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Effect of chia product supplement on anthropometric measures, blood pressure, glycemic-related parameters, lipid profile and inflammatory indicators: A systematic and meta-analysis

Omid Nikpayam [a,b], Ali Jafari [c,d], Ehsan Safaei [e], Niayesh Naghshi [f], Marziyeh Najafi [f], Golbon Sohrab [f,*]

[a] Health Management and Social Development Research Center, Golestan university of medical sciences, Gorgan, Iran
[b] Department of Nutrition, School of Health, Golestan University of Medical Sciences, Golestan, Iran
[c] Student Research Committee, Department of Nutrition, School of Health, Golestan University of Medical Sciences, Gorgan, Iran
[d] Systematic Review and Meta-analysis Expert Group (SRMEG), Universal Scientific Education and Research Network (USERN), Tehran, Iran
[e] Food Science and Human Nutrition Department, University of Florida, Gainesville, FL, USA
[f] Clinical Nutrition and Dietetics Department, Faculty of Nutrition Sciences and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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ABSTRACT

The present comprehensive systematic review and *meta*-analysis aimed to determine the effects of chia seed supplementation on anthropometric and metabolic factors. A systematic search was conducted for relevant studies up to June 2023. The *meta*-analysis included fourteen clinical trials comprising 729 participants. Statistical analysis demonstrated that chia supplementation had a significant effect on SBP (SMD = −0.41; 95% CI: −0.59, −0.22), DBP (SMD = −0.41; 95% CI: −0.65, −0.17), TC (SMD = −0.30; 95% CI: −0.48, −0.13), LDL-C (SMD = −0.30; 95% CI: −0.50, −0.11), and TG (SMD = −0.20; 95% CI: −0.38, −0.02), while the analysis did not illustrate any significant effect on other factors. The heterogeneity among included studies in terms of duration, dose, and participants is a major limitation of the present study. Based on the current *meta*-analysis results, chia supplementation could have beneficial effects on dyslipidemia and hypertension, helping to reduce the risk of cardiovascular disease.

1. Introduction

The prevalence of chronic diseases has been steadily increasing, posing significant challenges to both society and health systems worldwide (Anderson & Durstine, 2019). Optimal management of anthropometric measurements, blood pressure, glycemic-related parameters, lipid profiles, and inflammatory indicators plays a crucial role in maintaining overall health and well-being (Jenkins et al., 2002). These parameters serve as important indicators of metabolic health and are closely linked to the risk of developing chronic conditions, such as obesity, cardiovascular disease, and diabetes (Goodpaster & Sparks, 2017). As a result, there is a growing interest in identifying effective interventions that can improve these health markers and alleviate the burden of chronic diseases (Soriano et al., 2020). In recent years, there has been a noticeable surge in people's attention towards natural, herbal products, and dietary supplements as potential means of enhancing health outcomes (Thakkar et al., 2020). Among these products, chia seed supplementation has gained significant attention (Teoh et al., 2018).

Chia (Salvia hispanica L.) is an annual herbaceous plant belonging to the Lamiaceae family, characterized by its distinctive botanical traits (da Silva et al., 2017). Chia exhibits an impressive nutritional composition, containing approximately 486 kcal/100 g, 16% protein, 30% total lipids, 42% carbohydrates, and 34% dietary fiber, along with high concentrations of essential micronutrients such as polyphenols, carotenoids, vitamins, minerals, flavonoids, anthocyanins, and polyunsaturated fatty acids (PUFAs). Notably, chia seeds are renowned as one of the richest plant sources of omega-3 (-3) fatty acids, particularly alpha-linolenic acid (ALA), which constitutes around 60% of all fatty acids (da Silva et al., 2017; Kulczyński, Kobus-Cisowska, Taczanowski, Kmiecik, & Gramza-Michałowska, 2019; Montes Chañi et al., 2018; Silva, Verneque, Mota, & Duarte, 2021). Extensive research conducted on humans and animals over the past two decades has associated chia

* Corresponding author.
E-mail addresses: golbonsohrab@yahoo.com, golbonsohrab@sbmu.ac.ir (G. Sohrab).

