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The Anti-Obesity Effects of Green Tea: A Controlled, Randomized, Clinical Trial

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Abstract

Background: Obesity is a global health threatening issue with increasing prevalence in the developed and developing world. The limited efficacy and side effects of conventional treatments motivated the researchers to look for novel, safe, and effective therapeutic strategies.
Objectives: The current study aimed at investigating the anti-obesity effects of green tea in a population in North of Iran.
Methods: The current single-blind, placebo-controlled, parallel, clinical trial was conducted in Guilan outpatient clinic in Rasht, Iran, from January to December 2015. Eligible subjects were randomly allocated into 2 groups of green tea and control. In the GT Group, a cup of green tea and in the C group an equal amount of mineral water was taken 30 minutes after breakfast and lunch. The outcomes including body weight (BW), body mass index (BMI), hip circumference, waist circumference, and waist-to-hip ratio were measured at baseline, as well as 8 and 12 weeks after the intervention (T0,T_1, T_2).
Results: Finally, data obtained from 84 cases in groups GT (n = 41) and C (n = 43) were analyzed. No significant difference was observed in terms of baseline demographics and measurements between the 2 groups including male/female (P = 0.766), age (P = 0.376), weight (P = 0.846), height (P = 0.413), waist circumference (P = 0.619), hip circumference (P = 0.619), and waist-to-hip ratio (P = 0.301). According to the intragroup analyses, the trend of changes from baseline to 12 weeks after intervention were significant in both groups (P = 0.001); BW (79.88 $\pm$ 7.06 to 72.44 $\pm$ 6.82 kg) and (80.21 $\pm$ 7.16 to77.07 $\pm$ 7.22 kg) , BMI (29.95 $\pm$ 1.79 to 26.86 $\pm$ 2.59 kg/m^2) and (29.69 $\pm$ 2.1 to 27.07 $\pm$ 2.22 kg/m^2) , waist circumference (87.77$\pm$6.06 to 83.913 $\pm$ 6.13 cm) and (86.94 $\pm$ 8.05 to 85.23 $\pm$ 7.89 cm), and hip circumference (102.41 $\pm$ 7.35 to 98.3 $\pm$ 7.54 cm) and (101.02 $\pm$ 8.47 to 99.31 $\pm$ 8.81 cm) in GT and C groups, respectively. However no such difference was observed in waist/hip ratio in the GT and C groups (P = 0.087) and (P = 0.322), respectively. A significant difference was observed at T1 (P = 0.024 and P = 0.025) and T2 (P = 0.025 and P = 0.006), according to weight and BMI, respectively. However, the differences were not statistically significant based on the other variables.
Conclusions: Green tea could be a safe and effective choice for patients with obesity. However, further well-designed trials are required to confirm these findings.

Keywords: Green Tea, Obesity, EGCG

1. Background

Obesity is the result of an imbalance between calorie intake and energy expenditure, leading to excessive lipid accumulation in adipose tissue and is known as a medical health problem with increasing prevalence (1). It is a major risk factor for several diseases such as cardiovascular events, diabetes, hypertension, pulmonary disease, certain cancers, and osteoarthritis (2). It is shown that even 5% - 10% weight loss is associated with beneficial health effects (1). However, it should be noted that organized weight-loss programs including behavioral modification, pharmacotherapy, and surgical interventions fail to achieve complete satisfactory results and life style changes such as increased physical activity and low-fat diets often do not persist for a long term (3). Studies reported that the highest success rate of such conventional programs was 21% and adverse effects due to these interventions should

be considered as well (4). Thus, it is vital to search for effective anti-obesity alternatives with easy-to-use, tolerable, and cost-effective properties. Recently, natural herbal supplements are the focus of concentration and among them green tea is studied extensively (5-8). To make green tea, fresh leaves of Camellia sinensis are stewed rapidly by stream, and consequently fermentation is prevented. Green tea contains a mixture of catechin polyphenols and caffeine, which both play an important role in weight-loss and weight maintenance (9). It is noteworthy that in addition to its anti-obesity properties, several favorite effects are supposed for this plant including relaxation, cardiovascular protection, neuroprotection, anti- oxidant, anticancer, anti-inflammatory, and anti-thrombogenic effects (10-14).

