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Source: American Association For Cancer Research

Date Posted: 2003-10-29

Web Address: <http://www.sciencedaily.com/releases/2003/10/031029063913.htm>

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PHOENIX - Drinking green tea may do more than just thwart a head cold, according to research presented today at the American Association for Cancer Research Second Annual International Conference on Frontiers in Cancer Prevention Research. Green tea already is believed to help lower cholesterol and prevent heart disease, fight bacteria and dental cavities, and possibly aid weight loss. New studies are now suggesting the various potential anti-cancer benefits of the age-old beverage.

"Laboratory studies have suggested that green tea consumption may produce many health benefits, including the prevention of cancer, but the beneficial effects in humans are not clearly known," said CS Yang, Ph.D., of Rutgers University, N.J.

"Research is now showing how this novel chemopreventive agent might work at the molecular level and in the human population," he added.

Inhibition of VEGF Expression and Tumor Cell Growth in Breast Cancer Cells by Novel Synthetic Analogs of the Green Tea Catechin, Epigallocatechin-3-gallate (EGCG) (Abstract 1560)

EGCG (epigallocatechin-3-gallate) is the most abundant and active chemopreventive agent in green tea, and has been associated with reduced risk of breast, pancreatic, colon, esophageal and lung cancers in humans. However, EGCG has a low oral bioavailability, meaning that to sustain effective levels for biological activity, individuals would need to drink at least seven to eight cups of tea a day, or ingest large amounts of green tea polyphenol extract. Researchers from SRI International in Menlo Park, Calif., have successfully synthesized several EGCG analogs that inhibit the in vitro (in an artificial environment) growth of tumor cell lines with potencies equal to or greater than EGCG itself.

The investigators developed a chemical synthesis of cis racemic EGCG that allows them to modify the A-, B- and D-rings of EGCG independently of each other. Using this method, they created several different analogs (a chemical compound structurally similar, but different in composition). SR 13196, an analog modified in the B- and D-rings, displays significantly more potent growth inhibition of breast cancer cell lines when compared to EGCG. SR 13193, an analog modified in the D-ring, inhibits expression of the potent angiogenic factor VEGF (vascular endothelial growth factor) in breast cancer cells, similar to EGCG.

"These analogs are not only valuable tools to clarify how green tea may fight cancer, but are also potential chemopreventive drug candidates themselves, with perhaps better pharmacokinetic properties than have been seen with EGCG thus far," said SRI's Nurulain Zaveri, Ph.D., lead author of the study.

"Noting the success of the current findings, we plan to continue our studies with the novel EGCG analogs," she added.

Effect of a Four-Month Tea Intervention on Oxidative DNA Damage Among Heavy Smokers; Role of hogg1 Genotype (Abstract 1241)

Researchers are aware that DNA is susceptible to damage by reactive oxygen species; 8-OHdG (8-hydroxydeoxyguanosine) is one of the most abundant lesions formed during this damage. The most established pathway to repair this type of lesion is via the human 8-oxoguanine glycosylase (hogg1), a base excision repair enzyme, of which there are several different forms. Researchers at the Arizona Cancer Center in Tucson conducted a phase IIb randomized, controlled tea (green and black) intervention trial among heavy smokers, to study the effect of high

consumption of tea (four cups per day) on oxidative DNA damage as measured by urinary 8-OHdG, and to evaluate the role of the hogg1 genotype as an effect modifier.

"We found no significant interaction between smoking, hogg1 genotypes, and tea intervention in terms of level of urinary 8-OHdG," said Iman Hakim, M.D., Ph.D., of the Arizona Cancer Center and lead author of the study.

"This suggests that green tea may be effective in decreasing levels of urinary 8-OHdG among smokers, regardless of their hogg1 genotype, thus reducing DNA damage that would potentially lead to tumor development," she said.

