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Mini-Review

Green Tea Extract Thermogenesis-Induced Weight Loss by Epigallocatechin Gallate Inhibition of Catechol-*O*-Methyltransferase

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ABSTRACT Epidemiological studies have shown that intake of tea catechins is associated with a lower risk of cardiovascular disease. The antioxidative activity of tea-derived catechins has been extensively studied. Reports have shown that green tea extract intake is associated with increased weight loss due to diet-induced thermogenesis, which is generally attributed to the catechin epigallocatechin gallate. That catechin-polyphenols are known to be capable of inhibiting catechol-*O*-methyltransferase (the enzyme that degrades norepinephrine) is a possible explanation for why the green tea extract is effective in stimulating thermogenesis by epigallocatechin gallate to augment and prolong sympathetic stimulation of thermogenesis. Knowledge about thermogenesis-induced weight loss produced by green tea's epigallocatechin gallate and its ability to inhibit catechol-*O*-methyltransferase is important for health benefits and for prolonging the action of norepinephrine in the synaptic cleft.

KEY WORDS: • ***catechol*-O-*methyltransferase*** • ***epigallocatechin gallate*** • ***tea*** • ***thermogenesis***

INTRODUCTION

According to the Chinese legend, 4,000 years ago tea was discovered accidentally by the Emperor Shen Nung, as one day he was boiling water when a gust of wind blew leaves in from a tea tree. He was very pleased with the aroma and taste, and shortly after tea was invented.[1] Tea (*Camellia sinensis*, Family Theaceae) is consumed as one of the most popular beverages throughout the world. An estimated 2.5 million metric tons of dried teas are manufactured annually. The majority of tea beverage is prepared from three types of manufactured tea: green tea, oolong tea, and black tea. Green tea is prepared when the fresh leaves are processed rapidly to prevent "fermentation." Oolong tea is partially fermented tea products and has a unique flavor. Black tea is made by crushing to cause "fermentation" prior to the final drying of tea leaves. Of all the tea consumed in the world, 78% is black tea, which is usually consumed in the United States, Europe, Africa, and India; 20% is green tea, which is commonly consumed in Asian countries, especially in China and Japan; and 2% is oolong tea, which is produced in Southern China. Tea is usually prepared from tea bags infused in hot water in a proportion of 1 g of dried leaves to 100 mL of water. The resulting tea extract has a solid concentration of 0.35%. Green tea infusion contains approximately 30% catechins and 2% flavonols. Black tea infusion contains approximately 9% catechins, 4% theaflavins, and 3% flavonols.[2]

Green tea has been widely consumed in China and Japan for many centuries, and hence is regarded as safe.[3] Presently, 90% of green tea comes from China, and is cultivated on approximately 4 million acres of land. Tea's medicinal powers are so strongly believed in the Orient that the Chinese actually say that it is better to take green tea than to take medicine.[1] Green tea has more health benefits because of minimal processing and contains high quantities of pharmacologically active compounds. The active constituents are polyphenols, contributing to approximately 30% of green tea [epicatechin (EC), EC gallate (ECG), epigallocatechin (EGC), and EGC gallate (EGCG)].

Although tea leaves contain more than 2,000 components, most attention has been paid to the tea catechins. Catechins are the major components of tea polyphenols and constitute about 30–42% of the dry weight of green tea and 9% of the dry weight of black tea. The major catechins in fresh tea

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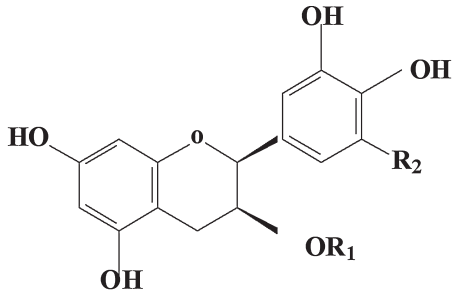


		R_1	R_2
Epigallocatechin gallate	EGCG	Gallate	OH
Epigallocatechin	EGC	H	OH
Epicatechin gallate	ECG	Gallate	H
Epicatechin	EC	H	H

FIG. 1. Major catechins in tea.

leaves are EGCG, EGC, ECG, and EC. The composition varies depending on the location of cultivation of tea plant, variety of plant, season of harvest, and manufacturing process. Catechins are colorless, water-soluble compounds that impart bitterness and astringency to tea infusion. The usual composition is 10–15% EGCG, 6–10% EGC, 2–3% ECG, and 2% EC. The structures of the major catechins are shown in Figure 1. EGCG is the most abundant catechin and has received by far the most attention in clinical study. In addition, flavonols such as quercetin and their glycosides, caffeine, theobromine, theophylline, and phenolic acids such as gallic acid are also present as minor constitutents. Caffeine usually accounts for 3–6% of the dry weight of brewed tea.

