GREEN TEA

The beverage of choice in the east, green tea shows promise as an anti-aging, cancer-fighting agent.

by Ivy Greenwell

Part I:
Anti-carcinogenic properties of green tea

One of the most exciting health developments of the nineties has been the discovery of the extraordinary anti-aging properties of green tea. Epidemiological observations have shown that people in green-tea consuming countries-mainly Japan and China-have very low rates of cancer. In Japan, the women who teach the tea ceremony, and thus drink more than the average amount of extra-strong green tea, are noted for their very low mortality rate and longevity; deaths from cancer are especially rare in this group.

The rates of breast, colon, skin, pancreatic, esophageal and stomach cancer have been found to be lower among drinkers of green tea. If those who consumed more than ten cups of green tea a day got cancer, it was at considerably older age, especially in women. Likewise, it has been noted that those Japanese smokers who consume a lot of green tea seem to enjoy protection against lung cancer. In fact, the Japanese have both the highest smoking rate and the lowest lung cancer rate in the industrialized world.

Western epidemiological studies have also tended to confirm that higher consumption of tea and coffee is associated with a lower risk of breast cancer. On the basis of a number of such epidemiological studies, it could be tentatively asserted that the higher the consumption of tea in general, and perhaps of green tea in particular, the lower the incidence of breast, prostate and lung cancer. The same probably holds true for colon, stomach, pancreatic and skin cancer. In vitro or animal research indicates that green tea may be effective against an even wider variety of types of cancer, including leukemia and glioma.

Research aimed at finding the active compounds in green tea revealed that its protective effects are due chiefly to catechins. Powerful polyphenolic antioxidants, catechins are astringent, water-soluble compounds that can be easily oxidized. They are a subgroup of flavonoids, weak phytoestrogenic compounds widely available in vegetables, fruit, tea, coffee, chocolate and wine. The antioxidant potential of both green and black teas, as measured by the Phenol Antioxidant Index, was found to be significantly higher than that of grape juice and red wines.

Green tea is manufactured from fresh, unfermented tea leaves; the oxidation of catechins is minimal, and hence they are able to serve as antioxidants. While the fermentation of tea leaves needed for the production of black tea produces some unique antioxidants such as theaflavins, bisflavonols and thearubigens (polymers of simple polyphenols), such fermentation reduces the catechin content, especially the strongly bioactive catechin called epigallocatechin gallate. Epigallocatechin gallate has been singled out by many researchers as particularly important for cancer prevention.

So far, most research has been done on green tea and the activity of its various catechin components; the research on complex polymeric polyphenols found in black tea is still in an early stage.

Numerous recent studies continue to confirm that green tea polyphenols have powerful anticarcinogenic, cardioprotective, neuroprotective and antimicrobial actions. In the first of the two articles on green tea, let us take a closer look at the anticarcinogenic properties of green tea.
The latest good news about green tea comes from a study done at the Karolinska Institute in Stockholm. A team of researchers headed by Dr. Yihai Cao found that green tea can block angiogenesis—the development of new blood vessels that tumors need in order to grow and metastasize. The authors gave mice the equivalent of two-to-three cups of green tea a day. When lung cancer was induced, the mice supplemented with green tea showed significantly less tumor growth. The scientists found that green tea suppressed the development of new blood vessels and prevented metastasis. They hypothesize the epigallocatechin gallate is the compound responsible for the suppression of angiogenesis.

In an interview, Dr. Cao explained that all solid tumors depend on angiogenesis for their growth. If green tea polyphenols can prevent angiogenesis, then this would go a long way toward explaining why green tea is effective in preventing so many kinds of cancer. Dr. Cao stressed that it takes long-term consumption of green tea in order to obtain these chemopreventive benefits.

The anti-angiogenic potential of green tea could also be used for the prevention and possibly even the treatment of degenerative eye disorders, such as diabetic retinopathy, that also depend on the development of new blood vessels. In addition, inhibition of angiogenesis may be another mechanism in which green tea helps prevent heart disease, since atherosclerotic plaque also needs to develop microcirculation to keep growing. (Note the recent news about how the anti-angiogenic drug endostatin slows the development of atherosclerosis.)