Although clinical studies supporting the anti-obesity effects of green tea, their findings were contradicted and equivocal. Also, the optimum consumption pattern is not well understood yet. On the other hand, the available data from similar clinical trials cannot be generalized to other populations as it is strongly supposed that people are genetically predisposed to the effect of epigallocatechin-3-gallate (EGCG)-caffeine mixtures with different extend (15). Considering the importance of the issue and lack of safe, long lasting, and effective strategies, green tea as a cost-effective and easy-to-use plant with the least side effects is worthy to be studied. To the authors' best knowledge; there were no similar studies in Iran. Accordingly, the current study aimed at investigating the effects of green tea on weight-loss in subjects with obesity in North of Iran.

2. Methods

Study design and participants: The current single-blind, placebo-controlled, parallel, clinical trial was conducted at Guilan outpatient clinic in Rasht, Iran, from January to December 2015. The trial protocol was approved by the research ethical committee of Guilan University of Medical Sciences (GUMS) and registered in Iranian registry of clinical trial (IRCT) (code: 201504086186N10). The clinic was a private center with different services; one was allocated to manage individuals with obesity. The objectives and the method of study were explained to the study candidates and the case selection was performed among them. The subjects were assured that they can withdraw from the study at any time and go on to the other treatment options. They were also assured about the publication of the study practical results, which could be feasible for them even if not allocated into the GT group. The subjects were interviewed for an initial screening including a complete medical and nutritional history and measurement of body weight (BW) and height, as well as waist and hip circumference. Based on 3-day diet records, caffeine intake and the diet energy balance were standardized as much as possible by the investigator (9). Caffeine-rich beverages such as energy drinks, colas, and coffee were introduced to patients and they were told to abstain from using them. They were also asked not to follow any other weight-loss programs during the study period. The subjects were selected among people with regular daily activity and were advised to do 30 minutes walking 3 times a week.

2.1. Inclusion Criteria

Generally, healthy males and females who consumed no more than 2 caffeinated beverages per day, within the age range of 18-50 years, BMI values of 24 - 35 kg/m^2, and low tea consumption (< 2 tea bag/day or < 4 g loose tea/day) were enrolled in the current study.

Exclusion criteria: Professional athletic, smoking, use of any medication-apart from over the counter and oral contraceptives, any medical or psychiatric complication, actively following a weight-loss program or a medically prescribed dietary regimen; losing or gaining > 2 kg BW in the 3 months before the intervention, pregnancy and breast feeding, a history of weight-reducing surgery, and eating disorder.

2.2. Sample Size

With a margin of error α = 0.05 and β = 10%, an expected power of 90% and a Z value of 1.28, it was calculated that a sample of at least 40 patients in each group was required. The probability of at least 10% drop out of the samples was considered.

Randomization and blindness: ninety-nine eligible patients were randomly allocated into either green tea (GT) or control (C) group using randomized, fixed, quadrant blocks. The subjects had an equal probability of being assigned into each of the 2 groups and were aware of their groups. The blind observer visited the cases at the mentioned measurement point times and recorded the data. Therefore, a single-blind trial was planned.

2.3. Preparation of Samples and Treatment

In group GT, a cup of green tea was prepared by immersing a green tea bag in 150 mL of 69-87°C water for 2 - 3 minutes (16) and in the group C, an equal amount of mineral water was taken 30 minutes after breakfast and lunch.

Intervention outcomes: the outcomes including BW, body mass index (BMI), and hip and waist circumferences were measured in the morning, while fasting and after voiding. In the standing position, a statiometer and a digital scale were used to measure height and weight of the

volunteers. BMI is defined as the body mass in kilograms divided by the square of the body height in meters. The waist circumference was measured at the site of the smallest circumference between the rib cage and the iliac crest and the site of the largest circumference between the waist and the thighs was taken as the landmarks of waist and hip measurement. The waist-to-hip ratio was calculated by dividing the waist circumference by the hip circumference. There were 3 measurement point times, at baseline, and 8 and 12 weeks after intervention (T0,T_1, T_2).

