

# Anti-obesity effects of green tea extracts on humans

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## Abstract

**Introduction:** Green tea is heavily promoted and sold over the counter for many illnesses, including obesity.

**Methodology:** Literature was reviewed focusing on the key words; tea, green tea, catechin, overweight, obesity, side effects, adverse effects, transient ischemic attack, stroke and liver function, up to December 2014.

**Results and discussion:** Majority of the studies on this topic were short term and involved only a small number of participants. Though these studies demonstrated very small reduction of weight, evidence was inadequate for the use of green tea as an anti-obesity agent. In this review, the effect of green tea on obesity and some possible harmful effects of green tea are discussed. Current evidence on green tea does not support the use of it as an anti-obesity agent. There are several reports of side effects. The liver side effects are a cause for concern.

**Conclusions:** Long term use of green tea as over the counter supplement should not be encouraged. Rather it should be considered a drink, very much like any other tea or coffee, till further evidence of efficacy and safety are proven.

**Key words:** green tea, catechin, caffeine, overweight and obesity

## Introduction

Obesity, the most prevalent metabolic disease worldwide, affects adults, adolescents and children by reaching epidemic proportions. Obesity is an excess of adipose tissue in relation to lean body mass. Body mass index (BMI) and waist circumference (WC) are used as surrogates for adiposity, on routine examinations (1). Obesity, especially central obesity is a risk factor for number of chronic diseases, including type 2 diabetes mellitus, ischaemic heart disease and hypertension (1, 2). Modest weight loss at 5-10% of the initial body weight, leads to reduction of risk of mortality and morbidity that have been linked with obesity and is a realistic goal (1, 3).

Judicial use of dietary agents combined with physical activity and reduction of energy consumption are safer than the surgical and pharmacological methods in controlling obesity (2, 4). Green tea, a non-fermented tea prepared by tea (*Camellia sinensis*, Theaceae) leaves, is a functional food ingredient and has been reported to have anti-obesity properties. Worldwide people consume this tea on a daily basis as a beverage, especially in Asian countries. Green tea, a dietary agent has been reported to

be effective in prevention of obesity by epidemiological and laboratory studies (2, 5-8). However, it has been found that it imparts some harmful effects such as hepatotoxicity if consumed in large quantities for a long period of time. Anti-obesity effects of green tea on humans are discussed in this review.

## Methodology

Literature was reviewed focusing on the key words; tea, green tea, catechin, overweight, obesity, side effects, adverse effects, transient ischaemic attack, stroke and liver function up to December 2014. Discussion is targeted on obesity, composition of green tea, mechanism of action, epidemiological and interventional studies, body weight maintenance, pharmacokinetics, harmful effects and transient ischemic attack.

## Results and discussion

### Composition of green tea

Tea (*Camellia sinensis*, Theaceae) is the most popular beverage next to water, consumed by over two-

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third of the world's population (4, 5, 9, 10). The main types of tea; black, oolong and green tea differ in terms of processing and chemical composition. Green tea is prepared by initial heating to inactivate the endogenous enzymes, while oolong and black tea are fermented. Tea leaves contain main energy sources; protein, carbohydrate, lipids and other health beneficial and flavoring components such as polyphenols, tannins, vitamins, minerals, volatile compounds, pigments and caffeine. Polyphenols and caffeine, the main components in a cup of tea are responsible for astringency and refreshment, respectively (11-13). Catechin, a colorless polyphenol is highly present in leaves at harvest and varied with the processing conditions and the variety of tea. Green tea preserves a large amount of catechins from oxidation than of others due to absence of fermentation step in processing (9). Furthermore, the amount of catechins in a cup of tea is highly variable, depending on preparation method adopted including the ratio of dry tea to water, temperature of water and the immersion time of leaves in hot water (9, 14-16).

Tea contains four major catechins; (-)-epicatechin (EC), (-)-epigallocatechin (EGC), (-)-epicatechin-3-gallate (ECG), and (-)-epigallocatechin-3-gallate (EGCG). EGCG is the most abundant and possesses the most potent anti-oxidative activity (2, 6, 14, 17-20). A cup of green tea contains 50-150 mg of catechins and 7.8-30 mg of caffeine (9, 21-23). Canned tea contains 0.3-35 mg of catechins/100 mL (24). Iced tea was found not to contain any flavanols (25). Average green tea catechin consumption in United Kingdom (200 mL cup) is 405.5 mg/day and in Japan (120 mL cup) is 200-400 mg/day (23, 26).

