Obesity Medicine 14 (2019) 100094

Contents lists available at ScienceDirect

Obesity Medicine

journal homepage: www.elsevier.com/locate/obmed

Original research

Effects of ginger powder supplementation on glycemic status and lipid profile in newly diagnosed obese patients with type 2 diabetes mellitus

Mohamed Hesham El Gayar[a], Maram M.M. Aboromia[a,*], Nesma Ali Ibrahim[a], Moustafa Hussein Abdel Hafiz[b]

[a] Department of Internal Medicine and Endocrinology, Faculty of Medicine, Ain Shams University, Egypt
[b] Department of Endocrinology, National Institute of Diabetes and Endocrinology (NIDE), Egypt

ARTICLE INFO

Keywords:
Ginger
T2DM
Glycemic status
Lipid profile
Obesity

ABSTRACT

Background: Diabetes is a huge problem affecting 387 million adults by a global prevalence of (8.3%) which is expected to rise to (10.1%) by 2035. Type 2 diabetes, a growing public health problem, is associated with increased morbidity and mortality.
Aim: To evaluate the effects of ginger powder supplementation on glycemic status, lipid profile and beta-cell function in obese Egyptian patients with new-onset type 2 Diabetes Mellitus.
Design: A randomized, single blind, placebo-controlled clinical trial, was performed on 80 subjects newly diagnosed with T2DM conducted at the National Institute of Diabetes and Endocrinology.Subjects were randomly divided into:**Group 1**: Ginger Group (GG), consumed three capsules daily, each capsule containing: 600-mg of ginger powder (total daily dose was 1.8 g), they also underwent certain diet and physical activity changes, and also received metformin as one 850-mg tablet twice a day with meals for a duration of 8 weeks.**Group 2:** Placebo Group (PG), which received capsules of the same color, size, and number as (Group 1) but containing wheat flour, they also underwent the same diet, physical activity, and metformin dosage as (Group 1) during the 8 weeks of the study.
Results: Ginger powder supplementation significantly reduced body mass index, fasting blood glucose,2-h postprandial blood glucose, glycated hemoglobin, total cholesterol, low density lipoprotein cholesterol, triglycerides, fasting insulin levels, and homeostasis model assessment-insulin resistance index(HOMA2-IR).Ginger also significantly increased high density lipoprotein cholesterol levels, beta cell function index (HOMA2-%β) & insulin sensitivity index (HOMA2-%S) in comparison to the placebo group.
Conclusion: Ginger supplementation could be an effective adjuvant therapy for patients with T2DM.

1. Introduction

Diabetes is a huge problem affecting 387 million adults by a global prevalence of (8.3%) which is expected to rise to (10.1%) affecting 592 million adults by 2035. Type 2 diabetes is associated with increased morbidity and mortality (Mahluji et al., 2013).

Cardiovascular diseases are the leading cause of morbidity and mortality in diabetic patients. Diabetic patients are 2-to-4-folds more prone to atherosclerosis. Dyslipidemia is the most important modifiable risk factor for atherosclerosis in diabetic patients. Diabetic control moderates diabetes-related dyslipidemia. Insulin resistance (IR) is the driving factor leading to type 2 diabetes and is an independent risk factor for cardiovascular diseases even in non-diabetic patients (Bhandari and Pillai, 2005).

Ginger the rhizome of the plant Zingiber officinal which also referred to as the "root" is indigenous to Southeast Asia where its cultivation dates back about 3000 years in India. Today, its use has spread to most of the inhabited world (Mahluji et al., 2013).

Several studies, have shown that ginger has different pharmacological effects, due to its different components such as gingerols and shogaols. So far, more than 40 antioxidant compounds are also detected in ginger (Shirdel et al., 2009). The main pharmacological actions of ginger and its isolated compounds include immunomodulatory, anticancer, anti-inflammatory, anti-apoptosis, glucose and lipid lowering effect and antiemetic (Ali et al., 2008).

Ginger has been shown to possess antidiabetic activity in a variety of studies. Other studies suggested that the response to ginger components depends on its dose concentration (Khandouzi et al., 2015).

* Corresponding author.
E-mail address: maramaboromia@med.asu.edu.eg (M.M.M. Aboromia).

https://doi.org/10.1016/j.obmed.2019.100094
Received 7 October 2018; Received in revised form 28 March 2019; Accepted 22 April 2019

Some experimental researches published on the antidiabetic, lipid lowering and anti-oxidative properties of ginger are controversial and more studies may be needed to clarify its role in protection and treatment of metabolic disorders (Khandouzi et al., 2015).

2. Patients and methods

This study was conducted at the Diabetes outpatient clinic of the National Institute of Diabetes and Endocrinology (NIDE) from January 2017 to January 2018.

2.1. Study type, design, participants and sample size

This was a randomized, single blind, placebo-controlled clinical trial. This study was conducted on eighty subjects aged from 30 to 60 years.

Sample size was determined based on the data from previous studies (Attari et al., 2016). To ensure that sample size, used in the study, could obtain the desired outcome for all relevant variables, the highest number of the calculated samples was considered. The sample size was computed as 32 per group. Regarding a possible loss to follow-up, a safety margin of 25% was determined, and therefore 40 patients were allocated in each group.

2.2. Inclusion criteria

Patients newly diagnosed type 2 diabetes mellitus according to The American Diabetes Association diagnosis criteria (American Diabetes Association, 2016), HbA_{1c} level $< 9\%$, BMI $\geq 30\,kg/m^2$, no pregnancy or lactation, no autoimmune disorder, no cardiac or renal diseases, no thyroid, chronic inflammatory diseases, or peptic ulcer, no regular consumption of ginger or other herbal drugs, no hypersensitivity to ginger, no consumption of lipid lowering drugs or oral contraceptive pills, and no consumption of any supplements 2 months before starting the study.

