Beneficial Effects of Green Tea—A Review

Article *in* Journal of the American College of Nutrition · May 2006

DOI: 10.1080/07315724.2006.10719518 · Source: PubMed

3 authors, including:

Carmen Cabrera
University of Murcia
46 PUBLICATIONS **3,966** CITATIONS

SEE PROFILE

Reyes Artacho
University of Granada
105 PUBLICATIONS **3,721** CITATIONS

SEE PROFILE

Review

Beneficial Effects of Green Tea—A Review

Carmen Cabrera, PhD, Reyes Artacho, PhD, Rafael Giménez, PhD

Departamento de Nutrición y Bromatología, Facultad de Farmacia, Universidad de Granada, Granada, SPAIN

Key words: green tea, polyphenols, catechins, antioxidant activity, human health

Tea is the most consumed drink in the world after water. Green tea is a 'non-fermented' tea, and contains more catechins, than black tea or oolong tea. Catechins are *in vitro* and *in vivo* strong antioxidants. In addition, its content of certain minerals and vitamins increases the antioxidant potential of this type of tea. Since ancient times, green tea has been considered by the traditional Chinese medicine as a healthful beverage. Recent human studies suggest that green tea may contribute to a reduction in the risk of cardiovascular disease and some forms of cancer, as well as to the promotion of oral health and other physiological functions such as anti-hypertensive effect, body weight control, antibacterial and antivirasic activity, solar ultraviolet protection, bone mineral density increase, anti-fibrotic properties, and neuroprotective power. Increasing interest in its health benefits has led to the inclusion of green tea in the group of beverages with functional properties. However, although all the evidence from research on green tea is very promising, future studies are necessary to fully understand its contributions to human health, and advise its regular consumption in Western diets, in which green tea consumption is nowadays limited and sporadic.

Key teaching points:

- Green tea contains numerous components with antioxidant activity: polyphenols (especially catechins), minerals, vitamins.
- Green tea contains more catechins than black or oolong teas.
- The strong antioxidant potential of catechins, and especially EGCG, are widely demonstrated *in vitro* and in animal studies. In addition, catechins possess antimutagenic, antidiabetic, anti-inflammatory, antibacterial and antiviral properties.
- Recent human studies suggest that green tea may contribute to reduce the risk of cardiovascular disease and cancer, and has another beneficial effect on health.
- Although research of green tea is very promising, future studies considering dietetic, environmental and life style factors, are necessary to fully understand its contribution to human health.

INTRODUCTION

Tea, a product made up from leaf and bud of the plant *Camellia sinensis*, is the second most consumed beverage in the world, well ahead of coffee, beer, wine and carbonated soft drinks [1–2]. Originating from China, tea has gained the world's taste in the past 2000 years. The economic and social interest of tea is clear and its consumption is part of many people daily routine, as an everyday drink and as a therapeutic aid in many illnesses.

Depending on the manufacturing process, teas are classified into three major types: 'non-fermented' green tea (produced by drying and steaming the fresh leaves to inactivate the polyphenol oxidase and thus, non oxidation occurs); 'semi-fermented' oolong tea (produced when the fresh leaves are subjected to a partial fermentation stage before drying); and 'fermented' black and red (*Pu-Erh*) teas which undergo a post-harvest fermentation stage before drying and steaming, although the fermentation of black tea is due to an oxidation catalyzed by polyphenol oxidase, and that of *Pu-Erh* tea is attained by using

Address reprint requests to: Carmen Cabrera, PhD, Dpto. Nutrición y Bromatología, Facultad de Farmacia, Campus Universitario de Cartuja, 18012-Granada, SPAIN. E-mail: carmenc@ugr.es.

Abbreviations: CI = confidence interval, DNA = deoxyribonucleic acid, DPPH = 2,2-diphenyl-l-picrylhydrazyl assay, DMPD = N,N-dimethyl-p-phenylendiamine assay, EC = (−)-epicatechin, ECG = (−)-epicatechin-3-gallate, EGC = (−)-epigallocatechin, EGCG = (−)-epigallocatechin-3-gallate, FRAP = ferric reducing ability of plasma assay, GA = gallic acid, GTP = green tea polyphenols, HDL = high density lipoproteins, HR = hazard ratio, LDL = low density lipoproteins, OR = odd ratio, ORAC = oxygen radical absorbance capacity assay, PCL = photochemiluminescence assay, RR = relative risk, TEAC = Trolox equivalent antioxidant capacity assay, TRAP = total radical-trapping antioxidant parameter assay, UV = ultraviolet.

Journal of the American College of Nutrition, Vol. 25, No. 2, 79–99 (2006)
Published by the American College of Nutrition

microorganisms [3–4]. McKay and Blumberg [4] reported a per capita mean consumption of tea in the world of 120 mL/day. Approximately 76–78% of the tea produced and consumed is black tea, 20–22% is green tea and less than 2% is oolong tea [5]. Black tea is consumed principally in Europe, North America and North Africa (except Morocco) while green tea is widely drunk in China, Japan, Korea and Morocco; oolong tea is popular in China and Taiwan [5–6]. In USA, the 80% of tea consumed is black ice tea [7].

Although health benefits have been attributed to green tea consumption since the beginning of its history, scientific investigations on this beverage and its constituents have been underway for less than three decades [4]. *In vitro* and animal studies, and clinical trials employing putative intermediary indicators of disease, particularly biomarkers of oxidative stress status, provide strong evidence that green tea polyphenols (GTP) may play a role in the risk and pathogenesis of several chronic diseases, especially cardiovascular disease and cancer, and related pathologies. In addition, several studies suggest a beneficial impact of green tea intake on bone density, cognitive function, dental caries and kidney stones, among other effects [4–5]. Over the last years, numerous epidemiological and clinical studies have revealed several physiological responses to green tea which may be relevant to the promotion of health and the prevention or treatment of some chronic diseases. However, the results from epidemiological and clinical studies of the relationship between green tea consumption and human health are mixed. For example, conflicting results between human studies may arise in part, from ignoring socioeconomic and lifestyle factors as well as by inadequate methodology to define tea preparation and intake [2,4–7].

Foodstuff can be regarded as functional if it is satisfactorily demonstrated to affect beneficially one or more target functions in the body, beyond adequate nutritional effects in a way which is relevant to either the state of well-being and health or the reduction of the risk of a disease [5,8–9], so green tea has been proved to have functional properties and at present, its consumption is widely recommended.

The aim of this article is to revise the most recent studies on green tea beneficial effects and to evaluate its potential interest in Western diets.

Green Tea Processing

Green tea is mainly produced from *Camellia sinensis* var. *sinensis*. The *Assan* type (*Camellia sinensis* var. *assamica*) has a too high content of polyphenols, which would make green tea taste excessively bitter [3]. The production of green tea is characterized by an initial heating process, which kills the enzyme polyphenol oxidase, which is responsible for the conversion of the flavanols in the leaf into the dark polyphenolic compounds that colour black tea. The other important process is rolling, in which leaves are cut and twisted. The final form of green tea depends on the particular variant being produced. The rolling stage is very similar to the operation with the same name in black tea production. Green tea production is restricted mainly to China and Japan [3,6]. Fig. 1 shows the principal differences between green and black tea processing.

Green Tea Composition

Green tea chemical composition is complex: proteins (15–20% dry weight) whose enzymes constitute an important fraction; aminoacids (1–4% dry weight) such as teanine or 5-*N*-ethylglutamine, glutamic acid, tryptophan, glycine, serine, aspartic acid, tyrosine, valine, leucine, threonine, arginine, lysine; carbohydrates (5–7% dry weight) such as cellulose, pectins, glucose, fructose, sucrose; lipids as linoleic and α-linolenic acids; sterols as stigmasterol; vitamins (B, C, E); xanthic bases such as caffeine and theophylline (Fig. 2); pigments as chlorophyll and carotenoids; volatile compounds as aldehydes, alcohols, esters, lactones, hydrocarbons, etc.; minerals and trace elements (5% dry weight) such as Ca, Mg, Cr, Mn, Fe, Cu, Zn, Mo, Se, Na, P, Co, Sr, Ni, K, F and Al. Due to the great importance of the mineral presence in tea, many studies have been carried out to determine their levels in green tea leaves and their infusions. For example, Costa *et al.* [1] observed large variations of the mineral content (Al, Ca, Mg and Mn) in green tea from different origins. Fernández-Cáceres *et al.* [10] determined the content of Al, Ba, Ca, Cu, Fe, K, Mg, Mn, Na, Sr, Ti, and Zn in 46 tea samples, and no clear differences were found between mineral content of green and black teas. Shu *et al.* [11] observed the great variations among different tea varieties in accumulating fluoride and aluminum. Fung *et al.* [12] indicated that black tea had higher Al and F concentrations than green tea. Xu *et al.* [13] reported that the content of Se in green teas was greatly increased by foliar application of Se-enriched fertilizers; moreover, the selenium-enriched green tea exhibited significantly higher antioxidant activity than regular green tea. Table 1 summarizes the mean chemical composition of green tea leaves in comparison with black tea leaves and its infusion.

Polyphenols constitute the most interesting group of green tea leaf components, and in consequence, green tea can be considered an important dietary source of polyphenols, particularly flavonoids. Flavonoids are phenol derivatives synthesized in substantial amounts (0.5–1.5%) and variety (more than 4000 identified), and widely distributed among plants [14]. The United States Department of Agriculture (USDA) has recently published a Database for the Flavonoid Content of Selected Foods [15]. The main flavonoids present in green tea include catechins (flavan-3-ols). The four major catechins are (−)-epigallocatechin-3-gallate (EGCG), that represents approximately 59% of the total of catechins; (−)-epigallocatechin (EGC) (19% approximately); (−)-epicatechin-3-gallate (ECG) (13.6% approximately); and (−)-epicatechin (EC) (6.4% approximately) [4]. Green tea also contains gallic acid (GA) and other phenolic acids such as chlorogenic acid and caffeic acid, and flavonols such as kaempferol, myricetin and quercetin [15].

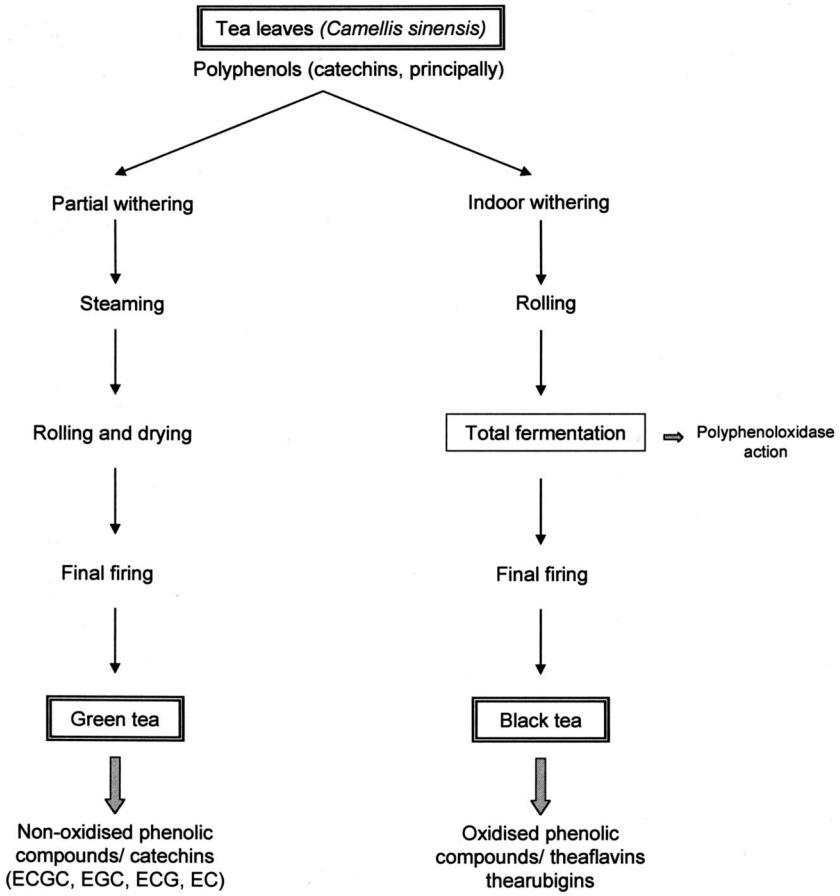

Fig. 1. Principal differences between green and black tea processing and its influence on the final polyphenols content.

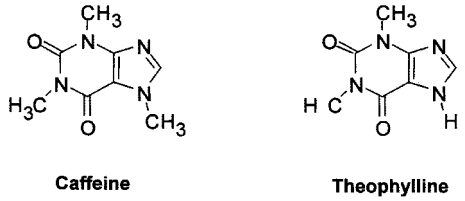

Fig. 2. Chemical structure of caffeine and theophylline.

Fig. 3 shows the chemical structure of GA and the four major catechins present in green tea. In black tea the polymerized catechins such as theaflavins and thearubigins predominate. Black and green teas both contain similar amount of flavonoids, however they differ in their chemical structure; green tea contains more catechins (simple flavonoids), while the oxidation undergone by the leaves in order to make black tea, converts these simple flavonoids into theaflavins and thearubigins [15].

The relative catechin content of green tea depends on how the leaves are processed before drying (a certain grade of fermentation and heating of tea leaves during the manufacturing process can result in polymerization of monopolyphenolic compounds such as the catechins, leading to conformational changes and thus modifying its properties. Other factors influencing catechin content are the geographical location and growing conditions (soil, climate, agricultural practices, fertilizers), the type of green tea (e.g., blended, decaffeinated, instant, . . .), and the preparation of the infusion (e.g., amount of the product used, brew time, temperature) [5,16]. McKay and Blumberg [5] reported that decaffeinating reduces slightly the

Table 1. Mean Composition (%) of Green Tea and Black Tea (and Its Infusion). From Belitz and Grosh [167]

Compound	Green tea*	Black tea*	Infusion†
Proteins	15	15	trace
Aminoacids	4	4	3.5
Fibre	26	26	0
Others carbohydrates	7	7	4
Lipids	7	7	trace
Pigments	2	2	trace
Minerals	5	5	4.5
Phenolic compounds‡	30	5	4.5
Oxidised phenolic compounds§	0	25	4.5

* Data refereed to dry weight of tea leaves.

† Black tea; infusion time: 3 min.

‡ Especially flavonoids.

§ Especially thearubigins and theaflavins.