2.4. Statistical Analysis

Statistical analyses were conducted using SPSS statistical software version 21 (SPSS Inc, Chicago, II). The data were expressed as mean ± standard error of mean (SEM). Chi-square test was applied to compare the categorical variables between the 2 groups. The Kolmogorov-Smirnov (K-S) test was used to determine the normality of the variables. Independent t test was employed to compare and assess the parametric data between the 2 groups and repeated measureless test to compare the parametric data in 3 measurement point times. The level of significance was set at 0.05 for P values.

3. Results

One hundred and ninety-two volunteers were screened for eligibility. Among them, 99 subjects were recruited for the trial and randomly divided into 2 groups of GT and C. During the study period, 15 subjects failed to attend the study visits for their personal reasons and were excluded. Finally, data collected from 84 cases were analyzed; GT (n = 41) and C (n = 43) (Figure 1). No significant difference was observed in terms of baseline demographics and measurements between the 2 groups; male/female (P = 0.766), age (P = 0.376), weight (P = 0.846), height (P = 0.413), waist circumference (P = 0.619), hip circumference (P = 0.619), waist-to-hip ratio (P = 0.301) (Table 1). According to the intragroup analysis, the trend of changes from baseline to 12 weeks after the intervention was significant in both groups (P = 0.001); BW (79.88 ±7.06 to 72.44 ± 6.82 kg) and (80.21 ± 7.16 to77.07 ± 7.22 kg) , BMI (29.95 ± 1.79 to 26.86 ± 2.59 kg/m^2) and (29.69 ± 2.1 to27.07 ± 2.22 kg/m^2) , waist circumference (87.77 ± 6.06 to 83.913 ± 6.13 cm) and (86.94 ± 8.05 to 85.23 ± 7.89 cm), and hip circumference (102.41 ± 7.35 to 98.3 ± 7.54 cm) and (101.02 ± 8.47 to 99.31 ± 8.81 cm) in the GT and C groups, respectively. However, no significant difference was observed in waist-to-hip ratio in the GT and C groups (P = 0.087) and (P = 0.322), respectively. A significant difference was observed at T1 (P = 0.024, P = 0.025) and T2 (P = 0.025, P = 0.006), according to weight and BMI, respectively. However, the difference between the groups was statistically insignificant based on other variables .The exact P-values are presented in Table 2. No subject reported any remarkable adverse effect due to this protocol, except of a mild gastric discomfort in few cases.

Table 1. Baseline Characteristics[a,b]

Variable	Green Tea	Placebo	P Value
Gender, (male/female)	15/26	16/27	0.766
Age, y	46.22 ± 6.44	47.68 ± 7.58	0.376
Weight, kg	79.88 ± 7.06	80.21 ± 7.16	0.846
Height, m	1.63 ± 0.06	1.64 ± 0.04	0.413
BMI, kg/m^2	29.95 ± 1.79	29.69 ± 2.01	0.562
Hip circumference, cm	102.4 ± 7.35	101.02 ± 8.47	0.454
Waist circumference, cm	87.77 ± 6.06	86.94 ± 8.05	0.619
Waist-to-hip ratio	0.85 ± 0.008	0.86 ± 0.01	0.301

[a] Groups were matched by characteristics; there were no statistically significant difference between the groups (P > 0.05)
[b] Values are expressed as mean ± SD.

4. Discussion

The current randomized, clinical trial was conducted in the free-living condition to investigate the anti-obesity properties of green tea. Experimental studies clarified that green tea containing caffeine and catechins, particularly EGCG, enhanced sympathetic activation, produced too much increase in fat oxidation, and led to the increase of 24-hour energy expenditure due to thermogenesis (9). The other suggested mechanisms involving the useful effects of green tea on people with obesity were desensitizing insulin-resistant muscles and also increase of adiponectin levels. Even a short-term ingestion of green tea extract could blunt glycemic response after a post-exercise glucose uptake. The suggested mechanism was that skeletal muscle glucose uptake might be altered by green tea supplementation (1, 2, 17-19).

