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Meta-analysis

Effect of green cardamom on lipoproteins, glycemic control and anthropometric parameters: A meta-analysis of randomized clinical trials

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SUMMARY

Introduction: The aim of this systematic review and meta-analysis was to summarize all the existing randomized controlled trials (RCTs) evidence and to evaluate the effects of green cardamom on lipoproteins, glycemic control and anthropometric parameters in healthy and/or with disease types compared with the control.

Method: Two independent authors systematically searched online databases including EMBASE, Scopus, PubMed, Cochrane Library, and Web of Science from inception until 30th July 2019. RCTs complying with the following criteria were included in this meta-analysis: human trials with either cross-over design or parallel design, trials with data on the effects of green cardamom on serum lipoproteins and glycemic control and anthropometric parameters with standard deviation and related 95% confidence interval for the both intervention and placebo groups. The heterogeneity among the included studies was assessed using Cochrane's Q test and I-square (I^2) statistic. Data were pooled using a random-effects model and weighted mean difference (WMD) was considered as the overall effect size.

Result: Seven trials were included in this meta-analysis. Triglycerides were significantly reduced after cardamom supplementation when compared with the control group. Cardamom intake from 3 small studies resulted in a significant increase in BMI when compared with the control group. However, cardamom supplementation did not have any significant effect on total cholesterol, LDL-cholesterol, HDL-cholesterol, fasting plasma glucose and body weight when compared with the control group.

Conclusion: This meta-analysis demonstrated that green cardamom intake significantly reduced triglycerides levels which may have played an indirect role in improved clinical symptoms in diseases with metabolic disorders.

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Practical applications

This meta-analysis demonstrated that green cardamom intake significantly reduced plasma triglycerides levels, but did not affect FPG, other lipids and lipoproteins and body weight. Therefore, green cardamom intake may have played an indirect role in improved clinical symptoms in diseases with metabolic disorders due to its effect on triglycerides levels.

1. Introduction

Herbal medicine is based upon spices and plants and although for centuries different cultures around the world have used traditional herbal medicine to treat many diseases, recently more and more attention has been paid on spices and plants in classical medicine as well [1]. Green cardamom from *Elettaria cardamomum* plant, known as "Queen of spice" is a member of ginger family (Zingiberaceae) [2,3]. It has been suggested that it might have antioxidative, anti-inflammatory, antimicrobial and anti-cancer effects [3–6]. The antioxidative effects of cardamom are mainly due to its polyphenols content, including flavonols (quercetin and kaempferol), flavone (luteolin) and anthocyanidin (pelargonidin) content [7]. It achieves antioxidant protection also by activation of the antioxidant enzymes [8]. According to some studies green cardamom may have beneficial effect on some lipoproteins, e.g. HDL-cholesterol, glucose and anthropometric parameters but the results are equivocal [9–11]. It seems that hypolipidemic effect of green cardamom may improve insulin function by reducing glucose and insulin levels [12].

Generally, flavonoids from green cardamom are effective in reducing glucose absorption [13], reducing fat storage [14], activating PGC-1α [15], enhancing glucose tolerance and inhibiting pancreatic lipase [16]. It has been also reported that 1,8-cineole, which is a major component of the green cardamom oil, significantly decreased fatty tissue mass and that it has vascular relaxant, anti-inflammatory, and antioxidant properties [17]. The proposed mechanisms include increase in antioxidant capacity and oxidation of fats [9], enhanced insulin activity and sensitivity due to increased glycogenesis and decreased gluconeogenesis [18], improvement in obesity and glycemic control by increased expression and activity of peroxisome proliferator-activated receptor gamma (PPAR-γ) [19], suppression of inflammation, nuclear factor-kappa B (NF-κB) [7] and cholesterol synthesis [20], as well as reducing oxidative stress [12]. However, the results of different studies are contradictory. For example, the results of Aghasi et al. [21] on patients with type 2 diabetes mellitus (T2DM) suggested that 3 g/day of green cardamom intake during 10 weeks, showed no significant changes in total cholesterol, LDL-cholesterol and HDL-cholesterol levels between the intervention and placebo groups. However, in another study by Azimi et al. [22], intake of 3 g/day of cardamom for 8 weeks in patients with T2DM resulted in a significant lipid-lowering effect on total cholesterol and LDL-cholesterol as well as increasing effect on HDL-cholesterol levels, but no significant change were observed in glycemic control, oxidative stress, inflammation and anthropometric parameters.

Daneshi-Maskooni et al. [23,24] demonstrated that 3 g/day of green cardamom during 3 months significantly decreased triglycerides, LDL-cholesterol and homeostatic model assessment for insulin resistance (HOMA-IR) score, and increased HDL-cholesterol, but did not have a significant effect on fasting plasma glucose (FPG), total cholesterol, body weight and body mass index (BMI) in overweight or obese patients with non-alcoholic fatty liver disease. Yaghooblou et al. [10] found that 3 g/day of green cardamom for 2 months in overweight and obese pre-diabetic women increased insulin sensitivity, and reduced total cholesterol and LDL-cholesterol. Since there is no meta-analysis analyzing the effects of green cardamom supplementation on serum lipoproteins, glycemic control and anthropometric parameters, this meta-analysis was performed to summarize all the existing randomized controlled trials (RCTs) evidence and to evaluate the effects of green cardamom on lipoproteins, glycemic control and anthropometric parameters in healthy and/or with disease types compared with the control.

