

REVIEWS: CURRENT TOPICS

Antiobesity effects of green tea catechins: a mechanistic review

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Abstract

Green tea catechins (GTC) are polyphenolic compounds present in the unfermented dried leaves of the plant, *Camellia sinensis*. Results from a number of randomized, controlled intervention trials have shown that consumption of GTC (270 mg to 1200 mg/day) may reduce body weight and fat. There are several proposed mechanisms whereby GTC may influence body weight and composition. The predominating hypothesis is that GTC influences sympathetic nervous system (SNS) activity, increasing energy expenditure and promoting the oxidation of fat. Caffeine, naturally present in green tea, also influences SNS activity, and may act synergistically with GTC to increase energy expenditure and fat oxidation. Other potential mechanisms include modifications in appetite, up-regulation of enzymes involved in hepatic fat oxidation, and decreased nutrient absorption. This article reviews the evidence for each of these purported mechanisms, with particular reference to studies in humans.

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1. Introduction

Obesity and the comorbidities associated with obesity remain a global health problem [1]. Recent estimates in the USA indicate that approximately one-third of the adult population is obese [2]. Although there are many proposed genetic and environmental factors that predispose individuals to weight gain, the fundamental cause of obesity is an imbalance between dietary intake and energy expenditure. Excess fat mass develops over time from a very small positive energy imbalance. In general, average weight gain per year is small, approximately 0.5 kg across all race, economic, and sex groups [3,4].

There are many dietary, and to a lesser extent, pharmacological strategies which have been shown to affect energy balance in a manner that results in successful weight reduction [5]. Such therapies typically affect one or more aspects of energy balance including appetite, nutrient absorption, or thermogenesis. Epidemiological evidence and several randomized controlled intervention trials have shown an inverse relationship between habitual tea consumption (predominately green tea) and levels of body fat and waist circumference [6,7]. While green tea contains an array of compounds, the putative antiobesity effects have been most commonly attributed to the polyphenolic fraction of green tea, specifically the catechins [8]. Green tea catechins (GTC) may affect multiple aspects of energy balance that, in aggregate, result in body weight and fat loss. In this paper, we review the relationships between GTC consumption and

body composition and discuss the purported mechanisms whereby GTC may confer antiobesity activity.

2. Green tea catechins

Green tea is brewed from the unfermented dried leaves of the plant, *Camellia sinensis*. Like other natural products, the leaves of this plant contain an array of phytochemicals that vary in concentration by the harvest season, age of the plant, climate, environmental conditions and processing conditions [9,10]. The predominant constituents of green tea, accounting for up to 35% of the dry weight, are the polyphenols, which include flavonols, flavones, and flavan-3-ols. (Table 1). Of these, 60–80% are the flavan-3-ols commonly known as catechins. By comparison, oolong and black tea, which are produced from partially fermented or completely fermented *C. sinensis* leaves, respectively, contain approximately half the catechin content of green tea [10,11].

Epigallocatechin-3-gallate (EGCG) is the most abundant catechin of green tea, representing 50–80% of the total catechin content [12]. It is also considered to be the most bioactive component of green tea [13]. Other minor catechins include epicatechin-3-gallate (ECG), epigallocatechin (EGC), epicatechin and catechin. The remaining solids of green tea include caffeine, theanine, theaflavins, thearubigins, quercetin, and other phenolics such as gallic acid and chlorogenic acid. GTC are absorbed in the intestine, however studies indicate large subject-to-subject variability in the pharmacokinetics of green tea catechins [14,15]. The bioavailability of GTC from supplements exceeds that of brewed tea, and the presence of food significantly blunts the absorption of GTC into circulation [12,14].

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Table 1
Flavonoid composition of brewed green tea^a

Components	Amount mg/100 g (100 ml)
Epigallocatechin 3-gallate	77.8±7.0
Epicatechin 3-gallate	19.7±2.8
Epigallocatechin	16.7±1.4
Epicatechin	8.3±0.5
Quercetin	2.7±0.3
Catechin	2.6±1.5
Gallocatechin	1.5±0.0
Thiarrubigins	1.1±1.1
Theaflavin	0.1±0.0
Total Flavonoids ^b	130.5

^a USDA Database for the Flavonoid Content of Selected Foods [11].

