Steep your genes in health: drink tea

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Tea, one of the most commonly consumed beverages in the world, has many health benefits. Tea polyphenols support health by promoting antioxidant enzymes, promoting apoptosis, preventing angiogenesis, and modulating epigenetic change. Considerable basic science and epidemiologic evidence supports the regular consumption of this tasty, inexpensive beverage.

Tea has been used for millennia in our world's oldest cultures as a common beverage and is currently the most widely consumed beverage in the world, after water. Currently, only 15% of Americans drink tea on a typical day (1). Yet, the typical American drinks at least one can of soda daily. What if we encouraged the increased use of green tea as a beverage instead?

Green tea has so many health benefits—from cancer prevention, heart disease prevention, reduction of plaque and gingivitis, reduction of insulin resistance, and reduction of hypertension, among others—that it could be considered a panacea. Tea has been consumed in China for over 4000 years, and the Kissa Yojoki (Book of Tea), written in 1191 by a Zen priest named Eisai, documents multiple medicinal uses for green tea.

Black, green, white, and oolong tea all come from the leaves of the *Camellia sinensis* plant, which grows indigenously in China, Japan, India, and Thailand. For black tea, the leaves are allowed to wither, ferment, and oxidize. For green tea, the plant leaves are steamed and parched immediately after they are picked. This difference in processing allows for a significant difference in the final phytochemical balance: black tea contains more theaflavins and thearubigins, and green tea contains more catechins. Both teas have been shown to have many health benefits, but this essay focuses on green tea.

Green tea contains a potent mix of phytochemicals, of which the catechins, epigallocatechin-3-gallate (EGCG) and epigallocatechin, have been well studied. EGCG is a polyphenol that makes up more than 40% of the total phenols within green tea (2). EGCG is an antioxidant and biologic response modifier in that it can modulate genetic expression (1). It can work as an antioxidant by scavenging free radicals as well as by acting as a metal chelator (3). EGCG affects genetic expression leading to inhibition of production of intracellular peroxides, prevention of angiogenesis, promotion of apoptosis (2), as well as a reduction in production of lipoxygenase, cyclooxygenase, and xanthine oxidase enzymes (4). Tea polyphenols down-regulate nuclear factor-kappa B and induce phase II enzymes such as glutathione S-transferase and superoxide dismutase (4).

One way of measuring an individual's level of oxidative stress is by measuring urinary 8-hydroxydeoxyguanosine (8-OHdG). In animal models, tea polyphenols have been shown to inhibit carcinogen-induced increases in urinary 8-OHdG.

EGCG also can inhibit angiogenesis. It inhibits the activity of matrix metallo-proteinases 2 and 9 and urokinase-plasminogen activator (4), thereby inhibiting degradation of extracellular matrix in preparation for angiogenesis. In addition, EGCG causes elevation of interleukin-12, which promotes antiangiogenesis, and suppresses interleukin-8, which promotes angiogenesis (5). EGCG also appears to block induction of vascular endothelial growth factor (2). Finally, EGCG has been shown to inhibit activation of the epidermal growth factor receptor and human epidermal growth factor receptor-2 and multiple downstream signaling pathways in cancer cell lines (6).

Another mechanism of action for EGCG is by induction of phosphorylation of serine residues on the p53 protein, thereby increasing the half-life of p53 (7). Increased transcriptional activity of p53 would promote apoptosis of abnormal cells.

Telomerase, required to maintain the length of telomeres in rapidly dividing cells, is highly expressed in cancer cells, while limited in normal cells (8). Berletch and colleagues demonstrated that EGCG affects both telomerase activity and the highly important process of methylation. Berletch incubated MCF-7 breast cancer cells and HL60 promyelocytic cells with EGCG and found reduced cellular proliferation and increased apoptosis in both cell lines. As a result of a time-dependent reduction in promoter methylation, the breast cancer cells had reduced expression of human telomerase reverse transcriptase that is essential for telomerase function (9).

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EPIDEMIOLOGIC STUDIES

Most epidemiologic studies investigating the effects of green tea consumption have been performed in Chinese and Japanese populations. In a population-based prospective cohort study, Kuriyama demonstrated a strong inverse association between increasing green tea consumption and mortality from cardiovascular disease (10). Many studies have not found a significant association with reduction of specific cancer risk: the Ohsaki study examined the risk of lung cancer in relation to green tea consumption and found no evidence that green tea consumption was associated with lung cancer or its prevention (11). Likewise, green tea has not been shown to be associated with a decreased risk of pancreatic cancer (12).