According to label claims, commercially available green tea formulations supply 150-800 mg catechins/day, 22.5-700 mg EGCG/d and 5.5-8.0 mg caffeine/day when taken as recommended. However, measured catechins contents were found to be 9-48% though the label claimed 100%, according to a study conducted in USA (27-32).

### **Mechanism of action**

Physiological functions of catechins are mainly ascribed to the gallate esters of 'epi' catechins (7, 10). Potential mechanisms by which catechins prevent development of overweight and obesity involve inhibition of adipocyte differentiation and proliferation, reduced fat absorption, inhibition of gastric and pancreatic lipases, increased energy expenditure and fat oxidation via stimulating thermogenesis by inhibition of catechol-O-methyl-transferase (COMT) which is a catecholamine-degrading enzyme, synergism with caffeine and suppression of fatty acid synthesis (17, 14, 33-37).

COMT inhibitory activity is possessed by all gallate-catechins and is highest for EGCG, a non-competitive inhibitor with half maximal inhibitory concentration (IC<sub>50</sub>)

of 70nM (38). However, inter-individual variability of COMT activity could vary as much as threefold and the effects of catechins on energy expenditure may vary depending on genetic variability in COMT activity (14, 39, 40). Besides, there is a large subject-to-subject variability in the pharmacokinetics of catechins (41).

### **Epidemiological and interventional studies**

Green tea is widely consumed in China, Japan, Korea and Morocco. Green tea has been considered by the traditional Chinese medicine as a healthful beverage. An epidemiological study revealed that 43% of Chinese were habitual tea drinkers and 96% of them were green or oolong tea consumers (42). The authors of this study found that longer the duration of tea consumption, lower the percent body fat, waist circumference (WC), hip circumference, and waist-to-hip ratio. Short term (375 mg catechins/d and 150 mg caffeine/d) as well as long term (570.4 mg catechins/d with regular exercise for 2 months) consumption of green tea increases fat utilization and energy expenditure in sedentary conditions (43, 44). The effect of EGCG (300 mg/d for 2 days) on fat oxidation is higher under post-prandial than fasting conditions in men (45). Long term ingestion of tea catechins stimulates dietary induced thermogenesis and dietary fat oxidation (34).

Two hundred and seventy (270) mg/d EGCG with 600 mg of caffeine a day has been reported to be the optimal concentration to produce an effect on macronutrient oxidation and to increase energy expenditure in sedentary conditions (46, 47). Beyond this threshold, the EGCG content of a compound containing a fixed dose of caffeine (600 mg/d) only produces a small non-significant additional increase in 24 h energy expenditure (46). However, the caffeine dose used here is twice as the habitual caffeine intake and may hinder the effects of EGCG. Table 1.0 shows the effect of different quantities of catechins and caffeine in tea on percentage body weight reduction of humans. Above studies show that 491 mg catechins/day resulted in lesser reduction in percentage of weight than 468, 458 and 444 mg catechins/day (9, 48, 49). The considerable higher percentage of weight loss with 666 mg catechins/day than with 680 mg EGCG/day may be due to lower body mass index (BMI) of subjects and the synergistic effect of all the catechins rather than from EGCG only (50, 51). BMI ranges of subjects used by Maki et al. were wider and they lost more weight (2.2 kg) than the subjects in the other study (1.7 kg), although both 625 and 583 mg catechins/day have shown similar weight reduction (20, 52).

Hsu et al. studied Tai women having 27.6 > BMI < 34.8 and the subjects had ingested capsules containing green tea extract three times daily 30 min after a meal (48). In other two studies Japanese adults had ingested beverages twice daily with meal (9, 49). BMIs of the subjects ranged from 22.5-30 with Kajimoto et al. and 24-35 with Wang et al.