2. Methods

2.1. Search and studies selection strategies

Scientific international databases, including EMBASE, Scopus, Cochrane Library, Web of Science and PubMed were searched for relevant studies published from inception until 30th July 2019. A search strategy was developed using the following MeSH and text keywords; "Intervention" OR "Cardamom" OR "cardamom" OR "cardamom" OR "cardamomum" OR "Intervention Study" OR "Intervention Studies" OR "controlled trial" OR "randomized" OR "random" OR "randomly" OR "placebo" OR "assignment" OR "clinical trial" OR "Trial" OR "assignment" OR "randomized controlled trial" OR "randomized clinical trial" OR "RCT" OR "blinded" OR "double blind" OR "double blinded" OR "clinical trial" OR "trials" OR "Pragmatic Clinical Trial" OR "Cross-Over Studies" OR "Cross-Over" OR "Cross-Over Study" OR "parallel" OR "parallel study" OR "parallel trial" AND outcomes ["triglycerides (TG) " OR "total-cholesterol (TC)" OR "LDL-cholesterol" OR "LDL-C″ OR "HDL-cholesterol" OR "HDL-C″ OR "fasting plasma glucose (FPG)" OR "body weight" OR "BMI". Search was confined to human clinical RCTs and those published in English. To avoid missing reports, we manually reviewed the reference list of articles and previous review studies.

2.2. Inclusion and exclusion criteria

Randomized controlled trials complying with the following criteria were included in this meta-analysis: human trials in healthy and/or with disease types, either cross-over design or parallel design, both female and male, trials with data on the effects of green cardamom on serum lipoproteins and glycemic control and anthropometric parameters with standard deviation (SD) and related 95% confidence interval (CI) for the both intervention and placebo groups) with a duration of equal or more than eight weeks. Other studies such as animal experiments, *in vitro* studies, case reports, observational studies, trials without a control group, and studies that did not achieve the least quality score were excluded from this meta-analysis. This scale is a 5-point scale for measuring the quality of randomized trials. In this measuring scale, studies that obtain at least 3 or more score are assessed as high quality [16].

2.3. Data extraction and quality assessment

Two independent authors (OA and EE) screened the articles based on the eligibility criteria. As the first step the titles and abstracts of studies were reviewed. Then, the full-text of relevant studies was assessed to ascertain the suitability of a study for the meta-analysis. Any disagreement was resolved by the judgment of the third author (ZA).

Following data were taken from selected studies: the first authors' name, study location, year of publication, sample size, age, study design, dosage of green cardamom, duration of the study,

type of disease, the mean and SD for serum lipoproteins and glycemic control and anthropometric parameters in each intervention group. The quality of the selected RCTs was independently assessed by the same authors using the Cochrane Collaboration risk of bias tool based on the following criteria: "randomization generation, allocation concealment, blinding of participants and outcome assessors, incomplete outcome data, and selective outcome reporting, and other sources of bias" [25].

2.4. Data synthesis and statistical analysis

The effects of green cardamom consumption on the changes of the following parameters were calculated: 1) FPG, 2) triglycerides, 3) total cholesterol, 4) LDL-cholesterol, 5) HDL-cholesterol, 6) body weight and 7) BMI. Weighted mean difference (WMD) with 95% CI was used for pooling data to determine the effect sizes. The change score approach was used to calculate the effect size of green cardamom intake on the analyzed parameters. The random-effect model was used to report the pooled effect sizes using 95% CI. To calculate the SD changes, the following formula was used: SD = square root [(SD pre-treatment)^2 (SD posttreatment)2 - (2R × SD pre-treatment × SD post-treatment)], correlation coefficient (R-value) was considered 0.8 [26]. When an SEM or SE was reported instead of SD, the SD was calculated based on the following formula: SD= SEM × $\sqrt{n}$ (n = sample size in each group).

2.5. Heterogeneity and publication bias

Heterogeneity of included studies was assessed using Cochrane's Q test (with significant P-value <0.1) and I-square test (I^2 greater than 50 percent showing significant heterogeneity). The funnel plot, as well as the Beggs's and Egger's regression tests was