2.3. Exclusion criteria

Diabetes duration more than 6 months, HbA1c level $\geq 9\%$, BMI $< 30\,kg/m^2$, Insulin therapy, any injectable or oral antidiabetic medication other than metformin, and any acute illnesses at the baseline or during the study, smoking, consumption of less than 80% of the capsules, any sensitivity due to ginger consumption reported by the patient or noticed after the outset of the study, consumption of vitamin, mineral or other nutritional supplements, and consumption of alcohol or narcotic drugs.

2.4. Dose, supplement preparation, and intervention duration

The Subjects were randomly allocated using a computer's random numbers into two groups:

Group 1: Ginger Group (GG)
Group 2: Placebo Group (PG)

GG consumed three capsules daily, each capsule containing: 600 mg of ginger powder (the total daily dose was 1.8 g), whereas PG received capsules of the same color, size, and number as GG but containing wheat flour, both after taking meals and for 8 weeks.

Dried rhizomes of ginger (Zingiber officinale Roscoe, Indian red [non-bleached] ginger) were purchased from a local spice dealer (Harraz Agricultural Seeds, Spices & Medical Plants Co., AKA Sheikh El Attarin, Cairo, Egypt). The ginger rhizomes were finely ground. Hard gelatin capsules (opaque dark green/opaque yellow) were purchased from (Jedco International Pharmaceuticals Co.). A Capsule Filling Machine was purchased online at Aliexpress.com from China. The capsules were either filled with 600 mg of ginger powder or wheat flour. The wheat flour capsules were buried in ginger powder for 2 weeks to render them identical in odor. Hence, participants were blind about the contents of the capsules they are receiving. Appropriate empty plastic jars with tight closure seals were purchased, each jar was filled with 42 capsules which was enough for 2 weeks. Participants received 1 jar at a time on day 1 and follow up visits on days 14, 28, and 42. These follow up visits were to insure that all patients complied with study interventions (lifestyle changes, metformin, and study capsules).

Once at the baseline, and again at the end, all subjects have been subjected to the following:

- **Full medical history taking** emphasizing the duration of diabetes mellitus, the type of current treatment, nutritional supplements, known sensitivity to ginger consumption and drug history in details.
- **Thorough clinical examination** including: Blood pressure and anthropometric measurements including; BMI and Waist/Hip ratio (WHR).
- Height, weight and waist and hip circumferences were measured with patients in an upright position with feet close together, arms at the side, wearing light clothing and no shoes.
- For measuring waist circumference, a measuring tape was placed at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest, at the end of a normal expiration. Hip circumference was measured around the widest portion of the buttocks, with the tape parallel to the floor (World Health Organization, 2008).
- Calculation of BMI: (BMI = weight in kilogram/height in meter square) (Speroff et al., 2005).

The ***World Health Organization (WHO)*** (World Health Organization, 2008) states that obesity is defined as a body mass index (BMI) above 30.0, and abdominal obesity is defined as a waist–hip ratio above 0.90 for males and above 0.85 for females.

2.5. Laboratory investigations

- Fasting and 2-h postprandial plasma glucose by end point colorimetric assay.
- HbA1c (%) measured using high performance liquid chromatography (HPLC).
- Lipid profile [triglycerides (TG), total cholesterol (TC), Low density lipoprotein cholesterol (LDL-C), and high density lipoprotein cholesterol (HDL-C)] measured using enzymatic hydrolysis and oxidation.
- Fasting serum insulin [by ELISA] to obtain homeostatic model assessment ($HOMA_2$) indices:

Insulin resistance ($HOMA_2$ - IR) Insulin sensitivity ($HOMA_2$ - %S) Beta-cell function ($HOMA_2$ - %β).

By the computer program HOMA Calculator v2.2.3 ***(University of Oxford, 2013).***

2.6. Methodology

- ***The first sample*** (8 h overnight fast) was used for measurement of fasting plasma glucose, fasting insulin, and HbA1c.
- ***The second sample*** (12 h fasting) was used for measurement of lipid profile. It was frozen at −20 C until assayed.

2.6.1. Principle of laboratory tests

2.6.1.1. Blood glucose. Glucose is oxidized by glucose oxidase into glucuronic acid and hydrogen peroxide, which, in the presence of peroxidase, reacts with 4-aminoantipyrine and phenol, forming red quinone compounds, the color intensity of which is proportional to the mount of glucose present in the sample (Trinder, 1969).

2.6.1.2. HbA1c. A venous whole blood specimen collected in EDTA was required. After centrifugation, the supernatant is injected into the HPLC system. The gradient separation via HPLC at 30 °C lasts 5 min. The chromatograms are recorded by an UV-detector. The quantification is performed with the delivered blood calibrator; the concentration is calculated via integration of peak heights respectively.

2.6.1.3. Serum lipid profile. Cholesterol esters are hydrolyzed, in the presence of cholesterol esterase (CHE), to cholesterol and fatty acid, total cholesterol is oxidized by cholesterol oxidase (CHOD) into 4-cholestan-3-one and hydrogen peroxide which, in the presence of peroxidase (POD), reacts with 4-aminoantipyrine (AT) and sodium 4-hydroxybenzoate, forming a red quinone derivative.The color intensity of this compound is proportional to the amount of total cholesterol present in the sample. LDL-C was calculated via the famous Friedewald equation:

$$LDL - C = \text{Total cholesterol} - HDL - C - (TG/5) \text{ in mg/dl.}$$

Triglycerides are hemolyzed by lipoprotein lipase (LPL) to glycerol. Glycerol is then phosphorylated to glycerol-3-phosphate by ATP in a reaction catalyzed by glycerol kinase. The oxidation of glycerol-3-phosphate is catalyzed by glycerol phosphate oxidase to form dihydroxyacetone phosphate and hydrogen peroxide (H_2O_2). In the presence of peroxidase, hydrogen peroxide affects the oxidative coupling of 4-chlorophenol and 4-aminoantipyrine to form a red color quinoneimine dye which is measured at 546 nm.

