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Green Tea minimally affects Biomarkers of Inflammation in Obese Subjects with Metabolic Syndrome

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Abstract

Objective—Green tea (*Camellia sinensis*) has shown to exert cardio-protective benefits in observational studies. The objective of this clinical trial was to assess the effects of green tea on features of metabolic syndrome and inflammation in obese subjects.

Methods—We conducted a randomized controlled trial in obese subjects with metabolic syndrome. Thirty-five subjects [age (mean±SE) 42.5±1.7 years, BMI 36.1±1.3 kg/m^2] completed the 8-week study and were randomly assigned to receive green tea (4 cups/day), green tea extract (2 capsules and 4 cups water/day), or no treatment (4 cups water/day). Both the beverage and extract groups had similar dosing of epigallocatechin-3-gallate (EGCG), the active green tea polyphenol. Fasting blood samples were collected at screening, four, and eight weeks of the study.

Results—Green tea beverage or extract supplementation did not significantly alter features of metabolic syndrome or biomarkers of inflammation including adiponectin, C-reactive protein (CRP), interleukin-6 (IL-6), interleukin-1β (IL-1β), soluble vascular cell adhesion molecule-1 (sVCAM-1), soluble intercellular adhesion molecule-1 (sICAM-1), leptin, or leptin:adiponectin ratio. However, both green tea beverage and extracts significantly reduced plasma serum amyloid alpha (SAA) versus no treatment ($p<0.005$).

Conclusion—This study suggests that the daily consumption of green tea beverage or extracts for 8 weeks was well tolerated but did not affect the features of metabolic syndrome. However, green tea significantly reduced plasma SAA, an independent CVD risk factor, in obese subjects with metabolic syndrome.

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Conflicts of interest: None

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Keywords

Green tea; Inflammation; Serum amyloid A; Metabolic syndrome

Introduction

A growing body of evidence indicates the role of green tea or its bioactive polyphenol, epigallocatechin gallate (EGCG), in significantly ameliorating features of metabolic syndrome, and subsequent risks for type 2 diabetes mellitus and cardiovascular disease (CVD) [1–3]. Metabolic syndrome, a constellation of several risk factors, including abdominal adiposity, hypertension, dyslipidemia (high triglycerides, low HDL), and impaired fasting glucose, has also been associated with chronic inflammation, insulin resistance and endothelial dysfunction [4,5]. Habitual consumption of green tea (*Camellia sinensis*), a popular beverage used in traditional Chinese medicine, has been associated with decreased risks for obesity [6], diabetes [7,8], hypertension [9], dyslipidemia [10,11], and CVD mortality [12–14] in several epidemiological studies. In selected clinical trials, green tea supplementation has been shown to significantly improve features of metabolic syndrome, such as, decreased abdominal adiposity indicated by waist circumference in obese subjects [15–17], reduced blood glucose and hemoglobin A_{1C} in pre-diabetic or diabetic patients [18,19], improved postprandial lipid responses in subjects with mild hypertriglyceridemia [20], and, increased flow-mediated dilation in smokers or subjects with endothelial dysfunction [21,22]. However, these epidemiological and clinical studies have been mostly conducted in populations in Asian countries with habitual green tea consumption. Also, in some trials outcomes are significant versus baseline but not control group, or are possibly confounded by the habitual caffeine intake by the subjects, or caffeine content in green tea. Thus, these limited human studies showing positive effects of green tea in metabolic syndrome, emphasize the need for further controlled intervention trials using decaffeinated green tea in populations with salient features of metabolic syndrome and CVD risk factors.

Clinical trials have reported mixed results on the effects of green tea on biomarkers of inflammation, which is associated with metabolic syndrome and CVD. In an uncontrolled study in male smokers, green tea consumption (600mL/day) for four weeks was shown to decrease P-selectin levels, suggesting a decrease in risk factors of atherosclerosis in these subjects [23]. In contrast, in a randomized controlled study, green tea intervention (900 ml green tea or 3.6g green tea polyphenols) for four weeks showed no effects on inflammatory markers such as C-reactive protein (CRP), interleukin-6 (IL-6), interleukin- 1β (IL-1β), or tumor necrosis factor-α (TNF-α) in healthy smokers [24]. In a postprandial study, green tea intake (6 g) versus controls improved endothelial function, but had no effects on biomarkers of inflammation in healthy individuals [25]. Studies in subjects with borderline diabetes or diabetes have shown no significant effects of green tea consumption (456mg green tea catechins for two months or 900ml of green tea for four weeks) on markers of inflammation [18,26]. Thus, based on these results, anti-inflammatory effects of green tea supplementation need further investigation in subjects with metabolic syndrome in controlled long-term intervention trials.

