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Can Green Tea Extract Promote Weight Loss?

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Green tea extract (GTE) is used in energy and pre-workout drinks due to its advertised effects of burning fat and boosting metabolism. Celsius Live Fit is a fitness drink and dietary supplement that claims to provide healthy energy, accelerate metabolism, and burn body fat during a workout. The key ingredients within this thermogenic drink are green tea leaf extract, caffeine, and ginger extract. The ingredients in these drinks may be successful in improving metabolic and thermogenic adaptations in the body (Lockwood et al., 2010). Thermogenic drinks may increase resting energy expenditure (REE), respiratory exchange ratio (RER), and glycerol appearance, an indication of the rate of lipolysis (a higher glycerol appearance reflects an increased breakdown of fat), which could lead to improvements in body composition overtime (Dalbo et al., 2008). The purpose of this research paper is to explore the effects of GTE on metabolism and weight loss. Many studies have explored the effects of combining GTE and exercise on health outcomes such as improvements in body composition, fat oxidation during exercise, and anti-inflammatory and metabolic markers.

Green Tea Extract

GTE is a popular dietary supplement that is derived from green tea plant leaves. Important components that make up green tea leaves are polyphenols, caffeine, amino acids, minerals, vitamins, and enzymes (Senanayake, 2013). Polyphenols are secondary metabolites that carry one or more hydroxyl groups and are known for their antioxidant properties and prevention of chronic diseases (Scalbert, Johnson, & Saltmarsh, 2005). Catechins, a group of polyphenols, more specifically flavonoids, which make up a substantial portion of green tea leaves and are found to be responsible for many of the benefits that accompany ingestion of green tea or GTE (Senanayake, 2013). The four main catechins that exhibit beneficial effects on factors relating to obesity are epigallocatechin-3-gallate (EGCG), epicatechin-3-gallate,

epigallocatechin (EGC), and epicatechin (Hodgson, Randell & Jeukendrup, 2013). The components that make up green tea leaves can be consumed via a GTE capsule, drink infused with GTE or by simply drinking green tea. Green tea is unfermented and is made by inactivating polyphenol oxidase via heat or steam in fresh leaves which inhibits catechin oxidation. Following this, the leaves are rolled, dried, and then packaged in tea bags, which are later soaked in hot water to make tea (Senanayake, 2013). GTE, on the other hand, is obtained by extracting water from green tea leaves. The extract can then be infused into drinks like Celsius, or added into capsules, which are then ingested (Kaur et al., 2008).

Effects of GTE at Rest

One of the benefits of ingesting GTE is its positive effect on metabolic processes in the body. GTE ingestion has been linked to increases in energy expenditure and a greater contribution of fat oxidation to total energy expenditure. A study by Hodgson et al. (2013) explored the effects of GTE supplementation at rest and during exercise. In this randomized, double-blind, parallel research study, it was hypothesized that there would be an increase in lipolysis at rest. Participants (27 males that were overall healthy and physically active) were divided into two groups, a GTE group (1200 mg catechins, 240 mg caffeine/day) and a placebo group (Hodgson et al., 2013); the drink was consumed for seven days. After seven days, the effect of GTE on participants was determined to increase metabolic processes at rest. Results showed positive changes such as a notable increase in lipolysis (increase in glycerol, reduction in TAGs, increased fat oxidation and increase in 3-hydroxybutrate), glycolysis (increase in lactaldehyde), and tricarboxylic acid cycle (increase in citrate) as well as reduced Cori cycle (reduction in alanine), amino acid catabolism (reduction in urea and creatine). This suggests GTE is capable of body composition changes like weight loss, but due to the brevity of the

research intervention, significant changes in weight could not be observed (Hodgson et al., 2013). These results lead to the conclusion that GTE, even at rest, is capable of inciting favorable changes in energy expenditure and fat oxidation.

