

Looking for anti-cancer compounds in the Sonoran Desert

Researchers isolate and test metabolites

By Susan McGinley

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Cancers that grow into numerous solid tumors in the body pose enormous difficulties for treatment. Their widespread placement eliminates surgery and radiation as options, leaving chemotherapy as the preferred medical choice. Yet adequate drugs are not currently available to treat major solid tumors such as those of the lung, breast, prostate, and colon. With these cancers on the rise in both Arizona and around the world, there is an urgent need to find a suitable treatment for the millions of patients who are affected.

Scientists have long turned to the Amazon rainforest to find plants that might save lives. Here in Arizona, they are searching our own backyard—the Sonoran Desert. A collaborative team of researchers from the University of Arizona’s College of Agriculture and Life Sciences (CALs), Arizona Health Sciences Center (AHSC), and the Arizona Cancer Center are testing natural compounds isolated from desert plants and microorganisms for their anti-cancer properties. The Arizona Disease Control Research Commission is funding the project.

“We began looking at desert plants because they are exposed to a lot of light, which speeds their metabolism,” says Leslie Gunatilaka, professor and associate director of the Southwestern Center for Natural Products Research and Commercialization, in the CALs Office of Arid Lands Studies. “This causes them to produce unique secondary metabolites, some of

which may have anti-cancer properties, specifically, tumor-fighting properties.”

During the three-year process Gunatilaka’s team has tested compounds from more than 500 plant species collected from open areas in the Arizona desert. Although the process involves numerous steps in progressively extracting and purifying active ingredients from plants, the group has found several compounds so far that have demonstrated antitumor properties in laboratory tests.

EACH PLANT IS METICULOUSLY ANALYZED

The researchers select compounds not only from plant parts—roots, stems, leaves, flowers, fruits and seeds—they’ve also extended their studies to include microorganisms living in the rhizosphere, the area immediately surrounding root surfaces. “We go out to the desert, select a plant, collect a little bit of root material without damaging the plant. We don’t uproot it,” Gunatilaka says. “We take a small piece of root back to the lab, isolate microorganisms, both bacteria and fungi. We grow them separately in selective media, isolate pure cultures of the organisms we want and then in turn grow those out.”

Next, the scientists extract cultures with organic solvents. The extracts contain large amounts of the secondary metabolites, which are tested in biological assays that use perpetual cancer cell lines for three types of cancers: breast cancer, non-small-cell lung cancer, and central nervous system (CNS) cancer.



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Of particular interest to Gunatilaka are the processes of angiogenesis and heat shock protein function activation. Angiogenesis is a process where a tumor begins to produce its own blood supply so it can grow even faster. His team is searching for plant extracts that can stop this mechanism and thus halt the tumor's spread in the body. Linda Meade-Tollin, a research assistant professor in the Department of Surgery at the AHSC, conducts assays to find out which extracts actively inhibit angiogenesis.

Heat shock proteins provide unusually good targets for anticancer drugs, according to Gunatilaka, because they facilitate the development of cancers by increasing the stability and activity of multiple mutant proteins within a cancer cell. Luke Whitesell, an associate professor in the Department of Surgery at the AHSC assists Gunatilaka in his search for compounds that activate the function of heat shock proteins.

Plant pathologists Hans VanEtten and Leland Pierson, in the Department of Plant Pathology, and Steven McLaughlin of the Office of Arid Lands Studies are also collaborating on the project. Members of Gunatilaka's research team include postdoctoral researchers Kithsiri Wijeratne and Guang Zhou, graduate students Tommy Turbyville and Todd Furbacher, and research specialist Anne Fritz.

"Once we find an active extract we fractionate it chemically to separate into single compounds," Gunatilaka explains. "Each fraction is tested using the same bioassay until we get a pure compound that shows activity. This can take several weeks to several months for each active extract." Both the chemical and physical properties of each pure compound are analyzed so the structure of the substance is fully understood. After that, the compound is tested in animal and later in human trials.

The procedure is slow, precise, and painstaking, and the identity of an effective compound is not released until it is included in a patented drug formula. According to Gunatilaka, it takes an average of 10-20 years and a minimum investment of 350 million dollars to develop an anticancer drug. One compound derived from a microbe will soon undergo animal trials in the laboratory of Robert Dorr, a pharmacologist at the Arizona Cancer Center. The National Cancer Institute is also evaluating the same compound using their panel of 60 cancer cell lines. About half a dozen other compounds also show promise.

HOW DOES THE HERBAL SUPPLEMENT PC SPES FIGHT PROSTATE CANCER?

Along with his search for anticancer compounds from Sonoran desert organisms, Gunatilaka is researching the effectiveness of an existing herbal formula that fights prostate cancer. PC SPES has been available in the U.S. for the last ten years. The PC stands for prostate cancer; SPES is Latin for "hope." The formula, which costs patients \$450 per month in out-of-pocket expenses (it is not covered by insurance) contains extracts of eight plants, seven from China and one from North America. Although the supplement is effective against the growth of the tumor, it is expensive and acts like an estrogen, which causes undesirable side effects in men.

"I got interested in this because PC SPES is an herbal supplement that has undergone at least six clinical trials in the United States and is proven to be effective," Gunatilaka says. "We have found antiangiogenesis activity in two of the plants." Prostate cancer is a solid tumor normally requiring a blood supply, which this formula apparently cuts off.

In a study that is just beginning, Gunatilaka is analyzing these plants to find the active compounds within them that fight prostate cancer. The Department of Defense has provided funding for Gunatilaka to isolate and characterize antiangiogenic compounds in PC SPES. By separating the active compounds from the other parts of the extracts, he hopes to remove the chemicals that cause the side effects. The pure compounds could then be incorporated into "novel drugs or combination therapies to cure hormone resistant, advanced metastatic PC," that would have fewer side effects. w

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