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Can EGCG Reduce Abdominal Fat in Obese Subjects?

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Original Research

Can EGCG Reduce Abdominal Fat in Obese Subjects?

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Key words: epigallocatechin gallate, catechins, obesity, abdominal fat

Objective: To evaluate metabolic effects of epigallocatechin gallate (EGCG) supplementation when combined with a program of regular aerobic exercise in overweight/obese post-menopausal women.

Methods: Thirty-eight overweight or obese postmenopausal women exercised at moderate intensity, viz. walking three times per week for 45 min at 75% of age-predicted maximum heart rate (HR), and took a 150 mg capsule of EGCG (Teavigo®) or placebo (lactose) twice daily for 12 weeks. Blood parameters (lipids, glucose and insulin), blood pressure, heart rate, arterial function and anthropometry were assessed at 0, 6 and 12 wk. At wk 0 and 12, body composition was assessed by dual energy X-ray absorptiometry (DXA) and abdominal fat was assessed by DXA and computed tomography (CT).

Results: Waist circumference ($p < 0.01$), total body fat ($p < 0.02$), abdominal fat (by DXA) ($p < 0.01$) and intra abdominal adipose tissue (by CT) ($p < 0.01$) were reduced in both treatment groups, with no difference between placebo and Teavigo®. Teavigo® significantly decreased resting HR ($p < 0.01$) and reduced plasma glucose in subjects with impaired glucose tolerance ($p < 0.05$).

Conclusions: Moderate consumption of EGCG can improve the health status of overweight individuals undergoing regular exercise by reducing HR and plasma glucose concentrations. Loss of body fat, however, may require a higher intake of EGCG, other catechins or addition of metabolic stimulants.

INTRODUCTION

The current obesity epidemic has intensified research into strategies to combat obesity and associated cardiovascular (CV) and metabolic risk [1]. In women the transition toward increased obesity, particularly abdominal adiposity, is most marked following menopause [2], bringing an increased risk of developing the metabolic syndrome [3] and CV disease [4]. Lifestyle changes such as increased physical activity and energy-restricted diets are recommended as primary interventions to reduce excess body fat and prevent the development of CV

and metabolic abnormalities [5]. However, increased consumption of certain bioactive nutrients such as omega-3 fatty acids may also reduce body fat through a variety of mechanisms, e.g. by increasing blood flow and hence delivery of fats to sites of metabolism and/or stimulating fat metabolism either directly or through changes in gene expression. We recently demonstrated that the ability of omega-3 supplementation to facilitate fat loss could be enhanced by a program of aerobic exercise [6]. Other bioactive nutrients which induce similar metabolic changes may also contribute to obesity prevention, especially when combined with regular exercise.

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Abbreviations: BMI = body mass index, BP = blood pressure, CT = computed tomography, CV = cardiovascular, DXA = Dual Energy X-Ray Absorptiometry, EC = epicatechin, ECG = epicatechin gallate, EGC = epigallocatechin, EGCG = epigallocatechin gallate, FMD = flow-mediated dilatation, GTN-D = glyceryl trinitrate-mediated dilatation, HR = heart rate, IAAT = intra abdominal adipose tissue.

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In recent years there has been increased interest in the health benefits of polyphenols, particularly flavonoids, which are found in plant-derived foods [7]. Dietary supplementation with flavonoids is associated with reduced CV mortality [8]. Flavonols are the predominant flavonoids found in tea, wine, cocoa, berries, apples and onions. They are comprised primarily of the catechins epigallocatechin gallate (EGCG), epigallocatechin (EGC), epicatechin gallate (ECG), and epicatechin (EC). Tea, in particular green tea in which EGCG is the most abundant catechin, has been investigated predominantly for its potential to prevent cancer [9] and CV disease [10]. However there is now evidence to suggest that green tea catechins, particularly EGCG, may have an additional metabolic role in reducing body fat [11].

Animal studies indicate that the consumption of green tea extracts containing catechins can increase fat oxidation at rest [12] and during physical activity [12, 13], can reduce body fat [14] and prevent the accumulation of fat mass when exposed to an obesogenic diet [15, 16]. Supplementation with EGCG alone has shown similar effects in preventing body fat accumulation in rodents exposed to a high fat diet [17,18]. These effects of green tea extracts and EGCG on body composition have been associated with changes in gene expression, which reduce lipogenic activity in adipose tissue and liver [17,18], and increase fatty acid oxidation in skeletal muscle [13].

