EGCG: Potent extract of green tea

Archeological evidence suggests that tea leaves steeped in boiling water were consumed as many as 5,000 years ago. Botanical evidence indicates that India and China were among the first countries to cultivate tea. Although the English are known for their love of tea, Americans invented the tea bag and began the practice of drinking iced tea in the early 1900s. Today, hundreds of millions of people drink tea around the world, and studies are now suggesting that one variety of tea in particular—green tea (Camellia sinensis)—has many health benefits.

The plant Camellia sinensis yields both green and black tea. The tea plant has long been cultivated in China. It's an evergreen shrub or tree that can grow to a height of 30 feet but usually is maintained at a height of 2 to 3 feet by regular pruning. The shrub is heavily branched, with young hairy leaves. The parts used are the leaf bud and the two adjacent young leaves together with the stem, broken between the second and third leaf. Older leaves are considered inferior in quality.

Green tea is produced by lightly steaming the fresh cut leaf, and the production of black tea involves allowing the leaves to oxidize. During oxidation, enzymes present in the tea convert polyphenols, which possess outstanding therapeutic action, to a different compound with different pharmacological effects. With green tea, oxidation doesn't take place because the steaming process inactivates these enzymes. Green tea is very high in polyphenols with potent antioxidant and anti-cancer properties. Oolong tea is partially oxidized.

Of the nearly 2.5 million tons of dried tea produced each year, only 20 percent is green tea. In other words, nearly four times as much black tea is produced and consumed compared to green tea. India and Sri Lanka are the major producers of black tea. Green tea is produced primarily in China, Japan and a few countries in North Africa and the Middle East.

The chemical composition of green tea varies with climate, season, horticultural practices and age of the leaf (position of the leaf on the harvested shoot). The major components of interest are the polyphenols. The term polyphenol denotes the presence of multiple phenolic rings. (A phenolic ring is a 6-carbon benzene ring with an attached hydroxyl (OH) group—also referred to as the hydroxyl functional group.) The major polyphenols in green tea are flavonoids (e.g., catechin, epicatechin, epicatechin gallate, epigallocatechin gallate (EGCG) and proanthocyanidins). Epigallocatechin gallate is viewed as the most significant active component. The leaf bud and first leaves are richest in epigallocatechin gallate. The usual concentration of total polyphenols in dried green tea leaves is around 8 to 12 percent.

Other compounds of interest in dried green tea leaves include caffeine (3.5 percent), an amino acid known as theanine (4 percent), lignan (6.5 percent), organic acids (1.5 percent), protein (15 percent) and chlorophyll (0.5 percent).

One cup of green tea will contain approximately 300 to 400 mg of polyphenols, but remember, only 8 to 12 percent of the entire cup will be polyphenols and a smaller portion will be of the most beneficial polyphenol epigallocatechin gallate.

Most of the studies on green tea have focused on the cancer protective aspects. Green tea polyphenols are potent antioxidant compounds that have demonstrated greater antioxidant protection than vitamins C and E in experimental studies.

In addition to exerting antioxidant activity on its own, green tea may increase the

activity of antioxidant enzymes. In one interesting study from the *Journal Cancer Research*, mice were fed green tea polyphenols via their drinking water for 30 days. Researchers discovered a significant increase in the activity of antioxidant and detoxifying enzymes (glutathione peroxidation, glutathione reductase and glutathione S-transferase, catalase and quinine reductase) in the small intestine, liver and lungs.

Let's examine the clinical applications of EGCG and look further into the research.

Clinical applications

Atherosclerosis
Population-based and clinical studies indicate that the antioxidant properties of green tea may help prevent atherosclerosis, particularly coronary artery disease. (Population-based studies refer to studies that follow large groups of people over time and/or studies that are comparing groups of people living in different cultures or with different dietary habits, etc.) In clinical practice, I employ 70 percent EGCG as a potent tool in my nutritional arsenal not only as an antioxidant, but to address arterial inflammation. Highly sensitive C-reactive protein (hs-CRP) is a marker of arterial inflammation. Inflammation also is believed to play a role in heart disease; EGCG is a potent anti-inflammatory.

