The Effect of Dietary Supplements Containing Green Tea, Capsaicin and Ginger Extracts on Weight Loss and Metabolic Profiles in Overweight Women: A Randomized Double-Blind Placebo-Controlled Clinical Trial

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Abstract

Background: This study was conducted to determine the effects of dietary supplements containing green tea, capsaicin and ginger extracts on weight loss and metabolic profiles among overweight women. Methods: This randomized double-blind placebo-controlled clinical trial was implemented among 50 overweight women. Participants were randomly divided into 2 groups. Group A received dietary supplements containing 125 mg green tea, 25 mg capsaicin and 50 mg ginger extracts (n = 25) group B received placebos (n = 25) twice with lunch and twice with dinner daily for 8 weeks. Results: Compared with placebo, taking dietary supplements containing green tea, capsaicin and ginger resulted in a significant decrease in weight (–1.8 ± 1.5 vs. +0.4 ± 1.2 kg, respectively, p < 0.001) and body mass index (BMI; –0.7 ± 0.5 vs. +0.1 ± 0.5 kg/m², respectively, p < 0.001). In addition, subjects who received green tea, capsaicin and ginger co-supplements had significantly decreased serum insulin concentrations (–2.6 ± 3.9 vs. –0.6 ± 2.0 μIU/mL, p = 0.02), homeostatic model of assessment for insulin resistance (–0.5 ± 0.8 vs. –0.05 ± 0.6, p = 0.01), and increased quantitative insulin sensitivity check index (+0.01 ± 0.01 vs. +0.001 ± 0.01, p = 0.008) and plasma glutathione (GSH) levels (+73.8 ± 120.6 vs. –28.3 ± 193.4 μmol/L, p = 0.03) compared with the placebo.

Conclusions: Our study indicated that taking green tea, capsaicin and ginger co-supplements for 8 weeks among overweight women had beneficial effects on weight, BMI, markers of insulin metabolism and plasma GSH levels.

Introduction

Obesity is currently emerging as a global epidemic, influencing more than 200 million men and almost 300 million women worldwide, accounting for 10% of the adult population [1]. The prevalence of this status among Iranian adults is 18.5% [2]. Previous studies have demonstrated that overweight increases the risk of chronic metabolic diseases such as type 2 diabetes mellitus (T2DM), hypertension and cardiovascular diseases (CVD) [3]. Importantly, overweight and obesity are associated with insulin resistance, which in turn can lead to hyperglycemia, lipid dis-
orders, oxidative stress and arterial hypertension [4]. On the other hand, the relationship between insulin resistance and oxidative stress in obese subjects has been confirmed [5].

To date, various approaches have been investigated to manage this public health issue, particularly much research has happened on the use of medicinal plants as a possible effective way for weight loss and also correction of metabolic disorders [6]. In a study by Chen et al. [7], it was observed that taking high-dose green tea extract in women with central obesity for 12 weeks led to a significant weight loss and to a consistent decrease in total- and low-density lipoprotein (LDL)-cholesterol levels without any side effects or adverse effects. In addition, combined capsaicin and green tea intake suppressed hunger and increased satiety more during negative than during positive energy balance [8]. In another study, the consumption of a dietary supplement containing epigallocatechin gallate (EGCG), capsaicins, piperine and L-carnitine for 8 weeks among overweight subjects decreased insulin resistance and LDL-cholesterol levels [9]. A significant decrease in body mass index (BMI), serum insulin, insulin resistance and a significant increase in insulin sensitivity were also seen following the administration of 2 g/day of ginger powder among obese women for 12 weeks [10].

However, these findings might in turn suggest the importance of green tea, capsaicin and ginger co-supplementation in the treatment of overweight patients; we hypothesized that green tea, capsaicin and ginger co-supplementation may contribute to the management of obesity and metabolic status. Co-supplementation of green tea, capsaicin and ginger may work better than a single supplementation alone. In addition, green tea, capsaicin and ginger co-supplementation might have a strong synergistic effect on weight loss, metabolic profiles and biomarkers of oxidative stress. Therefore, we hypothesized that green tea, capsaicin and ginger co-supplementation might affect weight and metabolic profiles in overweight women. This study was performed to determine the effects of green tea, capsaicin and ginger co-supplementation on weight loss, markers of insulin resistance, lipid concentrations and biomarkers of oxidative stress in overweight women.

