



## Systematic Review and Meta-analysis of the Effects of *Elettaria Cardamomum* Supplementation on Glycemic Indices and Anthropometric Measurements

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### ABSTRACT

**Background:** Type 2 diabetes mellitus (T2DM) is considered a problem for public health worldwide and cardamom (*Elettaria cardamomum*) as a spice which contains polyphenolic components may have a beneficial effect on the status of diabetes patients. This systematic review and meta-analysis aims to update the efficacy of cardamom intake on weight reduction and glycemic control. **Methods:** Electronic databases were searched up to December 2023 to identify eligible articles. Mean differences were pooled using a fixed effects model, and standard methods were used for the assessment of heterogeneity, sensitivity analysis, and publication bias. **Results:** Totally, eight studies were included in the final analysis. Analysis showed that cardamom intake attenuated serum level of insulin [standard mean difference (SMD): -0.64, 95% CI: -0.86 to -0.43,  $P < 0.001$ ], whereas changes of fasting blood glucose (SMD: -0.13, 95% CI: -0.33 to 0.06), weight (SMD: -0.01, 95% CI: -0.23 to 0.20) and body mass index (SMD: -0.05, 95% CI: -0.02 to 0.11) were not significant. **Conclusion:** According to the findings of the present meta-analysis, cardamom intake significantly declined serum insulin level but did not have any significant effect on fasting blood glucose, weight, and body mass index.

### Introduction

Type 2 diabetes mellitus (T2DM) is an endocrine disease identified by hyperglycemia and elevated insulin levels in the serum (DeFronzo *et al.*, 2015). T2DM is considered a public health problem worldwide due to its dramatic prevalence and public health consequences (Chen *et al.*, 2012). Various determinants are involved in the pathogenesis of T2DM such as genetic (Brunetti *et*

*al.*, 2014), age (Zoungas *et al.*, 2014), diet and lifestyle (Hu *et al.*, 2001), inflammation (Cruz *et al.*, 2013), and obesity (Schnurr *et al.*, 2020). In fact, obesity is considered a major risk factor for various chronic diseases and threatens public health (World Health Organization, 2020). The main characteristic of obesity is the accumulation of excessive fat tissue in the body which causes

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chronic low inflammation in the body (Amin *et al.*, 2019). Consequently, obesity increases the risk of insulin resistance and T2DM (Piché *et al.*, 2020). Nearly one-third of the population of the world is in the obese and overweight range (Chooi *et al.*, 2019). Previous studies indicated that the management of body weight and fat mass tissue had beneficial effects on glycemic control (Babio *et al.*, 2010). In fact, weight reduction decreases inflammatory markers in the body and improve the function of insulin receptors (Barazzoni *et al.*, 2018, Tutunchi *et al.*, 2020). Based on this, most of the interventions for the amelioration of hypoglycemia should be considered body weight (Koh-Banerjee *et al.*, 2004).

Cardamom (*Elettaria cardamomum*) is an herbal medicine that belongs to the ginger family (Zingiberaceae) and in some sources it is known as the queen of spices (Amma *et al.*, 2010). Cardamom natively grows in evergreen forests of the Western Ghats (Sinu and Shivanna, 2007). This spice is a rich source of polyphenolic components such as quercetin, kaempferol, luteolin, gallic acid, and pelargonidin (Deepa *et al.*, 2013). Previous studies expressed the desirable effect of cardamom on inflammation, oxidative stress (Kazemi *et al.*, 2017, Rahman *et al.*, 2017), and gastric lesions (Jamal *et al.*, 2006).

The effect of cardamom supplementation on anthropometric and glycemic variables is inconsistency in different clinical trials, such as Kazemi *et al.* who indicated that cardamom did not have any effects on weight and body mass index (BMI) in prediabetes patients (Kazemi *et al.*, 2017). Another study expressed that 12 weeks of cardamom supplementation significantly reduced weight and BMI (Daneshi-Maskooni *et al.*, 2019). The desirable effects of cardamom on fasting blood glucose (FBG) and insulin level were demonstrated in a clinical trial (Li *et al.*, 2017). The results were in line with the findings of the Aghasi *et al.*'s study regarding type 2 diabetes patients (Aghasi *et al.*, 2019). However, the findings of another study contradicted with others and did not have any significant effects on glycemic control (Fatemeh *et al.*, 2017).

Based on the previous studies, the beneficial effects of cardamom on glycemic control related to the stimulation expression of silent mating type information regulation 2 homolog-1 (SIRT-1). Many records indicated that SIRT-1 was involved in hemostasis of glucose by improving insulin secretion, protection pancreatic beta-cell as an antioxidant, declining inflammation via scrubbing free radicals, and positive effects on the adiponectin, adipogenesis, and hepatic glucose production (Kitada and Koya, 2013).

Given the controversy between the results of different studies, present systematic review and meta-analyses were aimed to assess all clinical trials published which investigated the effects of cardamom supplementation on weight, BMI, FBG and, insulin in the adult population.

## Materials and Methods

### Search strategy

This meta-analysis was conducted based on the guidelines of the preferred reporting items for systematic reviews and meta-analyses (PRISMA) (Page *et al.*, 2021). All studies were identified by an online search in the following databases: PubMed (<http://www.pubmed.com>), Scopus (<http://www.scopus.com>), ISI Web of Sciences (<http://www.webofscience.com>), and, Google Scholar up to December 2023. In this research, the authors used text word and medical subject's headings (mesh) by following keywords: "Elettaria cardamomum" OR "Cardamom" OR "Elettaria" AND "Clinical Trials" OR "Cross-Over Studies" OR "Double-Blind Method" OR "Single-Blind Method" OR "Random Allocation" OR "RCT" OR "Intervention Studies" OR "Intervention" OR "Controlled trial" OR "randomized" OR "randomized" OR "random" OR "randomly" OR "Placebos" OR "Assignment". Moreover, the reference list of eligible studies was screened to avoid missing relevant articles. Search strategy of different databases is presented in supplementary file.