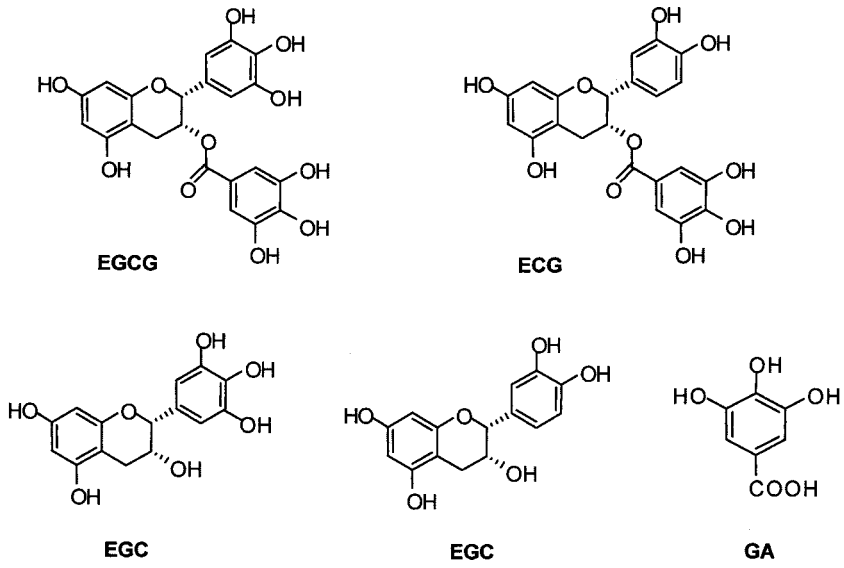

Fig. 3. Chemical structure of gallic acid and the four major catechins in green tea. GA, gallic acid; EGCG, (−)-epigallocatechin-3-gallate; EGC, (−)-epigallocatechin; ECG, (−)-epicatechin-3-gallate; EC, (−)-epicatechin.

tea catechin content; also, instant preparations and iced and ready-to drink teas present less content of catequins [16–17]. The production of bottled green tea beverage has encountered a browning problem mainly caused by the oxidation of catechins [18].

Wu and Wei [5] indicated that a cup of green tea (2.5 g of green tea leaves/200 mL of water) may contain 90 mg of EGCG. Lin *et al.* [19] analyzed 31 commercial teas, and detected that the levels of EGCG and total catechins were in the following order: green tea (old leaves) > green tea (young leaves) and oolong tea > black tea and *Pu-Erh* tea. Fernández *et al.* [20] determined the contents of GA, EGCG, EGC, EC and ECG, in a set of 45 tea samples, including black and green teas from different geographical origins (i.e. China, Japan, Kenya, Sri Lanka, and India); the GA levels were always higher in black tea because the amount of GA increases during the fermentation process due to its liberation from catechin gallates [21]. The amount of catechins were always higher in green tea; EGCG and EGC were the major catechins present with average contents of 7.358% and 3.955%, respectively; ECG presented values ranging between 0.910 and 3.556%. For black tea, EGCG and ECG were the catechins present in higher percentages, with average contents of 1.583 and 0.706%, respectively. Cabrera *et al.* [22] reported the mean content of the four major catechins (EGCG, EGC, ECG and EC) and gallic acid in 45 samples of different types of tea including black, red, oolong and green teas; the higher levels of EGCG appeared in green tea samples. Results are summarized in Fig. 4. However, Henning *et al.* [23] suggested that the large variation of the catechin content in tea is not taken into consideration in most of the epidemiological studies.

Bioavailability of Green Tea Catechins

The potential health effects of catechins depend not only on the amount consumed but on their bioavailability which appears to be very variable. In order to know the catechin bioavailability and metabolism, it is necessary to evaluate their biological activity within target tissues [24]. Following oral administration of tea catechins to rats, the four principal catechins (EC, ECG, EGC, and EGCG) have been identified in the portal vein, indicating that tea catechins are absorbed intestinally [25]. In rats given 0.6% GTP in their drinking water over a period of 28 days, plasma concentrations of EGCG were much lower than those of EGC or EC, even though the ratio of EGCG to EGC was 5:1 in the GTP solution. When the same GTP preparation was given to mice, plasma levels of EGCG were much higher than those of EGC and EC. So, there appear to be species differences in the bioavailability of EGCG compared to the other catechins [26]. In humans, EGCG may be less bioavailable than other green tea catechins. Catechin levels in human plasma reach their peak 2 to 4 h after ingestion [27]. A recent study in humans compared the pharmacokinetics of equimolar doses of pure EGC, ECG, and EGCG in 10 healthy volunteers; average peak plasma concentrations after a single dose of 1.5 mmol were 5.0 μmol/L for EGC, 3.1 μmol/L for ECG, and 1.3 μmol/L for EGCG. After 24 h, plasma EGC and EGCG returned to baseline, but plasma ECG remained elevated [28]. In humans, ECG has been found to be more highly methylated than EGC and EGCG, and EGCG has been found to be less conjugated than EGC and EC [29]. Unfortunately, little published data are available on tissue distribution of catechins in humans after green tea consumption; however, there are some interesting data from studies with animals. Kim *et al.* [26]

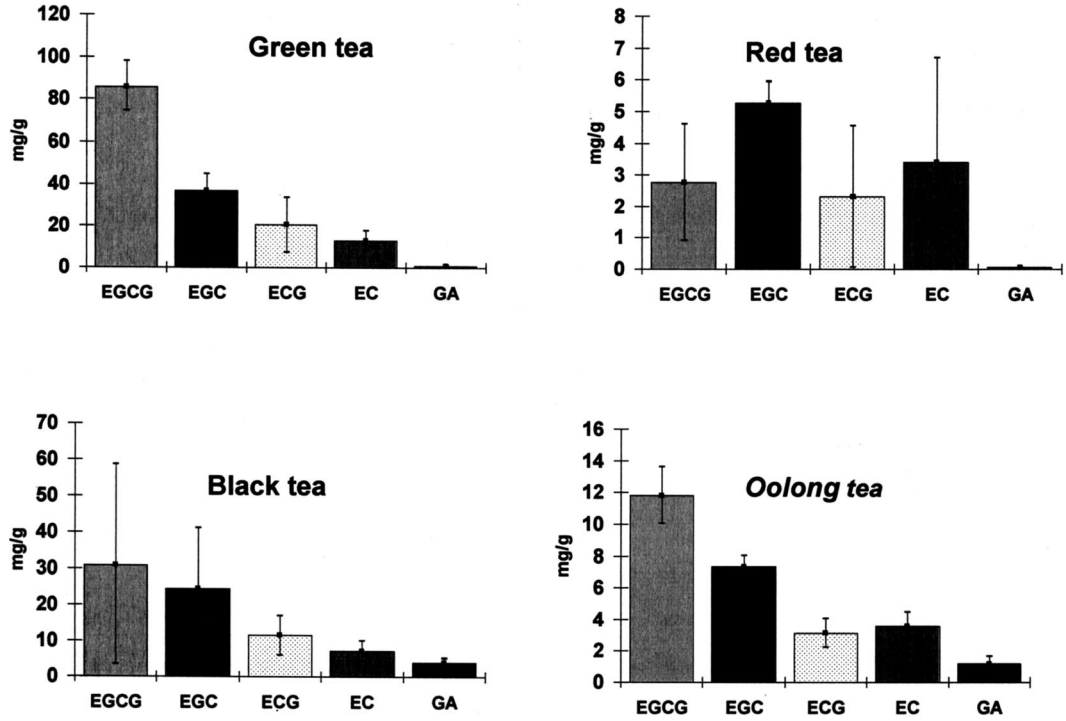

Fig. 4. Mean content of gallic acid and catechins in different types of tea (n = 45). Data refereed to dry weight of commercial samples (Source: Cabrera *et al.* [22]).

observed that when rats were given 0.6% GTP in their drinking water over a period of 28 days, substantial amounts of EGC and EC were found in the esophagus, large intestine, kidney, bladder, lung, and prostate; EGC and EC concentrations were relatively low in liver, spleen, heart, and thyroid; EGCG levels were higher in the esophagus and large intestine, but lower in other organs, likely due to poor systemic absorption of EGCG. Catechins are rapidly and extensively metabolized; studies in rats indicated that EGCG is mainly excreted through the bile, while EGC and EC are excreted through urine and bile. Determination of the actual bioavailability of metabolites in tissues may be much more important than knowledge of their plasma concentration, but data are still very scarce even in animals. Consequently, the metabolism and bioavailability of individual tea catechins and the pharmacokinetics of their metabolites require further clarification.

Lu *et al.* [30] reported that GTP have biological activities including modulation of key signal transduction pathways; however, the possible significance of these activities in inhibition of carcinogenesis *in vivo* depends on the polyphenol bioavailability. These authors observed that after oral administration of green tea to rats, about 14% of EGC, 31% of EC, and $<1\%$ of EGCG appeared in the blood; in mice, the bioavailability of EGCG was higher, but the biological activities of the catechin metabolites still need to be investigated. Inter-individual variations in the bioavailability of GTP can be substantial and may be due, in part, to differences in colonic microflora and genetic polymorphisms among the enzymes involved in polyphenol metabolism [31]. The effect of green tea drinking may also differ by genotype [32]. To sum up, there appear to be species differences in the bioavailability of EGCG compared to other tea catechins. Further research results are largely consistent in demonstrating that the addition of milk to tea does not interfere with catechin absorption [33–35], but milk may affect the antioxidant potential of tea, depending upon milk fat content, milk volume added, and the method used to assess this parameter [33–36]. Xu *et al.* [37] observed that the epimerisation reaction occurring in manufacturing canned and bottled tea drinks would not significantly affect antioxidant activity and bioavailability of total tea polyphenols.

Green Tea and Human Health

Green tea has been considered a medicine and a healthful beverage since ancient times. The traditional Chinese medicine has recommended this plant for headaches, body aches and pains, digestion, depression, detoxification, as an energizer and, in general, to prolong life. Green tea leaves contain three main components which act upon human health: xanthic bases (caffeine and theophylline), essential oils and especially, polyphenolic compounds. Caffeine acts mainly upon the central nervous system, stimulating wakefulness, facilitating ideas association and decreasing the sensation of fatigue [38]. Some of the effects caused by caffeine are influenced by theophylline tea content. Theophylline induces psychoactive activity, it also has a slightly inotrope and vasodilator effect, and a much

higher diuretic effect than caffeine. However, its most interesting effects can be seen at the bronchopulmonar and respiratory level. Theophylline causes a non-specific relaxation on the bronchial smooth muscle, and respiratory stimulation is also observed. Essential oils are in a great extent volatile and they evaporate from the beverage after some time, thus it is not very convenient to overextend the brewing time. Among their properties, the one of facilitating digestion must be highlighted [5,39]. Green tea is the type of tea with the higher percentage of essential oils [38–39]. However, green tea has received a great deal of attention especially due to its content of polyphenols, which are strong antioxidants and present important biological properties. Numerous studies have also demonstrated that the aqueous extract of GTP possesses antimutagenic, antidiabetic, antibacterial, anti-inflammatory, and hypocholesterolemic properties [21,40–44]. Beneficial effects in oral diseases such as protection against dental caries, periodontal disease, and tooth loss (which may significantly affect a person's overall health) have been also described [5]. Among all GTP, catechins and gallic acid have been especially considered to be the main players in the beneficial effects on human health next detailed.

Antioxidant Activity. Green tea is considered a dietary source of antioxidant nutrients: green tea is rich in polyphenols (catechins and gallic acid, particularly), but it also contains carotenoids, tocopherols, ascorbic acid (vitamin C), minerals such as Cr, Mn, Se or Zn, and certain phytochemical compounds. These compounds could increase the GTP antioxidant potential. GTP present antioxidant activity *in vitro* by scavenging reactive oxygen and nitrogen species and chelating redox-active transition metal ions; GTP can chelate metal ions like iron and copper to prevent their participation in Fenton and Haber-Weiss reactions [4,45–46]. They may also function indirectly as antioxidants through 1) inhibition of the redox-sensitive transcription factors; 2) inhibition of 'pro-oxidant' enzymes, such as inducible nitric oxide synthase, lipoxygenases, cyclooxygenases and xanthine oxidase; and 3) induction of antioxidant enzymes, such as glutathione-S-transferases and superoxide dismutases.

The antioxidant capacity of GTP has been assessed by several methods. For example, Cao *et al.* [47] using the oxygen radical absorbance capacity (ORAC) assay found that green tea has a much higher antioxidant activity against peroxyl radicals than vegetables such as garlic, kale, spinach and Brussels sprouts. Using the ferric reducing ability of plasma (FRAP) assay. Langley-Evans [48] found that the total antioxidant capacity of green tea is more potent than that of black tea. Saffari and Sadrzadeh [49] investigated the antioxidant capacity of EGCG using erythrocyte membrane-bound. ATPases as a model, and the results indicated that EGCG is a powerful antioxidant that is capable of protecting erythrocyte membrane-bound ATPases against oxidative stress. Several studies have shown that EGCG can act *in vitro* as an antioxidant by trapping proxyl radicals and inhibiting lipid peroxidation [49–50]. However, the antioxidant capacity of catechins determined *in vitro* is dependent upon the type of assay employed and it does not reflect factors such as bioavailability and metabolism. The fact that catechins are rapidly and extensively metabolized emphasizes the importance of demonstrating their antioxidant activity *in vivo* to better represent the physiological impact of green tea consumption. Frei and Higdon [51] reported that in order to determine whether or not GTP act as effective antioxidants *in vivo*, future studies in animals and humans should employ sensitive and specific biomarkers of oxidative damage of lipids, proteins and DNA.

Nevertheless, a substantial number of human intervention studies with green tea demonstrate a significant increase in plasma antioxidant capacity in humans after consumption of moderate amounts (1–6 cups/day); there are also initial indications which show that the enhanced blood antioxidant potential leads to a reduced oxidative damage in macromolecules such as DNA and lipids [2,4,23,28,37]. However, these authors indicated that the measurement of oxidative damage through biomarkers needs to be further established. McKay and Blumberg [4] reported that the repeated consumption of green tea and encapsulated green tea extracts for one to four weeks has been demonstrated to decrease biomarkers of oxidative status. Furthermore, Klaunig *et al.* [52] observed in a study with 40 male smokers in China and 27 men and women (smokers and non-smokers) in the United States, that oxidative DNA damage, lipid peroxidation, and free radical generation were reduced after consuming ~6 cups/day of green tea for seven days. Therefore, GTP may contribute to defenses against oxidative damages [5]. Erba *et al.* [53] suggest the ability of green tea, consumed within a balanced controlled diet, to improve overall the antioxidative status and to protect against oxidative damage in humans.