Recently, EGCG is used as the most bioactive component for weight-loss in a wide range of doses from 100 up to 8,568 mg/day (2). In the current study, large doses were avoided due to the lack of enough knowledge about the pharmacokinetic and bioavailability of high doses of green tea in human. Indeed, in correlation with the mentioned beneficial effects of green tea, a large body of evidence indicates that its extract can induce both antioxidant and prooxidant activities, which depends on the biological conditions and the dosage. EGCG might generate radical oxygen species (ROS) with cytotoxic properties

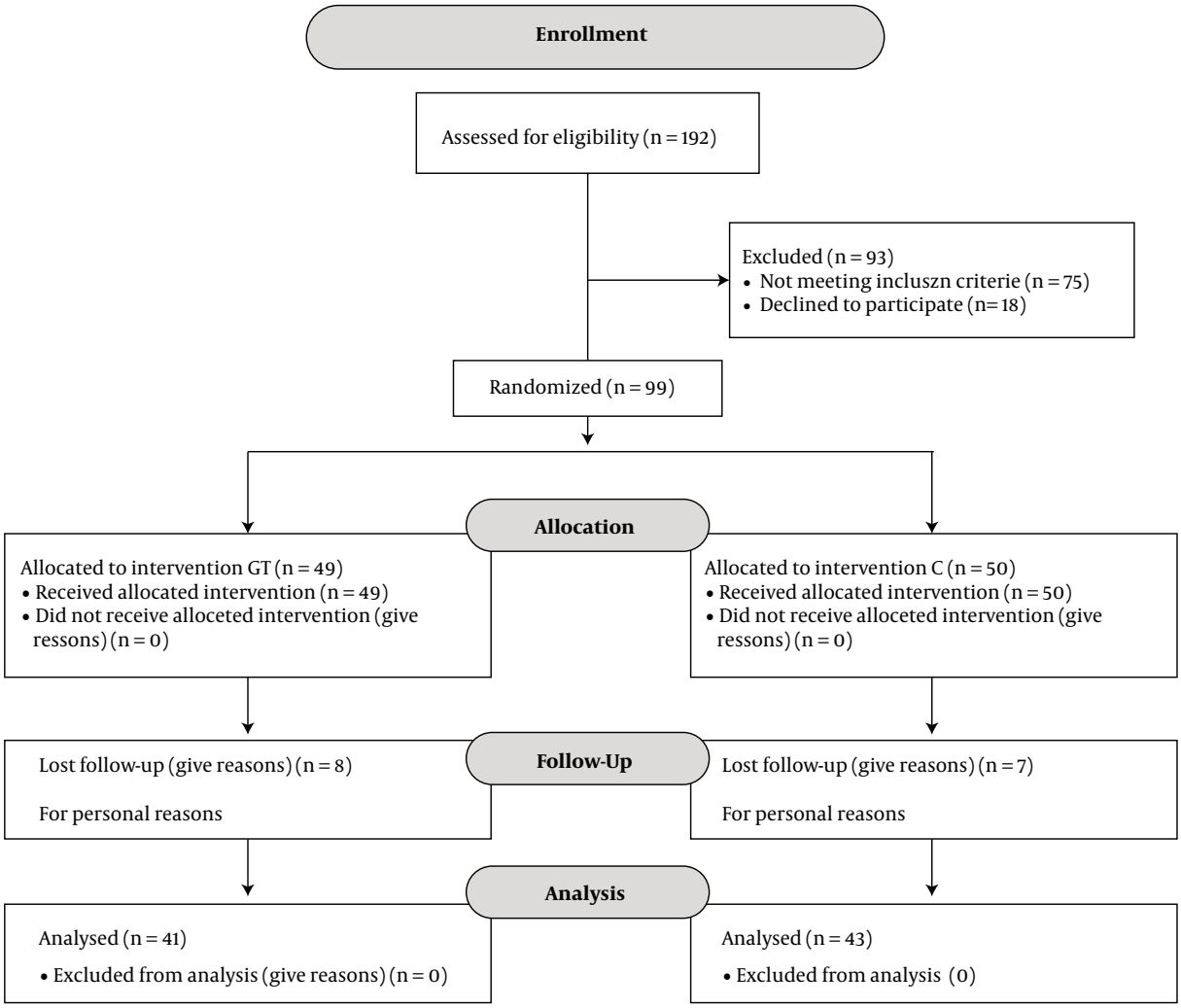

Figure 1. Study Flowchart

(10). Animal model studies showed that higher doses of EGCG induced pro-inflammatory responses, hemorrhagic lesions in stomach and intestine, oxidative stress in liver cells, enzyme rise, and acute hepatitis. Some other adverse effects such as nausea, vomiting, and abdominal dysfunction were reported as well (20-22).