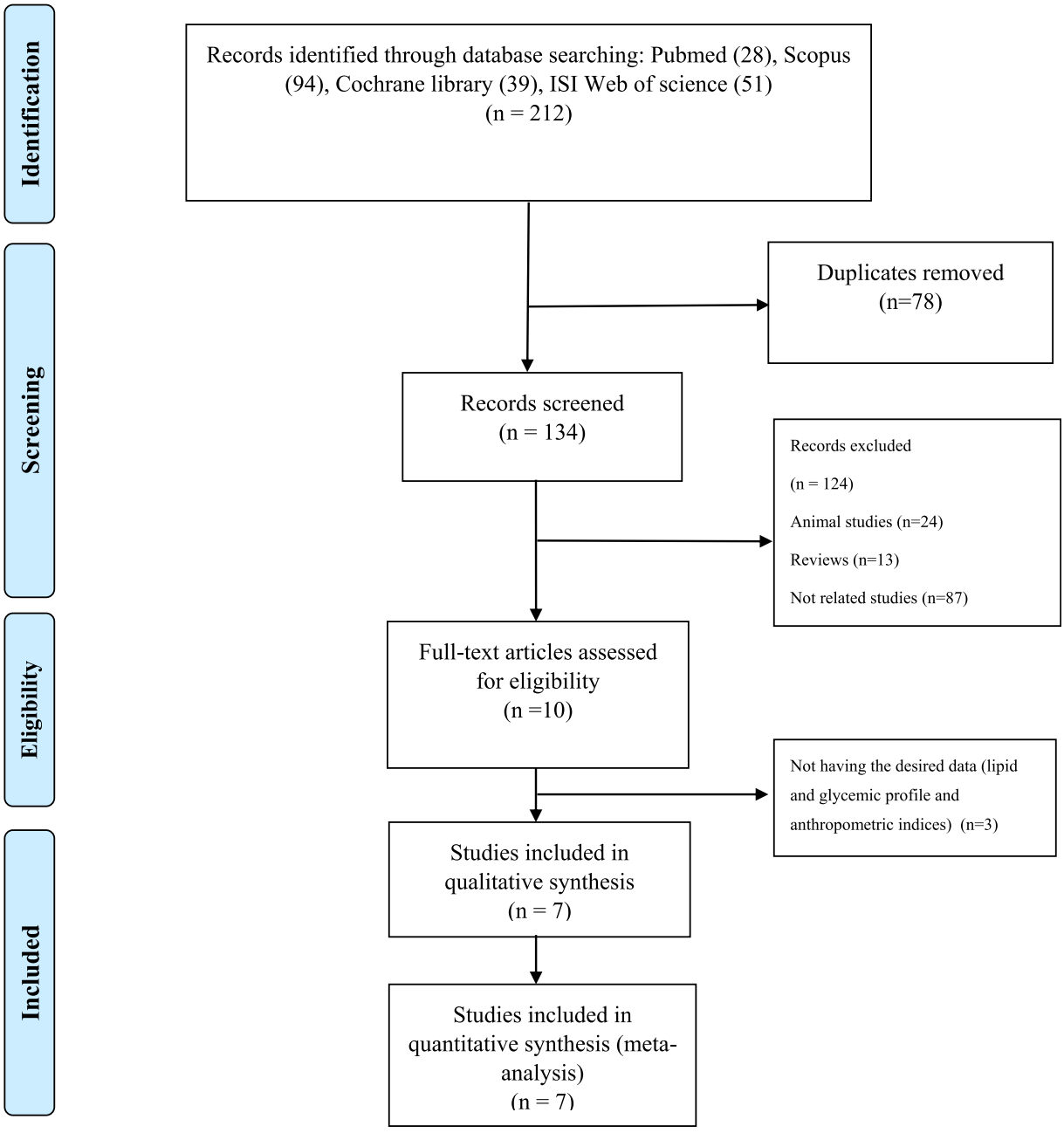


Fig. 1. Flowchart of the study selection for inclusion in the systematic reviews and meta-Analyses.

Table 1
Characteristics of included studies.

Studies	Publication year	Study design	Country	Participants	Sample size (intervention/ control)	Sex (intervention/ control)	Duration (Week/Month)	BMI (kg/m^2) (intervention/ control)	Age (years) (intervention/ control)	Intervention/control group
Aghasi et al. [21]	2019	R/DB/PC	Iran	Overweight or obese patients with type 2 diabetic	41/42	Male/Female (53%/47%)	10 W	29.06/29.1	53.9/53.3	Intervention group: 6 capsule contained 0.5 g of whole green cardamom powder (3000 mg) Placebo: 6 capsule contained 0.5 g rusk powder (3000 mg)
Kazemi et al. [27]	2017	R/DB/PC	Iran	Overweight or obese patients with pre-diabetic women	40/40	Female	8 W	29.7/29.3	30–70	Intervention group: 3 capsule contained 1 g of whole green cardamom powder (3000 mg) Placebo: 3 capsule with similar in shape, size, and appearance
Azimi et al. [22]	2014	R/SB/PC	Iran	Patients with type 2 diabetic	42/39	Male/Female (39.5%/60.5%)	8 W	28.96/28.4	51.59/53.64	Intervention group: 3 g dried powder from cardamom (3000 mg) Placebo: consumed three glasses of tea without any spices
Daneshi-Maskoon et al. [23]	2018	R/DB/PC	Iran	Overweight or obese patients with non-alcoholic fatty liver disease	43/44	Male/Female (62%/38%)	12 M	30.5/30.7	45.5/45	Intervention group: 6 capsule contained 0.5 g of green cardamom (3000 mg) Placebo: 6 capsule with similar in shape
Daneshi-Maskoon et al. [24]	2019	R/DB/PC	Iran	Overweight or obese patients with non-alcoholic fatty liver disease	43/44	Male/Female (62%/38%)	12 M	25–35	30–60	Intervention group: 6 capsule contained 0.5 g of green cardamom (3000 mg) Placebo: 6 similar capsule
Yaghooblou et al. [10]	2017	R/DB/PC	Iran	Overweight or obese patients with pre-diabetic women	40/40	Female	8 W	25–39.9	48.3/47.5	Intervention group: 3 capsule contained 1 g of whole green cardamom powder (3000 mg) placebo: 3 capsule contained 1g rusk powder (3000 mg)
Verma et al. [28]	2012	PC	India	Patients with ischemic heart disease	15/15	Male	12 W	NR	5–70	Intervention group: 4 capsule contained 0.75 g of whole green cardamom powder (3000 mg) Placebo: 4 capsule contained 0.75 lactose powder (3000 mg)

R: randomized, DB: double blind, SB: single blind, PC: placebo-control, NR: not-reported.