2.6.1.4. Fasting insulin. Insulin ELISA is a two-site enzyme immunoassay utilizing the direct sandwich technique with two monoclonal antibodies directed against separate antigenic determinants of the insulin molecule. Specimen, control, or the standard is pipetted into the sample well, then followed by the addition of peroxidase-conjugated anti-insulin antibodies. Insulin present in the sample will bind to anti-insulin antibodies bound to the sample well, while the peroxidase-conjugated anti-insulin antibodies will also bind to the insulin at the same time. After washing to remove unbound enzyme-labelled antibodies, 3, 3′, 5, 5′-Tetramethylbenzidine (TMB)-labelled substrate is added and binds to the conjugated antibodies. Acid is added to the sample well to stop the reaction, and the colorimetric endpoint is read on a microplate spectrophotometer set to the appropriate light wavelength.

2.6.1.5. Management of diabetes during the study. Both GG and PG participants were given the same prescribed diet with appropriate changes to make the protein, fat and carbohydrate ratio ideal (20: 20: 60). Each patient was provided with a diet chart, food exchange list. By learning the use of these food exchanges, patients could make the diet flexible to match their taste and keep their caloric needs constant.

All subjects were counseled about exercise programs to include:

- At least 150 min per week moderate-intensity aerobic activity, spread over at least 3 days per week with no more than 2 consecutive days without exercise.
- Reduce sedentary time = break up more 90 min spent sitting.

2.7. Metformin

Metformin is the preferred initial pharmacological agent for type 2 diabetes. Therefore, metformin was given as the initial pharmacological agent to all participants in both groups in addition to lifestyle changes (diet counseling, weight-loss education, and exercise) in the form of 500 mg tablets (available at NIDE outpatient clinic pharmacy) given twice daily after meals.

Table 1
The baseline characteristics, anthropometric & laboratory data of study participants.

	Groups at baseline			
	Ginger Group (n = 40)	Placebo Group (n = 40)	*t*-test	
	Mean ± SD	Mean ± SD	t	P-value
Sex (Male/Female)	19/21[a]	22/18[a]	0.450[b]	0.502
Age (years)	46.35 ± 9.53	46.10 ± 8.66	0.123	0.903
Systolic blood pressure (mmHg)	111.90 ± 3.73	111.73 ± 3.76	0.203	0.839
Diastolic blood pressure (mmHg)	71.03 ± 3.99	70.53 ± 4.40	0.532	0.596
WHR	1.09 ± 0.14	1.07 ± 0.12	0.855	0.395
BMI (kg/m2)	32.35 ± 1.51	32.28 ± 1.39	0.216	0.829
FBG (mg/dl)	172.03 ± 17.90	181.63 ± 18.80	2.339	0.022*
PPBG (mg/dl)	320.33 ± 35.82	284.43 ± 38.53	4.316	< 0.001**
HbA_{1c} (%)	8.05 ± 0.46	8.03 ± 0.54	0.245	0.807
TC (mg/dl)	268.40 ± 6.06	215.28 ± 26.41	12.400	< 0.001**
HDL-C (mg/dl)	39.80 ± 4.33	43.85 ± 7.32	3.0118	0.0035*
LDL-C (mg/dl)	164.53 ± 7.78	129.65 ± 17.92	11.295	< 0.001**
TG (mg/dl)	320.35 ± 13.14	206.90 ± 86.45	8.206	< 0.001**
Fasting serum Insulin (mIU/L)	20.74 ± 4.14	17.88 ± 2.50	3.741	< 0.001**
$HOMA_2$-%β	56.72 ± 1.93	46.45 ± 3.53	16.167	< 0.001**
$HOMA_2$-%S	34.39 ± 7.58	38.45 ± 6.39	2.587	0.012*
$HOMA_2$-IR	3.04 ± 0.65	2.67 ± 0.42	3.074	0.003*

[a] Number of males to females instead of Mean ± SD.
[b] Chi-square (X^2)-test instead of *t*-test. Non-significant > 0.05, Significant < 0.05*, highly significant < 0.001**.

Table 2
Anthropometric & laboratory data of study participants at the end of the study.

	Groups at end			
	Ginger Group (n = 40)	Placebo Group (n = 40)	*t*-test	
	Mean ± SD	Mean ± SD	t	P-value
BMI (kg/m2)	31.81 ± 1.21	32.31 ± 1.39	1.714	0.090
FBG (mg/dl)	120.88 ± 9.06	151.70 ± 13.23	12.156	< 0.001**
PPBG (mg/dl)	210.73 ± 21.72	206.68 ± 29.16	0.705	0.483
HbA_{1c} (%)	6.94 ± 0.38	7.26 ± 0.45	3.429	< 0.001**
TC (mg/dl)	237.30 ± 10.63	205.40 ± 19.52	9.076	< 0.001**
HDL-C (mg/dl)	42.05 ± 3.25	44.25 ± 7.34	1.7333	0.0870
LDL-C (mg/dl)	146.83 ± 9.81	129.28 ± 12.10	7.128	< 0.001**
TG (mg/dl)	242.10 ± 20.22	161.38 ± 77.27	6.392	< 0.001**
Fasting serum Insulin (mIU/L)	12.86 ± 2.59	13.21 ± 2.08	0.667	0.507
$HOMA_2$-%β	75.45 ± 2.32	50.64 ± 2.58	45.223	< 0.001**
$HOMA_2$-%S	59.11 ± 14.11	53.89 ± 10.03	1.909	0.060
$HOMA_2$-IR	1.78 ± 0.38	1.91 ± 0.33	1.733	0.087

3. Results

(see Tables 1–5, Fig. 1)

4. Discussion

Obesity is a pro-atherogenic condition that predisposes to cardiovascular disease (CVD) via its major associated risk factors such as; dyslipidemia, chronic low grade inflammation, insulin resistance, and type 2 diabetes mellitus. (Tzotzas et al., 2011).

This randomized, single blind, placebo-controlled study was

Table 3
Anthropometric & laboratory data of study participants at the baseline and at the end of the study in Ginger Group.