Effects of GTE and Exercise

Though GTE is capable of altering metabolic functioning at rest, these changes are further enhanced when GTE supplementation is combined with exercise. A study by Bagheri et al. (2019) explored the anti-inflammatory effects of GTE and endurance exercise on fat loss over an eight-week period. Obesity seems to be a growing problem in the modern world which leads to an increased risk of chronic diseases such as diabetes mellitus, metabolic syndrome, and cardiovascular diseases. A way to combat this is through the promotion of endurance exercise which has been found to lower pro-inflammatory biomarkers and produce an anti-inflammatory effect (Bagheri et al., 2019). This research aimed to explore the effect of combining endurance training and GTE in inactive, overweight women. In this randomized, double-blind study, 30 participants were assigned to one of three intervention groups [endurance training + placebo (ET+P), endurance training + GTE (ET+GTE) (GTE capsule: 500 mg, ~75% polyphenol catechins and 15 mg caffeine), and the control group – no exercise]. These participants were overweight, sedentary (did not engage in exercise for at least 6 months before the study) women (38.36 ± 3.16 years) who were healthy, not taking supplements or medications, and did not report any alcohol consumption (Bagheri et al., 2019).

In the Bagheri et al. (2019) intervention, GTE supplementation and endurance exercise differed between groups to observe effects on anthropometric measurements and plasma levels of inflammatory mediators (adiponectin, irisin, interleukin 6 (IL-6), tumor necrosis factor- α (TNF- α), and high-sensitivity C-reactive protein (hs-CRP)). Inflammatory mediators can be

indicative of adverse metabolic functioning and obesity, as an imbalance in anti-inflammatory and pro-inflammatory cytokines and adipokines can result from excess adipose tissue (Bagheri et al., 2019). Measures used to analyze results were the following: body weight on a digital scale, height with a medical sampler, body mass index (BMI), waist circumference, waist to hip ratio (WHR), and body fat percentage (BFP) using a multi-frequency bioelectrical impedance device were measured. Blood samples after fasting were obtained from the cubital vein to measure IL-6, TNF-a, irisin, adiponectin, and hs-CRP concentrations with the use of an enzyme-linked immunosorbent assay (Bagheri et al., 2019).

Bagheri et al. (2019) found that both exercise interventions significantly decreased body weight, BMI, BFP, and WHR, but the results of the group that received GTE were significantly greater than the placebo group ($P < 0.001$). As a result of the intervention, participants experienced a reduction in weight, BMI, BFP and WHR (Table 1). Additionally, the exercise interventions significantly increased adiponectin and decreased hs-CRP; again, these changes were greater in the GTE group when compared to the placebo ($P < 0.05$). There was no significant change observed in plasma levels of irisin and TNF-a in any group (Bagheri et al., 2019). The results of this research study indicate that combining GTE supplementation and endurance exercise is successful in increasing body composition changes as well as changes in anti-inflammatory and metabolic markers.

Table 1. Results of Exercise Interventions in the Bagheri et al. (2019) Intervention

Variables	ET+P	ET+GTE
Average Reduction in Weight (kg)	1.61	2.27
Average Reduction in BMI (kg/m^2)	0.64	0.84
Average Reduction in BFP	2.73%	4.48%
Average Reduction in WHR (m)	0.01	0.02

A comparable study by Dalbo et al. (2008) studied changes in energy expenditure and markers of lipolysis in response to ingesting a thermogenic drink, Celsius. The need for this study stemmed from data implicating that 31% of those living in the United States are obese and double that percentage, 65%, are considered overweight (Dalbo et al., 2008). Previous research found that thermogenic drinks are successful in promoting weight loss, burning more calories and fat, and increasing energy levels due to ingredients such as caffeine, catechins (found in GTE), and neurostimulants but there is a lack of research on thermogenic drinks and energy expenditure and circulating markers of lipolysis. Given this information, Dalbo et al. (2008) aimed to examine resting energy expenditure (REE) and markers of lipolysis in response to drinking a thermogenic drink such as Celsius (Dalbo et al., 2008). In this single-blind study, participants were assigned to either a placebo group or a thermogenic drink (TD) group based on age and fat-free mass. Participants in this research included 30 college-aged males and 30 college-aged females who were overall healthy. At the beginning of the study, anthropometric measures, body composition, REE, respiratory exchange ratio (RER), venous blood samples, glycerol analysis, and free fatty acid analysis were completed (Dalbo et al., 2008). During the intervention, participants consumed 336mL of either the TD or a non-caloric noncaffeinated placebo. After consuming the respective beverage, REE and RER were measured at 60-, 120-, and 180-minutes post-consumption, and serum glycerol and FFA concentrations were measured at 30-, 60-, 120-, and 180-minutes post-consumption. The results of this study demonstrated the success of thermogenic drinks in increasing REE when compared to the placebo ($p=0.004$), meaning that participants that drank the thermogenic drink rather than the placebo burned more calories at rest. Additionally, free fatty acid concentrations were significantly increased after consuming a thermogenic drink ($p=0.001$), but glycerol concentrations were not significantly