According to Japanese research, green tea reduces the levels of LDL or "bad" blood cholesterol, thereby reducing the risk of coronary heart disease. European studies have found that regular consumption of tea protects against heart disease, with one study documenting that the risk was 36 percent lower for tea drinkers. It is believed that the polyphenols in tea help prevent artherosclerosis.

Preliminary research also indicates that tea polyphenols may reduce the activity of platelets, which are the clotting agents of the blood. This is good, because "sticky" blood is more likely to form artery-blocking clots.

Green tea has demonstrated an ability to lower total cholesterol and raise HDL ("good") cholesterol in both animals and people. One population-based study found that men who drink green tea are more likely to have lower total cholesterol than those who do not drink green tea. Results from one animal study suggest that polyphenols in green tea may block the intestinal absorption of cholesterol and promote its excretion from the body.

EGCG has been reported to inhibit lipid peroxidation, an oxidative process implicated in several pathologic conditions, including atherosclerosis (Pietta et al.,1996). Keep in mind that the oxidation of LDL-cholesterol might be associated with an increased risk of heart disease.

In a cross-cultural correlation study of 16 cohorts, known as the Seven Countries Study, the average flavanol intake was inversely correlated with mortality rates of coronary heart disease after 25 years of follow-up (Hertog et al., 1995; Hollman et al.,1999).

Cancer
The cancer-protective effects of green tea have been reported in several population-based studies. For example, cancer rates tend to be low in countries such as Japan where green tea is regularly consumed. However, it is not possible to determine from these population-based studies whether green tea actually prevents cancer in people. Emerging animal and clinical studies are beginning to suggest that EGCG may play an important role in the prevention of cancer.

It has been suggested that EGCG and other tea catechins suppress tumor promotion by inhibiting the release of tumor necrosis factor-alpha, which is believed to stimulate tumor promotion and progression of initiated cells as well as premalignant cells (Fujiki et al., 2000). Furthermore, EGCG was shown to reduce specific binding of both the 12-Otetradecanoylphorbol-13-acetate (TPA)-type and the okadaic acid-type tumor promoters (the two major classes of tumor-promoting agents) to their receptors. This "sealing" effect of EGCG is achieved by its interaction with the phospholipid bilayer of the cell membrane (Fujiki et al., 1999). This is one reason why I will typically administer EGCG with glycophospholipids such as NT Factor or phosphatidylcholine.

When non-Hodgkin's lymphoma cells were transplanted into mice, green tea prevented 50 percent of the tumors from taking hold and significantly inhibited growth of the tumors (*Leukemia* 2000 Aug;14(8):1477-82).

Bladder cancer
A few studies have examined the relationship between bladder cancer and green tea consumption. In one study that compared people with and without bladder cancer, researchers found that women who drank black tea and powdered green tea were less likely to develop bladder cancer. A follow-up study by the same group of researchers revealed that bladder cancer patients (particularly men) who drank green tea had a substantially better 5-year survival rate than those who did not.

Breast cancer
Studies suggest that EGCG inhibits the growth of breast cancer cells, both in live animals and test tubes.

A Japanese study comparing 472 women with breast cancer who drank differing amounts of green tea indicates that EGCG may decrease both the severity of the initial diagnosis and the likelihood of recurrence. The researchers found that the women with Stage I, II and III breast cancers who drank five or more cups of green tea per day were less likely to have cancer that spread to the lymph nodes. In addition, the greater consumption of green tea by women with Stage I or II breast cancer was associated with lower incidence of recurrence. No correlation was shown with women who had Stage III cancers. Another Japanese study showed less overall incidence of cancer among 8,000 people who drank ten or more cups of green tea a day.