### Eligibility criteria

All clinical trials that evaluated the effects of cardamom intake on anthropometric variables and glycemic indexes were included in the present

study. Inclusion criteria included the following; 1- the study design was a randomized controlled trial 2- there was supplementation of cardamom or combination with other agents 3- there was sufficient reported information about both placebo and treatment groups 4- the study was published in English. The exclusion criteria in the present study included; 1- non-RCT studies, 2- a trial without a control group, 3- duplicate studies and animal studies, 4- a trial that evaluated the effects of cardamom only at the end of the trial.

#### **Data extraction and quality assessment**

Two independent reviewers (Najaf M, Papi S) screened the title and abstract of all the obtained studies through an electronic systematic search. A disagreement between investigators regarding study selection was resolved by a third independent reviewer (Nikpayam O). Finally, the required information was extracted from the included studies. The extracted relevant information included the first author's name, year of publication, study design, number and characteristics of participants in each group, intervention type and dose, duration of intervention, disease type, the effects of cardamom on FBG, insulin, weight, and BMI. The quality of included trials was evaluated using GRADE tool based on the Cochrane Handbook of systematic reviews of interventions. This tool consists of five variables: bias risk, consistency of results, directness, precision, and publication bias. GRADE results were categorized as "high," "medium," "low," and "very low." If any of the above variables are not met, the quality of a level will decrease (Guyatt *et al.*, 2008).

#### **Data analysis**

Statistical analysis in this meta-analysis was conducted by STATA software version 15. The effect size of cardamom intake on FBG, insulin, weight, and BMI was explicated through standard mean difference (SMD) with a 95% confidence interval (CI) from the fixed-effects model (using inverse variance method, Cohen statistic). The heterogeneity was assessed by I square test, and significant heterogeneity was defined as  $I^2 > 50\%$

with a P-value  $< 0.05$ . Sub-group analysis was performed for finding the probable source of heterogeneity among studies. For the influence of each study on pooled effect size, the authors used sensitivity analysis. Publication bias among the included studies was explored by funnel plots and also Egger's regression test and Begg's test.

## **Results**

### **Included studies**

Totally, 221 participants were identified after searching in Web of Sciences, Scopus, PubMed, and Google Scholar. After removing duplicate studies (114), 89 studies were excluded following screening the title and abstract, 18 studies remained for full-text evaluation, 10 studies were omitted due to not having the control group ( $n=1$ ), duplicated data ( $n=1$ ), being in Persian language ( $n=1$ ), and not having enough data to analyze ( $n=7$ ). Finally, 8 studies were included in this systematic review and meta-analysis (**Figure 1**).

### **Study characteristics**

Characteristics of included studies in the present systematic review and meta-analysis are presented in **Table 1**. All included studies were performed in Iran (Aghasi *et al.*, 2019, Azimi *et al.*, 2014, Azimi *et al.*, 2016, Cheshmeh *et al.*, 2021, Daneshi-Maskooni *et al.*, 2018, Fatemeh *et al.*, 2017, Kazemi *et al.*, 2017) except one study which was conducted in China (Li *et al.*, 2017). These studies were published between 2015 and 2021. Totally, 765 participants enrolled in these studies with 387 and 378 patients respectively in the treatment and control groups. Six studies were conducted on both genders and two studies were done only on women. The duration of supplementation with cardamom was from 8 weeks up to 16 weeks. The cardamom dosage in all studies was a 3-gram exception for one study which administrated 30-gram cardamom (Li *et al.*, 2017). The studies included in this meta-analysis reported no side effects associated with cardamom. The quality of enrolled studies is presented in **Table 2**.

### **Effects of cardamom on FBG**

The effects of cardamom intake on FBG are expressed in the **Figure 2**. According to the figure,

cardamom supplementation does not have significant effects on FBG; furthermore, there was no heterogeneity between included effects size. Also, subgroup analysis based on the duration of treatment, type of supplement, and mean age of patients did not show any considerable effect (Table 3). According to Begg's  $P$  (0.806) and Egger's  $P$  (0.896), and there was no publication bias between included studies. The funnel plot of studies is presented in the figure. 3. Sensitivity analysis revealed that excluding any one study did not have significant effects on SMD.

#### Effects of cardamom on insulin

Pooled findings of included studies indicated that cardamom supplementation significantly decreased the level of serum insulin, but there was heterogeneity between studies, as shown in Figure 4. So, subgroup analysis was conducted according to the duration of treatment, type of supplement, and mean age of participants. Analysis based on the duration of treatment showed that more than 8 weeks in comparison with less than 8 weeks,

supplementation with cardamom plus other agents vs. cardamom and people under 50 in comparison to those above 50 had a significant effect on serum level of insulin (Table 3). Statistical analysis did not show publication bias among included studies (Begg's  $P$  (0.086) and Egger's  $P$  (0.051). Funnel plot of studies was shown in Figure 5. Sensitivity analysis indicated that omitting each study did not change significantly the overall result.

#### Effects of cardamom on weight

Data analysis showed that cardamom supplementation had no effect on weight, and there was no heterogeneity between studies, which is shown in Figure 6. In addition, subgroup analysis findings are reported in Table 3. There was no publication bias between clinical trials investigating the cardamom impacts on weight (Begg's  $P=0.718$  and Egger's  $P=0.459$ ). The funnel plot of weight is reported in Figure 7. Also, sensitivity analysis indicated that excluding any of the clinical trials did not have any significant effects.