^b Total flavonoid content is estimated as the sum of individual flavonoids which include the following five subclasses: flavonols, flavones, flavanones, flavan-3-ols and anthocyanidins.

A typical brewed green tea beverage (250 ml) contains 50–100 mg catechins and 30–40 mg caffeine [12,16]. Preparation methods, including the amount of plant material used, brewing time, and water temperature, have all been reported to affect the composition of bioactive compounds in brewed tea [17]. Therefore, the concentration of bioactive components of green tea can vary widely. Standardized GTC beverages, supplements, and extracts have been developed for research or commercial purposes in an effort to provide uniform levels of GTC and/or EGCG. The majority of these products contain GTC that are equivalent to three or more servings of green tea.

3. Antiobesity effects of green tea catechins

Over the past 10 years, there have been a number of mostly small trials in humans showing favorable effects of GTC (270 to 1200 mg/d) on body weight [16,18–21] and body composition under free-living conditions [16,18–24], although not all studies showed consistent results [25–28]. A recent meta-analysis of 11 GTC trials reported an average body weight loss of 1.31 kg for subjects in the treatment groups relative to controls, with most intervention periods being approximately 12 weeks [29].

The majority of trials in humans showing reductions in body weight and fat mass with GTC consumption have examined subjects of Asian descent (see Ref. [29] for review). A recent meta-analysis of 11 trials showed that the average effect of GTC on body weight loss was larger for Asian participants (−1.51 kg) versus Caucasian participants (−0.82 kg) [29]. However, positive findings were reported by Maki et al. [24] who compared the effects of a high-GTC-beverage (625 mg/d GTC+39 mg caffeine) versus a control beverage (39 mg caffeine) in Caucasian subjects with increased central adiposity following a moderate-intensity exercise program (≥180 min/week) for 12 weeks. Reductions in abdominal fat area (−7.7 vs. −0.3%) and subcutaneous abdominal fat area (−6.2 vs. 0.8%), as measured by computerized tomography, were greater in the GTC group as compared to control, despite only a marginal difference in body weight loss (−2.2 vs. −1.0 kg). Other studies in Caucasian subjects have shown similar, favorable results [30], although it is plausible that subjects of Asian descent are more responsive to the effects of GTC potentially due to greater adiposity at a given body mass index compared to Caucasian subjects or other factors as discussed later in this review.

The favorable effects of GTC on obesity-related outcomes may be partly attributable to the caffeine component of green tea. Caffeine is known to independently increase energy expenditure, however daily caffeine intake (200 mg/d) has not resulted in greater body weight loss in longer-term feeding trials [31–33]. A recent meta-analysis of six randomized, controlled trials evaluating the antiobesity effects of

GTC (median 588 mg/d)+caffeine compared to caffeine alone showed significant reductions in body weight (−1.38 kg) and waist circumference (−1.93 cm) with the GTC+caffeine condition [7]. A meta-analysis indicated that studies providing GTC in the absence of caffeine did not result in significant differences in body weight or waist circumference relative to caffeine-free controls, although only two studies were included in the meta-analysis [28,34]. It is important to note that not all studies using GTC+caffeine mixtures produced favorable changes in body weight or body composition [25–27].

The effectiveness of GTC+caffeine on anthropometric changes may be influenced by habitual caffeine intake. Studies in which GTC+caffeine was consumed as part of a weight maintenance period following 4 weeks of a very-low-energy diet showed that weight and waist regain was attenuated in the subjects habitually consuming less than 300 mg/d of caffeine [35,36]. The authors speculated that GTC+caffeine may only be effective when habitual caffeine intake is below a certain threshold and that higher doses of GTC are necessary when habitual caffeine intakes are high. This is consistent with a recent trial in Thai men and postmenopausal women, a population that habitually consumes low levels of caffeine, in which consumption of low levels of GTC (141 mg/d)+caffeine (87 mg) as compared to a caffeine-free placebo for 8 weeks resulted in greater losses of body weight (−4.4 vs. −1.9 kg), waist circumference (−6.6 vs. −5.8 cm) and total body fat (−7.2 vs. −3.0%) [18].

