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Green Tea And COX-2 Inhibitors Combine To Slow Growth Of Prostate Cancer

ScienceDaily (Mar. 2, 2007) — Drinking a nice warm cup of green tea has long been touted for its healthful benefits, both real and anecdotal. But now researchers have found that a component of green tea, combined with low doses of a COX-2 inhibitor, could slow the spread of human prostate cancer.

In the March 1 issue of Clinical Cancer Research, researchers from University of Wisconsin-Madison demonstrate that low doses of the COX-2 inhibitor celecoxib, administered with a green tea polyphenol called pigallocatechin-3-gallate (EGCG), can slow the growth of human prostate cancer. Their experiments were performed in cell cultures and in a mouse model for the disease.

"Celecoxib and green tea have a synergistic effect -- each triggering cellular pathways that, combined, are more powerful than either agent alone," said Hasan Mukhtar, Ph.D., professor of dermatology at the University of Wisconsin and member of Wisconsin's Paul Carbone Comprehensive Cancer Center. "We hope that a clinical trial could lead to a preventative treatment as simple as tea time."

Previous research has linked the cyclooxygenase-2 enzyme, commonly known as COX-2, to many cancer types, including prostate cancer, said Mukhtar. Mukhtar and his colleagues have previously shown COX-2 inhibitors like celecoxib (known under the brand name Celebrex™) suppress prostate cancer in animal models. COX-2 inhibitors also have been shown to cause adverse cardiovascular effects when administered at high doses over long durations.

In 2004, Mukhtar and his colleagues demonstrated that green tea polyphenol EGCG has cancer-fighting abilities of its own. Their study, published in Cancer Research, showed that EGCG can modulate the insulin-like growth factor-1 (IGF-1)-driven molecular pathway in a mouse model for human prostate cancer, pushing the cells toward programmed cell death (apoptosis).

"We believed that COX-2 inhibitors may still prove beneficial if used in combination with complementary agents," Mukhtar said. "Our studies showed that the additive effect

of green tea enables us to utilize the cancer-fighting abilities of COX-2 inhibitors, but at lower, safer doses."

In this latest research, Mukhtar and his colleagues looked at the effects of the two substances on cultured human prostate cancer cells. Alone, both EGCG and NS-398, a COX-2 inhibitor similar to celecoxib, demonstrated the ability to slow cancer cell growth and limit the presence of known cancer-promoting proteins within the cell samples. Together, EGCG and NS-398 suppressed cell growth by an additional 15 to 28 percent.

The researchers repeated the experiment in mouse models of prostate cancer, using celecoxib and an oral suspension of the decaffeinated green tea polyphenol. By using pharmacy-grade celecoxib and actual tea, they had hoped to replicate real-life conditions. "The idea is that it would be easier to get people to drink green tea than it would be to take an additional dietary supplement," Mukhtar said.

In mice that were not treated with either substance, the tumor volume averaged 1,300 cubic millimeters, whereas mice given either the tea or celecoxib had tumors averaging 835 cubic millimeters and 650 cubic millimeters, respectively. Tumors taken from mice given both agents, however, measured on average a volume of 350 cubic millimeters.

In parallel to tumor growth inhibition, mice that received a combination of green tea and celecoxib registered a greater decrease in prostate specific antigen (PSA) levels compared to that in celecoxib alone or green tea alone treated animals. PSA is a protein produced by the cells of the prostate and is used as a marker for detection and progression of prostate cancer. These results, combined with a marked decrease in the presence of cancer-promoting proteins, offered clear indications that green tea and celecoxib, combined, could be useful in slowing prostate cancer growth, Mukhtar said.

"Prostate cancer typically arises from more than one defect in the cellular mechanics, which means that a single therapeutic might not work fighting a particular cancer long-term," Mukhtar said. "If tests in human trials replicate these results, we could see a powerful combined therapy that is both simple to administer and relatively cost effective."

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