Beehive extract shows potential as prostate cancer treatment

May 4 2012

An over-the-counter natural remedy derived from honeybee hives arrests the growth of prostate cancer cells and tumors in mice, according to a new paper from researchers at the University of Chicago Medicine.

Caffeic acid phenethyl ester, or CAPE, is a compound isolated from honeybee hive propolis, the resin used by bees to patch up holes in hives. Propolis has been used for centuries as a natural remedy for conditions ranging from sore throats and allergies to burns and cancer. But the compound has not gained acceptance in the clinic due to scientific questions about its effect on cells.

In a paper published in Cancer Prevention Research, researchers combined traditional cancer research methods with cutting-edge proteomics to find that CAPE arrests early-stage prostate cancer by shutting down the tumor cells' system for detecting sources of nutrition.

"If you feed CAPE to mice daily, their tumors will stop growing. After several weeks, if you stop the treatment, the tumors will begin to grow again at their original pace," said Richard B. Jones, PhD, assistant professor in the Ben May Department for Cancer Research and Institute for Genomics and Systems Biology and senior author of the study. "So it doesn't kill the cancer, but it basically will indefinitely stop prostate cancer proliferation."

Natural remedies isolated from plant and animal products are often marketed as cure-alls for a variety of maladies, usually based on vague

antioxidant and anti-inflammatory claims. While substances such as ginseng or green tea have been occasionally tested in laboratories for their medicinal properties, scientific evidence is commonly lacking on the full biological effects of these over-the-counter compounds.

"It's only recently that people have examined the mechanism by which some of these herbal remedies work," Jones said. "Our knowledge about what these things are actually doing is a bit of a disconnected hodge-podge of tests and labs and conditions. In the end, you're left with a broad, disconnected story about what exactly these things are doing and whether or not they would be useful for treating disease."

To study the purported anti-cancer properties of CAPE, first author Chih-Pin Chuu (now at the National Health Research Institutes in Taiwan) tested the compound on a series of cancer cell lines. Even at the low concentrations expected after oral administration, CAPE successfully slowed the proliferation of cultured cells isolated from human prostate tumors.

CAPE was also effective at slowing the growth of human prostate tumors grafted into mice. Six weeks of treatment with the compound decreased tumor volume growth rate by half, but when CAPE treatment was stopped, tumor growth resumed its prior rate. The results suggested that CAPE stopped cell division rather than killing cancerous cells.

To determine the cellular changes that mediated this effect, the researchers then used an innovative proteomics technique invented by Jones and colleagues called the "micro-western array." Western blots are a common laboratory tool used to measure the changes in protein levels and activity under different conditions. But whereas only one or a few proteins at a time can be monitored with Western blots, micro-western arrays allow researchers to survey hundreds of proteins at once from many samples.

Chuu, Jones and their colleagues ran micro-western arrays to assess the impact of CAPE treatment on the proteins of cellular pathways involved in cell growth – experiments that would have been prohibitively expensive without the new technique.

"What this allowed us to do is screen about a hundred different proteins across a broad spectrum of signaling pathways that are associated with all sorts of different outcomes. You can pick up all the pathways that are affected and get a global landscape view, and that's never been possible before," Jones said. "It would have taken hundreds of Westerns, hundreds of technicians, and a very large amount of money for antibodies."

The micro-western array results allowed researchers to quickly build a new model of CAPE's cellular effects, significantly expanding on previous work that studied the compound's mechanisms. Treatment with CAPE at the concentrations that arrested cancer cell growth suppressed the activity of proteins in the p70S6 kinase and Akt pathways, which are important sensors of sufficient nutrition that can trigger cell proliferation.

"It appears that CAPE basically stops the ability of prostate cancer cells to sense that there's nutrition available," Jones said. "They stop all of the molecular signatures that would suggest that nutrition exists, and the cells no longer have that proliferative response to nutrition."

The ability of CAPE to freeze cancer cell proliferation could make it a promising co-treatment alongside chemotherapies intended to kill tumor cells. Jones cautioned that clinical trials would be necessary before CAPE could be proven effective and safe for this purpose in humans. But the CAPE experiments offer a precedent to unlock the biological mechanisms of other natural remedies as well, perhaps allowing these compounds to cross over to the clinic.

"A typical problem in bringing some of these herbal remedies into the clinic is that nobody knows how they act, nobody knows the mechanism, and therefore researchers are typically very hesitant to add them to any pharmaceutical treatment strategy," Jones said. "Now we'll actually be able to systematically demonstrate the parts of cell physiology that are affected by these compounds."

Provided by University of Chicago Medical Center