Several mechanistic studies using animal models of obesity, metabolic syndrome and CVD also provide data substantiating the anti-obesity [27,28], anti-diabetic [29,30], anti-hypertensive [31,32], anti-hyperlipidemic [33,34], and anti-inflammatory [35,36] effects of green tea. Ramadan et al. [34] have reported the effects of a 28-day supplementation of green tea aqueous extracts in significantly alleviating hyperglycemia, dyslipidemia, and impaired liver function in male Wistar albino rats fed a cholesterol-rich diet. Ramesh et al.

[35] have shown anti-inflammatory effects of intraperitoneal administration of EGCG (100mg/kg body weight) in significantly reducing serum CRP levels and hematological markers of inflammation in rats fed an atherogenic diet versus the untreated group. Oral administration of EGCG (100 mg/kg body weight) in aged male Wistar albino rats fed a high-fat diet was also shown to significantly decrease CRP and TNF-α versus the unsupplemented group [36]. Thus, these animal studies show the benefits of green tea extracts or EGCG treatment in reversing high-fat diet induced inflammation and glucose and lipid abnormalities associated with metabolic syndrome. These potential benefits of green tea need to be confirmed in clinical trials, especially in US populations with increasing prevalence of obesity and metabolic syndrome [37].

Thus, the objective of our study was to test whether daily consumption of green tea beverage (4 cups/day) or extracts (2 capsules/day and 4 cups water/day) over a period of eight weeks would affect biomarkers of inflammation and features of metabolic syndrome versus age and gender matched no treatment (4 cups water/day) group, thereby lowering CVD risk factors in the US population with metabolic syndrome.

Materials & Methods

Subjects

Forty-one subjects with metabolic syndrome were recruited by flyers and e-mail advertisements at the General Clinical Research Center (GCRC) at University of Oklahoma Health Sciences Center (OUHSC). Subjects were included in the study if they had three of five features of metabolic syndrome as defined by the National Cholesterol education Program (NCEP), Adult Treatment Panel III (ATP III) guidelines [38]. Participants were excluded from the trial if they were under 21 years of age, had a pre-existing condition (e.g. diabetes, cancer, heart disease), liver or renal disorders, or anemia. Potential recruits were also excluded if they were consuming > 1g/day of antioxidants/fish oil supplements, were current smokers or used any kind of tobacco products, consumed alcohol on a regular basis (except social drinking), were pregnant or lactating or if their hemoglobin (Hb), white blood cells (WBC), platelets, liver, renal, or thyroid function tests were outside of the normal ranges. Subjects on stable medications (except hypoglycemic and hypolipidemic agents) were included in the study. Written informed consent was obtained from all potential recruits at the screening visit. The study was approved by the Institutional Review Board (IRB) at University of Oklahoma Health Sciences Center (OUHSC) and at Oklahoma State University (OSU).

Green tea beverage and extracts

Decaffeinated green tea bags were purchased from RC Bigelow Inc.© (Fairfield, CT). Four tea bags were steeped in 4 cups of boiled water (8 oz/cup) for 10 minutes. No sugar or milk was added to the tea, but artificial sweetener was used according to the preference of the participants. Each cup of green tea provided approximately 110mg of EGCG, 55 mg EGC, 45mg ECG, and 22mg EC. The decaffeinated green tea extract capsules were purchased from Solaray® (Park City, UT). The capsules were manufactured from the same lot numbers of raw materials. The label claimed 500 mg of green tea extract providing 400mg catechins and 250 mg EGCG. Other ingredients included in the capsule as filler were vegetable cellulose, magnesium stearate and silica. Each capsule contained approximately 230mg EGCG, 120mg EGC, 60mg ECG, and 25mg EC.