The current study indicated that the intake of 1200 mg/day EGCG plus 480 mg caffeine for 12 weeks had remarkable anti-obesity effects; the results were in agreement with those of other similar studies.

Chen et al. in a clinical trial examined the effects of low-dosage green tea extract (360 mg) on subjects with obesity and the results were disappointing; thereafter, they elevated the dosage to 8,568 mg and the results were superb. Therefore, they suggested that green tea effects on weight-loss were dose-dependent. The results of their study supported those of the current study; however, in addition to anthropometric data, they measured biochemical parameters and hormones, which could be the advantage of their work (2).

Hursel et al. in a meta-analysis reported just a small positive effect of green tea extract on weight-loss and weight maintenance (15). Wang et al. found that the daily consumption of 886 mg catechins and 198 mg caffeine for 90 days decreased the intra-abdominal fat (IAF), waist circumference, BW, and abdominal adiposity in moderately overweight Chinese subjects (23). Nagao et al. in Japan found that the daily administration of green tea containing 690 mg catechins for 12 weeks significantly decreased BW, BMI, waist circumference, and body fat mass in the in-

Table 2. Comparison of the Study Groups at T0, T1, and T2

Outcome	Baseline		8 w		12 w		P Value Between Groups
	Green Tea	Placebo	Green Tea	Placebo	Green Tea	Placebo	
Weight	79.88 ± 7.06	80.21 ± 7.16	72.86 ± 6.72	76.6 ± 7.23	72.44 ± 6.82	77.07 ± 7.22	0.0001
P Value	0.846		0.024		0.006		
BMI	29.95 ± 1.79	29.69 ± 2.1	28.61 ± 2.17	28.35 ± 2.15	26.86 ± 2.59	27.07 ± 2.22	0.0001
P Value	0.562		0.025		0.003		
Waist circumference	87.77 ± 6.06	86.94 ± 8.05	83.91 ± 6.02	84.97 ± 7.88	83.913 ± 6.13	85.23 ± 7.89	0.0001
P Value	0.619		0.521		0.426		
Hip circumference	102.41 ± 7.35	101.02 ± 8.47	98.61 ± 7.17	99.02 ± 8.71	98.3 ± 7.54	99.31 ± 8.8	0.0001
P Value	0.454		0.824		0.599		
Waist-to-hip ratio	0.85 ± 0.008	0.86 ± 0.014	0.85 18 ± 0.018	0.85 ± 0.017	0.85 ± 0.021	0.85 18 ± 0.018	0.372
P Value	0.301		0.117		0.387		

tervention group, compared with the control group (24).

Mielgo-Ayusto et al. in a randomized, double-blind, placebo-controlled trial revealed that consumption of 300 mg/day EGCG for 12 weeks did not enhance the energy-restricted diet-directive changes in body composition, energy, substrate metabolism, and cardiometabolic risk factors in females with obesity. Likewise, they did not report any significant reduction of BW. Their contradictory results might be due to the lower dosage of EGCG and the cases limited to female gender (25).

Auvichayapat et al. demonstrated that energy expenditure and fat oxidation increased by taking 100 mg/day EGCG with no impact on BMI and BW. Their findings were not completely in line with those of the current study, due to the lower dose of EGCG (100 mg/day), compared with 1,200 mg/day in the current study as well as different ethnicity and dietary patterns between the 2 studies. Moreover, authors suggested that the rebound tendency in BW occurred due to the dietary resistance was responsible for the failure of treatment in 8- and 12-week interventions (4).

Konvaks et al. investigated the effects of green tea on weight maintenance after BMI reduction and reported that although the energy expenditure was significantly higher in the green tea group, based on weight and BMI measures, no clinical improvements were obtained (26).