impacted (decreased) by ingesting the thermogenic drink ($p=0.18$) (Dalbo et al., 2008). The results of the Dalbo et al., 2008 research indicate that thermogenic drinks, and therefore GTE, are successful in improving resting energy expenditure and free fatty acid levels. Though results are promising, a problem that arose with these results is the fact that the safety and efficacy of ingesting thermogenic drinks daily over an extended period of time are unknown (Dalbo et al., 2008).

In response to Dalbo et al. (2008), Lockwood et al. (2010) launched a study to examine the safety and efficacy of thermogenic drinks that are successful in improving physiological responses to exercise. This research aimed at analyzing body composition, cardiorespiratory fitness & health, body strength, safety, and mood in response to aerobic and resistance exercise (5 days/week) and ingestion of Celsius, a thermogenic drink, containing GTE (Lockwood et al., 2010). In this randomized, double-blind study, participants were assigned to one of four groups [energy drink + exercise (EX-A), energy drink only (NEX-A), placebo + exercise (EX-B), and placebo only (NEX-B)]. Participants included 40 sedentary (engage in physical activity for <30 minutes/week), adult men (18-45 years old) that were overall considered healthy, but data from only 37 subjects were analyzed due to issues that arose during the intervention period. (Lockwood et al., 2010). During the intervention, participants ingested one drink/day (placebo or Celsius) for 10 weeks. Celsius includes 200mg of caffeine and ~180mg of GTE, while the placebo was canned identically and tasted the same with the same total energy, but no active ingredients that are found in Celsius. The exercise groups were supervised by trainers or specialists; they participated in aerobic exercise for three days per week and resistance training for two days per week, then kept track of their progress on a workout card. Food logs were used to analyze the nutritional habits of participants. Additionally, body composition,

cardiorespiratory and strength measurements were taken, clinical safety of thermogenic drinks was tested, and mood assessments were completed (Lockwood et al., 2010). Results showed that consuming Celsius before moderate-intensity exercise improved body composition by decreasing body fat, increasing lean muscle, and improving cardiorespiratory function and health, as well as improving endurance performance without a significant effect on mood. Participants in EX-A experienced a significantly greater reduction in fat mass (11.32%) and percent body fat (8.64%) ($p < 0.05$) when compared to EX-B (fat mass reduction = 0.57%; percent body fat reduction = 1.12%) and NEX-B (fat mass reduction = 0.42%; percent body fat reduction = 0.74%). Different from the Dalbo et al. (2008) study, the Lockwood et al. (2010) research also found that consuming thermogenic drinks over a prolonged time is determined to be safe, but also stated that without exercise thermogenic drinks do not have a significant effect on body composition after 10 weeks of ingestion each day (Lockwood et al., 2010). One of the most important take-away messages from this research is that thermogenic drinks are successful in improving body composition and functioning when ingested prior to exercise.

Additional evidence supporting the effects of GTE and exercise is presented in Ichinose et al. (2011) which reported that whole-body fat use during exercise is increased when GTE supplementation and moderate-intensity exercise are combined (Ichinose et al., 2011). Participants in this study included 12 overall healthy males (age: 23 ± 2 years, height: 172 ± 5 cm, weight: 67.3 ± 4.6 kg, BMI: 22.9 ± 1.5 kg/m², peak oxygen consumption (VO_{2peak}): 3.41 ± 0.29 L/min, ventilation threshold (VT): 1.94 ± 0.24 L/min, maximal heart rate (HR_{max}): 192 ± 11 beats per minute (bpm)). Participants were randomly placed into either a placebo group or a GTE group (572.8mg catechin, 76.7mg caffeine). Participants exercised on a cycle ergometer for 60 min/day, 3 days/week, for 10 weeks (Ichinose et al., 2011). The major finding