Epidemiological evidence from humans indicates that habitual tea consumption (predominantly green tea) for >10 years is associated with a smaller waist circumference and waist to hip ratio, and a lower percentage of body fat [19]. Consumption of green tea extracts has been shown to increase fat oxidation and energy expenditure, particularly if combined with a metabolic stimulant such as caffeine [20–22], and reduce total and abdominal fat [23,24]. Bérubé-Parent [20] showed that the daily consumption of a green tea extract with 600 mg of caffeine and 270–1200 mg of EGCG increased energy expenditure. Similarly, Dulloo et al. [22] reported that daily supplementation with a green tea extract containing 150 mg of caffeine and 270 mg of EGCG resulted in an increase in energy expenditure, but also reported an increase in fat oxidation. Boschmann et al [21] subsequently showed that the combination of 300 mg/d of pure EGCG with 200 mg/d of caffeine resulted in a greater increase in fat oxidation than the same, or a higher dose of EGCG (600 mg/d) or 200 mg/d of caffeine alone, thereby demonstrating a synergistic effect of 300 mg/d of EGCG and 200 mg/d of caffeine. Moreover, Duffy et al. [25] have shown that tea consumption can improve endothelial function. This may result in increased blood flow to active skeletal muscle which, in combination with potential EGCG induced changes in gene expression, could facilitate fat oxidation in exercising muscles. While these studies only examined effects of EGCG on energy expenditure, fat oxidation and vascular function, which might favour reductions in body fat, Hase et al. [23] and Nagao et al. [24] reported that supplementation with green tea extracts containing EGCG and caffeine

did reduce body fat. Hase et al. [23] supplemented healthy male volunteers daily for 12 weeks with a green tea extract containing 75 mg of caffeine and a total of 483 mg of catechins, of which 72 mg was EGCG, and found a significant reduction in abdominal fat assessed by computed-tomography. Nagao et al. [24] also assessed the effects of 12 weeks supplementation with green tea extracts on body fat in healthy males by supplementing with 75 mg of caffeine per day and 690 mg of catechins, of which 136 mg were EGCG, and reported a significant reduction in body fat assessed by bioelectrical impedance, and a significant reduction in subcutaneous fat assessed by CT. Therefore, these studies suggest that the combination of caffeine with EGCG can increase energy expenditure and fat oxidation, and reduce body fat.

The metabolic and circulatory benefits of supplementation with EGCG when combined with the thermogenic stimulus of caffeine, are similar to those induced by aerobic exercise [26,27] and might be potentiated by combining EGCG supplementation with a regular exercise program. Indeed, Shimatoyodome et al. [12] found that the greatest reductions in body fat in rodents occurred when green tea supplementation was combined with exercise, compared with green tea supplementation or exercise alone. Therefore, the aim of this study was to investigate the metabolic effects of a combination of EGCG and regular aerobic exercise in overweight/obese post-menopausal women.

MATERIALS AND METHODS

Subjects

Post-menopausal women (follicle stimulating hormone \geq 25 IU/L) aged 45–70 y and with body mass index (BMI) 25–39.9 kg/m² were recruited for a 12-wk intervention trial. Potential subjects attended a medical screening which included physical assessments (height, weight, vital signs, physical examination), clinical assessments (liver function, serum electrolytes, haematology) and electrocardiogram monitoring during a graded exercise test to confirm suitability for exercise training.

Subjects were excluded if they drank more than 3 cups of green tea per day, had habitual caffeine intake exceeding 300 mg (> 3–4 cups of coffee per day), had diabetes, liver, gastrointestinal or CV disease, abnormal thyroid function, took hypertensive, lipid-lowering or anti-obesity medications, had a known hypersensitivity or allergy to green tea and/or EGCG, were on a weight reduction program, a medically supervised diet or had lost more than 5 kg within the month prior to the study, smoked (> 10 cigarettes/d), were participating in any other study or had donated blood or had antibiotic therapy for more than 7 d in the 3 mos prior to commencement of the study. Ethics approval was obtained from both the University of Adelaide and the University of South Australia and written informed consent was obtained from all subjects prior to their participation. Forty-two women began the study.

