

The Effects of Coriander Seed Supplementation on Serum Glycemic Indices, Lipid Profile and Parameters of Oxidative Stress in Patients with Type 2 Diabetes Mellitus: A Randomized Double-Blind Placebo-Controlled Clinical Trial

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Research

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Abstract

Background: This research aimed to study the effect of coriander seed supplementation on serum glycemic indices, lipid profile and oxidative stress parameters in patients with type 2 diabetes mellitus (T2DM).

Methods: In this randomized double-blinded, placebo-controlled trial, eligible 40 T2DM patients aged 30-60 years were recruited from Sina Hospital (Tabriz, Iran) and randomly assigned into two groups to receive either coriander seed powder (1000 mg/day, n=20) or placebo (1000 mg/day, n=20) for 6 weeks. Anthropometric measurements, dietary intake, and biochemical parameters including fasting blood sugar (FBS), serum insulin, Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), total cholesterol (TC), triglyceride (TG), high- and low-density lipoprotein cholesterol (HDL-C and LDL-C), malondialdehyde (MDA), and total antioxidant capacity (TAC) were assessed before and after supplementation.

Results: Anthropometric measurements were not significantly different between intervention and placebo groups. Coriander seed supplementation led to significant within-group reductions in FBS (156.15 ± 23.19 to 130.30 ± 21.15), serum insulin (17.72 ± 0.47 to 17.12 ± 0.76), HOMA-IR (6.82 ± 0.95 to 5.52 ± 0.99), TC (183.85 ± 55.68 to 145.20 ± 31.36), TG (152.50 ± 37.59 to 130.40 ± 27.96), LDL-C (127.35 ± 23.45 to 111.40 ± 25.71), and MDA (1.65 ± 0.15 to 1.49 ± 0.15), whereas there were significant increases observed in serum TAC (1.93 ± 0.12 to 1.97 ± 0.09) ($P < 0.05$). Post-dose comparisons showed significant between-group differences for FBS, serum insulin, HOMA-IR, TC, TG, LDL-C, MDA, and TAC levels after adjusting for baseline values ($P < 0.05$).

Conclusions: Coriander seed supplementation was able to improve glycemic indices, lipid profile and oxidative stress status in T2DM and it may be useful complementary treatment in management of these patients.

Trial registration: The study protocol was registered on the Iranian Registry of Clinical Trials website (IRCT20190224042821N2) on 2019/Oct/11.

Background

Diabetes mellitus is a global health problem in the world. Type 2 diabetes mellitus (T2DM) is a metabolic disorder characterized by excessive glucose concentrations (hyperglycemia), increased insulin secretion, and insulin resistance [1–3]. The incidence rate of diabetes mellitus is growing fast in developing countries [5]. The T2DM is a leading cause of death among main 10 reasons of death worldwide [4]. The world prevalence of diabetes is high among populations aged 20–79 years old and estimated as 6.4% in 2010 [5]. The International Diabetes Association estimates that more than 382 million people worldwide have diabetes, predicted to rise to 592 million by 2035 [6].

Hyperglycemia, lipid profile abnormalities [6–8], impaired oxidant/antioxidant balance [9, 10], increased production of free radicals [11, 12], and impaired antioxidant defense system [13, 14] are among the main contributing factors in the etiology of diabetes and could potentially associate with diabetes-related complications. Oxidative stress is a prominent risk factor condition associated with the pathogenesis of T2DM [15]. Oxidative damages occur by the over-production of free radicals beyond the antioxidant capacities to impose cells with oxidative stress partly affects formation of lipid peroxidation products such as malondialdehyde (MDA) [17]. Several studies showed that MDA can potentially lead to the risk of insulin resistance and subsequently development of cardiovascular diseases [16]. Moreover, oxidative stress and insulin resistance are associated with increased concentrations of inflammatory biomarkers [17]. Therefore, controlling the oxidative stress might influence hyperlipidemia to better manage T2DM-related complications [17, 18].

The oral hypoglycemic agents could associate with various side effects, hence, adherence to these treatments is low; therefore, recently there is much attention paid to natural herbal remedies [20]. Herbal remedies can improve glycemic responses [19]. Coriander is one of the important herbs that has healing properties [20]. The main medicinal part of the plant is its fruit called coriander seed [22]. Coriander seeds are rich in bioactive compounds with strong antioxidant properties including flavonoids, polyphenols, carotenoids, steroids, tannins, limonene, linalool, α -pinen, β -caryophyllene, and γ -terpene [21]. The antioxidant properties of coriander seeds are mainly related to polyphenols and linalool (coriandol) [24]. Polyphenols can inhibit the oxidative stress by suppressing free radicals and coriandol by increasing the antioxidant defense system efficiency [22]. Recently, studies on animal models indicated beneficial effects of coriander seed on glycemic indices [23], lipid profile [22–25], and oxidative stress [25–27]. Only one clinical trial has been conducted on the effect of coriander seeds on type 2 diabetes [28]. Therefore, there is a limited number of studies regarding the effects of coriander seed on diabetes mellitus in human studies particularly no data exist to show its ameliorating effects on oxidative stress in T2DM patients, this clinical trial was planned to study the effects of coriander seed powder supplementation on serum glycemic indices, lipid profile and oxidative stress parameters in T2DM patients.