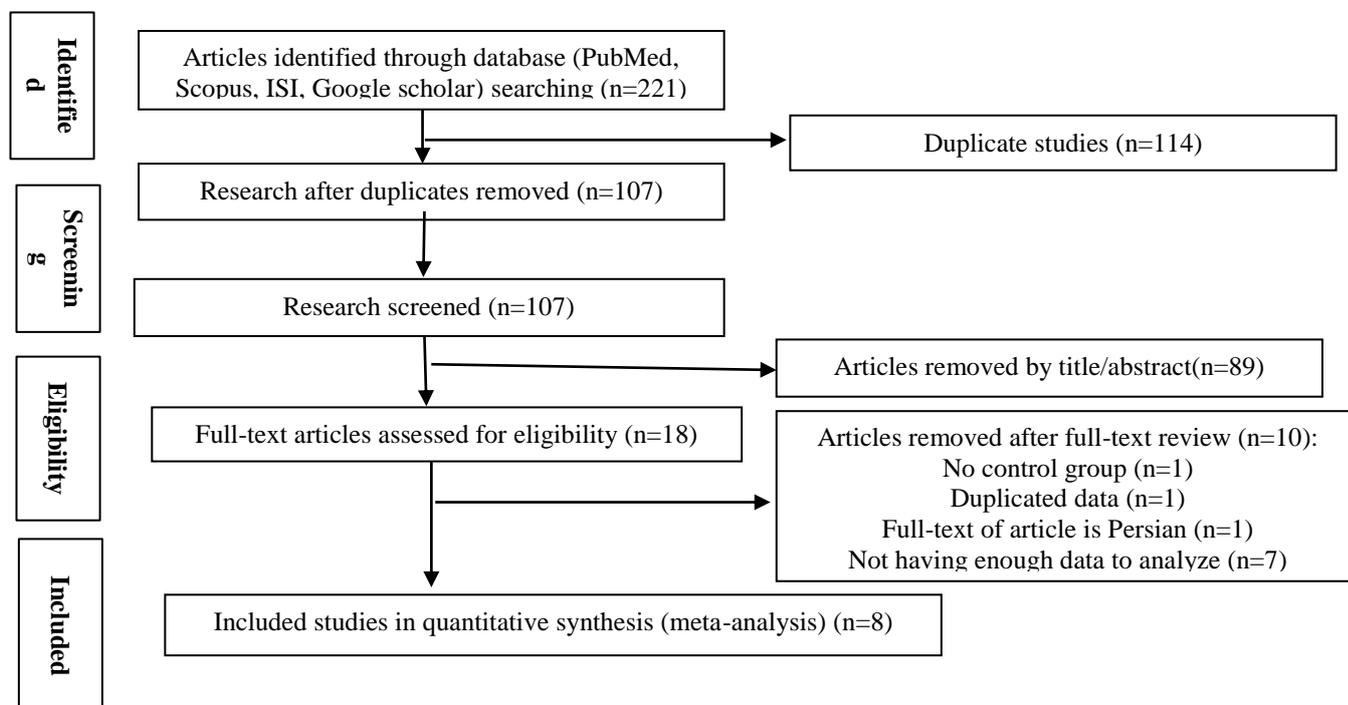


Figure 1. Flow chart of included studies.

Table 1. Characteristics of included studies.

| First author (year)     | Country | Type of disease                    | Participants (n) |                 | Age (year) |         | Dose (g) | Duration of treatment | Cardamom formulation                            |
|-------------------------|---------|------------------------------------|------------------|-----------------|------------|---------|----------|-----------------------|---|
|                         |         |                                    | Treatment        | Control         | Treatment  | Control |          |                       |   |
| Cheshmeh (2021)         | Iran    | PCOS                               | 99 <sup>a</sup>  | 95 <sup>a</sup> | 32.99      | 32.13   | 3        | 16 weeks              | Green cardamom powder capsule                   |
| Aghasi (2019)           | Iran    | T2DM                               | 41               | 42              | 53.90      | 53.30   | 3        | 10 weeks              | Green cardamom powder capsule                   |
| Daneshi-Maskooni (2018) | Iran    | NAFLD                              | 43               | 44              | 45.50      | 45.50   | 3        | 12 weeks              | Green cardamom powder capsule                   |
| Yaghooblou (2017)       | Iran    | Overweight or obese pre-diabetic   | 40*              | 40*             | 48.3       | 47.5    | 3        | 8 weeks               | Green cardamom powder capsule                   |
| Li (2017)               | China   | T2DM                               | 40               | 40              | 55.16      | 43.35   | 30       | 12 weeks              | Traditional Chinese medicine including cardamom |
| Kazemi (2017)           | Iran    | Overweight, and obese pre-diabetic | 40               | 40              | 48.30      | 47.50   | 3        | 8 weeks               | Green cardamom powder capsule                   |
| Azimi (2016)            | Iran    | T2DM                               | 42               | 39              | 54.33      | 53.64   | 3        | 8 weeks               | Green cardamom powder + black tea               |
| Azimi (2015)            | Iran    | T2DM                               | 42               | 39              | 51.59      | 53.64   | 3        | 8 weeks               | Green cardamom powder + black tea               |

<sup>a</sup>: Conducted exclusively on women; **NAFLD**: Non-alcohol fatty liver disease; **T2DM**: Type 2 diabetes mellitus ; **PCOS**: Polycystic ovary syndrome.

Table 2. Summary of findings and quality of evidence assessment using GRADE approach.

| Outcome measures      | Summary of findings       |                      |                           | Quality of evidence assessment (GRADE) |                           |                          |                               |                                  |
|-----------------------|---------------------------|----------------------|---------------------------|--|---------------------------|--------------------------|-------------------------------|----------------------------------|
|                       | None of patients (trials) | Effect size (95% CI) | Risk of bias <sup>a</sup> | Inconsistency <sup>b</sup>             | Indirectness <sup>c</sup> | Imprecision <sup>d</sup> | Publication bias <sup>e</sup> | Quality of evidence <sup>f</sup> |
| Insulin               | 411 (5)                   | -0.64 (-0.86,- 0.43) | Not Serious               | Serious                                | Serious                   | Not serious              | Not serious                   | Low                              |
| Fasting blood glucose | 411 (5)                   | -0.13 (-0.33, 0.06)  | Not Serious               | Not Serious                            | Serious                   | Not serious              | Not serious                   | Moderate                         |
| Weight                | 523 (5)                   | -0.02 (-0.19, 0.15)  | Not Serious               | Not Serious                            | Serious                   | Not serious              | Not serious                   | Moderate                         |
| Body mass index       | 606 (6)                   | -0.05 (-0.21, 0.11)  | Not Serious               | Not Serious                            | Serious                   | Not serious              | Not serious                   | Moderate                         |

