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Beneficial effects of green tea: A literature review

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Abstract

The health benefits of green tea for a wide variety of ailments, including different types of cancer, heart disease, and liver disease, were reported. Many of these beneficial effects of green tea are related to its catechin, particularly (-)-epigallocatechin-3-gallate, content. There is evidence from *in vitro* and animal studies on the underlying mechanisms of green tea catechins and their biological actions. There are also human studies on using green tea catechins to treat metabolic syndrome, such as obesity, type II diabetes, and cardiovascular risk factors.
Long-term consumption of tea catechins could be beneficial against high-fat diet-induced obesity and type II diabetes and could reduce the risk of coronary disease. Further research that conforms to international standards should be performed to monitor the pharmacological and clinical effects of green tea and to elucidate its mechanisms of action.

Background

In recent years, the health benefits [1] of consuming green tea, including the prevention of cancer [2] and cardiovascular diseases [3], the anti-inflammatory [4], antiarthritic [5], antibacterial [6], antiangiogenic [7], antioxidative [8], antiviral [9], neuroprotective [10], and cholesterol-lowering effects [11] of green tea and isolated green tea constituents are under investigation. However, adding green tea to the diet may cause other serious health concerns.

The health-promoting effects of green tea are mainly attributed to its polyphenol content [12], particularly flavanols and flavonols, which represent 30% of fresh leaf dry weight [1]. Recently, many of the aforementioned beneficial effects of green tea were attributed to its most abundant catechin, (-)-epigallocatechin-3-gallate (EGCG) [13-15]. Green tea extracts are more stable than pure epigallocatechin gallate, one of the major constituents of green tea, because of the presence of other antioxidant constituents in the extract [8]. In general, herbal medicines are complex mixtures of different compounds that often act in a synergistic fashion to exert their full beneficial effect [11]. However, relatively few herbal medicines have been well characterized and their efficacy demonstrated in systematic clinical trials as compared to Western drugs. This review article highlights the recent research on the efficacy, action mechanisms, and side effects of green tea and its catechins in *in vitro*, *in vivo*, and *ex vivo* systems [16].

The review on green tea and its catechins focused on language literature in English. The literature search was conducted in the following databases: Pubmed (1980-2009), EMBASE (1980-2009), Allied and complementary Medicine Database (AMED, 1985-2009) and China Journals Full Text Database (1975-2009). The keywords used were selected from the following terms: green tea, catechins, anticancer, diabetes, polyphenols, *in vivo* studies, general pharmacology and toxicology. The health benefits and adverse effects of green tea and its catechins were reviewed.

The authors read full articles and reached consensus after discussion. Articles included in the study covered the following effects of green tea: (1) the health benefits in humans and animals, (2) absorption of metal ions and drug-metabolizing enzymes, (3) antioxidation and inhibition of oxidative stress, (4) carbohydrate metabolism and diabetes mellitus, and (5) adverse effects. A total of 105 peer-reviewed papers in English were selected for this review.

Green tea

Tea is one of the most popular beverages consumed worldwide. Tea, from the plant *Camellia sinensis*, is consumed in different parts of the world as green, black, or Oolong tea. Among all of these, however, the most significant effects on human health have been observed with the consumption of green tea [17]. The first green

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tea was exported from India to Japan during the 17th century. It is estimated that about 2.5 million tons of tea leaves are produced each year throughout the world, with 20% produced as green tea, which is mainly consumed in Asia, some parts of North Africa, the United States, and Europe [18]. The association between tea consumption, especially green tea, and human health has long been appreciated [19,20]. Green tea and black tea are processed differently during manufacturing. To produce green tea, freshly harvested leaves are immediately steamed to prevent fermentation, yielding a dry, stable product. This steaming process destroys the enzymes responsible for breaking down the color pigments in the leaves and allows the tea to maintain its green color during the subsequent rolling and drying processes. These processes preserve natural polyphenols with respect to the health-promoting properties. As green tea is fermented to Oolong and then to black tea, polyphenol compounds (catechins) in green tea are dimerized to form a variety of theaflavins, such that these teas may have different biological activities.