Methods

Subjects

This randomized double-blind placebo-controlled trial was conducted at Diabetes Clinic of Sina Hospital administered by Tabriz University of Medical Sciences, Tabriz, Iran.

Inclusion criteria were: age 30-60 years, having T2DM for more than 3 years and satisfaction with the project. The exclusion criteria were: smokers, pregnant women, breast-feeding, any thyroid, liver, digestive, kidney and immune system dysfunction, cardiovascular diseases, uncontrolled T2DM and/or insulin-dependent diabetic patients, using non-steroidal anti-inflammatory drugs, hormone therapy, and taking antioxidant supplements during the last three months before the study.

The study protocol was approved by the Ethics Committee of Tabriz University of Medical Sciences (no.IR.TBZMED.REC.1398.677) and registered on the Iranian Registry of Clinical Trials website (IRCT20190224042821N2). All subjects were fully explained before recruitment and a written informed consent was obtained from each subject prior to the study enrolment.

Sample size was calculated based on FBS results reported by Parsaian *et al.* [30]. Considering a confidence level of 95% and power of 80%, 18 subjects were calculated for each group taking into account the likelihood of a dropout (20%), 22 subjects in each group were recruited (total sample size: 44 T2DM patients).

Study design and measurements

Diabetic patients referred to the Sina Diabetes Clinic who had a medical record in this center and were eligible for inclusion were explained about the plan. Individuals who were willing to participate in the project were divided into case and placebo groups based on the numbers inserted on their case (couple and individual). Of the 44 patients who met the inclusion criteria, there was lost to follow-up (n=4) due to dissatisfaction (Figure 1). Finally, 20 controls and 20 cases in each group were completed the interventions to conduct statistical analysis. First coriander seeds were washed, dried at room temperature, and then powdered with an electric mill. Then coriander seed powder was packed in 500 mg gelatin capsules. Corn starch was used to prepare the placebo (500 mg). The capsules were prepared using capsule filler under the aseptic conditions and 70% ethanol sterilized tool to prevent secondary contamination. The quality of the capsules was checked and cleaned with sterile cotton. The intervention or placebo group allocation was hidden from the researchers, and the coriander seed and placebo capsules were similar in appearance. Therefore, neither the participants nor the researchers were aware of the therapeutic assignments in this study. Patients were asked not to change the number and dosage of their medication (metformin and glibenclamide) and their physical activity during the study period. They were asked to take the capsules twice daily (30 min before lunch and dinner) during six weeks. The capsule intake guidelines were assessed by telephone interview once a week. At the end of study (the 6th week), patients were undergone re-examination.

Anthropometric assessments

At the beginning of trial, demographic characteristics were obtained and International Physical Activity Questionnaire (IPAQ) was completed to assess patients' physical activity level [29]. Furthermore, anthropometric measurements were performed at the beginning and at the end of the trial. Body weight was measured to the nearest 0.5 kg using a Seca scale (Hamburg, Germany), with the patients being barefoot and wearing light clothing. Height was also measured using a mounted tape, with the participants' arms hanging freely by their sides and recorded to the nearest 0.5 cm. Body mass index (BMI) was calculated by dividing weight (in kilograms) by the square of height (in meters). Waist circumference (WC) was obtained using an inelastic tape measure to the nearest 1 mm. The mid-point

between the last rib and the iliac crest was recorded as WC. Hip circumference (HC) was measured at the widest point of the hip. The waist to hip ratio (WHR) was calculated.

Nutritional assessments

Information regarding dietary intake was gathered using a 24-hour recall method for 3 days (including 2 working days and 1 weekend) a week before and at the end of supplementation. Total energy, macronutrients, and antioxidant vitamins intake were determined with the Nutritionist IV software program (First Databank Inc, Hearst Corp, San Bruno, CA, USA).

Laboratory assessments

At the beginning and at the end of the trial period, 5 mL of blood samples were taken from each patient after 12-hour overnight fasting. All serum samples were stored at -70 ° C until assay. Fasting blood sugar (FBS), serum total cholesterol (TC), triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C) were measured using the standard enzymatic colorimetric method by Auto-analyzer Bio-systems (Autoanalyzer, BS-200, MINDRAY chemistry analyzer, Germany, 2009) and Pars-Azmoon Diagnostic Kits (Tehran, Iran). Friedewald's formula was used to calculate low density lipoprotein cholesterol (LDL-C) [30]. Serum insulin concentration was determined by ELISA kit (Diameter, Italy and Bioassay Technology Laboratory, China). To measure insulin resistance, we used homeostatic model assessment of insulin resistance (HOMA-IR) based on the following formula: $HOMA-IR = \text{fasting insulin } (\mu\text{U/mL}) \times \text{fasting glucose (mg/dL)} / 405$ [31]. Serum concentration of malondialdehyde (MDA) was determined via thiobarbituric acid reactive substances (TBARS) method described by Bilici *et al.* [32]. Total antioxidant capacity (TAC) was measured using spectrophotometry method with a Randox kit (Randox Laboratories, Ltd., UK).

Statistical analysis

Data were analyzed by SPSS software version 21.0 (SPSS, Inc, Chicago, IL, USA). Kolmogorov-Smirnov test was used to check the normality of the data. Quantitative and qualitative data were reported as mean \pm standard deviation and frequency (percentage), respectively. Differences between variables before and after study were compared by paired t-test. Comparisons between groups were made by chi-squared test, independent sample t-test or Mann-Whitney U test, as appropriate. Analysis of covariance (ANCOVA) was used to find any differences between the two groups at the end of the study, adjusting for baseline values. P-value less than 0.05 was considered statistically significant.