Green tea has also been shown to help prevent metastasis. Cancer cells secrete special enzymes called collagenases in order to penetrate and colonize various tissues. It is the metastatic process that is lethal, not the primary tumor. Hence finding substances that can prevent metastasis is of prime importance in fighting cancer. A study done at the University of Shizuoka in Japan found that epigallocatechin gallate does in fact inhibit the secretion of collagenases by tumor cells (in this study, highly metastatic lung cancer cells), thus arresting their ability to invade normal tissue. Black tea theaflavins were also effective. There is also additional evidence that green tea polyphenols help inhibit angiogenesis, or the growth of new blood vessels that nourish the tumor.

Two of the green tea polyphenols, epigallocatechin-3-gallate and epicatechin-3-gallate, have been found to be effective inhibitors of 5 alpha-reductase type I, reducing the synthesis of DHT, a potent form of testosterone implicated in causing prostate enlargement and prostate cancer. Epigallocatechin gallate has also been found to be the most potent catechin in inducing apoptosis in human prostate cancer cells when tested on various cell lines. Together with lycopene and selenium, green tea should be considered as a special prostate-protective agent.

Breast Cancer

A recent Japanese study explored in greater detail the epidemiological findings on green tea’s protection against breast cancer. In this case, women with stage I, II and III breast cancer were assessed in terms of their green tea consumption. It was found that "premenopausal women who consumed more green tea had a lower number of lymph node metastases. In postmenopausal women greater consumption of green tea correlated with increased expression of the estrogen and progesterone receptor, which implies more differentiated tumor cells and better prognosis." Finally, in a seven-year follow it was found that "women with stage I or II cancer who consumed five or more cups of green tea a day had approximately half the recurrence rate of those women who consumed four cups or less."

One way in which green tea helps protect against breast cancer is by enhancing glucuronization of estrogens in the liver, a process through which estrogens are rendered inactive by being conjugated with glucuronic acid, a form in which they are excreted from the body. Perhaps it is mainly this mechanism that also accounts for lower estradiol levels found in those Japanese women who consume a significant amount of green tea. (Another mechanism might involve higher levels of sex hormone binding globulin found in women who consume green tea; the authors caution, however, that this might be due to caffeine.)

Besides human epidemiological studies, we also have experimental animal studies showing that green tea catechins provide significant protection against breast cancer. One study found that after exposure to a strong mammary carcinogen (DMBA), the survival rate in the group of rats fed a diet enriched with 1% green tea catechins was 93.8%, compared with only 33.3% in the control group. The tumors in the green tea group were also significantly smaller.

Epigallocatechin gallate alone was also found to inhibit tumor growth of human mammary cancer transplanted into mice. A study done at the College of Pharmacy at the University of Arizona likewise singled out epigallocatechin gallate as the most effective of the green tea catechins in its anticancer effects in regard to breast cancer, colon cancer and melanoma.

Green tea has also shown promise in other areas. For one, it enhances the effectiveness of chemotherapy in ovarian cancer. A study done at the University of Shizuoka, Japan, discovered that oral administration of green tea or theanine, an amino acid found in the leaves of green tea, synergized with the chemotherapy drug Adriamycin in lowering tumor weight. Adriamycin alone was ineffective. Theanine nearly tripled the concentration of adriamycin in the tumor tissue, while decreasing adriamycin levels in healthy tissue. In a more recent study, the same authors showed that theanine also synergizes with Adriamycin to inhibit liver metastases of ovarian cancer. This adds to the growing evidence that natural agents such as green tea can greatly enhance the effectiveness of...
Leukemia is yet another disease where green tea may prove effective as an adjuvant therapy for treatment. The particularly bioactive catechin in green tea, epigallocatechin gallate, was found to inhibit the proliferation of human and mouse leukemic cells in vitro. Even at the lower concentration, DNA synthesis by leukemic cells was reduced by more than 50%, while normal cells were unharmed. Another study, using the leukemic blast cells from patients with acute myeloblastic leukemia, a particularly aggressive and often deadly form of leukemia, found that epigallocatechin gallate inhibited the effect of tumor necrosis factor alpha and other growth factors. Yet another study found that green tea extract is a potent nucleoside transport inhibitor, interfering with tumor cells' repair of DNA after chemotherapy. Thus green tea extract "markedly potentiated" the effectiveness of chemotherapy. These findings suggest that epigallocatechin gallate and green tea extract could be used as a nontoxic adjuvant therapy for leukemia. It would also be interesting to examine how green tea polyphenols synergize with such established anti-leukemic alternative treatments as retinoic acid, Vitamin D3, DMSO, curcumin and esculetin.