Antimutagenic and Anticarcinogenic Potential. Lifestyle-related diseases, including cancer, are also characterized as aging-related diseases, where aging may be the most potent causal factor. Therefore, prevention of lifestyle-related diseases will depend on slowing the aging process and avoiding the clinical appearance the disease. Dietary components that are capable of retarding cellular aging and inhibiting the growth of cancer cells without affecting the growth of normal cells are receiving considerable attention for the development of novel cancer-preventive approaches [54–56]. The role of green tea in protection against cancer has been supported by ample evidence from studies in cell culture and animal models [54]. Animal studies have shown that green tea inhibit carcinogenesis of the skin, lung, oral cavity, esophagus, stomach, liver, kidney, prostate and other organs [55,57–60]. In some studies, the inhibition correlated with an increase in tumor cell apoptosis and a decrease in cell proliferation [56]. Today, green tea is accepted as a cancer preventive on the basis of numerous *in vitro*, *in vivo* and epidemiological studies. The Chemoprevention Branch of the National Cancer Institute has initiated a plan

for developing tea compounds as cancer-chemopreventive agents in human trials [61]. The chemopreventive effects of green tea depend on: (1) its antioxidant action; (2) the specific induction of detoxifying enzymes; (3) its molecular regulatory functions on cellular growth, development and apoptosis; and (4) a selective improvement in the function of the intestinal bacteria flora. D'Alessandro *et al.* [62] also indicated that an important aspect of cancer risk is related to inflammatory response; currently, anti-inflammatory agents are used in chemopreventive strategies. The inflammatory response involves the production of cytokines and proinflammatory oxidants such as hypochlorous acid and peroxynitrite produced by neutrophils and macrophages, respectively. These oxidants react with phenolic tyrosine residues on proteins to form chloro- and nitrotyrosine. Green tea catechins and soy isoflavones have also been shown to be chemopreventive; the aromatic nature of polyphenols makes them potential targets of hypochlorous acid and peroxynitrite, and these reactions may create novel pharmacophores at the site of inflammation. In addition, a major mechanism of the anticarcinogenic activity of green tea in animals is the impairment of the interaction of carcinogens with DNA leading to mutations. Nevertheless, the antimutagenic activity of green tea as well as its underlying mechanisms must be reviewed, and the role of GTP, the postulated bioactive components, and caffeine must be critically evaluated. EGCG from green tea especially imparts a growth inhibitory effect on cancer cells [56,63–64]. EGCG possesses promising anticancer potential due to its antioxidant, antimutagenic and chemopreventive properties [65–66].

Rosengren [67] indicated that the green tea catechins reduce the proliferation of breast cancer cells *in vitro* and decrease breast tumor growth in rodents. Furthermore, *in vitro* studies have demonstrated that the combination of EGCG and tamoxifen is synergistically cytotoxic to breast cancer cells; these results suggest that the catechins have significant potential in the treatment of breast cancer. Mittal *et al.* [56] reported that the treatment with EGCG decreased cell viability at different stages studied (approx. 80% inhibition) in human breast carcinoma MCF-7 cells, but had no adverse effect on the growth of normal mammary cells. These authors found that this treatment inhibited telomerase activity (40–55%); telomerase is elevated in >90% of breast carcinomas and therefore has received much attention as a target for breast cancer therapy and cancer diagnostic research. According to Wu *et al.* [68], green tea drinkers showed a significantly reduced risk of breast cancer; compared to women who did not drink green tea regularly (i.e., less than once a month). Furthermore, there was a significant trend of decreasing risk with increasing amount of green tea intake. Two studies in Japanese women diagnosed with breast cancer indicate that green tea consumption is inversely associated with the rate of recurrence, especially in the early stages of breast cancer [69–70]. Zhou *et al.* [71] also reported that breast cancer is significantly less prevalent among Asian women, whose diets contain high intake of soy products and green tea. These authors suggested that dietary soy phytochemical concentrate plus green tea may be used as a potential effective dietary regimen for inhibiting progression of estrogen-dependent breast cancer.

Zhang *et al.* [72] reported that ovarian cancer risk declined with increasing frequency and duration of green tea consumption. Green tea is also an effective chemopreventive agent to human prostate cancer. In the same line of research, Yu *et al.* [73] reported that EGCG inhibited the growth of prostate cancer adenoma cells and induced apoptosis. Jian *et al.* [74] conducted a case-control study in China in order to investigate whether green tea consumption has an etiological association with prostate cancer. Prostate cancer risk declined with increasing frequency, duration and quantity of green tea consumption. The dose-response relationships were also significant, suggesting that green tea is protective against prostate cancer. Yamamoto *et al.* [59] reported that GTP could be applied to enhance the effectiveness of chemo/radiation therapy to promote cancer cell death while protecting normal cells.

On the one hand, epidemiological studies have suggested that high consumption of green tea protects against the development of chronic active gastritis and decreases the risk of stomach cancer; in addition, the ingestion of green tea before fasting protects the intestinal mucosa against atrophy [75]. On the other hand, Borrelli *et al.* [76] concluded in a systematic review, that an inverse association does not seem to exist between green tea consumption and the risk of gastric and intestinal cancer, although green tea did show a protective effect on adenomatous polyps and chronic gastritis [76]. In the same way, Hoshiyama *et al.* [66] and Koizumi *et al.* [77] found no association between green tea consumption and the risk of stomach cancer; these authors indicated that green tea consumption had no protective effect against stomach cancer, and suggested the implication of other factors such as age, smoking, socioeconomic status, *Helicobacter pylori* infection, history of pectic ulcer, and family history of stomach cancer along with certain dietary components. Sasazuki *et al.* [78] reported an inverse association between green tea consumption and distal gastric cancer among women; however, these authors indicated that more prospective studies with detailed information are needed to confirm the role of green tea in the occurrence of gastric cancer. Il'yasova *et al.* [7] examined the association between black tea consumption and colon cancer in a population-based study in North Carolina, and concluded that, contrary to expectation, black tea drinking did not decrease the risk of colon cancer. However, it is important to remark that major risk factors for colorectal cancer are family history of colorectal cancer, exposure to non-steroid anti-inflammatory drugs, certain meat cooking practices, smoking, low physical activity and an elevated body mass index, and elevated intake of red meat and alcoholic beverages. Data on the effects of green tea in the prevention of this type of cancer are not available.

Several authors have noted that some epidemiological studies have generated inconsistent results [54,79]. Some of these

Table 2. Epidemiological Studies on the Association between Green Tea Consumption and Cancer Risk

Country	Type of study/subjects	Green tea consumption	Health effects	Reference
Breast cancer				
Japan	Prospective study 1160 female invasive breast cancer (mean age = 51.5 y)	≥6 cups/day 3–5 cups/day 0–2 cups/day	A decrease of the risk of cancer recurrence is observed with a consumption of ≥3 cups/day of tea (HR = 0.69, 95% CI = 0.22–0.84). This decrease is mainly in early stage cases.	Inoue *et al.* [70]
USA	Case-control study Asian-american women 501 breast cancer patients and 594 controls	>85.7 mL/day 0–85.7 mL/day no drinkers	There is a significant trend of decreasing risk of breast cancer with increasing amount of tea intake, (OR = 1, 95% CI = 0.51–0.99; OR = 0.71, 95% CI = 0.51–0.99; OR = 0.53, 95% CI = 0.35–0.78) respectively, in association with no, 0–85 mL/day and >85.7 mL/day.	Wu *et al.* [68]
Japan	Pooled of two prospective studies with 35004 women	5 cups/day <1 cups/day	Tea intake is not associated with a lower risk of breast cancer (RR for women drinking >5 cups/day compared with <1 cup/day = 0.84, 95% CI = 0.57–1.24).	Suzuki *et al.* [168]
Ovarian cancer				
China	Case-control study 254 ovarian cancer patients and 652 controls	Validated questionnaire	Increasing frequency and duration of tea drinking can reduce the risk of ovarian cancer (OR = 0.39 for those drinking tea daily, OR = 0.23 for those drinking tea for >30 years, compared with non tea drinkers).	Zhang *et al.* [72]
Prostate cancer				
China	Case-control study 130 prostate adenocarcinoma patients and 274 controls	Face-to-face interview using a structured questionnaire (Almost all the tea consumed is green tea)	The prostate cancer risk declined with increasing: frequency (non-drinkers for tea drinking OR = 0.28, 95% CI = 0.17–0.47), duration (OR = 0.12, 95% CI = 0.06–0.26 for drinking tea over 40 years) and quantity of tea consumption (OR = 0.09, 95% CI = 0.04–0.21) for those consuming more than 1.5 kg of tea leaves yearly and OR = 0.27, 95% CI = 0.15–0.48 for those drinking more than 1 L/day).	Jian *et al.* [74]
Gastro-intestinal cancer				
Japan	Case-control study 887 gastric cancer and 28619 control age: 20–79 y	6 cups/day 3–5 cups/day 1–2 cups/day never	Consumption of more than 6 cups/day *vs* never drinking decreased the risk of gastric cancer.	Huang *et al.* [169]
Japan	Cross-sectional study 636 men and women mean age: men: 59.2 y, women: 60.4 y	≥10 cups/day 0–9 cups/day	Consumption of more than 10 cups/day reduces the risk of chronic atrophic gastritis (OR = 0.59, 95% CI = 0.42–0.86).	Shibata *et al.* [170]
Japan	Cross-sectional study 566 men age: 50–55 y	≥5 cups/day 3–4 cups/day <3 cups/day	No relationship between tea consumption and risk of chronic atrophic gastritis (OR = 0.7, 95% CI = 0.5–1.2).	Kuwahara *et al.* [171]
Japan	Prospective cohort study 8552 adults	≥10 cups/day 4–9 cups/day <3 cups/day	Consumption of more than 10 cups/day decrease the risk of stomach cancer (OR = 0.69, 95% CI = 0.23–1.88) and colorectal cancer (OR = 0.56, 95% CI = 0.22–1.4).	Nakachi *et al.* [88]
Japan	Prospective cohort study 14873 men and 23667 women Hiroshima atomic bomb survivors	≥5 cups/day 2–4 cups/day 0–1 cups/day	No relation between tea consumption and reduced risk of stomach cancer (OR = 0.95, 95% CI = 0.76–1.2), colon cancer (OR = 1.0, 95% CI = 0.76–1.4) or rectum cancer (OR = 1.3, 95% CI = 0.77–2.1).	Nagano *et al.* [79]
China	Case-control study 166 chronic atrophic gastritis, 133 gastric cancer and 433 controls	21 cups/week 1–21 cups/week never	Significant inverse association between tea drinking and gastric cancer (OR = 0.39, 95% CI = 0.15–1.01) or chronic atrophic gastritis (OR = 0.52, 95% CI = 0.28–0.99).	Setiawan *et al.* [172]

(*Table continues*)

Table 2. *Continued*

Country	Type of study/subjects	Green tea consumption	Health effects	Reference
Japan	Prospective cohort study 11902 men and 14409 women (mean age: 46.4 y)	≥5 cups/day 3–4 cups/day 1–2 cups/day <1 cup/day	No association with risk of gastric cancer men: (OR = 1.16, 95% CI = 0.9–2.6), women: (OR = 0.8, 95% CI = 0.5–1.3).	Tsubono *et al.* [173]
Japan	Prospective cohort study 30370 men and 42481 women	≥10 cups/day 5–9 cups/day 3–4 cups/day 1–2 cups/day <1 cup/day	No association between tea consumption and stomach cancer death; men: (OR = 1.00, 95% CI = 0.5–2), women: (OR = 0.7, 95% CI = 0.3–2).	Hoshiyama *et al.* [174]
Japan	Prospective cohort study 18746 men and 26184 women	Every day 3 times/week <3 times/week	No association between tea consumption and stomach cancer death; men: (OR = 1.11, 95% CI = 0.75–1.63), women: (OR = 1.43, 95% CI = 0.78–2.62).	Fujino *et al.* [175]
Japan	Case-control study 157 incident stomach cancer and 285 controls	≥10 cups/day 5–9 cups/day 3–4 cups/day 1–2 cups/day <1 cup/day	No inverse association between tea consumption and the risk of stomach cancer.	Hoshiyama *et al.* [66]
Esophageal cancer				
China	Prospective interventional study 778 esophageal precancerous lesion	Intervention group: 5 mg/day of decaffeinate green tea (DGT) for 12 months.	DGT trial did not show apparent difference between the treatment and placebo group in alleviating the esophageal precancerous lesions and abnormal cell proliferation.	Wang *et al.* [176]
Bladder cancer				
Japan	Prospective cohort study 14873 men and 23667 women Hiroshima atomic bomb survivors	A mail survey	Tea consumption is not related to risk of bladder cancer	Nagano *et al.* [177]
Lung cancer				
China	Case-control study 649 lung cancer women and 675 controls women	Face-to-face interviews	Among non-smoking women, consumption of green tea was associated with a reduced risk of lung cancer (OR = 0.65, 95% CI = 0.45–0.93), and the risks decreased with increasing consumption.	Zhong *et al.* [178]
Cancer incidence				
Japan	Prospective study 38540 people (14.873 men, mean age 52.8 y and 23667 women, mean age 58.8 y)	≥5 times/day 2–4 times/day 1 time/day never	Tea consumption is unrelated to incidence of cancers under study. (RR = 1, 95% CI = 0.91–1.1, and RR = 0.98, 95% CI = 0.88–1.1 for all cancer consuming tea twice to four times per day and five or more times per day, as compared with those consuming tea once per day or less).	Nagano *et al.* [79]

HR = hazard ratio; OR = odd ratio; RR = relative risk; CI = confidence interval.

studies related tea consumption with reduced risk of cancer. In a similar way, other authors found that tea lacks protective activity against certain human cancers; these results raise questions about the actual role of green tea components in human cancer that need to be addressed. For example, Arab and Il'yasova [80] provided a brief synopsis of 30 studies aimed at examining tea consumption as a factor in the incidence of colon and rectal cancers; the 30 papers examined populations in 12 countries and provided data on consumption of both black and green tea. These studies do not provide consistent evidence to support the theory from animal studies and basic research of tea being a potent chemopreventive agent. A negative association is stronger in observational epidemiologic studies of rectal cancer than in colon cancer. There is no consistent adjustment for important potential confounders of any tea relationship, such as coffee and alcohol consumption and physical activity levels. Finally, these authors indicated that the assessment of tea in most of these studies was based on a single question and

therefore may have significant measurement error compared with more recent studies specifically aimed at assessing green tea consumption. Table 2 summarizes some recent epidemiological studies on the association of green tea consumption and cancer risk.