Table 2
The effects of cardamom on glycemic control, serum lipids and anthropometric measurements.

Variables	Number of effect sizes	Weighted mean difference	95% CI	P- value	Heterogeneity	
					I^2 (%)	P- value heterogeneity
FPG (mg/dl)	4	−0.98	−2.45, 0.49	0.191	0.0%	0.592
TC (mg/dl)	5	−7.51	−20.37, 5.36	0.253	96.5%	<0.001
LDL-C (mg/dl)	5	−6.58	−16.51, 3.36	0.194	95.4%	<0.001
TG (mg/dl)	5	−14.25	−28.34, −0.17	0.047	98.2%	<0.001
HDL-C (mg/dl)	5	1.31	−0.28, 2.89	0.106	95.6%	<0.001
Body weight (kg)	3	0.14	−0.19, 0.46	0.406	0.0%	0.845
BMI (kg/m^2)	4	0.07	0.01, 0.12	0.024	0.0%	0.516

FPG, fasting plasma glucose; TC, total cholesterol; LDL-C, low density lipoprotein cholesterol; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; BMI, body mass index.

used to determine the publication bias. Both STATA 11.0 (Stata Corp., College Station, TX) and Review Manager 5.3 (Cochrane Collaboration, Oxford, UK) were applied for data analysis.

3. Results

3.1. Study selection

We identified 212 studies; 78 duplicate articles were detected and removed. After screening, 134 articles based on title and abstract, 124 articles were removed because they were either performed on animals, or were review articles or were unrelated studies. 3 publications were excluded based on low full-text quality assessment. Finally, 7 articles [10,21–24,27,28] were included in our systematic review and meta-analysis. Of these, 5 trials [10,21,22,24,28] reported the effect of cardamom on serum lipoproteins, 4 trials [10,21,22,24] on FPG, 3 articles [22,23,27] on body weight and 4 studies [21–23,27] on BMI. Flowchart of study selection summarized in Fig. 1.

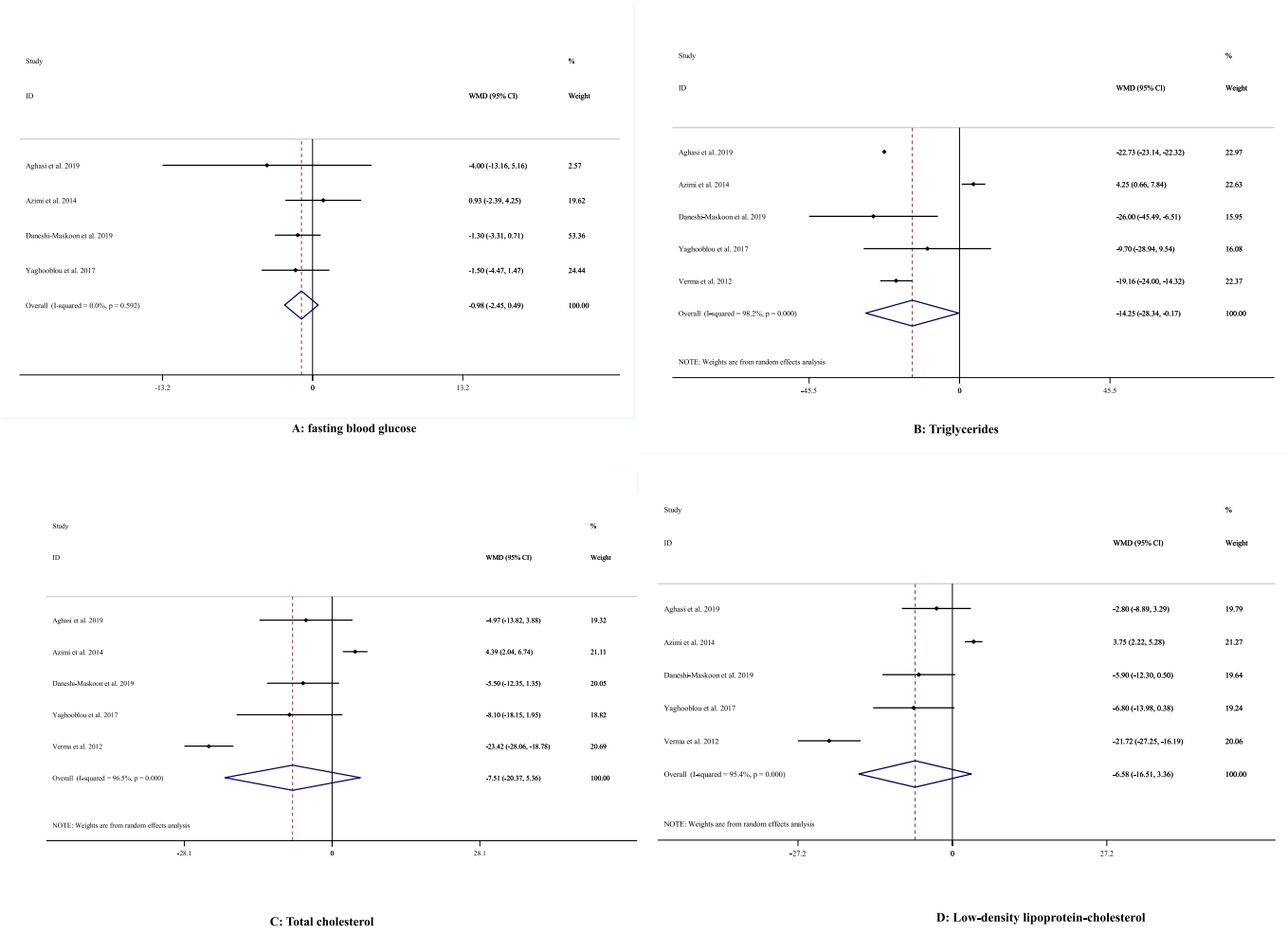
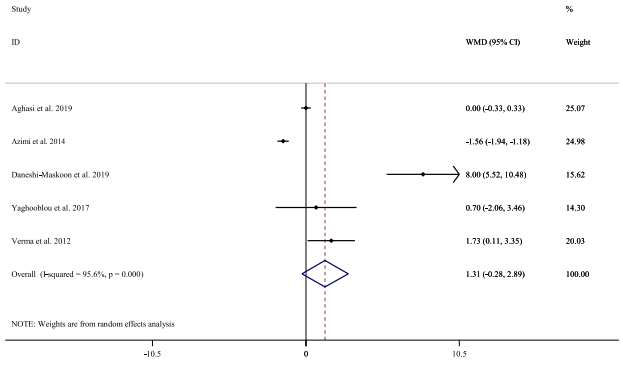
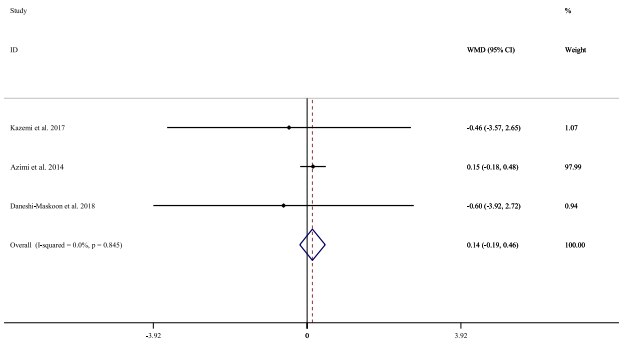


