



Green tea and health: An overview

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Abstract

Tea is the most widely consumed beverage in the world, except water. Recently, numerous researches have discovered the strong antioxidant potential mostly in green tea. This property is essentially due to catechins belonging to the polyphenolic flavonoids. These compounds are strong scavengers of free radicals and oxidants that could develop many ailments such as cancer, cardio-vascular disorders, inflammatory diseases, etc. Recent *in vitro*, animal and human studies have reported that green tea or its catechins may prevent cancer development, reduce cholesterol levels and hypertension, protect neurodegenerative diseases, improve dental health, etc. Although the antioxidant potential of green tea is evident, the results from epidemiological and clinical studies of the relationship between green tea and prevention of these diseases in humans are mixed. More controlled, well-designed clinical trials are needed to determine the effectiveness of green tea in human chemoprevention. The aim of this overview article is to revise the most recent medicinal studies of green tea, its chemical composition, its catechin pharmacokinetics and its side-effects.

Key words: Green tea, antioxidants, catechins, cardiovascular and neurodegenerative diseases, cancer, oral health, pharmacokinetics, side-effects.

Introduction

Tea plant (*Camellia sinensis*, Theaceae) is an evergreen shrub, cultivated at altitudes up to about 2000 m (7,000 feet), in approximately 30 countries, mainly in East and South Asia (China, India, Japan, Sri-Lanka, Burma, Vietnam, Cambodia, Indonesia), but also in Argentina, Kenya, etc.^{1,2}. Historically, it seems that tea was first used in China about five thousand years ago by the Chinese Emperor Shen Nung in 2737 B.C. Surprisingly, he discovered the delicious flavor of tea when wild tea leaves accidentally fell into his pot of boiling water^{3,4}. Nowadays, tea is the most widely consumed beverage in the world, after water. In the market, three main tea types: green, black and oolong, are all prepared from the leaves of the same *Camellia sinensis* plant. The difference among them is due to the processing method called fermentation. Green tea is unfermented tea, produced by steaming or pan-frying the fresh-cut tea leaves at moderated temperatures². The heating process inactivates the enzymes present in tea leaves, thereby avoiding the oxidation of tea polyphenolic antioxidants. Black tea is fermented tea, obtained by allowing the leaves to oxidize. During fermentation, enzymes in leaves oxidize many polyphenolic compounds, giving it the strongest flavor, darkest color, and lowest content of antioxidants. Oolong tea (Oolong - a Chinese word meaning "black dragon"), a semi-fermented tea, is developed in 19th century by partial auto-oxidation process, giving oolong its unique flavor, and also its partial loss of antioxidants¹⁻⁴. About 2.5 million tons of dried tea are manufactured each year, of which 78 percent are black tea, 20 percent green tea and 2 percent oolong tea⁴.

Beside the three main tea types, white tea, recently introduced

in the market, is the most precious Chinese tea. White tea is produced in the province of Fukien or Fujian (China) with very young leaves and buds of the same *Camellia sinensis* plant by an unfermented processing method. White tea contains more polyphenolic antioxidants than green tea. Scientific studies on white tea are still scarce, but some authors have reported that white tea is more potent for health protection than green tea^{5,6}.

Recently, numerous researches have discovered the strong antioxidant potential mostly in green tea. The antioxidant properties of green tea essentially reside in catechins belonging to the polyphenolic flavonoids. These compounds are strong scavengers of free radicals and oxidants that may develop many serious ailments such as cancer, cardio-vascular disorders, inflammatory diseases, etc. Recent studies in *in vitro*, in animals and in humans have shown that green tea or its catechins may prevent cancer development, reduce cholesterol levels and hypertension, decrease the risk of stroke and heart attack, protect neurodegenerative diseases, improve dental health, etc.

The aim of this overview article is to revise the most recent medicinal studies of green tea, its chemical composition, its catechin pharmacokinetics, its side-effects and also to present some our discussion about green tea and health.

