



Tobacco Tech

Looking to the Future of Tobacco

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New pharmaceutical company to use natural compounds from plants

Kentucky agriculture may soon have a new role in the natural products industry, thanks to an entrepreneurial company called Yaupon Therapeutics, Inc. With its name derived from an Indian word meaning "tree leaf," Yaupon is poised to become a success story for Kentucky agriculture, the University of Kentucky and the pharmaceutical community. The biggest winners, however, may be the patients who will eventually benefit from the new medical drugs being developed.

Several years of research funding from the former Tobacco & Health Research Institute (now the Kentucky Tobacco Research & Development Center or KTRDC) enabled Drs. Peter Crooks and Linda Dwoskin of the UK College of Pharmacy to begin extensive research on certain plant natural products. They found five compounds that could potentially be developed for pharmaceutical use; three of these are now ready for advanced development.

"If we are successful in developing pharmaceuticals that come from plants, then the farmer may some day have the ability to grow specialty crops for the pharmaceutical industry," said Robert Alonso, president and chief executive officer of Yaupon. "This in turn will hopefully help people to further appreciate nature and farming as valuable resources."

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One of Yaupon's target products, lobeline, is being developed to help drug users hooked on methamphetamines to overcome addiction.



A compound from the Lobelia plant is on track to become a new pharmaceutical for use in overcoming methamphetamine addiction.

Derived from the common plant *Lobelia inflata*, also known as cardinal flower, lobeline is the most advanced of the three products. With clinical testing anticipated in 2004, lobeline may be on the market within four years.

Another useful natural product comes from the Middle Eastern "black seed" plant (*Nigella sativa*), and

fights cancer by killing malignant cells while protecting vital organs against the damaging effects of chemotherapy. Unlike lobeline, the black seed compound still requires pre-clinical testing, with market introduction anticipated in approximately seven years.

"KTRDC is very pleased that the work of Drs. Crooks and Dwoskin is becoming an enterprise which may assist Kentucky farmers and advance

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Pharmaceutical company cont.

the natural products industry," says Dr. Maelor Davies, director of KTRDC. "We are excited to explore the possibilities that plants like Lobelia which produce useful natural products may represent new prospects for Kentucky agriculture."



A substance isolated from the "black seed" plant (pictured above) shows great potential in fighting malignant cancer cells.

Tobacco Tech is an occasional series published by KTRDC to inform growers and others about exciting new possibilities for tobacco and other crops. Topics will provide information on our cutting-edge biotechnology research program and our efforts to stimulate new crop opportunities for Kentucky tobacco farmers.

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Wasp is source of new technology for crop protection

A parasitic wasp that lays its eggs in other insects is the source for new technology being developed by scientists at the University of Kentucky Department of Entomology and the Kentucky Tobacco Research & Development Center (KTRDC).

Seemingly like a scene from a scary movie, the parasitic wasp lays eggs and releases specialized cells called teratocytes into an insect host, such as a caterpillar. The teratocytes then release a protein that paralyzes the host so the wasp larvae can feed on it.

Drs. Bruce Webb (Entomology) and Indu Maiti (KTRDC) reasoned that if teratocytes had that effect on the host, then perhaps the unique protein that they secrete could be genetically introduced into plants to provide protection against insect pests like the tobacco budworm and tobacco hornworm.

They successfully isolated, and expressed in tobacco, the gene encoding teratocyte secretory protein (TSP14) from the predatory wasp. Budworm and hornworm larvae (caterpillars) were then allowed to feed on these transgenic plants, with remarkable results as shown in the picture below. When given a choice, the caterpillars avoided chewing on the leaves of the TSP14-expressing plant. And when the TSP14 plant was the only leaf available the larvae experienced a higher mortality rate and grew more slowly than did the larvae eating leaf tissue of control plants.

According to the researchers, "These observations indicate that TSP14 has anti-feedant activity. Our results demonstrate the potential for introduction of the TSP14 genes into plants in order to achieve protection against lepidopteran pests."

There is an increasing need to find alternatives to the commonly used "BT" strategy to protect crops against insect damage. Drs. Webb and Maiti are now exploring the formation of a company to develop their exciting and promising new technology toward this goal.