Subjects and Methods

Trial Design

The current study was an 8-week randomized, double-blind, placebo-controlled clinical trial.

Participants

This study was a randomized double-blind clinical trial in which 50 women aged 18–50 years and who were overweight or obese (BMI ≥25 kg/m²) during January 2016 to March 2016 in Kashan, Iran were included. Exclusion criteria were as follows: pregnancy or lactation, individuals aged <18 or >50 years, BMI <25 kg/m², subjects with hypertension, thyroid, diabetes or cardiovascular disorders or anti-obesity medications.

Ethics Statements

This research was conducted in accordance with the Declaration of Helsinki and informed consent was taken from all participants. The trial was approved by the Ethics Committee of Kashan University of Medical Sciences (KUMS) and was registered in the Iranian website for registration of clinical trials (http://www.irct.ir: IRC2015122712438N15).

Study Design

At first, all subjects were categorized according to weight (25–29.9 and ≥30 kg/m²) and age (<35 and ≥35 years). Then, participants in each block were randomly allocated into 2 treatment groups to take either dietary supplements containing green tea, capsaicin and ginger (n = 25) or placebo (n = 25) for 8 weeks. Participants were requested not to change their ordinary physical activity and not to take any nutritional supplements during the 8-week trial. All persons completed 3-day food records and 3 physical activity records at the study baseline and end-of-the trial. Daily macro- and micro-nutrient intakes were analyzed by nutritionist IV software (First Databank, San Bruno, CA, USA). In this study, physical activity was described as metabolic equivalents (METs) in hours per day. To determine the METs for each patient, we multiplied the times (in hour per day) reported for each physical activity by its related METs coefficient by standard tables [11].

Intervention

In the treatment group, participants received dietary supplement containing 125 mg green tea, 25 mg capsaicin and 50 mg ginger twice with lunch and twice with dinner daily for 8 weeks. Dietary supplements and placebo (paraffin) capsules were produced by the department of the formulation of Barij Medicinal Plants Research Center (Barij Essence Pharmaceutical, Kashan, Iran) [12]. To produce dietary supplement hard capsules, at first green tea, capsaicin and ginger essential oil was dissolved in poly ethylene glycol 4,000 in 25°C; then it was en-coated into a capsule [12]. Analysis of green tea, capsaicin and ginger capsules was done in the laboratory of Barij Essence, Kashan, Iran by the high-performance liquid chromatography method [12]. Following analysis of green tea, it was detected that the major components were polyphenols including EGCG, epicatechin gallate, epicatechins, flavanols and caffeine. Furthermore, the major compound of ginger included gingerols, zingerone and shogaols. The appearance of the placebo capsules, such as color, shape, size and packaging, was identical to that of green tea, capsaicin and ginger [12].

Treatment Adherence

Every 4 weeks, subjects were taking enough supplements and placebos to last 3 days after their next scheduled visit and were instructed to return all unused supplements and placebos at each visit. The remaining supplements and placebos were counted and subtracted from the number provided to determine the number.
taken. To increase the compliance, all participants received short messages on their cell phones to take supplements and placebos every day.

Assessment of Anthropometric Measures
The weight and height of participants were determined in an overnight fasting status using a standard scale (Seca, Hamburg, Germany) at the onset of the study and after 12-weeks’ treatment. BMI was calculated as weight in kilograms divided by height in meters squared. All anthropometric measures were performed by a trained nutritionist.

Assessment of Outcomes
The primary endpoint of this study was weight and BMI. The secondary outcomes of the current study included markers of insulin metabolism, lipid profiles and biomarkers of oxidative stress.

