

Ginger and diabetes: A mini-review.

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Abstract

Background: Ginger is one of the most well liked spices in the world. In more recent times interest has shifted towards possible effects of ginger on cancer, blood clotting, inflammation and pain. However, lesser attention has been given to metabolic diseases such as diabetes. Animal studies and human trials have shown promising results.

Methods: A comprehensive search was made in PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/>) and The University of Linköping's electronic research database (www.bibl.liu.se.e.bibl.liu.se/?l=sv). The goal was to gather information about human research on the topic ginger and diabetes mellitus in randomized and/or controlled clinical trials or meta-analyses in order to review the scientific evidence. The following search terms were used in various combinations: Diabetes; Glucose; Insulin; Cardiovascular; Ginger; Zingiber Officinale; Meta-analysis; Randomized; Controlled; Clinical Trial.

Results: The PubMed search yielded several randomized and/or controlled clinical trials on the topic of the effects of ginger on diabetes mellitus or diabetes-related measurements such as glucose or insulin or lipids. The search also yielded four meta-analyses. The individual clinical trials found had already been included in the four meta-analyses, except for one trial that was published after the last inclusion date in the most recent meta-analysis. The meta-analyses all showed that ginger consumption could have profitable effects on glucose and lipid metabolism in patients with diabetes and other risk factors. In the clinical trials significant reductions in fasting blood glucose, HbA1c, total cholesterol, LDL, and triglycerides were seen as well as an increase in HDL. Additionally, a trial published after the last inclusion date in the most recent meta-analysis also exhibited reductions in glucose and lipids in diabetics consuming ginger.

Conclusions: Current scientific research shows that ginger consumption can have a favorable impact on measurements of glucose and lipids in patients with diabetes. The results are as of now only applicable to Iranian and Indian populations and further trials are warranted in Western populations.

Keywords: Ginger, Diabetes.

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Introduction

Ginger is one of the most well liked spices in the world. From its origin in Southeast Asia it has spread to Europe and has a long tradition within alternative medicine as a cure for diverse diseases. Throughout history ginger has often been used to alleviate vomiting, intestinal disturbances and colds. In more recent times interest has shifted towards possible effects of ginger on cancer, blood clotting, inflammation and pain. However, little attention has been given to metabolic diseases such as diabetes. Animal studies and human clinical trials have shown promising results. Experimental research in animals both *in vitro* and *in vivo* has shown that ginger can have effects on carbohydrate metabolism, insulin sensitivity and lipids. Moreover, such studies have also been able to show positive results on diabetic complications in the liver, kidneys, nerves and eyes [1].

The key enzymes controlling carbohydrate metabolism associated with hyperglycemia and type 2 diabetes are α -amylase and α -glucosidase. Ginger extract has *in vitro* been able to inhibit the enzymes α -amylase and α -glucosidase and

the inhibiting effect correlated with gingerol and shogaol in the extract [2]. Diabetes mellitus is characterized by defects in insulin release and/or insulin sensitivity. *In vitro* studies have also shown that extract from ginger and gingerol could increase glucose uptake in muscles and fat cells. *In vivo* studies have shown an increase in plasma insulin levels accompanied by reduced glucose levels.

Furthermore, animal studies have shown protective effects of ginger on β -cells and restored insulin levels, and several animal models with diabetes and hyperlipidemia have shown reduced levels of cholesterol, LDL, triglycerides and increased HDL. To be more specific, STZ-induced (injection of streptozotocin) type 2 diabetic animal models have been used to study the effects of ginger on diabetes. One study evaluated the antihyperglycaemic effect of aqueous extract of ginger administered orally on a daily basis in three different doses (100, 300, 500 mg/kg body weight) for a period of 30 days to STZ-induced diabetic rats. Results revealed a dose-dependent antihyperglycaemic effect with a decrease of plasma glucose levels by 38% and 68% on the 15th and 30th day, respectively, after the rats were given 500 mg/kg ginger [3]. In another study, an aqueous extract

of raw ginger, 500 mg/kg, was administered intraperitoneally daily for a period of 7 weeks to STZ-induced diabetic rats. The STZ-injected rats exhibited hyperglycemia accompanied with weight loss, indicating their diabetic condition. Raw ginger was significantly effective in lowering serum glucose, cholesterol and triacylglycerol levels in the ginger-treated diabetic rats compared with the control diabetic rats. The ginger treatment also resulted in a significant reduction in urine protein levels [4].