Composition of Green Tea

Several chemical components of green tea have been identified and determined. The most abundant constituents of green tea are catechins belonging to the flavan-3-ol class of flavonoids. The major four catechins in green tea leaves are: (-)-epigallocatechin

gallate (EGCG), (-)-epigallocatechin (EGC), (-)-epicatechin gallate (ECG), and (-)-epicatechin (EC). They are all polyphenolic compounds^{1-4,6-9}. Dried green tea leaves generally contain 8-12% total polyphenols. These compounds account for 78% of the antioxidant potential of green tea. Among them, epigallocatechin gallate (EGCG) is considered the most active compound with 32% effect. It is about 25-100 times more potent as an antioxidant than vitamins C and E^{1-4,6-9}. During the black tea preparation by fermentation with polyphenol oxidase *in situ*, catechins partially change into oligomeric quinones, including theaflavine, theaflavine acid and thearubigene, or to the non-water-soluble flavonoids such as quercetin, kaempferol and myricetin which impart the characteristic taste and color properties of black tea^{1-4,6-9}. Therefore, the antioxidant properties of these transformed products become reduced or inactive. Thus, ECGC concentrations are 4-6 times greater in green tea than in black tea and 2-3 times greater than in oolong tea^{4,6-10}.

Caffeine, theobromine and theophylline, the principal alkaloids, account for about 4% of the dry weight, of which 3.5% caffeine. Green tea has about 1/10-1/6 as much caffeine as coffee, about 1/3 as black tea and about 1/2 as oolong tea. In addition, there are phenolic acids such as gallic acids and amino acids such as theanine (5-N-ethylglutamine), a characteristic amino acid of tea. A cup (200 mL) of green tea contains about 142 mg EGCG, 65 mg EGC, 28 mg ECG, 17 mg EC, and 76 mg caffeine⁶⁻⁹.

Green tea contains B-vitamins and ascorbic acid, which are destroyed by enzymatic oxidation during the black tea processing. The essential oil contains more than 300 components including aldehydes, phenylethyl alcohols, phenols, hexenal, hexenol, linalool, dihydroactinidiolide and p-vinylphenol^{4,6-9}. Many minerals are present in green tea, including fluoride, calcium, magnesium, chromium, zinc, copper, aluminum, selenium, etc.^{4,6-9}.

Medicinal Studies of Green Tea

In the last two decades, several hundred scientific publications have described the *in vitro* and *in vivo* medicinal effects of green tea. Most of them have reported its benefits on health, especially on the prevention of numerous pathologies such as cancer, cardiovascular disorders, neurodegenerative diseases, dental caries, obesity, etc. We develop herein some main studies of green tea cited in the most recent scientific literature.

Antioxidant activity: The human body constantly produces unstable molecules called oxidants such as free radicals, superoxides, singlet oxygen, peroxynitrite, etc. To become stable, oxidants steal electrons from other molecules and, in the process, damage cell proteins and genetic material. This damage may leave the cell vulnerable to cancer. Antioxidants are substances that help the human body to scavenge and eliminate oxidants. Like other antioxidants, the tea polyphenols (catechins) selectively inhibit specific enzyme activities that lead to cancer¹⁰. They may also target and repair DNA aberrations caused by oxidants. Many chronic and inflammatory pathologies such as arthritis, cancer, neurodegenerative diseases, hypercholesterolemia, etc. are a result of oxidative stress and subsequent generation of free radicals. Green tea polyphenols are potent free radical scavengers due to the hydroxyl groups and the aromatic rings present in their chemical structure. The hydroxyl groups on the aromatic rings (phenols) can form complexes with free radicals and neutralize

them, preventing the progression of the disease process. In addition, green tea polyphenols enhance the actions of many antioxidant enzymes such as glutathione reductase, glutathione-S-transferase and superoxide dismutase in the liver, thereby accelerating neutralization and elimination of toxic compounds, and are also capable of chelating metal ions, such as iron, that can generate radical oxygen species^{3,13}. Tea polyphenols may increase the antioxidant capacity of some tissues, decreasing their susceptibility to tumor formation. Numerous *in vitro*, animal and human studies using different cell lines, organ targets, animal models and clinical trials have demonstrated the strong antioxidant and radical scavenging properties of green tea and its constituents such as EGCG (epigallocatechin gallate)¹⁰⁻¹⁹. However, some authors have reported the lack of these activities in humans^{20,21}.

Cancer: During the 1980s cohort studies have observed that Asian populations who regularly consume green tea have lower rates of cancer. Since then, scientists have focused researches to find out why green tea can reduce or prevent cancer in humans by using different *in vitro* and *in vivo* experiments. There is considerable research evidence that green tea is associated with reduced risk of various forms of cancer^{9,22-24}.