Green tea may also have a positive effect on chromosome damage in bone marrow. Aflatoxin, a carcinogenic mold-produced toxin commonly found in peanut butter and grain products, is known to cause damage to chromosomes in rat bone marrow cells. One study discovered that giving rats aqueous green tea extract 24 hours before inoculation with aflatoxin gained considerable protection from this damage. Black tea and coffee were not effective, although caffeine helped prevent damage if given 2 hours before the inoculation. The authors concluded that green tea "potently suppressed" chromosome damage in the bone marrow.

A more recent study, done at the Fels Institute for Cancer Research at Temple University in Philadelphia, found that the addition of .5% of instant green tea powder to the diet of rats changed the metabolism of aflatoxin toward the formation of non-toxic hydroxylated metabolites, and decreased the binding of aflatoxin to liver-cell DNA, significantly decreasing the resulting number of precancerous cells. The authors conclude that green tea protects against aflatoxin-induced liver cancer.

Green tea also inhibited liver damage caused by exposure to 2-nitropropane. Even more important, green tea also protected against liver injury caused by galactosamine, which happens to be an animal model of viral hepatitis.

Another type of cancer where high consumption of green tea seems to make a difference is stomach cancer. Men who consumed 7 cups or more of green tea a day had a 31% lower risk of stomach cancer. A Japanese in vitro study found that both green tea extract and epigallocatechin gallate caused a concentration- and time-dependent growth inhibition and apoptosis (programmed cell death) in a line of human stomach cancer cells.

A recent animal study done at the Alabama A&M University discovered that phytic acid (found in beans and grains) and green tea synergize to significantly reduce the number of preneoplastic lesions. Again, this points to the general principle that two or more natural agents are more effective together.

Protection against radiation-induced DNA damage is yet another area where green tea has had positive effects. A recent National Cancer Institute study found that green tea catechins can protect cells against radiation damage. Using chromatid breaks as a marker for unrepaired DNA strand breaks, it was found that all catechins except, interestingly, epigallocatechin gallate, significantly reduced DNA radiation damage. Curcumin had a similar effect. The authors speculate that the protective mechanism is due to the ability of polyphenols to scavenge the particularly dangerous hydroxyl radical. They conclude that catechins and other plant polyphenols can protect human cells against radiation damage.

One interesting recent study compared the effects of epigallocatechin gallate, curcumin (a powerful anticarcinogenic compound from the curry spice turmeric), and the combination of both on an in-vitro model of oral cancer. It was found that epigallocatechin gallate helped arrest tumor cell growth in a different cell-cycle stage than curcumin. When the two compounds were combined, growth inhibition was enhanced, suggesting a synergistic effect.

Likewise, a study using human lung cancer cell culture found that a combination of catechins rather than epigallocatechin gallate alone was more effective at producing apoptosis (programmed cell death), and the effect was synergistically increased when catechins were combined with other anti-cancer agents such as tamoxifen (a protein kinase antagonist). This provides additional support for the multi-agent approach to cancer.

Smoking may cause damage to the DNA of various cells, including lymphocytes. One type of damage is sister-chromatid exchange (SCE). SCE rates were found to be elevated in smokers who did not consume green tea. Those smokers who did consume green tea had SCE rates comparable to those of nonsmokers, in spite of the fact that their average daily intake was only 3 cups per day. Coffee failed to show a protective effect.

An animal study, however, did show that caffeine is an important chemopreventive agent in lung cancer protection, and that black tea also has an effect.

Skin cancer, and the protective effects of catechins on the skin, have been studied extensively. Ultraviolet radiation is known to
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concentrations of epigallocatechin gallate, cancer cells exhibited telomere shortening and senescence. Thus, inhibition of
telomerase could be one of the main anticarcinogenic mechanisms of catechins.

The most recent study, done at Purdue University and presented at the 1998 meeting of the American Society for Cell Biology, discovered another major mechanism. The authors, the husband and wife team of Dorothy and James Morre, claim that the main
tumor-inhibitory mechanism of green tea may stem from its ability to interfere with the enzyme quinol oxidase, generally referred to
as NOX. This enzyme is required for growth by both normal and malignant cells. While normal cells express NOX only when dividing, tumor cells express it all the time. The tumor form of the enzyme is called t-NOX, or tumor-associated NOX. Drugs that inhibit tNOX also inhibit tumor growth.