Studies have shown that the catechin called EGCG is the most abundant and active compound responsible for most of green tea's role in promoting good health.[2] EGCG is a very powerful and potent anticancer, anti-inflammatory, and antioxidant constituent of green tea.[4] Recent scientific research has shown its ability to improve weight loss.

Essentially, the two ways to treat obesity are to reduce energy intake or to increase energy expenditure.[5] Total daily energy expenditure is composed of three factors: thermic effect of physical activity, resting metabolic rate, and thermic effect of feeding (diet-induced thermogenesis).[6] To a large extent thermogenesis is under the control of the sympathetic nervous system, as norepinephrine (NE) has the ability to control biochemical pathways that lead to an increased rate of mitochondrial oxidation, with poor coupling of ATP synthesis, hence leading to an increase in heat production.[7] Therefore, a rational approach for obesity management could be an interference with the sympathetic nervous system and the heat-producing neurotransmitter NE.[5]

The target for pharmocological interference in the NE modulatory pathway is the enzyme catechol-*O*-methyltransferase (COMT). COMT is present in most tissues in soluble and membrane-bound forms. The main function of COMT is to eliminate the various catecholic compounds (NE) by decreasing their hydrophilicity by methylation, and then further sulfation/glucuronidation is usually needed for effective elimination from the body.[8] Tea catechins have been shown *in vitro* to inhibit COMT.[9] Green tea's EGCG acts on the NE modulatory pathway and exerts a thermogenic effect, that is, an anti-obesity action by the inhibition of COMT.[10] Therefore, through EGCG's inhibition of COMT, there is a prolonged effect of NE on the α- and β-adrenergic receptors at the postsynaptic cleft of the nerve terminal, which increases the cyclic adenosine monophosphate concentration and thermogenesis.[3,7]

Knowledge about thermogenesis-induced weight loss from green tea's EGCG and its ability to inhibit COMT is a very important factor in human diet for health benefits, and also for prolonging the action of NE in the synaptic cleft.

EGCG INHIBITION OF COMT

An increase in body fat and weight greatly increases the risks of adverse health consequences.[1] Therefore, the health care community is increasingly focused on factors that positively affect health and well-being, such as increased physical activity and proper diet. Since diet affects total daily energy expenditure, considerable attention has been given to diet-induced thermogenesis in an attempt at solving the weight management puzzle. Research has found that green tea's EGCG stimulates thermogenesis through the inhibition of COMT, therefore prolonging the effect of NE on thermogenesis. However, the inhibition of COMT by EGCG remains to be further characterized. The journal articles cited in this review are all focused on green tea and thermogenesis but vary, as they all together cover the effects on mice, rats, obese individuals, healthy men, and nonobese men and women. Caffeine is also a main focus in the these articles as it is a main component of green tea, and also exerts a thermogenic effect on a different pathway through the inhibition of phosphodiesterase, therefore increasing the cellular amount of cyclic adenosine monophosphate and increasing thermogenesis.

The following three experiments used the same green tea extract—AR25, commercially named EXOLISE® (Arkopharma, Bedford, MA). The capsule of 375 mg was obtained by alcohol extraction from dry tea leaves of unfermented *C. sinensis*. It is an 80% ethanolic dry extract standardized at 25% catechins, with approximately 70% EGCG. The percentage content of caffeine is 5–10%. The ingestion of the green tea extract capsules from the human studies provided a daily total of 150 mg of caffeine and 375 mg of catechins, with 270 mg of EGCG. High performance liquid chromatography analysis of green tea extract is given in Figure 2.

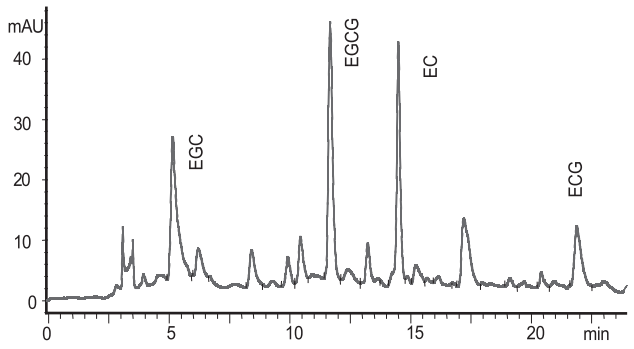


FIG. 2. High performance liquid chromatography profile of green tea extract.