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seeds with improvements in insulin resistance, abnormal lipid profiles, glucose tolerance, and even obesity (Chicco, D'Alessandro, Hein, Oliva, & Lombardo, 2009; Coates, 2011; da Silva et al., 2017; Ho et al., 2013; Marineli Rda et al., 2015; Rui et al., 2018; V. Vuksan et al., 2017; V. Vuksan et al., 2010). Furthermore, current evidence suggests that the hypoglycemic, antibacterial, hypotensive, and immunostimulatory properties of chia seed components contribute to the enhancement of blood lipid profiles (Kulczyński et al., 2019).

Previous studies have shown the efficacy of chia seed supplementation in improving anthropometric and lipid profiles (Oliveira-de-Lira et al., 2018; V. Vuksan et al., 2017). In addition, in-vivo and in-vitro studies have revealed the beneficial effects of chia on insulin resistance, lipid oxidation and oxidative stress (LUCINI MAS, Sabatino, Theumer, Wunderlin, & Baroni; Maturana et al., 2023). Also in a review studies chia has been proposed as a functional food which improve the health status (Agarwal et al., 2023; Jeelani et al., 2023). In a clinical trial, Quaresma et al. reported that chia flour intake had no significant effects on anthropometric indices, fasting blood glucose, and insulin levels in adult women with central obesity (Quaresma, de Oliveira Siais, Grangeiro É, & Rosado, 2022). Similarly, another trial conducted in this field showed no significant effect in improving the lipid profiles of individuals undergoing chia intervention (Nieman et al., 2009). Additionally, a systematic review and *meta*-analysis published in 2018 found no significant effects of chia seed supplementation on anthropometric or glycemic-related parameters. However, subgroup analysis suggested that higher doses of chia seeds were significantly associated with lower postprandial blood glucose levels (Teoh et al., 2018). Since the publication of this *meta*-analysis (Teoh et al., 2018), several clinical trials investigating the effects of chia seed supplementation on anthropometric and glycemic-related parameters have been published, potentially influencing the overall effect size. In addition, based on the supplementary file of the previous *meta*-analysis (Teoh et al., 2018) the number of studies entered into the final analysis for each variable was very low which resulted in not providing an overall effect size from all available effect sizes and, demonstrating a comprehensive conclusion associated with the effects of chia seed on the anthropometric and metabolic factors. Due to it, the present systematic review *meta*-analysis tries to consider all of the studies related to the effects of chia on the anthropometric indices and metabolic factors to provide a consistent conclusion.

Understanding the effects of chia product supplementation on anthropometric measures, glycemic control, blood pressure, lipid profile and inflammatory parameters can have significant implications for individuals seeking natural interventions to optimize their health. Furthermore, the findings of this systematic review and *meta*-analysis can provide valuable insights to healthcare professionals, policymakers, and researchers, guiding future research and interventions related to chia product supplementation. By addressing the research gaps in the existing literature and providing a comprehensive analysis, this study aims to contribute to the growing body of knowledge in the field and provide a valuable resource for the readers and potential consumers of chia products.

2. Method

This study adhered to the guidelines provided in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) (Moher, Liberati, Tetzlaff, Altman, & PRISMA Group*, 2009), as well as followed the recommendations outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al., 2019).

2.1. Registration

The systematic review and *meta*-analysis were registered in PROSPERO (International Prospective Register of Systematic Reviews), a recognized database for systematic reviews. The registration number CRD42023431811 was obtained to ensure transparency and adherence to the review process.

2.2. Strategy and data sources

A comprehensive systematic search was conducted to identify relevant studies from multiple databases. The search was performed from the inception of the databases until June 2023. The databases searched included PubMed, Scopus, and Web of Science. Additionally, alternative sources such as ProQuest for dissertations and theses, conference papers, and Google Scholar were explored. The search strategy utilized a combination of keywords and search terms related to chia product supplementation, anthropometric measures, blood pressure, glycemic-related parameters, lipid profile, and inflammatory indicators. The search queries were created using Boolean operators (e.g., AND, OR) to ensure robustness. Our search strategy is detailed in Supplementary Table 1. The titles, abstracts, and full texts of the retrieved studies were screened for eligibility by two independent reviewers. Any discrepancies were resolved through consensus or the involvement of a third reviewer.