Methods

A comprehensive search was made in PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/>) and The University of Linköping’s electronic research database (www.bibl.liu.se.e.bibl.liu.se/?l=sv). The goal was to gather information about human research on the topic ginger and diabetes mellitus in randomized and/or controlled clinical trials or meta-analyses. The following search terms were used in various combinations: Diabetes; Glucose; Insulin; Cardiovascular; Ginger; Zingiber Officinale; Meta-analysis; Randomized; Controlled; Clinical Trial.

Results

The PubMed search yielded several randomized and or controlled clinical trials on the topic of the effects of ginger on diabetes mellitus or diabetes-related measurements such as glucose or insulin or lipids. The search also yielded four meta-analyses. The individual clinical trials found had already been included in the four meta-analyses, except for one trial that was published after the last inclusion date in the most recent meta-analysis. Here follows a short description of the four meta-analyses. The individual trials can be viewed in Table 1.

Meta-analysis 1

Daily et al. published 2015 a systematic review and meta-

analysis on the effects of ginger on diabetes [5]. The authors of the article found five randomized clinical trials that fit their inclusion criteria: Andallu et al. [6]; Mahluji et al. [7]; Arablou et al. [8]; Mozaffari-Khosravi et al. [9]; Khandouzi et al. [10]. Four of these were deemed as high quality studies with a duration of 8 weeks and one study was deemed as low quality with a study duration of 4 weeks. All patients had had diabetes mellitus for at least between 2 and 10 years and none had serious diabetic complications. The patients received ginger powder in doses of between 1.6 and 3.0 grams/day and between 30 to 84 days of intervention. Four of the studies were performed in Iran and one in India, and four of the studies used a two-arm parallel design (ginger and placebo) and one study used a four-arm parallel design. The main result of the meta-analysis was that ginger supplement significantly lowered fasting glucose by -18.74 mg/dl (-34.70; -2.77) and HbA1c levels by -1.66% (-2.04; -1.29), but did not show any significant effects on fasting insulin levels or HOMA-IR. The authors concluded that their “meta-analysis along with the supporting evidence from animal and cellular studies strongly suggests that ginger has efficacy for the management of blood glucose levels and that the effects are both preventive and therapeutic for Type 2 diabetes”. Furthermore, they stated that “the major limitation of this study was the relatively few clinical trials available for the meta-analysis and the modest number of participants in each trial, however, that was offset by the consistency of the results” [5].

Meta-analysis 2

Mazidi et al. published 2016 a systematic review and meta-analysis on the effects of ginger on inflammation, lipids and glucose [11]. The authors looked for articles in the literature up until July 2016. They found nine trials that fit their inclusion

Table 1. Trials Performed with Ginger Supplementation in Diabetes Patients.

Reference /Country/ Publication Year	Number of Patients (Ginger/ Placebo); Age (Years)	Intervention/Placebo-treatment	Duration of Intervention	Effect Size; *p<0.05
[6] India 2003	N=8/N=8; 40-60	Ginger powder capsule 500 mg 2x3 per day/ Corn starch tablet 500 mg 2x3 per day	30 Days	FPG: -17* mg/dl
[7] Iran 2013	N=28/N=30; 38 -65	Ginger powder capsule 1000 mg 1x3 per day/Corn starch tablet 1000 mg 1x3 per day	8 Weeks	FPG: 6.1 mg/dl HbA1c: -3.5% Insulin: -13* µU/ml HOMA: -8.1*
[8] Iran 2014	N=33/N=30; 30 - 70	Ginger powder capsule 800 mg 1x2 per day / Wheat flour powder capsule 800 mg 1x2 per day	12 Weeks	FPG: -9.1* mg/dl HbA1c: -1.0* % Insulin: -3,7* µU/ml HOMA: -1.7*
[9] Iran 2014	N=40/N=41; Mean age 50	Ginger powder capsule 1000 mg 1x3 per day/ Microcrystalline cellulose capsule 1000 mg 1x3 per day	8 Weeks	FPG: -18.17* mg/dl HbA1c: -0.4* % Insulin: -7.4* mU/L HOMA: -1.04*
[10] Iran 2015	N=22/N=19; 20-60	Ginger powder capsule 1000 mg 1x2 per day/Lactose powder capsule 1000 mg 1x2 per day	12 Weeks	FPG: -19* mg/dl HbA1c: -0.77* %
[12] Iran 2015	N=45;20-60	Ginger powder capsule 3 g per day/Lactose capsules 3 g per day	12 Weeks	FPG: -19.41* mg/dl HbA1c: -0.77* % Insulin: -1.46* µU/mL
[14] Iran 2012	N=40/N=41; N/A	Ginger powder capsule 3 g per day/ N/A	8 Weeks	FPG : -18.18* mg/dl
[15] Iran 2015	N=41/N=39; Mean age 54,5	3 g ginger rhizome in 3 cups black tea per day/3 cups black tea	8 Weeks	FPG : -1.02 mg/ml
[17] Iran 2017	N=23/N=22; 30-60	Ginger powder capsule 500 mg 2 x 2 per day/ Wheat flour capsule 500 mg 2 x 2 per day	10 Weeks	FPG: -26.3* mg/ml HbA1c: -0.38* %