Antimutagenic, anticarcinogenic and antiangiogenic effects: Numerous *in vitro* researches have demonstrated the green tea activity against various mutagens and carcinogens²⁵⁻²⁹. Green tea and its polyphenols have also been shown to inhibit angiogenesis in *in vitro* proliferation studies and *in vivo* angiogenesis assays^{22,30-33}. Angiogenesis is a crucial process that may account for part of the mechanism of the cancer-preventive effect of green tea²². Abnormal angiogenesis occurs in rheumatoid arthritis, diabetic retinopathy and cancer growth and metastasis²². The polyphenol components of green tea, especially EGCG (epigallocatechin gallate), have been shown *in vitro* to inhibit cellular proliferation and stimulate apoptosis of various cancer cell lines, including prostate, lymphoma, colon, lung, etc.

The mechanisms of antimutagenesis and anticarcinogenesis of green tea and its EGCG are antioxidation, induction of phase II enzymes, inhibition of TNF α expression and release, inhibition of cell proliferation, and induction of apoptosis. Cell cycle arrest and apoptosis induced by green tea are probably the two most significant factors^{34,35}. However, the site of action and the mechanisms of cancer-preventive activity by green tea and its polyphenols are not clearly understood. EGCG has been implicated in the inhibition of gene expression such as tumor necrosis factor, vascular endothelial growth factor and nitric oxide synthase, and the modulation of several cancer-related proteins including ornithine decarboxylase, matrix metalloproteinase, cyclooxygenase and urokinase^{34,35}. Many observations have raised the possibility that green tea catechins, in addition to their antioxidative properties, also affect the molecular mechanisms involved in angiogenesis, extracellular matrix degradation, regulation of cell death and multidrug resistance³³. According to Yang *et al.*³⁵, the relevant mechanisms of cancer prevention by tea polyphenols, except their redox properties, are related to their direct binding to target molecules, including the inhibition of selected protein kinases, matrix metalloproteinases and DNA methyltransferases.

Animal studies: Green tea and its constituents have been shown by different investigators to inhibit or prevent some forms of organ

tumorigenesis and angiogenesis in different animal model systems^{12,36}. This includes lung, colon, prostate, skin and liver cancers, etc.³⁷⁻⁴¹. In most of these experiments, reduction in tumor number and tumor size has been observed in the tea-treated group, and in some experiments, decreased tumor incidence has also been described. The green tea constituent, epigallocatechin-3-gallate (EGCG), and the black tea constituents, theaflavins, have also been shown to be effective. Most promising are the consistent findings that green tea or tea polyphenol administration prevented carcinogen-induced increases in the oxidized DNA base, 8-OHdG, in animal models of skin, lung, colon, liver and pancreatic cancer¹².

Clinical trials and cohort studies: *In vitro* and animal studies provide strong evidence that green tea polyphenols may possess the bioactivity to prevent or inhibit some forms of cancer. However, the results from epidemiological and clinical studies of the relationship between green tea and cancer prevention are mixed^{9,10,22-24,42}. Some cohort studies have supported a protective role of tea against the development of cancer. Studies conducted in Japan have revealed that a significant delay in cancer onset was associated with increased intake of green tea^{43,44}.

Prostate cancer: Jian *et al.* have recently found in a case-control study in China that the prostate cancer risk declined with increasing frequency, duration and quantity of green tea consumption^{9,45}. However, no association between tea intake and prostate cancer has been observed in a retrospective cohort study of the 1970–1972 Nutrition Canada Survey participants^{42,46}. It is noteworthy that this epidemiological study in Canada was most relevant to black tea.

Breast cancer: A clinical trial conducted in Japan and recently an epidemiological survey in Asian American women have found that increased consumption of green tea was closely associated with decreased recurrence of early stages of breast cancer and with significant delay in this cancer onset, respectively⁴⁷⁻⁴⁹. The results of a recent meta-analysis of epidemiological studies have indicated a lower risk for breast cancer with green tea consumption and have suggested a possible late-stage, promotional effect of black tea on breast carcinogenesis⁵⁰. Based on some published data about tea and hormones, Wu and Yu⁵¹ have suggested that the preventive effect of green tea against breast cancer may be related to decreased blood estrogen levels found in green tea drinkers, while increased levels of this hormone were found in black tea ones. Green tea may enhance glucuronidation of estrogens in the liver, a metabolism process through which estrogens are transformed into water-soluble conjugates to be rapidly excreted in the urine.