The catechin content, primarily EGCG, EGC, ECG, and EC, in green tea leaves (tea bags) and capsules were analyzed using the procedure described previously by Seeram et al. [39]. Briefly, 100mg of green tea leaves or extract powder were weighed and sonicated for 10

minutes in methanol:water (1:1). The extracts were filtered (0.22μm) and analyzed on a Waters column (Symmetry C18, 100 mm × 4.6 mm, 3.5 μm). Mobile phase consisted of acetonitrile and 0.2% aqueous phosphoric acid under binary linear gradient conditions. The wavelength was detected at 278nm and catechins were quantified using reference standards. All solvents were HPLC grade and purchased from Pharmco (Brookfield, CT). Catechin standards (EGCG, EGC, ECG & EC) were purchased from Sigma Aldrich Co. (St. Louis, MO). The HPLC-UV detection system consisted of a Waters 600 Controller multisolvent delivery system pump, a Waters 717plus Auto sampler, a Waters 2487 Dual λ Absorbance Detector, and Empower Pro software, Build 1154 (Waters, Milford, MA).

Study protocol

This was a randomized controlled trial with a single blind and permuted block randomization design. To account for the effects of age and gender on the variables of interest, participants were recruited into trios matched for age (± 5 years) and gender. The age and gender for a trio was determined by the first participant assigned to that trio. The next consecutive participant that met the matching criteria of that trio was assigned as the second participant of that trio, and so on. Each trio had one participant in each of the three intervention groups: green tea (4 cups/day), green tea extracts (2 capsules, 4 cups water/day), or no treatment (4 cups water/day). While trios were filled consecutively with participants meeting the matching parameters, the intervention to which the first, second, and third participants in the trio were assigned was pre-determined by random permutation.

Participants in the no treatment and green tea extract groups came in for follow-up visits at 2, 4, 6, & 8 weeks and were provided with containers to measure 4 cups of water to be consumed on a daily basis. Those in the extract group received a 2-week supply of capsules during their follow-up visits and were instructed to take 2 capsules a day, morning and evening at least 6–8 hours apart. Compliance was confirmed by pill count. The green tea beverage group made daily visits to the GCRC for a fresh supply of tea. This was to ensure compliance and consistency since, in our opinion, instructing subjects to prepare the tea themselves and drink 4 cups a day for 8 weeks would introduce inconsistencies and lack of compliance. Subjects in the green tea group consumed 2 cups of green tea in the morning at the GCRC and were provided with another 2 cups in a container and asked to consume at least 6–8 hours later in the day. Participants were told not to reheat the tea which they consumed later in the day, but to drink it straight from the container. The Bionutrition unit at the GCRC prepared the green tea for the subjects and monitored compliance. All subjects were asked to refrain from any other source of green tea or related supplements other than that provided by the study, and to maintain their usual diet, physical activity and lifestyle while enrolled in the study. Bionutrition staff was instructed not to discuss diet or weight issues with participants to avoid potential confounding factors which may arise as a result of daily visits of the tea group versus weekly visits of the extract and no treatment groups at the clinic. Subjects were compensated during their follow-up visits. Since we compared the effects of green tea beverage or green tea extract capsules with water, it was not possible to blind the participants to the interventions. However, the laboratory personnel and GCRC nurses were blinded to the particpants' intervention group; the recruitment and Bionutrition staff at the GCRC was not involved in physical measurements or laboratory analyses. Participants were asked not to discuss or mention their intervention with the GCRC nurses. Dietary data were collected at screen and eight weeks of the study.

Body weight, height, blood pressure and waist circumference were measured by trained personnel at GCRC. At screening visit, fasting serum samples were drawn and sent to the University of Oklahoma Medical Center (OUMC) Laboratory for analyses of fasting glucose, lipid profile {total cholesterol, triglycerides, low-density lipoproteins (LDL), high-density lipoproteins (HDL)}, and other blood variables [hemoglobin (Hb), platelets, white

blood cells (WBC), liver enzymes, creatinine, body urea nitrogen (BUN), electrolytes, albumin, total protein, and thyroid-stimulating hormone (TSH)]. Fasting EDTA-plasma samples were collected at screen, four and eight weeks of the study, separated by centrifugation (3000 rpm for 10 min at 4°C) and stored at −80°C for subsequent analyses of biomarkers of inflammation.