2.3. Inclusion and exclusion criteria and data extraction

Studies were selected for inclusion in the *meta*-analysis based on predetermined criteria, considering the following factors: (a) only randomized controlled trials (RCTs) were included to ensure high-quality evidence, (b) studies involving human participants of any gender, and health status were considered, (c) studies investigating the effect of chia product supplementation, alone or in form of co-supplementation, on anthropometric measures, blood pressure, glycemic-related parameters, lipid profile, and inflammatory indicators were included, (d) studies reporting relevant outcomes, such as changes in body weight, body mass index (BMI), waist circumference, blood pressure, fasting blood glucose levels, lipid profile parameters, and inflammatory markers, were considered. Studies were excluded from the analysis based on the following criteria: (a) non-human studies or studies conducted on animal models, (b) non-English articles, and (c) lack of relevant data or outcomes of interest.

A standardized data extraction form was used to extract relevant data from the selected studies. The extraction process involved collecting information on study design, sample size, intervention duration, participant characteristics, chia product supplementation details (dosage, frequency, and duration), outcome measures, and other relevant data necessary for the *meta*-analysis.

2.4. Data synthesis and quality assessment

The titles and abstracts of all records obtained through the search strategy were carefully examined by two reviewers (A.J and N.N), under the supervision of a senior reviewer (O.N), in accordance with the selection criteria. Detailed information regarding the studies, including study size, outcome measures, participants' baseline characteristics, details of the intervention and comparison groups, as well as the time points for data collection and outcome reporting, were extracted from the full texts of the selected studies. This extraction process was carried out by the same two reviewers (A.J and N.N), and the extracted information was cross-checked for accuracy and consistency.

To evaluate the methodological quality of the included studies, we used the Cochrane Collaboration tool (Higgins et al., 2019), as described by Higgins (Higgins et al., 2011). This tool enables the assessment of the risk of bias in the studies. The reviewers categorized the methodological quality of each study as "low risk," "high risk," or "unclear risk" based on the criteria provided by the Cochrane Collaboration tool. This assessment allowed for a comprehensive evaluation of the quality and potential biases in the included studies.

2.5. Statistical analysis

The effect size was assessed using the standard mean difference (SMD), specifically Hedges' g, accompanied by 95% confidence intervals (CI). In cases where the studies did not provide the standard deviations (SDs) for changes and only reported for baseline and end of the trial, the SD for net change was calculated based on the Follmann method (Follmann, Elliott, Suh, & Cutler, 1992), assuming a correlation coefficient (R) of 0.5. In cases where the Standard error (SE) was provided, SD was assigned based on the follow formula, SD: SE × sqrt (n), where n is the sample size in each group. For the *meta*-analysis, a random-effects model (DerSimonian and Laird) was employed to combine the data, based on the results of the heterogeneity test. The assessment of heterogeneity involved the visual inspection of forest plots, the $\chi 2$ test to evaluate the associated p-value, and the calculation of the I2 statistic. Substantial statistical heterogeneity was considered if the p-value was<0.05 or if the I2 value exceeded 50%. Sensitivity analyses were performed to evaluate the robustness of the findings. Subgroup analyses based on study characteristics or exclusion of studies with a high risk of bias were conducted to assess the impact of these factors on the overall results. Additionally, to evaluate publication bias, Begg's and Egger's tests were applied, accompanied by funnel plots for visual examination of asymmetry. To conduct the statistical analyses, Stata software version 15 was utilized.

3. Result

3.1. Study selection

A total of 1807 studies were obtained from electronic database searches. After removing duplicates (n = 382), 1425 articles remained. Subsequently, 1408 articles were excluded based on an evaluation of