Results

Forty patients with T2DM completed this clinical trial (20 patients in each coriander seed and placebo groups as described in Fig. 1). No adverse events were reported in patients supplemented with coriander seed and/or placebo. General characteristics, medication intake and physical activity level of study patients are shown in Table 1. The variables been normalized before the analyses. At baseline, there was no significant difference between the two groups in terms of general characteristics, medication intake and physical activity level (Table 1).

Table 1
General characteristics, medication intake and physical activity level of the study participants

Variable	Placebo group (n = 20)	Coriander seed group (n = 20)	p*
Age (year)	47.60 ± 8.7	50.00 ± 7.48	0.329
Diabetes duration (year)	3.38(2.29)	3.64(1.57)	0.432
Sex	9 (45)	10 (50)	0.752
Male	11 (55)	10 (50)	
Female			
Education	6 (30)	5 (25)	1.000
Primary	4 (20)	3 (15)	
Under diploma	9 (45)	10 (50)	
Diploma	1 (5)	2 (25)	
Higher education			
Physical activity level	13 (48.1)	14 (51.9)	0.255
Low	7 (53.8)	6 (46.2)	
Moderate	0 (0.0)	0 (0.0)	
High			
Glibenclamide(5mg)	11 (55)	12 (60)	0.749
Not used	9 (45)	8 (40)	
Using ≥ 1/day			
Metformin (500mg)	13 (65)	11 (55)	0.519
1 tablet/day	7 (35)	9 (45)	
2–3 tablet/day			
Data were expressed as mean ± SD for quantitative variables, or number (percent) for categorical variables.			
P < 0.05 was considered significant.			
* P values indicate comparison between groups (Chi-squared test, Independent sample t-test, or Mann-Whitney U test, as appropriate).			

Anthropometric measurements and dietary intake analysis of patients throughout the study are shown in Table 2 and Table 3, respectively. At baseline, there was no significant difference between the two groups in anthropometric measurements and dietary intake (p > 0.05). Furthermore, no significant changes were

seen within and/or between coriander seed and placebo groups in anthropometric measurements and dietary intake after 6 weeks ($p > 0.05$).

Table 2
Anthropometric measurements of subjects at baseline and after 6 weeks

Variable		Placebo group (n = 20)	Coriander seed group (n = 20)	p*
Weight (Kg)	Baseline	74.05 ± 12.18	73.51 ± 12.35	0.888**
	After 6 weeks	74.05 ± 12.59	73.26 ± 12.56	0.636*
	MD (95% CI)	0.02(-0.52, 0.56)	-0.27(-1.16, 0.61)	
	P***	0.920	0.532	
BMI (Kg/m ²)	Baseline	31.25 ± 5.07	30.88 ± 5.17	0.797**
	After 6 weeks	31.26 ± 5.24	30.76 ± 5.25	0.628*
	MD (95% CI)	0.01(-0.22, 0.24)	-0.11(-0.52, 0.26)	
	P***	0.995	0.523	
WC (cm)	Baseline	97.20 ± 12.19	96.78 ± 11.22	0.897**
	After 6 weeks	97.01 ± 9.76	96.35 ± 10.68	0.855*
	MD (95% CI)	-0.19(-1.47, 1.07)	-0.43(-1.93, 1.07)	
	P***	0.760	0.560	
WHR	Baseline	0.90 ± 0.06	0.89 ± 0.06	0.778**
	After 6 weeks	0.90 ± 0.06	0.89 ± 0.06	0.848*
	MD (95% CI)	0.009(-0.001, 0.02)	-0.001(-0.02, 0.01)	
	P***	0.941	0.894	
MD: mean difference; CI: confidence interval; BMI: body mass index; WC: waist circumference; WHR: waist to hip ratio.				
Data were expressed as mean ± SD.				
P < 0.05 was considered significant.				
* P values indicate comparison between groups (and ANCOVA test, adjusted for baseline values, after 6 weeks).				
** P values indicate comparison between groups (independent sample t-test at baseline)				
*** P values indicate comparison within groups (paired t-test).				

Table 3
Dietary intake of subjects at baseline and after 6 weeks

Variable		Placebo group (n = 20)	Coriander seed group (n = 20)	p*
Energy (Kcal/d)	Baseline	1949.73 ± 68.39	1955.50 ± 96.14	0.820*
	After 6 weeks	1961.58 ± 90.02	1961.58 ± 90.02	0.531**
	MD (95% CI)	11.85(-24.83,48.53)	6.08(-36.65,48.81)	
	p***	0.818	0.553	
Carbohydrate (g/d)	Baseline	275.70 ± 17.78	277.50 ± 17.59	0.822*
	After 6 weeks	276.65 ± 19.38	276.40 ± 17.96	0.743**
	MD (95% CI)	0.95(-7.58,9.48)	-1.1(-9.26,7.06)	
	p***	0.490	0.753	
Protein (g)	Baseline	81.42 ± 11.31	78.35 ± 11.45	0.866*
	After 6 weeks	81.40 ± 9.32	78.00 ± 8.03	0.755**
	MD (95% CI)	-0.02(-4.77,4.73)	-0.35(-4.89,7.06)	
	p***	0.533	0.633	
Fat (g)	Baseline	63.91 ± 5.85	63.80 ± 6.35	0.326*
	After 6 weeks	63.12 ± 5.78	63.60 ± 6.36	0.755**
	MD (95% CI)	-0.79(-3.46,1.88)	-0.20(-3.12,2.72)	
	p***	0.125	0.855	

Data were expressed as mean ± SD.