in this research was the hastening of reducing respiratory exchange ratio by GTE supplementation, in comparison to exercise alone. Additionally, carbohydrate oxidation during exercise was significantly lower in the GTE group after training ($p < 0.05$), indicating an increase in fat oxidation during exercise (Ichinose et al., 2011). These results show that exercise, when combined with GTE supplementation, is successful in increasing fat oxidation throughout the body further supporting the benefits of GTE on body composition.

A final study that supports the benefits of the combination of GTE and exercise is by Venables et al. (2008) which aimed to determine the effect of GTE in conjunction with moderate-intensity exercise on glucose tolerance and fat oxidation. In this crossover study, 12 overall healthy males (age: 26 ± 2 years; weight: 75.1 ± 3.2 kg; BMI: 23.9 ± 0.8 kg/m²; maximal oxygen consumption ($\dot{V}O_{2max}$): 50.9 ± 2.1 mL/kg · min) participated in study A and study B, with at least one week in between trials (Venables et al., 2008). In study A participants exercised at 50% of their maximal workload; in study B participants were assessed by an oral-glucose-tolerance test. Prior to the interventions, participants either took a GTE supplement (340mg polyphenols and 136mg EGCG) or a placebo. (Venables et al., 2008). The main findings from this research state that GTE is successful in increasing fat oxidation when combined with moderate-intensity exercise.

Amount of GTE Needed to Cause Effect

Ingestion of GTE has shown promising benefits in relation to anti-obesity factors and body composition, but this intake must meet requirements to have an effect. Research over time has used varying amounts of GTE supplementation to have an effect on participants. The key aspects to be considered when ingesting GTE are catechin content and caffeine content. Hodgson et al. (2013) supplemented with 1200mg catechins and 240mg caffeine/day; Bagheri et al. (2019)

supplemented with a 500mg GTE capsule, made up of ~75% polyphenol catechins and 15 mg caffeine; Dalbo et al. (2008) supplemented with 336 mL of thermogenic drink, containing both caffeine (200mg) and GTE (15% EGCG); similarly, Lockwood et al. (2010) supplemented with one Celsius drink, containing both caffeine (200mg) and GTE (15% EGCG); finally, Ichinose et al. (2011) supplemented with 572.8mg catechin and 76.7mg caffeine. Though the supplementation between studies varies, each research study had positive results due to GTE supplementation. Hodgson, Randell & Jeukendrup (2013) compared various studies to better determine the amount of GTE needed to produce desirable results. Research found that usually, a standard cup of green tea contains 100 to 300mg catechins as well as 50 to 90mg of caffeine. GTE supplement, on the other hand, usually contains on average around 200mg of catechin and 6mg of caffeine per capsule (Hodgson, Randell, & Jeukendrup, 2013).

The amount of catechins and caffeine present will vary depending on the method of GTE ingestion (drinking green tea, GTE capsule, or thermogenic drink with GTE), but the effect may be different depending on the intake duration. Short-term effects (within 24 hours) on resting metabolism were seen through supplementation of 270mg/d of EGCG and 150mg/day of caffeine (Dulloo et al., 1999). Further supporting these findings, Berube-Parent et al. (2005) found that GTE supplementation increased energy expenditure at rest over a short period, but a ceiling effect was observed at 270mg/day of ECGC (Berube-Parent et al., 2005). Results are still not definite, but it can be concluded that around 300mg of catechins within GTE are needed to observe a short-term effect on resting metabolism (Hodgson, Randell, & Jeukendrup, 2013). Similar results were also seen on resting metabolism over longer periods (12 weeks), though supplementation was higher at 750mg/d of catechins. It was found that over longer periods of time, higher doses of catechins (593mg/day versus 78mg/d) were more successful in improving

resting metabolism (Hodgson, Randell, & Jeukendrup, 2013). Shorter versus longer-term effects of GTE on fat metabolism during exercise has not been studied as intensely, but most results indicate some improvement in metabolic processes when exercise is combined with GTE; though further research is warranted (Hodgson, Randell, & Jeukendrup, 2013).