While both black and green tea infusions inhibited tNOX in various cancer lines, green tea was able to achieve these results at much
greater dilutions, indicating higher concentrations of the active compound or compounds. By selectively testing for active
compounds, the authors of the study concluded that epigallocatechin gallate was the active agent responsible for inhibiting tNOX

While the inhibition of telomerase and of tNOX may be the chief anticarcinogenic mechanisms of green tea polyphenols, or at least
two very important ones, there is little doubt that green tea catechins act along several different pathways and interact with a variety
of enzymes to produce their anti-cancer effects.

It should also be noted that green tea lowers serum glucose and consequently insulin (this will be discussed in detail in the second
article on green tea). Since elevated insulin is a potent growth factor for many kinds of tumors, as well as a pro-inflammatory and
immunosuppressive hormone, the lowering of insulin in itself should help prevent cancer or, in cases of existing cancer, slow down
its growth.

While green tea, and possibly black tea as well, show great promise mainly as chemopreventive agents, there is now mounting
evidence that the active compounds in tea are an effective adjuvant therapy for the treatment of cancer, particularly when combined
with other natural anti-cancer agents such as curcumin, or with conventional drugs such as tamoxifen or chemotherapy. Finally, tea
and green tea extract can also be used for prevention of recurrence and metastasis.

Obviously, the anti-cancer mechanisms of green tea polyphenols are complex, and not yet completely understood. Research at the
level of molecular genetics is particularly promising. We already do know enough to state with certainty that green tea is an effective
chemopreventive agent. And we also know that it is best to use several anti-cancer agents (including all the major antioxidants) for synergistic prevention along all the possible pathways. Green tea works along so many pathways that it is simply an indispensable part of any serious cancer-prevention program.

Part II: Cardio-protective properties of green tea
Caution: It should be noted that catechins belong in the broader category of very bioactive compounds known as catechols, which themselves have the power to damage cells unless they are properly methylated. When megadoses of green tea extract are used, care should be taken to obtain comprehensive nutritional support to provide sufficient synergistic antioxidants and methylating agents.

Challa A et al. Interactive suppression of aberrant crypt foci induced by azoxymethane in rat colon by phytic acid and green tea. Carcinogenesis 1999; 20:2023-26


Chung FL et al. Inhibition of lung carcinogenesis by black tea in Fischer rats treated with a tobacco-specific carcinogen: Caffeine as an important constituent. Cancer Res 1998;58:4096-4101


Hara Y. Influence of tea catechins on the digestive tract. J Cel Biochem 1997; Suppl 27: 52-58


Hirose M et al. Inhibition of mammary gland carcinogenesis by green tea catechins and other naturally occurring antioxidants in female Sprague-Dawley rats pretreated with MDBA. Cancer Lett 1994; 83:149-56


Ito Y et al. Chromosome aberrations induced by aflatoxin B1 in rat bone marrow cells in vivo and their suppression by green tea. Mutat Res 1989; 222:253-61


Lean ME et al. Dietary flavonols protect diabetic human lymphocytes against oxidative damage to DNA. Diabetes 1999; 48:176-81


Morre D, Morre DJ. Findings on epigallocatechin gallate and tNOX inhibition presented at the 38th annual meeting of the American Society for Cell Biology; summary available at http//www.uns.purdue.edu


Pashka AG et al. Induction of apoptosis in prostate cancer cell lines by the green tea component, epigallocatechin gallate.

Reuters. Green tea blocks angiogenesis. Internet Health News, 3-31-1999

Sai I, Kai S et al. Protective effects of green tea on hepatotoxicity, oxidative DNA damage and cell proliferation in the rat liver, induced by repeated oral administration of 2-nitropropane. Food Chem Toxicol 1998; 6:1043


Sugiyama T, Sadzuka Y. Combination of theanine with doxorubicin inhibits hepatic metastasis of M5076 ovarian sarcoma. Clin Cancer Res 1999; 5:413-16


Valcic S et al. Inhibitory effect of six green tea catechins and caffeine on the growth of four selected human tumor cell lines. Anticancer Drugs 1996; 7:461-68


Yan YS. Effect of Chinese tea extract on the immune function of mice bearing tumors and their antitumor activity. Chung Hua Yu Fang 1992; 26:5-7