**Table 1. Effect of green tea on body weight reduction**

Composition		Intake period/ week	Body weight reduction %	Reference
Catechin/ (mg/d)	caffeine/ (mg/d)			
172 (EGCG)	138	06	1.6 <sup>S</sup>	Bajerska et al., 2010 [50]
236	97	24	1.5 <sup>NS</sup>	Stendell-Hollis et al., 2010 [53]
300 (EGCG)	low habitual caffeine intake	12	0.1 <sup>NS</sup>	Hill et al., 2007 [47]
444	50	12	0.7 <sup>S</sup>	Kajimoto et al., 2005 [49]
458	104	12	1.0 <sup>NS</sup>	Wang et al., 2010 [9]
468	126	12	1.0 <sup>NS</sup>	Wang et al., 2010 [9]
491	27.3	12	0.3 <sup>NS</sup>	Hsu et al., 2008 [48]
583	130	12	2.3 <sup>S</sup>	Nagao et al., 2007 [20]
625	115	12	2.3 <sup>S</sup>	Maki et al., 2009 [52]
665.9	50	12	1.0 <sup>S</sup>	Kajimoto et al., 2005 [49]
680 (EGCG)	49	06	0.8 <sup>S</sup>	Bajerska et al., 2010 [50]
690	75	12	3.2 <sup>S</sup>	Nagao et al., 2005 [27]
886	198	12	1.7 <sup>S</sup>	Wang et al., 2010 [9]

S- Significant and NS- Non-significant at  $p < 0.05$

(9,49). High catechin:caffeine ratio given by Hsu et al. and low bioavailability of catechins when given as capsules compared to the beverage form may have caused lesser reduction in percentage body weight (48). Furthermore, Tai women may be less sensitive to catechins.

Two hundred and thirty six (236) mg catechins/day caused 1.5% weight reduction while 458 mg catechins/day accounted for 1% reduction (9, 53). This can be justified by longer duration of treatment with frequent dosing which had led to stable catechin and caffeine plasma concentrations, by Stendell-Hollis et al., compared to Wang et al. (9, 53).

All these studies have been of short duration, most lasting 12 weeks. Most of the research have failed to show a clinically significant, i.e. 5-10%, weight loss. However, 5.5% and 14.3% weight losses have been reported by Diepvens et al. and Pierro et al., respectively (38, 54). In the former study, reduction was due to 1207 mg catechins/day and 300 mg caffeine/day with hypocaloric diet in healthy females while the latter was due to 300 mg/day of Monoselect Camellia® (a preparation containing a standardized green tea extract complexed with phospholipids amount of catechins was not cited) with hypocaloric diet (38, 54). However, when compared with placebo, green tea has no effect on body weight or body composition (54).

Table 2 shows the WC reduction in several studies with catechins. Significant decrease in total fat area was

observed with the doses of 690, 666 and 444 mg catechins/day; reduction in visceral fat area with 666, 583 and 444 mg catechins/day were observed; reduction in subcutaneous fat area was observed with 690 and 583 mg catechins/day; and reduction in abdominal fat area was observed with 625 mg of catechins/day during exercise (20, 27, 49, 52).

Catechins render better results on body weight and WC when combined with dietary control, physical activity and caffeine intake than ingesting catechins alone. Furthermore, maintaining the ratio of catechins:caffeine around 1:1 is important in weight reduction strategies (50).

### Body weight maintenance

Habitual high caffeine (270 mg EGCG + 150 mg caffeine/day) consumption was found to reduce the body weight, fat mass and WC more than in low caffeine consumption, through thermogenesis and fat oxidation. Weight maintenance after weight loss was not affected by green tea, supplying caffeine (104 mg/d) and catechins (573 mg/d) for 13 weeks, in overweight and moderately obese humans (55). However, habitual high caffeine consumption was associated with a higher weight regain compared with habitual low caffeine consumption (55).

Administration of EGCG and caffeine with diet supplying  $\approx 10\%$  total energy from protein is effective for weight maintenance following weight loss in overweight and moderately obese humans (3). However, considerably

Table 2. Effect of green tea on WC reduction

Composition		WC reduction/cm	Reference
Catechin/ (mg/d)	caffeine/ (mg/d)		
236	-	0.9 <sup>NS</sup>	Stendell-Hollis et al., 2010 [53]
300(EGCG)	-	1.0 <sup>S</sup>	Hill et al., 2007 [47]
375 in an uncontrolled study	-	4.1 <sup>NS</sup>	Chantre et al., 2002 [33]
444	-	0.9 <sup>S</sup>	Kajimoto et al., 2005 [49]
458	104	1.1 <sup>NS</sup>	Wang et al., 2010 [9]
468	126	1.3 <sup>NS</sup>	Wang et al., 2010 [9]
491	-	1.7 <sup>S</sup>	Hsuet al., 2008 [48]
583	-	0.7 <sup>S</sup>	Nagao et al., 2007 [20]
625	-	0.9 <sup>NS</sup>	Maki et al., 2009 [52]
666	-	0.8 <sup>S</sup>	Kajimoto et al., 2005 [49]
690	75	3.4 <sup>S</sup>	Nagao et al., 2005 [27]
886	198	1.9 <sup>S</sup>	Wang et al., 2010 [9]
1207	-	4.5 <sup>S</sup>	Diepvens et al., 2006 [54]

S- Significant and NS- Non-significant at  $p < 0.05$

high level of hunger and lower satiety were reported in this diet and may result in weight gain with additional intake of meals or snacks (3). Although both green tea-caffeine mixture and high protein diets have proven to be effective in weight maintenance followed by weight loss, synergistic effect has not been reported (3).