<sup>a</sup>: Risk of bias based on the Cochrane risk of bias tool. This tool assesses selection bias, performance bias, detection bias, attrition bias, and reporting bias; <sup>b</sup>: Downgraded if there was a substantial unexplained heterogeneity ( $I^2 > 50\%$ ,  $P < 0.10$ ) that was unexplained by subgroup analyses; <sup>c</sup>: Downgraded if there were factors present relating to the participants, interventions, or outcomes that limited the generalizability of the results. Participants of the included studies were from different health conditions; <sup>d</sup>: Downgraded if 95% confidence interval (95% CI) crossed the minimally important difference (MID) for benefit or harm; <sup>e</sup>: Downgraded if there was an evidence of publication bias using funnel plot; <sup>f</sup>: Since all the included studies were randomized controlled trials, the certainty of the evidence was graded as high for all outcomes by default and then downgraded based on prespecified criteria. Quality was graded as high, moderate, low, very low.

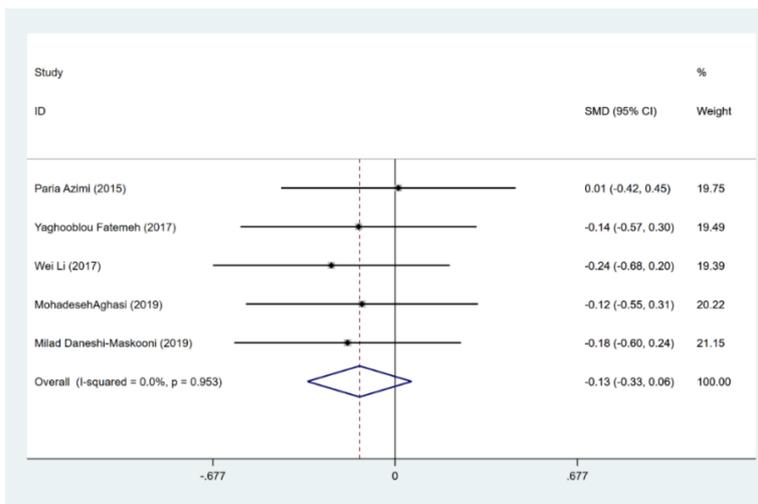


Figure 2. Forest plot of the cardamom supplementation on fasting blood glucose.

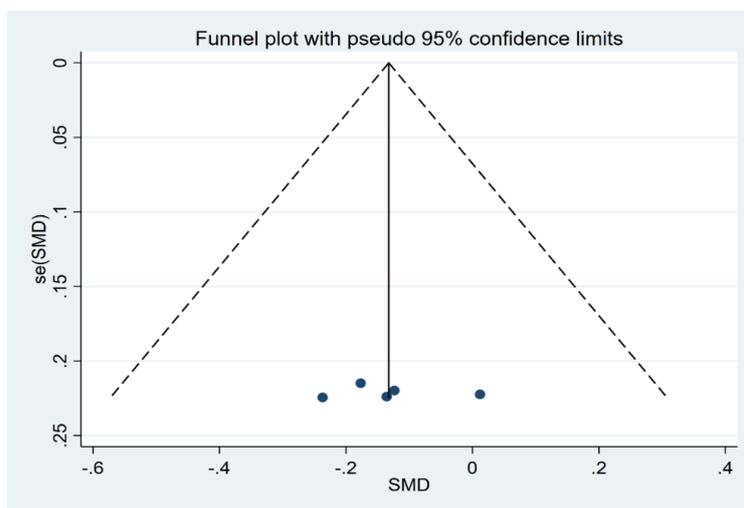


Figure 3. Funnel plot of the cardamom supplementation on fasting blood glucose.

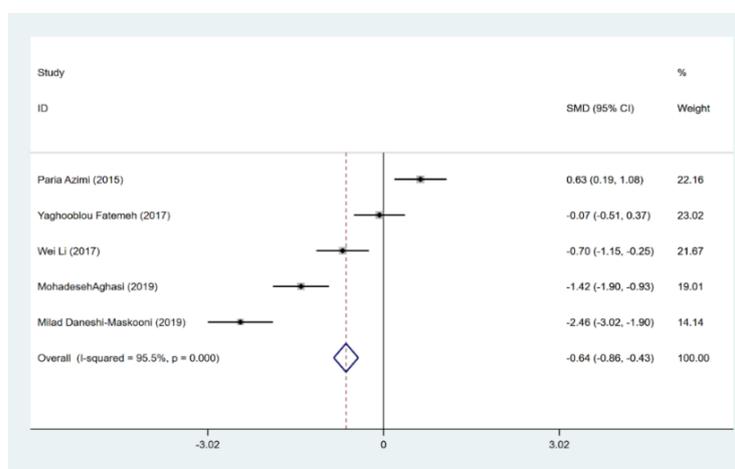
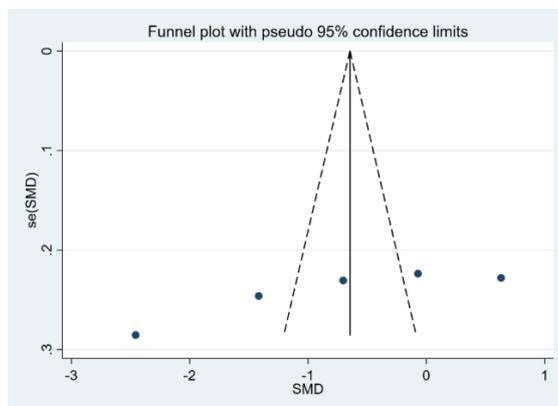


Figure 4. Forest plot of the cardamom supplementation on insulin.