Biomarkers of inflammation

Plasma concentrations of CRP, Adiponectin, IL-6, IL-1β, sICAM-1, sVCAM-1, and leptin were determined using ELISA kits (R&D Systems, Inc. Minneapolis, MN) according to the manufacturer's protocol. The plasma was diluted in diluent buffer in the following ratio: 1/10000, 1/10000, 1/1, 1/100, 1/1000, 1/1000, and 1/100 respectively. The minimum detectable level was 15.625, 62.5, 9.375, 0.04, 15.625, 15.625 and 31.25 pg/ml, for each assay, respectively. The inter-assay CV was 6.24, 3.59, 3.10, 2.56, 3.51, 7.59, and 11.68%, respectively. Plasma levels of SAA were determined using ELISA kit (Invitrogen Corporation, Camarillo, CA), based on the manufacturer's guidelines. The minimum detectable level was <4ng/mL. Plasma samples were diluted 200-fold in diluent buffer and the average inter-assay CV was 6.8% for SAA.

Statistical analyses

All measures had descriptive statistics calculated and graphs drawn to look for outliers. Outliers due to data errors were corrected where possible or removed. Pair wise differences (green tea versus no treatment and green tea extracts versus no treatment) between the three groups at baseline were assessed using student t-tests.

Changes in measurements over the eight week study period were assessed by calculating the difference between the pre- (baseline) and post- (8 weeks) intervention measurements. Differences between the green tea or green tea extract group and the no treatment group were tested essentially using t-tests for paired data: differences calculated for the green tea and green tea extract groups were conditioned on their respective no treatment group; the difference seen in the no treatment participant was subtracted from the difference seen in each corresponding green tea and green tea extract participant within the age and gender matched trio. These conditional differences for the green tea and green tea extract groups were then assessed as being different from zero (no change) using student t-tests. All statistical tests were two-tailed with a conservative Bonferroni adjustments for multiple hypothesis testing in which alpha was set at 0.005. SPSS for Windows (version 15.0, SPSS Inc., 2006) was used for the statistical calculations.

Results

Forty-one individuals were recruited for the study. Two people withdrew due to relocation and personal reasons, and four were withdrawn on account of starting cholesterol (1) and glucose lowering (1) medications during the study, and for smoking (2). Thus, a total of 35 subjects completed the study with a mean age of 42.5±1.7 years and a mean BMI of 36.1±1.3 kg/m^2 at screening visit. No significant differences were noted in baseline characteristics except for total and LDL- cholesterol levels which were significantly higher in the no treatment group in comparison to those taking green tea extracts (Table 1).

Out of fifteen trios created throughout the two-year study period, eleven were completed or had a no treatment and tea or no treatment and supplement pair which could be used for comparisons. Trios without a no treatment participant had to be excluded from data analyses. Consequently, a total of 29 subjects were used in data analyses, forming 11 green tea – no treatment and 7 green tea extract – no treatment pairs.

Plasma concentrations of adiponectin, CRP, IL-6, IL-1β, sVCAM-1, sICAM-1, leptin and leptin: adiponectin ratio were not significantly affected by green tea beverage or extract supplementation for eight weeks versus age and gender-matched no treatment group (Table 2). However, the green tea beverage group showed a non-significant decrease in IL-6 levels (37%, p=0.3) compared to baseline. Pair wise comparisons showed a significant decrease in plasma SAA in green tea beverage (14.4%, $p<0.005$) and green tea extract (24.5%, $p<0.005$) groups versus no treatment subjects at eight weeks of the study (Table 2).

Green tea beverage or green tea extract supplementation did not significantly affect features of metabolic syndrome as defined in this study [38], including waist circumference, systolic and diastolic blood pressure, triglycerides, HDL, and fasting glucose versus no treatment group. The prevalence of the features of metabolic syndrome was the highest for low HDL (94%), followed by enlarged waist circumference (91%), elevated systolic and/or diastolic blood pressure or on blood pressure medications (71%), elevated triglycerides (54%), and impaired fasting glucose (20%) among the study subjects. Plasma concentrations of safety parameters including AST, ALT, BUN, creatinine, Hb, platelets, WBC, electrolytes, albumin, total protein, and TSH remained unaltered by green tea beverage or extract supplementation for all participants.

Discussion

To our knowledge, this is the first study investigating the effects of decaffeinated green tea supplementation on biomarkers of inflammation and features of metabolic syndrome in obese population in the US. Our study results show that green tea beverage or extract supplementation selectively lower plasma SAA versus the no treatment group. However, green tea intervention did not affect inflammatory markers including CRP, IL-6, IL-1β, sVCAM-1, sICAM-1, adiponectin and leptin or features of metabolic syndrome.