Green tea and thermogenesis: interactions among catechin-polyphenols and caffeine and their sympathetic activity

Dulloo *et al*.[3] performed two experiments. The first experiment found that the green tea extract possesses thermogenic properties that are greater than can be accounted for by its caffeine content *per se*. The second experiment found that brown adipose tissue (BAT) thermogenesis may also be attributed to an interaction between its high EGCG content and caffeine on sympathetically released NE.

The studies were performed with five male Sprague-Dawley rats, 7–8 weeks old. Two fragments, 10–12 mm long and about 1 mm thick, of interscapular BAT (IBAT) were dissected out from the middle part of the fat pad. The tissues were then perfused with Krebs-Ringer bicarbonate buffer. The respiratory rates of IBAT fragments were measured by a method involving repeated oxygen uptake determinations.

In the first experiment, the comparison was done on the effects of the green tea extract AR25 and caffeine under two conditions: unstimulated state and stimulated state with subthreshold concentrations of ephedrine to mimic a small increase in sympathetic activity. The results shown in Figure 3A (intact tissue) indicate statistically that higher mole of oxygen (MO_2) values occur with the green tea extract than with caffeine at 100 μM and at 250 μM. Therefore, caffeine does not increase basal IBAT MO_2 (as it has to be in millimolar concentration to stimulate IBAT respiration rate), and green tea extract, containing an isomolar concentration of caffeine, resulted in significant increases in IBAT MO_2 above basal levels in a dose-dependent fashion.

The experiment was repeated with IBAT tissues from chemically sympathectomized animals. The animals were treated with 6-hydroxydopamine for denervation, where 90% or more of NE in IBAT is reduced, because of the chemical destruction of the sympathetic nerve endings and hence depletion of the NE stores. The results shown in Figure 3B (sympathectomized) indicate that the effects of green tea on MO_2 were considerably blunted. Therefore, the blunted effect on BAT thermogenesis in sympathectomized animals cannot be attributed to postsynaptic tissue damage, but it is due to the depletion of NE stores following chemical sympathectomy. This suggests that the interaction requires intact sympathetic neural innervation. Hence, the effects on thermogenesis are likely to be highly dependent upon the release of endogenous NE from the sympathetic nerves innervating this tissue.

In the second experiment, the effect of EGCG on the *in vitro* respiration rate of IBAT was tested to obtain direct evidence that catechin-polyphenols contribute to the efficacy of the green tea extract in potentiating thermogenesis. The results shown in Figure 4A indicate that only at 200 μM has EGCG induced a small, statistically significant, increase in MO_2 relative to basal values. However, at 200 μM, with the combination of EGCG plus caffeine, there was a 2.4-fold increase of MO_2 in IBAT relative to basal values, indicating a synergistic interaction.

In another study, shown in Figure 4B, the combination of caffeine and EGCG was studied under stimulated conditions,