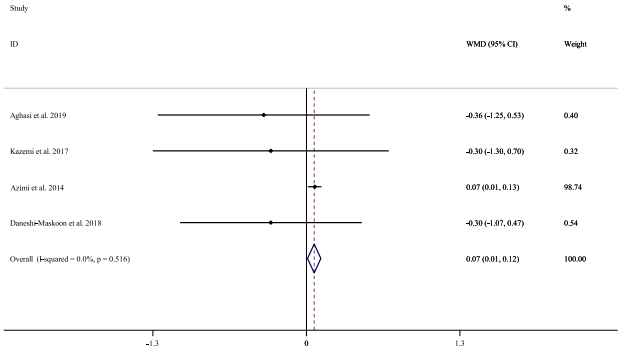
Fig. 2. A–G. Meta-analysis metabolic profiles and anthropometric measurements weighted mean difference estimates for A) fasting blood glucose (mg/dl), B) triglycerides (mg/dl), C) total cholesterol (mg/dl), D) Low-density lipoprotein-cholesterol (mg/dl), E) High-density lipoprotein-cholesterol (mg/dl), F) body weight (kg) G) Body mass index (kg/m2) in the cardamom and control groups.



E: High-density lipoprotein-cholesterol



F: Body weight



G: Body mass index

Fig. 2. (*continued*).

3.2. Characteristics of the included studies

The general characteristics of eligible studies are outlined in Table 1. These articles were published between 2012 and 2019 and were performed in Iran [10,21–24,27] and India [28]. Study duration ranged from 2 to 3 months. The dosage in all the included studies [10,21–24,27,28] was 3000 mg/day. Study design in all studies [10,21–24,27,28] was parallel. Five studies [21–24,28] were performed on subjects of both sexes and two studies [10,27] were done on women. Sample size in eligible trials ranged from 30 [28] to 87 [23,24]. In total, 528 subjects were enrolled in these trials, of which 264 individuals were randomized to the cardamom group and 264 subjects to the control group. Mean age of the participants ranged from 30 to 70 years and the mean baseline BMI varied from 25 to 39.9 kg/m^2. Participants in these studies were patients with pre-diabetes [10,27], T2DM [21,22], non-alcoholic fatty liver disease [23,24] and ischemic heart disease [28].

