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*Research Article*

# Effects of Supplementation with Ginger (*Zingiber officinale Roscoe*) on Serum Glucose, Lipid Profile and Oxidative Stress in Obese Women: A Randomized, Placebo-Controlled Clinical Trial

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**ABSTRACT**

***Background:*** The hypoglycemic, hypolipidemic and antioxidative effects of ginger in type 2 diabetic patients have been recently noticed. However given the very limited data on obesity, the present study was furthered to investigate those beneficial effects of ginger supplementation in obese women. ***Methods:*** In this clinical trial, 80 eligible obese women (aged 18-45 yr.) were randomly divided into two groups of ginger (receiving 2 g ginger powder as two 1g tablets per day) or placebo (corn starch to the same amount) for 12 weeks. Serum levels of glucose, lipid profile, malondialdehyde (MDA) and total antioxidant capacity (TAC) were determined before and after the intervention. ***Results:*** At the end of intervention, significant reductions of serum glucose, total cholesterol (TC), Triglyceride (TG), the TC/HDL.c and LDL.c/HDL.c ratios and increase of HDL.C were observed in both study groups. However, the decrease of serum TG was significantly (percent change: -20.51% vs. -4.92%; $p$=0.006) and the glucose reduction was non-significantly (percent change: -7.51% vs. -6.16%; $p$=0.669) more pronounced in the ginger group versus placebo. Moreover the concentration of MDA increased in ginger group ($p$=0.005) and TAC decreased in placebo group ($p$=0.029) as compared to the baseline without any significant difference between groups. ***Conclusion:*** Our findings revealed a minor beneficial effect of ginger powder supplementation on serum glucose and a moderate, significant effect on TG, as compared to the placebo. However ginger consumption did not cause any significant effect on serum MDA and TAC levels.

## Introduction

The global epidemic of obesity has become a major public health issue over the world. Obesity increases the risk of numerous chronic diseases including type-2 diabetes mellitus (T2DM), cardiovascular diseases, osteoarthritis and certain types of cancers and overall is associated with elevated morbidity and mortality.[1,2]

The occurrence of a low-grade chronic inflammation in obese subjects has been implicated in development of a cluster of metabolic abnormalities along with obesity such as impaired glucose regulation, insulin resistance, hypertriglyceridemia, hypercholesterolemia and low serum HDL.C levels.[3,4] In addition, elevated oxidative stress during obesity is another key mediator for its adverse effects.[5,6]

Although the preferred intervention for obesity management is dietary modulation and physical activities,[7] but using natural products such as herbal medicines may also help to lose weight and reduce some complications of obesity.[8]

The rhizome of ginger (*Zingiber officinale Roscoe*, family Zingiberaceae) is a well-known food spice and medicinal plant over the world.[9] It has long been used as a remedy for some diseases such as vomiting, joint and muscular pain, indigestion and cold-induced syndrome. The main ginger derived bioactive compounds are gingerol and shogaol.[10,11] There are some scientific evidences regarding various pharmacological activities of ginger powder, extract or its bioactive components including anti-inflammatory and antioxidant,[12,13] antifungal and antibacterial,[14,15] antiemetic[16-18] and anti-cancer[19,20] effects. Moreover, ginger is generally considered as a safe herbal medicine according to existing data and also the FDA's report on its safety.[18]

Regarding the hypoglycemic and hypolipidemic effects

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of ginger, it has been shown that the ethanolic extract of ginger can decrease blood glucose[21] and plasma lipids[22,23] in streptozotocin induced diabetic rats. Whereas, in the non-diabetic animals there are some inconsistent findings.[24,25] In this regard, scientific researches in humans are very limited and yield different results in diabetic[26-29] and non-diabetic patients.[30-32] It seems that ginger can decrease serum glucose level, especially its elevated level by some default mechanisms such as increased gene expression of GLUT-4, insulin receptors and enhanced b-cell functions.[33] Moreover ginger maybe decrease lipid profile using decreased fat absorption, cellular cholesterol biosynthesis and increased cholesterol conversion to bile acids.[9,33]

To our knowledge, the effect of ginger on blood glucose, lipid profile and oxidative stress in obese subjects has been investigated just in one pilot study by Atashak et al.[34,35] According to their results, ginger consumption versus placebo didn't cause any significant change in serum glucose, lipid profile, MDA and TAC levels. Consequently, the present randomized double blind placebo controlled study aimed to investigate those beneficial effects of ginger in obese women.