FPG=Fasting plasma glucose; N/A= Information not found

criteria. Eight trials were performed in Iran and one trial was performed in USA. The trials were published between 2008 and 2015 and the population studied varied between 10 and 88 individuals. Mean age was between 24 and 58 years. 1.0 to 3.0 grams/day of ginger was used in the intervention groups and the length of study varied between 2 and 3 months. Four of the included trials were based on diabetic patients, two of the trials included dialysis patients, two of the trials included patients with overweight and finally one trial was based on patients with hyperlipidemia. Three of the four trials that included patients with diabetes were the same trials as studied by Daily et al. [5] in the above mentioned meta-analysis. The fourth was done by Shidfar et al. and published 2015 [12]. The main results showed a significant reduction in serum CRP concentration by -0.84 mg/L (-1.38 ; -0.31), fasting blood glucose by -1.35 mg/dl (-2.04 ; -0.58), HbA1c by -1.01% (-1.28 ; -0.72) and triglycerides by -1.63 mg/dl (-3.10 ; -0.17). Furthermore, there was a significant elevation in HDL by 1.16 mg/dl (0.52 ; 1.08). The authors concluded that their “systematic review showed that ginger supplementation can improve CRP level, glycaemia indexes, and lipid profile, which can be useful for the prevention and management of CVD” [11].

Meta-analysis 3

Jafarnejad et al. published 2017 a meta-analysis on the effects of ginger on glucose and lipids in patients with diabetes or hyperlipidemia [13]. The authors searched the literature up until October 2016 and found nine randomized controlled trials that fit the inclusion criteria. Three of the nine trials were based on patients with hyperlipidemia and six trials were based on patients with diabetes. Four of the six diabetes trials had been included in the meta-analyses by Daily et al. [5] and Mazidi et al. [11]. The other two diabetes trials had been published by Talaei et al. [14] and Azimi et al. [15]. Compared with the control group the intervention group that received ginger reduced the weighted mean difference in triglycerides by -8.84 (-11.95 ; -5.73), total cholesterol by -4.42 (-8.70 ; -0.13) and fasting blood glucose by -14.93 (-19.83 ; -10.04). Moreover, there was a significant increase in HDL by 2.87 (0.88 ; 4.86). The authors concluded that “their meta-analysis supported the idea that ginger had effects on glucose and lipids, that side effects were limited, and that effects could be dependent upon the underlying disease” [13].

Meta-analysis 4

The most recent meta-analysis and systematic review found was published by Zhu et al. [16]. The authors’ goal was to evaluate the effect of ginger on diabetes and components of the metabolic syndrome. The authors searched the literature up until May 2017. They found a total of ten randomized controlled trials with a combined total of 490 included individuals. Five of the ten trials were based on diabetes patients and these trials were the same as included in the previously mentioned meta-analyses in this mini-review, with the exception that Talaei et al. [14], Azimi et al. [15] and Khandouzi et al. [10] were not included. The other five trials were based on patients with overweight (three), patients on dialysis (one) and patients with hyperlipidemia (one). Nine trials were performed in Iran and

one in India. Compared with the control group the intervention group with ginger consumption reduced the weighted mean difference of HbA1c by -1.00% (-1.56 ; -0.44), fasting insulin by -1.62 (-2.20 ; -1.05), HOMA-IR by -0.59 (-1.01 ; -0.17), triglycerides by -24.8 (-36.1 ; -13.5), total cholesterol by -8.22 (-16.0 ; 0.45), LDL by -6.66 (-12.4 ; -0.88), and finally increased HDL by 1.34 (0.03 ; 2.65). The authors concluded that their “systematic review and meta-analysis provide convincing evidence for the effects of ginger on glucose control, insulin sensitivity, and improvement of blood lipid profile. Based on the positive effects and negligible side effects, ginger may be a promising adjuvant therapy for diabetes mellitus type 2 and the metabolic syndrome [16]”.

