A Biopesticidal Tree Begins to Blossom

Neem seed oil has insect toxicologists buzzing about its potential as a source of natural insecticides

EVER SINCE THE EARLY 1970S, WHEN researchers ushered in a brave new world of genetic engineering, agricultural visionaries have talked of doing away with toxic pesticides by producing insect-resistant strains of crop plants. But the design of "robo-plants" is only one of the more publicized approaches to natural pest control. Perhaps the hottest development in the field is coming not from the gene-splicers' high-tech labs but from a lowly tree, called neem, that grows widely in Africa and Asia.

Revered for centuries by the people of India for its ability to ward off insects and improve human health, neem has now become the favorite flora of Western firms that have begun buying up tons of neem seeds a year in the hopes of cashing in on what one neem researcher calls a "gift from God." Chemicals derived from the seeds ward off more than 200 species of insects, including some of the world's most tenacious pests: locusts, gypsy moths, and cockroaches. But toxicological testing to date shows that the neem products are much safer for other species than are synthetic insecticides, many of which work by poisoning nerve cell functions. "I won't go so far as to say it will knock all the synthetics out of the market," says Murray Isman, an insect toxicologist at the University of British Columbia in Vancouver, but "there's a pretty good market for neem, because there's a lot of momentum out there for growers to shy away from synthetic neurotoxins."

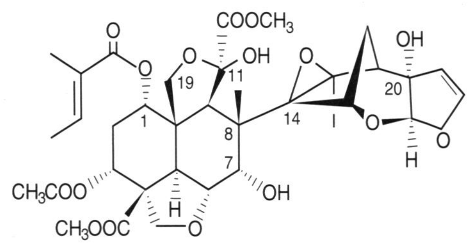
The excitement over neem and other natural insecticides reflects the urgency with which researchers are searching for alternatives to conventional synthetic pest-killers. Driven by concern about the synthetics' toxicity to animals—humans included—and the penchant of insects to develop resistance to the insecticides, farmers and others who need ways of doing in harmful pests have begun steering away from synthetics in favor of biological pest-control methods that can do the job with fewer toxic side effects.

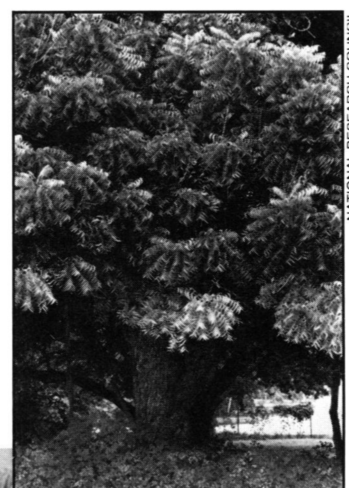
Already neem is carving a niche in the biopesticide market. W.R. Grace Co. of New York City recently began distributing a neem-based biopesticide, Margosan-O, for use in greenhouses, commercial nurseries, forests, and homes, and several other firms worldwide are developing neem-based products. Even the National Research Council (NRC) is caught up in "neemania." A few weeks ago, it released a report entitled "Neem: A tree for solving global problems." After reviewing the literature, an NRC panel concluded that "the tree is probably the single best source of biopesticides around," proclaims the panel chair, Eugene Shultz, who is an engineer at Washington University in St. Louis. In addition to discussing neem's natural insecticides, the report points up the tree's potential as a source of medicines and spermicides as well (*Science*, 17 January, p. 275). The goal of the report, explains Noel Vietmeyer, NRC study director, is to wake up entrepreneurs who might want to invest in neem and also develop a new cash crop for Third World countries where the tree primarily grows.

Neem's value comes as no surprise to researchers in India who have been studying its bacteria- and insect-killing properties for 70 years. But the West mostly ignored neem until the early 1970s, when anecdotal reports of the tree's insect-fighting ability began to intrigue researchers looking for more natural pesticides. The reports also caught the attention of Robert Larson, a timber importer, who heard about the tree while in India in 1971. A few months later Larson's firm, Vikwood Ltd. of Sheboygan, Wisconsin, began importing neem seeds and having them assayed as a potential insecticide.