## Materials and Methods:

### *Study design*

The present randomized, double-blind, placebo-controlled clinical trial was conducted on 80 obese women aged 18-45 yr. and BMI of 30-40 kg/m$^2$. The sample size was determined based on data from previous study.[36] By considering a 90% power and a 5% significance level, at least 28 cases were necessitated in each group. But assuming a 40% drop-out, 40 cases were assigned in each group.

The eligible obese women were recruited voluntarily, through a general announcement across the city of Tabriz., Iran. The exclusion criteria were age under 18 or over 45, BMI>40, clinically diagnosed diabetes mellitus, cardiovascular disease, hypo or hyperthyroidism, gallstone, deep depression, pregnancy, breast feeding or menopause, being on a weight lowering diet, taking medications that could influence weight, subjects with high physical activity, smoking, taking nutritional supplements and being hypersensitive to ginger.

The study was approved by the Ethics Committee of Tabriz University of Medical Science (reference number 92154) and the study was registered on the Iranian Registry of Clinical Trials (http://www.irct.ir) with the identification No. 201311172017N18.

### *Tablets preparation*

Dried rhizomes of ginger (*Zingiber officinale Roscoe*, Chinese yellow ginger) were purchased from a local market in Tabriz. The ginger rhizomes were finely ground and then prepared as tablets containing 1 gram ginger powder in each (Pharmaceutics laboratory, Faculty of Pharmacy, Tabriz University of Medical Science). Likewise, the placebo tablets consisted of corn starch and other excipients in order to match the weight of ginger tablet. The tablets were placed in the identical bottles and were labeled with 2 codes by a third person not directly involved in our study. As well as a slight amount of ginger powder was added to the placebo tablets containers to give ginger odor.

### *Intervention*

A written consent form was taken from all participants prior to the intervention. Subjects (N=80) were randomly assigned to the ginger or placebo group (N=40) using a random number table. Subjects in each group were instructed to take 2 tablets per day (30 minutes before meal) for 12 weeks.[26,29] Tablets were being given to the participants monthly. Participants were also asked to maintain their dietary and exercise pattern throughout the study.

### *Measurements*

Blood samples (5 cc) were collected at the beginning and end of 12 weeks intervention after a 10-12 hr. overnight fasting (water permitted). Serum samples were separated by centrifugation and stored at -80 ºC until analysis.

The concentrations of serum glucose, Total cholesterol (TC), HDL.C and Triglyceride (TG) were measured by enzymatic colorimetric methods with commercial kits (Pars Azmoon Co., Tehran, Iran) on an automatic analyzer (Abbott, model Alcyon 300, USA). Serum LDL.C was calculated according to the Friedewald equation.[37] Since the TC/HDL.C and LDL.C/HDL.C ratios determine the relative risk of coronary artery disease, they were also calculated.

Serum malondialdehyde (MDA) level, as a marker of lipid peroxidation and oxidative stress was measured through reaction with thiobarbituric acid (TBA) as a TBA reactive substance (TBARS) to produce a pink colored complex. Then, its fluorescence intensity was measured at 547 nm with excitation at 525 nm by a spectrofluorimeter (Kontron, model SFM 25A, Italy).[38] Moreover, total antioxidant capacity (TAC) was assessed by Ferric Reducing-antioxidant Power (FRAP) method.

In addition, Body mass index (BMI) was calculated from the measurement of height and weight, using calibrated equipment every 4 weeks, according to the following formula: weight (kg)/height (m$^2$).