4. Antiobesity mechanisms of green tea catechins

The mechanisms whereby GTC influence body weight and body composition remain an active area of investigation. Much of the work in humans has focused on the effects of GTC on thermogenesis and substrate oxidation, both of which are mediated by sympathetic nervous system activity. Other potential mechanisms include modifications in appetite control, down-regulation of enzymes involved in hepatic lipid metabolism, and decreased nutrient absorption. Evidence for each of these purported mechanisms, with particular reference to studies in humans, will be presented (Fig. 1).

4.1. Energy expenditure

The sympathetic nervous system (SNS) plays a major role in the regulation of energy expenditure and lipolysis. Substances that stimulate or prolong the presence of norepinephrine (NE), a key mediator of SNS activity, increase energy expenditure and promote the oxidation of fat. In 1975, Borhardt and Huber provided evidence that GTC inhibits catechol O-methyltransferase (COMT), the enzyme that degrades norepinephrine, thus prolonging the action of sympathetically-released NE in the synaptic cleft [37]. Caffeine, naturally present in green tea, also influences SNS activity via inhibition of phosphodiesterase, the enzyme which rapidly degrades intracellular cyclic adenosine monophosphate (cAMP), a signal released in response to NE [38]. It is plausible that when consumed together, GTC and caffeine act synergistically, resulting in pronounced effects on the SNS and thus, energy expenditure and lipolysis.

This hypothesis has been explored in a number of trials in humans by measuring changes in energy expenditure after consumption of GTC+caffeine. In aggregate, most acute studies with GTC+caffeine mixtures (including studies using oolong tea) have shown modest increases in 24-h energy expenditure relative to caffeine-free controls (3–4%) [39–42,45]. Long-term studies on energy expenditure suggest that this effect persists over time [18]. Dulloo et al. [41] conducted one of the first studies in young men following a single dose of encapsulated GTC [375 mg (270 mg EGCG)+150 mg caffeine]. Subjects showed a 4% increase in 24-h energy expenditure following the GTC treatment, whereas there was no change following 150 mg caffeine alone (Table 2). Although