Stomach cancer: Several case-control studies recently conducted in Japan and China showed a protective effect of green tea on stomach cancer and gastritis, especially an inverse association between green tea consumption and distal gastric cancer among women^{42,52-55}. In contrast, a recent case-control study conducted in Japan found no protective effect of green tea consumption against this tumor⁵⁶.

Colorectal cancer: Studies on the effects of green tea on colon or rectal cancer have produced conflicting results. Some epidemiological investigations conducted in Japan and China have shown a protective effect on colorectal cancers, while other cohort studies have not found any benefits^{42,52,57,58}.

Other cancers: Other studies of green tea's ability to prevent

lung, pancreas, bladder or other cancer forms have yielded similarly mixed results^{22,24,36,42,49}. Further research is needed before green tea can be recommended for cancer prevention in humans.

Cardiovascular diseases: Hypertension: Recent studies of green tea polyphenols in hypertensive animals have demonstrated the evidence linking reduced blood pressure with tea intake^{9,42,59,60}. In humans, some recent epidemiological studies have shown that green tea consumption could reduce high blood pressure^{9,60-62}. However, other studies have not supported a hypotensive effect of tea^{42,63}.

Atherosclerosis: According to some cohort investigations, tea consumption may reduce the development and progression of atherosclerosis in adult and elderly people^{42,60,64,65}. As elevated plasma total homocysteine concentration is an independent risk factor for atherosclerosis and cardiovascular disease, a strong inverse relation between green tea consumption and homocysteine levels has also been reported by some cohort studies^{42,66}. In contrast, high consumption of coffee and black tea may increase plasma total homocysteine concentrations in humans⁶⁷.

LDL-cholesterol: Antioxidants present in food and beverage may delay atherogenesis by preventing the oxidation of low density lipoprotein cholesterol (LDL-cholesterol or still called "bad cholesterol") and thus reducing cardiovascular risk factor. The susceptibility of LDL to oxidation is inhibited *in vitro* by extracts of green and black tea^{42,68}. This activity of green tea has been also observed in some cohort studies^{42,69-71}. However, no effect of consumption of green and black tea on plasma lipid and antioxidant levels and on LDL oxidation in smokers has been observed in another investigation²⁰.

Coronary heart disease (CHD): Several cohort studies conducted in Europe, Japan and USA have reported a strong reduction of coronary heart disease mortality and stroke incidence in association with tea consumption^{42,43,60,70-74}. Tea type used from European and American cohorts is probably derived from consumption of black tea, while the use of green tea is certain from Japanese cohort^{42,73}. However, some other cohort studies have shown no inverse association between the tea intake and the risk of CHD^{42,70}.

These diverging experimental and epidemiological results emphasize the need for specially designed well-controlled studies of tea or tea flavonoids using early markers of CHD, such as endothelial dysfunction or atherosclerotic progression as an endpoint⁷⁵. Indeed, green tea and its polyphenols represent a promising tool in the prevention of a variety of cardiovascular disorders, and may be in the future an adjuvant therapy for these chronic diseases.

Neurodegenerative diseases: The neuroprotective activity of green tea and its polyphenols, especially EGCG (epigallocatechin-3-gallate), has been proven by several recent *in vitro* and *in vivo* studies using different cell lines and animal models⁷⁶⁻⁷⁸. Recent publications have suggested that green tea polyphenols possibly protect against Parkinson's and Alzheimer's diseases and other neurodegenerative symptoms^{9,79-85}. It has been reported in a recent study that high doses of EGCG significantly reduce the formation of β -amyloid proteins in the brains of mice that are altered to develop Alzheimer's disease⁷⁹. An abnormal buildup of β -amyloid plaque in the brain is implicated in the nerve damage and memory