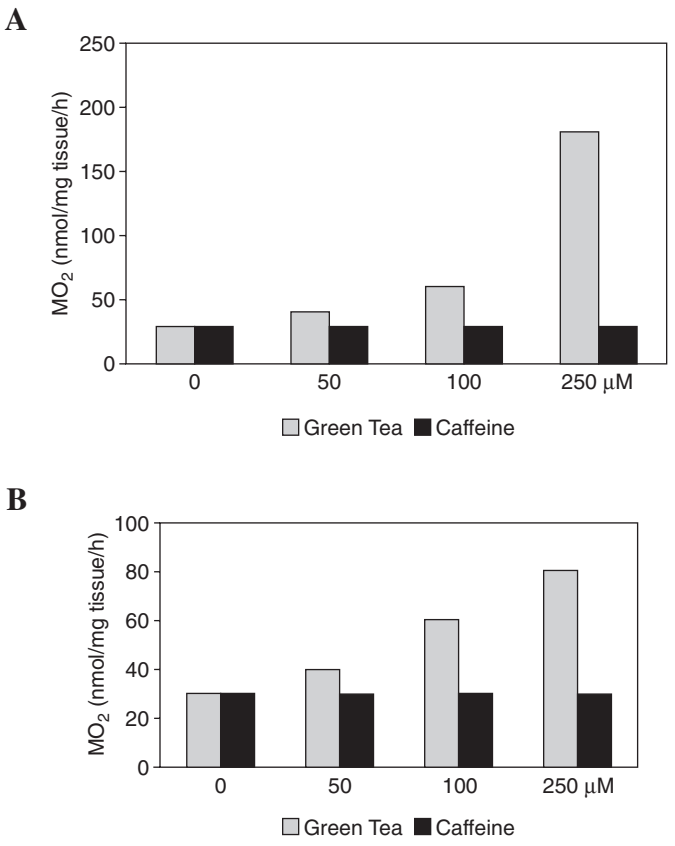


FIG. 3. Respiration rates (MO_2) of IBAT from intact rats (**A**) and from rats chemically sympathectomized (**B**) in response to caffeine or to green tea extract containing isomolar concentrations of caffeine. The data are presented in the absence or presence of a low concentration of ephedrine (an enhancer of NE release). Modified from Dulloo *et al*.[3]

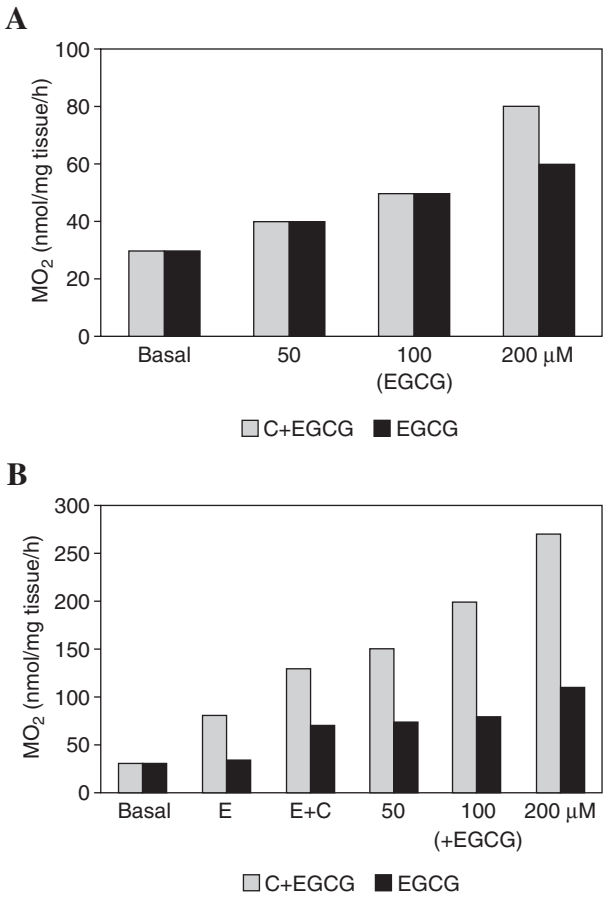


FIG. 4. Respiration rates (MO_2) of IBAT in response to EGCG alone or in combination with caffeine (C) in the unstimulated state (**A**) and EGCG in the stimulated state induced by low doses of ephedrine (E) and caffeine (C) (**B**). In all measurements, caffeine was administered at 100 μM (a low subthreshold concentration that in its own right does not increase MO_2), and in the study shown in (B), ephedrine was administered at 0.1 and 0.25 μM, which in its own right either did not increase basal MO_2 (broken line) or significantly increased basal MO_2 between 50% and 100% (solid line). The shaded areas represent the synergistic increases in tissue thermogenesis in response to the interaction between EGCG and caffeine in the absence (A) or in the presence (B) of an increase in NE release (induced by ephedrine). Modified from Dulloo *et al*.[5]

where a subthreshold concentration of ephedrine (0.1 μM and 0.25 μM) was used to increase the NE release. Two subsets are shown: the dashed line represents data where ephedrine did not increase IBAT MO_2, and the solid line represents data where there was significant stimulation of IBAT MO_2. Both show that EGCG increases IBAT MO_2; as shown with the dashed lines at 200 μM, there is a 2.8-fold increase in MO_2 relative to basal values, and a 70% increase in MO_2 relative to that for ephredrine plus caffeine. Also, as shown by the solid line at 100 and 200 μM, the combination increased basal MO_2 values by 5.7-fold and 7.4-fold, respectively, or by 40% and 90%, respectively, relative to ephedrine and caffeine combined. Since the IBAT MO_2 is severalfold higher with an increase in NE in the synaptic cleft, these data show that EGCG cannot increase the release of NE, only act on it, and prolong the effect for thermogenesis.

