

GREEN TEA

(Camellia sinensis)

Green Tea and Women's Health



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PROFESSIONAL RESOURCES

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BACKGROUND AND USES

Of the many botanicals in women's health, it has become increasingly apparent that green tea has a unique diverse list of indications in the prevention and treatment of conditions pertinent to women. These conditions include breast cancer, ovarian cancer, cervical dysplasia, polycystic ovarian syndrome, and weight management. This is not an exhaustive list of the benefits of green tea by any means. Other significant research can be found in the areas of lipid management, cardiovascular disease, influenza prevention, type 2 diabetes, liver disease, cognitive impairment and many different cancers other than breast and ovarian cancer. The focus of this article is the former list, but any practitioner of botanical medicine who has made themselves aware of the many uses of green tea, will likely find themselves a robust user.

ACTIVE CONSTITUENTS

Derived from the tea plant *Camellia sinensis*, green tea is very high in polyphenols, which have potent antioxidant and anti-tumor properties. The major polyphenols in green tea are flavonoids, including catechin, epicatechin, epicatechin gallate, epigallocatechin gallate, and proanthocyanidins. Epigallocatechin gallate (EGCG) is thought to be the most significant active component of green tea. Products with higher EGCG content are thought to be more potent. Other compounds in green tea include vitamin C, a very small amount of caffeine, theanine, lignins, organic acids, protein and chlorophyll.

MECHANISMS OF ACTION

The catechins in green tea are thought to have anti-inflammatory activity by COX-1 and COX-2 inhibition, leukotriene inhibition, and nitric oxide synthetase activity. Green tea flavonoids might also reduce lipoprotein oxidation, reduce proliferation of vascular smooth muscle and inhibit the release of arachidonic acid from platelets. However, when used in humans, green tea has not yet shown any consistent effect on cardiovascular risk factors.

CLINICAL RESEARCH SUMMARY

A study was recently published in JAMA to investigate the associations between green tea consumption and all-cause and cause-specific mortality. It is called the Ohsaki study, a population-based, prospective cohort study.¹ This study included Japanese adults aged 40-79 without a history of stroke, coronary heart disease or cancer, at initiation of the study. They were followed for up to 11 years for all cause mortality and for up to 7 years for cause-specific mortality. Green tea consumption was inversely

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associated with mortality due to all causes and inversely associated with cardiovascular disease. This inverse association for all-cause mortality association and for cardiovascular disease was stronger in women and even a greater association with cardiovascular disease. Unfortunately, there was no beneficial effect of green tea consumption and reducing the hazard ratio of cancer mortality.

Despite lack of clarity regarding green tea and cancer prevention in humans, there are mechanisms of action of green tea that are compelling: Green tea may protect against some kinds of cancers by preventing blood vessel growth in tumors, inducing apoptosis, reducing oxidative DNA damage, inhibiting tumor promoters, inhibiting hormones and growth factors with the receptor sites, reducing free radical generation and inhibiting important enzyme systems necessary for cancer promotion and proliferation.

Breast Cancer

Epigallocatechin gallate (EGCG) and epigallocatechin (EGC) reduce the proliferation of human breast cancer cells in vitro and inhibit breast tumor growth. Animal studies have demonstrated the effects of green tea on reducing as well as preventing breast tumors and inhibiting various enzymes and cell signaling systems. EGCG has demonstrated the ability to inhibit the growth of human breast and prostate tumors transplanted into athymic mice.² Green tea extracts given to female rats significantly decreased DMBA-induced mammary tumor burden, invasive tumors, and significantly delayed the onset of a first tumor.³

Another study in which Sprague-Dawley rats were fed 1% green tea catechins in the diet, was effective in reducing breast tumor promotion, but not the progression of breast cancer.⁴ Several in vitro studies have found green tea reduced the rate of proliferation of breast cancer cells.^{5,6}

More recently, green tea extract and EGCG affected angiogenic factor vascular endothelial growth factor (VEGF) expression.⁷ The extract or the EGCG significantly decreased the levels of the VEGF peptide secreted into the medium of human breast cancer cells. The green tea was also able to suppress the expression of protein kinase C, a VEGF transcription modulator, and decrease the RNA levels of VEGF. Inhibition of VEGF transcription appears to be involved in the antiangiogenic effects of green tea. The implication being that green tea could inhibit blood supply to breast cancer tumors or breast cancer cell target sites by inhibiting VEGF and may have potential use for breast cancer treatment and prevention.