P < 0.05 was considered significant.

* P values indicate comparison between groups (and ANCOVA test, adjusted for baseline values, after 6 weeks).

** P values indicate comparison between groups (independent sample t-test at baseline)

*** P values indicate comparison within groups (paired t-test).

Variable		Placebo group (n = 20)	Coriander seed group (n = 20)	p*
Vitamin E (mg/d)	Baseline	3.85 ± 1.81	3.60 ± 1.94	0.588*
	After 6 weeks	3.50 ± 2.1	3.80 ± 2.2	0.346**
	MD (95% CI)	-0.35(-1.25,0.55)	0.20(-0.75,1.15)	
	p***	0.685	0.786	
Vitamin C (mg/d)	Baseline	121.17 ± 68.45	113.67 ± 70.54	0.735*
	After 6 weeks	112.36 ± 65.00	119.13 ± 45.43	0.532**
	MD (95% CI)	-8.81(-39.44,21.82)	5.46(-21.76,32.68)	
	p***	0.402	0.943	
Data were expressed as mean ± SD.				
P < 0.05 was considered significant.				
* P values indicate comparison between groups (and ANCOVA test, adjusted for baseline values, after 6 weeks).				
** P values indicate comparison between groups (independent sample t-test at baseline)				
*** P values indicate comparison within groups (paired t-test).				

As illustrated in Table 4, there was no significant difference in serum glycemc indices, lipid profile and oxidative stress parameters between the two study groups at baseline ($p > 0.05$). Compared to baseline, FBS, serum insulin and HOMA-IR levels decreased significantly in the coriander seed group ($p < 0.001$, $p = 0.003$ and $p < 0.001$, respectively). Moreover, significant decrease in serum TC, TG, and LDL-C was observed in the coriander seed group ($p < 0.001$), whilst changes in serum HDL-C were not significant ($p = 0.428$). In addition, significant increase in serum TAC level and significant decrease in serum MDA level were observed in coriander seed group ($p < 0.001$). In the placebo group, except for serum TC level which had a statistically significant increase ($p = 0.042$), all other variables did not change significantly ($p > 0.05$) compared with baseline. At the end of the study, results of ANCOVA test showed statistically significant differences between the two studied groups in FBS ($p < 0.001$), serum insulin ($p = 0.001$), HOMA-IR ($p < 0.001$), TC ($p < 0.001$), TG ($p < 0.001$), LDL-C ($p < 0.001$), TAC ($p < 0.001$) and MDA ($p < 0.001$) levels, after adjusting for baseline values. Age, sex, drug use and physical activity were controlled for as confounding factors.

Table 4

Serum glycemetic indices, lipid profile and oxidative stress parameters of subjects at baseline and after 6 weeks

Variable		Placebo group (n = 20)	Coriander seed group (n = 20)	p*
FBS (mg/dl)	Baseline	161.15 ± 25.17	156.15 ± 23.19	0.517**
	After 6 weeks	160.85 ± 26.01	130.30 ± 21.15	< 0.001*
	MD (95% CI)	-0.30(-1.83, 1.23)	-25.85(-32.63,-19.07)	
	P***	0.685	< 0.001	
Insulin (µU/mL)	Baseline	17.80 ± 50	17.72 ± 0.47	0.628**
	After 6 weeks	17.92 ± 0.63	17.12 ± 0.76	0.001*
	MD (95% CI)	0.12(-0.27 ,0.52)	-0.60(-0.98,-0.22)	
	P***	0.514	0.003	
HOMA-IR	Baseline	7.08 ± 1.12	6.82 ± 0.95	0.436**
	After 6 weeks	7.13 ± 1.27	5.52 ± 0.99	< 0.001*
	MD (95% CI)	0.05(-0.10,0.20)	-1.30(-1.60,-1.01)	
	P***	0.514	< 0.001	
TC (mg/dl)	Baseline	155.73 ± 68.39	183.85 ± 55.68	0.162**
	After 6 weeks	161.58 ± 69.02	145.20 ± 31.36	< 0.001*
	MD (95% CI)	5.85(0.24,11.46)	-38.65(-58.35,-18.95)	
	P***	0.042	0.001	

MD: mean difference; CI: confidence interval; FBS: fasting blood sugar; HOMA-IR: homeostatic model assessment of insulin resistance; TC: total cholesterol; TG: triglyceride; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; TAC: Total antioxidant capacity; MDA: malondialdehyde.

Data were expressed as mean ± SD.

P < 0.05 was considered significant.

* P values indicate comparison between groups (and ANCOVA test, adjusted for baseline values, after 6 weeks).