In Figure 5, the last study presented, it is shown that EGCG produces an increase in MO_2 at 100 μM with added ephedrine, in contrast to its lack of effect alone. This is due to the increase in release of NE, where EGCG can then have a prolonged effect on and increase thermogenesis.

These three studies combined suggest that the efficacy of green tea extract to potentiate BAT thermogenesis is due to the interaction between EGCG and caffeine with the sympathetically released NE. EGCG enzymatic degradation of COMT would cause a reduction in the degradation of NE and therefore prolong the action of sympathetically released NE on adrenoreceptors. Plus, caffeine would increase the NE-induced cyclic adenosine monophosphate activation in the cell, by inhibiting phosphodiesterase-induced degradation of intracellular cyclic adenosine monophosphate. Also, green tea extract was found to be more effective than were equivalent amounts of caffeine in stimulating peripheral tissue thermogenesis. Therefore, as shown in vitro, caffeine and EGCG by inhibitory actions on two different enzyme systems would work together to increase the action of NE on thermogenesis.

Efficacy of a green tea extract rich in catechin-polyphenols and caffeine in increasing 24-hour energy expenditure and fat oxidation in humans

Dulloo *et al*.[5] designed a study for 10 healthy men based on the fact that green tea extract, containing caffeine and catechins, has thermogenic properties via sympathetic activation of NE and therefore plays a role in body composi-

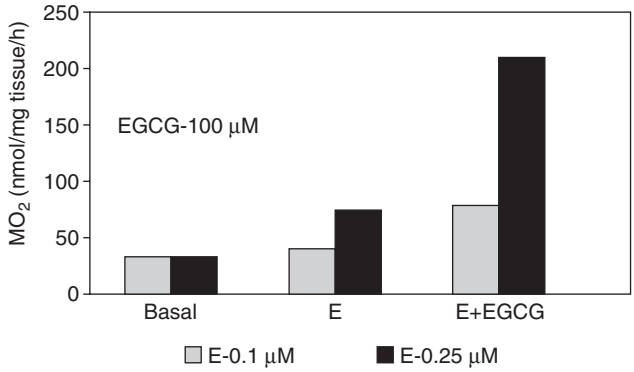


FIG. 5. Respiration rates (MO_2) of IBAT in response to EGCG in the stimulated state induced by relatively low doses of ephedrine. In all measurements, EGCG was administered at 100 μM (a low subthreshold concentration that in its own right does not increase MO_2), and ephedrine was administered at 0.1 or 0.25 μM. The shaded areas represent the synergistic increases in tissue thermogenesis in response to the interaction between EGCG and ephedrine. Modified from Dulloo *et al*.[3]

Table 1. Energy Expenditure During Diurnal, Nocturnal, and Total 24-Hour Periods

	Energy expenditure			
	Placebo	*Caffeine*	*Green tea*	P
Diurnal	6,463 ± 386	6,547 ± 383	6,754 ± 352	<.01
Nocturnal	3,075 ± 149	3,053 ± 145	3,112 ± 140	NS
Total 24-hour	9,538 ± 521	9,599 ± 518	9,867 ± 488	<.01

Data are from Dulloo *et al.*[5] NS, not significant.

tion. The objective was to show the extent to which daily administration of capsules containing a green tea extract that is comparable to the amount of polyphenols and caffeine commonly consumed in green tea beverages in an Asian community would stimulate thermogenesis and increase daily energy expenditure in humans. Also, they showed that the effects of green tea extract on the metabolic rate in humans is greater than that explained by caffeine content *per se*.

The subjects were recruited from the students and staff at the University of Geneva, Geneva, Switzerland. The 10 men were on average approximately 25 years old and had a body mass index of 25 kg/m^2. Questionnaires eliciting medical and nutritional histories were obtained. Noneligible subjects included smokers, competitive athletes, persons who participated in intense physical exercise, or those who had a history of weight loss. Eligiblity criteria included 8–30% body fat, consumption of a typical Western diet with 35–40% fat contributing to dietary energy intake, and intake of methylxanthines ranged from 100 to 200 mg/day.