loss seen in Alzheimer's disease. Tea flavonoids (catechins) have been reported to possess divalent metal chelating, antioxidant and anti-inflammatory activities, to penetrate the brain barrier and to protect neuronal death in a wide array of cellular and animal models of neurological diseases⁸⁰. Emerging evidence has shown that tea catechins may have many additional mechanisms of action by affecting numerous sites, potentiating endogenous antioxidants and eliciting dual actions during oxidative stress, ischemia and inflammation. Catechins have proven to modulate apoptosis at various points in the sequence, including altering expression of anti- and proapoptotic genes⁸¹. According to Mandel *et al.*^{80,82}, the neuroprotective mechanisms of green tea catechins consist in their brain-permeable, nontoxic, transitional metal (iron and copper)-chelatable/radical scavenger properties. Daily intake of green tea catechins efficiently protects the penumbra from irreversible damage due to cerebral ischemia and consequent neurologic deficits⁸⁴. A recent cohort study in elderly Japanese have shown that green tea helps slow the age-related decline in brain function seen as declining memory, cognitive impairment, dementia and Alzheimer's disease⁸⁵. However, more cohort and clinical studies need to be undertaken for the knowledge of green tea neuroprotection.

Arthritis: Recent animal studies have reported possible anti-inflammatory and arthritis-preventing effects of green tea thanks to its strong antioxidant activities. Some American researchers have found that green tea antioxidants postpone the beginning of and decrease in the severity of one type of arthritis in mice by reducing the expression of inflammatory mediators such as cyclooxygenase 2, interferon and tumor necrosis factor in the arthritic joints of the mice fed green tea polyphenols^{71,86}. These results are promising and could create future research that may lead to new arthritis treatments in humans.

Oral health: Green tea can prevent dental caries and some oral infections thanks to its catechins and fluoride content. Information from both human and animal studies have demonstrated how green tea works against bacteria that cause cavities in teeth^{9,42,87}. Green tea extracts inhibit bacteria such as *Escherichia coli*, *Streptococcus salivarius* and *Streptococcus mutans* that are responsible for dental caries^{9,42,71}. Several human studies have shown that bacteria present in dental plaque stopped growing when people rinsed their mouths with tea five times for 30 seconds over a 15 minute period^{42,71,88}. Another benefit of green tea consumption is observed with periodontal disease: green tea short circuits the damaging effects of the bacteria most responsible for gum disease, *Porphyromonas gingivalis*⁸⁹. Overall, green tea experiments have shown promising results for the oral health.

Other medicinal effects: Some animal and human studies have suggested that green tea and its catechins may help regulate glucose in the body and prevent the development of type 2 diabetes^{70,71,90}. Due to the growing obesity pandemic, green tea are being increasingly investigated in cell, animal and human studies for the search of its eventual anti-obesity effects. Studies conducted with human subjects have reported reduced body weight and body fat, as well as increased burn fat and thermogenesis⁹¹. Green tea consumption has also been associated with increased bone mineral density and could help prevent

osteoporosis^{9,42,71}. Green tea also appears to protect the liver from the damaging effects of toxic substances such as alcohol and also from the galactosamine-induced hepatitis in rats^{92,93}. More research in all these areas would be helpful.

Pharmacokinetics of Green Tea Catechins

Knowledge of the absorption and metabolism of green tea polyphenols is crucial to understand the fate of these compounds and their metabolites in the body in order to evaluate their biological activity in clinical trials. Some pharmacokinetic studies of different main tea catechins, green tea extracts (Polyphenon E) or tea infusion have been investigated in animals and humans^{49,94-102}. Absorbed catechins: epigallocatechin gallate (EGCG), epicatechin gallate (ECG), epigallocatechin (EGC) and epicatechin (EC), are extensively metabolized and converted to conjugated forms (glucuronides and sulphates) predominantly in the liver and some are methylated by catechol-O-methyl transferase⁷⁵. Van Amelsvoort *et al.*⁹⁸ have found that the catechin levels in plasma after ingestion were significantly different: EGC rose quickly with a short elimination half-life ($t_{1/2}$ elim. = 1.7 h), ECG was intermediate in rise but slowest in decline ($t_{1/2}$ elim. = 6.9 h), EGCG was slowest in rise but intermediate in decline ($t_{1/2}$ elim. = 3.9 h). Unlike EGC and EC, EGCG and ECG were mostly present as the free form in human plasma and in low quantities in human urine, whereas EGC and EC were mostly in the conjugated forms. It is noteworthy that only the free form of catechins, and not their conjugates, are biologically active. Over 90% of the total urinary EGC and EC, almost all in the conjugated forms, were excreted between 0 and 8 h^{96,97}. According to Cooper *et al.*⁴⁹, for EGCG to have therapeutic efficacy in selective killing of cancer cells, it has been suggested that the polyphenols must be present in the blood at a certain minimal level of about 100 nmol/L. The effect of the polyphenols is reversible. If the polyphenols are taken away even after up to 8 hours, cancer cells *in vitro* resume normal rates of growth. The polyphenols are eliminated rapidly from the blood or metabolized. Even in cell culture they may not survive in the medium for more than a few hours at nanomolar concentrations.

