The effect of ginger on blood sugar and urine protein in patients with type 2 diabetes mellitus; a clinical trial

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ABSTRACT

Introduction: The prevalence of diabetes mellitus has been increasing exponentially and its complications are a major cause of morbidity and mortality. Ginger is one of the herbal remedies which has preventive effects on nephropathy in animal models in some studies.

Objectives: We aimed to investigate the effect of ginger on urine protein analysis and blood glucose levels in diabetic patients.

Patients and Methods: In a clinical trial, 98 patients with type 2 diabetes were randomly divided into two groups; the intervention group received 500 mg of Zingiber as capsule, daily in addition to routine therapies, since control group received only conventional treatments for diabetes. Before and after intervention, blood glucose, urine microalbumin and hemoglobin A1c (HbA1c) were measured.

Results: The findings showed that Zingiber decreased HbA1c levels in diabetic patients (P=0.006), however, it did not have a significant effect on fasting blood glucose (P=0.179), 2 hours post-prandial glucose levels (P=0.272), and the microalbuminuria quantity in urine (P=0.109).

Conclusion: In our study, the hypoglycemic short-term effects of ginger observed as a reduction of HbA1c, however its effect on reducing blood glucose levels [FBS and 2 hours postprandial glucose (2hpp)] was not significant, therefore ginger can be considered as a supplementary agent in the treatment of diabetes. However it is recommended to conduct more studies to obtain results with more reliability.

Trial registration: The trial protocol was approved by the Iranian Registry of Clinical Trial (identifier: IRCT2017103025732N27; https://www.irct.ir/trial/21503, ethical code; IR.SEMUMS.REC.1395.207).

Implication for health policy/practice/research/medical education: Diabetes is a leading cause of morbidity and mortality. Diabetes in its early stages is curable by using herbal medicine. Since antiquity, diabetes has been treated with plant medicines. Recent scientific investigation has confirmed the efficacy of many of the herbs, some of which are remarkably effective. Zingiber has long term effect on diabetes and can be useful in prevention of diabetes complications.

Ginger is a genus of grassy perennial Zingiberaceae family commonly referred to as the root of the plant, the part used is the scientific name *Zingiber officinale*. Although ginger is commonly referred to as the root of the plant, the part used is essentially the swollen underground stem of the plant. Ginger is a genus of grassy perennial Zingiberaceae family with about 70 species native to southeastern Asia with narrow, straw-like stems and shiny green arrowhead leaves that grow from tuberous rhizome (9,10). Their flowers are yellowish-green with a purple edge and creamy spots and small conical inflorescence with dense ears with stems growing out of ground in the summer (11). Among the ginger properties, one can state strengthening the immune system, anti-inflammatory properties, protective effects against colorectal cancer, anti-nausea and anti-thyroid effects in pregnant women, strong antioxidant effect, liver detoxifier, anti-hyperglycemia, anti-constipation and anti-palpitation (9-14).

Ginger has a protective effect and helps improve the kidney damage of diabetic patients (10). For instance, ginger antioxidants are gingerol, shogaols, and some phenolic derivatives of ketones, resulting in the loss of free radicals in the organs of the body, including the kidneys (13,15).

Ginger extract can help improve long-term diabetes control, resulting in increased insulin secretion and insulin release, as well as increased glucose clearance is in the peripheral tissues responding to insulin (9). Ginger kidney protective effect can be similar to metformin and prevent phosphorylation due to AMP-activated protein kinase activity (16,17).

A substance in ginger called gingerol is effective in increasing the use of glucose by cells without the need for insulin. Moreover, it is seen that insulin sensitivity increases drastically and therefore serum insulin decreases while using it. Moreover, the levels of low-density lipoprotein cholesterol and triglyceride in their blood have decreased (9). Ginger reacts with serotonin receptors since the effect of these receptors reverses insulin secretion. Accordingly, treatment with ginger reduces the level of glucose by 35% and increases insulin in the plasma by 10%. Ginger inhibits the synthesis of inflammatory factors in the body, as well as having a reverse effect to that of hyperglycemia in the body (18,19).

However, the high consumption of ginger may cause heartburn, interactions with cardiac and diabetic drugs and stimulate central nervous system disorders. Moreover, pregnant women, those with kidney and bile stones, and those using blood diluents should be careful the excessive use.

**Objectives**

Given its antioxidant and anti-inflammatory properties, we examine the effect of ginger on changes of blood glucose and microalbuminuria in diabetic patients.