	Ginger Group			
	Baseline	End	Paired *t*-test	
	Mean ± SD	Mean ± SD	t	P-value
BMI (kg/m2)	32.35 ± 1.51	31.81 ± 1.21	7.918	< 0.001**
FBG (mg/dl)	172.03 ± 17.90	120.88 ± 9.06	35.910	< 0.001**
PPBG (mg/dl)	320.33 ± 35.82	210.73 ± 21.72	47.233	< 0.001**
HbA_{1c} (%)	8.05 ± 0.46	6.94 ± 0.38	57.511	< 0.001**
TC (mg/dl)	268.40 ± 6.06	237.30 ± 10.63	40.595	< 0.001**
HDL-C (mg/dl)	39.80 ± 4.33	42.05 ± 3.25	11.332	< 0.001**
LDL-C (mg/dl)	164.53 ± 7.78	146.83 ± 9.81	39.337	< 0.001**
TG (mg/dl)	320.35 ± 13.14	242.10 ± 20.22	67.387	< 0.001**
Fasting serum Insulin (mIU/L)	20.74 ± 4.14	12.86 ± 2.59	29.317	< 0.001**
$HOMA_2$-%β	56.72 ± 1.93	75.45 ± 2.32	34.632	< 0.001**
$HOMA_2$-%S	34.39 ± 7.58	59.11 ± 14.11	23.083	< 0.001**
$HOMA_2$-IR	3.04 ± 0.65	1.78 ± 0.38	27.620	< 0.001**

Table 4
Anthropometric & laboratory data of study participants at the baseline and at the end of the study in the Placebo Group.

	Placebo Group			
	Baseline	End	Paired *t*-test	
	Mean ± SD	Mean ± SD	t	P-value
BMI (kg/m2)	32.28 ± 1.39	32.31 ± 1.39	0.774	0.444
FBG (mg/dl)	181.63 ± 18.80	151.70 ± 13.23	31.446	< 0.001**
PPBG (mg/dl)	284.43 ± 38.53	206.68 ± 29.16	41.680	< 0.001**
HbA_{1c} (%)	8.03 ± 0.54	7.26 ± 0.45	38.885	< 0.001**
TC (mg/dl)	215.28 ± 26.41	205.40 ± 19.52	8.248	< 0.001**
HDL-C (mg/dl)	43.85 ± 7.32	44.25 ± 7.34	2.082	0.044*
LDL-C (mg/dl)	129.65 ± 17.92	129.28 ± 12.10	0.248	0.805
TG (mg/dl)	206.90 ± 86.45	161.38 ± 77.27	10.392	< 0.001**
Fasting serum Insulin (mIU/L)	17.88 ± 2.50	13.21 ± 2.08	52.421	< 0.001**
$HOMA_2$-%β	46.45 ± 3.53	50.64 ± 2.58	15.705	< 0.001**
$HOMA_2$-%S	38.45 ± 6.39	53.89 ± 10.03	25.363	< 0.001**
$HOMA_2$-IR	2.67 ± 0.42	1.91 ± 0.33	43.386	< 0.001**

Table 5
Mean change in various parameters in both groups.

	Mean change from baseline			
	Ginger Group	Placebo Group	*t*-test	
	Mean ± SD	Mean ± SD	t	P-value
BMI (kg/m2)	−0.54 ± 0.43	−0.03 ± 0.25	7.266	< 0.001**
FBG (mg/dl)	−51.15 ± 9.01	−29.93 ± 6.02	12.390	< 0.001**
PPBG (mg/dl)	−109.60 ± 14.68	−77.75 ± 10.10	11.306	< 0.001**
HbA_{1c} (%)	−1.11 ± 0.12	−0.77 ± 0.12	12.483	< 0.001**
TC (mg/dl)	−31.10 ± 4.85	−9.88 ± 7.57	14.932	< 0.001**
HDL-C (mg/dl)	2.25 ± 1.26	0.40 ± 1.22	6.6713	< 0.001**
LDL-C (mg/dl)	−17.70 ± 2.85	−0.37 ± 9.42	11.138	< 0.001**
TG (mg/dl)	−78.25 ± 7.34	−45.53 ± 27.71	7.221	< 0.001**
Fasting serum Insulin (mIU/L)	−7.88 ± 1.70	−4.67 ± 0.56	11.346	< 0.001**
$HOMA_2$-%β	18.73 ± 3.42	4.19 ± 1.69	24.105	< 0.001**
$HOMA_2$-%S	24.72 ± 6.77	15.44 ± 3.85	7.534	< 0.001**
$HOMA_2$-IR	−1.27 ± 0.29	−0.75 ± 0.11	10.427	< 0.001**

designed to determine whether 8-week ginger supplementation could influence glycemic status, lipid profile, and insulin level. It was conducted on 80 obese patients, newly diagnosed with T2DM. Participants allocated randomly using computer selection according to their electronic numbers into two groups; **Group 1:** Ginger Group (GG) included 40 patients who consumed one 600 mg powdered rhizome of ginger capsule before each meal (total daily dose was 1.8 g), and **Group 2:** Placebo Group (PG) included 40 patients who consumed wheat flour capsules of the same color, size, and number as those of ginger capsules. Metformin therapy of 500 mg twice daily was prescribed for both groups as well as life style modification as recommended by ADA 2017 guidelines (American Diabetes Association, 2016).

Regarding glycemic indices, our results found a highly significant statistical difference ($P < 0.001$) between the mean change (reduction) from the baseline of fasting blood glucose in GG -51.15 ± 9.01 mg/dl and in PG -29.93 ± 6.02 mg/dl, which indicates that ginger powder supplementation for 8 weeks significantly reduced FBG in newly diagnosed T2DM in obese patients compared with placebo. Our results also found a highly significant statistical difference ($P < 0.001$) between the mean change (reduction) of 2-h postprandial blood glucose in GG -109.60 ± 14.68 mg/dl and in PG -77.75 ± 10.10 mg/dl, which indicates that ginger powder supplementation for 8 weeks significantly reduced PPBG compared with placebo. We also found a highly significant statistical difference ($P < 0.001$) between the mean change (reduction) of HbA1c in GG -1.11 ± 0.12% and in PG -0.77 ± 0.12%, which indicates that ginger powder supplementation significantly reduced HbA1c compared with placebo.