This was a double blind study, as each subject was randomly assigned one of three treatments for 6 weeks and orally took the capsular form three times per day, two capsules with breakfast, lunch, and dinner. The three treatments included (1) the green tea extract AR25 containing 50 mg of caffeine and 90 mg of EGCG, (2) 50 mg of caffeine, and (3) a placebo that consisted of cellulose as inert filler. Each subject spent 24 hours in the respiratory chamber on three occasions within 5–10-day intervals. The following conditions were the same for each respiratory chamber trial: energy intake, nutrient composition of the diet, sedentary lifestyle pattern, pattern of physical activity, meal pattern, and time period for sleeping. Caffeine products were not consumed 24 hours before the respiratory chamber. Also, during the first 8 hours of each trial, the heart rate was monitored with a portable frequency meter and showed no significant differences.

The daily energy expenditure was continuously monitored by indirect calorimetry during the stay in the respiratory chamber. Also, urinary nitrogen was measured by the method of Kjeldahl, and catecholamines were measured by liquid chromatography with electrochemical detection.

In Table 1, diurnal, nocturnal, and total 24-hour energy expenditure values are presented for placebo, caffeine, and green tea extract. Diurnal energy expenditure was significantly higher during treatment with green tea extract than during treatment with placebo or caffeine by 4.5% and 3.2%, respectively. Also, total daily energy expenditure with green tea extract was significantly higher than that with both the placebo and caffeine by 3.5% and 2.8%, respectively. There was an increase in energy expenditure in six of the 10 subjects after treatment with green tea extract, ranging from 266 to 836 kJ, and only two of the 10 subjects with caffeine.

In Table 2, the values for urinary excretion of catecholamines are shown. Urinary NE and its precursor dopamine tended to be highest during treatment with green tea extract; however, the only significant change was for daily energy expenditure of NE. This observation is consistent with the inhibiting effect of green tea on COMT, as the reduction in NE degradation causes a spillover of NE into the circulation, and hence higher urinary excretion of NE.

This experiment is the first to show in humans that tea has a potential influence on energy expenditure since dietary intake and diet composition were identical during all treatments, and the subjects maintained the same feeding and physical activity patterns during each 24-hour respiratory chamber trial. The 4% increase in 24-hour energy expenditure treatment with green tea extract reflects its stimulatory effect on thermogenesis. Also, the effects of green tea on thermogenesis cannot be solely explained on the basis of caffeine content since it failed to alter the energy expenditure with an amount of caffeine equivalent to that in the extract. Therefore, the metabolic effects resulted from ingredients other than caffeine in the green tea extract, and caffeine may have enabled a synergistic interaction with other bioactive ingredients in the green tea to promote catecholamine-induced thermogenesis.

Green tea extract and its activity for the treatment of obesity

Chantre and Lairon[2] performed a 3-month open study with moderately obese patients on the effects of the green

Table 2. Urinary Catecholamines During Diurnal, Nocturnal, and Total 24-Hour Periods

	Catecholamines (nmol)			
	Placebo	*Caffeine*	*Green tea*	P
Diurnal				
Epinephrine	66 ± 16	49 ± 4	55 ± 7	NS
NE	106 ± 15	127 ± 24	146 ± 23	NS
Dopamine	893 ± 173	946 ± 160	1,086 ± 179	NS
Nocturnal				
Epinephrine	12 ± 4	19 ± 4	15 ± 3	NS
NE	54 ± 5	61 ± 11	73 ± 7	NS
Dopamine	694 ± 80	632 ± 126	803 ± 105	NS
Total 24 hours				
Epinephrine	78 ± 13	67 ± 4	70 ± 8	NS
NE	160 ± 14	187 ± 29	219 ± 27	<.05
Dopamine	1,587 ± 187	1,578 ± 165	1,889 ± 241	NS

Data are from Dulloo *et al.*[5] NS, not significant.