3.3. Effect of cardamom on serum lipoproteins, glycemic control and anthropometric indices

Five included studies with 361 participants analyzed the effects of cardamom supplementation on triglycerides, total cholesterol, LDL-cholesterol and HDL-cholesterol levels. Pooling their data based on random-effects model, we found that triglycerides were significantly reduced after cardamom supplementation (WMD: −14.25 mg/dL, 95% CI; −28.34 to −0.17, P = 0.047) when compared with the control group (Table 2 & Fig. 2B). However, cardamom supplementation did not have any significant effects on total cholesterol (WMD: −7.51 mg/dL, 95% CI; −20.37 to 5.36, P = 0.253) (Table 2 & Fig. 2C), LDL-cholesterol (WMD: −6.58 mg/dL, 95% CI; −16.51 to 3.36, P = 0.194) (Table 2 & Fig. 2D) and HDL-cholesterol levels (WMD: 1.31 mg/dL, 95% CI; −0.28 to 2.89, P = 0.106) (Table 2 & Fig. 2E). However, there was significant heterogeneity between studies, we conducted stratified analysis to explore potential sources of heterogeneity. The results of the sub-group analysis have demonstrated that cardamom intake had significant effect on reducing TG levels in studies with duration ≥12 weeks (WMD: −19.55 mg/dL, 95% CI; −24.25 to −14.86, P < 0.001) and non-diabetic patients (WMD: −19.00 mg/dL, 95% CI; −23.56 to −14.44, P < 0.001). In addition, cardamom intake had a significant impact on reducing TC (WMD: −12.86 mg/dL, 95% CI; −25.47 to −0.25, P = 0.046) and LDL-cholesterol levels (WMD: −11.50 mg/dL, 95% CI; −21.71 to −1.28, P = 0.027) in non-diabetic patients. On the other hand, subgroup analysis showed that long-term intervention (≥12 weeks) increased HDL-cholesterol levels (Table 3).

The impact of cardamom supplementation on FPG was assessed in 4 studies which included 331 participants. The pooled estimates showed that there was no significant effect of cardamom on FPG,

Table 3
Subgroup analyses of cardamom intake on lipid profiles.

	NO	WMD (95%CI)	P within group	P heterogeneity	I^2
Subgroup analyses of cardamom intake on TG levels					
Trial duration (week)					
<12	3	−9.41 (−31.46, 12.63)	0.403	<0.001	99.1%
≥12	2	−19.55 (−24.25, −14.86)	<0.001	0.504	0.0%
Diabetes status					
T2DM	2	−9.30 (−35.74, 17.13)	0.491	<0.001	99.5%
Non-diabetic	3	−19.00 (−23.56, −14.44)	<0.001	0.497	0.0%
Subgroup analyses of cardamom intake on TC levels					
Baseline serum TC (mg/dl)					
<200	3	−1.76 (−10.33, 6.79)	0.686	0.013	77.2%
>200	2	−14.84 (−32.39, 2.69)	0.097	0.001	90.5%
Trial duration (week)					
<12	3	−1.76 (−10.33, 6.79)	0.686	0.013	77.2%
≥12	2	−14.84 (−32.39, 2.69)	0.097	0.001	90.5%
Diabetes status					
T2DM	2	0.65 (−8.32, 9.63)	0.886	0.039	76.5%
Non-diabetic	3	−12.86 (−25.47, −0.25)	0.046	0.001	85.2%
Subgroup analyses of cardamom intake on LDL-C levels					
Baseline serum LDL-C (mg/dl)					
>100	1	−2.80 (−7.51, 1.91)	0.244	–	–
<100	4	−7.54 (−19.38, 4.29)	0.212	<0.001	97.4%
Trial duration (week)					
<12	3	−1.58 (−8.41, 5.24)	0.650	<0.001	90.2%
≥12	2	−13.82 (−29.32, 1.68)	0.081	<0.001	94.6%
Diabetes status					
T2DM	2	0.88 (−5.47, 7.25)	0.785	0.008	85.7%
Non-diabetic	3	−11.50 (−21.71, −1.28)	0.027	<0.001	91.5%
Subgroup analyses of cardamom intake on HDL-C levels					
Baseline serum HDL-C (mg/dl)					
<50	3	3.69 (−2.43, 9.81)	0.238	0.005	81.1%
>50	1	−1.56 (−5.42, 2.30)	0.428	–	–
Trial duration (week)					
<12	3	−0.34 (−2.93, 2.23)	0.793	0.705	0.0%
≥12	1	8.00 (5.23, 10.76)	<0.001	–	–
Diabetes status					
T2DM	2	−1.40 (−5.07, 2.26)	0.452	0.804	0.0%
Non-diabetic	2	4.45 (−2.70, 11.60)	0.223	0.002	89.8%

CI, confidence interval; TG, triglycerides; TC, total cholesterols; LDL-C, Low-density lipoprotein cholesterol; HDL-C, High-density lipoprotein cholesterol; T2DM, type 2 diabetes mellitus; WMD, weighted mean differences.

when compared with the control group (WMD: −0.98 mg/dL, 95% CI; −2.45 to 0.49, P = 0.191) (Table 2 & Fig. 2A).

Pooling effect sizes from 3 trials which included 248 patients, we found that cardamom administration had no significant effect on body weight when compared with the control group (WMD: 0.14 kg, 95% CI; −0.19 to 0.46, P = 0.406) (Table 2 & Fig. 2F). Four trials with 331 subjects, reported an increasing effect of cardamom on BMI. Pooled results from fix-effect model demonstrated a significant increasing effect of cardamom on BMI. Cardamom intervention from 3 small studies resulted in a significant increase in BMI when compared with controlled group (WMD: 0.07 kg/m^2, 95% CI; 0.01 to 0.12, P = 0.024) (Table 2 & Fig. 2G).