**Table 3.** Results of subgroup analysis of the included studies in meta-analysis.

| Variable                     | Duration of treatment |          | Type of supplement |                         | Mean age |       |
|------------------------------|-----------------------|----------|--------------------|-------------------------|----------|-------|
|                              | < 8 week              | > 8 week | Cardamom           | Cardamom + other agents | < 50     | > 50  |
| <b>Insulin</b>               |                       |          |                    |                         |          |       |
| No. of comparisons           | 2                     | 3        | 2                  | 3                       | 2        | 2     |
| SMD                          | 0.27                  | -1.40    | -0.04              | -1.86                   | -0.48    | -0.31 |
| 95%CI                        |                       |          |                    |                         |          |       |
| Lower                        | -0.04                 | -1.69    | -0.3               | -2.23                   | -1.32    | -0.64 |
| Higher                       | 0.59                  | -1.12    | 0.21               | -1.49                   | -0.63    | 0.01  |
| P-value                      | 0.086                 | 0.0      | 0.0                | 0.006                   | 0.001    | 0.061 |
| I <sup>2</sup> (%)           | 79.4                  | 91.3     | 88.2               | 86.9                    | 97.3     | 96.6  |
| P-heterogeneity              | 0.028                 | 0.001    | 0.001              | 0.006                   | 0.001    | 0.001 |
| <b>Fasting blood glucose</b> |                       |          |                    |                         |          |       |
| No. of comparisons           | 2                     | 3        | 3                  | 2                       | 3        | 2     |
| SMD                          | -0.06                 | -0.18    | -0.15              | 0.11                    | -0.18    | -0.06 |
| 95%CI                        |                       |          |                    |                         |          |       |
| Lower                        | -0.37                 | -0.43    | -0.39              | -0.42                   | -0.43    | -0.36 |
| Higher                       | 0.25                  | 0.07     | 0.10               | 0.20                    | 0.07     | 0.25  |
| P-value                      | 0.697                 | 0.160    | 0.481              | 0.250                   | 0.152    | 0.718 |
| I <sup>2</sup> (%)           | 0.0                   | 0.0      | 0.0                | 0.0                     | 0.0      | 0.0   |
| P-heterogeneity              | 0.640                 | 0.953    | 0.984              | 0.431                   | 0.950    | 0.665 |
| <b>Weight</b>                |                       |          |                    |                         |          |       |
| No. of comparisons           | 3                     | 2        | 3                  | 2                       | 3        | 2     |
| SMD                          | 0                     | -0.03    | -0.04              | 0.02                    | -0.04    | 0.02  |
| 95%CI                        |                       |          |                    |                         |          |       |
| Lower                        | -0.25                 | -0.27    | -0.24              | -0.29                   | -0.24    | -0.29 |
| Higher                       | 0.25                  | 0.20     | 0.17               | 0.33                    | 0.17     | 0.33  |
| P-value                      | 0.999                 | 0.775    | 0.735              | 0.899                   | 0.735    | 0.899 |
| I <sup>2</sup> (%)           | 0.0                   | 0.0      | 0.0                | 0.0                     | 0.0      | 0.0   |
| P-heterogeneity              | 0.975                 | 0.938    | 0.997              | 0.999                   | 0.997    | 0.999 |
| <b>Body mass index</b>       |                       |          |                    |                         |          |       |
| No. of comparisons           | 3                     | 3        | 4                  | 2                       | 3        | 3     |
| SMD                          | 0.01                  | -0.09    | -0.09              | 0.06                    | -0.08    | 0.00  |
| 95%CI                        |                       |          |                    |                         |          |       |
| Lower                        | -0.24                 | -0.29    | -0.27              | -0.25                   | -0.29    | -0.25 |
| Higher                       | 0.27                  | 0.12     | 0.10               | 0.37                    | 0.13     | 0.25  |
| P-value                      | 0.920                 | 0.403    | 0.366              | 0.733                   | 0.446    | 0.995 |
| I <sup>2</sup> (%)           | 0.0                   | 0.0      | 0.0                | 0.0                     | 0.0      | 0.0   |
| P-heterogeneity              | 0.884                 | 0.980    | 0.998              | 0.999                   | 0.987    | 0.823 |

SMD: standard mean difference



**Figure 5.** Funnel plot of the cardamom supplementation on insulin.

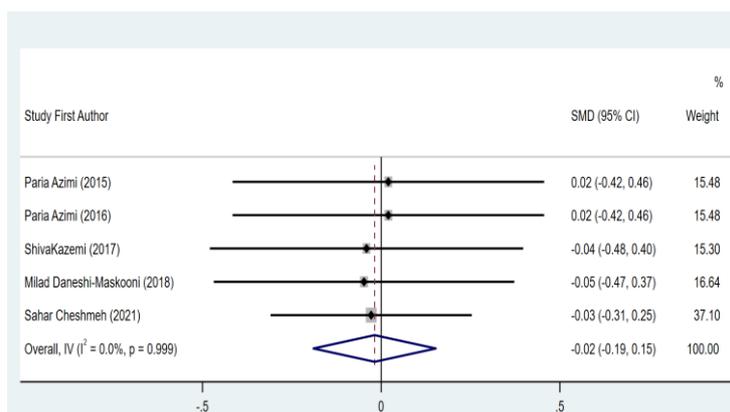


Figure 6. Forest plot of the cardamom supplementation on weight.

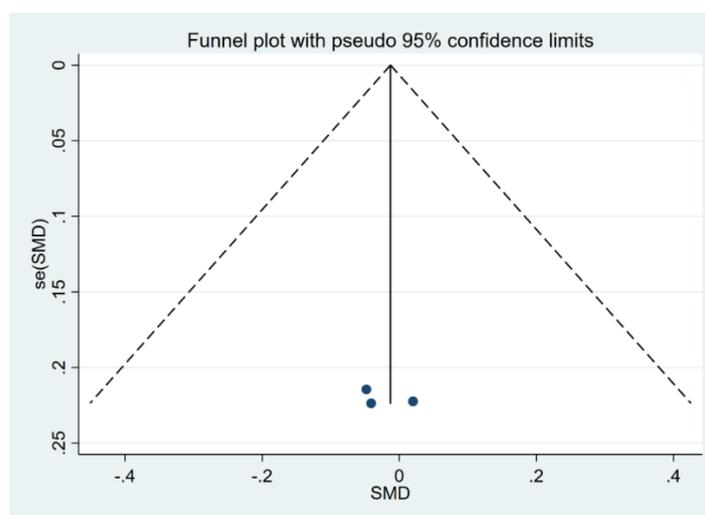


Figure 7. Funnel plot of the cardamom supplementation on weight.