SAA, a family of apolipoproteins expressed in hepatocytes and adipocytes has been shown to increase oxidative stress, decrease endothelial nitric oxide synthase (eNOS) activity, and impair reverse cholesterol transport by HDL particles [40–43]. A cross-sectional study among overweight or obese postmenopausal women has shown lower SAA levels among women with higher quality dietary patterns versus those with lower scores [44]. A 6-week green tea polyphenol supplementation significantly decreased SAA and severity of colitis in an animal model of chronic inflammation at dietary achievable doses [45]. However, catechin supplementation for six weeks in apo E-deficient mice had no effects on plasma SAA [46]. Clinical studies investigating the effects of dietary factors including polyphenols on SAA are limited. Previously, Nantz et al [47]. have reported that green tea polyphenols significantly reduced SAA in healthy adult volunteers. The subjects took 200 mg of decaffeinated green tea extracts twice a day for 3 weeks. In contrast, polyphenols from soy, instead of green tea, showed no effect on plasma SAA. In a 3-month study involving a one month control phase, followed by one month each of high- and low-soy isoflavone intervention, no treatment differences were observed on plasma SAA among hypercholesterolemic men and postmenopausal women [48]. In our study, administration of green tea beverage or extract, equivalent to approximately 440mg or 460mg EGCG, respectively, was effective in reducing SAA in obese subjects with metabolic syndrome. In comparison to our study, the null effects reported by Jenkins et al. [48] may be explained by the short duration of each intervention, differences in study sample, and possible differential effects of soy flavonoids versus green tea flavonoids in lowering SAA. Cardiovascular epidemiology has shown SAA to be an independent predictor for cardiovascular disease in women with suspected myocardial ischemia and for early mortality in patients with acute coronary syndromes [49,50]. Furthermore, baseline serum SAA in our subjects with metabolic syndrome (mean±SE, 53.0±1.0 μg/mL) was higher than the levels reported by

Nantz et al. [47] or Jenkins et al. [48] in their healthy or hypercholesterolemic subjects, respectively, and was comparable to SAA reported in women with advanced CVD [50]. Thus, our data suggest the possible anti-inflammatory role of green tea flavonoids in reducing elevated SAA in obese subjects with metabolic syndrome. However, this observation needs to be confirmed in larger clinical trials.

CRP, an acute phase protein synthesized by the liver has shown to be a powerful predictor of cardiovascular risk compared to other inflammatory markers [51,52]. In our study subjects with metabolic syndrome, all participants had baseline CRP level >3mg/L (mean±SE, 6.2±1.2 mg/L), a high-risk category for CVD [53]. Serum CRP has been inversely associated with dietary flavonoid intake in US adults, especially with the intakes of foods and beverages high in flavonols (onions, apples, tea), anthocyanidins (berries), procyanidins (dark chocolate) and isoflavones (soy) [54,55]. However, limited clinical data exist on the effects of tea flavonoids on CRP. Both acute and chronic (4 weeks) consumption of 450ml and 900ml of black tea, respectively, showed no effects on CRP in patients with coronary artery disease [56]. Acute consumption of green tea (6g) by smokers failed to show any effects on CRP compared to the matched caffeine or water group [25]. In another 4-week study among smokers, de Maat et al. [24] reported no effects of green tea intervention (3.6g polyphenols) on plasma CRP levels. We report similar findings in our 8-week study which showed no effects of green tea (960ml) or green tea extract (870mg green tea catechins) supplementation on plasma CRP levels. It is possible that a higher dose of green tea flavonoids or a combination of different flavonoids might be effective in lowering CRP and this remains an area of further investigation.