### Pharmacokinetics

After ingestion peak plasma concentrations ( $C_{max}$ ) of catechins were reached rapidly and gradually reduced to undetectable levels in 24 h (19, 56, 57).  $C_{max}$ , time to reach  $C_{max}$  and elimination half-life of EGCG rise in a dose dependent manner (19, 41). Caffeine or other catechins have been reported to affect the pharmacokinetics of EGCG (19, 74). Bioavailability of EGCG is higher than that of EGC and EC (19).

Oral bioavailability of catechins from supplements exceeds that of brewed tea (14). A significant fraction of the orally administered catechins is eliminated presystemically or is decomposed during intestinal absorption and in blood (11, 19, 41). This can result from ingestion of catechins with meals, transportation of absorbed EGCG back into intestine by P-gp, multi drug resistance gene product, and/or ionization of catechins when stomach pH is increased (3, 11, 39, 41). In contrast, Van het Hof et al. found that addition of skimmed milk has no effect on bioavailability of catechins (56). However, the percentage of milk added to tea used in this study is lower than that used in previous studies (56). Catechins were found in human saliva, blood and

urine after mouth rinsing and oral administration of catechins as solutions (11).

The catechins are metabolized by the liver and kidneys, and excreted in bile and urine (11). They are subjected to extensive biotransformation including methylation, glucuronidation, sulfation and ring-fission metabolism (11). In plasma, EGCG and EGC have been reported to be mostly present in the free form (41, 57). EGC and EC have been detected in plasma and urine, predominantly as glucuronic acid and sulfate conjugates (19). Free EC levels were very low or undetectable in plasma (19, 41). In physiological conditions, it is very likely that EGCG is oxidatively decomposed, but not (+)-catechin (11). The decomposition of EGCG and EGC was found in a short time, even at pH 7.4 (11).

### Harmful effects

Green tea has been widely consumed in China and Japan for many centuries and is generally regarded safe (39). Table 3.0 summarizes the health effects of green tea intake in different quantities of catechins, caffeine and flavanols.

However, several cases were reported on hepatotoxicity of green tea intake in different products consumed for  $\geq 1$  month as shown in Table 4. In all cases, patients had taken the relevant product of green tea extract for weight maintenance and had not any history of liver disease, alcohol use and risk factors for viral hepatitis. According to case reports of consumption of

**Table 3. Effect of green tea on health**

<i>Composition/ (mg/d)</i>	<i>Time duration of the intake</i>	<i>Health effects</i>	<i>Reference</i>
886 catechins and 198 caffeine	90 days	No differences of liver function tests	Wang et al., 2010 [9]
844 catechins	14 days	Alter the activity of the enzymes cytochrome P-450 2D6 and 3A4	Donovan et al., 2004 [58]
800EGCG	4 weeks	No alteration of phenotypic indices of CYP1A2, CYP12D6, and CYP12C9, but resulted in a small reduction in CYP3A4 activity	Chow et al., 2006 [59]
670 flavanols	3 weeks	No alterations of markers of liver and kidney function in healthy men	Frank et al., 2009 [60]
625 catechins and 39 caffeine	12 weeks	No liver toxicity	Maki et al., 2009 [52]
666 catechins			Kajimoto et al., 2005 [49]
800EGCG	4 weeks	No significant changes in blood counts and blood chemistry profiles	Chow et al., 2003 [57]
300EGCG	12 weeks	No adverse effects	Hill et al., 2007 [47]
583 catechins	12 weeks		Nagao et al., 2007 [20]
Population based study, Japan		No significant association between liver cancer risk and green tea consumption	Inoue et al., 2009 [61]
Increased consumption of green tea, meta analysis		Reduce the risk of liver disease	Jin et al., 2008 [62] Sing et al., 2011 [63]

green tea-based supplements, histological examination revealed inflammatory, cholestatic or necrotic liver damage depending on the subject (2). In ~20% of case reports, additional liver damage following re-challenge with the same preparation was observed (2). However, no clear determinants for the type of pathology observed have been reported (2). US Pharmacopoeia Dietary Supplements Information Expert Committee has proposed that all green tea extract products should bear a label that suggests consumption together with food because of the possibility of severe liver problems (17).