Study Design

Subjects were allocated to one of two groups which were balanced by age, BMI and fasting blood glucose. The groups were then randomly assigned to either of the two treatments. All subjects were required to run or walk for 45 minutes, 3 times per week at a HR which corresponded to 75% of their age predicted maximum in a protocol described previously [6]. One exercise group took 2 Teavigo® capsules/d containing 150 mg of EGCG (total EGCG intake 300 mg/d), while the other group took 2 placebo (lactose) capsules/d. Subjects consumed one capsule just prior to breakfast and the other prior to the evening meal, except on the three days per week when they performed their exercise training when one of the two capsules was taken 1 h prior to exercise.

Outcome measures were assessed and compared across each intervention group at wk 0, 6 and 12, with the exception of body composition (by DXA and CT), which was assessed at wk 0 and 12 only. Subjects attended two clinic visits at each of these time points where blood samples were collected and CV and anthropometric assessments were performed in a fasted state. All subjects were instructed to maintain their normal diet and physical activity patterns (in addition to completing their required exercise sessions) during the study. Subjects completed a 5 d physical activity diary (adapted from Bouchard et al [28]) and a weighed food record (analysed using *Foodworks Professional Edition*: Xyris Software, Version 3.02).

Clinical Assessments

Arterial Compliance, Blood Pressure, Heart Rate and Endothelial Function. Resting (supine) blood pressure (BP), HR and indices of arterial compliance were derived using the HDI/Pulsewave CR-2000 Cardiovascular Profiler (Hypertension Diagnostics Inc., Eagan, MN, USA). Assessments of endothelium-dependent flow-mediated dilation (FMD) and direct glyceryl trinitrate-induced (GTN-D) vasodilation were made using two dimensional B-mode ultrasound (LOGIQ 5, GE Medical Systems, Wisconsin, USA). The protocol for these procedures has been described previously [6].

Anthropometry. Measures of body weight, height, waist and hip circumference were taken at each time point (i.e. wk 0, 6 and 12), as previously described [29].

Total Body & Abdominal Composition. Body composition and abdominal fat were assessed in all subjects at wk 0 and 12 using DXA (*Lunar Prodigy*: General Electric, Madison, USA). Abdominal fat content calculated by DXA was determined for the body segment bordered superiorly and inferiorly by the lowest point of the rib cage and the uppermost aspect of the iliac crests respectively, and extended laterally to the outer edge of the rib cage [30]. Subcutaneous and intra abdominal adipose tissue (IAAT) was determined using single slice CT (Toshiba Aquilion; Toshiba Medical Systems, Japan). The protocol for these assessments has been described previously [29].

Laboratory Analyses

Blood Sample Collection, and Standard Clinical Laboratory Analysis. Fasting blood (10–12 h overnight) was obtained at each visit by direct venipuncture of a forearm vein. Standard clinical laboratory analyses were performed at the screening visit (wk 0) and subsequently at wk 6 and 12. These measures included follicle stimulating hormone (for inclusion criteria only), insulin, glucose, blood lipids, adipocytokines (adiponectin and leptin), haematology, liver function and serum electrolytes.

Statistical Analysis

Statistical analysis was performed using *Statistica for Windows* (Version 5.1, StatSoft Inc, Tulsa, USA). Based on previous estimates of variance in abdominal adiposity [31], 24 subjects (12 volunteers per group) provided 90% power at $p < 0.05$ to detect a 5% change in abdominal fat mass. Given that this population was unaccustomed to exercising it was anticipated that the drop out rate could be as high as 40%. Therefore, it was determined that 42 volunteers would provide sufficient numbers for the start of the trial. The student t-test was used to compare group means at base. Analysis of variance (ANOVA) with repeated measures was used to determine the effect of the treatment, time of measurement, and their interactions on the dependent variables. Where appropriate, analysis of covariance (ANCOVA) with repeated measures was used. Where ANOVA or ANCOVA showed a statistically significant main effect, pairwise comparisons were performed using Tukey's test for differences between means. A p value of ≤ 0.05 was considered statistically significant. Results are presented as means \pm SEM.

RESULTS

Subjects

Of the 42 subjects who began the study, 4 were withdrawn from the trial (one due to a knee injury and 3 were non-compliant) leaving a total of 38 subjects who completed the study requirements ($n = 19$ per treatment group). Their baseline (wk 0) characteristics are shown in Tables 1 and 2. There were no differences between groups for any of these characteristics.