Diepevens et al. found that green tea extract (600 mg EGCG) had no effect on BW and BMI in females with obesity. Their results were in contrast to those of the current study; although in addition to the lower applied dosage, there were remarkable differences between the studied populations (3).

Yan Xu in an experimental rat model on a full fat diet found that green tea extract had significant anti-obesity effects. Moreover, the anti-inflammatory properties of green tea were also observed. They suggested it as a potential intervention against obesity. In line with these findings, fat accumulation, blood lipid, and leptin levels decreased during the green tea intervention (27). Westerterp-Plantenga et al. showed that 270 mg EGCG exhibited weight maintenance in habitually low caffeine consumers, supported by relatively greater thermogenesis and fat oxidation. They proposed green tea as a novel dietary component with anti-obesity properties. Furthermore, it could control correlated conditions such as fatty liver and insulin resistance (1). Totally, accumulating evidence suggests that green tea remains positive effects on fat metabolism, even if sometimes in clinical indexes such as weight, BMI, and anthropometric measurements could not be highlighted. However, similar studies discovered disparate results partly justified by the following suggested mechanisms. In relation to the current study, several possible mechanisms are declared. In the control group, the results were significantly better in T1, compared with baseline; however, this superiority was not kept constantly till T2. It can be explained by this theory that maybe the positive effects of green tea gradually increased. In other words, during T0 and T1 weight reduction in both groups were the result of controlled diet and exercise, but during T1 and T2 the effects of green tea was significant and also dietary resistance might be partly responsible. Moreover, the placebo effects of green tea in the current study cannot be ignored as the subjects were aware of the type of drink. Considering the fact that belief and positive attitude towards a therapeutic regimen play a significant role in its efficacy, the current study finding might be affected.

In addition, according to previous data, the applied

dosage of EGCG and caffeine were in effective range, though not classified as the highest dosage, not in the low limit either. The type of administration was a cup of beverage instead of capsules. Theoretically, consuming tea causes a longer gastric emptying time, compared with capsules (4).

Theoretically, it can be claimed that the achieved significant differences between the groups were due to the green tea effects, as it was tried to match the groups by a well-designed randomization. Anyway, experimental models were not the same as human studies in a free living condition. Although studies attempted to eliminate confounding factors including physical activity, diet, and regular caffeine consumption, it was not easy to control subjects tightly regarding the effective factors, which was perfectly done in the experimental studies. In addition, differences among the applied protocols regarding the case selection, dosage of EGCG and caffeine, timing and form of administration, capsule or beverage form, were partly responsible. It is strongly proposed that genetic background of individuals might contribute to the achieved data. Also, in different areas with different climatic conditions, which affect their foodstuff and type of nutrition, lipolytic activation of green tea could not be the same either (4). It was demonstrated that the anti-obesity effects of green tea were more dominant in a mild negative energy balance, compared with a severe negative balance; of course, the type of diet was not the same in all studies. Moreover, studies performed in a weight maintenance period might have different findings, compared with the ones conducted in a weight-loss period. All in all, although several useful effects of green tea are confirmed, it seems that its safe and optimal doses are still ambiguous; thus, routine consumption is not recommended before achieving practical knowledge on the advantages of green tea to human.

Limitation: There were certain limitations in the current study; for example, the small sample size. In addition, obesity related hormones, biomedical data, and clinically remarkable parameters such as lipid profile, as well as systolic and diastolic blood pressure were not measured. Although waist-to-hip ratio, one of the measured variables, is known as a predictor of the risk of cardiovascular diseases and type 2 diabetes via the potential intermediates of blood lipid profile, blood pressure, and glycemic phenotypes (28), it was not noted as the limitation of the study. The follow-up time was not long enough to uncover if this result is steady without any adverse effects such as hepatic toxicity. Also, placebo effect was not ruled out in the current study.

4.1. Conclusions

The current study revealed that green tea could be an alternative to treat patients with obesity. It was well tolerated with no significant adverse effects. However, further well-designed, large-scale trials with longer follow-up periods are recommended to find the optimum dosage in regard to safety and effectiveness to prevent or treat obesity before recommending it to be supplemented among the adults with obesity.

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Footnotes

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