Table 1 Composition (%) of green tea, black tea, and black tea infusion [21]

Compound	Green Tea*	Black tea*	Infusion*
Protein	15	15	trace
Amino acids	4	4	3.5
Fiber	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
Oxidized phenolic compounds§	0	25	4.5

* Data refer to dry weight of tea leaves.
† Infusion time: 3 minutes
‡ Especially flavonoids
§ Especially thearubigins and theaflavins

Green tea composition

The chemical composition of green tea is complex: proteins (15-20% dry weight), whose enzymes constitute an important fraction; amino acids (1-4% dry weight) such as theanine or 5-*N*-ethylglutamine, glutamic acid, tryptophan, glycine, serine, aspartic acid, tyrosine, valine, leucine, threonine, arginine, and lysine; carbohydrates (5-7% dry weight) such as cellulose, pectins, glucose, fructose, and sucrose; minerals and trace elements (5% dry weight) such as calcium, magnesium, chromium, manganese, iron, copper, zinc, molybdenum, selenium, sodium, phosphorus, cobalt, strontium, nickel, potassium, fluorine, and aluminum; and trace amounts of lipids (linoleic and α-linolenic acids), sterols (stigmasterol), vitamins (B, C, E), xanthic bases (caffeine, theophylline), pigments (chlorophyll, carotenoids), and volatile compounds (aldehydes, alcohols, esters, lactones, hydrocarbons). Due to the great importance of the mineral presence in tea, many studies have determined their levels in tea leaves and their infusions (Table 1) [21]. Fresh leaves contain, on average, 3-4% of alkaloids known as methylxanthines, such as caffeine, theobromine, and theophylline [22]. In addition, there are phenolic acids such as gallic acids and characteristic amino acid such as theanine present [22].

Green tea contains polyphenols, which include flavanols, flavandiols, flavonoids, and phenolic acids; these compounds may account for up to 30% of the dry weight. Most of the green tea polyphenols (GTPs) are flavonols, commonly known as catechins. Products derived from green tea are mainly extracts of green tea in liquid or powder form that vary in the proportion of polyphenols (45-90%) and caffeine content (0.4-10%). The major flavonoids of green tea are various catechins, which are found in greater amounts in green tea than in black or Oolong tea [23]. There are four kinds of catechins mainly find in green tea: epicatechin, epigallocatechin, epicatechin-3-gallate, and EGCG [24]. The preparation methods influence the catechins both quantitatively and qualitatively; the amount of catechins also varies in the original tea leaves due to differences in variety, origin, and growing conditions [25]. The preparation of fresh green tea cannot totally extract catechins from the leaves; therefore, the concentration found differs from the absolute values determined through the complete extraction of leaves [26]. Moreover, catechins are relatively unstable and could be quantitatively and qualitatively modified during the time frame of an experiment [27,28]. Thus, comparison of ingested doses in animal studies is not possible because the catechin quantification before administration is often not known.

Health benefits of green tea in humans and animals

Studies using animal models show that green tea catechins provide some protection against degenerative diseases [29]. Some studies indicated that green tea has an antiproliferative activity on hepatoma cells and a hypolipidemic activity in hepatoma-treated rats, as well as the prevention of hepatoxicity [29] and as a preventive agent against mammary cancer post-initiation [29]. Green tea catechins could also act as antitumorigenic agents [30] and as immune modulators in immunodysfunction caused by transplanted tumors or by carcinogen treatment [29]. Moreover, green tea, its extract, and its isolated constituents were also found to be effective in preventing oxidative stress [31] and neurological problems [32].

Green tea consumption has also been linked to the prevention of many types of cancer, including lung,

colon, esophagus, mouth, stomach, small intestine, kidney, pancreas, and mammary glands [33]. Several epidemiological studies and clinical trials showed that green tea (and black and Oolong teas to a lesser extent) may reduce the risk of many chronic diseases [34]. This beneficial effect has been attributed to the presence of high amounts of polyphenols, which are potent antioxidants. In particular, green tea may lower blood pressure and thus reduce the risk of stroke and coronary heart disease. Some animal's studies suggested that green tea might protect against the development of coronary heart disease by reducing blood glucose levels and body weight [35]. However, all these data are based on middle-aged animals' populations, not the elderly populations, which nutritional status tends to be more adversely influenced by age-related biological and socioeconomic factors [36].