Colorectal cancer
One of the main reasons I began my research into sourcing and formulating a potent EGCG supplement was due to my family history of colon cancer (as well as prostate cancer). A study at the Linus Pauling Institute at Oregon State University on mice that were genetically predisposed to develop tumors in their intestines revealed after 12 weeks of treatment that mice that were given green tea had significantly fewer tumors than mice that received no treatment (*Carcinogenesis*, February 2003).

Phenol sulfotransferases are involved in cancer growth, and EGCG was shown to inhibit this activity in a human colon cancer call line (*Biol Pharm Bull* 2000 Jun;23(6):695-9).

Chinese scientists discovered that EGCG inhibits angiogenesis (the production of new blood vessels) in mice inoculated with human colon cancer. This blocking of new blood vessel growth may be an important part of the overall anti-cancer action of polyphenols because it impedes tumor growth. Esophageal cancer studies in laboratory animals have found that green tea polyphenols inhibit the growth of esophageal cancer cells. However, results of studies in people have been conflicting. In fact, some evidence suggests the hotter the tea (or any other hot beverage), the greater the risk of developing esophageal cancer. However, researchers reporting on a case-

control study found that Chinese men and women who drink green tea have a reduced risk of up to 60 percent of developing esophageal cancer (*Journal of the National Cancer Institute*, June 1, 1994).

Lung cancer
Consumption of green tea was found to be associated with a reduced risk of lung cancer among non-smokers but not among smokers. Also among non-smokers, the risks of lung cancer decreased with increasing tea consumption (*Epidemiology* 2001 Nov; 12(6):695-700).

Treatment of human lung cancer cell line A549 cells with EGCG significantly inhibited the expression levels of hnRNP B1 mRNA and the elevated levels of hnRNP B1 protein, both of which are constitutively elevated in cancer cells.
Furthermore, EGCG inhibited the promoter activity of hnRNP A2/B1 gene expression, preventing lung cancer (*International Journal of Oncology* 20: 1233-1239, 2002).

Pancreatic cancer
Researchers in Japan determined whether EGCG affects proliferative and invasive activity of human pancreatic carcinoma cells. The results indicate that the growth of all three pancreatic carcinoma cells (PANC-1, MIA PaCa-2 and BxPC-3) was significantly suppressed by EGCG treatment in a dose-dependent manner. EGCG may be a potent biologic inhibitor of pancreatic carcinoma, reducing their proliferative and invasive activity (*Pancreas*, July 2002).

Prostate cancer
In my opinion, EGCG is the most important component of green tea to the prostate cancer patient. The first evidence of its ability to induce prostate cancer apoptosis (programmed cell death) was published in *Cancer Letters* back in 1998 (130(1-2):1-7 1998 Aug 14).

Its pharmacologic activity extends beyond its action as an antioxidant. EGCG acts against urokinase, an enzyme often found in large amounts in human cancers, inhibits ornithine decarboxylase (a rate-limiting enzyme closely associated with tumor promotion), and blocks type 1 5-alpha-reductase (5AR). Inhibitors of 5AR may be effective in the treatment of 5 alpha dihydrotestosterone-dependent abnormalities, such as benign prostate hyperplasia, prostate cancer and certain skin diseases.

Urokinase breaks down the basement membrane of cell junctions, which may be a key step in the process of tumor cell metastasis as well as tumor growth. EGCG attaches to urokinase and prevents these actions.

EGCG was shown to inhibit growth and induce regression of human prostate and breast cancers in athymic mice (Liao S, Umekita Y, Guo J et al. “Growth inhibition and regression of human prostate and breast tumors in athymic mice by tea epigallocatechin gallate.” *Cancer Letters* 96:239-243, 1995).

Skin cancer
Studies suggest that EGCG and green tea polyphenols have anti-inflammatory and anti-cancer properties that may help prevent the onset and growth of skin tumors. Topical application of EGCG may prevent UV-B-induced immunosuppression and precancerous cell changes after UV-B exposure (*J Leukoc Biol.* 2001;69:719-726).