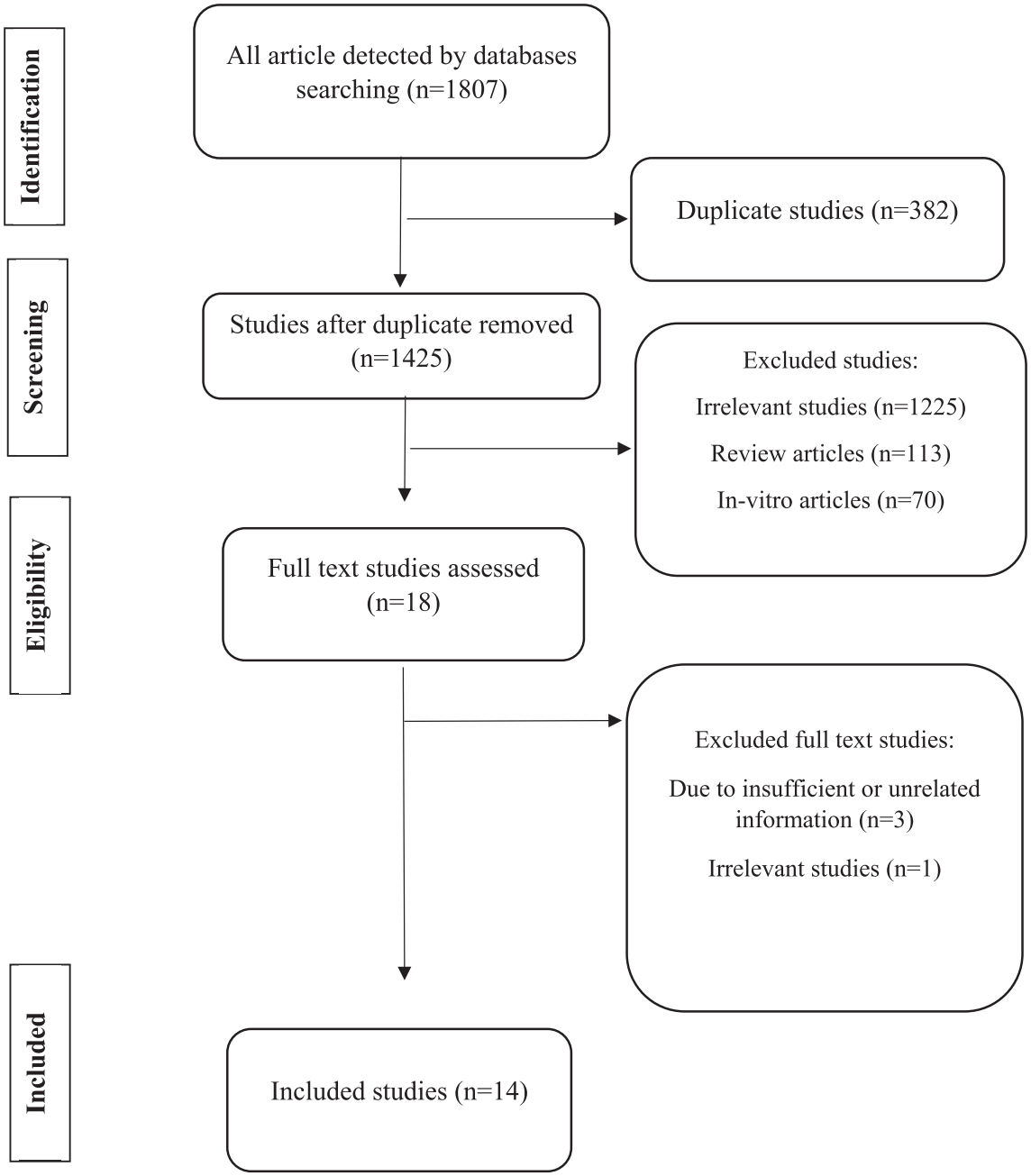

Fig. 1. Literature search and study selection process.

their titles and abstracts. Out of the initial pool, 18 studies were considered relevant and underwent a detailed examination in their full-text form. The studies excluded from the full-text review, along with the reasons for their exclusion, can be found in Supplementary Table 2. Ultimately, 14 studies were included in the analysis. Fig. 1 provides the PRISMA flow diagram. The general characteristics of the included studies are outlined in Table 1. The total number of participants in all the included studies was 729 (Intervention = 366 and control = 363), and they were included in the final analysis. The treatment duration varied between 8 and 24 weeks across the studies. In terms of quality assessment, seven trials were identified as having a high risk of bias (Guevara-Cruz et al., 2012; Nieman et al., 2009; Nieman et al., 2012; Laura Sampaio Quaresma, de Oliveira Siais, Grangeiro, & Rosado, 2023; Vázquez-Manjarrez et al., 2021; Vladimir Vuksan et al., 2007; Zbinden-Foncea et al., 2023), while six trials were considered to have either some concerns or a low risk of bias (Alwosais, Al-Ozairi, Zafar, & Alkandari, 2021; Oliveira-de-Lira et al., 2018; Toscano et al., 2014; Toscano, Toscano, Tavares, da Silva, & Silva, 2015; V Vuksan et al., 2017; Zurbau et al., 2021) in terms of quality (Table 2).