Tea components possess antioxidant, antimutagenic, and anticarcinogenic effects and could protect humans against the risk of cancer by environmental agents [37]. Sano *et al*. [38] reported the inhibitory effects of green tea leaves against tert-butyl hydroperoxide-induced lipid peroxidation, and a similar antioxidant effect on the kidney was observed after oral administration of the major tea polyphenol EGCG. The antioxidative potency of crude catechin powder and individual catechins was tested in experiments using the active oxygen method. Crude catechins reduced the formation of peroxides far more effectively than dl-α-tocopherol [39]. Shim *et al*. [40] studied the chemopreventive effect of green tea among cigarette smokers and found that it can block the cigarette-induced increase in sister chromatid exchange frequency.

The effectiveness of green tea in treating any type of diarrhea and typhoid has been known in Asia since ancient times [41-43]. Green tea catechins have an inhibitory effect on *Helicobacter pylori* infection [44,45]. 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 [46-48]. Furthermore, Weber *et al*. [9] observed that adenovirus infection is inhibited *in vitro* by green tea catechins.

In humans, Hirasawa and Takada [49] studied the antifungal activity of green tea catechins against *Candida albicans* and the convenience of a combined treatment with catechins and lower doses of antimycotics, which 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 effect was considered independent of smoking status, hormone replacement therapy, coffee drinking, and the addition of milk to tea [50]. Park *et al*. [51] observed the positive effects of green tea extracts and GTPs on the proliferation and activity of bone cells. 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 [52,53]. Green tea strengthens the immune system action because it protects it against oxidants and radicals. Recent studies suggested that GTPs might protect against Parkinson's and Alzheimer's diseases and other neurodegenerative diseases [10,54]. Studies have demonstrated GTP neuroprotectant activity in cell cultures and animal models, such as the prevention of neurotoxin-induced cell injury [54]. Green tea is considered to be useful for insect stings due mainly to its anti-inflammatory effects and its capacity to stop bleeding [55,56]. Some studies have suggested an inverse association between green tea consumption and the risk of kidney stone formation [41,57]. In an experimental cataractogenesis system, green tea acted by preserving the antioxidant defense system of the lens [58]. Skrzydlewska *et al*. [59] indicated a beneficial effect of green tea in alcohol intoxication. In addition to all of these reported properties, which have helped the recognition of green tea as functional food by some authors [60], green tea is also currently used in the preparation of a variety of foods, pharmaceutical preparations, dentifrices, and cosmetics [61].

Tea has been shown anticarcinogenic effects against breast cancer in experimental studies [62]. However, epidemiologic evidence that tea protects against breast cancer has been inconsistent [62]. A case-control study was conducted in southeastern China between 2004 and 2005 [63]. The incidence cases were 1009 female patients aged 20-87 years with histologically confirmed breast cancer, and the 1009 age-matched controls were healthy women randomly recruited from breast disease clinics. Information on duration, frequency, quantity, preparation, and type of tea consumption as well as diet and lifestyle were collected by face-to-face interviews using a validated and reliable questionnaire. In comparison with non-tea drinkers, green tea drinkers tended to reside in urban settings, to have more education, and to consume more coffee, alcohol, soy, vegetables, and fruits. After adjusting established and potential confounding factors, green tea consumption was associated with a reduced risk of breast cancer. Similar dose-response relationships were observed for duration of drinking green tea, number of cups consumed, and new batches prepared per day.

Hsu *et al*. [64] demonstrated the effects of supplementation with decaffeinated green tea extract (catechins) on hemodialysis-induced reactive oxygen species, atherosclerotic disease risk factors, and proinflammatory cytokines. The pharmacokinetics of one oral dose of

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