Our findings are partly supported by Andallu and his colleagues (Andallu et al., 2003) which found that the mean glucose level in the blood was reduced significantly in T2DM men following the administration of 3 g of ginger per day for 30 days. It has been also found that consumption of 1.6 g & 2 g (Khandouzi et al., 2015) of ginger per day for 12 weeks reduced FBG and HbA1c in T2DM patients.

Another study found that consumption of 3 g of ginger per day for 8 weeks significantly decreased FBG and HbA1c in T2DM patients (Mozaffari-Khosravi et al., 2014). Also, Shidfar et al. (2015) found that 3 g/day of ginger supplementation for 3 months significantly decreased blood glucose and HbA1c in T2DM patients. Ginger was also found to decrease FBG up to 20% in patients undergoing continuous ambulatory peritoneal dialysis (CAPD), a reduction that was significant in comparison with placebo. More recently, another clinical trial showed that daily consumption of 2 g of ginger reduced FBG and HbA1c in T2DM patients (Shidfar et al., 2015).

On the other hand, Mahluji et al. (2013) found that taking 2 g of ginger per day for 2 months has no significant effect on FBG and HbA1c in T2DM patients. Another team of researchers showed that daily administration of 2 g of ginger powder for 12 weeks in obese women had no significant effect on FBG, versus placebo (Attari et al., 2016). Furthermore, it has been reported in patients with coronary artery disease that 4 g of ginger powder for 3 months had no effect on the level of blood glucose.

We couldn't compare our results about PPBG, as to our knowledge, our study is the first study to investigate the ginger effect on PPBG in T2DM.

Many researchers speculate that the hypoglycemic and other pharmacological activities of ginger is due to its phenols, polyphenols and flavonoids. It seems that ginger decreases blood glucose by antagonistic activity against serotonin receptors and its blockage. Also ginger may inhibit the intestinal glucosidase and amylase enzymes activity and thereby reduce absorption of glucose. One of the possible effects of ginger hydro-alcoholic extract is inhibition of the hepatic glycogen phosphorylase enzyme to prevent glycogen breakdown in liver and also inhibition of hepatic glucose phosphatase enzyme. On the other hand, it increases the activity of enzymes involved in glycogen synthesis (Shanmugam et al., 2011).

Regarding lipid profile, our results found a highly significant statistical difference ($P < 0.001$) between the mean change (reduction) from the baseline of TC in GG - 31.10 ± 4.85 mg/dl (11.6%) & in PG -9.88 ± 7.57 mg/dl (4.6%), which indicates that ginger powder

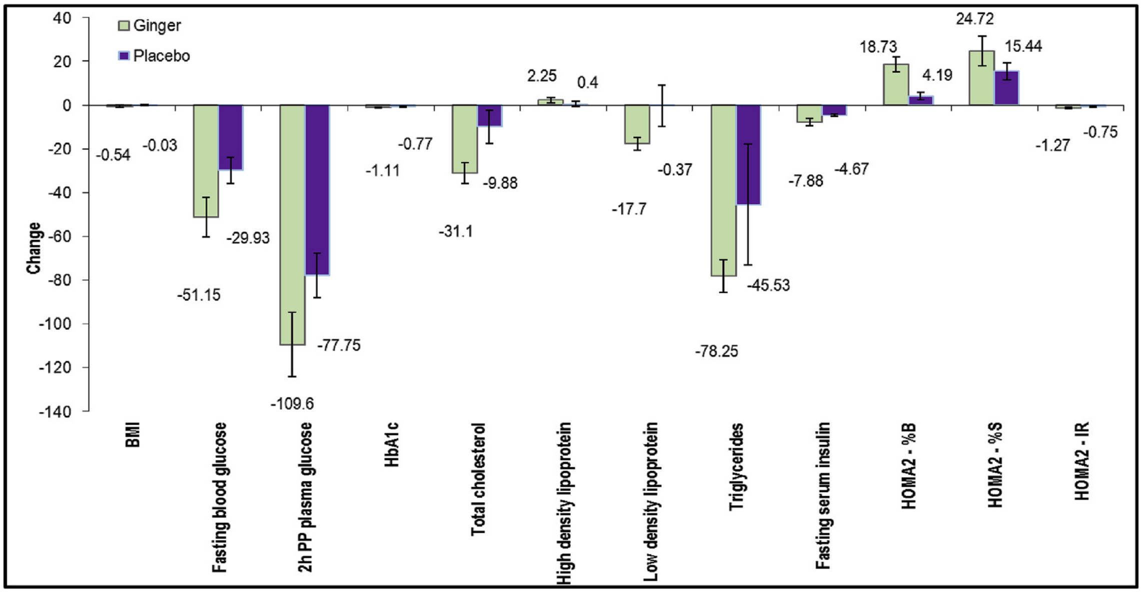

Fig. 1. Comparison between both groups regarding the mean changes from baselines.

supplementation for 8 weeks significantly reduced TC in newly diagnosed T2DM in obese patients compared to placebo. We also found a highly significant statistical difference ($P < 0.001$) between the mean change (reduction) from the baseline of LDL-C in GG -17.70 ± 2.85 mg/dl (10.8%) & in PG -0.37 ± 9.42 mg/dl, which indicates that ginger powder supplementation for 8 weeks significantly reduced LDL-C compared with placebo. Our study also revealed a highly significant statistical difference ($P < 0.001$) between the mean change (reduction) from the baseline of TG in GG - 78.25 ± 7.34 mg/dl (24.4%) & in PG -45.53 ± 27.71 mg/dl (22%), which indicates that ginger powder supplementation for 8 weeks significantly reduced TG compared with placebo. There was also a highly significant statistical difference ($P < 0.001$) between the mean change from the baseline of HDL-C in GG 2.25 ± 1.26 mg/dl & in PG 0.40 ± 1.22 mg/dl, which indicates that ginger powder supplementation for 8 weeks significantly increased HDL-C compared with placebo.