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Breast tumors which are HER-2 neu positive may also be especially susceptible to green tea. EGCG inhibited mouse mammary tumor HER-2 neu cell growth in vitro,⁸ and dose of green tea polyphenols slowed the growth of estrogen receptor-negative breast cancer cell lines.¹²

In 1998, a study found that the more green tea pre-menopausal women with stage I and stage II breast cancer consumed, the fewer metastasized lymph nodes they developed.⁹ Additionally, postmenopausal women who consumed green tea experienced an increased progesterone and estrogen status – a finding usually associated with less aggressive forms of breast cancer. No benefit was seen in stage III breast cancer patients. In stage I and II patients, there was a 16.7% recurrence rate for those consuming five cups or more of green tea (with an average of eight cups) per day. For those who consumed four or fewer cups per day (with an average of two), there was a 24.3% recurrence rate. Disease-free survival was also significantly improved in stage I and stage II breast cancer patients who had a greater consumption of green tea, compared to those who consumed less green tea.

Another Japanese study compared 472 women with breast cancer and different intakes of green tea and found that EGCG may decrease the severity of the initial diagnosis and the incidence of recurrence.¹⁰

Epidemiologic studies, both case-control and cohort in design, have examined the association between tea intake and breast cancer. A meta-analysis of 13 papers provided data on green tea and black tea.¹¹ For black tea, there were conflicting results in case-control versus cohort studies. Of the eight case-control studies, there was a minor inverse association between black tea and risk of breast cancer. Five cohort studies demonstrated a modest increase in risk associated with black tea intake. However, the results for green tea indicated a lower risk for breast cancer with green tea consumption.

Another mechanism of green tea is in its ability to inhibit aromatase. In the Shanghai Women's Health Study, a cohort of 74,942 Chinese women, there was a time-dependent interaction between green tea consumption and age of onset of breast cancer.¹² "Age at breast cancer onset was significantly later for breast cancer patients who drank green tea than for those who did not, among premenopausal women who began drinking tea and were diagnosed with breast cancer before menopause, and among postmenopausal women who both began drinking tea and were diagnosed with breast cancer after menopause. On the other hand, the study found that among postmenopausal breast cancer patients, green tea drinkers who started before menopause had comparable age at onset to the nondrinkers." In women who started drinking green tea ages 25 years or younger had a lower risk of developing pre-

menopausal breast cancer. Compared with non-tea drinkers, women who started tea drinking at 25 years of age or younger had an increased risk of postmenopausal breast cancer, suggesting that regular green tea intake may delay the onset of breast cancer.

Ovarian Cancer

Green tea and its components have been shown to downregulate the expression of specific proteins involved in inflammation, cell signaling, cell motility and angiogenesis in epithelial ovarian cancer cell lines in the laboratory setting. In addition, studies have shown that green tea can induce apoptosis (cell death) and could even enhance the effects of an ovarian chemotherapeutic drug, cisplatin. Human observational studies also show significant associations between green tea consumption and decreased rates of ovarian cancer as well as a better prognosis in those with ovarian cancer. The specifics of these findings can be found in an important recent systematic review of the laboratory, animal and human studies investigating the effects of green tea for ovarian cancer prevention and treatment was published in 2012.¹³ Within that review, four epidemiological studies showed a significant dose-response relationship.^{14,15,16,17}

In other research, investigators evaluated the association between tea consumption (mainly black tea) and the risk of ovarian cancer in women aged 40-76. During an average of 15 years and in 61,057 women, tea consumption was inversely associated with ovarian cancer risk.¹⁸ Compared with women who rarely or never consumed tea, those who drank 2 or more cups daily had a hazard ratio of 0.54 (95% CI, 0.31-0.91) for ovarian cancer. Risk reduction was independent of age of menarche, age at first birth, age at menopause, family history of breast cancer and use of hormone replacement therapy.