### *Statistical Analyses*

The data were analyzed using SPSS software (version 21.0; IBM Corp., Armonk, NY, USA). Normality of variables was examined using the Kolmogorov-Smirnov test. Differences at baseline among treatment groups were assessed by independent sample *t*- test.

Differences between groups at the end of intervention were analyzed using the analysis of covariance (ANCOVA) with the baseline values and BMI

differences employed as covariates. Paired sample *t*-test was used to assess within groups differences before and after the supplementation. Results are reported as mean ± SD and the significance level was set at $p<0.05$.

## Results

From eighty volunteer women who were recruited the study, 10 participants did not complete the study as shown in figure 1. One person from the ginger group withdrew because of pregnancy and nine participants from the placebo group dropped out because of travelling (n=2), pregnancy (n=3), using antidepressant agents (n=2), diagnosed hypothyroidism (n=1) and taking corticosteroids for rheumatoid arthritis (n=1). In addition, there wasn't any report of the adverse effects of ginger or placebo.

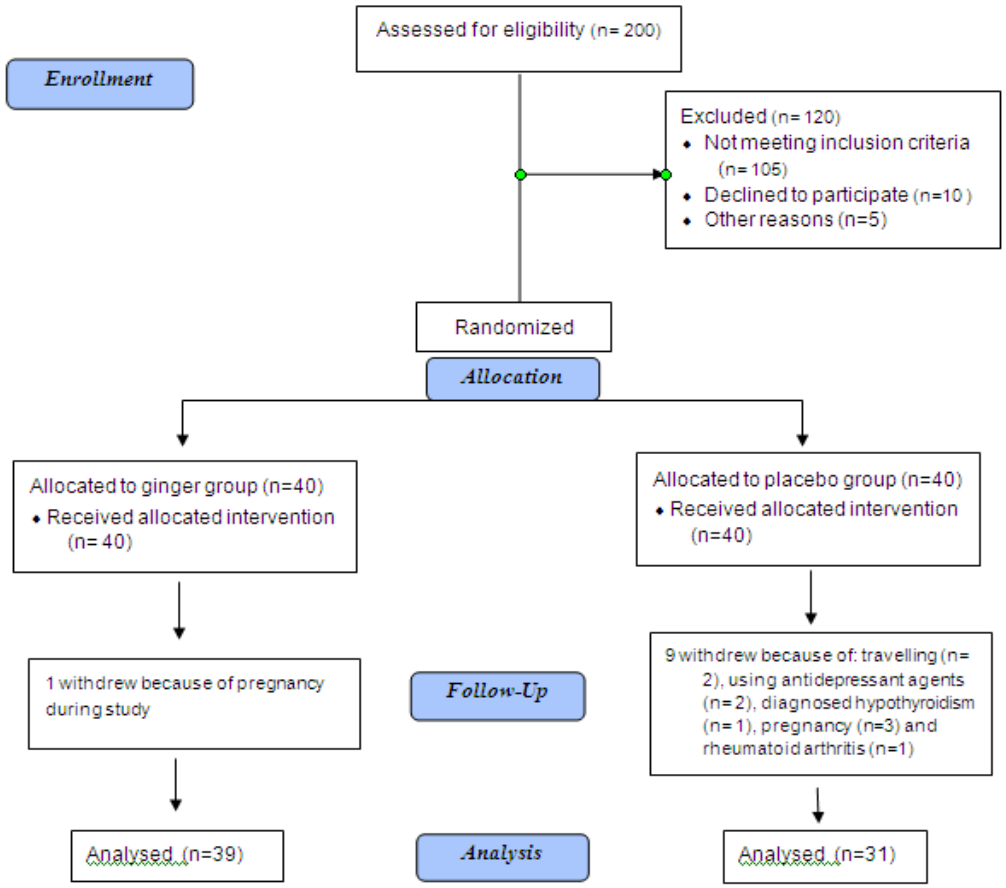


**Figure 1.** The consort flowchart describing the progress of the patients through the trial.

**Table 1.** Baseline characteristics of the participants in both groups.

| Parameters | Ginger group(n= 39)* | Placebo group(n= 31)* | *P value* ** |
|---|---|---|---|
| Age (y) | 35.25±7.30 | 34.54±7.91 | 0.699 |
| BMI (kg/m2) | 34.34±3.61 | 35.46±3.41 | 0.192 |
| Glucose (mg/dl) | 94.20±13.50 | 94.48±15.31 | 0.936 |
| TG (mg/dl) | 139.89±64.77 | 158.22±84.31 | 0.307 |
| TC (mg/dl) | 181.69±30.34 | 192.45±45.34 | 0.240 |
| LDL-C (mg/dl) | 104.92±25.29 | 109.64±39.15 | 0.544 |
| HDL-C (mg/dl) | 48.76±10.97 | 51.16±10.50 | 0.359 |
| LDL-C/HDL-C | 2.25±0.69 | 2.15±0.69 | 0.576 |
| TC/HDL-C | 3.89±1.00 | 3.84±0.84 | 0.827 |
| MDA (nmol/ml) | 2.02±1.24 | 2.29±1.3 | 0.380 |
| TAC (U/L) | 1.36±0.24 | 1.40±0.24 | 0.571 |

Values are mean ± SD.
* Baseline data are shown just for study subjects who completed the study