However, some slight divergence about pharmacokinetic profiles of tea catechins is found in the literature. This may be due to the forms of catechins utilized e.g. pure catechins, tea extracts or tea infusion and also to the administration mode, e.g. fasting condition or with meal. More research in pharmacokinetic studies is needed to understand the factors which affect the bioavailability and biotransformation of catechins, and to explore the biological activities of these compounds.

Side-effects

Green tea is generally considered safe and non-toxic. A recent animal study on acute and short-term toxicity of a high-concentration EGCG extract of green tea has reported that no adverse effect is observed for a level of 500 mg EGCG preparation/kg/day¹⁰³. The same authors have also concluded that this preparation is not genotoxic after testing high ECGC concentrations by different classical *in vitro* and *in vivo* assays¹⁰⁴. Another study in healthy individuals has related that an oral dose containing 800 mg ECGC is well-tolerated when taken under the fasting condition⁹⁶. It should be noted that the amount of catechins in 3 cups of green tea is between 240 and 320 mg².

However, due to the presence of caffeine and polyphenols, some side-effects have been reported with long-term or excessive use of green tea: insomnia, nervousness, anxiety, irritability, loss of appetite, gastric irritation, hyperacidity, vomiting, constipation or diarrhea, palpitation, vertigo, headache^{1,2,4}. Although rare, allergic reactions to green tea with symptoms such as difficulty of breathing, swelling of lips, tongue or face, may occur^{1,2}. Tea contains fluoride and aluminium in high levels. Classical teas provide 1.32 to 4.18 ppm of fluoride (1 part per million= 1mg/L)⁴. Fluorine is both benefic and toxic element for body. It is an essential mineral for bone and tooth health, but an excess can cause fluorosis, a disease characterized by mottled teeth and skeletal fragility. Fluorosis has been observed in some region of China such as Tibet with people after long-time drinking of brick tea. The fluorine concentration of brick tea is 200-300 times higher than ordinary green tea and black tea because brick tea (tea compressed into brick shape) is made from old stems and leaves of the tea tree, but ordinary green tea and black tea are made from tender leaves and buds¹⁰⁵. Aluminium levels in tea ranged from 46 to 58 µg/L referred to dry weight⁹. Black tea contains nearly six-fold more Al than green tea⁹. Aluminium is a toxic mineral for brain, bone and kidney. As tea is a good metal chelating agent, researchers have discovered that aluminium is accumulated in tea in a complex, rather than ionic, form, which is less absorbable, and thereby, no or less adverse effect on health^{4,106}. By the same explanation, drinking tea may contribute to iron deficiency, and in infants, tea has been associated with impaired iron metabolism and microcytic anemia^{1,2}.

Contra-indications

People with stomach ulcers, psychological disorders (particularly anxiety), tachycardia and kidney disorders should not take green tea. It is recommended that children, pregnant and breastfeeding women also avoid consumption of green tea^{1,2}. As green tea has antifolate activity, one of its anticancer mechanisms, some authors suggest that green tea consumption during pregnancy may have an increased risk of fetus malformation such as spina bifida because folic acid helps ensure normal fetus development¹⁰⁷. Moreover, green tea is not to be consumed by patients suffering from iron deficiency anemia, while it is recommended for patients with genetic hemochromatosis⁹.