### Effects of cardamom on BMI

Pooled 5 clinical trials together showed cardamom intake had no significant effect on BMI, with no heterogeneity as shown in **Figure 8**. Moreover, the results of the subgroup analysis are presented in **Table 3**. No publication bias was

discovered among the studies on BMI (Begg's  $P=0.327$  and Egger's  $P=0.309$ ). The funnel plot of included studies is expressed in **Figure 9**. Sensitivity analysis for studies that considered the effect of cardamom on BMI did not show any significant effect on SMD by excluding any studies.

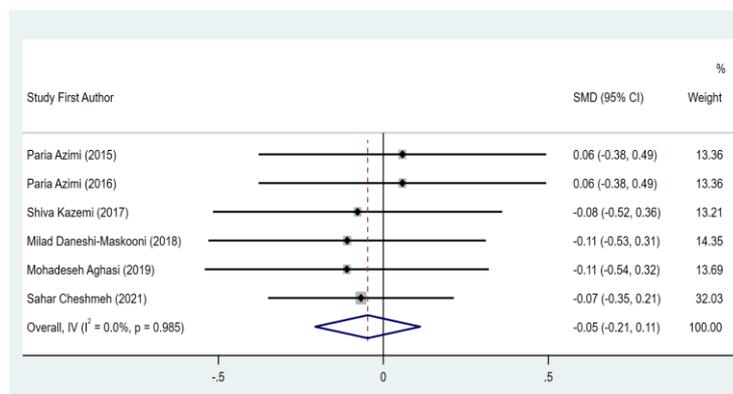


Figure 8. Forest plot of the cardamom supplementation on body mass index.

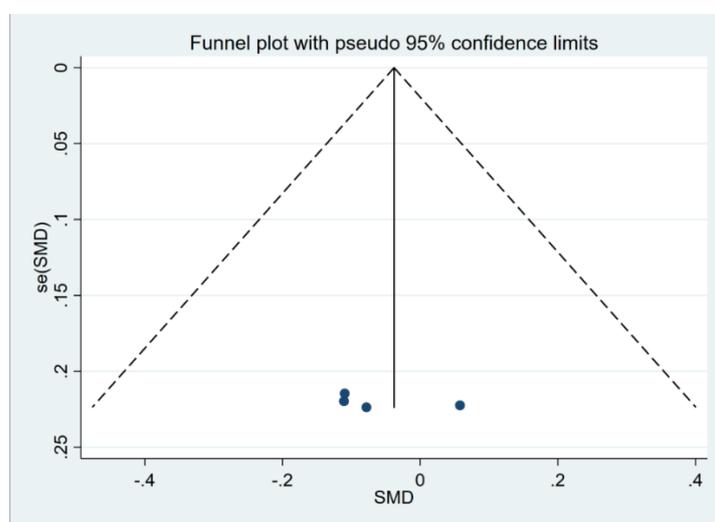


Figure 9. Funnel plot of the cardamom supplementation on body mass index.

## Discussion

Previous systematic reviews and meta-analyses did not consider all published studies on the effects of cardamom supplementation in human subjects, which may have introduced bias in the reported results. The study did not evaluate the effect of cardamom supplementation on insulin levels. Instead, it focused on updated systematic reviews and meta-analyses that examined the impact of cardamom intake on anthropometric variables and glycemic control. The findings indicated that cardamom intake improved serum insulin levels, but had no effect on weight, BMI, or FBG.

However, most of the included studies showed beneficial effects on FBG, but analysis in the present meta-analysis did not show any significant

effect. Subgroup analysis based on the duration of treatment, type of supplement, and mean age of subjects illustrated that although cardamom supplementation had a greater effect when subjects were younger than 50, via supplementation just with cardamom and more than 8 weeks, these effects were insignificant. Overall cardamom administration had a considerable effect on the serum insulin level. The finding of subgroup analysis according to the duration of supplementation, type of supplement, and mean age of participants showed that cardamom intake could decrease the level of serum insulin when the duration of treatment was more than 8 weeks in comparison to less than 8 weeks. In addition, cardamom exclusively had a significant effect on

insulin compared with cardamom with other ingredients; in addition, cardamom was more effective when the mean age of patients was under 50. However, it did not have any remarkable effect on weight. But, analysis based on the duration of treatment, type of supplement, and mean age of participants indicated that supplementation exclusively with cardamom for more than 8 weeks' in patients above 50 was more helpful in weight management. Based on the findings of the included studies, cardamom consumption did not have any substantial effect on BMI. Subgroup analysis revealed that cardamom had a more significant impact on BMI when supplementation was conducted for more than 8 weeks compared to less than 8 weeks. Additionally, cardamom was more effective than the combination of cardamom with other ingredients in patients younger than 50 years old compared to those aged 50 and older.

Negligible effect of cardamom on weight, BMI, and FBG in present study may be associated with different reasons including high heterogeneity among included studies to the quantity analysis, small number of studies in subgroup analysis which were conducted to eliminate heterogeneity among studies, mean of weight or BMI of participants in studies which were not very high (Aghasi *et al.*, 2019, Azimi *et al.*, 2014, Kazemi *et al.*, 2017), administration cardamom in combination with other substances in some studies (Azimi *et al.*, 2014, Azimi *et al.*, 2016, Li *et al.*, 2017), and studies that have been performed on samples with different disease (Azimi *et al.*, 2016, Daneshi-Maskooni *et al.*, 2018, Kazemi *et al.*, 2017). The contradictions among all the mentioned causes hinder the ability to make a definitive decision.