Biochemical Assessment
Blood samples (10 mL) were obtained after 12 h of overnight fasting at the study baseline and after 8-week intervention at Kashan reference laboratory. An enzymatic method (Pars Azmun, Tehran, Iran) was utilized to determine FPG, serum triglycerides, total-, LDL-, and high-density lipoprotein (HDL)-cholesterol. All inter- and intra-assay coefficient of variations (CVs) for FPG and lipid concentrations were less than 5%. Serum insulin levels were quantified using an ELISA kit (DiaMetra, Milano, Italy) with intra- and inter-assay CVs 2.5 and 5.1% respectively. The homeostatic model of assessment for insulin resistance (HOMA-IR), HOMA-B and the quantitative insulin sensitivity check index (QUICKI) were assessed based on suggested formulas [13]. Plasma total antioxidant capacity (TAC) and total glutathione (GSH) were determined using the FRAP method developed by Benzie and Strain [14] and by the method of Beutler and Gelbart [15] respectively. All inter- and intra-assay CVs for biomarkers of oxidative stress were less than 5%. Measurements of markers of insulin metabolism, lipid concentrations and biomarkers of oxidative stress were performed in a blinded fashion.

Sample Size
To calculate sample size, we used the standard formula suggested for clinical trials by considering type one error (α) of 0.05 and type 2 error (β) of 0.20 (power = 80%). Based on a previous study [16], we used 1.89 kg as SD and 1.7 kg as the difference in mean (d) of weight loss as key variable. Based on this, we needed 21 persons in each group. Assuming 4 dropouts in each group, the final sample size was determined to be 25 persons per group.

Randomization
Randomization assignment was conducted by the use of computer-generated random numbers. Randomization and allocation were concealed from the researchers and persons until the final analyses were completed. The randomized allocation sequence, enrolling participants and allocating them to interventions, was conducted by a trained staff at the clinic.

Statistical Methods
To evaluate whether the study variables were normally distributed or not, we applied the Kolmogorov–Smirnov test. Analyses were conducted based on an intention-to-treat (ITT) principle. To detect differences in anthropometric measures as well as in macro- and micro-nutrient intakes between the 2 groups, we used Student t test to independent samples. To evaluate the effects of green tea, capsaicin and ginger co-supplementation on weight loss, metabolic profiles and biomarkers of oxidative stress, we used one-way repeated measures analysis of variance. Adjustment for changes in baseline values of biochemical parameters, age and BMI at the study baseline was performed by analysis of covariance using general linear models. The p value of <0.05 were considered statistically significant. All statistical analyses used the Statistical Package for Social Science version 18 (SPSS Inc., Chicago, IL, USA).

Results
At the screening visit, 170 persons were screened in the diet therapy clinic. One hundred subjects of the 170 screened persons were excluded from the first visit. Then, among 70 participants who were evaluated for eligibility, 20 subjects were excluded because they were not living in Kashan (n = 6) and were unable to commit to study (n = 14; Fig. 1). During the treatment phase of the study, 2 persons from the placebo group (withdrawn due to personal reasons [n = 2]) and 3 persons from the intervention group (withdrawn due to personal reasons [n = 3]) were excluded. However, as the analysis was done based on the ITT principle, all 50 obese women were included in the final analysis. On average, the rate of compliance in our study was high, such that more than 90% of capsules were consumed throughout the study in both groups. No side effects were reported following the administration of capsules in obese women throughout the study.

The mean age and height of the study participants were not statistically different among green tea, capsaicin and ginger co-supplements and placebo groups (Table 1). Baseline weight and BMI, and METs were not significantly different comparing the 2 groups. After 8 weeks of intervention, compared with placebo, taking dietary supplements containing green tea, capsaicin and ginger resulted in a significant decrease in weight (−1.8 ± 1.5 vs. +0.4 ± 1.2 kg, respectively, p < 0.001) and BMI (−0.7 ± 0.5 vs. +0.1 ± 0.5 kg/m², respectively, p < 0.001).

Comparison of dietary intakes of study subjects throughout the study showed no significant changes in macro-nutrient intakes among the 2 groups (Table 2).

Subjects who received green tea, capsaicin and ginger co-supplements had significantly decreased serum insulin concentrations (−2.6 ± 3.9 vs. −0.6 ± 2.0 μIU/mL, p = 0.02), HOMA-IR (−0.5 ± 0.8 vs. −0.05 ± 0.6, p = 0.01), and increased QUICKI (+0.01 ± 0.01 vs. +0.001 ± 0.01, p = 0.008) and plasma GSH levels (+73.8 ± 120.6 vs. −28.3 ± 193.4 μmol/L, p = 0.03) compared with the placebo (Ta-
Administration of green tea, capsaicin and ginger co-supplements had no significant effects on FPG, lipid concentrations and TAC compared with the placebo. When we adjusted the analysis for baseline values of biochemical parameters, age and BMI at the study baseline, the above-mentioned findings remained significant (data not shown).