Table 3. Evolution of Body Weight Loss (Modified from Chantre and Lairon[2])

	Baseline	*Week 4*	*Week 8*	*Week 12*
Number of subjects	70	68	63	66
Mean (kg)	75.99 ± 8.85	74.64 ± 8.93	73.97 ± 9.02	72.49 ± 8.97

Table 4. Evolution of Waist Circumference (Modified from Chantre and Lairon[2])

	Baseline	*Week 4*	*Week 8*	*Week 12*
Number of subjects	70	68	63	66
Mean (cm)	94.41 ± 11.72	90.6 ± 10.86	89.98 ± 10.91	88.27 ± 10.8

tea extract AR25 in France from June 1999 to December 1999. The 70 patients were between the ages of 20 and 69 years, with a body mass index between 24 and 32 kg/m^2. The exclusion criteria included history of serious systemic disease, including diabetes, significant cardiac, renal, hepatic, or endocrine disorders, and pregnancy or lactation, as well as consumption of drugs capable of influencing body weight within the previous month. The initial screening visit included a medical history and physical examination. For 12 weeks, each subject took two capsules in the morning and two capsules midday of the green tea extract AR25. Body weight was evaluated every 4 weeks until week 12, and waist circumference was measured at each visit. Also, sitting heart rate and blood pressure was measured at each visit.

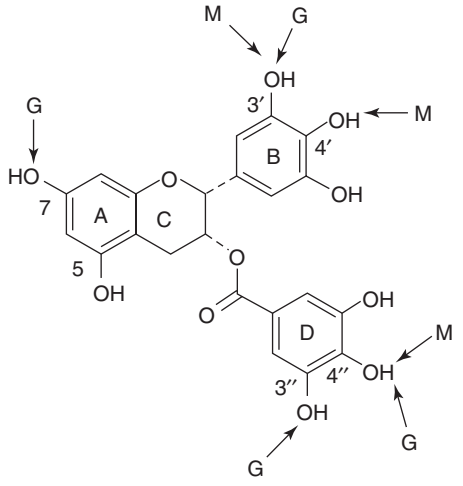
During the course of the study a continuing decrease of body weight was observed as well as waist circumference as shown in Tables 3 and 4. The mean body weight was decreased by 4.60% and waist circumference by 4.48%. Also, no significant differences in blood pressure were observed.[2] The results show that the green tea extract AR25 in humans can lower body weight and waist circumference. Even though this is an open uncontrolled design, it is very noticeable that body weight decreased by 4.6% in 3 months.

Enzymology of methylation of tea catechins and inhibition of COMT by EGCG

Lu *et al.*[11] performed a study where they provided basic information on mice, rats, and humans on the methylation of EGCG and suggested that EGCG may inhibit COMT-catalyzed methylation of endogenous and exogenous compounds.

Eight-week-old female CF-1 mice and five male Sprague-Dawley rats were sacrificed after 1 week on the diet. The liver and intestine were promptly removed and washed with ice-cold saline, and samples were pooled for preparation of microsomes and cytosol by differential ultracentrifugation. The EGCG was synthesized and purified in the laboratory. The possible sites of methylation and glucuronidation of EGCG were determined and are shown in Figure 6.

This study shows that EGCG potently inhibits the activities of COMT. Using EGC and 3,4-dihydroxy-L-phenylalanine as substrates, EGCG, 4″-*O*-methyl-EGCG, and 4′,4″-di-*O*-methyl-EGCG were all potent inhibitors of COMT. It was found that since EGCG is a gallated catechin, it has a 60-fold higher activity than nongallated catechins (EGC and EC) in inhibiting COMT activity. The noncompetitive inhibition of COMT by 4″-*O*-methyl-EGCG and 4′,4″-di-*O*-methyl-EGCG suggests that they inhibit COMT by binding to a site other than the catechol binding site. Displayed in Figure 7 is the concentration-dependent inhibition of COMT activity by EGCG, showing that as the level of EGCG increases, that of the COMT substrate decreases, therefore suggesting that EGCG is inhibiting the action of COMT on endogenous and exogenous compounds.



EGCG

FIG. 6. A summary of possible sites of methylation (M) and glucuronidation (G) of EGCG.[11]

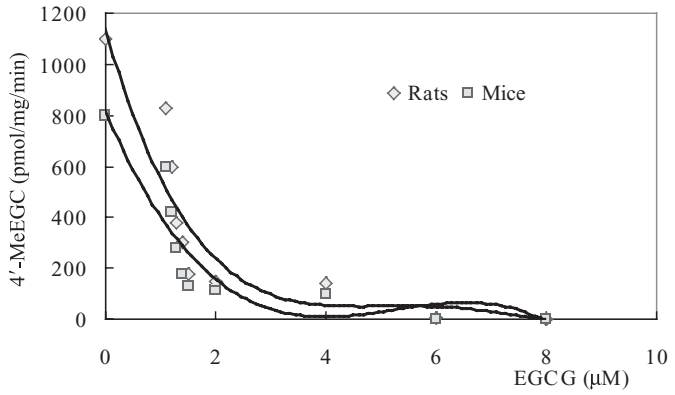


FIG. 7. Concentration-dependent inhibition of COMT activity by EGCG (modified from Lu *et al.*[11]).