By 1980, interest in neem had picked up to the point that an international congress was held in Rottach-Egern, Germany. About that time, researchers had begun deciphering how neem oil works. It contains several limonoids, a class of chemicals that act as feeding deterrents and growth regulators in insects. The most potent of these proved to be a compound called azadirachtin, a tetranortriterpenoid. Currently impossible to synthesize, azadirachtin is similar in structure to the insect hormone ecdysone, which is needed for molting during insect development. And one way that azadirachtin apparently works is by blocking ecdysone's action, thereby preventing larval insects from shedding their external skeletons and maturing. "You can stop a generation of insects by killing off all the immatures so they don't become adults and reproduce," says James F. Walter, manager of biochemical engineering at Grace's Washington Research Center in Columbia, Maryland.

Neem-esis to insects. *Azadirachtin, an active ingredient of oil from neem-tree seeds, interferes with insect molting, reproduction, and digestion. The USDA's James Locke has been testing it against the chrysanthemum leafminer.*





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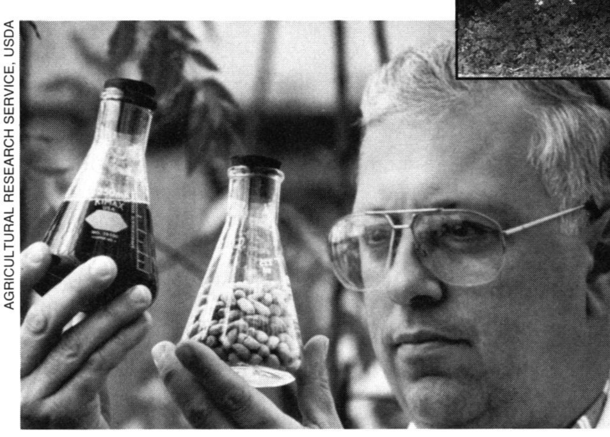

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But that's not the only subtle way that azadirachtin kills insects. Indeed, toxicologists say they're amazed at the variety of effects that it has. "It's been called a feeding deterrent, it's been called an insect growth regulator, it has a lot of properties depending on what insect you're talking about," says David Warthen, a chemist at the U.S. Department of Agriculture's Insect Chemical Ecology Laboratory in Beltsville, Maryland, who has studied neem oil for 10 years. Researchers also have found that neem inhibits the formation of chitin, a polysaccharide that makes up insect exoskeletons. And neem disrupts mating and sexual communication, causes sterility, and decreases gut motility, preventing an insect from swallowing, says Warthen. That wide variety of effects helps explain why azadirachtin is effective against so many different types of insects. In addition to cockroaches and the gypsy moth, neem victims include aphids as well as two of California's most hated agricultural pests, the medfly and the "poinsettia biotype" of the sweet potato whitefly, which farmers recently dubbed the "superbug" because it has destroyed about $120 million worth of California crops since last October and has survived eradication attempts with standard pesticides.

Another plus for azadirachtin is that even though it's toxic to a wide spectrum of insect pests, it doesn't seem to affect many pest predators. When testing it on an aphid-infested field, for example, Isman found that the aphids died out after several days, while aphid predators, such as ladybugs and lacewings, showed no ill effects. According to James C. Locke, a plant pathologist in the U.S. Department of Agriculture's Agricultural Research Service (ARS) who's tested neem extract against the chrysanthemum leafminer, that selectivity may reflect the fact that plants take in the azadirachtin and circulate it through their leaves. Aphids and other insects that feed on the leaves are therefore affected, while nonfeeders escape.

Researchers hope that because azadirachtin mainly affects physiological processes specific to insects and other arthropods, such as molting and chitin synthesis, it will have little toxicity for higher animals. And so far those hopes are being fulfilled. In 1979, Larson contracted out neem toxicity studies to a chemistry consulting firm, Madison, Wisconsin-based D&S Associates. According to tests submitted to the Environmental Protection Agency (EPA), Margosan-O, a neem extract containing 3000 parts per million azadirachtin, was nontoxic when fed to mallard ducks, bobwhite quail, and rats. Margosan-O didn't cause an adverse immune response when injected into rats, nor was it mutagenic in the Ames test, which assays for potential carcinogens by testing for their ability to cause mutations in bacteria. The EPA refused to comment on more extensive toxicity tests under way at Grace. Neem "isn't a panacea for pest control," says Isman, who's tested neem against biopesticides such as the pyrethrins, which are obtained from chrysanthemum leaves. "But of all the natural insecticides I've worked on, it's easily the best," he says.