### Discussion

Our study indicated that taking green tea, capsaicin and ginger co-supplements for 8 weeks among overweight women had beneficial effects on weight, BMI, markers of insulin metabolism and plasma GSH levels, but did not affect FPG, lipid and TAC concentrations. To...
our knowledge, this study is the first one to evaluate the beneficial effects of green tea, capsaicin and ginger co-supplements on weight loss and metabolic status in overweight women. It must be kept in mind that due to lack of evidence about the appropriate dosage of green tea, capsaicin and ginger co-supplements for overweight women, we used the dose of green tea based on a previous study in overweight and moderately obese subjects [17]. In addition, the appropriate dosage of capsaicinoids to reduce energy intake is not clear in different studies. In previous studies, the dosage of capsaicinoids was varied from 0.4 mg [18] to 33 mg [19]. However, the dosage of green tea in this study was lower than that used by others [7, 20]; we believe that further studies are needed to confirm our findings.

Overweight persons are susceptible to metabolic diseases including coronary heart disease, T2DM, certain types of cancer and osteoarthritis [21]. This study demonstrated that taking green tea, capsaicin and ginger co-supplements for 8 weeks among overweight women led to a significant decrease in weight and BMI compared with the placebo. Supporting the concept of our study, Chen et al. [7] demonstrated that 12 weeks of treatment with high-dose green tea extract in women with central obesity resulted in a significant weight loss. In addition, Canton and Lairon [22] investigated the effects of green tea extract in moderately overweight persons (average BMI 28.9 kg/m²) and observed a 3.5-kg decrease in body weight versus baseline for 12 weeks. A randomized controlled trial was launched in subjects with obesity and metabolic syndrome (median BMI 36.3 kg/m²), and body weight (2.5 kg) was significantly decreased following an 8-week supplementation with encapsulated green tea extracts [16]. In another study, Belza et al. [23] the impact of a bioactive supplement combining capsaicin, tyrosine, catechins, caffeine and calcium was tested in the context of a diet-based weight-reducing program. Mentioned results showed that the supplement increased thermogenesis and accentuated body fat loss by 0.9 kg over 8 weeks. Furthermore, this is also in line with a recent study by Lopez et al. [24] who demonstrated that a supplement containing caffeine and capsaicin for 8 weeks accentuated body weight and fat loss during a weight loss program. A significant decrease in BMI was also seen following the supplementation with 2 g/day of ginger powder among obese women for 12 weeks [10]. Green tea, capsaicin and ginger appear to complement each other by acting on the various pathways of the sympathetic nervous system at the cellular and molecular levels. Tea catechins prolong the effect of norepinephrine-mediated thermogenesis by inhibiting catechol O-methyltransferase and suppressing the degradation of norepinephrine at the synaptic cleft [25]. In addition, caffeine in green tea extract also prolongs the thermogenic signal of norepinephrine by inhibiting phosphodiesterase-induced degradation of intracellular cyclic AMP [26]. On the other hand, capsaicin increases energy metabolism via β-adrenergic pathway and thermogenic action [27]. In human studies, test-meals enriched with capsaicin increased both energy expenditure and lipid oxidation [27, 28]. In addition, increasing thermogenesis and energy expenditure by catecholamine-releasing action and increasing the lipolysis of

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<th>Table 2. Dietary intakes of study participants throughout the studya</th>
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<td>Energy, kcal/day</td>
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<td>Cholesterol, mg/day</td>
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aData are means ± SDs.
bObtained from paired-samples t tests.
MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid; TDF, total dietary fiber.
white adipose tissue by ginger may be explained as
reasons for further weight loss. Overall, the strongest
treatment showed the most significant effects on energy
expenditure, suggesting that synergism of bioactive in-
gredients is of importance. Previous studies have shown
that a combination of bioactive ingredients has a stronger
energy intake–reducing effect than treatment with single
ingredients. Toubro et al. [30] observed that body weight
loss following the intake of ephedrine/caffeine mixture
was greater than only caffeine and ephedrine. Further-
more, Dulloo et al. [31] demonstrated that stimulating
effects of green tea on energy expenditure and substrate
oxidation due to caffeine and tea catechins were greater
than explained by the active compounds given individu-
ally. Recent studies have focused on the effects of combin-
ing bioactive ingredients and have shown energy intake
or appetite-reducing effects in both short-
[32] and long-term studies [33]. These results support our findings
that capsaicin + green tea + ginger can induce consider-
able changes in energy expenditure.