**Patients and Methods**

**Study design**

In this clinical trial study, 116 individuals over 18 years of age admitted to endocrinology clinic of Kowsar hospital in Semnan, Iran with type 2 diabetes mellitus, were divided into two groups using blocked randomization with randomly selected block sizes. The inclusion criteria were patients more than 18 years old who treated with insulin...
or glucose lowering drugs with non-nephrotic proteinuria and a GFR more than 50 mL/min/1.73 m². The exclusion criteria were being pregnant or lactating women, patients with liver illness, or symptomatic biliary or kidneys stones, active malignancies, alcohol users, active infections and warfarin users. The patients were randomly assigned to receiving ginger (case), control groups using random allocation sampling method, and underwent intervention in three months. Five patients from the intervention group were excluded from the study (one patient due to acute cholecystitis and four patients due to loss to follow up). Forty-eight patients in the intervention group received 500 mg of ginger as 250 mg capsules (Goldaru Pharmaceutical Company) besides receiving blood glucose drugs before lunch and before dinner for 12 weeks. Three patients in the control group excluded due to loss to follow up and 50 patients in the control group received no medicines and only received the same drugs that they had already used. Prior to the intervention and after that, the fasting blood glucose (FBS) and postprandial blood glucose 2 hours after meals 2 hours postprandial glucose (2hpp), hemoglobin A1c (HbA1c) and the value of urine microalbumin was measured. A checklist containing demographic and laboratory data for before and after intervention was applied.

**Ethical issues**

The research followed the tenets of the Declaration of Helsinki. This paper was extracted from the thesis of Haniyeh Movahed, at the department of internal medicine, Semnan University of Medical Sciences. Moreover, the study protocol was registered in the Iranian Registry of Clinical Trials (identifier: IRCT2017103025732N27; https://www.en.irdt.ir/trial/21503). The study was approved by the ethics committee of the Semnan University of Medical Sciences (#IR.SEMUMS.REC.1395.207). Additionally, informed consent was obtained from all of the patients.

**Statistical analysis**

Data were analyzed by SPSS 23. The chi-square, Shapiro-Wilk test, $t$ test (or Mann-Whitney U test) and Median tests were used to compare two related groups. $P<0.05$ was considered to indicate the significance level.

**Results**

In this study, 116 patients with type 2 diabetes mellitus were enrolled, 18 patients excluded from study during recruitment and follow-up. Finally 98 patients were entered to statistical analysis, 48 of them were ginger and 50 were as the control group. Therefore, the study was conducted on 48 patients. Mean ($±SD$) of age in the ginger group was 61.2 $±$ 10.7 years and the control group was 59.6 $±$ 7.9 years ($P=0.414$) (Table 2). The youngest and the oldest patient were 41 years old. The ginger group was similar to the control group in terms of age ($P=0.944$; Table 1).

![Consort flow diagram of the study.](http://journalrip.com)}
years and 86 years in the ginger group and 47 years and 78 years in the control group, respectively.

In the ginger group 41.7% and in the control group 36% of patients can be described as overweight or obese (Table 3).

Mean ± standard deviation of FBS before and after intervention in both groups is shown in Table 4. Mean FBS in ginger patients decreased by different 2.38 units, while in the control group increased by 1.46 units; however FBS was not significantly different in the groups (P = 0.197).

The mean 2-hour postprandial blood sugar in the ginger group decreased by 2.17 units on average while it increased by 7.36 in the control group. Similarly, two-hour hyperglycemic changes were not significantly different between the two groups (Table 5) (P = 0.272).

The mean HbA1c in the ginger group decreased by 0.42 units on average and 0.10 in the control group. HbA1c changes were significantly different between the two groups (Table 6) (P = 0.006).

The mean urinary microalbumin in patients receiving ginger decreased by 1.15 units on average and in the control group decreased by 1.12 units. However, urinary microalbumin changes were not significantly different between the two groups (Table 7) (P = 0.109).

### Discussion

One hundred patients with type 2 diabetes randomly were assigned to ginger and control groups (50 patients received ginger and 50 were as the control group). During the first month after receiving ginger, two patients (7.66%) from the ginger recipient group started to grow digestive problems as the most common complication of ginger and were excluded from the study. The group receiving ginger and 66% of the control group were females. The two groups were homogenous regarding gender. The results showed that ginger significantly reduces HbA1c levels in diabetic patients, with no significant effects on the level of FBS and 2hpp glucose and urine micro-albumin levels. Numerous studies conducted on the effects of ginger on diabetes focused on animal models. Alshathly et al assessed the ginger therapeutic effect against functional and structural alteration in the liver of diabetic rats and concluded that ginger as a natural safe herbal medication has antioxidant, anti-diabetic effect and can be used to support liver functions in diabetic status (20).

In another study by Li et al, ginger has shown prominent protective effects on diabetic nephropathy and other complications in the liver, eye, and neural system (21).

The antioxidant and anti-inflammatory effects of ginger have been examined in human studies. Araujo et al indicated that ginger has hypoglycemic potential and reduces diabetic complications (22). Kulkarni et al reported that ginger is effective as an anti-inflammatory and antioxidant supplement along with anti-TB therapy as it possesses strong free radical scavenging property too (23).