Anti-Hypertensive Effect And Cardiovascular Disease Risk. Green tea has long been believed to possess hypotensive effects in popular Chinese medicine. However, conflicting results have been shown among trials and animal studies on the relation between tea consumption and blood pressure. Epidemiological evidence about the long-term effect of green tea on hypertensive risk is also inconsistent. Negishi *et al.* [81] observed that both black and green tea polyphenols attenuate blood pressure increases, through their antioxidant properties, in stroke-prone spontaneously hypertensive rats, but the amounts of polyphenols used in this experiment correspond approx. to those 1L of tea. Recently, some epidemiological studies indicated that green tea consumption slightly reduces blood pressure. Yang *et al.* [82] concluded that habitual moderate strength green tea or oolong tea consumption, 120 mL/day or more for 1 year significantly reduces the risk of developing hypertension in the Chinese population. Hodgson *et al.* [83] reported that long-term regular ingestion of green tea may have a favorable effect on blood pressure in older women. However, other studies do not support a hypotensive effect of green tea [4]. Singh *et al.* [84], and Murakami and Ohsato [85] reported that dietary green tea intake preserves and improves arterial compliance and endothelial function. Green tea consumption has also been inversely associated with the development and progression of atherosclerosis, which is consistent with the former observations. Geleijnse *et al.* [86] in their prospective Rotterdam study with 3454 adults, 55 years of age or older, and with a follow-up duration ranging from two to three years, examined aortic atherosclerosis via X-ray measurement of calcified deposits in the abdominal aorta; the odds ratio (OR) for drinking 125–250 mL (1–2 cups) of black tea daily was 0.54 (95% CI = 0.32–0.92) and decreased to 0.31 (95% CI = 0.16–0.59) when >500 mL/day (more than four cups) were consumed. Data on green tea are reported by Sasazuki *et al.* [87] who in a cross sectional study of 512 coronary patients (302 men and 210 women) established that green tea may be protective against coronary atherosclerosis in men (OR = 0.5, 95% CI = 0.2–1.2 for consumption of 2–3 cups, and OR = 0.4, 95% CI = 0.2–0.9 for ≥4 cups per day as compared with a consumption of one cup per day or less), but not in women. Nakachi *et al.* [88] in a prospective cohort study of 8522 men and women concluded that consuming ≥10 cups/day is linked with a decreased relative risk (RR) of death from cardiovascular disease in men (RR = 0.58, 95% CI = 0.34–0.99) and in women (RR = 0.82, 95% CI = 0.49–1.38).

Epidemiological studies suggest that green tea consumption is associated with a reduced cardiovascular disease risk, but the mechanisms for these observations have remained uncertain. Several studies have demonstrated that green tea may affect the cardiovascular function through mechanisms of action related to LDL-cholesterol oxidation [4,89]. The oxidation of LDL-cholesterol, associated with a risk for atherosclerosis and heart disease, is inhibited by green tea due to EC and EGCG antioxidant activity. The *in vitro* antioxidant activity of EGCG on LDL oxidation was stronger than that of EC [90]. In accordance with these observations, Trevisanato and Kim [91] indicated that GTP may slow atherogenesis by reducing the oxidative modification of LDL-cholesterol and associated events such as foam cell formation, endothelial cytotoxicity and induction of proinflammatory cytokines. Gomikawa and Ishikawa [90] suggested that catechins suppressed the susceptibilities of human LDL to oxidation by $CuSO_4$ *in vitro* and plasma oxidation *in vivo* after ground green tea ingestion. Recent bioavailability studies indicate that GTP can accumulate in the body at concentrations comparable to those employed *in vitro* by several investigators [31]. Other data report that catechins have been shown to reduce plasma cholesterol levels and the rate of cholesterol absorption. Raederstorff *et al.* [92] investigated the dose-response and the mechanism of action of EGCG on these parameters in rats which were fed a diet high in cholesterol and fat; after 4 weeks of treatment, total cholesterol and LDL-cholesterol plasma levels were significantly reduced in the group fed 1% EGCG when compared to the non-treatment group. Plasma triglycerides and HDL-cholesterol did not change significantly. These authors suggested that one of the underlying mechanisms by which EGCG affects lipid metabolism is by interfering with the micellar solubilization of cholesterol in the digestive tract, which then in turn decreases cholesterol absorption. Yokozawa *et al.* [93] reported that the administration of GTP effectively inhibited LDL-cholesterol oxidation and elevated serum antioxidative activity. Furthermore, GTP increased the levels of HDL-cholesterol, leading to dose-dependent improvement of the atherogenic index. Thus, GTP may exert an antiatherosclerotic action by virtue of its antioxidant properties and by increasing HDL-cholesterol levels. Consistent with these results are the data reported by Hertog *et al.* [94] that demonstrated an inverse correlation between catechin intake and coronary heart disease mortality after a 25-year follow-up of 12763 men from seven different countries. Similarly, another research showed that men and women from the Boston Area Health study who consumed one or more cups per day of green tea in the previous year had a 44% lower risk of myocardial infarction than those who drank no tea [95]. Recently, Peters *et al.* [96] have provided a meta-analysis that suggested a decrease in the rate of cardiovascular disease outcomes with increasing green tea consumption. Through seven studies the incidence rate of myocardial infarction was estimated to decrease by 11% with an increase in green tea consumption of three cups per day (RR = 0.89; 95% CI = 0.79–1.019). In addition, an inverse association of green tea intake and myocardial infarction and its genetic variation has been found by Hirano *et al.* [97] and Ohmori *et al.* [98].

Impaired endothelium-derived nitric oxide activity contributes to the pathogenesis of atherosclerosis, and in coronary circulation, it has been linked with future cardiovascular disease events. Furthermore, this endothelial dysfunction is associated with increased oxidative stress and may be reversed by antioxidant interventions [4]. Duffy *et al.* [99] observed that tea consumption improved flow-mediated dilation, in association with an increased plasma catechin concentration ($p < 0.001$). No effects were observed with an equivalent dose of caffeine (200 mg) or on endothelium-independent nitroglycerin-mediated dilation. As flow-mediated dilation is blunted in coronary heart disease patients compared to healthy subjects, these results suggest that green tea reverses endothelial vasomotor dysfunction. Hertog *et al.* [100] reported no association of catechin by tea intake with ischemic heart disease incidence in a 14-year follow-up of 334 men, 45 to 59 years of age, conducted in Caerphilly, Wales. According to McAnlis *et al.* [101], the discrepancy between the effect of green tea *in vivo* and *ex vivo*, on the susceptibility of LDL-cholesterol to oxidation may be due to the inability to achieve concentrations *in vivo* as great as those obtained with the former methods. The possible variations between the different studies may be also due to their ignorance of socioeconomic and lifestyle factors associated with the green tea drinking (i.e., geographical differences, social class, body mass index, healthy lifestyle, higher prevalence of smoking, higher fat intake, alcohol intake, coffee consumption).

Oral Health. Oral diseases including dental caries, periodontal disease, and tooth loss may significantly impact a person's overall health. Among these, dental caries is a multifactorial infectious disease in which nutrition, microbiological infection, and host response play important roles. Earlier reports in experimental animals and humans suggested that green tea consumption (without added sugar) reduces dental caries [5,102–103]. Linke and LeGeros [104] indicated that frequent intake of green tea can significantly decrease caries formation, even in the presence of sugars in the diet. *In vivo* animal studies have shown that specific pathogen-free rats infected with *Streptococcus mutans* and then fed with a cariogenic diet containing GTP have significantly lower caries scores [105]. Supplementing drinking water of rats with 0.1% GTP along with a cariogenic diet also significantly reduced total fissure caries lesions [5]. Recent findings of Okamoto *et al.* [106] suggest that green tea catechins may have the potential to reduce periodontal breakdown resulting from the potent proteinase activity of *Porphyromonas gingivalis*. In addition, green tea decoctions inhibit α-amylase in human saliva, reducing maltose release by 70% and effectively lowering the cariogenic potential of starch-containing food [4]. Similarly, Zhang and Kashket [107] reported that green tea extracts inhibits human salivary amylase and may reduce the cariogenic potential of starch-containing food such as crackers and cakes because it may reduce the tendency of this kind of food to serve as slow-release sources of fermentable carbohydrate. It is likely that the cariogenic challenge in a cariogenic diet may be reduced by the simultaneous presence of green tea in the diet.

Apart from their polyphenol content, both green and black tea, are a natural source of fluoride and an effective vehicle for fluoride delivery to the oral cavity. According to Simpson *et al.* [108], after cleansing the mouth with tea, approximately 34% of the fluoride is retained and shows a strong binding ability to interact with the oral tissues and their surface integuments. This fluoride content may have a beneficial impact on caries and may carry out a wide range of biological activities including prevention of tooth loss and oral cancer [106,109]. Nonetheless, the data have suggested that GTP extract may be responsible for the noted effects on oral health and it has been also demonstrated that GTP rather than fluoride contribute to anticariogenic potential [5,105] by inhibition of oral bacteria growth such as *Escherichia coli*, *Streptococcus salivarius*, and *Streptococcus mutans*. Several studies have indicated that GTP inhibit growth, acid production, metabolism, and glucosyltransferase enzyme activity of *S. mutans* and dental plaque bacteria [5]. In consequence, green tea has been considered as functional food for oral health and is widely used in toothpaste formulation.

Solar Ultraviolet Protection. Epidemiological, clinical and biological studies have shown that solar ultraviolet (UV) light is a complete carcinogen and repeated exposure can lead to the development of various skin disorders including melanoma and non-melanoma skin cancers. EGCG is considered to be a topic protector agent against some types of radiation, since it prevents skin disease, photoaging and potential cancer problems due to prolonged exposure [109–111]. It seems that the rest of catechins also favour this action [5,109–110]. Katiyar [111] indicated that topical treatment or oral consumption of GTP inhibits chemical carcinogen or UV radiation-induced skin carcinogenesis in different laboratory animal models. Topical treatment of GTP or ECCG and oral consumption of GTP resulted in prevention of UVB-induced inflammatory responses, immunosuppression and oxidative stress, which are the biomarkers of several skin disease conditions. Topical application of GTP and EGCG prior to exposure of UVB protects against UVB-induced local as well as systemic immune suppression in laboratory animals. This fact was associated with the inhibition of UVB-induced infiltration of inflammatory leukocytes. The *in vitro* and *in vivo* animal and human studies have suggested that GTP are photoprotective in nature, and can be used as pharmacological agents for the prevention of solar UVB light-induced skin disorders including photoaging, melanoma and non-melanoma skin cancers [4–5,109,111].

Body Weight Control. Obesity has increased at an alarming rate in recent years and is now a worldwide health problem. Current interest in the role of functional foods in weight control has focused on plant ingredients capable of interfering with the sympathoadrenal systems [112]. The effects of long-term feeding with tea catechins have been widely studied, and some investigators suggest a potential role of green tea in body

weight control. In addition, caffeine and theanine have been found to strengthen polyphenol effects on body weight control and fat accumulation in mice [113]. *In vitro* studies with green tea extracts containing 25% of catechins have shown its capacity (in conditions similar to physiological ones) to significantly inhibit the gastric lipase, and in a lower extent also the pancreatic lipase. Thus, the lipolysis of long-chain triglycerides is reduced in a 37% [114]. *In vitro* studies have also shown that green tea extracts interfere in the fat emulsification process, which occurs before enzymes act, and is indispensable for lipid intestinal absorption [114–115]. Green tea also exhibits a fatty acid synthase inhibitor activity [116]. In addition, green tea may have thermogenic properties not only attributable to its caffeine content, but to the joint-effect of caffeine and catechins. EGCG can act upon AMPc levels by increasing the energetic expenditure [114]. Dulloo *et al.* [112] using a green tea extract rich in catechins and caffeine, concluded that green tea has thermogenic properties and promotes fat oxidation beyond than those explained by its caffeine content *per se*; the green tea extract may play a role in the control of body composition via sympathetic activation of thermogenesis, fat oxidation, or both. Dulloo *et al.* [117] indicated that the thermogenic properties of green tea could reside primarily in an interaction between its high content in catechins and the presence of caffeine with sympathetically released noradrenaline; since polyphenols are known to be capable of inhibiting catechol-o-methyl-transferase (the enzyme that degrades noradrenaline), and caffeine of inhibiting trancellular phosphodiesterases (enzymes that break down noradrenaline-induced AMPc). Such a synergistic interaction between polyphenols and caffeine to increase and prolong sympathetic stimulation of thermogenesis could be of value in assisting the management of obesity. Kovacs *et al.* [118] reported that weight maintenance after 7.5% of body weight loss in overweight and moderately obese subjects was not affected by green tea treatment and that regular caffeine consumption affected weight maintenance in green tea treatment. According to some authors, green tea extracts (with a 25% of catechins content) may be advisable for overweight treatment in patients whose body mass index ranges between 25 and 29.9 kg/m^2, only if they do not present special sensitiveness to xantic bases [118]. Wu *et al.* [119] indicated that an inverse relationship may exit among regular green tea consumption, body fat percentage, and body fat distribution, especially for subjects who have maintained the habit of tea consumption for more than 10 years.

Glucose Tolerance and Insulin Sensitivity. Epidemiological observations and laboratory studies have shown that green tea has an effect on glucose tolerance and insulin sensitivity. Anderson and Polansky [120] reported that green tea increases insulin activity, and that the predominant active compound is EGCG; these same authors indicated that addition of lemon to the tea did not affect the insulin-potentiating activity but the addition of 50 g of milk per cup decreased the insulin-potentiating activity similar to 90%. Wu *et al.* [121] examined the effect of green tea supplementation on glucose tolerance and insulin sensitivity in rats; rats were divided into two groups: a control group was fed with standard chow and deionized distilled water, while the other was fed with the same chow diet but with green tea instead of water (0.5 g of lyophilized green tea powder dissolved in 100 mL of deionized distilled water); after 12 weeks of green tea supplementation, this group had lower fasting plasma levels of glucose, insulin, triglycerides, and free fatty acid than the control rats. In addition, GTP significantly increased basal and insulin-stimulated glucose uptake of adipocytes [4]. Some investigations have also shown that EGCG does not only regulate the glucose level in blood, but also may rehabilitate damaged *beta*-cells, which are responsible for producing insulin [4,119].