** P values indicate comparison between groups (independent sample t-test at baseline)

*** P values indicate comparison within groups (paired t-test).

Variable		Placebo group (n = 20)	Coriander seed group (n = 20)	p*
TG (mg/dl)	Baseline	170.70 ± 77.78	152.50 ± 37.59	0.354**
	After 6 weeks	171.65 ± 79.38	130.40 ± 27.96	< 0.001*
	MD (95% CI)	0.95 (-4.13,6.03)	-22.10(-32.03,-12.17)	
	P***	0.700	< 0.001	
LDL-C (mg/dl)	Baseline	133.35 ± 21.31	127.35 ± 23.45	0.402**
	After 6 weeks	133.00 ± 21.03	111.40 ± 25.71	< 0.001*
	MD (95% CI)	-0.35(-1.38,0.68)	-15.95(-20.79,-11.11)	
	P***	0.487	< 0.001	
HDL-C (mg/dl)	Baseline	33.80 ± 6.35	33.21 ± 5.85	0.764**
	After 6 weeks	33.60 ± 6.36	33.12 ± 5.78	0.782*
	MD (95% CI)	-0.20(-0.56,0.16)	-0.10(-0.36,0.16)	
	P***	0.258	0.428	
TAC (mmol/L)	Baseline	1.88 ± 0.14	1.93 ± 0.12	0.210**
	After 6 weeks	1.88 ± 0.14	1.97 ± 0.09	< 0.001*
	MD (95% CI)	0.001(-0.003,0.004)	0.04 (0.02, 0.06)	
	P***	0.789	< 0.001	
MDA (nmol/mL)	Baseline	1.67 ± 0.14	1.65 ± 0.15	0.613**
	After 6 weeks	1.68 ± 0.14	1.49 ± 0.15	< 0.001*

MD: mean difference; CI: confidence interval; FBS: fasting blood sugar; HOMA-IR: homeostatic model assessment of insulin resistance; TC: total cholesterol; TG: triglyceride; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; TAC: Total antioxidant capacity; MDA: malondialdehyde.

Data were expressed as mean ± SD.

P < 0.05 was considered significant.

* P values indicate comparison between groups (and ANCOVA test, adjusted for baseline values, after 6 weeks).

** P values indicate comparison between groups (independent sample t-test at baseline)

*** P values indicate comparison within groups (paired t-test).

Variable	Placebo group (n = 20)	Coriander seed group (n = 20)	p*
MD (95% CI)	0.01(-0.01, 0.02)	-0.15(-0.22,-0.09)	
P***	0.213	< 0.001	
MD: mean difference; CI: confidence interval; FBS: fasting blood sugar; HOMA-IR: homeostatic model assessment of insulin resistance; TC: total cholesterol; TG: triglyceride; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; TAC: Total antioxidant capacity; MDA: malondialdehyde.			
Data were expressed as mean ± SD.			
P < 0.05 was considered significant.			
* P values indicate comparison between groups (and ANCOVA test, adjusted for baseline values, after 6 weeks).			
** P values indicate comparison between groups (independent sample t-test at baseline)			
*** P values indicate comparison within groups (paired t-test).			

Discussion

Findings showed acceptable efficacy of supplementation by coriander seeds among the study population with T2DM. Serum glucose levels decreased significantly in the coriander seed group compared to baseline measures and those in the placebo group. Accordingly, Aissaoui *et al.* [33] study who indicated significant post-intervention changes in coriander seed supplemented obese hyperlipidemic and hyperglycemic rats. Similar results were also discussed by Parsaian *et al.* in T2DM patients [30], showed the hypoglycemic effect of coriander seed including stimulating glucose utilization by peripheral tissues, especially muscle and adipose tissue, increasing hepatic glucose uptake, decreasing hepatic glucose production and gluconeogenesis, and increasing the activities of glucose 6-phosphatase and glycolysis by polyphenols and flavonoids extracted from coriander [33]. Furthermore, inhibiting glucosidase and amylase activities as well as decreasing glucose release and absorption in the gastrointestinal tract via SGLT1 transporter suppression have also been suggested to play a role in reducing glycemia [28]. By contrast, Al-Suhaimi *et al.* [34] showed no changes in serum glucose level after coriander seed administration in healthy adult male rabbits. Contrast to present findings, Nyakudya *et al.* [35], showed increased serum levels of glucose after five weeks of coriander intervention but this increase was not statistically significant. Present results showed that coriander seed supplementation led to significant decrease in serum levels of insulin compared to baseline and placebo group. In a study by Aissaoui *et al.* [33], reduction in serum insulin was also observed following coriander seed supplementation but was not statistically significant. In addition, insulin resistance improved significantly in the coriander seed group compared to baseline and placebo group. This finding was also in accordance with a previous

investigation [33]. It seems that coriander seed increases insulin signaling, thereby reducing insulin resistance by enhancing insulin sensitivity [33].

Dyslipidemia is an important risk factor for the development of atherosclerosis in patients with T2DM [24].