Tea consumption may also enhance the survival of women with epithelial ovarian cancer. A cohort of 254 women with confirmed ovarian cancer was followed for a minimum of 3 years. The survival was greater with tea drinkers who consumed at least 1 cup of green tea per day compared to non tea drinkers.¹⁹

Cervical Dysplasia and HPV/Cervical Cancer

Green tea has recently been shown to influence numerous mechanisms which are favorable towards preventing and/or treating HPV related lesions. Epigallocatechin-3-gallate has been shown to inhibit epidermal growth factor receptor (EGFR) signaling pathway.²⁰ EGFR activation is required for cervical cell proliferation which suggests agents which inhibit EGFR may be of important therapeutic value in prevention and treatment of cervical dysplasia and genital warts. Two other in vitro studies demonstrated EGCG inhibits the growth of human cervical cancer

cell lines, induces apoptosis, inhibits telomerase activity in cervical cell lines and has a role in regulation of gene expression.^{21,22}

Perhaps the most encouraging of the studies was an investigation of the clinical efficacy of green tea extracts delivered vaginally and/or orally in patients with HPV infected cervical lesions. Fifty-one patients with cervical lesions ranging from chronic cervicitis, mild dysplasia, moderate dysplasia and severe dysplasia were divided into four groups as compared with 39 controls.²³ A green tea polyphenol vaginal product was applied locally twice a week to 27 patients. 20 of the 27 patients using the vaginal green tea product showed a response. An oral 200 mg EGCG capsule was taken orally every day for eight to 12 weeks in six patients and three out of the six showed a response. Group three consisted of eight patients using the vaginal product and the oral capsule. Six of eight showed a response. Group 4 consisted of 10 patients using a higher dose EGCG capsule (amount not stated). Six out of the 10 patients with this higher dose EGCG oral capsule only, showed a response. Overall, 35 of 51 (69%) response rate was noted for the green tea products compared with a 10% response rate in the untreated controls. The mechanisms involved appear to be apoptosis, cell cycle arrest, modification of gene expression and anti-tumor effects, specifically, inhibition of cell proliferation. These results demonstrate green tea extracts in the form of a vaginal delivery and an oral capsule are effective strategies for treating cervical lesions.

Uterine Fibroids

In an in vitro study and nude mouse model, EGCG inhibited the proliferation and induced apoptosis in rat uterine leiomyoma cells in vitro and in vivo.²⁴ This may lead to a potential of green tea extract for the prevention and treatment of uterine leiomyoma in women.

Bone Density

Green tea is emerging as having some potential effect on bone remodeling and part of the current paradigm shift in nutritional influences on bone. Moving beyond the historic focus on minerals and other essential nutrients, bone is highly responsive to phytochemicals. Though nonessential, they can support bone density through osteoblast and osteoclast cell biochemistry and support bone homeostasis in ways that are very different from calcium, vitamin D, etc. Of the phytochemicals, polyphenols appear to be highly influential.

One specific review describes the effect of green tea or its bioactive components on bone health, with an emphasis on the following²⁵: 1) the prevalence and etiology of osteoporosis; 2) the role of oxidative stress and antioxidants in osteoporosis; 3) green tea composition and bioavailability; 4) the effects of green tea and its active components on osteogenesis osteoblastogenesis, and osteoclastogenesis from human epidemiological, animal, as well as cell culture studies; 5) possible mechanisms explaining the osteoprotective effects of green tea bioactive compounds; 6) other bioactive components in tea that benefit bone health; and 7) a summary and future direction of green tea and bone health research and the translational aspects. In general, tea and its bioactive components might decrease the risk of fracture by improving bone mineral density and supporting osteoblastic activities while suppressing osteoclastic activities.

Weight loss

Green tea may also play a role in weight management. An increase in fat and calorie metabolism may be caused by the caffeine, catechin and theanine constituents. They appear to stimulate thermogenesis as a means of increasing fat burning and inhibiting fat absorption. In addition, individuals who take green tea extract have been observed to expend more energy and burn more calories than those who do not.²⁶ In this study demonstrating the thermogenic properties and fat oxidation of green tea, done in Geneva in 1999, the higher dose used contained 50 mg of caffeine and 90 mg of EGCG per 2 capsules. According to this study, dosing is 2 caps with breakfast and 2 caps with lunch.