** *P* values are based on the independent sample *t*- test

The baseline characteristics of the study subjects are given in Table 1. Prior to the intervention, there was no statistically significant differences between groups in any of measured parameters ($p$> 0.05).

As shown in Table 2, ginger supplementation for 12 weeks significantly reduced serum glucose ($p$<0.0001), TC ($p$=0.037), TG ($p$<0.0001), TC/HDL.C ($p$<0.0001) and LDL.C/HDL.C ($p$=0.023), while increased MDA ($p$=0.005) and HDL.C ($p$<0.0001) as compared to the baseline. In the placebo group, there was also significant reductions of serum glucose ($p$=0.008), TC ($p$=0.024), TG ($p$=0.018), TC/HDL.C ($p$=0.003), LDL.C/HDL.C ($p$=0.005) and TAC (p= 0.029) along with significant increase in serum HDL.C ($p$<0.0001). Serum level of LDL.C had no significant change in any groups.

**Table 2.** Effect of 12 weeks ginger supplementation compared to the placebo on some biochemical parameters in obese women.

| Parameters | Ginger group | | | Placebo group | | | |
|---|---|---|---|---|---|---|---|
| | Before intervention | After intervention | *Changes (%)*[a] | Before intervention | After intervention | *Changes (%)*[a] | *P value*[†] |
| Glucose (mg/dl) | 94.20±13.50 | 86.17±8.25* | -7.51±9.67 | 94.48±15.31 | 87.54±10.51* | -6.16±12.12 | 0.669 |
| TG (mg/dl) | 139.89±64.77 | 103.35±42.87* | -20.51±26.58 | 158.22±84.31 | 135/58±60.02* | -4.92±36.96 | 0.006 |
| TC (mg/dl) | 181.69±30.34 | 173.02±29.5* | -4.05±12.93 | 192.45±45.34 | 176.38±46.44* | -6.83±24.43 | 0.848 |
| LDL-C (mg/dl) | 104.92±25.29 | 100.56±28.68 | -2.69±23.77 | 109.64±39.15 | 96.11±47.77 | -4.04±80.23 | 0.583 |
| HDL-C (mg/dl) | 48.76±10.97 | 51.81±10.95* | 6.60±1.95 | 51.16±10.50 | 53.96±10.67* | 5.68±2.63 | 0.107 |
| LDL-C/HDL-C | 2.25±0.65 | 2.05±0.81* | -8.68±21.93 | 2.15±0.69 | 1.40±0.60* | -42.93±113.02 | 0.013 |
| TC/HDL-C | 3.89±1.00 | 3.49±0.98* | -9.91±11.97 | 3.84±0.84 | 2.87±0.86* | -26.05±54.67 | 0.023 |
| MDA (nmol/ml) | 2.02±1.24 | 3.46±2.60* | 95.47±232.04 | 2.29±1.30 | 2.68±1.74 | 50.24±175.44 | 0.434 |
| TAC (U/L) | 1.36±0.24 | 1.35±0.25 | -0.13±15.18 | 1.40±0.24 | 1.31±0.25* | -5.22±12.14 | 0.150 |