A total of 118 smokers with hogg1 data completed the four-month intervention trial, which estimated the main effects and interaction effect of green and black tea consumption on urinary 8-OHdG. Researchers also studied whether the effect of treatment varied by hogg1 status of the individual. After adjusting for baseline measurements and other potential factors, assessment revealed a highly significant decrease in 8-OHdG (-31 percent) after four months of drinking decaffeinated green tea. No change was seen among smokers assigned to the black tea group, and no significant difference was seen in the level of urinary 8-OHdG by hogg1 genotype.

Chemoprevention Trial of Green Tea Polyphenols in High-Risk Population of Liver Cancer: Modulation of Urinary Excretion of Green Tea Polyphenols 8-hydroxydeoxyguanosine (Abstract 1286) and of Aflatoxin Biomarkers (Abstract 1287)

Green tea polyphenols (GTP) are highly effective chemopreventive agents in inhibiting a variety of cancer-induced tumors in models for different targets, including liver tumors. Researchers recently evaluated the role of GTP on two biomarkers for liver cancer, aflatoxin markers and urinary excretion of 8-hydroxydeoxyguanosine (8-OHdG), and affirmed the effectiveness of GTP in reducing these risk factors. The study involved 124 people aged 20 to 55, both HBsAg (hepatitis-B surface antigen) and aflatoxin (AF)-albumin adducts positive, who were randomly divided into three groups and treated daily with either low-dose GTP (500 mg, n=42), high-dose GTP (1,000 mg, n=41) or placebo (n=41) for three months. Aflatoxin is a naturally occurring poisonous substance produced by mold that can be found in blood serum, plasma or urine (albumin).

In the first arm of the study, urine samples were collected at day 0, one month and three months to assess urinary 8-OHdG and GTP biomarkers (EGC and EC). After adjusting for urinary creatinine levels, results showed a trace amount of GTP, including similar levels of EGC and EC in the baseline samples for all three groups. Levels of EGC and EC in samples collected at one month were dose-dependently elevated in treated groups, as EGC increased 1.7-fold in both treated groups, and EC increased 2.2-fold in the low-dose group and 3.5-fold in the high-dose group. Samples collected at three months showed similar patterns.

Though levels of 8-OHdG at baseline were comparable for all three groups and did not show obvious changes at one month, urinary 8-OHdG at three months was greatly reduced in GTP-treated groups, as compared to that in the placebo group. The results suggest that urinary EGC and EC are good biomarkers for GTP intake, and GTP treatment reduces urinary excretion of 8-OHdG.

In the second arm of the study, blood and urine samples were collected at day 0, one month and three months to assess AF (aflatoxin) biomarkers. Levels of AF-albumin adduct at baseline were comparable for all three groups. Sample levels collected at 1-month were significantly decreased in the high-dose group, as compared with the placebo group. At three months, the levels of AF-albumin adduct were significantly decreased in the low-dose and high-dose groups, as compared with the baseline levels.

"These results demonstrate that green tea polyphenol treatment effectively inhibits phase I enzyme activities and enhances the phase II enzyme activities," said Jia-Sheng Wang, M.D., Ph.D., of the Texas Tech University System, and lead investigator of the study.

"At the same time, we see the value of green tea polyphenols in reducing excretion of 8-OHdG. All of this is good news for the prevention and early detection of liver cancer," he added.

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Founded in 1907, the American Association for Cancer Research is a professional society of more than 21,000 laboratory, translational, and clinical scientists engaged in cancer research in the United States and in more than 60 other countries. AACR's mission is to accelerate the prevention and cure of cancer through research, education, communication, and advocacy. Its principal activities include the publication of five major peer-reviewed scientific journals: Cancer Research; Clinical Cancer Research; Molecular Cancer Therapeutics; Molecular Cancer Research; and Cancer Epidemiology, Biomarkers & Prevention. AACR's annual meetings - next year in Orlando, Fla., March 27-31 - attract more than 15,000 participants who share new and significant discoveries in the cancer field. Specialty meetings like this one, held throughout the year, focus on the latest developments in all areas of cancer research. -----