Significant decreases in serum levels of TC, TG, and LDL-C were found in the intervention group supplemented coriander seed compared to baseline and placebo group. Our study was consistent with results of previous studies in animal models [22–25] that indicated a significant decrease in serum cholesterol after coriander seed administration. Moreover, Parsaian *et al.* [28] reported the potential effects of coriander seed supplementation in lowering serum cholesterol in T2DM patients. Cholesterol lowering mechanisms of coriander seed are presumably attributable to the decreased cholesterol biosynthesis particularly by inhibition of β -Hydroxy β -methylglutaryl-CoA (HMG-CoA) reductase, a key enzyme in cholesterol biosynthesis, increasing cholesterol degradation to fecal bile acids and increasing lecithin-cholesterol acyl transferase (LCAT) [25, 28]. In addition, flavonoids and polyphenols that present in coriander seed may be responsible for its hypolipidemic and hypoglycemic effects [28]. Decrease in serum LDL-cholesterol can also be due to decreased LDL synthesis or an increased LDL metabolism [25]. Moreover, decrease in serum TG may be due to the stimulation of TG degradation through increased lipoprotein lipase expression and activity as well as decreased TG synthesis and its secretion [25]. Inconsistent with our results, Al-Suhaimi *et al.* [34] study showed no decrease in serum levels of cholesterol after the intervention in healthy male rabbits. This lack of cholesterol reduction might be attributed to the low dose of coriander seed used in that study. According to our study, changes in serum levels of HDL-C were not significant compared to baseline and placebo group. Our study was in line with Parsaian *et al.* [28] study who reported no significant changes in serum HDL-C after coriander seed supplementation. Our study was not similar with Dhanapakiam *et al.* [24] who proved that HDL-C levels increased after coriander seed consumption probably due to the removal of cholesterol from the tissues and directing it to the liver by HDL-C. In addition, Aissaoui *et al.* [33] indicated that coriander seed decreased serum HDL-C significantly which was probably due to the large changes in blood cholesterol levels.

Diabetes mellitus is associated with increased reactive oxygen species, lipid peroxidation, and impaired antioxidant defense system [39]. Lipid peroxidation can lead to various products including MDA which is the most important toxin. Previous studies showed that plasma concentration of MDA elevated significantly in patients with diabetes mellitus [36, 37]. TAC is recognized as a reliable marker for measuring the cumulative action of all antioxidants in plasma and other body biologic fluids [39]. Both TAC and MDA seem as important markers to detect the status of oxidative stress [38]. To the best of our knowledge, present study was the first research assessing the effects of coriander seed supplementation in T2DM. According to our results, coriander seed increased serum levels of TAC and decreased serum levels of MDA significantly compared to baseline and placebo group. Previous animal studies showed the role of coriander seed in scavenging superoxide anion and hydroxyl radicals [25–27]. Coriander seed contains phenolic compounds which might exert antioxidant activity, thereby it could reduce lipid

peroxidation and related markers in tissues [28]. This indicates that coriander seed extract might interact with the accumulation of peroxy radicals and act as chain breaking antioxidant against lipid peroxidation [26]. The active components of coriander seed can take part as electron donors, which can react with free radicals to generate stable forms of radicals and thereby terminate the radical chain reaction [26].

The limitations of the current study were small number of participants and short duration of supplementation. The strengths of our study were conducting a double-blind, randomized, placebo-controlled design. We evaluated dietary energy and nutrients intake at baseline and at the end of trial to find any confounders. Also, coriander seed powder seemed to be well tolerated by participants.

Conclusion

Present study demonstrated that coriander seed powder supplementation decreased serum glucose, insulin, insulin resistance, TC, TG, LDL-C, and MDA levels and increased serum TAC level significantly in T2DM patients. These findings suggest that coriander seed can be useful in management of diabetic patients.

Abbreviations

T2DM: type 2 diabetes mellitus; FBS: fasting blood sugar; IPAQ: international physical activity questionnaire; BMI: body mass index; WC: waist circumference; HC: hip circumference; WHR: waist to hip ratio; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; HOMA-IR: homeostatic model assessment of insulin resistance; MDA: malondialdehyde; TBARS: thiobarbituric acid reactive substances; TAC: total antioxidant capacity; ANCOVA: analysis of covariance; HMG-CoA: β -hydroxy β -methylglutaryl-CoA.

Declarations

Ethics approval and consent to participate

All procedures followed were in accordance with the ethical standards of the Ethical Committee of Tabriz University of Medical Sciences.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable.

Authors' Contributions

SZ, AB, and SP conceived the idea, participated in study design, performed the experiments, supervised the entire work, conducted the statistical analysis, and helped with drafting of manuscript. AMM participated in the performance of the experiments. All authors have read and approved final version of the manuscript.

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References

1. Maritim A, Sanders a, Watkins Iii J. Diabetes, oxidative stress, and antioxidants: a review. *J Biochem Mol Toxicol*. 2003;17(1):24–38.
2. Ramakrishna V, Jaikhani R. Oxidative stress in non-insulin-dependent diabetes mellitus (NIDDM) patients. *Acta diabetologica*. 2008;45(1):41–6.
3. Abou-Seif MA, Youssef A-A. Evaluation of some biochemical changes in diabetic patients. *Clin Chim Acta*. 2004;346(2):161–70.
4. Nolan CJ, Damm P, Prentki M. Type 2 diabetes across generations: from pathophysiology to prevention and management. *The Lancet*. 2011;378(9786):169–81.
5. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Res Clin Pract*. 2010;87(1):4–14.