Other Effects. Green tea catechins have been reported to have antibacterial and antiviral activity. Green tea effectiveness against any type of diarrhoea and typhoid has been known in Asia since ancient times [4,68,119]. Nowadays it is also known that it inhibits the reproduction and growth of many bacteria, among which some types of *Salmonella*, *Clostridium* or *Bacillus* can be named. Takabayashi *et al.* [122] and Yee *et al.* [123] reported an inhibitory effect of green tea catechins on *Helicobacter pylori* infection. Moreover, it has been shown that green tea has not effect over intestinal flora, which is a great advantage against other bactericide agents. Regarding its antiviral action, green tea is well known for preventing tobacco crops from being invaded by the 'mosaic virus' of tobacco. Recent investigations have confirmed that catechins completely inhibit its growth and reproduction [3]. Effects of green tea against the influenza virus, especially in its earliest stage, as well as against the *Herpes simplex* virus have also been demonstrated [124–126]. Furthermore, Weber *et al.* [127] observed that adenovirus infection is inhibited *in vitro* by green tea catechins. Hirasawa and Takada [128] indicated the antifungal activity of green tea catechins against *Candida albicans*, and the convenience of a combined treatment with catechins and lower doses of antimycotics; this treatment may help to avoid the side effects of antimycotics.

Green tea consumption has also been associated with increased bone mineral density, and it has been identified as an independent factor protecting against the risk of hip fractures; this fact has been considered independent of smoking status, hormone replacement therapy, coffee drinking and the addition of milk to tea [129]. Park *et al.* [130] observed the positive effects of green tea extracts and GTP on the proliferation and activity of bone cells. Wu and Wei [5] indicated that bone mineral density may be influenced by several chemical compounds that are contained in tea extracts (i.e., caffeine, phytostrogen, fluoride, . . .).

Green tea polyphenols are known to have anti-fibrotic properties on the skin and on the arteries. The proliferation of hepatic stellate cells is closely related to the progression of liver fibrosis in chronic liver diseases, and EGCG has a potential inhibitory effect on the proliferation of these cells [131–132].

Green tea strengthens the immune system action since green tea protects it against oxidants and radicals. Bayer *et al.* [133] suggest that oral intake of green tea could act as an adjunctive therapy for prevention of transplant rejection in humans. The neuroprotective power of complex extracts rich in flavonoids like those of *Ginkgo biloba*, green tea or lyophilized red wine have been demonstrated in several studies [134–135]. Recent studies suggest that GTP possibly protect against Parkinson's and Alzheimer's diseases and other neurodegenerative diseases [44,136]. GTP have demonstrated neuroprotectant activity in cell cultures and animal models, such as the prevention of neurotoxin-induced cell injury; the biological effects of GTP may benefit patients with Parkinson's disease, but further in-depth studies are needed to investigate the safety and effectiveness of green tea in humans and to determine the different mechanisms of green tea in neuroprotection [44]. In the same way, the neuroprotective effects of the theanine contained in green tea are a focus of considerable attention, and further studies are warranted [134].

Finally, the following health effects of green tea consumption have also been described. Green tea is considered to be useful for insect stings due mainly to its antiinflammatory effects and its capacity to stop bleeding [137–138]. Some studies have suggested an inverse association between green tea consumption and the risk of kidney stone formation [4,139]. In addition, green and black tea extracts led to a retardation of the progression of lens opacity in rats with cataracts induced by selenite [140]. Gupta *et al.* [141] reported that green tea acts by preserving the antioxidant defense system of the lens. Skrzydlewska *et al.* [142] indicated a beneficial effect of green tea in alcohol intoxication. Besides all the above mentioned properties, which have helped to the recognition of green tea as functional food by some authors [143], it is not to forget its current use in the preparation of a variety of food, pharmaceutical preparations, dentifrices and cosmetics [144]. This additional use is mainly due to its antioxidant activity, which makes it a natural, efficient and safe preservative.

Green Tea Nutritional Value

Green tea consumption contributes to the overall daily fluid intake, and if sugar is not added, the calories intake is insignificant; besides, the caffeine intake is lower than in coffee, black tea or cola soft-drinks. In addition, green tea contribution to the dietary intake of antioxidant compounds (catechins and other phytochemical substances, certain vitamins as vitamin C, and minerals as Mn, Cr, Se, Zn) is very interesting to promote human health and well being, and more relevant than that other non-alcoholic beverages widely consumed. The Mn content is high, and tea is considered a rich source of this essential element [21,145]. Manganese is a constituent of three metalloenzymes (i.e., arginase, pyruvate carboxylase, and Mn-superoxide dismutase) and it activates a large number of enzymes, such as glycosyl transferases, involved in mucopolysaccharide synthesis [146]. Manganese deficiency can cause abnormalities in the metabolism of carbohydrates, glycosaminoglycans, and cholesterol [147]. Chromium, selenium and zinc play also an important role in human metabolism, and interest in these elements is increasing since there are reports relating trace element status and oxidative diseases. Chromium is involved in carbohydrate and lipid metabolism; the most frequent sign of Cr deficiency is altered glucose tolerance; this nutrient has been associated with diabetes and cardiovascular diseases [146]. Beneficial effects of dietary Cr supplementation, particularly in groups in which deficiencies are frequent, have been reported [147]. Garcia *et al.* [148] measured through duplicate diet sampling the Cr dietary intake in Spain and detected that the most elevated intakes are related to high consumption of infusions, especially tea and coffee. Selenium functions through selenoproteins, several of which are oxidant defense enzymes; Se acts as enzymatic cofactor of glutathione peroxidase in the elimination of peroxide radicals from the organism. Epidemiological studies have shown the possible effects of Se in the prevention and regression of cancer [146–147]. Most Se is ingested in food, but food derived from vegetables has a variable Se content depending on the zone where they have been cultivated [149]. Zinc enzymes participate in a wide variety of metabolic processes including carbohydrate, lipid, and protein synthesis or degradation. This element is required for deoxyribonucleic and ribonucleic acid synthesis; it may also play a role in stabilizing plasma membranes [147]. Zinc has been recognized as a cofactor of the superoxide dismutase enzyme, which is involved in protection against oxidative processes [146]. Recently there has been a development of terminology and change in conceptual approaches towards setting nutrient recommendations from adequate to optimum nutrition [150]. Regarding antioxidant minerals, the US Food and Nutrition Board has set an Adequate Intake for Mn at 2.3 and 1.8 mg/day for adult men and women, respectively, and a Tolerable Upper Intake Level at 11 mg/day for adults. Chromium Adequate Intake values are 35 and 25 μg/day for young men and women, respectively. The Recommended Dietary Allowance for Zn is 8 and 11 mg/day for adult men and women, respectively; the Tolerable Upper Intake Level for adults is 40 mg/day. The selenium Recommended Dietary Allowance and Tolerable Upper Intake Level for adults is 55 and 400 μg/day, respectively [151–152]. Table 3 summarizes data on the content of minerals with antioxidant activity in green tea.

In addition, green tea contains more vitamin C than black and oolong teas [153]; the total content of vitamin C in tea leaves decreased during the manufacturing process of fermented teas [154], however bibliographical data on vitamin C content in green tea are scarce. Due to the fact that green tea consumption in the occidental diets (except Morocco) is scarce and occasional, its contribution to the total antioxidant dietary intake is low [155]. For example, Pulido *et al.* [156] evaluated the contribution of the most consumed beverages to the antioxidant intake in the Spanish diet; the intake is estimated at 1623 mg of vitamin E and 598 mg of vitamin C by FRAP procedure. Tea only contributes to 3–5% of the total, whereas

Table 3. Antioxidant Minerals Content in Green Tea Leaves (Data Referred to Dry Weight)

Mineral	Content (mean; range)	Class (origin)	Reference
Cr	238.6 ng/g	sencha (Japan)	Cabrera *et al.* [22]
	291.0 ng/g	jasmine (Japan)	Cabrera *et al.* [22]
	219.8 ng/g	Kokaicha (Japan)	Cabrera *et al.* [22]
	111.9 ng/g	Bancha (Japan)	Cabrera *et al.* [22]
	141.7 ng/g	Paimutan (China)	Cabrera *et al.* [22]
	118.4 ng/g	gunpower (China)	Cabrera *et al.* [22]
Mn	699 μg/g (160–1500)	A set of samples (China)	Xie *et al.* [21]
	1069.7 μg/g	sencha (Japan)	Fernández-Cáceres *et al.* [10]
	1021.5 μg/g	gunpower (China)	Fernández-Cáceres *et al.* [10]
	714.9 μg/g	jasmine (China)	Fernández-Cáceres *et al.* [10]
	500.7 μg/g	sencha (Japan)	Cabrera *et al.* [22]
	354.1 μg/g	jasmine (Japan)	Cabrera *et al.* [22]
	651.3 μg/g	Kokaicha (Japan)	Cabrera *et al.* [22]
	987.6 μg/g	Bancha (Japan)	Cabrera *et al.* [22]
	236.6 μg/g	Paimutan (China)	Cabrera *et al.* [22]
	518.9 μg/g	gunpower (China)	Cabrera *et al.* [22]
Se	0.18* μg/g (0.03–7.5)	A set of samples (China)	Xie *et al.* [21]
	455 $\pm$ 184 ng/g	"high Se tea" (China)	Yoshida *et al.* [179]
	92.9 ng/g	sencha (Japan)	Cabrera *et al.* [22]
	89.7 ng/g	jasmine (Japan)	Cabrera *et al.* [22]
	48.5 ng/g	Kokaicha (Japan)	Cabrera *et al.* [22]
	80.1 ng/g	Bancha (Japan)	Cabrera *et al.* [22]
	75.1 ng/g	Paimutan (China)	Cabrera *et al.* [22]
	70.2 ng/g	gunpower (China)	Cabrera *et al.* [22]
Zn	39.4* μg/g (20–60)	A set of samples (China)	Xie *et al.* [21]
	24.6 μg/g	sencha (Japan)	Fernández-Cáceres *et al.* [10]
	28.4 μg/g	gunpower (China)	Fernández-Cáceres *et al.* [10]
	44.3 μg/g	jasmine (China)	Fernández-Cáceres *et al.* [10]
	78.1 ng/g	sencha (Japan)	Cabrera *et al.* [22]
	78.6 ng/g	jasmine (Japan)	Cabrera *et al.* [22]
	76.1 ng/g	Kokaicha (Japan)	Cabrera *et al.* [22]
	65.0 ng/g	Bancha (Japan)	Cabrera *et al.* [22]
	75.1 ng/g	Paimutan (China)	Cabrera *et al.* [22]
	57.5 ng/g	gunpower (China)	Cabrera *et al.* [22]

* Geometric mean.

coffee and red wine are the main contributors. However, all the above mentioned properties of green tea, demonstrate that it can be considered an alternative to other widely consumed drinks, which have a higher content of energy and/or caffeine, and are richer in sugars, alcohol, CO_2, etc. Besides, drinking tea is an optimum way of fighting thirst due to its refreshing properties, its slightly bitter taste, its low binding effect and its fruity and agreeable smell [149,157]. Its preparation is easy, uncomplicated and varied (lemon, mint, cinnamon, . . . can be added to it).

Harmful Effects of Tea Over Consumption

Harmful effects of tea over consumption (black or green) are due to three main factors: (1) its caffeine content, (2) aluminum presence, and (3) the effects of tea polyphenols on iron bioavailability. A day-long consumption of green tea improved the cognitive and psychomotor performance of healthy adults in a manner similar to coffee, but green tea (which contains less caffeine) is less likely than coffee to disrupt sleep quality at night [4]. Lin *et al.* [19] compared the caffeine content in the same type of tea but manufactured by different fermentation processes, and concluded that the caffeine level presented the following order: black tea > oolong tea > green tea > fresh tea leaf. Cabrera *et al.* [22] determined the caffeine content in a total of 45 tea samples, including 'fermented' teas (red and black teas), oolong tea and green tea samples; the results showed that caffeine presence is higher in the case of black teas (41.5–67.4 mg/g), whereas green and oolong teas show a mean caffeine content of 32.5 and 29.2 mg/g, respectively. Fernandez *et al.* [20] also reported that caffeine content is higher in the case of 'fermented' teas, showing values between 2.4 and 4.8%, whereas 'non-fermented' teas show caffeine levels ranging between 1.47 and 3.86%. Table 4 includes data on the caffeine content in beverages widely consumed. The caffeine content in green tea may vary according to the type of tea and the form of preparation (i.e., brewing time); generally, bagged tea produces a higher percentage of caffeine than tea leaves [3]. In any case, although green tea caffeine content is low, its consumption is not advisable in cases of special sensitiveness to xanthic bases. The negative effects

Table 4. Caffeine Content in Food and Beverages

Product	Caffeine content*
Normal coffee	80–115 mg/150 mL†
Espresso coffee	108–180 mg/150 mL
Instant coffee	65 mg/150 mL
Decaffeinated coffee	1–3 mg/150 mL
Green tea (3 min brewing time)	15–25 mg/150 mL
Black tea (3 min brewing time)	40–70 mg/150 mL
Oolong tea	18–33 mg/150 mL
Decaffeinated tea	0.6–3 mg/150 mL
Iced tea	70 mg/360 mL
Cocoa milk shake	5 mg/240 mL
Hot chocolate	4 mg/150 mL
Plain chocolate (bar)	15 mg/20 g
Milk chocolate (bar)	5 mg/20 g
Cola soft drink	38–46 mg/360 mL

* A consumption higher than 200 mg/day is not advisable.

† Quantities vary according to the beverage preparation.

produced by caffeine are nervousness, sleep disorders, vomits, headaches, epigastric pain, tachycardia [38–39]. Theophylline negative effects are similar to those of caffeine, but they only occur with high quantities intake. Thus, green tea should not be taken by patients suffering from heart conditions or major cardiovascular problems. Pregnant and breast feeding women should drink no more than 1–2 cups/day, since it can cause an increase in heart rhythm. It is also convenient to control the concomitant consumption of green tea and some drugs, due to its diuretic effects [39].