Our results are in agreement with a previous study where the administration of 3 g of ginger per day for 30 days significantly reduced TC, TG, LDL-C, and significantly increased HDL-C in T2DM men. Our findings are also supported by another study which also showed that the administration of 3 g of ginger per day in hyperlipidemic non diabetic patients for 45 days significantly reduced TC, TG and significantly increased HDL-C while reduced LDL-C but not with a statistical significance (Alizadeh-Navaei et al., 2008).

Our results are inconsistent with Atashak et al. which found that consumption of 1 g of ginger per day for 10 weeks had no significant effect on TC, TG, LDL-C, and HDL-C in obese men (Atashak et al., 2011). More recently, another study found that supplementation with 3 g of ginger per day for 6 weeks also had no significant effect on TC, TG, LDL-C, and HDL-C in obese women with breast neoplasms (Karimi et al., 2015).

Other studies had more conflicting but partly supporting results. Mahluji et al. (2013) found that receiving 2 g of ginger per day for 2 months significantly reduced TG, and LDL-C but had no significant effect on TC, and HDL-C in T2DM patients. However, Arablou et al. (2014)found that consumption of 1.6 g of ginger per day for 12 weeks significantly reduced TC, and TG but had no significant effect on LDL-C, and HDL-C in T2DM patients. Furthermore, a couple of studies reported that ginger supplementation significantly reduced TG only but had no significant effect on TC, LDL-C, and HDL-C (Attari et al., 2016).

Ginger extract consumption can result in accumulation of active ingredients within the cells, as well as in the cell plasma membrane, thus affecting cellular enzymes, and plasma membrane receptors. It has been shown that ginger extract consumption reduces the cellular uptake of oxidized LDL, possibly due to the steric modification of plasma lipoprotein receptors (modification of the spatial relationships of atoms in plasma lipoprotein receptor molecules) (Fuhrman et al., 2000).

The hypotriglyceridemic effect of ginger may be due to increasing lipoprotein lipase enzyme activity and therefore hydrolysis of circulatory TG and decreasing serum TG. Ginger also reduces the Carbohydrate-responsive element-binding protein (ChREBP) gene expression in the liver. ChREBP, a transcriptional regulator of lipid and glucose metabolism, mediates activation of several regulatory enzymes of glycolysis and lipogenesis. Reduced ChREBP expression, decreases the expression of ACC1 [a subunit of acetyl-CoA carboxylase (ACC)], fatty acid synthase, Stearoyl-CoA desaturase-1 (SCD1), and glucose-6-phosphatase, glucogenic and lipogenic proteins and decreases fat accumulation in the liver, reduces serum TG and improves insulin resistance. Ginger can increase hepatic cholesterol 7a-hydroxylase enzyme activity and the conversion of cholesterol into bile acids, resulting in reduced serum cholesterol concentration. Also there are observations that the compounds in ginger inhibit the biosynthesis of cholesterol in the liver of rats. In addition to the effect of ginger on increasing bile secretion, increased fecal excretion of cholesterol and phospholipids by ginger can also reduce cholesterol levels (Gao et al., 2012).

Insulin resistance, as a common metabolic abnormality in type 2 diabetes, is an underlying trait for many cardiovascular and metabolic disorders such as hypertension and dyslipidemia provoking a widespread interest in developing new insulin sensitization agents. In the present study, $HOMA_2$ indices were determined as the predictors of beta cell function ($HOMA_2$-%β), insulin sensitivity ($HOMA_2$-%S), and insulin resistance ($HOMA_2$-IR).

Regarding Insulin level and $HOMA_2$ indices: our results showed a highly significant statistical difference ($P < 0.001$) between the mean change (reduction) from the baseline of fasting insulin level in GG -7.88 ± 1.70 mIU/L & in PG -4.67 ± 0.56 mIU/L, which indicates that ginger powder supplementation for 8 weeks significantly reduced fasting insulin level compared with placebo. Our results also showed a highly significant statistical difference ($P < 0.001$) between the mean changes (increase) from the baseline of $HOMA_2$-%β in GG 18.73 ± 3.42 & in PG 4.19 ± 1.69, which indicates that ginger supplementation significantly increased $HOMA_2$-%β compared with placebo. Our study also found a highly significant statistical difference ($P < 0.001$) between the mean change (increase) from the baseline of

$HOMA_2$-%S in GG 24.72 ± 6.77 & in PG 15.44 ± 3.85, which indicates that ginger supplementation significantly increased $HOMA_2$-%S compared with placebo. Our results also showed a highly significant statistical difference ($P < 0.001$) between the mean change (reduction) from the baseline of $HOMA_2$-IR in GG -1.27 ± 0.29 & in PG -0.75 ± 0.11, which indicates that ginger supplementation significantly reduced $HOMA_2$-IR compared with placebo.

Our results are in agreement with some previous studies. Mahluji et al. (2013) found that receiving 2 g of ginger per day for 2 months significantly reduced fasting plasma insulin levels and HOMA-IR in T2DM. Arablou et al. (2014) found that consumption of 1.6 g of ginger per day for 12 weeks significantly reduced insulin resistance determined by HOMA-IR, and insulin sensitivity determined using quantitative insulin-sensitivity check index (QUICKI) in T2DM patients. Shidfar et al. (2015) also found that 3 g/day of ginger supplementation for 3 months induced a statistically significant reduction in insulin level and insulin resistance in T2DM patients. Attari et al. (2016) also found that consumption of 2 g of ginger for 12 weeks in obese women induced a significant reduction in serum insulin and HOMA-IR index along with significant increase in QUICKI in ginger compared to placebo.

However, a contrary to our results, ginger consumption (1 g/day) for 10 weeks did not cause any significant change in fasting serum insulin and HOMA-IR in obese men. Furthermore, Karimi et al. (2015) found that supplementation with 3 g of ginger for 6 weeks in obese women with breast neoplasms had no significant effect neither on inulin level nor insulin resistance. Although, Mozaffari-Khosravi et al. (2014) found that consumption of 3 g of ginger per day for 8 weeks in T2DM patients had no significant effect neither on fasting insulin level nor HOMA indices but significantly increased QUICKI and concluded that ginger is effective in lowering insulin resistance. The fact that all the indices did not come to the same consequences may be due to the disparity in sensitivity or properties of these indices or due to other causes.