In individuals with a usually low caffeine intake, a green tea-caffeine combination improved weight loss through thermogenesis and fat oxidation.²⁷

Polycystic ovarian syndrome

Green tea's ability to increase the production of sex-hormone-binding globulin and its thermogenic effect also provides a rationale for its use in women with polycystic ovarian syndrome (PCOS).²⁸ By increasing sex hormone-binding globulin, some free testosterone can be bound up, thereby reducing some of the testosterone-related problems seen in women with PCOS such as hair thinning, acne and facial hair. Obesity is another consideration in approximately 50% of PCOS women. Green tea may be helpful in not only increasing SHBG, but also in the thermogenic effects and weight loss potential.

ADVERSE EFFECTS/CAUTIONS/CONTRAINDICATIONS

Some individuals are negatively affected by the small amount of caffeine in green tea and its stimulating effect, leading to nervousness, insomnia, dizziness, agitation, restlessness, confusion and anxiety. These effects are more common when using higher doses of green tea. Some individuals may also have an increase in blood pressure or pulse, especially if consumed in higher amounts and in those who already have even mild hypertension. Allergic reactions can occur and tend to include cough, dyspnea, loss of consciousness and asthma. Rare anaphylaxis reactions can occur to the caffeine in green tea.

Another consideration is withdrawal from the green tea. Although uncommon, withdrawal symptoms have been known to occur, including anxiety, restlessness, muscle tension, nausea and vomiting.

Combining ephedra with caffeine can increase the risk of adverse events including hypertension, seizures, and temporary loss of consciousness. Avoid use during pregnancy and while nursing. Infants whose nursing mothers consume caffeine could suffer from sleep disorders.

The Natural Medicines Comprehensive Database lists the following drugs as have potential adverse interactions with green tea: Adenosine, Alcohol, amphetamines, cimetidine, clozapine, cocaine, contraceptives, disulfiram, ephedrine, estrogens, fluconazole, lithium, monamine oxidase inhibitors, nicotine, quinolone antibiotics, theophylline, verapamil and clopidogrel, ticlopidine, heparin and warfrain.

ADULT DOSING

When dosing green tea capsules, those containing 300 mg of green tea extract with 95% polyphenols, 80% catechins and 55% EGCG, 1 capsule is approximately equal to 3 cups of green tea. The normal amount of green tea consumed traditionally by Japanese adults is about three cups per day, providing about 240 to 320 mg of polyphenols. Green tea suppositories are also now available for use in HPV and cervical dysplasia management.

SUMMARY OF CLINICAL CONCEPTS

1. Breast Cancer stage I or II = 2-3 green tea extract capsules (containing 95% polyphenols, 80% catechines and 55% EGCG per day) per day or 5-8 cups of tea daily.
2. Ovarian cancer prevention = 1 cup per day
3. Ovarian cancer treatment adjunct = 2 cups per day
4. Cervical atypia = green tea suppositories twice weekly plus one green tea extract capsule per day
5. Cervical dysplasias = as part of a comprehensive systemic and local treatment strategy, also include one green tea capsule daily and green tea suppositories twice weekly
6. Weight loss = 2 caps of green tea extract with breakfast and 2 with lunch (2 caps = 50 mg caffeine and 90 mg of EGCG)
7. PCOS= 250-500 mg of green tea extract per day (95% polyphenols, 80% catechins, 45% EGCG)

ABOUT THE AUTHOR

Dr. Tori Hudson, Naturopathic Physician, graduated from the National College of Naturopathic Medicine (NCNM) in 1984 and has served the college in several capacities, including: Medical Director, Associate Academic Dean, and Academic Dean. She is currently a clinical professor at The National College of Naturopathic Medicine (NCNM), Southwest College of Naturopathic Medicine and Bastyr University. Dr Hudson has been in practice for 28 years, is the medical director of her clinic, "A Woman's Time" in Portland, Oregon, and director of product research and education for VITANICA.

Dr. Hudson was awarded the 1990 President's award from the American Association of Naturopathic Physicians for her research in women's health, the 1999 prestigious Naturopathic Physician of the Year award, the 2003 NCNM Alumni Pioneer Award., and the 2009 Natural Products Association Pioneer Award.

She is a nationally recognized author (book: Women's Encyclopedia of Natural Medicine second edition, McGraw Hill 2008), speaker, educator, researcher, and clinician. Dr. Hudson serves on several editorial boards and advisory panels, including on the Scientific Advisory Board of *Gaia Herbs Professional Solutions*.

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