Ginger group: n= 39; Placebo group: n= 31
TC: total cholesterol; TG: triglyceride; MDA: malondialdehyde; TAC: total antioxidant capacity
[a] Mean percent changes ± SD
* $P$ < 0.05 significantly different from baseline.
† *P values* indicate the comparison between groups by analysis of covariance (ANCOVA) with the baseline values and BMI differences, employed as covariates.

In the present study, ginger consumption significantly decreased the body weight, BMI, waist circumference (WC), and hip circumference (HC) as compared to the placebo while there was no difference between groups in energy and macronutrients intake during the study (data not shown).[39]

Furthermore, the results of ANCOVA test (the baseline values and BMI differences employed as covariates) revealed that ginger consumption significantly decreased serum TG ($p$=0.006) compared to the placebo and surprisingly there was significant reductions of TC/HDL.C ($p$=0.023) and LDL.C/HDL.C ($p$=0.013) in placebo versus ginger group (see Table 2). However, there were no significant difference in changes of glucose, other fractions of lipid profile, MDA and TAC between groups ($p$> 0.05).

## Discussion

Obesity has emerged over the past thirty years as a major public health issue and at least, 2.8 million adults die each year from its comorbidities.[40] Combating obesity has been under scientific investigation for many years. Regarding the popularity of using medicinal plants for treatment or prevention of diseases, the present study aimed to assess hypoglycemic, hypolipidemic and anti-oxidative effects of ginger supplementation in obese women.

Our results revealed that serum glucose level was significantly decreased in both study groups after 12 weeks intervention, albeit it was more noticeable but statistically non-significant in the ginger vs. placebo group.

Evidences from experimental studies show significant blood glucose lowering effect of ginger treatment in animals.[22,41-43] Whereas, in humans the results are inconsistent. In our previous study, daily administration of 2 g ginger powder for 8 weeks in T2DM patients increased insulin sensitivity, but like the finding of present study had no significant effect on serum fasting glucose, versus placebo.[26] Besides, our results are in agreement with that obtained by Bordia et al.[32] They showed that high dose of ginger powder consumption

(4 g/day) for 3 months in non-diabetic patients with coronary artery disease had no significant effect on blood glucose level. Moreover, this finding is also supported by a most relevant pilot study that ginger consumption (1 gr/day) for 10 weeks did not cause any significant change in fasting serum glucose levels in obese men.[34] In contrast, Mozaffari-Khosravi et al.[28] and Khandouzi et al.[29] recently demonstrated that ginger powder supplementation (3 g for 8 weeks and 2 g for 12 weeks, respectively) significantly decreased fasting blood sugar and Hemoglobin A1c in T2DM patients compared to the placebo.

To the best of our knowledge, relatively few interventional studies have investigated the effect of ginger consumption on blood glucose in non-diabetic population with normal serum glucose range. While, the hypoglycemic effect of ginger in diabetic patients still remains uncertain, it seems that ginger consumption has the most therapeutic effects in hyperglycemic people. Hence, our different results with some of these studies[28,29] may be due to the normal fasting blood glucose level of our participants at baseline.