By 1985, the safety data were sufficient for the EPA to grant Larson a license for Margosan-O for nonagricultural uses. In 1988 Larson sold the product rights to Grace, which earlier this year began distributing Margosan-O to consumers. Grace is completing the battery of toxicity texts needed for general pesticide registration for food crops and probably will apply to the EPA for a license for Margosan-O use on food crops later this year, says Jow-Lih Su, a development manager for commercial planning at Grace. Meanwhile, Grace is putting into place a network of neem seed sources so it can ensure a constant supply of the seeds and reduce their price, right now at roughly $300 per ton.

If the EPA does register Margosan-O for use on food crops, sales "could be very substantial," says Peter Boer, Grace's executive vice president and chief technical officer. Current sales of natural insecticides, including the pyrethrins, which have been sold commercially for many years, and their synthetic mimics amount to about $450 million per year in the United States. That figure could climb to $813 million annually by 1998, according to the NRC report. For comparison, about $2 billion worth of synthetic insecticides are sold annually in the United States. Insect toxicologists say the success predicted for neem and other plant-derived pesticides in the R&D pipeline probably won't spell the end of the synthetics. Nevertheless, like pioneering plants, neem and other budding biopesticides are beginning to establish themselves in a forest of synthetics. ■ RICHARD STONE

Human Ancestor Found—In Museum

For years, paleoanthropologists have been searching the hot and dusty Rift Valley of Africa, which winds through Ethiopia, Kenya and Tanzania, for the oldest fossil specimens of early human ancestors. Now it seems that they could have come in from the heat and done some of their work in the cool of a museum. Last week it turned out that the oldest known fossil from the *Homo* lineage that leads to modern humans has been sitting in a tray in the National Museum of Kenya for more than 25 years.

Nobody knew that that's what the fossil fragment was, however, until a team led by Yale University paleoanthropologist Andrew Hill gave it a closer look. "The site [where the fossil was found, Lake Baringo in Kenya] was never dated, and no one paid much attention to this specimen," says Hill. But beginning a few years ago, Hill's team took another look at the skull fragment. Last week, they announced in *Nature* that state-of-the art dating methods reveal the fragment to be 2.4 million years old—making it the earliest member of the genus *Homo* by about half a million years.

The new date helps fill in a major gap in the evolutionary history of early hominids in East Africa. Until the redating, the oldest known fossil from the genus *Homo* was found near Lake Turkana in Kenya and dated to 1.9 million years. But the new date for the skull fragment places *Homo* in the African landscape at a time when the first stone tools—crude chips found in Ethiopia—were made: 2.6 million to 2.4 million years ago. The fragment also provides evidence for a theory that *Homo* was born at a time of dramatic climate change, when a global cooling altered the environment so drastically that it may have been the key event leading to a burst of new mammalian species.

The 3-inch fragment was discovered in the mid-1960s by a team led by John Martyn of Bedford College in London, and even at the time, the discoverers noted that it had hominid features. But it was mostly forgotten until members of Hill's team reexamined it and realized it wasn't just another hominid fossil but a member of the genus *Homo*. Steven Ward of the Northeastern Ohio University College of Medicine determined that it had anatomical features characteristic of *Homo*. Meanwhile, geologist Al Deino of the Geochronology Center of the Institute of Human Origins in Berkeley, California, used a new technique called single-crystal laser-fusion argon-argon dating on volcanic deposits above and below the spot where the skull fragment was found. The method works by using a laser to melt feldspar crystals found in volcanic samples until they release their trapped internal gases. The ratio of two of these gases—isotopes of argon—changes over time. Hence by measuring the ratio, the method can date the rocks.

When the dates came in, they led the Hill team to conclude that the specimen is "the earliest securely known fossil of our own genus found so far." Hill has already begun searching near Lake Baringo for other early hominid specimens. So far, he says they've found "a complete pig skeleton, a whole monkey, a giant land turtle—but no hominids." They plan to return early this summer, however, in search of other early human ancestors. ■ ANN GIBBONS