Regarding aluminum presence in black and green tea, some studies revealed the high capacity of this plant to accumulate Al. This aspect is important for patients with renal failures because Al can be accumulated by the body, resulting in neurological diseases; it is therefore necessary to control the intake of food with high amounts of this metal [1]. The possible connection between elevated tissue Al content and problems such as osteomalacia and neurodegenerative disorders (i.e., Alzheimer's disease) has awakened interest in Al intake via diet [158]. Minoia *et al.* [159] found concentrations of Al in green and black teas (as infusions) accounting for 431–2239 μg/L, whereas in coffee they found lower concentrations (9.1–30.8 μg/L). In a study carried out in Italy, these authors estimated the tea contribution to the total Al dietary intake as 665 μg/week (considering a weekly mean consumption of 2 cups). According to several authors, Al dietary intake must not exceed 6 mg/day in order to avoid potentially toxic levels [160]. López *et al.* [158] evaluated Al presence in food and beverages widely consumed in Spain, and found that Al levels in tea ranged from 43.42 to 58.04 μg/g referred to dry weight of the solid product, and from 13.91 to 27.45 μg/L in the corresponding infusions; levels in coffee samples varied between 25.6 and 29.08 μg/g referred to dry weight of the solid product, and from 7.12 to 9.14 μg/L in the corresponding infusions. Costa *et al.* [1] observed that black tea contains nearly six-fold more Al than green tea, and the extraction of Al in black teas was higher than the one observed in green teas; the Al concentrations in the tea infusions were constant after 5 min of extraction. These authors also indicated that the variations between different samples may be due to different soil conditions as well as different harvesting periods, and the influence of the water quality. Following this line of study, several authors considered that this element does not seem to be much more bioavailable in tea than in other dietary sources [1,161]. Even so, it cannot be ignored that tea infusions may contain particularly bioavailable and neurotoxic compounds such as Al maltolate, but this is currently speculative [161]. At this respect, Costa *et al.* [1] reported that the composition of Al species could vary depending on the method of tea production, and for non-fermented teas, most of the leached Al is mainly found in large or small organic compounds; in organic complexes with small molecular masses, such as citrates, the Al-complexes are more bioavailable than in inorganic complexes (such as hydroxide), but generally, Al is poorly absorbed by the body. Thus, future studies designed to accurately assess the presence and bioavailability of Al in green tea leaves is necessary.

Several studies have demonstrated that black tea appears to inhibit the bioavailability of non-heme iron by 79% to 94% when both are consumed concomitantly; the impact of this interaction depends on the iron intake and iron status of the individual [162–163]. Likewise, green tea catechins may have an affinity for iron, and green tea infusions can cause a significant decrease of the Fe bioavailability from the diet [164]. On the one hand, some authors affirm that tea should not be consumed by patients suffering from anaemia. For example, iron deficiency anaemia among children in Saudi Arabia and the United Kingdom may be exacerbated by the regular consumption of tea with meals [165–166]. On the other hand, this effect may be of benefit to patients with genetic hemochromatosis [4]. It is worth noting that the interaction between tea and iron can be mitigated by the addition of lemon or consuming tea between meals.

Conclusions

Green tea has been consumed in China and other Asian countries since ancient times in order to maintain and improve health. Nowadays, green tea is considered one of the most promising dietary agents for the prevention and treatment of many diseases and consequently, it is being studied extensively worldwide. Numerous studies in a variety of experimental animal models have demonstrated that aqueous extract of the mayor GTP designed as catechins (EGCG, EGC, ECG and EC) possess antioxidant, antimutagenic, antidiabetic, anti-inflammatory, antibacterial and antiviral, and above all, cancer-preventive properties. Epidemiological studies suggest that consumption of green tea may have a protective effect against the development of several cancers. Preclinical studies of green tea

and its polyphenolic components have demonstrated antimutagenic and anticarcinogenic activity, and inhibition of growth of tumor cell lines and animal tumor models, including cancer. Green tea may also have chemopreventive properties, and enhancement of chemotherapeutic agents has been demonstrated. In addition, several epidemiological studies with humans have demonstrated that regular green tea consumption has beneficial effects and it shows a significant rate of protection against the development of some oral diseases and against solar radiations. It also contributes to body weight control and to the rise of bone density as well as being able to stimulate the immune system. Furthermore, green tea consumption has been recently reported to act positively against neurodegenerative diseases such as Parkinson and Alzheimer disease. Catechin antioxidant power is also strengthened by the presence of other phenolic compounds, vitamin C and minerals such as Cr, Mn, Se, and Zn, although specific data regarding this fact are still scarce.

However, conflicting results between cohort studies conducted in different countries may also arise from confusion in the frequency and timing of intake, and the marked contrasts in the socioeconomic and lifestyle factors associated with tea drinkers. It is also important to consider the type of tea or its preparation (e.g., short time *vs.* long brewing time and hot tea *vs.* iced tea) due to the marked impact of these factors on polyphenol content and concentration. It is also important to draw attention on the need of further-in-depth studies on the nature and mechanisms of the active green tea compounds, on the bioavailability of the different catechins in humans, and appropriate dose levels to act as functional food.

Since green tea beneficial health effects are being increasingly proved, it could be advisable to encourage the regular consumption of this widely available, tasty and inexpensive beverage as an interesting alternative to other drinks, which do not only show the beneficial effects of green tea, but are also more energetic, do contain more caffeine (green tea contains less caffeine than black tea, coffee or cola soft-drinks), are rich in additives and/or CO_2. While no single food item can be expected to provide a significant effect on public health, it is important to note that a modest effect between a dietary component and a disease having a major impact on the most prevalent causes of morbidity and mortality, i.e., cancer and heart disease, should merit substantial attention. Taking all this into account, it would be advisable to consider the regular consumption of green tea in Western diets.

ACKNOWLEDGMENT

We thank M.J. Martinez-Vique for revising the English grammar of the original manuscript. We thank Antiguo Tostadero (specialized tea shop) for its cooperation and interest in this research.

REFERENCES

1. Costa LM, Gouveia ST, Nobrega JA: Comparison of heating extraction procedures for Al, Ca, Mg and Mn in tea samples. Ann Sci 18:313–318, 2002.
2. Rietveld A, Wiseman S: Antioxidant effects of tea: Evidence from human clinical trials. J Nutr 133:3275–3284, 2003.
3. Willson KC: "Coffee, Cocoa and Tea." New York: CABI Publishing, 1999.
4. McKay DL, Blumberg JB: The role of tea in human health: An update. J Am Coll Nutr 21:1–13, 2002.
5. Wu CD, Wei GX: Tea as a functional food for oral health. Nutrition 18:443–444, 2002.
6. Zuo Y, Chen H, Deng Y: Simultaneous determination of catechins, caffeine and gallic acids in green, Oolong, black and *Pu-erh* teas using HPLC with a photodiode array detector. Talanta 57:307–316, 2002.
7. Il'yasova D, Martín C, Sandler RS: Tea intake and risk of colon cancer in African-Americans and Whites: North Carolina colon cancer study. Cancer Causes Control 14:676–772, 2003.
8. Diplock AT, Aggett PJ, Ashwell M, Bornet F, Fern EB, Roberfroid MB: Scientific concepts of functional foods in Europe consensus document. Br J Nutr 81:1–27, 1999.
9. Roberfroid MB: Global view on functional foods: European perspectives. Br J Nutr 88:133–138, 2002.
10. Fernández-Cáceres PL, Martin MJ, Pablos F, González AG: Differentiation of tea (*Camelia sinensis*) varieties and their geographical origin according to their metal content. J Agric Food Chem 49:4775–4779, 2001.
11. Shu WS, Zhang ZQ, Lan CY, Wong MH: Fluoride and aluminum concentrations of tea plants and tea products from Sichuan Province, PR China. Chemosphere 52:1475–1482, 2003.
12. Fung KF, Zhang ZQ, Wong JWC, Wong MH: Aluminum and fluoride concentrations of the three tea varieties growing at Lantau Island, Hong Kong. Environ Geochem Health 25:219–232, 2003.
13. Xu J, Zhu SG, Yang FM, Cheg LC, Hu Y, Pan GX, Hu QH: The influence of selenium on the antioxidant activity of green tea. J Sci Food Agric 83:451–455, 2003.
14. Vison J, Dabbagh Y, Serry M, Jang J: Plant flavonoids, especially tea flavonols, are powerful using an *in vitro* oxidation model for heart disease. J Agric Food Chem 43:2800–2802, 1995.
15. USDA: "USDA Database for the Flavonoid Contents of Selected Foods." Beltsville: US Department of Agriculture, 2003.
16. Hakim I, Harris R, Weisgerber U: Tea intake and squamous cell carcinoma of the skin: Influence of type of tea beverages. Cancer Epidemiol Biomarkers Prev 9:727–731, 2000.
17. Arts I, Van De Putte B, Hollman O: Catechins contents of foods commonly consumed, in the Netherlands. Tea, wine, fruit juices, and chocolate milk. J Agric Food Chem 48:1752–1757, 2000.
18. Wang LF, Kim DM, Park JD, Lee CY: Various antibrowning agents and green tea extract during processing and storage. J Food Process Pres 27:213–225, 2003.
19. Lin YS, Tsai YJ, Tsay JS, Lin JK: Factors affecting the levels of tea polyphenols and caffeine in tea leaves. J Agric Food Chem 51:1864–1873, 2003.
20. Fernández PL, Pablos F, Martín MJ, González AG: Study of

catechin and xanthine profiles as geographical tracers. J Agric Food Chem 50:1833–1839, 2002.
21. Xie M, Von Bohlen A, Klockenkämper R, Jian X, Günther K: Multielement analysis of Chinese tea (*Camellia sinensis*) by total-reflection X-ray fluorescence. Z Lebensm Unters For 207: 31–38, 1998.
22. Cabrera C, Giménez R, López MC: Determination of tea components with antioxidant activity. J Agric Food Chem 51:4427–4435, 2003.
23. Henning SM, Fajardo-Lira C, Lee HW, Youssefian AA, Go VLW, Heber D: Catechin contents of 18 teas and green tea extract supplement correlates with the antioxidant capacity. Nutr Cancer 45:226–235, 2003.
24. Manach C, Scalbert A, Morand C, Rémésy C, Jiménez L: Polyphenols: food sources and bioavailability. Am J Clin Nutr 79: 727–747, 2004.
25. Okushio K, Matsumoto N, Kohri T, Suzuki M, Nanjo F, Hara Y: Absorption of tea catechins into rat portal vein. Biol Pharm Bull 19:326–329, 1996.
26. Kim S, Lee MJ, Hong J: Plasma and tissue levels of tea catechins in rats and mice during chronic consumption of green tea polyphenols. Nutr Cancer 37:41–48, 2000.
27. Yang CS, Chen L, Lee MJ, Balentine D, Kuo M, Schantz SP: Blood and urine levels of tea catechins after ingestion of different amounts of green tea by human volunteers. Cancer Epidemiol Biomarkers Prev 7:351–354, 1998.
28. Higdon JV, Frei B: Tea catechins and polyphenols: health effects, metabolism, and antioxidant functions. Crit Rev Food Sci Nutr 43:89–143, 2003.
29. Chow HH, Cai Y, Alberts DS: Phase I pharmacokinetic study of tea polyphenols following single-dose administration of epigallocatechin gallate and polyphenon E. Cancer Epidemiol Biomarkers Prev 10:53–58, 2001.
30. Lu H, Meng XF, Lee MJ, Li C, Maliakal P, Yang CS: Bioavailability and biological activity of tea polyphenols. Food Factors in Health Promotion and Disease Prevention Symposium Series 851:9–15, 2003.
31. Scalabert A, Williamson G: Dietary intake and bioavailability of polyphenols. J Nutr 130:2073S–2085S, 2000.
32. Loktionov A, Bingham S, Vorster H, Jerling J, Runswick S, Cummings J: Apolipoprotein E genotype modulates the effect of black tea drinking on blood lipids and blood coagulation factors: A pilot study. Br J Nutr 79:133–139, 1998.
33. Leenen R, Roodenburg A, Tijburg L, Wiseman S: A single dose of tea with or without milk increases plasma antioxidant activity in humans. Eur J Clin Nutr 54:87–92, 2000.
34. Van het Hof K, Kivits G, Weststrate J, Tijburg L: Bioavailability of catechins from tea: The effect of milk. Eur J Clin Nutr 52:356–359, 1998.
35. Hollman PC, Van Het Hof K, Tijburg L, Katan MB: Addition of milk does not affect the absorption of flavonols from tea in man. Free Radic Res 34:297–300, 2001.
36. Langley-Evans S: Consumption of black tea elicits and increases in plasma antioxidant potential in humans. Int J Food Sci Nutr 51:309–315, 2000.
37. Xu JZ, Yeung SY, Chang Q, Huang Y, Chen ZY: Comparison of antioxidant activity and bioavailability of tea epicatechins with their epimers. Br J Nutr 91:873–881, 2004.
38. Varnam AH, Sutherland JP: "Beverages: Technology, Chemistry and Microbiology." London: Chapman & Hall, 1994.
39. Bruneton J: "Pharmacognosie. Phytochimie. Plantes Médicinales." Paris: Technique et Documentation-Lavoisier, 2001.
40. Feng Q, Kumagai T, Torii Y, Nakamura Y, Osawa T, Uchida K: Anticarcinogenic antioxidants as inhibitors against intracellular oxidative stress. Free Radic Res 35:779–788, 2001.
41. Amantana A, Santana-Rios G, Butler JA, Xu MR, Whanger PD, Dashwood RH: Antimutagenic activity of selenium-enriched green tea toward the heterocyclic amine 2-amino-3-methylimidazo[4,5-f] quinoline. Biol Trace Elem Res 86:177–191, 2002.
42. Embola CW, Sohn OS, Fiala ES, Weisburger JH: Induction of UDP-glucuronosyltransferase 1 (UDP-GT1) gene complex by green tea in male F344 rats. Food Chem Toxicol 40:841–844, 2002.
43. Kondo T, Ohta T, Igura K, Hara Y, Kaji D: Tea catechins inhibit angiogenesis endothelial cell growth, migration *in vitro*, measured by human and tube formation through inhibition of VEGF receptor binding. Cancer Lett 180:139–144, 2002.
44. Pan TH, Jankovic J, Le WD: Potential therapeutic properties of green tea polyphenols in Parkinson's disease. Drugs Aging 20: 711–721, 2003.
45. Kim JH, Kang BH, Jeong JM: Antioxidant antimutagenic and chemopreventive activities of a phyto-extract mixture derived from various vegetables, fruits and oriental herbs. Food Sci Biotechnol 12:631–638, 2003.
46. Skrzydlewsja E, Augustyniak A, Ostrowska J, Luczaj W, Tarasiuk E: Green tea protection against aging-induced oxidative stress. Free Radic Biol Med 33:555, 2002a.
47. Cao G, Sofic E, Prior R: Antioxidant capacity of tea and common vegetables. J Agric Food Chem 44:3426–3431, 1996.
48. Langley-Evans S: Antioxidant potential of green and black tea determined using the ferric reducing power (FRAP) assay. Int J Food Sci Nutr 51:181–188, 2000.
49. Saffari Y, Sadrzadeh SMH: Green tea metabolite EGCG protects membranes against oxidative damage in vitro. Life Sci 74:1513–1518, 2004.
50. Zhang MH, Luypaert J, Pierna JAF, Xu QS, Massart DL: Determination of total antioxidant capacity in green tea by near-infrared spectroscopy and multivariate calibration. Talanta 62: 25–35, 2004.
51. Frei B, Higdon JV: Antioxidant activity of tea polyphenols *in vivo*: Evidence from animal studies. J Nutr 133:3275–3284, 2003.
52. Klaunig J, Xu Y, Han C, Kamendulis L, Chen J, Heiser C, Gordon M, Mohler E: The effect of tea consumption on oxidative stress in smokers and nonsmokers. Proc Soc Exp Biol Med 220:249–254, 1999.
53. Erba D, Riso P, Bordoni A, Foti P, Biagi PL, Testolin G: Effectiveness of moderate green tea consumption on antioxidative status and plasma lipid profile in humans. J Nutr Biochem 16: 144–149, 2005.
54. Chung FL, Schwartz J, Herzog CR, Yang YM: Tea and cancer prevention: Studies in animals and humans. J Nutr 133:3268–3274, 2003.
55. Lambert JD, Yang CS: Mechanisms of cancer prevention by tea constituents. J Nutr 133:3262–3267, 2003.
56. Mittal A, Pate MS, Wylie RC, Tollesfsbol TO, Katiyar SK: EGCG down regulates telomerase in human breast carcinoma