3.4. Publication bias

Publication bias assessment was done based on begg's regression tests and visual inspection of funnel plot (Fig. 3A–G). Results demonstrated no evidence of bias related with triglycerides (P = 0.806), total cholesterol (P = 0.806), LDL-cholesterol (P = 0.462), HDL-cholesterol (P = 1.000), FPG (P = 1.000), body weight (P = 0.296) and BMI (P = 1.000).

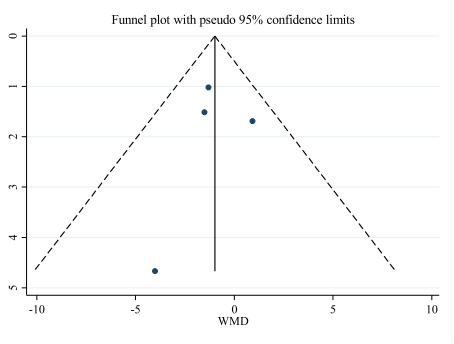
3.5. Quality assessment

The quality of the studies was evaluated on the basis of the Cochrane tool, and its results are summarized in Table 4. Most studies indicated adequate quality for key factors [10,21–24,27]. One had fair quality for random Sequence Generation, allocation concealment and other sources of bias [28], and in related with blinding of participants personnel two studies had low quality [22,28].

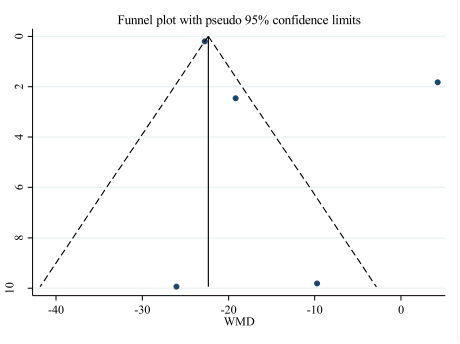
4. Discussion

This is the first meta-analysis of RCTs evaluating the effects of green cardamom on FPG, serum lipoproteins and anthropometric parameters. This meta-analysis demonstrated that green cardamom intake significantly reduced triglycerides levels and significantly increased BMI, but did not have a significant effect on FPG, other lipids and lipoproteins and body weight. Although BMI statistically significant, it marginal improvement.

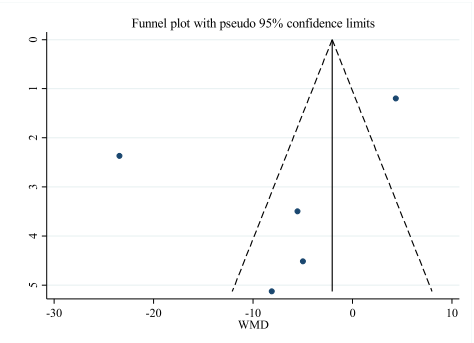
Today, a growing interest exists in patients with metabolic disorders for using dietary supplements in order to control insulin resistance and dyslipidemia [29]. In our meta-analysis of RCTs, green cardamom intake significantly reduced triglycerides levels and significantly increased BMI, but did not have a significant effect on FPG, other lipids and lipoproteins and body weight. Overall, pooling information from all qualified RCTs, provides more precise and powerful evidence than those from the individual studies. However, these studies are heterogeneous with respect to study duration, green cardamom dose, the characteristics of participants, sampling method, age ranges, differences between intervention and control groups, allocation concealment, cross-over design or parallel design, dietary intake of participants, and the assessment



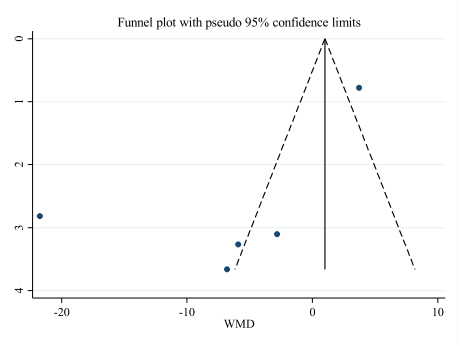
A: fasting blood glucose



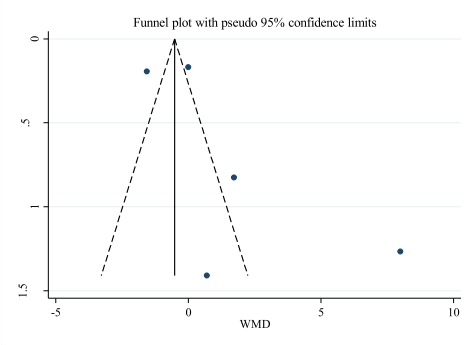
B: Triglycerides



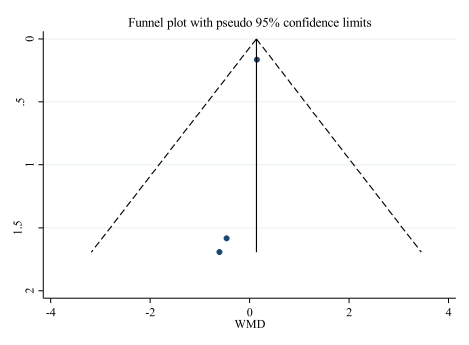
C: Total cholesterol



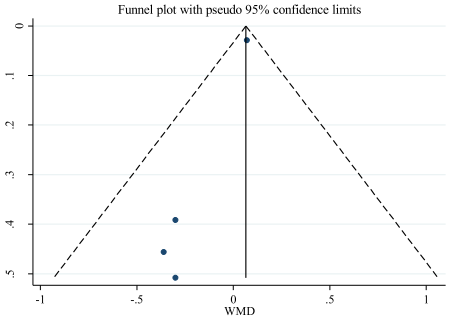
D: Low-density lipoprotein-cholesterol



E: High-density lipoprotein-cholesterol



F: Body weight



G: Body mass index

Fig. 3. A–G. Funnel plot representing publication bias in the studies reporting the impact of cardamom intake on A) fasting blood glucose, B) triglycerides, C) total cholesterol, D) Low-density lipoprotein-cholesterol, E) High-density lipoprotein-cholesterol, F) body weight G) Body mass index.