Circulating levels of adipocytokines, such as IL-6, IL-1β and adhesion molecules like sVCAM-1 and sICAM-1 expressed in vascular endothelium, have been associated with increased risks of cardiovascular events in apparently healthy subjects or in patients with existing CAD [57–60]. While limited in vitro data show the inhibitory effects of green tea polyphenols or EGCG on IL-1β and/or IL-6 synthesis [61,62] and/or expression of VCAM-1 [63], human studies are inadequate and remain inconclusive. Lee et al. [23] showed a selective effect of green tea beverage in lowering P-selectin, an adhesion molecule in smokers in an uncontrolled 4-week study. However, no effects were seen in IL-6 in type 2 diabetic subjects following green tea intervention for 4 weeks [26]. We found no significant change in circulating levels of cytokines or adhesion molecules in our study subjects with metabolic risk factors. Thus, flavonoid modulation of cytokines and adhesion molecules in a clinical setting appears to be selective and warrants further investigation. Also, baseline mean concentrations of IL-6 (23.5±12.0 μg/L), IL-1β (0.22±0.02 pg/mL), sVCAM-1 (250.1±24.2 ng/mL) and sICAM-1 (107.3±9.7 ng/mL) were lower in our subjects with metabolic syndrome in comparison to previously reported levels in subjects with metabolic syndrome or advanced CVD [59,60,64,65], and this may account for the null effects of green tea intervention. Furthermore, certain classes of anti-hypertensive medications, such as angiotensin II antagonists and angiotensin converting enzyme inhibitors, have been shown to exert anti-inflammatory effects [66,67]. Since a significant number of our study subjects were on stable medications for hypertension, this could possibly contribute to the observed null effects of green tea intervention on inflammatory markers including CRP, IL-6, IL-1β or adhesion molecules.

Adiponectin, an anti-inflammatory adipocytokine has shown to be reduced in subjects with metabolic syndrome versus subjects with null or fewer features of metabolic syndrome [68,69]. Subjects in our study had mean baseline adiponectin concentrations of 2.0±0.4 mg/L, which are comparable to previously reported studies in which subjects in the lowest quartile of adiponectin (< 5.0 mg/L) had highest incidence or risks of metabolic syndrome [70,71]. Green tea catechins have been shown to up regulate adiponectin expression in

mouse preadipocyte cells [72]. However, in our study, green tea supplementation had no significant effects on adiponectin levels. Our results are comparable to previously reported dietary intervention studies in which adiponectin levels were unaltered: following green tea supplementation in type 2 diabetic subjects [26], after significant diet-induced weight loss [73], or in obese subjects on a very low-calorie diet [74]. Thus, the role of dietary factors in modulating adiponectin levels needs further investigation. We also measured leptin: adiponectin ratios in our study, which however showed no significant effects. Leptin, a hormone secreted by adipose tissue has been positively correlated with obesity and metabolic syndrome [75,76]. In our study, the average baseline leptin concentrations of 39.0±7.2 ng/mL are higher than previously reported studies in subjects with metabolic syndrome [77,78]. A combination of soy, black and green tea polyphenols was shown to significantly reduce serum leptin concentrations in both male and female mice, though the effects cannot be attributed to green tea per se [79]. While green tea polyphenols and leptin levels have not been previously correlated in humans, our data suggest that the cardio protective effects of green tea are not mediated via circulating leptin levels in obese subjects.

Furthermore, the baseline values for individual components of metabolic syndrome, including glucose and lipid profiles, were mildly elevated in our study subjects. The mean baseline values for blood pressure, glucose, triglycerides and total cholesterol were either normal or slightly elevated in the green tea, green tea extract or no treatment group. Also, the recently updated definition of metabolic syndrome has unifying criteria, and requires the cut points for waist circumference to be specific to the population being studied, and the country of study setting [80]. In light of this new definition, our sample size of primarily US adult women has only two significant abnormal features out of five: elevated waist circumference and low HDL-cholesterol levels, with blood pressure slightly above the cut points and normal glucose and slightly elevated triglycerides. Thus, mild prevalence of metabolic syndrome in conjunction with low concentrations of interleukins and adhesion molecules in our subjects may contribute to the overall lack of positive effects of an eight-week green tea intervention on these variables. On the other hand, in future studies, a higher dose of green tea or longer study duration may be effective in decreasing elevated CRP or increasing low adiponectin levels in subjects with metabolic syndrome. Other limitations of our study involve a high female: male ratio, and a small study sample which limits generalizability to a larger population. Also, genetic variations in phase-II metabolizing enzymes [81] may affect the overall metabolism, clearance and thus physiological effects of green tea polyphenols and were not accounted for in this study.