6. Chakrabarti S, Khan ZA, Cukiernik M, Fukuda G, Chen S, Mukherjee S. Alteration of endothelins: a common pathogenetic mechanism in chronic diabetic complications. *Journal of Diabetes Research*. 2002;3(4):217–31.
7. Brownlee M. Biochemistry and molecular cell biology of diabetic complications. *Nature*. 2001;414(6865):813.
8. King GL, Brownlee M. The cellular and molecular mechanisms of diabetic complications. *Endocrinol Metab Clin North Am*. 1996;25(2):255–70.
9. Evans JL, Goldfine ID, Maddux BA, Grodsky GM. Oxidative stress and stress-activated signaling pathways: a unifying hypothesis of type 2 diabetes. *Endocr Rev*. 2002;23(5):599–622.
10. Sasaki H, Zhu L, Fukuda S, Maulik N. Inhibition of NF kappa B activation by pyrrolidine dithiocarbamate prevents in vivo hypoxia/reoxygenation-mediated myocardial angiogenesis. *Int J Tissue React*. 2000;22(4):93–100.
11. Perez-Matute P, Zulet MA, Martinez JA. Reactive species and diabetes: counteracting oxidative stress to improve health. *Curr Opin Pharmacol*. 2009;9(6):771–9.
12. Nishikawa T, Kukidome D, Sonoda K, Fujisawa K, Matsuhisa T, Motoshima H, et al. Impact of mitochondrial ROS production on diabetic vascular complications. *Diabetes Res Clin Pract*. 2007;77(3):41-S5.
13. Bonnefont-Rousselot D, Bastard J, Jaudon M, Delattre J. Consequences of the diabetic status on the oxidant/antioxidant balance. *Diabetes metabolism*. 2000;26(3):163–77.
14. Opara EC, Abdel-Rahman E, Soliman S, Kamel WA, Souka S, Lowe JE, et al. Depletion of total antioxidant capacity in type 2 diabetes. *Metab Clin Exp*. 1999;48(11):1414–7.
15. Kangralkar V, Patil SD, Bandivadekar R. Oxidative stress and diabetes: a review. *Int J Pharm Appl*. 2010;1(1):38–45.
16. Rains JL, Jain SK. Oxidative stress, insulin signaling, and diabetes. *Free Radic Biol Med*. 2011;50(5):567–75.
17. Garcia C, Feve B, Ferre P, Halimi S, Baizri H, Bordier L, et al. Diabetes and inflammation: fundamental aspects and clinical implications. *Diabetes Metab*. 2010;36(5):327–38.
18. Pooya S, Jalali MD, Jazayery AD, Saedisomeolia A, Eshraghian MR, Toorang F. The efficacy of omega-3 fatty acid supplementation on plasma homocysteine and malondialdehyde levels of type 2 diabetic patients. *Nutrition Metabolism Cardiovascular Diseases*. 2010;20(5):326–31.
19. Rajeshwari U, Andallu B. Medicinal benefits of coriander (*Coriandrum sativum* L.). *Spatula DD*. 2011;1(1):51–8.
20. Mohammed SF, Al-Gburi OSH, Abbas ER. Effect of *Corianderum sativum* on live weight gain, lipids, hematological and some blood parameters of Awassi female and male lambs. *Advances in Environmental Biology*. 2017;11(4):19–23.
21. Paarakh PM. *Coriandrum sativum* Linn. "â€". *Review Pharmacologyonline*. 2009;3:561–73.

22. Hosseinzadeh H, Qotbi A, Ahmad A, Seidavi A, Norris D, Brown D. Effects of different levels of coriander (*Coriandrum sativum*) seed powder and extract on serum biochemical parameters, microbiota, and immunity in broiler chicks. *The Scientific World Journal*. 2014;2014.
23. Aissaoui A, Zizi S, Israili ZH, Lyoussi B. Hypoglycemic and hypolipidemic effects of *Coriandrum sativum* L. in *Meriones shawi* rats. *J Ethnopharmacol*. 2011;137(1):652–61.
24. Dhanapakiam P, Joseph JM, Ramaswamy V, Moorthi M, Kumar AS. The cholesterol lowering property of coriander seeds (*Coriandrum sativum*): mechanism of action. *J Environ Biol*. 2007;29(1):53.
25. Joshi SC, Sharma N, Sharma P. Antioxidant and lipid lowering effects of *Coriandrum sativum* in cholesterol fed rabbits. *International Journal of Pharmacy Pharmaceutical Sciences*. 2012;4(3):231–4.
26. Deepa B, Anuradha C. Antioxidant potential of *Coriandrum sativum* L. seed extract. 2011.
27. Msaada K, Jemia MB, Salem N, Bachrouch O, Sriti J, Tammar S, et al. Antioxidant activity of methanolic extracts from three coriander (*Coriandrum sativum* L.) fruit varieties. *Arabian Journal of Chemistry*. 2017;10:3176-S83.
28. Parsaeyan N. The effect of coriander seed powder consumption on atherosclerotic and cardioprotective indices of type 2 diabetic patients. 2012.
29. Moghaddam MB, Aghdam FB, Jafarabadi MA, Allahverdipour H, Nikookheslat SD, Safarpour S. The Iranian Version of International Physical Activity Questionnaire (IPAQ) in Iran: content and construct validity, factor structure, internal consistency and stability. *World applied sciences journal*. 2012;18(8):1073–80.
30. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical chemistry*. 1972;18(6):499–502.
31. Antuna-Puente B, Faraj M, Karelis A, Garrel D, Prud'homme D, Rabasa-Lhoret R, et al. HOMA or QUICKI: is it useful to test the reproducibility of formulas? *Diabetes Metab*. 2008;34(3):294–6.
32. Bilici M, Efe H, Köroğlu MA, Uydu HA, Bekaroğlu M, Değer O. Antioxidative enzyme activities and lipid peroxidation in major depression: alterations by antidepressant treatments. *J Affect Disord*. 2001;64(1):43–51.
33. Aissaoui A, Zizi S, Israili ZH, Lyoussi B. Hypoglycemic and hypolipidemic effects of *Coriandrum sativum* L. in *Meriones shawi* rats. *J Ethnopharmacol*. 2011;137(1):652–61.
34. Al Suhaimi E. Effect of *Coriandrum sativum*, a common herbal medicine on endocrine and reproductive organ structure and function. *The Internet Journal of Alternative Medicine*. 2009;7(2):1540–2584.
35. Nyakudya T, Makaula S, Mkumla N, Erlwanger K. Dietary supplementation with coriander (*Coriandrum sativum*) seed: Effect on growth performance, circulating metabolic substrates, and lipid profile of the liver and visceral adipose tissue in healthy female rats. *International Journal of Agriculture and Biology*. 2014;16(1).