Table 4
Risk of bias assessment of the studies included in this meta-analysis.

Studies	Random Sequence Generation	Allocation concealment	Selective outcome reporting	Other sources of bias	Blinding of participants personnel	Blinding of outcome assessors	Incomplete outcome data
Aghasi et al. [21]	L	L	L	L	L	H	L
Kazemi et al. [27]	L	U	L	L	L	H	L
Azimi et al. [22]	L	U	L	L	H	H	L
Daneshi-Maskoon et al. [23]	L	L	L	L	L	U	L
Daneshi-Maskoon et al. [24]	L	L	L	L	L	H	L
Yaghooblou et al. [10]	L	U	L	L	L	U	L
Verma et al. [28]	H	H	L	H	H	H	L

Abbreviation; L: low-risk of bias, H: high-risk of bias, U: unclear-risk of bias.

method of BMI status/weight change. In particular, the wide variation in the amount and formulation of green cardamom may be the most important contributor to the heterogeneity seen in our results. In a study by Aghasi et al. [21], green cardamom at a dosage 3 g/day during 10 weeks decreased insulin levels, HbA1c levels, HOMA-IR score and triglycerides levels by increase in sirtuin-1(SIRT1) levels in patients with T2DM. Yaghooblou et al. [10] showed that 3 g/day of cardamom supplementation to pre-diabetic subjects for 8 weeks was associated with an improvement in insulin sensitivity and decreased total cholesterol and LDL-cholesterol concentrations. However, these findings were not significant when compared with the placebo group. In patients with ischemic heart disease cardamom consumption significantly reduced serum total cholesterol, LDL-cholesterol and triglycerides levels [30]. Another study in patients with T2DM showed that consumption of 3 glasses of black tea plus 3 g cardamom daily improved total cholesterol, triglycerides, LDL-cholesterol and HDL-cholesterol levels when compared with the control group [22]. The beneficial effects were seen following the intake of 500 mg of green cardamom three times a day for 12 weeks in overweight or obese NAFLD patients decreasing FPG, insulin, triglycerides, and LDL-cholesterol levels, increasing HDL-cholesterol and decreasing the grade of fatty liver [24].

Cardamom has a high content of polyphenolic compounds, including kaempferol, luteolin, quercetin, gallic acid, pelargonidin, caffeic acid and limonene [31]. The underlying mechanism of beneficial effects of green cardamom on serum triglycerides levels may be related to improvement in insulin resistance [32]. It was shown that insulin resistance is directly associated with plasma triglycerides concentrations [33]. Circulating lipoprotein lipase, an enzyme which is regulated by insulin, hydrolyzes triglycerides in lipoproteins. This enzyme is inhibited in subjects with insulin-resistance, which has hypertriglyceridemia as a consequence [34]. Another possible mechanism of green cardamom effects on serum lipoproteins may be by its effects on PPARs. SIRT1 is associated with lipid metabolism by the activation of PPAR-γ [35]. It is very difficult to explain how green cardamom could increase BMI without having any significant effect on body weight.

The current meta-analysis is among rare studies that summarize findings from earlier studies on the effects of green cardamom intake on lipoproteins, glycemic control and anthropometric parameters. Therefore it is important to consider some imitations of this meta-analysis when interpreting the results and producing conclusions. This study has some limitations. One of the most important is that patients in the included studies had different diseases such as pre-diabetes, T2DM, non-alcoholic fatty liver disease and ischemic heart disease which might have an influence on the results. Moreover, due to the heterogeneity between studies, evident from the variations in duration of green cardamom intake, the dosage and frequency of green cardamom used, results should be interpreted with caution. Green cardamom in different forms and by different methods were obtained that may have different effects on metabolic profiles and anthropometric parameters. The number of studies and sample size of participant's study that finally entered to the meta-analysis was low. Daneshi-Maskoon et al. [24] and Yaghooblou et al. [10] have significantly different BMI and age distribution. This could have greatly affected the results. Due to the small number of studies, we could not re-analyze without these two studies. So further studies are needed to reach a definitive conclusion.

5. Conclusions

This meta-analysis demonstrated that green cardamom intake significantly reduced plasma triglycerides levels and significantly increased BMI, but did not affect FPG, other lipids and lipoproteins and body weight. Although BMI statistically significant, it marginal improvement. Therefore, green cardamom intake may have played an indirect role in improved clinical symptoms in diseases with metabolic disorders due to its effect on triglycerides levels.

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Author contributions

ZA contributed in conception, data collection and manuscript drafting. OA, EE, ZR, BB, FK, SHD and SM contributed in conception, data collection and manuscript drafting. All authors read and approved the final version of the paper.

Declaration of Competing Interest

None declared.

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