There are some evidence that one potential factor in the etiology of IR is limited cellular antioxidant defenses against oxidative stress. Many studies have shown that treatment with antioxidants improves glucose transport and tolerance in type 2 diabetic patients and animals with IR. Ginger contains lots of antioxidants including gingerols, shogaols, paradols and zingerones. It is possible that they act by increasing the GLUT4 protein, insulin receptors and improving β-cells function It seems that ginger's effect on insulin sensitivity is through the activation of PPARγ or up regulation of adiponectin. Isa et al. (2008) stated that the 6- gingerol and 6-shogaol in ginger, up regulate adiponectin and 6-shogaol has agonistic activity with PPARγ.

Regarding BMI, the results of our study showed that consumption of ginger powder for 8 weeks resulted in a highly significant statistical reduction in BMI(mean change in GG vs PG -0.54 ± 0.43 vs −0.03 ± 0.25 respectively, $P < 0.001$).

Our finding is in agreement with Attari et al. (2016) who also found that consumption of 2 g of ginger for 12 weeks resulted in a slight, but statistically significant decrease in BMI in obese women.

Our finding is inconsistent with some other studies where no significant effect on BMI was observed after consumption of ginger: 1 g/day for 10 weeks in obese men; 2 g/day for 2 months in T2DM patients (Mahluji et al., 2013); 1.6 g/day for 12 weeks in T2DM patients; and 3 g/day for 8 weeks in T2DM patients (Mozaffari-Khosravi et al., 2014).

Such disparity in results, is attributed to the fact that the present study is the first study to investigate the effects of ginger powder supplementation in obese patients with new-onset T2DM, and explained by a Danish clinical cohort study (combined with self-reported past weight history) on 588 patients newly diagnosed with T2DM which found that patients generally follow a course of declining average weight average 5.7 years after the diagnosis of T2DM, and these weight developments are related primarily to recent weight changes Each kg of weight gain during the year preceding the diagnosis was associated with a weight loss of 0.2 kg during the follow up period (de Fine Olivarius et al., 2015).

Animal studies also had contradictions. Ginger aqueous extracts significantly decreased body weight, body fat mass and serum leptin levels in obese diabetic rats compared to the control group. In contrast, Wadikar and Premavalli showed that, ginger juice significantly increased weight gain and decreased leptin levels in rats. However, other researchers demonstrated that rodents treated with a high-fat diet (HFD) containing 6-gingerol had significant lower weight gain, fat accumulation, and circulating level of leptin, compared to HFD control (Saravanan et al., 2014).

As there are very limited clinical studies in this regard, it is difficult to compare our results. Overall, it seems that ginger could influence body weight and body composition through some mechanisms such as (Mahluji et al., 2013) increasing thermogenesis and energy expenditure by catecholamine-releasing action (Bhandari and Pillai, 2005); increasing the lipolysis of white adipose tissue; and (Shirdel et al., 2009) inhibition of the lipase enzyme and the intestinal absorption of dietary fat (Pulbutr et al., 2011).

To our knowledge, our present study is one of the few studies to investigate the effects of ginger powder supplementation to newly diagnosed obese T2DM patients. The inconsistency with some experimental studies may be attributable to (Mahluji et al., 2013) the disparity of subjects across those studies as regards type & duration of diabetes, existence of obesity, baseline HbA1c, and the severity of insulin resistance (Bhandari and Pillai, 2005); the disparity in pharmacological form, chemical composition, and the preparation method of administered ginger extract; rhizome used, and storage time (Henriksen, 2006).

Overall, the reexamination of the previous studies indicated that research to date as to the impact of ginger powder on sugar indices of diabetic patients has been very constrained. Moreover, the results of the researches conducted on human and animals have turned out to be contradictory. This contradiction may be the consequence of the disparity in participants response. And this disparity in response can be the sequel of the patients' difference at the onset of research, experimental group weight, the severity of insulin resistance and other measured indices at the beginning of the study. The high percentage of the patient's compliance in consuming capsules can be regarded as a strong point of the study.

5. Conclusion

Ginger significantly reduced BMI, FBG, PPBG, HbA_{1c}, TC, LDL-C, TG, fasting insulin level, and HOMA2-IR. Ginger also significantly increased HDL-C, HOMA2-%β, and HOMA2-%S. Ginger is considered a safe and effective adjuvant antidiabetic agent; and has beneficial effects on lipid profile, insulin resistance, and promoting weight loss.

Conflict of ineterests

I declare there is no conflict of ineterests.

Funding

No funding concerning this research.

Ethical approval

This research was approved by the ethical committee in ain shams university and informed consent was obtained from each patient.

References

Ali, B.H., Blunden, G., Tanira, M.O., Nemmar, A., 2008. Some phytochemical, pharmacological and toxicological properties of ginger (Zingiber officinale Roscoe): a review of recent research. Food Chem. Toxicol. Int. J. Publ. Br. Ind. Biol. Res. Assoc. 46,