36. Braxas H, Rafrat M, Hasanabad SK, Jafarabadi MA. Effectiveness of genistein supplementation on metabolic factors and antioxidant status in postmenopausal women with type-2 diabetes mellitus. Canadian Journal of Diabetes. 2019.
37. Černe D, LUKAČ BAJALO J. Oxidative stress assays for disease risk stratification. Acta Pharmaceutica. 2006;56(1):1–17.

Figures

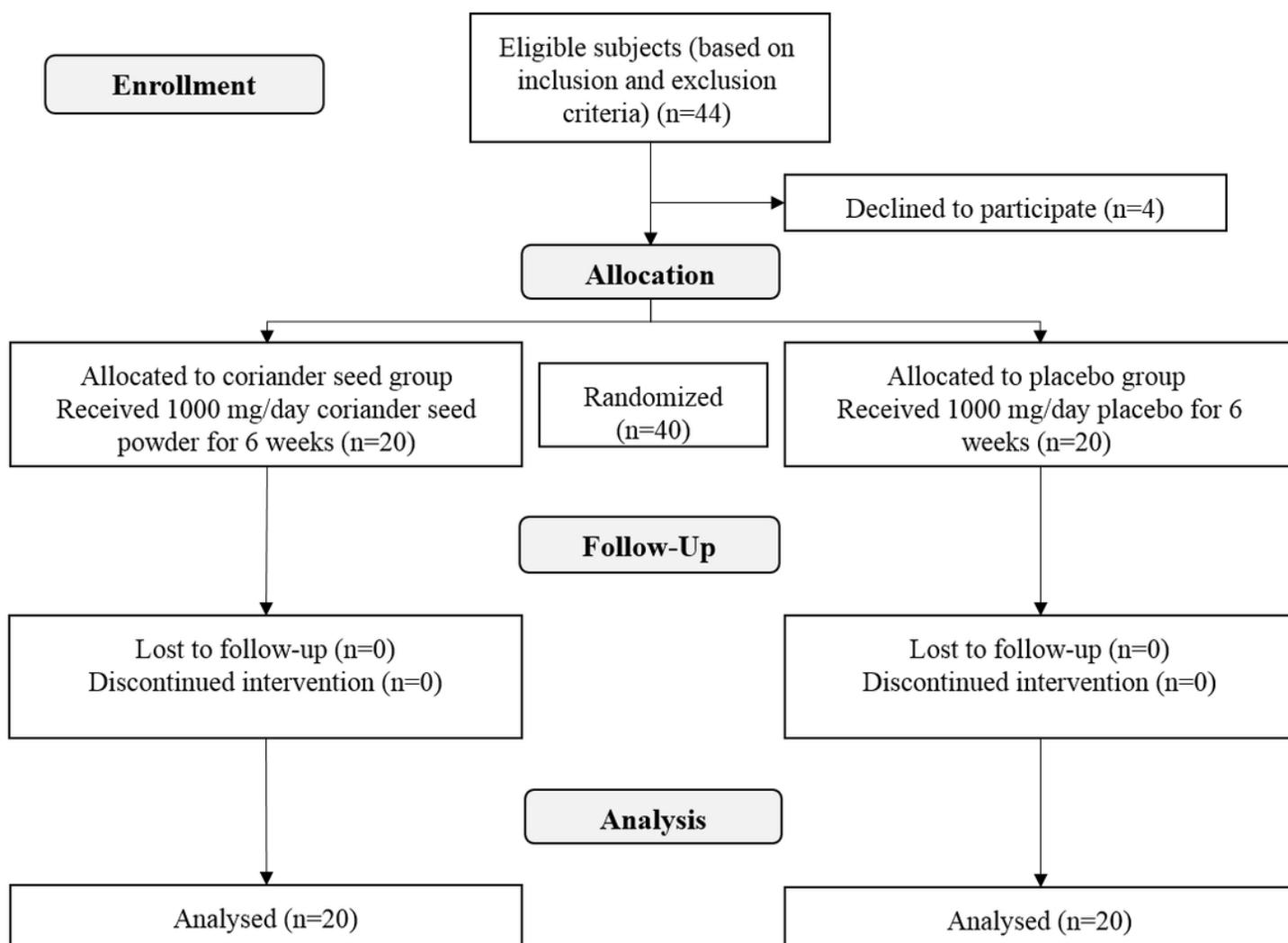


Figure 1

Study Flow Diagram