Stomach cancer
Laboratory studies have found that green tea polyphenols inhibit the growth of stomach cancer cells in test tubes. The exposure of human stomach cancer KATO III cells to EGCG led to both growth inhibition and the induction of programmed cell

death (apoptosis) (*Oncol Rep*, 5(2):527-9 1998 Mar-Apr).

Skin health
Interesting research using pooled human keratinocytes (skin cells) to study the normal growth of the skin cells alone and compared it to the growth of the cells when exposed to EGCG revealed that EGCG reactivated dying skin cells. Cells that migrate toward the surface of the skin normally live about 28 days, and by day 20, they basically sit on the upper layer of the skin getting ready to die and slough off. Current research seems to show that EGCG reactivates them.

The skin consists of three layers: the epidermis (outer layer), dermis (mid-layer) and hypodermis (inner layer). Skin researcher Dr. Hsu learned that green tea polyphenols aren't absorbed beyond the epidermis, so any benefits are limited to that outer layer of skin. But the benefits, he stressed, seem significant.

Dr. Hsu thinks that EGCG may be a fountain of youth for skin cells. When exposed to EGCG, the old cells found in the upper layers of the epidermis appear to start dividing again. They make DNA and produce more energy. They are reactivated. In addition, the researchers found that EGCG accelerates the differentiation process among new cells.

Combining these effects of EGCG on skin cells in different layers of the epidermis, there may be potential benefits for skin conditions as diverse as aphthous ulcers, psoriasis, rosacea, wrinkles and wounds. Perhaps scar tissue could be prevented from forming with EGCG therapy. Diabetics with slow healing wounds may benefit from EGCG supplementation. As a faculty member of the American College for Advancement in Medicine who teaches an anti-aging workshop, I put all my patients with skin care concerns on EGCG.

Joint health
Since green tea is a potent antioxidant and anti-inflammatory (it's been shown to decrease the production of inflammatory prostaglandin E2), it's a great tool to employ for patients with osteoarthritis, rheumatoid arthritis and bursitis. Numerous patients with arthritic complaints feel better while on EGCG, which play a role in their tailored nutritional therapy program of diet, supplementation and exercise.

Some interesting research in Europe shows that EGCG protects cartilage destruction in test-tube models of cartilage loss that mimic what happens in the arthritic joint.

Inflammatory bowel disease (IBD)
Green tea may help reduce inflammation associated with Crohn's disease and ulcerative colitis, the two types of IBD. In addition, if green tea proves to be helpful for preventing colon cancer, this would be an added benefit for those with IBD because they are at a higher risk for the disease. In a recent study, scientists may have uncovered one of the mechanisms behind this effect. It was determined that EGCG can inhibit interleukin 8 (IL-8), a pro-inflammatory cytokine. Researchers believe their results require further study, and trials are currently underway. I had the pleasure of listening to a lecture in San Antonio, Texas at the American College of Nutrition conference in October 2002. I met Dr. Craig J. McClain, who is currently using EGCG on IBD patients with very good results. After that conference, I began my research into developing the highest quality EGCG supplement in the United States.

Diabetes
Green tea traditionally has been used to control blood sugar in the body. Animal studies suggest that green tea may help prevent the development of type 1 diabetes

and slow the progression once it has developed. People with type 1 diabetes produce little or no insulin, a hormone that ushers glucose (sugar) into cells. EGCG may help regulate glucose in the body because it has a slight inhibition on carbohydrate digesting enzymes. Though more research in this area is needed, I routinely employ EGCG in all my diabetic patients, particularly because of their increased risk of cardiovascular disease and for their high requirement for antioxidants.

Liver disease
Population-based studies have shown that men who drink more than 10 cups of green tea per day are less likely to develop disorders of the liver. Green tea also appears to protect the liver from the damaging effects of toxic substances such as alcohol. Animal studies have shown that green tea helps protect against the development of liver tumors in mice.

Results from several animal and human studies suggest that EGCG may help treat viral hepatitis (inflammation of the liver from a virus).

Additionally, green tea has hepatoprotective qualities that include killing dangerous intestinal bacterial strains (clostridium and Escherichia coli), promoting the growth of friendly bacteria in the intestine and lowering excessive iron levels in the liver that would interfere with ribavirin and interferon treatment for hepatitis C.