3.2. Effects of chia supplement on anthropometric measures

Fig. 2 outlines the impact of chia supplements on anthropometric measures. Eight articles examined the effect of chia supplements on BMI and concluded that there was no significant effect (SMD = −0.1; 95% CI: −0.33, 0.13, P = 0.401). Furthermore, there was no heterogeneity among the studies (I^2: 8.3%, P = 0.366).

A total of twelve trials assessed the effects of chia supplements on body weight. The analysis indicated that chia supplements did not have a significant effect on weight (SMD = −0.08; 95% CI: −0.27, 0.11, P = 0.416), and there was no heterogeneity among the studies (I2: 0.00%, P = 0.984).

In eight trials investigating the impact of chia supplements on waist circumference (WC), the *meta*-analysis revealed that chia supplements did not affect WC (SMD = − 0.20; 95% CI: −0.43, 0.02, P = 0.079). Similarly, there was no heterogeneity among these studies (I^2: 0.00%, P = 0.433).

Additionally, eight trials examined the effect of chia supplements on body fat. The *meta*-analysis showed that chia supplements did not have an impact on body fat (SMD = 0.02; 95% CI: −0.21, 0.24, P = 0.888), and no heterogeneity was observed among the studies (I^2: 0.00%, P = 0.826).

The sensitivity analysis conducted for BMI, weight, WC, and body fat revealed that the exclusion of any of the studies did not affect the overall findings. Additionally, there was no evidence of publication bias for BMI (Begg's P = 0.327 and Egger's P = 0.242), weight (Begg's P = 0.532and Egger's P = 0.459), WC (Begg's P = 0.624 and Egger's P = 0.804), and body fat (Begg's P = 0.652 and Egger's P = 0.721).

3.3. Effects of chia supplement on blood pressure

Fig. 3 provides an overview of the impact of chia supplements on blood pressure. Thirteen studies were included in the analysis of chia supplement's effect on systolic blood pressure (SBP), revealing a significant reduction (SMD = −0.41; 95% CI: −0.59, −0.22, P < 0.0001), but there was high heterogeneity among the included studies (I2: 63.7%, P = 0.001).

The overall findings from a *meta*-analysis of nine trials assessing the effect of chia supplements on diastolic blood pressure (DBP) indicated a significant reduction (SMD = −0.41; 95% CI: −0.65, −0.17, P:0.001). However, high heterogeneity was observed among these studies (I2: 92.4%, P < 0.0001).

The sensitivity analysis demonstrated that the pooled results for SBP and DBP did not change significantly when any of the studies were removed. Furthermore, there was no evidence of publication bias in the studies examining SBP (Begg's P = 0.128 and Egger's P = 0.108) and DBP (Begg's P = 0.851 and Egger's P = 0.170).

3.4. Effects of chia supplement on glycemic-related parameters

Fig. 4 provides an overview of the impact of chia supplements on glycemic-related parameters. Overall, fourteen studies investigated the effect of chia supplements on fasting blood glucose (FBG), and the *meta*-analysis results showed that chia supplements did not have a significant effect on FBG (SMD = −0.03; 95% CI: −0.2, 0.14, P = 0.723), with high heterogeneity among the studies (I2: 73.2%, P < 0.0001).

Five trials reported the effect of chia supplements on HbA1c levels. The pooled effect size of these five studies did not reveal a significant reduction in HbA1c (SMD = −0.20; 95% CI: −0.45, 0.05, P = 0.117), with no heterogeneity among the studies (I2: 20.8%, P = 0.282).

The effect of chia supplements on insulin levels was evaluated in five randomized controlled trials (RCTs). According to the analysis findings,

Table 1
Characteristics of trials included in the *meta*-analysis.