MCF-7 cells, leading to suppression of cell viability and induction of apoptosis. Int J Oncol 24:703–710, 2004.
57. Inoue M, Tajima K, Hirose K, Hamajima N, Takezaki T, Kuroishi T, Tominaga S: Tea and coffee consumption and the risk of digestive tract cancers: Data from a comparative case-referent study in Japan. Cancer Causes Control 9:209–216, 1998.
58. Bianchi G, Cerhan J, Parker A, Putnam S, See W, Lynchi C, Cantor K: Tea consumption and risk of bladder and kidney cancers in a population-based case-control study. Am J Epidemiol 151:377–383, 2000.
59. Yamamoto T, Hsu S, Lewis J, Wataha J, Dickinson D, Singh B, Bollag WB, Lockwood P, Ueta E, Osaki T, Schuster G: Green tea polyphenols causes differential oxidative environments in tumor versus normal epithelial cells. J Pharmacol Exp Ther 301:230–236, 2003.
60. Laurie SA, Miller VA, Grant SC, Kris MG: Phase I study of green tea extract in patients with advanced lung cancer. Cancer Chemother Pharmacol 55:33–38, 2005.
61. Siddiqui IA, Afaq F, Adhami VM, Ahmad N, Mukhtar H: Antioxidants of the beverage tea in promotion of human health. Antioxid Redox Signal 6:571–582, 2004.
62. D'Alessandro T, Prasain J, Benton MR, Botting N, Moore R, Darley-Usmar V, Patel R, Barnes S: Polyphenols, inflammatory response, and cancer prevention: Chlorination of isoflavones by human neutrophils. J Nutr 133:3773–3777, 2003.
63. Lin YL, Lin JK: (−)-Epigallocatechin-3-gallate blocks the induction of nitric oxide synthase by down-regulating lipopolysaccharide-induced activity of transcription factor NF-kB. Mol Pharmacol 52:467–472, 1997.
64. Chen J, Han C: The protective effect of tea on cancer: Human evidence. In Bidlach WR, Omaye ST, Meshin MS, Topham DK (eds): "Phytochemicals as Bioactive Agents." Lancaster: Technomic, pp 131–150, 2000.
65. Yamamoto T, Lewis J, Wataha J, Dickinson D, Singh B, Bollag WB, Ueta E, Osaki T, Athar M, Schuster G & Hsu S: Roles of catalase and hydrogen peroxide in green tea polyphenol-induced chemopreventive effects. J Pharmacol Exp Ther 308:317–323, 2004.
66. Hoshiyama Y, Kawaguchi T, Miura Y, Mizou T, Tokui N, Yatsuya H, Sakata K, Kondo T, Kikuchi S, Toyoshima H, Hayakawa N, Tamakoshi A, Ohno Y, Yoshimura T: A nested case-control study of stomach cancer in relation to green tea consumption in Japan. Br J Cancer 90:135–138, 2004.
67. Rosengren RJ: Catechins and the treatment of breast cancer: Possible utility and mechanistic targets. Drugs 6:1073–1078, 2003.
68. Wu AH, Yu MC, Tseng CC, Hankin J, Pike MC: Green tea and risk of breast cancer in Asian Americans. Int J Cancer 106:574–579, 2003.
69. Nakachi K, Suemasu K, Suga K, Takeo T, Imai K, Higashi Y: Influence of drinking green tea on breast cancer malignancy among Japanese patients. Jpn J Cancer Res 89:254–261, 1998.
70. Inoue M, Tajima K, Mizutani M, Iwata H, Iwase T, Miura S, Hirose K, Hamajima N, Tomonaga S: Regular consumption of green tea and the risk of breast cancer recurrence: follow-up study from the Hospital-based Epidemiologic Research Program at Aichi Cancer Center (HERPACC), Japan. Cancer Lett 167:175–182, 2001.
71. Zhou JR, Yu LY, Mai ZM, Blackburn GL: Combined inhibition of estrogen-dependent human breast carcinoma by soy and tea bioactive components in mice. Int J Cancer 108:8–14, 2004.
72. Zhang M, Binns CV, Lee AH: Tea consumption and ovarian cancer risk: A case-control study in China. Cancer Epidemiol Biomarkers Prev 11:713–718, 2002.
73. Yu NH, Yin JJ, Shen SR: Growth inhibition of prostate cancer cells by epigallocatechin in the presence of Cu^{2+}. J Agric Food Chem 52:462–466, 2004.
74. Jian L, Xie LP, Lee AH, Binns CW: Protective effect of green tea against prostate cancer: A case-control study in southeast China. Int J Cancer 108:130–135, 2004.
75. Asfar S, Abdeen S, Dashti H, Khoursheed M, Al-Sayer H, Mathew T, Al-Bader A: Effect of green tea in the prevention and reversal of fasting-induced intestinal mucosal damage. Nutrition 19:536–540, 2003.
76. Borrelli F, Capasso R, Russo A, Ernst E: Systematic review: green tea and gastrointestinal cancer risk. Aliment Pharmacol Ther 19:497–510, 2004.
77. Koizumi Y, Tsubono Y, Nakaya N, Nishino Y, Shibuya D, Matsuoka H, Tsuji I: No association between green tea and the risk of gastric cancer: Pooled analysis of two prospective studies in Japan. Cancer Epidemiol Biomarkers Prev 12:472–473, 2003.
78. Sasazuki S, Inoue M, Hanaoka T, Yamamoto S, Sobue T, Tsugane S: Green tea consumption and subsequent risk of gastric cancer by subsite the JPHC study. Cancer Causes Control 15: 483–491, 2004.
79. Nagano J, Kono S, Preston DL, Mabuchi K: A prospective study of green tea consumption and cancer incidence, Hiroshima and Nagasaki (Japan). Cancer Causes Control 12:501–508, 2001.
80. Arab L, Il'yasova D: The epidemiology of tea consumption and colorectal cancer incidence. J Nutr 133:3310–3318, 2003.
81. Negishi H, Xu JW, Ikeda K, Njelekela M, Nara Y, Yamory Y: Black and green tea polyphenols attenuate blood pressure increases in stroke-prone spontaneously hypertensive rats. J Nutr 134:38–42, 2004.
82. Yang YC, Lu FH, Wu JS, Wu CH, Chang CJ: The protective effect of habitual tea consumption on hypertension. Arch Intern Med 164:1534–1540, 2004.
83. Hodgson JM, Devine A, Puddey IB, Chan SY, Beilin LJ, Prince RL: Tea intake is inversely related to blood pressure in older women. J Nutr 133:2883–2886, 2003.
84. Singh AK, Seth P, Anthony P, Husain MM, Madhavan S, Mukhtar H, Maheshwari RK: Green tea constituent epigallocatechin-3-gallate inhibits angiogenic differentiation of human endothelial cells. Arch Biochem Biophys 401:29–37, 2002.
85. Murakami T, Oshato K: Dietary green tea intake preserves and improves arterial compliance and endothelial function. J Am Coll Cardiol 41:271–274, 2003.
86. Geleijnse J, Launer L, Hofman A, Pols H, Witteman J: Tea flavonoids may protect against atherosclerosis: The Rotterdam Study. Arch Intern Med 159:2170–2174, 1999.
87. Sasazuki S, Kodama H, Yoshimasu K, Liu Y, Washio M, Tanaka K, Tokunaga S, Kono S, Arai H, Doy Y, Kawano T, Nakagaki O, Takada K, Koyanagi S, Hiyamuta K, Nii T, Shirai K, Ideishi M, Arakawa K, Mohri M, Takeshita A: Relation between green tea consumption and the severity of coronary atherosclerosis among Japanese men and women. Ann Epidemiol 10:401–408, 2000.

88. Nakachi K, Matsuyama S, Miyake S, Suganuma M, Imai K: Preventive effects of drinking green tea on cancer and cardiovascular disease: Epidemiological evidence for multiple targeting prevention. Biofactors 13:49–54, 2000.
89. Ishikawa T, Suzukawa M, Ito T, Yoshida H, Ayaori M, Nishiwaki M, Yonemura A, Hara Y, Nakamura H: Effect of tea flavonoid supplementation on the susceptibility of low-density lipoprotein to oxidative modification. Am J Clin Nutr 66:261–266, 1997.
90. Gomikawa S, Ishikawa Y: Effects of catechins and ground green tea drinking on the susceptibility of plasma and LDL to the oxidation *in vitro* and *ex vivo*. J Clin Biochem Nutr 32:55–68, 2002.
91. Trevisanato S, Kim Y: Tea and health. Nutr Rev 58:1–10, 2000.
92. Raederstoff DG, Schlachter MF, Elste V, Weber P: Effect of EGCG on lipid absorption and plasma lipid levels in rats. J Nutr Biochem 14:326–332, 2003.
93. Yokozawa T, Nakagawa T, Kitani K: Antioxidative activity of green tea polyphenol in cholesterol-fed rats. J Agric Food Chem 50:3549–3552, 2002.
94. Hertog M, Kromhout D, Aravanis C, Blackburn H, Buzina R, Fidanza F, Gianpaoli S, Jansen A, Menotti A, Nedeljkovic S, Pekkarinen M, Simic B, Toshima H, Feskens E, Hollman P, Katan M: Flavonoid intake and long-term risk of coronary heart disease and cancer in the Seven Countries Study. Arch Intern Med 155:381–386, 1995.
95. Sesso H, Gaziano J, Buring J, Hennekens C: Coffee and tea intake and the risk of myocardial infarction. Am J Epidemiol 149:162–169, 1999.
96. Peters U, Poole C, Arab L: Does tea affect cardiovascular disease? A meta-analysis. Am J Epidemiol 154:495–503, 2001.
97. Hirano R, Momiyama Y, Takahashi R, Taniguchi H, Kondo K, Nakamura H, Ohusuzu F: Comparison of green tea intake in Japanese patients with and without angiographic coronary artery disease. Am J Cardiol 90:1150–1153, 2002.
98. Ohmori R, Momiyama Y, Takahashi R, Taniguchi H, Nakamura H, Kondo K, Ohsuzu F: Inverse association of green tea intake with myocardial infarction (MI) and its genetic variation. Atheroscler Suppl 4:21, 2003.
99. Duffy SJ, Keaney Jr JF, Holbrook M, Gokce N, Swerdloff P, Frei B, Vita JA: Short- and long-term black tea consumption reverses endothelial dysfunction in patients with coronary artery disease. Circulation 104:151–156, 2001.
100. Hertog M, Sweetnam P, Fehily A, Elwood P, Kromhout D: Antioxidant flavonols and ischemic heart disease in a Welsh population of men: The Caerphilly study. Am J Clin Nutr 65: 1489–1494, 1997.
101. McAnlis G, McEneny J, Pearce J, Young I: Black tea consumption does not protect low density lipoprotein from oxidative modification. Eur J Clin Nutr 52:202–206, 1998.
102. Elvin-Lewis M, Vitale MK, Opjas T: Anticariogenic potential of commercial teas. J Prosther Dent 6:273–276, 1980.
103. Mitscher LA, Jung M, Shankel D: Chemoprotection: a review of the potential therapeutic antioxidant properties of green tea (*Camellia sinensis*) and certain of its constituents. Med Res Rev 17:327–332, 1997.
104. Linke HAB, LeGeros RZ: Black tea extract and dental caries formation in hamsters. Int J Food Sci Nutr 54:89–95, 2003.
105. Otake S, Makimura M, Kuroki T: Anticaries effects of polyphenolic compounds from Japanese green tea. Caries Res 25:438–442, 1991.
106. Okamoto M, Sugimoto A, Legun KP, Nakayama K, Kamaguchi A, Maeda N: Inhibitory effect of green tea catechins on cysteine proteinases in Porphyromonas gingivalis. Oral Microbiol Immunol 19:118–120, 2004.
107. Zhang J, Kashket S: Inhibition of salivary amylase by black and green teas and their effects on the intraoral hydrolysis of starch. Caries Res 32:233–236, 1998.
108. Simpson A, Shaw L, Smith AJ: The bio-availability of fluoride from black tea. J Dent 29:15–21, 2001.
109. Lee MJ, Lambert JD, Prabhu S, Meng XF, Lu H, Maliakal P, Ho CT, Yang CS: Delivery of tea polyphenols to the oral cavity by green tea lavels and black tea extract. Cancer Epidemiol Biomarkers Prev 13:132–137, 2004.
110. Elmets CA, Singh D, Tubesing K, Matsui M, Katiyar S, Mukhtar H: Cutaneous photoprotection from ultraviolet injury by green tea polyphenols. J Am Acad Dermatol 44:425–432, 2001.
111. Katiyar SK: Skin photoprotection by green tea: Antioxidant and immunomodulations effects. Curr Drug Targets 3:234–242, 2003.
112. Dulloo AG, Duret C, Rohrer D, Girardier L, Mensi N, Fathi M, Chantre P, Vandermander J: Efficacy of a green tea extract rich in catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans. Am J Clin Nutr 70: 1040–1045, 1999.
113. Zheng G, Sayama K, Okubo T, Junefa LR, Oguni I: Anti-obesity effects of three major components of green tea, catechins, caffeine and theanine in mice. In vivo 18:55–62, 2004.
114. Juhel C, Armand M, Pafumi Y, Rosier C, Vandermander J, Larson D: Green tea extract (AR25®) inhibits lipolysis of triglycerides in gastric and duodenal medium *in vitro*. J Nutr Biochem 11:45–51, 2000.
115. Chantre P, Lairon D: Recent findings of green tea extract AR25® (exolise) and its activity for the treatment of obesity. Phytomedicine 9:3–8, 2002.
116. Tian WX, Li LC, Wu XD, Chen CC: Weight reduction by Chinese medicinal herbs may be related to inhibition of fatty acid synthase. Life Sci 74:2389–2399, 2004.
117. Dulloo AG, Seydoux J, Girardier L, Chantre P, Vandermander J: Green tea and thermogenesis: interactions between catechin-polyphenols, caffeine and sympathetic activity. Int J Obes Relat Metab Disord 24:252–258, 2000.
118. Kovacs EM, Lejeune MP, Nijs I, Westerterp-Plantenga MS: Effects of green tea on weight maintenance after body-weight loss. Br J Nutr 91:431–437, 2004.
119. Wu CH, Lu FH, Chang CS, Chang TC, Wang RH, Chang CJ: Relationship among habitual tea consumption, percent body fat, and body fat distribution. Obes Res 11:1088–1095, 2003a.
120. Anderson RA, Polansky MM: Tea enhances insulin activity. J Agric Food Chem 50:7182–7186, 2002.
121. Wu LY, Juan CC, Hsu YP, Hwang LS: Effect of tea green supplementation on insulin sensitivity in Sprague-Dawley rats. J Agric Food Chem 52:643–648, 2004.
122. Takabayashi F, Harada N, Yamada M, Murohisa B, Oguni I: Inhibitory effect of green tea catechins in combination with sucralfate on *Helicobacter pylori* infection in Mongolian gerbils. J Gastroenterol 39:61–63, 2004.