Oral bolus dosing results in greatly increased  $C_{max}$  of EGCG compared with dietary administration and divided doses of the same total daily dose (2, 57). Caffeine content, presence of aluminum, and the affinity of catechins on iron are the major harmful effects of over consumption of tea (5). Green tea extracts may exert diuresis, excess gas, nausea, heartburn, stomachache, abdominal pain, diarrhea, dizziness, headache, muscle pain, increased levels of transaminases and serum bilirubin, blood pressure elevation and decreased dietary iron absorption (2, 5, 33, 46, 57). The incidence of gastrointestinal adverse events increased at higher doses

under fasting conditions and with bolus dosing (41, 57). Green tea consumption is not advisable in cases of special sensitiveness to xanthic bases (5). Negative effects produced by caffeine are nervousness, sleep disorders, vomiting, headache, epigastric pain, tachycardia, palpitation, anxiety, restlessness, dizziness and high blood pressure (5, 39). Even though, acute caffeine consumption may alter some cardiovascular variables, chronic ingestion of caffeine has little or no health consequences (39).

Supplements of green tea contain much higher catechin and caffeine doses than green tea beverages, in different dosage forms and may cause harmful effects (2). One capsule has been reported to be equal to 5-7 cups of tea. These capsules are usually taken more than one a day. Furthermore, United Kingdom tea council has recommended intake of 3-4 cups of tea per day for health benefits and intake of >6 cups of tea is not beneficial to health (58-63).

### **Green tea and transient ischemic attack**

A meta analysis from nine studies involving 4378

**Table 4. Hepatotoxicity of green tea extract**

<i>Composition</i>	<i>Age/year</i>	<i>Gender</i>	<i>Time duration of the intake/Month</i>	<i>Harmful effect</i>	<i>Reference</i>
720 mg/day green tea extract	44	Female	6	Acute liver toxicity with hepatitis	Molinari et al., 2006 [66]
Green tea extract	37	Female	4	Nausea, abdominal pain and jaundice	Bonkovsky, 2006 [67]
'Hydroxycut'; green tea extract	27	Male	1	Fatigue and jaundice	Stevens et al., 2005 [68]
'Euphoria'; herbal product including green tea	45	Female	1	Jaundice	Jimenez-Encarnacion et al., 2012 [69]
'SlimQuick'; herbal product including green tea	24	Female	3	Jaundice	Weinstein et al., 2012 [70]
'Fat burners'; green tea	28	Female	1	Jaundice	Krishna et al., 2011 [71]
'Hydroxycut' or	31	Female	3	Jaundice	Chen et al., 2010 [72]
'Herbalife' products; green tea extract	37 53		4 12		
'Hydroxycut'; green tea extract	23	Female	2	Jaundice	Rashid and Grant, 2010 [73]

strokes among 194, 965 individuals has revealed that daily consumption of either green or black tea equaling three cup per day could prevent the onset of ischemic stroke (64). Furthermore, regardless of their country of origin, individuals consuming  $\geq 3$  cups of tea per day had a 21% lower risk of stroke than those consuming  $< 1$  cup per day (absolute risk reduction, 0.79; CI, 0.73 to 0.85) (64).

However, according to a case report, transient ischemic attack-like symptoms could possibly be attributed to one or more components of oolong tea, especially when consumed in large quantities (65).

## Conclusions

Catechins render a very modest effect on reducing body weight and waist circumference when combined with dietary control, physical activity and caffeine intake than ingesting catechins alone. However, 300 mg/d of Monoselect Camellia® is the only preparation that showed a clinically and statistically significant weight loss (14.3%). Nevertheless, this study was conducted with hypocaloric diet. Except very few studies most have been conducted for twelve week duration. Hence, further large randomized, long term studies are needed to determine whether this product demonstrates an anti-obesity effect with or without hypocaloric diet. Contrasting results have been found when green tea is

used to maintain weight following weight loss. Current evidence on green tea does not support the use of it as an anti-obesity agent. There are several reports of side effects. The liver side effects are a cause for concern. Therefore long term use of green tea as over the counter supplement should not be encouraged. Rather it should be considered a drink, very much like any other tea or coffee, till further evidence of efficacy and safety are proven.

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