commensurately better at stunting growth.

"Furthermore," writes Nathanson in a report of his research in the Oct. 12 SCIENCE, "the concentrations of caffeine found naturally in undried tea leaves (0.68 to 2.1 percent) or coffee beans (0.8 to 1.8 percent) were sufficient to kill most [tobacco hornworm] larvae." This immediately suggested to him Mother Nature's purpose for putting the substances in plants at such high levels: to protect the plant. To test the hypothesis, he sprayed caffeine, theophylline or the synthetic methylxanthine IBMX onto tomato leaves, a natural food of the insect. All three discouraged feeding — and, where doses were high enough, resulted in the insects' death.

If insects are given "the opportunity to walk away from the food, they will," explains Nathanson. However, given no alternative food — as in his experiments — the insects will munch away, eventually developing problems with coordination. "It seems that the incoordination becomes a problem particularly when they try to molt," he adds. It's a difficult activity for the insects under the best of conditions, he says. Once they lose coordination, many find themselves unable to shed their old skin, and die in the process, although this is not the primary cause of death in most insects.

Nathanson initially focused on the tobacco hornworm because of factors such as its ease in rearing on both natural and synthetic diets. But subsequent work with IBMX, a more potent methylxanthine, has shown the compounds will also discourage feeding by butterfly larvae, mealworm larvae and milkweed-bug nymphs at concentrations of 0.3 percent or less. The chemical is even more potent against mosquito larvae: It killed them at concentrations of just 0.0007 percent. Although two species of adult flour beetles survived diets of up to 3 percent IBMX without symptoms, long-term studies showed that just one-tenth of that amount was sufficient to prevent their reproduction.

Nathanson's research indicates that the methylxanthines work primarily by blocking action of an essential enzyme, phosphodiesterase. Cells use the enzyme to break down cyclic-AMP, a compound necessary for neurotransmitter action. If cyclic-AMP levels build to high enough concentrations, cell metabolism becomes seriously unbalanced and can result in death.

Exploiting that principle further, Nathanson has shown that when low doses of methylxanthines are delivered along with pesticides based on insect hormones that increase the production of cyclic-AMP, the toxicity of the combination can be 50-fold greater than that of the hormone-based pesticide alone. And because humans lack cell receptors for these hormones, Nathanson says it may one day prove possible to create such a combination pesticide that is toxic only to the insects. — *J. Raloff*

Suit filed against hormone-gene work

Experiments targeted at increasing the growth rate and adult size of farm animals have come under attack by an opponent of genetic engineering and an animal protectionist. Jeremy Rifkin of the Foundation of Economic Trends and Michael W. Fox of the Humane Society of the United States, both in Washington, D.C., have filed a suit in a U.S. District Court to halt experiments involving the transfer of the human growth hormone gene into pigs and sheep. These experiments are under way at the U.S. Department of Agriculture's (USDA's) research center in Beltsville, Md.

The experiments are an agricultural application of work published last winter in which mice receiving the human growth hormone gene produced the human hormone and grew to be twice the size of normal mice (SN: 12/24/83, p. 412). Scientists at the University of Pennsylvania in Philadelphia and at the University of Washington in Seattle who participated in the mouse experiments are now collaborating with the USDA scientists. They are currently using the human gene because it has been extensively studied, but plan eventually to use livestock growth hormone genes.

Hundreds of pig and sheep embryos have been injected with the human gene, and about 50 animals of each species have been born. The experiments so far have not succeeded in producing giant pigs or sheep, but the scientists are working to determine whether the human growth hormone gene is present in the animals and whether it functions.

The plaintiffs claim that transferring genetic traits between animal species is "a violation of the moral and ethical canons of civilization, poses a grave potential threat to the biological integrity of each species, and represents a new and insidious form of cruelty toward animals by robbing them of their unique genetic makeup."

Officials at the USDA were unwilling to comment on the moral aspects of the sheep and pig experiments. However, the department released a statement saying, "Work being done in domestic animals is a repeat of experiments conducted in mice." It reports that the gene transferred is not human DNA but a chemical replica of it. The statement points out that the USDA experiments have been approved by the "appropriate" committee, the recombinant DNA advisory committee of the National Institutes of Health — *J.A. Miller*

Gene-splice pesticides

As an initial step toward regulation of pesticides developed with genetic engineering techniques, the U.S. Environmental Protection Agency (EPA) has announced it will require notification before companies can release into the environment certain types of microbial pesticides for small-scale field testing. This "interim policy" applies to pesticides that include naturally occurring microorganisms to be used in environments where they do not naturally occur and microorganisms genetically altered by scientists.

The EPA will have 90 days to evaluate the proposed test plan for risk to public health. "Although EPA does not have reason to believe that any harmful conditions will necessarily occur, the agency believes it should take a closer look at direct releases ... into the environment," says John Moore of EPA. "With genetic engineering, EPA is venturing out into a complex new world." The agency plans to prepare a policy statement later this year on how the pesticide and toxic substances laws will affect the biotechnology industry. □