Factors that Influence GTE

GTE has been found to be successful in increasing metabolism and fat oxidation in multiple studies but there are variables that can influence this effect of GTE. To start, the bioavailability and bioactivity of catechins are an important factor in the efficacy of GTE supplementation. Enough biologically active catechins must be introduced to the body to exhibit the benefits of GTE (Hodgson, Randell, & Jeukendrup, 2013). Additionally, when conducting research, to continue to adequately test the effect of GTE on participants, methods of measuring fat oxidation must be reproducible and extremely sensitive. Another factor that should be considered when interpreting results is differences in clinical populations as participant demographics, such as ethnicity may lead to differences in the observed efficacy of GTE (Hodgson, Randell, & Jeukendrup, 2013).

Adverse Effects of GTE

Although there are many positives to ingesting GTE, there can also be negative side effects that should be taken into consideration. Many of the proposed adverse effects of ingesting large amounts of GTE are due to an overconsumption of caffeine, rather than the green tea itself or the catechins within. A study by Nawab & Farooq (2015) explained that the caffeine content in an average cup of green tea (around 50mg) is not problematic, but when GTE is being used for weight loss, a much larger amount of caffeine is ingested, which can be as high as five times as much. This is when the caffeine can lead to a risk of upset stomach, tremors, insomnia, and

restlessness (Nawab & Farooq, 2015). Another important consideration has to do with iron absorption in the body. Tannins, which make up a considerable portion of green tea, commonly bind to non-heme iron in the body when ingested. This in turn can lead to problems with digestion and absorption of iron, possibly leading to iron deficiency, in which one can experience irritability, heartbeat arrhythmias, headaches, shortness of breath, and feeling weak (Nawab & Farooq, 2015). Green tea has also been found to interfere with folate when ingested, which is an essential component of protecting DNA from unwanted alterations due to cancer. Folate is also important in preventing anemia, making red blood cells, and protecting individuals from heart disease (Nawab & Farooq, 2015). Another problem that can arise with excess green tea consumption is dehydration. As green tea is a natural diuretic, it can lead to increased voiding and therefore depleted electrolyte levels and dehydration (Nawab & Farooq, 2015). Before taking GTE supplementation, individuals should also consult with their doctor, as it has been found that green tea can interfere with some medications such as lithium, blood thinners, and MAOI inhibitors. Additionally, in combination with other medications or supplements, liver toxicity, and oxidative stress can occur with GTE supplementation (Nawab & Farooq, 2015). Other adverse outcomes to excessive green tea intake (5-6L/d) could lead to nausea, bloating, indigestion, and diarrhea, while excessive consumption of caffeine in green tea can lead to headache, loss of appetite, vomiting, dizziness, confusion, and psychomotor agitation (Nawab & Farooq, 2015). While very excessive amounts of GTE would have to be consumed (>five times the normal ~50mg of supplement or 5-6L of green tea) to produce many of these undesirable side effects, they should be taken into consideration when ingesting GTE, particularly for weight loss.

Conclusion

Widespread research has shown that GTE is successful in promoting an increase in fat oxidation and increased metabolism when combined with exercise. Some studies have found GTE is also successful in increasing energy expenditure and fat oxidation at rest, but these results may not be chronic. For optimal results, GTE should be consumed regularly in combination with moderate-intensity exercise to exhibit an effect on body weight and metabolism. The most drastic results are seen when a thermogenic drink is consumed within about 15 minutes before beginning exercise, but excessive intake should be avoided due to potentially adverse effects. Promising benefits, such as body composition changes, increased fat oxidation during exercise, and changes in anti-inflammatory and metabolic markers have been observed as a result of combining GTE and exercise. Based on the research studied, GTE supplementation (~270mg) should be taken (in capsule form, in a cup of green tea, in a thermogenic drink) shortly before beginning exercise to produce the most successful results, such as increased fat oxidation and changes in anti-inflammatory and metabolic markers, as well as improvements in body composition.