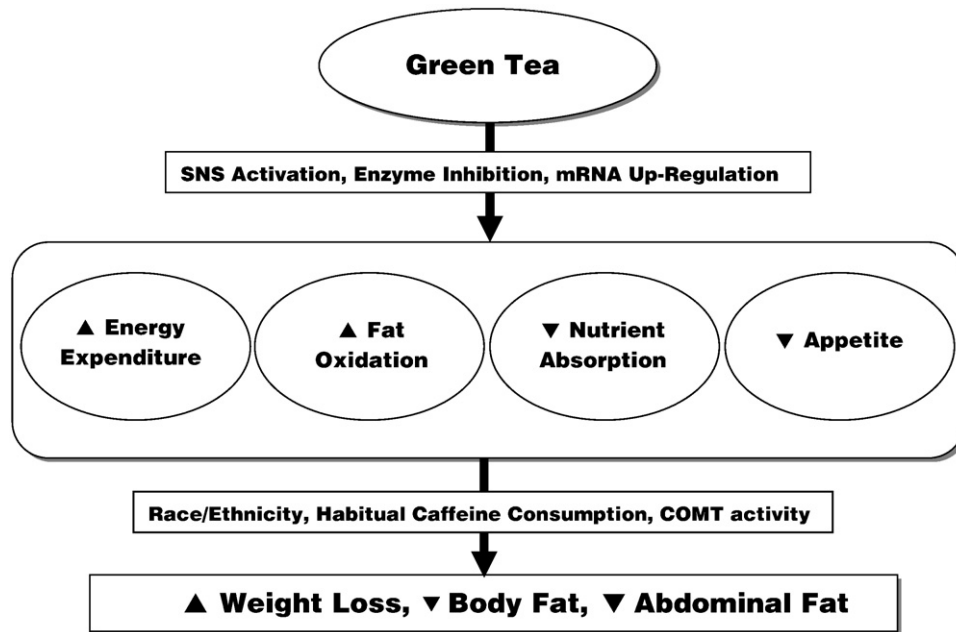


Fig. 1. Proposed antiobesity mechanisms of green tea.¹

¹ These are factors for which there are data or strong theoretical reasons to believe that they are important in the antiobesity activity of green tea. There are insufficient data to systematically evaluate other factors such as the role of gender or physical activity on outcomes such as weight loss and body composition.

the absence of an effect on energy expenditure following this dose of caffeine is in conflict with other studies, the data suggest that GTC in combination with caffeine promotes increased 24-h energy expenditure. The notion that a GTC+caffeine combination is necessary to elicit an effect on 24-h energy expenditure is in agreement with results from other studies where EGCG or GTC alone failed to increase energy expenditure [43,46].

Caffeine is known to independently stimulate energy expenditure in a dose-dependent manner, with doses as low as 100 mg showing effects [31,33]. With the exception of Dulloo et al. [41], the few studies that have compared catechin+caffeine mixtures to an equivalent amount of caffeine have failed to show meaningful increases in energy expenditure (Table 2). For example, Gregersen et al. [44] compared the effects of different doses of GTC (493–840 mg+150 mg caffeine) on 14-h energy expenditure in young men. There was a nonsignificant trend toward increased energy expenditure (<2%) on the GTC treatment with the highest dose of EGCG (607 mg) only as compared to 150 mg caffeine alone. However, the treatment was administered in five small doses over 11 h, which may be below the threshold needed to elicit a positive response on energy expenditure.

Rumpler et al. [39] evaluated the effects of oolong tea at full strength (612 mg catechins+270 mg caffeine) and oolong tea at half strength (306 mg catechins+135 mg caffeine) compared to a caffeine-containing control (270 mg caffeine) and caffeine-free control (water) in young men. Results showed greater 24-h energy expenditure (~3%) for both the full-strength oolong tea and caffeine treatments relative to water. There were no differences between the full-strength tea and caffeine control conditions. Bérubé-Parent et al. [42] compared the effects of three doses of EGCG (600, 900 and 1200 mg) on 24-h energy expenditure in men at a fixed dose of caffeine (600 mg). Compared to a caffeine-free placebo, all doses of EGCG increased energy expenditure by 8%, without any apparent effect of increased doses of EGCG. However, this high level of caffeine may increase SNS activity to a level that would mask incremental effects of GTC catechins on energy expenditure. Therefore, whether GTC or catechins (e.g., EGCG) increase energy

expenditure independent of caffeine and the actual magnitude of the increase remain to be elucidated.

It has been recently proposed that the effects of GTC on energy expenditure may vary depending on genetic variability in COMT enzyme activity [29]. A single nucleotide polymorphism [Val(158) Met SNP, rs4680] leads to either a methionine (Met) or valine (Val) substitution at codon 158, resulting in a three- to fourfold reduction in COMT activity in humans carrying this allele [47]. Differences in COMT activity have been previously shown to influence energy expenditure following anti-depressant therapy, such that individuals with the low-activity COMT enzyme allele are at increased risk for weight gain [48]. Therefore, it is plausible that variations in COMT activity may influence the effects of GTC on energy expenditure. Interestingly, Asian populations show a higher frequency of the high-activity COMT enzyme allele, or the Val/Val polymorphism, whereas Caucasian populations exhibit a higher frequency of the low-activity COMT enzyme allele, or the Met/Met polymorphism [49,50]. Thus, a potential explanation for why studies examining GTC effects on energy expenditure in Asian populations have shown more favorable results versus those in Caucasian subjects may be that individuals of Asian descent are more sensitive to the effects of GTC on energy expenditure and other SNS-mediated outcomes (Table 2).