123. Yee YK, Koo MWL, Szeto ML: Chinese tea consumption and lower risk of Helicobacter infection. J Gastroenterol Hepatol 17:552–555, 2002.
124. Toda M, Okubo S, Ohnishi R, Shimamura T: Antibacterial and bactericidal activities of Japanese green tea. J Nippon Med Sch 44:669–672, 1989.
125. Mukoyama A, Ushijima H, Nishimura S, Koike H, Toda M, Hara Y, Shimamura T: Inhibition of rotavirus and enterovirus infections by tea extracts. Jpn J Med Sci Biol 44:181–186, 1991.
126. Yam TS, Shah S, Hamilton-Miller JM: Microbiological activity of whole and fractionated crude extracts of tea (*Camellia sinensis*), and of tea components. FEMS Microbiol Lett 152:169–174, 1997.
127. Weber JM, Ruzindana-Umunyana A, Sicar S, Cowan J: Adenovirus infection is inhibited *in vitro* by green tea catechins. J Clin Virol 28:S91, 2003.
128. Hirasawa M, Takada K: Multiple effects of green tea catechin on the antifungal activity of antimycotics against *Candida albicans*. J Antimicrob Chemother 53:225–229, 2004.
129. Muraki S, Yamamoto S, Ishibashi H, Horiuchi T, Hosoi T, Suzuki T, Orimo H, Nakamura K: Green tea drinking is associated with increased bone mineral density. J Bone Miner Res 18:S241–S241, 2003.
130. Park H, Ko S, Kim J, Kim S: Effects of green tea extracts and polyphenols on the proliferation and activity of bone cells. J Bone Miner Res 18:S342, 2003.
131. Dorchies OM, Wagner S, Waldhauser KM, Buetler TM, Ruegg UT: Anti-fibrotic properties of green tea catechins on mouse muscle cell cultures. Neuromuscul Disord 13:639, 2003.
132. Sakata R, Ueno T, Nakamura T, Sakamoto M, Torimura T, Sata M: Green tea polyphenols epigallocatechin-3-gallate inhibits platelet-derived growth factor-induced proliferation of human hepatic stellate cell line LI90. J Hepatol 40:52–59, 2004.
133. Bayer J, Gomer A, Demir Y, Amano H, Kish DD, Fairchild PS, Heeger PP: Effects of green tea polyphenols on murine transplant-reactive T cell immunity. Clin Immunol 110:100–108, 2004.
134. Kakuda T: Neuroprotective effects of the tea components theanine and catechins. Biol Pharm Bull 25:1513–1518, 2002.
135. Dajas F, Rivera F, Blasina F, Arredondo F, Echeverri C, Lafon L, Morkio A, Heizen H: Cell cultura protection and *in vivo* neuroprotective capacity of flavonoids. Neurotox Res 5:425–432, 2003.
136. Weinreb O, Mandel S, Amit T, Youdim MB: Neurological mechanisms of green tea polyphenols in Alzheimer's and Parkinson's diseases. J Nutr Biochem 15:506–516, 2004.
137. Sagesaka-Mitane Y, Miwa M, Okada S: Platelet aggregation inhibitors in middle-aged Japanese men and women. Ann Epidemiol 7:280–284, 1997.
138. Dvorakova K, Dorr RT, Valcies S, Timmermann B, Alberts DS: Pharmacokinetics of the green tea derivative, EGCG, by the topical route of administration in mouse and human skin. Cancer Chemother Pharmacol 43:331–335, 1999.
139. Ishizuk H, Eguchi H, Oda T, Ogawa S, Nakagawa K, Honjo S, Kono S: Relation of coffee, green tea, and caffeine intake to gallstone disease in middle-age Japanese men. Eur J Epidemiol 18:401–405, 2003.
140. Thiagarajan G, Chandani S, Sundari CS, Rao SH, Kulkarni AV, Balasubramanian D: Antioxidant properties of green and black tea, and their potential ability to retard the progression of eye lens cataract. Exp Eye Res 73:393–401, 2001.
141. Gupta SK, Halder N, Srivastava S, Trivedi D, Joshi S, Varma SD: Green tea (*Camellia sinensis*) protects against selenite-induced oxidative stress in experimental cataractogenesis. Ophthalmic Res 34:258–263, 2002.
142. Skrzydlewska E, Ostrowska J, Stankiewicz A, Farbiszewski R: Green tea as a potent antioxidant in alcohol intoxication. Addict Biol 7:307–314, 2002b.
143. Ferrari CKB, Torres EAFS: Biochemical pharmacology of functional foods and prevention of chronic diseases of aging. Biomed Pharmacother 57:251–260, 2003.
144. Arburjai T, Natsheh FM: Plants used in cosmetics. Phytother Res 17:987–1000, 2003.
145. Powell JJ, Burden TJ, Thompson RP: *In vitro* mineral availability from digested tea: a rich dietary source of manganese. Analyst 123:1721–1724, 1998.
146. Mann J, Truswell AS: "Essentials of Human Nutrition." New York: Oxford University Press, 1998.
147. Shils ME, Olson JA, Shike M: "Modern Nutrition in Health and Disease." Malvern: Lea and Febiger, 1994.
148. García E, Cabrera C, Lorenzo ML, Sánchez J, López MC: Daily dietary intake of chromium in southern Spain measured with duplicate diet sampling. Br J Nutr 86:391–396, 2001.
149. Fennema OR: "Food Chemistry." New York: Dekker, 2000.
150. Younger KM: Dietary Reference Standards. In Gibney MJ, Vorster HH, Kok FJ (eds): "Introduction to Human Nutrition." Oxford: Blackwell Science, pp 116–124, 2002.
151. Institute of Medicine: "Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium and Carotenoids." Washington: National Academy Press, 2000.
152. Institute of Medicine: "Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium and Zinc." Washington: National Academy Press, 2002.
153. Hasegawa N, Niimi N, Odani F: Vitamin C is one of the lipolytic substances in green tea. Phytother Res 16:91–92, 2002.
154. Shimada K, Takahashi M, Haji A, Kaminohara M, Matsuda N, Nomura A, Sawano E, Saeki K: Changes in contents and extractabilities of some ingredients in tea leaves during manufacturing process of green tea (sencha). J Jpn Soc Food Sci 43:695–702, 1996.
155. García-Closas R, Berenguer A, Tormo JM, Sánchez MJ, Quiros JR, Navarro C, Arnaud R, Dorronsoro M, Chirlaque MD, Barricarte A, Ardanaz E, Amiano P, Martínez C, Agudo A, González CA: Dietary sources of vitamin C, vitamin E and specific carotenoids in Spain. Br J Nutr 91:1005–1011, 2004.
156. Pulido R, Hernández-García M, Saura-Calixto F: Contribution of beverages to the intake of lipophilic and hydrophilic antioxidants in the Spanish diet. European J Clin Nutr 57:1275–1282, 2003.
157. Fisher C, Scott TR: "Food Flavours. Biology and Chemistry." Cambridge: The Royal Society of the Chemistry, 1997.
158. López FF, Cabrera C, Lorenzo ML, López MC: Aluminum content in foods and beverages consumed in the Spanish diet. J Food Sci 65:206–210, 2000.

159. Minoia C, Sabbioni E, Ronchi A, Gatti A: Trace element reference values in tissues from inhabitants of the European Community. IV. Influence of dietary factors. Sci Total Environ 141:181–195, 1994.
160. Massey RC, Taylor D: "Aluminum in Food and the Environment." London: Royal Society of Chemistry, 1991.
161. Flaten TP: Aluminum in tea concentrations, speciation and bioavailability. Coordin Chem Rev 228:385–395, 2002.
162. Tuntawiroon M: Dose-dependent inhibitory effect of phenolic compounds in foods on non-heme iron absorption in men. Am J Clin Nutr 53:554–557, 1991.
163. Hurrell RF: "Prospects for improving the iron fortification of foods." In Fomon S, Zlotkin S (eds): "Nutricional anemias." New York: Raven Press, pp 193–208, 1992.
164. Hamdaoui MH, Chabchob S, Heidhili A: Iron bioavailability and weight gains to iron-deficient rats fed a commonly consumed Tunisian meal "bean seeds ragout" with or without beef and with green or black tea decoction. J Trace Elem Med Biol 17:159–164, 2003.
165. Al-Othaimeen A, Osman A, Al-Orf S: Prevalence of nutritional anaemia among primary school girls in Riyadh City, Saudi Arabia. Int J Food Sci Nutr 50:237–243, 1999.
166. Gibson S: Iron intake and iron status of preschool children: Associations with breakfast cereals, vitamin C and meat. Public Health Nutr 2:521–528, 1999.
167. Belitz DH, Grosch W: "Química de los Alimentos." Zaragoza: Acribia, 1997.
168. Suzuki Y, Tsubono Y, Nakaya N, Suzuki Y, Koizumi Y, Tsuji I: Green tea and the risk of breast cancer: pooled analysis of two prospective studies in Japan. Br J Cancer 90:1361–1363, 2004.
169. Huang X, Tajima K, Hamajima N, Inoue M, Takezaki T, Kuroishi T, Hirose K, Tominaga S, Xiang J, Tokudome S: Effect of life styles on the risk of subsite-specific gastric cancer in those with and without family history. J Epidemiol 9:40–45, 1999.
170. Shibata K, Moriyama M, Fukushima T, Kaetsu A, Miyazaki M, Une E: Green tea consumption and chronic atrophic gastritis: a cross-sectional study in a green tea production village. J Epidemiol 10:310–316, 2000.
171. Kuwahara Y, Kono S, Eguchi H, Hamada H, Shinchi K, Imanishi K: Relationship between serologically diagnosed chronic atrophic gastritis, Helicobacter pylori, and environmental factors in Japanese men. Scand J Gastroenterol 35:476–481, 2000.
172. Setiawan VW, Zhang ZF, Yu GP: Protective effect of green tea on the risk of chronic gastritis and stomach cancer. Int J Cancer 92:600–604, 2001.
173. Tsubono Y, Nishino Y, Komatsu S, Hsieh C, Kanemura S, Tsuji I, Nakatsuka H, Fukao A, Satoh H, Hisamichi S: Green tea and the risk of gastric cancer in Japan. New Engl J Med 344:632–636, 2001.
174. Hoshiyama Y, Kawaguchi T, Miura Y, Mizoue T, Tokui N, Yatsuya H, Sakata K, Kondo T, Kikuchi S, Toyoshima H, Hayakawa N, Tamakoshi A, Ohno Y, Yoshimura T: A prospective study of stomach cancer death in relation to green tea consumption in Japan. Br J Cancer 87:309–313, 2002.
175. Fujino Y, Tamakoshi A, Ohno Y, Mizoue T, Tokui N, Yoshimura T: Prospective study of education background and stomach cancer in Japan. Prev Med 35:121–127, 2002.
176. Wang LD, Zhou Q, Feng CW, Liu B, Qi YJ, Zhang YR, Gao SS, Fan FM, Zhou Y, Yang CS, Wei JP, Zheng S: Intervention and follow-up on human esophageal precancerous lesion in Henen, northern China, a high-incidence area for esophageal cancer. Gan To Kagaku Ryoho 29:159–172, 2002.
177. Nagano J, Kono S, Preston DL, Mabuchi K: Bladder-cancer incidence in relation to vegetable and fruit consumption: a prospective study of atomic-bomb survivors. Int J Cancer 86:132–138, 2000.
178. Zhong L, Golberg MS, Gao YT, Hanley JA, Parent ME, Jin F: A population-based case-control study of lung cancer and green tea consumption among women living in Shanghai, China. Epidemiology 12:695–700, 2001.
179. Yoshida M, Kimura Y, Abe M, Ando T, Tachi H, Fukunaga K: Quantitative evaluation of selenium contained in tea by high performance liquid chromatography. Nutr Sci Vitaminol 47:248–252, 2001.

Received March 18, 2005; revision accepted December 20, 2005.