First author, Year	Country	Study population	Mean age (Year) In/P	Participant (N) In/P	Dose of supplement	Type of supplement	Duration of treatment
Zbinden-Foncea, 2023	Chile	Healthy young	22.4 ± 3.1	6/6	50 gr	chia flour	8 weeks
Sampaio Quaresma, 2022	Brazil	Obese women	NR	11/9	30 gr	Chia flour	12 weeks
Alwosais, 2021	Kuwait	T2DM	51.8/52.7	20/22	40 gr	Chia seed	12 weeks
Vazquez-Manjarrez, 2021	Mexico	Hypercholesterolemia	NR	32/30	4 gr	Chia seed	8 weeks
Zurbau, 2021	Canada	T2DM	60.0/59.0	52/52	60 gr	Chia seed	24 weeks
Guevara-Cruz, 2019	Mexico	Healthy young	NR	11/10	4 gr	Chia seed	8 weeks
Guevara-Cruz, 2019	Mexico	MetS	NR	18/17	4 gr	Chia seed	8 weeks
Guevara-Cruz, 2019	Mexico	MetS and obese	NR	111/9	4 gr	Chia seed	8 weeks
Oliveira-de-Lira, 2018	Pernambuco	Obese women	35.00/31.58	19/19	6 gr	Chia oil	8 weeks
Vuksan, 2017	Canada	T2DM	60.00/60.00	27/31	30 gr/1000 Kcal	Salba-chia	24 weeks
Toscano, 2015	Brazil	Obese or overweight	48.8/ 51.4	19/7	35 gr	Chia flour	12 weeks
Toscano, 2014	Brazil	Hypertensive	48.8/51.4	19/7	35 gr	Chia flour	12 weeks
C.Nieman, 2012	USA	Obese or overweight	60.40/58.40	16/26	25 gr	Whole chia seed	10 weeks
C.Nieman, 2012	USA	Obese or overweight	57.2/58.40	14/26	25 gr	milled chia seed	10 weeks
Guevara-Cruz, 2012	Mexico	MetS	NR	32/35	4 gr	Chi seed	8 weeks
C.Nieman, 2009	USA	Overweight	NR	14/14	50 gr	Chia seed	12 weeks
C.Nieman, 2009	USA	Overweight	NR	25/23	50 gr	Chia seed	12 weeks
Vuksan, 2007	Canada	T2DM	64.00/64.00	20/20	37 gr	Salba chia	12 weeks

Abbreviations: In, Intervention; MetS, Metabolic syndrome; NR, No Response; P, Placebo; T2DM, Type 2 Diabetes Mellitus.

Table 2
Quality of trials included in the *meta*-analysis.

Study, year	Random sequence generation	Allocation concealment	Blinding of participants & personnel	Blinding of outcome assessment	Incomplete outcome data	Selective outcome reporting	Other sources of bias	Overall quality
Zbinden-Foncea, 2023	L	L	H	H	L	L	L	High risk of bias
Sampaio Quaresma, 2022	L	U	H	H	H	L	L	High risk of bias
Alwosais, 2021	L	L	U	L	L	L	L	Low risk of bias
Vazquez-Manjarrez, 2021	L	L	L	H	H	L	L	High risk of bias
Zurbau, 2021	L	L	L	H	L	L	L	Fair
Guevara-Cruz, 2019	L	L	L	H	L	L	L	Fair
Oliveira-de-Lira, 2018	L	U	L	H	L	L	L	Fair
Vuksan, 2016	L	L	L	H	L	L	L	Fair
Toscano, 2015	L	U	L	H	L	L	L	Fair
Toscano, 2014	L	U	L	H	L	L	L	Fair
C.Nieman, 2012	L	H	L	H	L	L	L	High risk of bias
Guevara-Cruz, 2012	L	L	L	H	H	L	L	High risk of bias
C.Nieman, 2009	L	H	H	H	L	L	L	High risk of bias
Vuksan, 2007	L	L	H	H	U	L	L	High risk of bias

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

chia supplements did not have a significant effect on insulin levels (SMD = 0.07; 95% CI: −0.17, 0.32, P = 0.568). Moreover, there was no heterogeneity observed among the included studies (I2: 32.4%, P = 0.205).