Discussion

Firstly, several meta-analyses in recent years, based on mainly controlled, randomized or controlled and randomized trials, have shown that ginger consumption could have profitable effects on glucose and lipid metabolism in patients with diabetes. In the trials significant reductions in fasting blood glucose, HbA1c, total cholesterol, LDL, and triglycerides were seen as well as an increase in HDL. The four meta-analyses presented in this mini-review included altogether eight independent clinical trials based on patients with diabetes. Almost all of the individual trials had either excluded patients on insulin from the beginning of the trial or excluded patients which for any reason during the course of the trial got their hypoglycemic medication altered by their physician. None of the four meta-analyses had cited each other, i.e. the latter had not cited the former meta-analysis/analyses which could mean that the authors were not attentive to each other’s work or that they had other reasons not to cite. The meta-analysis by Zhu et al. [16] published most recently stated in the beginning of their discussion: “To the best of our knowledge, this is the first article to evaluate the effects of ginger on type 2 diabetes mellitus and components of the metabolic syndrome”; a statement that seems false since the other meta-analyses determined the same parameters on similar populations.

Secondly, after the last inclusion date in May 2017 into the meta-analyses, there have been published further trials on the topic. One of these is a study published by Makhdooni Arzati et al. [17]. The study was performed in Iran between 2015 and 2016 on 45 patients with diabetes type 2. Patients were 30 to 60 years old and had had diabetes for one to ten years. They were randomized by permuted randomized block design to either the intervention with 2 grams of grounded ginger or placebo with 2 grams of white flour. The ginger and flour were taken as two capsules of 500 mg two times a day for 10 weeks. There were no differences in demographics between the groups at baseline. Compared with placebo, ginger reduced fasting blood glucose -26.3 mg/dL \pm 35.3 vs. 11.9 mg/dL \pm 38.6, and HbA1c, -0.38% \pm 0.35 vs. 0.22% \pm 0.29, significantly. Moreover, the LDL/HDL-ratio was significantly reduced in the intervention group. Thus, single clinical trials published after the inclusion of trials into the above mentioned meta-analyses studied in this mini-review continue to show similar results, i.e. favorable effects of ginger on diabetes.

Thirdly, of all the included trials in the meta-analyses there was only one trial performed on a Western population [18]. All other trials were mostly performed in Iran and some in India. This single trial was a randomized, cross-over trial performed in the USA on a limited number of patients (10 overweight men in their forties) without diabetes. The effect of the intervention, 2 grams of ginger powder dissolved in water, was evaluated within few hours. The results did not show any significant effects of ginger powder on inflammatory markers, glucose, insulin or lipids. Thus, based on the evidence from clinical trials in this mini-review we cannot draw any certain conclusions about how ginger would affect diabetes and other risk factors in a Western population. On the other hand, there has been quite a movement of Middle Eastern individuals to Western countries over the years. One question that might be asked is if these migrated individuals continue to eat ginger to the same extent as they did in their home country or if they conform to Western diets losing the protective effects of ginger consumption? Thus, trials performed with ginger on diabetes patients in Western countries are highly warranted.

Along the same lines, clinical trials performed with ginger on diabetes patients with previous cardiovascular diseases such as ischemic heart disease or stroke would be pertinent in the future. A trial by Bordia et al. studied whether ginger consumption would be useful in patients with coronary heart disease [19]. It was a non-randomized but placebo-controlled trial with 30 patients on intervention and 30 patients on placebo. The intervention group consumed 4 grams of ginger for three months. There were no differences in glucose or lipid values between the groups. The trial was not a study on diabetes patients.

Fourthly, longitudinal studies or cross-sectional studies can give information about possible relationships between consumption of foods and diseases/risk factors but can never for certain be proof of cause and effect. One good example of this is a recently published cross-sectional study by Wang et al. [20], where the prevalence of chronic diseases and ginger consumption was studied in 4628 individuals from China (1823 men; 2823 females) ages 18 - 77 years old. Information came from questionnaires and medical records. The results showed statistically significant associations between ginger consumption and coronary heart disease and hypertension. The higher the ginger consumption the lower the prevalence of heart disease or hypertension. Interestingly, there was no significant association what so ever between ginger consumption and diabetes or hyperlipidemia. This is noteworthy regarding the results obtained in this mini-review on clinical trials, but it exemplifies the difficulties in interpreting results from cross-sectional studies. However, the study by Wang et al. [20] studied a Chinese population, which cannot be equaled with populations from the Middle East or India.

Conclusion

Several meta-analyses in recent years, based on mainly randomized controlled clinical trials, have shown that ginger consumption could have profitable effects on glucose and lipid metabolism in patients with diabetes and other risk populations. The results are as of now only applicable to Iranian and Indian populations and further trials are highly warranted in Western populations.

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