KU NEWS RELEASE

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Contact: <u>Joe Monaco</u>, KU News Service, 785-864-7100

Newly discovered plant-based molecules showing cancer-fighting potential

Physalis longifolia

Native Medicinal Plant Research Program

LAWRENCE – To the casual observer, the wild tomatillo is just your everyday, run-of-the-mill weed.

But to University of Kansas scientists Barbara Timmermann, Kelly Kindscher and Mark Cohen, this common North American plant might be the key to a new line of cancer-fighting treatments based on molecules present in nature.

The three KU researchers have discovered 14 new compounds in the wild tomatillo that are showing significant anti-cancer properties in preclinical testing. The new compounds, known as withanolides, are already showing promise in combating a number of different cancers and tumors – without any noticeable side effects or toxicity.

"We're excited by the preliminary results," said Timmermann, a medicinal chemist and co-director of KU's Native Medicinal Plant Research Program, which comprises scientists from various KU departments to examine native plants as remedies, supplements or pharmaceutical agents. "While our research is still in the early stages, we're optimistic that some of these 14 molecules could lead to new plant-based drugs or dietary supplements."

Timmermann and her colleagues – Kindscher is a senior scientist at the Kansas Biological Survey, and Cohen is a surgical oncologist and translational clinician scientist at the University of Kansas Medical Center – describe the new withanolides in the November 2011 edition of the Journal of Natural Products. Additionally, their discovery is one of only 31 breakthrough technologies to earn a coveted presentation slot at the University Research & Entrepreneurship Symposium, a showcase of the nation's most promising new university-based technologies for industry leaders, venture capitalists and entrepreneurs, April 18 in Cambridge, Mass. The symposium is designed to develop financial or industrial partnerships to advance new technologies into the marketplace.

"It's a big deal for us to be invited to this symposium," said Timmermann, a renowned expert in pharmacognosy, the study of natural drugs. "We're in an elite group."

The wild tomatillo, whose formal scientific name is <u>Physalis longifolia</u>, is common in the Plains states and throughout North America. While researchers have studied other plants in the Physalis genus, the KU team is the first to examine the longifolia species as a source of potentially useful therapeutic compounds.

What inspired Timmermann and her colleagues to examine the wild tomatillo? It began with a bioprospecting project in South America in the late 1990s, when Timmermann discovered a plant with a compound that showed anti-cancer potential. Due to cost, distance, intellectual property issues and trade regulations, returning to South America to collect more of the plant wasn't practical. So Timmermann teamed up with Kindscher to identify Midwestern plants that could have the same type of compounds as the South American plant.

"Our research led us to Physalis longifolia, which is a fairly common plant throughout the Midwest," Timmermann said. "And from there, we discovered not only the molecule we were seeking, but also the 14 new compounds, most of which have turned out to be even more potent than the original one we were looking for. Discovery is a beautiful thing when it happens like that."

In addition, Timmermann and Kindscher's research indicates that the Pueblo Indians and other indigenous populations throughout North America used this and other species of wild tomatillo fruits as food, with no apparent ill effects.

"The anthropological record seems to show that the fruits of Physalis longifolia aren't toxic." Timmermann said.

So far, Cohen's laboratory at KU Medical Center has demonstrated that these novel compounds have potent anticancer activity in melanomas, thyroid cancer, head and neck squamous cell cancer, breast cancer, glioblastoma brain tumors, and certain leukemias. These compounds can drastically shrink – or in some cases even completely dissolve – aggressive cancers in mouse models without any noticeable side effects or toxicity. In addition, other studies indicate these compounds may have anticancer activity against both esophageal cancers and pancreatic cancers.

The discovery is the latest to emerge from the Native Medicinal Plant Research Program, which was launched in 2009 with funding from Heartland Plant Innovations, a private organization that received startup funding through the Kansas Bioscience Authority. The program targets plants of the Great Plains used by Native American tribes and uses modern science to examine their chemical structures to discover the compounds responsible for their healing properties and determine which might have wound-healing, anti-inflammatory, antioxidant and even anti-cancer powers that could benefit human health.

"The Native Medicinal Plant Research Program epitomizes multidisciplinary collaboration by bringing together different KU departments," Timmermann said. "For example, our Kansas Biological Survey has expertise in plant collection, ecological assessment and taxonomy. Our School of Pharmacy can isolate, chemically characterize and modify the molecules to unravel their mechanism of action. And physician scientists such as Dr. Mark Cohen at KU Medical Center are investigating the compounds in animal cancer models. And of course, as a backdrop to all this, we have a world-class KU Cancer Center that recently submitted its application for National Cancer Institute designation. So it's a great multidisciplinary effort."

Regarding the 14 new compounds, Timmermann cautioned that it's still early in the research process, and that even if the compounds prove viable, the entire process from the lab bench to animal trials to human trials to regulatory approval could take a decade before they turn up in a supplement or pharmaceutical product. But she described the discovery as among the more exciting of her career – and it appears others agree, as evidenced by Cohen's invitation to present the discovery at next month's University Research & Entrepreneurship Symposium.

"For our discovery to be one of just 31 technologies to be presented in Cambridge is very exciting," she said. "It speaks well of our work and, more broadly, of the interdisciplinary research being done at KU."

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kunews@ku.edu | (785) 864-3256 | 1314 Jayhawk Blvd., Lawrence, KS 66045