Antioxidant properties
Researchers at the University of Kansas feel that EGCG is at least 100 times more effective than vitamin C and 25 times better than vitamin E at protecting cells and their genetic material, DNA, from damage believed to be linked to cancer, heart disease and other potentially life-threatening illnesses. EGCG, carries twice the antioxidant punch of resveratrol, found in red wine.

University of Kansas researcher Dr. Mitscher says, “I’m not making any claims, but, used in conjunction with a healthful diet and exercise program, it’s like an insurance policy. It increases your odds of avoiding or postponing diseases associated with free radicals.”

The early evidence of antioxidant properties of EGCG came from the experimental data that showed EGCG-induced inhibition of soybean lipoxygenase. (Ho et al., 1992). Later, it was reported that EGCG inhibited TPA-induced oxidative DNA base modification in HeLa cells, inhibited Cu2+-mediated oxidation of low density lipoprotein (LDL), reduced tert-butyl hydroperoxide-induced lipid peroxidation and blocked the production of reactive oxygen species derived from NADPH-cytochrome P450-mediated oxidation of the cooked meat carcinogen, 2-amino-3methylimidazo[4,5-f]quinoline (Surh, 1999).

Green tea, which is water soluble, has another advantage over vitamin E. Excessive amounts of antioxidants found in green tea are excreted by the body. The body absorbs and retains fat-based vitamins such as vitamin E, even at potentially harmful levels.

The antioxidant activity of EGCG helps tremendously to combat post-exercise muscle soreness.

Weight loss
Studies suggest that EGCG may boost metabolism and help burn fat. In a French study, resting metabolic rate increased by 4 percent after 90mg of EGCG was consumed three times per day.

Scientists at the University of Chicago's Tang Center for Herbal Medicine Research have found that EGCG caused rats to lose up to 21 percent of their body weight. Rats injected with EGCG derived from green tea leaves lost their appetites and consumed up to 60 percent less food after seven days of daily injections. EGCG seems to desensitize leptin receptors (leptin may play a role in appetite) in the study animals (*Endocrinology*, March 2003). Researchers suspect that EGCG may work through other hormonal systems that control appetite and body weight that we don't know about yet.

I recommend EGCG as part of my weight loss protocols even though I'm not exactly sure how it works. The three theories of EGCG-assisted weight loss are increasing metabolic rate, preventing the digestion of some carbohydrate (akin to a "starch blocker" effect) or reducing appetite. I have noticed an increase in my own metabolic rate since regularly taking 70 percent EGCG. I noticed beneficial effects in my weight loss patients with some saying that they note a reduction in appetite.

EGCG is rapidly replacing ephedra as a weight loss supplement.

70 percent EGCG, the ultimate green tea supplement
A few green tea products on the market reach a maximum of 55 percent EGCG. Our green tea extract, sourced and formulated by me personally, contains the highest quantity of EGCG available in supplement form. Each 500 mg capsule contains 70 percent EGCG.

When beginning EGCG as a supplement, it would be wise to make sure you also are taking probiotics. Sometimes I recommend that patients take probiotics one or two weeks prior to introducing EGCG. Additionally, I recommend a change in diet. Remember that EGCG may act as a starch blocker. If candida overgrowth is present in the intestines, one might experience some mild gastrointestinal discomfort. Additionally, there is some evidence that EGCG is anti-fungal, which can promote a "die off" response that might also induce mild gastrointestinal discomfort. Taking probiotics prior to and during EGCG supplementation and while changing your diet (at the very least remove all refined carbohydrates) will prevent any mild gastrointestinal discomfort.

I developed our green tea extract to be free of caffeine, so it is not a stimulant and is safe for caffeine-sensitive individuals or for those wishing to remain caffeine free. Additionally, our EGCG is free of vitamin K, making it safe to take with blood thinning medication.

EGCG should not be used during pregnancy.

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