Effects on Energy Intake and Expenditure, Total Body and Abdominal Composition

Energy intake (kJ) and background energy expenditure (kJ) remained constant throughout the intervention for both treatment groups. Subjects in both treatments groups showed significant reductions in total body fat ($p < 0.02$), abdominal fat (determined by DXA; $p < 0.01$), IAAT (determined by CT; $p < 0.01$), waist circumference ($p < 0.01$) and waist to hip ratio

Table 1. Baseline (Wk 0) Characteristics and Effects of Treatment on Energy Intake, Energy Expenditure and Body Composition

	PLACEBO		TEAVIGO®	
	Baseline	Change by Week 12	Baseline	Change by Week 12
Energy intake (kJ/day ⁻¹)	7626 ± 384	477 ± 429	7755 ± 360	343 ± 459
Energy expenditure (kJ/day ⁻¹)	3410 ± 534	-11 ± 181	3428 ± 295	-99 ± 222
Body mass (kg)	81.05 ± 2.01	-0.45 ± 0.27	79.92 ± 1.73	0.08 ± 0.21
Body mass index (kg/m ²)	31.39 ± 0.73	-0.16 ± 0.10	30.65 ± 0.59	0.03 ± 0.08
Total body fat mass (kg)	36.9 ± 1.4	-0.8 ± 0.2*	36.4 ± 1.1	-0.2 ± 0.3*
Total body lean mass (kg)	40.0 ± 0.9	0.2 ± 0.2	39.4 ± 0.8	-0.1 ± 0.2
% Body fat	47.85 ± 0.78	-0.7 ± 0.22	47.82 ± 0.67	0.04 ± 0.34
Abdominal fat mass (g)	2311 ± 124	-87 ± 32*	2406 ± 121	-70 ± 25*
Visceral fat area (cm ²)	128.7 ± 10.7	-12.0 ± 3.9*	134.6 ± 8.4	-6.5 ± 5.1*
Subcutaneous fat area (cm ²)	372.9 ± 16.0	-3.9 ± 8.5	374.3 ± 15.2	-1.3 ± 5.0
Waist circumference (cm)	104.7 ± 2.0	-2.69 ± 0.55*	102.4 ± 1.8	-1.02 ± 0.64*
Hip circumference (cm)	113.5 ± 1.5	-0.81 ± 0.37	112.6 ± 1.0	-0.38 ± 0.47
Waist to hip ratio	0.92 ± 0.01	-0.017 ± 0.005*	0.909 ± 0.01	-0.006 ± 0.006*

Data are mean ± SEM. Significant change from baseline, **p*<0.01.

Table 2. Baseline (Wk 0) Characteristics and Effects of Treatment on Metabolic and Cardiovascular Biomarkers

	PLACEBO		TEAVIGO®	
	Baseline	Change by Week 12	Baseline	Change by Week 12
Plasma glucose (mmol · l ⁻¹)	5.53 ± 0.11	-0.01 ± 0.06	5.39 ± 0.10	-0.09 ± 0.10
Fructosamine (μmol · l ⁻¹)	244.21 ± 2.82	3.65 ± 4.21	242.7 ± 3.40	4.06 ± 2.85
Plasma insulin (mU · l ⁻¹)	8.08 ± 1.03	-0.55 ± 0.77	10.99 ± 1.82	-3.2 ± 1.52
Adiponectin (ng · ml ⁻¹)	13.30 ± 1.14	-0.6 ± 0.9	13.04 ± 1.60	-0.5 ± 1.0
Leptin (ng · ml ⁻¹)	36.93 ± 4.03	-3.3 ± 1.5	34.33 ± 3.37	0.7 ± 1.6
Systolic blood pressure (mmHg)	122.58 ± 3.28	0.79 ± 1.63	125.2 ± 2.96	0.04 ± 2.02
Diastolic blood pressure (mmHg)	69.46 ± 1.73	1.35 ± 0.99	70.93 ± 1.35	0.75 ± 1.45
Resting Heart rate (bpm)	61.7 ± 2.1	1.0 ± 0.3	64.5 ± 1.7	-3.6 ± 1.1**
Small artery compliance (ml · mmHg ⁻¹ · 100)	5.47 ± 0.69	0.57 ± 0.78	5.47 ± 0.64	0.31 ± 0.54
Large artery compliance (ml · mmHg ⁻¹ · 10)	14.30 ± 0.81	-0.04 ± 0.44	14.41 ± 0.72	0.58 ± 0.55
FMD (%)	5.77 ± 0.81	-0.38 ± 0.98	5.96 ± 0.70	-0.41 ± 0.82
GTN-D (%)	26.10 ± 1.35	-0.35 ± 1.46	24.25 ± 1.10	0.55 ± 1.05

Data are mean ± SEM.

