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Unlocking the secrets of medicinal plants

Age-old herbal remedies-one from the South Pacific and the other from China-promise significant benefits in combating cancer and hypertension.

BY RICK BOGREN

Researchers at the LSU AgCenter, working with scientists in the LSU School of Veterinary Medicine and the Pennington Biomedical Research Center in Baton Rouge and at the LSU Health Sciences Center in New Orleans, are unlocking the secrets of two plants with potential medicinal benefits. One is noni, a small tree cultivated in Polynesia and Hawaii that researchers believe can prevent cancer. The other is eucommia, also known as the hardy rubber tree, native to the central region of China, which contains compounds that could lower high blood pressure.

"Most of the herbal dietary supplements we see in the U.S. market are purely based on traditional knowledge without further quality control and subsequent pre-clinical and clinical evaluations," says Dr. Zhijun Liu, a researcher in the LSU AgCenter's School of Renewable Natural Resources.

Liu says natural products from these plants, however, are difficult to use as medicines because of inconsistencies in how they're produced. "Botanical extracts are either not standardized or are standardized without reference to the active ingredients," he says. "This has been a key flaw in the quality control of botanical extracts."

Manufacturing without knowing what is responsible for therapeutic activities risks the loss of the key ingredients in the process and results in inconsistent clinical effects. "To be effective, the active ingredients must be concentrated enough to achieve a therapeutic effect," Liu says.

Scientists at the LSU Health Sciences Center in New Orleans, led by Dr. Conrad Hornick in the Department of Physiology and Dr. Eugene Woltering in the Stanley S. Scott Cancer Center, discovered that noni fruit juice can inhibit angiogenesis-the process by which new blood vessels grow-in a human tissue-based model. They passed their discovery on to Liu for analysis.

The collaborative work of these researchers presents convincing evidence along with a botanical prototype product for treatment and prevention of re-occurrence of all solid tumors, malignant or benign, that rely on angiogenesis to grow and spread.

"All adult angiogenic processes are caused by disease, with the exception of a few physiological processes like menses and placental formation," Liu explains. "Tumors cannot grow beyond the size of a pin head without first inducing new blood vessel formation. Inhibiting angiogenesis can thus prevent cancer from developing beyond the simple limits of existing blood vessels. Noni juice completely blocked the angiogenic response in our test at a 10 percent concentration, but was only partially active at a lower concentration."

The researchers believe noni juice could be a perfect cancer preventative for long-term use. While standard chemotherapeutic drugs are all designed to be toxic-harming both healthy and cancerous tissues to varying degrees-targeted therapies such as angiogenic inhibitors directed toward specific receptors or growth-factor pathways offer great hope in managing cancer.

To confirm their hypothesis, the researchers conducted a series of experiments at the LSU AgCenter and the LSU Health Sciences Center.

"First, we attempted to characterize the active fractions of noni juice," Liu says. Using a process called column chromatography, his team found that one of four initial fractions was active. Following two more rounds of fractionation, they found two sub-sub-fractions that contain active ingredients.

While the process revealed that noni juice contains more than one active compound responsible for antiangiogenic activity, the active ingredients are in low concentrations. The researchers are now isolating and purifying the active compounds, which will then be characterized using nuclear magnetic resonance and mass spectrometry at the LSU Chemistry Department in Baton Rouge. Once the active compounds are identified, they will be used as chemical markers to standardize what the researchers call "Super Noni."

"The Super Noni product is extremely practical for clinical use," Liu says. "The exact therapeutic dosing regimen will have to be determined in human clinical trials, but it is obvious that this refined noni extract offers a great advantage in designing clinically effective yet practical dosing regimens for cancer therapy and prevention trials."

In another collaborative project, an ancient herbal use for maintaining healthy blood pressure has been scientifically validated—a rare occurrence for a botanical product. Eucommia bark has been used in traditional Chinese herbalism for over 3,000 years. It was believed to aid the development of strong bones and the healing of tissue, in addition to lowering blood pressure. Liu and his colleagues are working to verify the extract's effect on blood pressure and standardize it for clinical use.

"Standardizing the eucommia extract is the key to quality control and any relevant clinical utility," Liu stresses. Botanical extracts, he notes, are mixtures of naturally occurring compounds, which is quite different from typical pharmaceuticals based on a single active ingredient. That means a botanical extract may be effective because of the way its components work together—what Liu refers to as "beneficial synergism."

The researchers have completed a three-phase study of the extract. First, they developed a protocol for standardization and produced the extract. Then, they studied the standardized extract for safety and efficacy in hypertensive rats to provide data for evaluation in human subjects. Finally, they tested the safety and efficacy in human subjects based on information from the rat study.

The standardized eucommia bark extract was evaluated in hypertensive rats under the direction of Dr. David Baker of the LSU School of Veterinary Medicine. It lowered blood pressure in male rats in eight days, and the effects diminished within 24 hours.

The researchers then gained approval to evaluate the extract on human subjects. Dr. Frank Greenway, medical director at Pennington, has completed an eight-week, randomized, double-blind human clinical trial, with initial results showing the standardized extract is safe and effective in lowering blood pressure.

"These indications are encouraging, and they support use of the extract for maintaining a healthy blood pressure," Liu says. "The positive results from this project certainly set a precedent that an ancient use can become a modern use through scientific evaluations. That should be good news to Americans 55 years old or older, who stand a 90-percent chance of developing high blood pressure."