In another study, Tzeng et al examined the effect of ginger on nephropathy in diabetic rats. The results showed an increase in creatinine clearance, a decrease in blood glucose, and a decrease in (10). The result of the review by Li et al showed the protective and preventive effects of ginger in diabetes mellitus, diabetes complications, and other metabolic diseases. The results of this review show that ginger has an anti-hyperglycemic
Effect of ginger on blood sugar

In a study by AL-Qattan et al., the hypoglycemic effects of garlic and ginger on diabetic rats were assessed. The results of the study showed the hypoglycemic effects of garlic and ginger, reduced progression of diabetic nephropathy in the samples examined (3). The results of our study regarding the level of blood glucose and urine protein were in contrast to empirical studies. It seems that the difference between human and animal studies can be one of the reasons for this inconsistency. In our study, comparing HbA1c in the two groups showed a significant decrease in the ginger recipient group. Our study did not show the decreasing effect of ginger on microalbuminuria. However, our results were based on short-term period study (3 months), regarding positive effects of ginger on reducing HbA1c, which may be seen in the long-term follow-up as in the study by Qattan-Al et al. (3). Ramudu et al. examined the protective and therapeutic effects of ginger against histopathologic changes of gentamicin-induced tubular toxicity in an animal nephropathy model. Animals from the gentamicin treatment group had a significant decrease in serum creatinine. Gingerol-enriched fraction reduced GM-induced nephrotoxicity, and this effect is due to reductions in oxidative stress and inhibition of inflammatory gene expression (25).

However, comparing microalbuminuria in the two groups in our study did not show a significant difference, which may be due to the short term design of our study and need to be reviewed over a period of more than 12 weeks to reach various outcomes. In some studies, hypoglycemic effects of ginger have been examined in human studies as well (26,27).

<table>
<thead>
<tr>
<th>Group</th>
<th>2-hour postprandial blood glucose</th>
<th>Difference</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before intervention</td>
<td>After intervention</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Median</td>
</tr>
<tr>
<td>Ginger</td>
<td>189</td>
<td>51.7</td>
<td>186</td>
</tr>
<tr>
<td>Control</td>
<td>201.3</td>
<td>62.9</td>
<td>185.5</td>
</tr>
<tr>
<td>P value</td>
<td>0.550</td>
<td>0.031</td>
<td>0.197</td>
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</tbody>
</table>

Table 5. Mean ± standard deviation of two-hour postprandial blood glucose in ginger diabetic patients and control group

<table>
<thead>
<tr>
<th>Group</th>
<th>Hemoglobin A1c</th>
<th>Difference</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before intervention</td>
<td>After intervention</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Median</td>
</tr>
<tr>
<td>Ginger</td>
<td>7.5</td>
<td>1.1</td>
<td>7.3</td>
</tr>
<tr>
<td>Control</td>
<td>7.6</td>
<td>1.2</td>
<td>7.6</td>
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<tr>
<td>P value</td>
<td>0.662</td>
<td>0.053</td>
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Table 6. Mean ± standard deviation, median, and amplitude of hemoglobin A1c quartile before and after treatment and their changes in two groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Urinary microalbumin level</th>
<th>Difference</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before intervention</td>
<td>After intervention</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Median</td>
</tr>
<tr>
<td>Ginger</td>
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<td>24.3</td>
<td>27</td>
</tr>
<tr>
<td>Control</td>
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<td>51.1</td>
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<tr>
<td>P value</td>
<td>0.557</td>
<td>0.667</td>
<td>0.109</td>
</tr>
</tbody>
</table>

Table 7. Mean ± standard deviation, median, and amplitude of urinary microalbumin levels before and after treatment and their changes in two groups
It was observed that extract of ginger significantly reduced body weights and serum lipid levels in the treated rats. In the same order, serum glucose significantly decreased ($P < 0.05$) after 8-day and moreover, elevations in the measured biochemical parameters were significantly ($P < 0.05$) attenuated in rats treated with the ginger extract (28).

In the review study by Daily et al, the effects of ginger on type 2 diabetes have been investigated in several randomized clinical trials. The study has stated the significant effects of ginger on reducing FBS and HbA1c resemble our study (27). Reduction in FBS levels and 2 hours after meals were seen in the group receiving ginger, which is similar to the human studies in our study (27).

Although the level of blood glucose (FBS and 2hpp) reduction in our study was not significantly different between the group receiving ginger and the control group, this is inconsistent with the studies mentioned. In our study, ginger consumption had significant reduction in HbA1c, similar to those of other studies (3,28), showing the long-term effects of ginger on reducing and controlling blood glucose levels.

**Conclusion**
In our study, the hypoglycemic effects of ginger were observed in in short-term follow up. Although its effect on reducing blood glucose levels (FBS and 2hpp) was insignificant. Its effect on the reduction of HbA1c was significant and perhaps ginger can be considered a supplementary agent in the treatment of diabetes. However, getting results with a greater degree of confidence requires more studies.

**Limitations of the study**
Given some of the limitations of our study, such as the lack of cooperation of some patients in using ginger, it is recommended to conduct studies with more sample size and multiple centers to obtain results with more reliability.

**Conflicts of interest**
There was no conflict of interests.

**Ethical considerations**
Ethical issues (including plagiarism, data fabrication, and double publication) were completely observed by the authors.

**Authors’ contribution**
Conception and design: MF and MY; Literature search and data acquisition: HM; Drafting the manuscript: MF, MY and HM; Analysis and interpretation of data: RG; Critical revision of the manuscript for important intellectual content: MF, MY. All authors read and approved the final paper.

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**References**