We have shown that green tea, capsaicin and ginger
co-supplementation for 8 weeks among overweight wom-
en was associated with a significant reduction in serum
insulin, HOMA-IR and a significant elevation in QUICKI
compared with the placebo but did not influence FPG,
HOMA-B and lipid profiles. Green tea has been shown to
influence plasma levels of lipids and insulin resistance in
a majority of animal studies. However, the results of hu-
man studies have been controversial. In agreement with
our study, the consumption of green tea for 6 months re-
sulted in improved glucose homeostasis in overweight
breast cancer survivors [34]. Furthermore, capsaicin in-
take improved glucose homeostasis in diabetic rats
[35]. A 3-month supplementation with 3 g/day ginger also im-
proved glycemic indices in patients with T2DM [36]. A
meta-analysis study demonstrated that the administra-
tion of green tea beverages or extracts resulted in signifi-
cant reductions in serum total- and LDL-cholesterol
concentrations, but no effect on HDL-cholesterol was
observed [37]. Insulin resistance and metabolic dysfunc-
tion [39]. Insulin resistance is considered to be respons-
able for the development of all constituents of the meta-
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tion [39]. Obesity is associated with hyper-
nase activation, modulating the expression of genes involved in metabolism, particularly in adipose tissue [40] and decreasing apoptosis of β-cells by potentiating insulin/IGF-1 signaling [35]. The discrepancies between findings of this study and those of previous reports might be explained by doses of green tea, capsaicin and ginger supplements used, the intervention time, clinical characteristics of the participants such as variation in baseline levels of metabolic profiles.

Findings of this study have shown that combined green tea, capsaicin and ginger intake for 8 weeks among overweight women led to a significant increase in plasma GSH levels but unchanged plasma TAC concentrations. In line with the findings of our study, the consumption of green tea increased GSH levels among weight-trained men for 7 days [41]. Capsaicin and curcumin co-supplementation for 8 weeks in hypercholesterolemic rats increased GSH levels [42]. In addition, Wistar rats administered capsaicin (3 mg/kg) for 3 consecutive days indicated a reduction in oxidative stress in the liver and other tissues [43]. Treatment with gingeroil (50 mg/kg body weight) also decreased oxidative stress in rats [44]. Increased oxidative stress in obese subjects may play a role in T2DM development [45] and CVD [46]. GSH plays an important role in the protection of cells and tissue structures due to detoxication of xenobiotics, free radicals, peroxides, and regulation of immune function [47]. Catechins of green tea could have direct or indirect antioxidant properties [47]. Increased activities of GSH reductase, GSH transferase and catalase following the consumption of capsaicin and ginger may explained their antioxidant effects [42, 44].

Some of the main strengths of our study were assessment of markers of insulin metabolism, lipid concentrations, biomarkers of oxidative and its randomized design. Few limitations must be taken into account when our results are interpreted. We did not evaluate the beneficial effects of green tea, capsaicin and ginger co-supplementation on thyroid hormones and inflammatory cytokines. Furthermore, the sample size was small and the duration of the intervention was short in this study. Further studies with a bigger sample size and a longer duration of the intervention are needed to confirm our findings.

Taken together, our study indicated that taking green tea, capsaicin and ginger co-supplements for 8 weeks had beneficial effects among overweight women in terms of their weight, BMI, markers of insulin metabolism and plasma GSH levels, but did not affect FPG, lipid, and TAC concentrations.

Acknowledgements

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Authors’ Contributions

Z.A. and M.T. contributed in conception, design, statistical analysis and drafting of the manuscript. M.T., N.F., S.T., M.M., H.A., and F.K. contributed in data collection and manuscript drafting. Z.A. supervised the study. All authors approved of the final version for submission.

Disclosure Statement

The authors declare that they have no financial or other conflicts of interest.

Clinical Trial Registration Number


References