4.2. Alterations in fat metabolism

Another potential mechanism whereby GTC induce antiobesity effects may relate to changes in fatty acid oxidation and metabolism. Under the influence of the SNS, NE stimulates lipolysis in peripheral tissues (adipose, liver, skeletal muscle), releasing free fatty acids into circulation and up-regulating hepatic lipid metabolism. Augmenting sympathetic stimulation by inhibition of COMT and phosphodiesterase would, theoretically, be expected to increase fat oxidation [43]. Studies in rodents support this hypothesis [51,52]; however, studies in humans have shown mixed results on the respiratory quotient (RQ), an indicator of the ratio of fat to carbohydrate oxidation (Table 2). Dulloo et al. [41] reported that GTC (375 mg+150 mg

Table 2
Effects of green tea catechins on energy expenditure and RQ in humans under resting conditions^a

Authors, year	Duration	Population	Treatment	Energy Expenditure ^b	RQ/Substrate oxidation ^b
Auvichayapat et al., 2008 [18]	12 wk	n=60 Thai men/women	• 141 mg GTC+87 mg caffeine • Caffeine-free placebo	• ↑ REE (+3.2%)	• ↓ RQ (-3.6%) ^c
Belza et al., 2009 [19]	1 d	n=12 Caucasian men	• 500 mg GTE (125 mg GTC) • 50 mg caffeine • Caffeine-free placebo	• ↔ 4 h EE • ↑ 4 h EE (+6.0%)	–
Berube-Parent et al., 2005 [42]	1 d	n=12 Caucasian men	• 270 mg EGCG+600 mg caffeine • 600 mg EGCG+600 mg caffeine • 900 mg EGCG+600 mg caffeine • 1200 mg EGCG+600 mg caffeine • Caffeine-free placebo	• ↑ 24 h EE (+8.0%) • ↑ 24 h EE (+8.0%) • ↑ 24 h EE (+8.0%) • ↑ 24 h EE (+8.0%)	• ↔ RQ • ↔ RQ • ↔ RQ • ↔ RQ
Boschmann et al., 2007 [43]	2 d	n=6 Caucasian men	• 300 mg EGCG+0 mg caffeine • Caffeine-free placebo	• ↔ 4 h EE	• ↓ RQ (-3.5%)
Dulloo et al., 1999 [41]	1 d	n=10 Caucasian men	• 375 mg GTC (270 mg EGCG)+150 mg caffeine • 150 mg caffeine • Caffeine-free placebo	• ↑ 24 h EE (+4.0%) • ↔ 24 h EE	• ↓ RQ (-3.4%) • ↔ RQ
Gregersen et al., 2009 [44]	1 d	n=15 Caucasian men	• 607 mg EGCG+150 mg caffeine • 572 mg EGCG+150 mg caffeine • 494 mg GTC (mixed)+150 mg caffeine • 150 mg caffeine • Caffeine-free placebo	• ↔ 14 h EE • ↔ 14 h EE • ↔ 14 h EE • ↔ 14 h EE	• ↔ RQ • ↔ RQ • ↔ RQ • ↔ RQ
Komatsu et al., 2003 [40]	Acute	n=11 Japanese women	• Green tea (156 mg EGCG+161 mg caffeine) • Oolong tea (81 mg EGCG+77 mg caffeine) • Water	• ↑ 2 h EE (50 kJ/2h) • ↑ 2 h EE (111 kJ/2 h)	• ↔ RQ • ↔ RQ
Rudelle et al., 2007 [45]	3 d	n=31 Caucasian men/women	• 540 mg GTC (282 mg EGCG)+300 mg caffeine+633 mg calcium • Caffeine-free control	• ↑ 24 h EE (4.6%)	• ↔ fat ox
Rumpler et al., 2001 [39]	3 d	n=12 Caucasian men	• Oolong tea (612 mg catechins+270 mg caffeine) • Oolong tea (306 mg catechins+135 mg caffeine) • 270 mg caffeine • Water	• ↑ 24 h EE (2.9%) • ↔ 24 h EE • ↑ 24 h EE (3.4%)	• ↑ fat ox (12%) • ↔ fat ox • ↑ fat ox (8%)
Westerterp-Plantenga et al., 2005 [36]	3 mo	n=76 Caucasian men/women	• 270 mg EGCG+150 mg caffeine • Caffeine-free placebo	• ↑ EE ^d	• ↓ RQ ^d