Conclusion

Green tea beverage or extract supplementation of obese subjects with metabolic syndrome for 8 weeks was well tolerated and reduced circulating SAA versus no treatment group, but did not affect other biomarkers of inflammation (CRP, IL-6, IL-1β, sICAM-1, sVCAM-1), adiponectin, and features of metabolic syndrome. Thus, green tea may be included as part of a comprehensive strategy involving diet, exercise, and specific dietary supplementations aimed at reversing inflammation, endothelial dysfunction and cardiovascular risk factors in subjects with metabolic syndrome.

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Table 1

Baseline characteristics, safety parameters and features of Metabolic Syndrome at 0 and 8 weeks in Green Tea study (n=35)[1]

Variables	Green Tea		No treatment		Green tea extract
N	**13**		**12**		**10**
Gender (female/male)	10/3		10/2		7/3
Age (years)	42.8±2.6		44.6±3.2		39.5±3.0
P value		0.66[2]		0.26[3]	
Weight (kg)					
0 wk	96.4±4.7		102.7±6.6		106.2±7.5
8 wk	94.5±4.5		103.2±6.6		105.7±7.2
P value		0.28[2]		0.80[3]	
Waist circumference (inches)					
0 wk	41.3±1.1		42.5±2.0		45.3±2.5
8 wk	41.7±1.4		42.2±1.7		44.8±2.1
P value		0.83[2]		0.34[3]	
Systolic blood pressure (mm Hg)					
0 wk	132.0±3.5		130.0±2.6		128.0±3.3
8 wk	127.6±3.1		127.3±2.6		127.9±2.1
P value		0.94[2]		0.86[3]	
Diastolic blood pressure (mm Hg)					
0 wk	83.0±2.2		80.0±2.1		82.0±1.7
8 wk	80.1±2.5		80.3±2.6		82.7±2.3
P value		0.96[2]		0.48[3]	
Glucose (mmol/L)					
0 wk	5.0±0.2		4.9±0.2		4.7±0.2
8 wk	4.9±0.1		4.8±0.2		4.6±0.4
P value		0.55[2]		0.74[3]	
HbA_{1C} (%)					
0 wk	5.5±0.1		5.6±0.1		5.5±0.1

Variables	Green Tea		No treatment		Green tea extract
N	13		12		10
8 wk	5.7±0.1		5.5±0.1		5.4±0.1
P value		0.43[2]		0.54[3]	
Total cholesterol (mmol/L)					
0 wk	5.0±0.3		5.48±0.27		4.4±0.4*
8 wk	4.9±0.2		5.43±0.23		4.3±0.3*
P value		0.16[2]		0.84[3]	
LDL-cholesterol (mmol/L)					
0 wk	3.16±0.26		3.73±0.24		2.59±0.25*
8 wk	2.98±0.23		3.71±0.18		2.55±0.23
P value		0.21[2]		0.08[3]	
HDL-cholesterol (mmol/L)					
0 wk	1.04±0.05		1.08±0.05		0.98±0.13
8 wk	1.01±0.03		1.11±0.02		0.97±0.12
P value		0.92[2]		0.38[3]	
Triglycerides (mmol/L)					
0 wk	1.9±0.3		1.5±0.2		1.82±0.31
8 wk	2.0±0.3		1.6±0.3		1.79±0.28
P value		0.48[2]		0.76[3]	
AST (U/L)					
0 wk	24.7±2.1		27.5±3.4		28.7±4.5
8 wk	23.7±1.7		28.4±3.5		29.0±4.2
P value		0.84[2]		0.67[3]	
ALT (U/L)					
0 wk	28.2±3.4		36.5±7.3		33.8±6.6
8 wk	27.5±3.2		34.7±6.8		32.5±5.8
P value		0.88[2]		0.73[3]	
BUN (mg/dL)					
0 wk	10.5±0.7		11.5±1.2		10.8±0.6
8 wk	9.7±0.6		12.3±1.6		11.6±0.7