DISCUSSION

Long-term oral consumption of green tea or EGCG-containing extracts may mimic some of the acute EGCG effects that may be beneficial to health. Long-term consumption of green tea may influence the incidence of obesity, diabetes, and cardiovascular disease.[11]

In the study by Dulloo *et al.*,[3] there were no reported side effects and no significant differences in heart rate across treatments observed in the 8 hours that the subjects were assessed in the respiratory chamber. Also, in the study of Chantre and Lairon,[2] there were no significant differences in blood pressure. However, there were side effects reported such as abdominal pain, diarrhea, and an increase of transaminases. Nonetheless, 94% of the subjects and 96% of the investigators found the AR25 extract to be well or very well tolerated. Therefore, the green tea extract is distinct from sympathomimetic drugs, as these drugs are limited by their adverse cardiovascular effects and are particularly inappropriate for obese individuals with hypertension and other cardiovascular implications.

It could be argued that other tea flavonoids in the green tea extract AR25, such as quercetin and myricetin, may have affected the inhibition of COMT in the human trials, since they have been shown to inhibit COMT *in vitro*. However, with the small amounts present and their absorption when taken orally being doubtful, there is only a small chance that they were a contributing factor.[9] It also has been proposed that many *S*-adenosyl methionine-dependent methyltransferases, including DNA methyltransferases and COMT, have a common catalytic domain structure, and it is possible that EGCG/methylated EGCG can bind to certain sites on the catalytic domain of DNA methyltransferase and inhibit its activity.[8,12]

While there is an increasing interest in green tea's role in promoting good health, the bioavailability and biotransformation of EGCG are not well understood, even though several studies on this topic have been published. The knowledge base of the absorption, metabolism, and tissue distribution is limited.[10,11] The kinetic parameters of EGCG methylation by human liver and the contribution of methylation to the biotransformation of EGCG remain unknown.[8] An example of how green tea needs to be used at the right composition and the right form to exert a pharmacologically significant effect is the study performed by Martinet *et al.*,[13] where they demonstrated that 12 plant preparations (including green tea) had no effect on energy expenditure. However, the green tea preparation they used was not the standardized green tea extract that was developed and tested in the previous experimental and clinical designs that has been shown to have thermogenic properties.

Dulloo *et al.*[5] showed by testing with 10 healthy men that the 24-hour energy expenditure increased approximately 4%. It is generally accepted that thermogenesis contributes 8–10% of daily energy expenditure (760–950 kJ) in a typical sedentary man. Therefore, this 4% increase (328 kJ) due to green tea extract would extrapolate to a 35–43% (75–100 kJ) increase in the thermogenesis compartment of daily energy expenditure. This may seem small for a single day; however, the long-term effects are significant as a lower caloric expenditure of 75 kJ/day theoretically would result in nearly 8 lb of weight loss per year.[14] Therefore, oral administration of the green tea extract stimulated thermogenesis that has the potential to influence body weight by changes in energy expenditure.[5] Also, another study performed by Landsberg *et al.*[15] showed that the NE turnover rate in IBAT of the rat demonstrated an increase in sympathetic activity in response to overfeeding.

Also, evidence suggests that a diminished sympathetic nervous system activity may contribute to the diminished energy expenditure leading to obesity. Therefore, the regulation by green tea extract of the sympathetic nervous system activity by heat-producing NE has an important role in weight management.[16]

Further studies are necessary to evaluate and document the observed weight-reducing action of green tea extract, especially in patients with much greater obesity.[2] Further studies on effects of tea catechins on the metabolism of catecholic hormones and their related disease are warranted. The potential interactions between EGCG and catecholic hormones or drugs should also be considered.[8]

CONCLUSIONS

All of the experimental and clinical studies reported here strongly suggest that the green tea extract, rich in catechins and caffeine, is an effective potentiator of sympathetically mediated thermogenesis and a natural substance for the management of obesity. *In vitro*, green tea extract was shown to exert a stimulation of thermogenesis, possibly mediated by a reduction in enzymatic degradation of NE and prolongation of action of sympathetically released NE. In human studies there was an observed significant increase of energy expenditure, lowering of body weight, decrease in waist circumference, and no change in heart rate or blood pressure.

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