GTE, green tea extract; EE, energy expenditure; REE, resting energy expenditure.

^a Table includes studies available in English.

^b Study outcomes are summarized as significantly increasing (↑), decreasing (↓), or producing no change (↔) in EE or RQ/substrate oxidation relative to the placebo or control condition.

^c Significant difference at 8 weeks only.

^d EE and RQ were increased and decreased, respectively, in subjects habitually consuming low levels of caffeine plus the EGCG+caffeine treatment during a 3 month weight maintenance period following a 4-week very low energy weight loss diet.

caffeine) decreased RQ by 3.4% relative to a caffeine-free placebo, suggesting an increase in fat oxidation, whereas there was no effect of caffeine alone (150 mg). A similar effect (−3.5%) was observed following an acute dose of 300 mg EGCG in Caucasian men [43]. Other acute feeding studies have not shown changes in fat oxidation relative to caffeine-free controls [40,42,44]. However, it has been suggested that the effects of GTC on fat oxidation are cumulative over time, a hypothesis that is supported by evidence in animal studies [6,52]. GTC, particularly EGCG, up-regulated the expression of several genes involved in hepatic beta-oxidation in mice following 1 month of feeding, including acyl-CoA oxidase and medium chain acyl-CoA dehydrogenase [52]. This was accompanied by a decrease in the expression of hepatic fatty acid synthase and an increase in beta-oxidation by 285% compared to control mice following a low-fat diet. Such findings were not apparent 24 h after feeding GTC. As such, acute feeding studies may not reflect the potential chronic effects of GTC on fat oxidation and substrate utilization.

Evidence on the long-term effects of GTC on fat oxidation is sparse. Auvichayapat et al. [18] evaluated RQ following GTC ingestion (141 mg GTC+87 mg caffeine) versus a caffeine-free control as part of a weight loss program in Thai men and women. Values for RQ were not different at week 4 from baseline or between groups, but declined significantly at week 8 (−3.6%, $P<.05$ versus baseline and the control group). By week 12, RQ returned to levels observed at baseline, however the study authors indicated that compliance with the intervention program was compromised during the last 4 weeks of the trial.

Indirect evidence from intervention trials suggests that GTC may alter fat metabolism by promoting lipolysis from specific fat depots. The fat depots of the abdomen appear to be more responsive to NE-induced lipolysis than those in other depots [53]. Abdominal fat is more lipolytically active than lower body adipose depots, altering fatty acid uptake and release in a way that selectively reduces abdominal adipose tissue more so than peripheral fat depots. Nagao et al. [22] evaluated the effects of a brewed green tea beverage (~75 mg caffeine) with added GTC (583 mg) as compared to a caffeine-matched control beverage (96 mg GTC) in Japanese men and women undergoing treatment for diabetes, a population with high prevalence of increased abdominal adiposity. At the end of the 12 week intervention period, body weight did not differ between the GTC and control groups; however, waist circumference was significantly reduced (−3.3 cm) in those consuming the GTC. Maki et al. [24] reported similar results in Caucasian men and women with increased abdominal adiposity following a 12-week intervention period with GTC (624 mg+39 mg caffeine) and an exercise program (≥ 180 min/week). Total abdominal fat area, and particularly subcutaneous abdominal fat area measured with computed tomography, were significantly reduced (−7.7 and −6.2 cm², respectively) at week 12 versus the control group, despite there being no significant difference between groups in body weight loss (−2.2 vs. −1.0 kg).