References

- Bagheri, R. Rashidlamir, A., Ashtary-Larky, D., Wong, A., Alipour, M., Motevalli, M.S., Chebbi, A., Laher, I., & Zouhal, H. (2019). Does green tea extract enhance the anti-inflammatory effects of exercise on fat loss? *British Journal of Clinical Pharmacology*, 85(4), 753-762. <https://doi.org/10.1111/bcp.14176>
- Berube-Parent, S., Pelletier, C., Dore, J., & Tremblay, A. (2005). Effects of encapsulated green tea and Guarana extracts containing a mixture of epigallocatechin-3-gallate and caffeine on 24 h energy expenditure and fat oxidation in men. *British Journal of Nutrition*, 94(3), 432-436. doi:10.1079/BJN20051502
- Dalbo, V.J., Roberts, M.D., Stout, J.R., & Kerksick, C.M. (2008). Acute effects of ingesting a commercial thermogenic drink on changes in energy expenditure and markers of lipolysis. *Journal of the International Society of Sports Nutrition*, 5(6).
- Dulloo, A.G., Duret, C., Rohrer, D., Girardier, I., Mensi, N., Fathi, M., Chantre, P., & Vandermander, J. (1999). Efficacy of green tea extract rich in catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans. *The American Journal of Clinical Nutrition*, 70(6), 1040-1045. <https://doi.org/10.1093/ajcn/70.6.1040>
- Hodgson, A.B., Randell, R.K., Boon, N., Garczarek, U., Mela, D.J., Jeukendrup, A.E., & Jacobs, D.M. (2013). Metabolic response to green tea extract during rest and moderate-intensity exercise. *The Journal of Nutritional Biochemistry*, 24(1), 325-334. <https://doi.org/10.1016/j.jnutbio.2012.06.017>
- Hodgson, A.B., Randell, R.K., & Jeukendrup, A.E. (2013). The effect of green tea extract on fat oxidation at rest and during exercise: Evidence of efficacy and proposed mechanisms. *Advances in Nutrition*, 4(2), 129-140. <https://doi.org/10.3945/an.112.003269>
- Ichinose, T., Nomura, S., Someya, Y., Akimoto, S., Tachiyashiki, K., & Imaizumi, K. (2011). Effect of endurance training supplemented with green tea extract on substrate metabolism during exercise in humans. *Scandinavian Journal of Medicine & Science in Sports*, 21(4), 598-605. <https://doi.org/10.1111/j.1600-0838.2009.01077.x>
- Kaur, T., Pathak, C.M., Pandhi, P., & Khanduja, K.L. (2008). Effects of green tea extract on learning, memory, behavior and acetylcholinesterase activity in young and old male rats. *Brain and Cognition*, 67(1), 25-30. <https://doi.org/10.1016/j.bandc.2007.10.003>
- Lockwood, C.M., Moon, J.R., Smith, A.E., Tobkin, S.E., Kendall, K.L., Graef, J.L., Cramer, J.T., & Stout, J.R. (2010). Low-calorie energy drink improves physiological response to exercise in previously sedentary men: A placebo controlled efficacy and safety study. *Journal of Strength and Conditioning Research*, 24(8), 2227-2238.
- Nawab, A. & Farooq, N. (2015). Review on green tea constituents and its negative effects. *The Pharma Innovation Journal*, 4(1), 21-24.

Scalbert, A., Johnson, I.T., & Saltmarsh, M. (2005). Polyphenols: Antioxidants and beyond. *The American Journal of Clinical Nutrition*, 81(1), 215S-217S. <https://doi.org/10.1093/ajcn/81.1.215S>

Senanayake, N. (2013). Green tea extract: Chemistry, antioxidant properties and food applications – A review. *Journal of Functional Foods*, 5(4), 1529-1541. <https://doi.org/10.1016/j.jff.2013.08.011>

Venables, M.C., Hulston, C.J., Cox, H.R., & Jeukendrup, A.E. (2008). Green tea extract ingestion, fat oxidation, and glucose tolerance in healthy humans. *The American Journal of Clinical Nutrition*, 87(3), 778-784. <https://doi.org/10.1093/ajcn/87.3.778>