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Variables	Green Tea	No treatment	Green tea extract
N	13	12	10
P value	0.78[2]	0.85[3]	
Creatinine (μmol/L)			
0 wk	70.7±8.8	70.7±8.8	80.0±8.8
8 wk	72.6±7.8	68.5±8.4	81.6±7.4
P value	0.64[2]	0.73[3]	
Albumin (g/L)			
0 wk	39.0±1.0	39.0±1.0	38.0±1.0
8 wk	38.3±0.9	37.8±0.8	39.2±0.9
P value	0.72[2]	0.66[3]	
Hemoglobin (g/L)			
0 wk	138.0±4.0	136.0±3.0	140.0±5.0
8 wk	141.0±4.1	135.7±2.6	141.0±5.2
P value	0.74[2]	0.83[3]	
White blood cells (K/mm^3)			
0 wk	6.8±0.6	6.2±0.4	7.5±0.4*
8 wk	7.0±0.7	6.5±0.6	7.2±0.3
P value	0.68[2]	0.77[3]	
Antihypertensive medication users (%)	55	24	90
ACEIs (%)	16	0	10
ARBs (%)	0	0	20
BBs (%)	15	8	10
CCBs (%)	8	0	10
Diuretics (%)	16	8	30
Combinations (%)	0	8	10
Aspirin users (%)	8	8	0
Multi-vitamin users (%)	38.5	8	30
Herbs/botanical users (%)	0	17	10

[1]Values are means±SE

[2] p- value for paired t-test for Green tea versus No treatment

[3] p-value for paired t-test for Green tea extract versus No treatment

* significantly different from no treatment ($p<0.05$)

ACEIs- angiotensin converting enzyme inhibitors, ARBs- angiotensin receptor blockers, BBs-beta blockers, CCBs- calcium channel blockers

Table 2

Markers of inflammation and atherosclerosis in subjects with metabolic syndrome following 8-week supplementation of green tea beverage or extract versus controls[1]

Variables	Green tea		No treatment		Green tea extract
N	11		11		7
Adiponectin (mg/L)					
0 wk	1.9±0.3		2.4±0.4		1.6±0.3
8 wk	2.2±0.4		3.3±0.9		1.5±0.3
Conditional difference		−0.1±0.6		−0.5±0.7	
P value		0.88[2]		0.53[3]	
C-reactive protein (mg/L)					
0 wk	5.1±0.9		6.1±1.2		7.4±1.5
8 wk	8.0±1.8		6.3±1.3		8.6±1.8
Conditional difference		3.2±2.2		2.7±2.2	
P value		0.24[2]		0.26[3]	
Interleukin-6 (μg/L)					
0 wk	21.5±6.7		30.2±14.2		18.9±14.7
8 wk	13.5±4.1		22.9±9.4		20.5±17.6
Conditional difference		−1.9±5.9		17.6±14.2	
P value		0.76[2]		0.67[3]	
Interleukin-1β (pg/mL)					
0 wk	0.20±0.04		0.20±0.03		0.25±0.1
8 wk	0.23±0.10		0.30±0.10		0.2±0.02
Conditional difference		0.01±0.02		−0.01±0.05	
P value		0.62[2]		0.91[3]	
sVCAM-1 (ng/mL)					
0 wk	284.6±24.7		224.3±27.9		241.3±20.0
8 wk	286.8±32.8		201.9±20.0		314.7±44.9
Conditional difference		6.0±43.2		70.1±44.7	
P value		0.89[2]		0.17[3]	
sICAM-1 (ng/mL)					

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Variables	Green tea		No treatment		Green tea extract
N	11		11		7
0 wk	119.0±9.10		107.6±10.8		94.8±9.30
8 wk	119.6±13.5		88.1±8.70		131.0±25.2
Conditional difference		29.1±27.2		49.0±31.0	
P value		0.32[2]		0.16[3]	
Leptin (ng/mL)					
0 wk	37.9±8.0		44.0±7.2		36.3±6.5
8 wk	38.4±7.8		48.7±8.5		41.8±8.5
Conditional difference		0.7±3.4		4.5±6.9	
P value		0.84[2]		0.53[3]	
Leptin/Adiponectin					
0 wk	24.9±6.5		17.6±3.9		26.7±5.5
8 wk	23.4±6.5		19.3±3.9		36.2±9.2
Conditional difference		1.6±8.9		11.3±11.5	
P value		0.85[2]		0.36[3]	
Serum amyloid A (μg/mL)					
0 wk	52.7±0.6		52.0±1.3		54.2±1.1
8 wk	45.1±0.6		62.2±1.2		40.9±0.4
Conditional difference		−18.5±1.8		−21.5±1.1	
P value		0.00001[2]		0.00001[3]	

[1] Values are means±SE

[2] p- value for paired t-test using conditional difference for Green tea versus No treatment

[3] p-value for paired t-test using conditional difference for Green tea extract versus No treatment