Drug interactions

Due to the presence of polyphenols and caffeine in green tea, certain medicines could interact with green tea. The polyphenols (catechins) may decrease the absorption and thus the activity of the following drugs: atropine, codeine, ephedrine, warfarin and clozapine. The caffeine may interact with the following drugs heightening their effects to dangerous levels: ephedrine, pseudoephedrine, theophylline, and aminophylline. The caffeine may inhibit the hemodynamic effects of adenosine, or reduce the sedative effects of benzodiazepines (mitazolam, diazepam, etc.), or increase blood pressure in people taking β-blockers (propranolol, metropolol)^{2,108-111}.

However, some association of green tea with drugs may be useful (synergistic effect). Green tea may increase the effectiveness of certain antibiotics such as levofloxacin by reducing bacterial resistance to treatment¹¹². The combination of green tea and chemotherapy medications, specifically doxorubicin, adriamycin,

sulindac, tamoxifen, etc. have increased the effectiveness of these medications in laboratory tests, but these results have not yet been demonstrated in clinical studies¹¹³⁻¹¹⁶.

It is reminded that this list of drug interaction with tea is not exhaustive and still not valid in clinical therapies.

Dosage

About 3 cups (750 mL) of green tea infusion per day (providing 240-320 mg of polyphenols) is an average daily dose. However, in some studies, subjects drank up to 10 cups (2,500 mL) a day in order to obtain medicinal benefits from green tea beverage^{1,2}. To prepare a tea infusion, 1 teaspoon (3-3.5 g) of dried green tea leaves or 1 tea bag (2-2.2 g) is poured or plunged into about 250 mL of boiling water, then steeped for 3-5 min. Capsules and tablets containing standardized extracts of polyphenols with dosage from 100 to 500 mg are available in the market. A daily dose of 300-400 mg of polyphenols is typical for these products². Many of these standardized products are decaffeinated. Tea infusion must be taken as soon as possible (within a couple of hours) and becomes darker with time because of the oxidization of polyphenols with air and eventually with light.

Discussion

In vitro and animal studies have provided strong evidence that green tea polyphenols possess the antioxidant, antimutagenic, anticarcinogenic and antiangiogenic properties to prevent or inhibit some forms of cancer. These laboratory studies have also demonstrated their chemopreventive activities against certain cardiovascular disorders, neurodegenerative symptoms, arthritis, obesity, dental caries, etc. However, the results from epidemiological and clinical studies of the relationship between green tea and prevention of these diseases are mixed. Why are there these controversies between experimental studies and investigations in humans? We observe that the results of these cohort studies are more positive in Japan and China than in Western countries. Indeed, these types of studies are complex and it is difficult to find out the exact causes of these divergences. Lifestyle condition may be one of these causes. Dietary type differences between these people may explain the conflicting results of these cohort studies. It is well-known that there are good food and bad food. The association of green tea with good food may prevent these chronic diseases, while with bad food, no tea chemoprevention could be found. The list of good food and bad food is long and varied. Briefly, good food could be defined here as food rich in antioxidants, vitamins etc. and poor in carcinogens and mutagens that are often produced by cooking, contrary to bad food. In addition, Western people prefer black tea, while Asian people like green tea. It is reminded that polyphenol concentrations are five times greater in green tea than black tea. Even in green tea, the antioxidant levels may considerably vary between manufacturers and between batches because of variation of fabrication process, soil, weather, storage, etc. Polyphenols are unstable molecules, they are easily oxidized by air and by light, and consequently can lose all their health benefits. Tea preparation may also influence polyphenol content and availability. For example, antioxidants are not found in "iced tea", except caffeine, because of its preparation and storage. For clinical trials, the control of polyphenol levels in tea before assay must be imperative. Pharmacokinetic studies are also helpful to understand

the factors which affect the bioavailability and metabolism of catechins and consequently, their biological activities. More well-designed and controlled clinical trials are needed to assess the effectiveness of green tea in human chemoprevention. In addition, dietary recommendations must be developed so that people would accept to change their lifestyle.

Conclusions

While the results of experimental studies on green tea and its polyphenols have been promising for the prevention of many serious chronic diseases, those of epidemiological and clinical studies are still not convincing because of lifestyle differences and of lack of standardized methods. However, the antioxidant potential of green tea is certain. The consumption of green tea with other good food can help the body to neutralize free radicals and other toxic products and in consequence, to maintain a good health. Briefly, the health benefits of green tea may be primarily preventive, still not therapeutic. It would be reminded that your health is not only in your plate, but also in your cup, and vice versa.

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