Obesity is a condition in the body in which adipose tissues are incremented and is considered an increase in body weight and accumulation of excessive fat (Fernández-Sánchez *et al.*, 2011). Given that metabolism energy expenditure reduces along with aging, aging is considered a risk factor for obesity (Ebrahimzadeh Attari *et al.*, 2018, Geisler and Müller, 2017), which may due to the cardamom supplementation being more effective in older patients. Most studies lasting more than 8

weeks that administered only cardamom for supplementation highlight its beneficial effects related to the type of intervention.

Polyphenols improved weight and glycemic control throughout the activation of SIRT-1; in fact, polyphenolic compounds elevated SIRT-1 expression (Chaudhary and Pfluger, 2009, Chung *et al.*, 2010). SIRT-1 belongs to a family of highly conserved nicotinamide adenine dinucleotide (NAD<sup>+</sup>)-dependent enzymes with deacetylate residues of acetylated lysine (Coppari, 2012). The findings of this study showed that cardamom intake did not have any significant effects on body weight but 3 out of 5 studies reported a decreasing trend in body weight (Aghasi *et al.*, 2019, Azimi *et al.*, 2016, Daneshi-Maskooni *et al.*, 2019). SIRT-1 contributes to weight control by regulating peroxisome proliferator-activated receptor gamma (PPAR- $\gamma$ ) and adipogenesis (Kitada and Koya, 2013). Furthermore, a critical stage in the activation of mitochondrial fatty acid oxidation is PGC-1- $\alpha$  deacetylation by Sirt-1 (Chaudhary and Pfluger, 2009). SIRT-1 also contributes to glucose homeostasis by a different mechanism such as SIRT-1 downregulates mitochondrial uncoupling proteins-2 (UCP-2) and deacetylates the FOXO transcription factors stimulate insulin secretion, protects from pancreatic  $\beta$ -cells against oxidative stress, release adiponectin and regulation of hepatic gluconeogenesis (Chaudhary and Pfluger, 2009, Kitada and Koya, 2013).

There are some limitations in the present systematic meta-analysis. First, the protocol of the present study did not register in PROSPERO due to we didn't report it in the text. Second, included studies in the current systematic meta-analysis were different in terms of target populations, type of supplement (exclusive cardamom vs. combination of cardamom with other substance) and duration of treatment; however, the authors tried to minimize heterogeneity via subgroup analysis. Third, they could not perform an analysis on the effects of cardamom intake on hemoglobin A1c because the included studies have not reported this variable; so, it is proposed that future studies evaluate the effects of cardamom intake on hemoglobin A1c. Fourth, all

the included clinical trials were carried out in Iran; therefore, the authors could not generalize the results of this meta-analysis worldwide, although statistical analysis did not show publication bias for included studies. Finally, despite that subgroup analysis, the authors could not find a source of heterogeneity in the analysis of results of the insulin. The present systematic meta-analysis had several strengths and was an updated systematic meta-analysis that included new trials to the analysis and considered all sources of heterogeneity for a better decision. Furthermore, based on the Cochrane collaboration's tool, overall quality of all the included studies were good.

### Conclusion

According to the findings of the present meta-analysis, cardamom intake might improve insulin levels but did not have any effects on weight, BMI, and FBG. It seems that further investigations with various dosages of cardamom, intervention period, nationality, and indicators need to decide about the potential effects of cardamom intake on weight reduction and glucose hemostasis; therefore, according to the results of this systematic meta-analysis cardamom intake is not recommended for glycemic control and weight management.

### Authors' contributions

O Nikpayam, G Sohrab, and M Najafi were involved in data curation. O Nikpayam and Najafi M conducted formal analysis. O Nikpayam, A Ostadrahimi designed the methodology and supervised the work. Nikpayam O, G Sohrab, and M Najafi wrote the original draft. All authors finally read the manuscript and approved it for publishing.

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### References

- Aghasi M, et al. 2019. Beneficial effects of green cardamom on serum SIRT1, glycemic indices and triglyceride levels in patients with type 2 diabetes mellitus: a randomized double-blind placebo controlled clinical trial. *Journal of the science of food and agriculture*. **99** (8): 3933-3940.
- Amin MN, et al. 2019. How the association between obesity and inflammation may lead to insulin resistance and cancer. *Diabetes & metabolic syndrome: clinical research & reviews*. **13** (2): 1213-1224.
- Amma K, Rani MP, Sasidharan I & Nisha VNP 2010. Chemical composition, flavonoid-phenolic contents and radical scavenging activity of four major varieties of cardamom. *International journal of biological & medical research*. **1** (3): 20-24.
- Azimi P, Ghiasvand R, Feizi A, Hariri M & Abbasi B 2014. Effects of cinnamon, cardamom, saffron, and ginger consumption on markers of glycemic control, lipid profile, oxidative stress, and inflammation in type 2 diabetes patients. *Review of diabetic studies*. **11** (3): 258.
- Azimi P, et al. 2016. Effect of cinnamon, cardamom, saffron and ginger consumption on blood pressure and a marker of endothelial function in patients with type 2 diabetes mellitus: A randomized controlled clinical trial. *Blood pressure*. **25** (3): 133-140.
- Babio N, Balanza R, Basulto J, Bulló M & Salas-Salvadó J 2010. Dietary fibre: influence on body weight, glycemic control and plasma cholesterol profile. *Nutricion hospitalaria*. **25** (3): 327-340.
- Barazzoni R, Gortan Cappellari G, Ragni M & Nisoli E 2018. Insulin resistance in obesity: an overview of fundamental alterations. *Eating and weight disorders-studies on anorexia, bulimia and obesity*. **23**: 149-157.
- Brunetti A, Chiefari E & Foti D 2014. Recent advances in the molecular genetics of type 2 diabetes mellitus. *World journal of diabetes*. **5** (2): 128.
- Chaudhary N & Pfluger PT 2009. Metabolic benefits from Sirt1 and Sirt1 activators. *Current opinion in clinical nutrition & metabolic care*. **12** (4): 431-437.
- Chen L, Magliano DJ & Zimmet PZ 2012. The worldwide epidemiology of type 2 diabetes mellitus-present and future perspectives. *Nature*

*reviews endocrinology*. **8** (4): 228-236.