The authors of the present review hypothesize that the effects of GTC may be greatest under conditions of elevated NE release, such as during exercise. Venables et al. [54] reported that healthy Caucasian men ingesting three capsules of GTC (340 mg polyphenols/

capsule+0 mg caffeine) in the 24-h preceding a moderate-intensity exercise session increased fat oxidation by 17% as compared to a caffeine-free placebo, suggesting that GTC amplify the effects of exercise on fat oxidation, possibly through increased lipolysis. Ota et al. [55] showed similar results in young Japanese men consuming a GTC beverage (570 mg+40 mg caffeine) as part of an exercise program (90 min/week) for 8 weeks. Fat oxidation was increased in the GTC group under both exercising and sedentary conditions as compared to a placebo. Unfortunately, neither study included a nonexercise condition that would allow for direct comparison. Hill et al. [28] failed to show differences in abdominal fat in overweight and obese Caucasian women consuming 300 mg/d EGCG (0 mg caffeine) as part of a moderate-intensity exercise program (135 min/week) for 12 weeks compared to a placebo. Therefore, the available data are inconclusive regarding the relationship between GTC intake and exercise. Whether habitual caffeine intake, race/ethnicity or exercise intensity/duration further influence the effects of GTC on fat metabolism remains to be determined.

4.3. Appetite inhibition

Substances known to increase hepatic fatty acid oxidation, such as beta-adrenergic agonists, decrease voluntary food intake in rats [56,57]. It has been hypothesized that energy status within the liver, primarily the production of ATP, triggers signals to the appetite-regulating centers of the brain by vagal sensory neurons [58–60]. As such, when hepatic fatty acid oxidation is low and there is a concomitant decrease in ATP levels, appetite is increased. Consumption of medium-chain fatty acids and 1,3-diacylglyceride oil, ingredients that increase hepatic fatty acid oxidation, have been shown to reduce food intake in human subjects [61,62]. Given the evidence that GTC may increase hepatic fat oxidation, it is plausible that appetite may be altered by GTC.

Studies in animals provided with GTC or EGCG are inconsistent with regards to effects on food intake [13,52,63]. When GTC or EGCG were provided orally, there was no decrease in voluntary food intake [51,64–66]. Conversely, Kao et al. [63] showed that rats treated with EGCG by intraperitoneal injection had a reduction in food intake of 50–60% versus control rats. Studies on voluntary food intake in humans are limited, although Belza et al. [19] conducted a short-term trial in normal weight men. Subjects consumed 8% (~95 kcal) less energy at an ad libitum meal 4 h following consumption of 500 mg green tea extract versus placebo. Additionally, Gregersen et al. [44] assessed subjective appetite sensations with visual analog scales while subjects were housed in a respiratory chamber for 14 h. There were no significant differences between GTC and placebo.

Several longer feeding studies have assessed subjective appetite by visual analog scales or indirectly, via evaluation of diet records. Auvichayapat et al. [18] measured appetite in men and women ingesting a GTC supplement (141 mg GTC+87 mg caffeine) for 12 weeks. Appetite scores did not differ from baseline or between the active or placebo groups. Other studies which have analyzed food intake by 3-day diet records have also failed to show differences in reported energy intake over time, despite favorable outcomes for body weight or body fat [16,24]. However, such self-reported diet recalls may not be sensitive enough to detect small changes in dietary intake that may have an effect on body weight and fat mass over time.