Abbreviations: FMD = flow-mediated dilatation, GTN-D = glyceryl trinitrate-mediated dilatation.

Significantly different from placebo; ***p*<0.01.

(*p*<0.01) by wk 12 (Table 1). However, there were no differences between treatment groups for any of these parameters.

Effects on CV and Metabolic Biomarkers

Arterial compliance, endothelial function and BP did not change as a result of either treatment, although a significant reduction in HR was observed in subjects supplemented with Teavigo® (Table 2, *p*<0.01). Blood lipids (triglycerides, total cholesterol, high-density lipoprotein and low-density lipoprotein cholesterol), adiponectin, leptin, insulin and glucose were also unaffected by either treatment. However, Teavigo® reduced plasma glucose concentrations by 0.27 mmol/L (i.e. ≈5%) in subjects with impaired glucose tolerance (*n* = 7) as determined by fasting glucose levels >5.5 mmol/L (see Fig. 1; *p*<0.05). Measures of liver function, haematology and serum electrolytes remained within healthy ranges throughout the

intervention, indicating that there were no adverse effects of treatment.

DISCUSSION

The aim of this study was to compare effects of EGCG versus placebo supplementation on total and abdominal fat and CV risk factors in overweight or obese post-menopausal women undergoing regular aerobic exercise. The results suggest that exercise-induced changes in body composition, particularly in abdominal fat, are not enhanced by a daily dose of 300 mg of EGCG (Teavigo®). Moreover, this treatment had minimal impact on CV or metabolic health, except for a reduction in resting HR and fasting blood glucose (in subjects with impaired glucose tolerance).

The results of this trial contrast with findings of animal studies [17,18] and other human trials [20,22–24]. In rodents

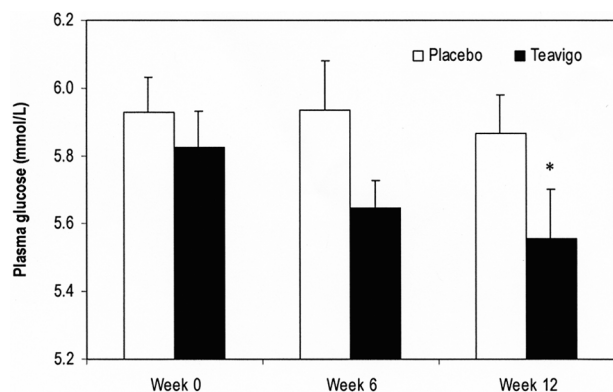


Fig. 1. Plasma glucose in subjects with impaired glucose tolerance. *Significantly different from placebo, $p < 0.05$.

green tea extracts containing EGCG can improve body composition [17,18], while in humans EGCG in combination with caffeine can increase fat oxidation and energy expenditure [20–22] and reduce total and abdominal fat [23,24]. Using a double-blind cross-over design, Bérubé-Parent et al. [20] examined the effects of combining varying doses of EGCG (90–400mg) with a fixed dose of caffeine (200 mg) on energy expenditure. They observed an 8% increase in 24 hr energy expenditure with all caffeine+EGCG doses compared with a cellulose placebo. Similarly, using the same study design, Dulloo et al. [22] examined the effects of consuming a green-tea extract containing 270 mg EGCG combined with 150 mg caffeine per day on energy expenditure. The combination of EGCG and caffeine increased 24 hr energy expenditure by 4% compared with caffeine alone or a placebo. Similarly, Boschmann et al. [21] reported an increase in fat oxidation with either 300 or 600 mg EGCG/d and an exponential synergism in fat oxidation when EGCG was combined with caffeine.