The mechanisms responsible for hypoglycemic effect of ginger are not entirely clear, this might result from the increased gene expression of GLUT-4, insulin receptors and enhanced b-cell functions.[33] Moreover, Rani et al. suggested that major components of ginger , specially gingerols, improve blood glucose level by inhibition of key enzymes relevant to type 2 diabetes, α-glucosidase and α-amylase.[44]

The other finding of present study was a significant decrease of TG in ginger group compared to the placebo and surprisingly significant reductions of TC/HDL.C and LDL.C/HDL.C in placebo versus ginger group. There were no significant differences in changes of other lipid profile fractions between groups. The observed beneficial effects of ginger and placebo on serum lipid profile maybe due to the empathy effect, reduction of weight and energy intake in both group as mentioned in our previous article.[39] However it should be noted that this is not the first study that the subjects in placebo group have improvements in some parameters; even more than the intervention effects, without any other explanation for this. Generally, although there are some evidences for the hypolipidemic effect of ginger, however these findings were not consistent for all fractions of lipid profile.

Nammi et al.[25] reported that ethanolic extract of Z. officinale decreased total cholesterol, LDL cholesterol, triglycerides, free fatty acids and phospholipids in high-fat diet-fed rats in a dose dependent manner. However, no significant change in serum HDL cholesterol was observed. In contrast, Prasad et al. showed that 21 days treatment with ginger-juice in rats significantly reduced the serum TC level and increased HDL.C, while the LDL-C and TG remained unchanged.[45]

In this regards, there are relatively few clinical trials. Alizade et al.[31] reported the hypolipidemic effect of ginger whereas Bordia et al.[32] and Atashak et al.[34] demonstrated that ginger powder didn't have any significant effects on blood lipid profiles in coronary artery disease and obese men, respectively. Moreover, Andalu et al demonstrated that consuming dry ginger powder (3gr/day) for 30 days, significantly decreased total cholesterol, LDL, and VLDL cholesterol in diabetic patients.[46]

Such discrepancy of results may be attributed to differences in shape of administered ginger (powder or extract), preparation method, target disease and duration of study. The hypolipidemic effect of ginger may be due to decreased fat absorption (e.g. decreased pancreatic lipase) and increased cholesterol conversion to bile acids. Besides, it was reported that ginger can inhibit cellular cholesterol biosynthesis through reduction of hepatic farnesyl diphosphate synthetase.[9,33]

Obesity is usually accompanied by elevated oxidative stress, which is a key mediator for obesity related complications.[5,6] In our study, ginger consumption didn't have significant effect on TAC and MDA levels, as compared to the placebo. However, there were significant intragroup differences in MDA and TAC in ginger and placebo groups respectively. Although our results revealed that the MDA level increased in both groups, especially in ginger group; in contrast the decrease of TAC in ginger group was lower than that in placebo group which may be confirmed the antioxidative effect of ginger.

Contrary to our finding, most experimental studies especially on diabetic animals indicated that ginger extract or its purified bioactive compounds have great potential to limit oxidative stress and lipid peroxidation.[47,48] It was also shown that ginger polyphenols, specifically free pholyphenolic compounds significantly increased the activity of antioxidant defense system enzymes, including superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and glutathione reductase (GR) in streptozotocin induced diabetic rats.[49] However, there are limited clinical trials in this regards and contrary to animal studies, all of them examined ginger powder effects and often no significant difference in serum MDA level was reported between ginger and placebo groups.[30,35,50] Of course, a significant decrease of serum MDA level in T2DM patients has been reported previously.[29] One explanation for this controversy, is using independent t-test to compare groups instead of more reliable ANCOVA test.

Taken together, this is the first clinical trial aimed to investigate the effect of ginger on some metabolic features of obesity. A potential limitation of this study is that we cannot generalize our results to men. The other limitation is that we couldn't measure the other biomarkers of oxidative stress such as serum oxidized LDL.c (ox-LDL), nitric oxide (NO) and catalase levels. Moreover, as a suggestion for future researches, ginger

supplementation in higher dose along with weight lowering diet maybe need, to reach more effectiveness.
In conclusion, our findings demonstrated a minor beneficial effect of 2 g ginger powder supplementation for 12 weeks on serum glucose and a moderate, significant effect on TG, as compared to the placebo. However ginger consumption did not cause any significant effect on serum MDA and TAC levels. Further clinical trials may be required to explore ginger's efficacy in obese people.

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## Conflict of interest
There is no conflict of interest in this study.

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