4.4. Reduced nutrient absorption

Decreased nutrient absorption in the gastrointestinal tract has been proposed as a potential mechanism explaining the antiobesity effects of GTC. In vitro data suggest that GTC may reduce glucose absorption by inhibiting gastrointestinal enzymes involved in

nutrient digestion, in particular, α -amylase and α -glucosidase activity [67,68]. Cellular studies have also shown that GTC decreases glucose uptake in intestinal cells and inhibits the sodium-dependent glucose transporter [69,70]. Indeed, Zhong et al. [71] reported that test meals containing a mixture of green tea (100 mg ECG and 300 mg EGCG), black tea and mulberry tea resulted in carbohydrate malabsorption of 25% (~60 kcal) compared to placebo in healthy adults, as assessed by breath hydrogen analysis. Similar results have been reported in animal studies [72]. Studies in both rats and humans have also reported decreased blood glucose levels following an oral glucose tolerance test when coadministered with oral intakes of GTC and EGCG [54,72–75].

Interestingly, the timing of green tea catechin intake may differentially affect the absorption and metabolism of glucose. Park et al. [75] reported that when GTC (specifically EGCG and ECG) were administered one hour prior to a glucose load, circulating glucose levels actually exceeded those of the water control. They speculate that GTC, and in particular, the gallated catechins, inhibit circulating glucose uptake via competitive inhibition of glucose transporters located throughout the body. The increase in glucose was accompanied by an increase in insulin levels. Therefore, it is possible that GTC hinder absorption of glucose within the intestine when co-ingested, which would decrease circulating glucose, but GTC may also decrease transport of circulating glucose into peripheral tissues when consumed prior to a glucose-containing meal, resulting in higher levels of plasma glucose and insulin. Whether this temporal effect of GTC on blood glucose and insulin levels influences acute and long-term efficacy of GTC on energy expenditure, fat oxidation or weight loss remains to be determined.

It has been reported that GTC may also disrupt fat digestion and absorption. Chan et al. [76] showed that hamsters supplemented with GTC produced feces with increased concentrations of total fatty acids, neutral sterols and acidic sterols compared with a control group, however other data do not support this finding [77,78]. GTC may modify fat absorption by disrupting several critical steps in the digestion and transport of lipids across the enterocyte. Juhel et al. [79] reported that GTC inhibited gastric and pancreatic lipase activity. Perhaps related to this, GTC, particularly EGCG, has been shown to disrupt normal micelle formation by decreasing lipid solubility and size dose-dependently in in vitro biliary micelle models [80–83]. In vitro studies have also shown that GTC has the capacity to form complexes with specific transporters that reside on the brush border membrane, which might reduce the uptake of lipids by the enterocytes [84].

Whether this mechanism plays a meaningful role in humans is not presently known. Zhong et al. [71] did not show any effect of a green tea extract (100 mg ECG and 300 mg EGCG) on fat malabsorption using breath $^{13}\text{CO}_2$ analysis. To the best of our knowledge, the effect of GTC on fecal fat excretion in humans has not been reported in the literature. However, Hsu et al. [85] showed that a polyphenol-enriched oolong tea increased fecal fat content by ~50% (~90 kcal/3 days fecal collection) as compared to a placebo. There was a trend for greater excretion of fecal cholesterol during the oolong tea period.

5. Conclusion

Over the last decade, there have been a number of intervention trials showing reductions in body weight and fat after chronic consumption of GTC with caffeine. Early mechanistic work suggested that GTC may increase energy expenditure, stimulating thermogenesis to a greater degree than caffeine alone. However, as indicated in this review, more recent investigations have not universally supported that hypothesis. The relationship between GTC and caffeine and thermogenesis is, at present, unclear, and future work should seek to clarify the influence of habitual caffeine intake and individual

differences in COMT enzyme activity on energy expenditure under both acute and chronic study conditions. Other possible mechanisms, including increased fat oxidation, decreased appetite, and disrupted nutrient absorption, may also play roles in the antiobesity effects of GTC. These mechanisms may also be influenced, at least in part, by concomitant caffeine intake and variations across populations in enzyme activities. Furthermore, the influences of dose, method of intake (e.g., empty or full stomach, supplement, brewed beverage, etc.), duration of intake, sex, degree of adiposity and potential positive interaction with physical activity merit further inquiry in both mechanistic studies and randomized, controlled intervention trials.

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