- Cheshmeh S, et al.** 2021. Green cardamom plus low-calorie diet can decrease the expression of inflammatory genes among obese women with polycystic ovary syndrome: a double-blind randomized clinical trial. *Eating and weight disorders-studies on anorexia, bulimia and obesity*. **27** (2): 821-830.
- Chooi YC, Ding C & Magkos F** 2019. The epidemiology of obesity. *Metabolism*. **92**: 6-10.
- Chung S, et al.** 2010. Regulation of SIRT1 in cellular functions: role of polyphenols. *Archives of biochemistry and biophysics*. **501** (1): 79-90.
- Coppiari R** 2012. Metabolic actions of hypothalamic SIRT1. *Trends in endocrinology & metabolism*. **23** (4): 179-185.
- Cruz NG, et al.** 2013. The linkage between inflammation and type 2 diabetes mellitus. *Diabetes research and clinical practice*. **99** (2): 85-92.
- Daneshi-Maskooni M, et al.** 2018. Green cardamom increases Sirtuin-1 and reduces inflammation in overweight or obese patients with non-alcoholic fatty liver disease: a double-blind randomized placebo-controlled clinical trial. *Nutrition & metabolism*. **15** (1): 63.
- Daneshi-Maskooni M, et al.** 2019. Green cardamom supplementation improves serum irisin, glucose indices, and lipid profiles in overweight or obese non-alcoholic fatty liver disease patients: a double-blind randomized placebo-controlled clinical trial. *BMC complementary and alternative medicine*. **19** (1): 59.
- Deepa G, Ayesha S, Nishtha K & Thankamani M** 2013. Comparative evaluation of various total antioxidant capacity assays applied to phytochemical compounds of Indian culinary spices. *International food research journal*. **20** (4): 1711.
- DeFronzo RA, et al.** 2015. Type 2 diabetes mellitus. *Nature reviews disease primers*. **1** (1): 1-22.
- Ebrahimzadeh Attari V, et al.** 2018. A systematic review of the anti-obesity and weight lowering effect of ginger (*Zingiber officinale* Roscoe) and its mechanisms of action. *Phytotherapy research*. **32** (4): 577-585.
- Fatemeh Y, et al.** 2017. The effect of cardamom supplementation on serum lipids, glycemic indices and blood pressure in overweight and obese pre-diabetic women: a randomized controlled trial. *Journal of diabetes & metabolic disorders*. **16** (1): 40.
- Fernández-Sánchez A, et al.** 2011. Inflammation, oxidative stress, and obesity. *International journal of molecular sciences*. **12** (5): 3117-3132.
- Geisler C & Müller MJ** 2017. Impact of fat-free mass quality and detailed body composition on changes of resting energy expenditure with age. *Current nutrition reports*. **6**: 111-121.
- Guyatt GH, et al.** 2008. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *British medical journal*. **336** (7650): 924-926.
- Hu FB, et al.** 2001. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. *New England journal of medicine*. **345** (11): 790-797.
- Jamal A, Javed K, Aslam M & Jafri M** 2006. Gastroprotective effect of cardamom, *Elettaria cardamomum* Maton. fruits in rats. *Journal of ethnopharmacology*. **103** (2): 149-153.
- Kazemi S, et al.** 2017. Cardamom supplementation improves inflammatory and oxidative stress biomarkers in hyperlipidemic, overweight, and obese pre-diabetic women: A randomized double-blind clinical trial. *Journal of the science of food and agriculture*. **97** (15): 5296-5301.
- Kitada M & Koya D** 2013. SIRT1 in type 2 diabetes: mechanisms and therapeutic potential. *Diabetes & metabolism journal*. **37** (5): 315-325.
- Koh-Banerjee P, et al.** 2004. Changes in body weight and body fat distribution as risk factors for clinical diabetes in US men. *American journal of epidemiology*. **159** (12): 1150-1159.
- Li W, Wang M, Wu W, Bai Y & Wang Q** 2017. Curative effect of traditional Chinese medicine combined with metformin hydrochloride on diabetes and its effect on TNF- $\alpha$ , MCP-1 and NO. *Biomedical research*. **28** (19): 8529-8532.

- Page MJ, et al.** 2021. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *International journal of surgery*. **88**: 105906.
- Piché M-E, Tchernof A & Després J-P** 2020. Obesity phenotypes, diabetes, and cardiovascular diseases. *Circulation research*. **126 (11)**: 1477-1500.
- Rahman MM, et al.** 2017. Cardamom powder supplementation prevents obesity, improves glucose intolerance, inflammation and oxidative stress in liver of high carbohydrate high fat diet induced obese rats. *Lipids in health and disease*. **16 (1)**: 151.
- Schnurr TM, et al.** 2020. Obesity, unfavourable lifestyle and genetic risk of type 2 diabetes: A case-cohort study. *Diabetologia*. **63 (7)**: 1324-1332.
- Sinu PA & Shivanna K** 2007. Pollination ecology of cardamom (*Elettaria cardamomum*) in the Western Ghats, India. *Journal of tropical ecology*. **23 (4)**: 493-496.
- Tutunchi H, et al.** 2020. A systematic review of the association of neuregulin 4, a brown fat-enriched secreted factor, with obesity and related metabolic disturbances. *Obesity reviews*. **21 (2)**: e12952.
- World Health Organization** 2020. Overweight and obesity, [https://www.oecd.org/en/publications/health-at-a-glance-asia-pacific-2020\\_26b007cd-en.html](https://www.oecd.org/en/publications/health-at-a-glance-asia-pacific-2020_26b007cd-en.html).
- Zoungas S, et al.** 2014. Impact of age, age at diagnosis and duration of diabetes on the risk of macrovascular and microvascular complications and death in type 2 diabetes. *Diabetologia*. **57 (12)**: 2465-2474.