Hase et al. [23] and Nagao et al. [24] investigated the effects of 12 weeks of supplementation with high and low doses of green tea catechins on body fat reduction in normal weight to obese volunteers. Hase et al. [23] reported that subjects receiving a high catechin dose (total catechins; 483 mg, EGCG; 301 mg) had a reduction in total body fat (assessed using bioelectrical impedance) and abdominal fat (assessed by CT), while subjects receiving a low catechin dose (total catechins; 119 mg, EGCG; 32 mg) did not, although these reductions in fat were not significantly different between treatments. However, Nagao et al. [24] reported greater reductions in body weight, total body fat (assessed by bioelectrical impedance) and abdominal fat (by CT) with a total catechin dose of 690 mg (containing 136 mg EGCG), compared to a control dose of 22 mg (containing 3.1 mg EGCG). This reduction in abdominal fat was due to a significant decrease in subcutaneous fat, with only a trend for a greater reduction in intra abdominal adipose tissue compared with placebo.

These effects of EGCG on fat loss may be mediated through activation of an EGCG receptor which regulates energy intake

and expenditure [32]. Animal studies have demonstrated that EGCG can up-regulate several lipid metabolizing enzymes, including acetyl CoA carboxylase [33] and fatty acid synthase [34]. Together, these data suggest that green tea catechins, particularly EGCG, have the potential to reduce body fat in humans, and this effect may be enhanced when combined with a metabolic stimulant.

In rodents, Shimatoyodome et al. [12] found that the addition of a green tea extract (80.3% catechins by weight of which EGCG represented 40.6%) to the diet (0.5% w/w) combined with regular aerobic exercise, resulted in a greater attenuation of visceral fat accumulation (87%) compared with green tea supplementation (58%) or exercise (37%) alone. However, despite reported increases in fat oxidation in other studies [20–22], we found that taking 300mg EGCG/d did not reduce body fat beyond the effect of aerobic exercise alone in overweight/obese postmenopausal women. Increases in energy expenditure and changes in body composition have been observed with similar [20,23] or lower [22,24] intakes of EGCG, although the total intake of catechins was greater in these studies. It is unclear whether EGCG is the exclusive mediator of potential metabolic benefits or if other catechins are equally or more efficacious than EGCG [35].

There is evidence to suggest that green tea consumption can improve circulatory function by inhibiting smooth muscle proliferation, preventing platelet aggregation, neutralising free radicals and promoting vasorelaxation [10]. Both short (2 h) and long-term (4 wk) tea consumption has been shown to improve endothelium-dependent vasodilatation in coronary artery disease patients [25]. This improvement may be attributable to EGCG, which has been shown to activate endothelial nitric oxide synthase [36,37] and increase nitric oxide release [37,38]. However, it appears that the sustained improvement of endothelial function [25] can be attributed to the total flavonoid intake rather than a single catechin such as EGCG [35]. It is therefore possible that the lack of effect of EGCG on endothelial function in this study was due to a lower overall consumption of catechins, an argument which may apply equally to the lack of effect on body composition. As the plasma level of EGCG appears to be exponentially related to EGCG intake [39], it may be possible to elicit significant effects on body composition with marginally higher intakes of EGCG.

Although supplementation with EGCG did not alter fat metabolism in this study, we observed a reduction in plasma glucose in subjects with impaired glucose tolerance, although the long-term regulation of glucose (fructosamine) did not change. This is in accordance with results from other studies investigating the effects of tea catechins on glucose metabolism. Hosoda et al. [40] administered 1500mL of oolong tea (EGCG content, 386 mg) or water for 30 days to type 2 diabetics taking hyperglycemic medication. Oolong tea significantly reduced fasting blood glucose and fructosamine concentrations, while there were no changes in

subjects consuming water. In a study investigating the acute effects of green tea on glucose metabolism [41], 1.5 g green tea powder in 150 mL of water significantly improved glucose tolerance in healthy subjects compared to administration of hot water alone. Green tea catechins may lower plasma glucose by increasing the uptake and translocation of the GLUT4 protein in skeletal muscle [14].

CONCLUSION

A daily intake of 300 mg of EGCG (Teavigo®) superimposed on a program of regular exercise has no demonstrable effects on body composition but may improve plasma glucose levels in subjects with glucose intolerance. We suggest that a greater total catechin intake or addition of a metabolic stimulant such as caffeine may be needed to alter body composition.

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