Several case-control studies performed in China, however, have shown statistically significant inverse associations of tea drinking with gastric, pancreatic, colorectal, lung, and breast cancers (13–16). A case-control study of 130 incident prostate cancer patients matched to 274 hospital inpatients without malignancies found that prostate cancer risk declined with increasing frequency, duration, and quantity of green tea consumption; the odds ratio for green tea drinkers compared with nondrinkers was 0.28 (95% confidence interval [CI], 0.17–0.47) (17).

A prospective study in Sweden looked at the association between tea consumption (both green and black) and risk of ovarian cancer in 61,057 women. There was an inverse association with the risk of ovarian cancer, and each additional cup of tea per day was associated with an 18% lower risk of ovarian cancer (multivariate hazard ratio, 0.82; 95% CI, 0.68–0.99) (18). A Canadian prospective cohort study of 49,613 women enrolled in the National Breast Screening Study found that tea intake was not associated with ovarian cancer risk, but there was a borderline positive association with coffee use (19).

CLINICAL TRIALS

An exciting study out of Italy randomized 60 volunteers with high-grade prostate intraepithelial neoplasia to a double-blind placebo-controlled study in which patients were randomized to 600 mg green tea catechins per day or placebo. After 1 year, only one tumor was diagnosed among the 30 men treated with green tea catechins, compared with nine cancers in the 30 placebo-treated men ($P \leq 0.01$) (20).

A Korean study looking at the effects of green tea extracts on preinvasive disease of the cervix showed a 69% response rate compared with a 10% response rate in untreated controls ($P < 0.05$) (21).

Another randomized, double-blind, placebo-controlled study looked at use of green tea polyphenols and association with oxidative DNA damage in patients who were seropositive for hepatitis B surface antigen as well as aflatoxin-albumin adducts. After 3 months, 8-OHdG levels decreased significantly in the groups treated with green tea polyphenols ($P = 0.007$) (22). Similarly, increased tea consumption was associated with a highly significant decrease in urinary 8-OHdG in smokers after 4 months of drinking decaffeinated green tea ($P = 0.002$), though no change in urinary 8-OHdG was seen among those drinking black tea (23).

Figure. Green tea. Photo: Curt Humphreys.

In Japan, a group of 136 patients with a history of colorectal adenomas removed by endoscopic polypectomy and then confirmed 1 year later to be polyp free at colonoscopy were randomized into groups of 71 patients given 1.5 g green tea extract per day and 65 patients without supplementation. Twelve months later, repeat colonoscopy was performed in 125 patients, with adenomas found in 31% of the control group and 15% of the green tea extract group ($P < 0.05$) (24).

Other chronic inflammatory disorders besides cancer are also impacted by green tea consumption. Epidemiologic studies show an inverse relationship between green tea consumption and mortality from cardiovascular disease, particularly with stroke mortality (11). Oral administration of 500 mg green tea catechins has been shown to significantly decrease plasma oxidized low-density lipoprotein (25). A small study from the United Kingdom demonstrated an increase in fat oxidation during moderate-intensity exercise and improvement in insulin sensitivity and glucose tolerance following acute ingestion of green tea extract (26).

POSSIBLE ADVERSE REACTIONS

Green tea can cause nausea, particularly when taken on an empty stomach. It does contain caffeine and can be associated with central nervous system hyperstimulation, such as insomnia, agitation, or tremors, although these effects are more likely to be noted with extremely high doses of green tea, such as 5 to 6 L of green tea per day (27). Typically, an 8-oz serving of brewed tea could be expected to contain approximately 30 to 50 mg caffeine, compared with 115 to 170 mg of caffeine in an 8-oz serving of brewed coffee. Tea does contain a compound called L-theanine, which tends to be relaxing and counteracts the effects of the caffeine within it.

There have been at least 14 case reports of hepatotoxicity, most associated with weight loss that contained multiple herbal supplements including *Camellia sinensis.* In Bonkovsky's report of a woman who developed abdominal pain and jaundice twice in association with a weight loss product containing *Camellia sinensis,* he noted that most of the reports of hepatotoxicity associated with products containing *Camellia sinensis* presented

with a mixed hepatocellular-cholestatic picture, and all resolved following discontinuation of the supplement (28).

PRACTICAL ASPECTS

There are thousands of varieties of green tea, which vary greatly in terms of taste and quality. Typically one would use water that is not quite boiling, and pour it over the tea, letting the leaves steep for approximately 2 to 3 minutes. If the tea leaves are left in the hot water too long, they start releasing tannins, which impart a bitter taste to the tea (interestingly, steeping green or black tea for a longer period of time, such as 15 minutes, gives a bitter drink that can be used as a home remedy for diarrhea). Avoid adding ice to your drink, as this leads to precipitation of the beneficial polyphenols on the ice. For best results, share with a friend and relax while you sip on this healthy beverage *(Figure)!*

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