409–420.
Alizadeh-Navaei, R., Roozbeh, F., Saravi, M., Pouramir, M., Jalali, F., Moghadamnia, A.A., 2008. Investigation of the effect of ginger on the lipid levels. A double blind controlled clinical trial. Saudi Med. J. 29 (9), 1280–1284.
American Diabetes Association, 2016. Classification and diagnosis of diabetes. Diabetes Care 39 (Suppl. 1) January 2016.
Andallu, B., Radhika, B., Suryakantham, V., 2003. Effect of aswagandha, ginger and mulberry on hyperglycemia and hyperlipidemia. Plant Foods Human Nutr. (Formerly Qualitas Plantarum) 58 (3), 1–7.
Arablou, T., Aryaeian, N., Valizadeh, M., Sharifi, F., Hosseini, A., Djalali, M., 2014. The effect of ginger consumption on glycemic status, lipid profile and some inflammatory markers in patients with type 2 diabetes mellitus. Int. J. Food Sci. Nutr. 65 (4), 515–520.
Atashak, S., Peeri, M., Azarbayjani, M.A., Stannard, S.R., Haghighi, M.M., 2011. Obesity-related cardiovascular risk factors after long-term resistance training and ginger supplementation. J. Sport. Sci. Med. 10 (4), 685.
Attari, V.E., Ostadrahimi, A., Jafarabadi, M.A., Mehralizadeh, S., Mahluji, S., 2016. Changes of serum adipocytokines and body weight following Zingiber officinale supplementation in obese women: a RCT. Eur. J. Nutr. 55 (6), 2129–2136.
Bhandari, U., Pillai, K.K., 2005. Effect of ethanolic extract of Zingiber officinale on dyslipidaemia in diabetic rats. J. Ethnopharmacol. 97 (2), 227–230.
de Fine Olivarius, N., Siersma, V.D., Køster-Rasmussen, R., Heitmann, B.L., Waldorff, F.B., 2015. Weight changes following the diagnosis of type 2 diabetes: the impact of recent and past weight history before diagnosis. Results from the Danish Diabetes Care in General Practice (DCGP) study. PLoS One 10 (4), e0122219.
Fuhrman, B., Rosenblat, M., Hayek, T., Coleman, R., Aviram, M., 2000. Ginger extract consumption reduces plasma cholesterol, inhibits LDL oxidation and attenuates development of atherosclerosis in atherosclerotic, apolipoprotein E-deficient mice. J. Nutr. 130 (5), 1124–1131.
Gao, H., Guan, T., Li, C., Zuo, G., Yamahara, J., Wang, J., Li, Y., 2012. Treatment with ginger ameliorates fructose-induced Fatty liver and hypertriglyceridemia in rats: modulation of the hepatic carbohydrate response element-binding protein-mediated pathway. Evid. Based Complement Altern. Med. 2012.
Henriksen, E.J., 2006. Exercise training and the antioxidant α-lipoic acid in the treatment of insulin resistance and type 2 diabetes. Free Radic. Biol. Med. 40 (1), 3–12.
Isa, Y., Miyakawa, Y., Yanagisawa, M., Goto, T., Kang, M.S., Kawada, T., Tsuda, T., 2008. 6-Shogaol and 6-gingerol, the pungent of ginger, inhibit TNF-α mediated down-regulation of adiponectin expression via different mechanisms in 3T3-L1 adipocytes. Biochem. Biophys. Res. Commun. 373 (3), 429–434.
Karimi, N., Roshan, V.D., Bayatiyani, Z.F., 2015. Individually and combined water-based exercise with ginger supplement, on systemic inflammation and metabolic syndrome indices, among the obese women with breast neoplasms. Iran. J. Cancer Prev. 8 (6).
Khandouzi, N., Shidfar, F., Rajab, A., Rahideh, T., Hosseini, P., Taheri, M.M., 2015. The effects of ginger on fasting blood sugar, hemoglobin A1c, apolipoprotein B, apolipoprotein AI and malondialdehyde in type 2 diabetic patients. Iran. J. Pharm. Res. (IJPR) IJPR 14 (1), 131.
Mahluji, S., Attari, V.E., Mobasseri, M., Payahoo, L., Ostadrahimi, A., Golzari, S.E., 2013. Effects of ginger (Zingiber officinale) on plasma glucose level, HbA1c and insulin sensitivity in type 2 diabetic patients. Int. J. Food Sci. Nutr. 64 (6), 682–686.
Mozaffari-Khosravi, H., Talaei, B., Jalali, B.A., Najarzadeh, A., Mozayan, M.R., 2014. The effect of ginger powder supplementation on insulin resistance and glycemic indices in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled trial. Complement. Ther. Med. 22 (1), 9–16.
Pulbutr, P., Thunchomnang, K., Lawa, K., 2011. Rats and high fat diet-fed rats. Int. J. Pharmacol. 7 (5), 629–634.
Saravanan, G., Ponmurugan, P., Deepa, M.A., Senthilkumar, B., 2014. Anti- obesity action of gingerol: effect on lipid profile, insulin, leptin, amylase and lipase in male obese rats induced by a high-fat diet. J. Sci. Food Agric. 94 (14), 2972–2977.
Shanmugam, K.R., Mallikarjuna, K., Kesireddy, N., Reddy, K.S., 2011. Neuroprotective effect of ginger on anti-oxidant enzymes in streptozotocin-induced diabetic rats. Food Chem. Toxicol. 49 (4), 893–897.
Shidfar, F., Rajab, A., Rahideh, T., Khandouzi, N., Hosseini, S., Shidfar, S., 2015. The effect of ginger (Zingiber officinale) on glycemic markers in patients with type 2 diabetes. J. Complement. Integr. Med. 12 (2), 165–170.
Shirdel, Z., Mirbadalzadeh, R., Madani, H., 2009. Anti diabetid and Anti lipidemic effect of Ginger in Alloxan Monohydrate diabetic rats in comparison with glibenclamide. Iran. J. Diabetes & Lipid Disord. 9 (1), 7–15.
Speroff, L., Glass, R.H., Kase, M.J., 2005. Ovulation and polycystic ovary syndrome. Clin. Gynecol. Endocrinol. Infertil. 7 (12), 287–520.
Trinder, P., 1969. Determination of glucose in blood using glucose oxidase with an alternative oxygen receptor. Ann. Clin. Biochem. 6, 24–27.
Tzotzas, T., Evangelou, P., Kiortsis, D.N., 2011. Obesity, weight loss and conditional cardiovascular risk factors. Obes. Rev. 12 (5).
World Health Organization, 2008. WHO STEPwise approach to surveillance (STEPS). In: Waist Circumference and Waist-Hip Ratio: Report of a WHO Expert Consultation, Geneva, 8-11 December 2008.