The sensitivity analysis revealed that the pooled effect sizes of FBG, HbA1c, and insulin did not significantly change when any of the studies were removed. Additionally, there was no evidence of publication bias in the studies examining FBG (Begg's P = 0.938 and Egger's P = 0.596), HbA1c (Begg's P = 0.851 and Egger's P = 0.647), and insulin (Begg's P = 0.624 and Egger's P = 0.666).

3.5. Effects of chia supplement on lipid profile

Fig. 5 provides an overview of the effects of chia supplements on lipid profile. The impact of chia supplements on total cholesterol (TC) levels was assessed in eleven trials, and the pooled standardized mean difference (SMD) analysis showed that chia supplements had a significant effect on TC (SMD = −0.30; 95% CI: −0.48, −0.13, P = 0.001), with no heterogeneity observed among the studies (I^2: 26.2%, P = 0.172).

A total of twelve studies investigated the effect of chia supplements on LDL cholesterol (LDL-C) levels. The *meta*-analysis results demonstrated a significant reduction in LDL-C (SMD = −0.30; 95% CI: −0.50, −0.11, P = 0.002), although heterogeneity was observed among the studies (I^2: 62.7%, P = 0.002).

The pooled effect size of twelve studies indicated a significant decrease in HDL cholesterol (HDL-C) concentration with chia supplements (SMD = −0.28; 95% CI: −0.47, −0.09, P = 0.005), and there was no heterogeneity observed among the studies (I^2: 77.2%, P = 0.001).

Out of thirteen studies, thirteen trials reported the effect of chia supplements on triglyceride (TG) concentration. The *meta*-analysis showed that chia supplement significantly reduces the levels of TG (SMD = −0.20; 95% CI: −0.38, −0.02, P = 0.027), and high heterogeneity was observed among the studies (I^2: 67.1%, P = 0.000).

The sensitivity analysis for TC, LDL-C, HDL-C, and TG indicated that excluding any of the studies did not significantly affect the pooled effect size. Additionally, there was no evidence of publication bias for TC (Begg's P = 0.815 and Egger's P = 0.779), LDL-C (Begg's P = 0.404 and Egger's P = 0.838), HDL-C (Begg's P = 0.404 and Egger's P = 0.632), and TG (Begg's P = 0.655 and Egger's P = 0.711).

3.6. Effects of chia supplement on inflammatory factors

Fig. 6 provides information on the effects of chia supplements on inflammatory factors. In total, six studies investigated the effect of chia supplements on high-sensitivity C-reactive protein (hs-CRP). The *meta*-analysis results indicated that chia supplements did not have a significant effect on hs-CRP (SMD = −0.09; 95% CI: −0.34, 0.16, P = 0.495), with high heterogeneity observed between the studies (I^2: 93.6%, P < 0.0001).

Four trials reported the effect of chia supplements on tumor necrosis factor-alpha (TNF-α) levels. The pooled effect size of these five studies showed no significant reduction in TNF-α with chia supplements (SMD = −0.02; 95% CI: −0.34, 0.30, P = 0.908), and there was no heterogeneity among the studies (I2: 0.00%, P = 0.915).

The effect of chia supplements on interleukin-6 (IL-6) levels was evaluated in four RCTs. According to the analysis findings, chia supplements did not have a significant effect on IL-6 levels (SMD = 0.04; 95% CI: −0.28, 0.35, P = 0.028). Additionally, there was no heterogeneity observed among the included studies (I2: 0.00%, P = 0.992).

The sensitivity analysis showed that the pooled effect sizes of hs-CRP, TNF-α, and IL-6 did not significantly change when any of the studies were removed. Furthermore, there was no evidence of publication bias for hs-CRP (Begg's P = 0.404 and Egger's P = 0.009), TNF-α (Begg's P = 1.000 and Egger's P = 0.804), and IL-6 (Begg's P = 0.327 and Egger's P = 0.088).

3.7. Subgroup analysis

Table 3 provides an overview of the subgroup analysis based on treatment duration, type of supplementation and the dosage of the chia supplement. The results indicated that chia supplementation had a more favorable effect on SBP in studies with a treatment duration of over 10

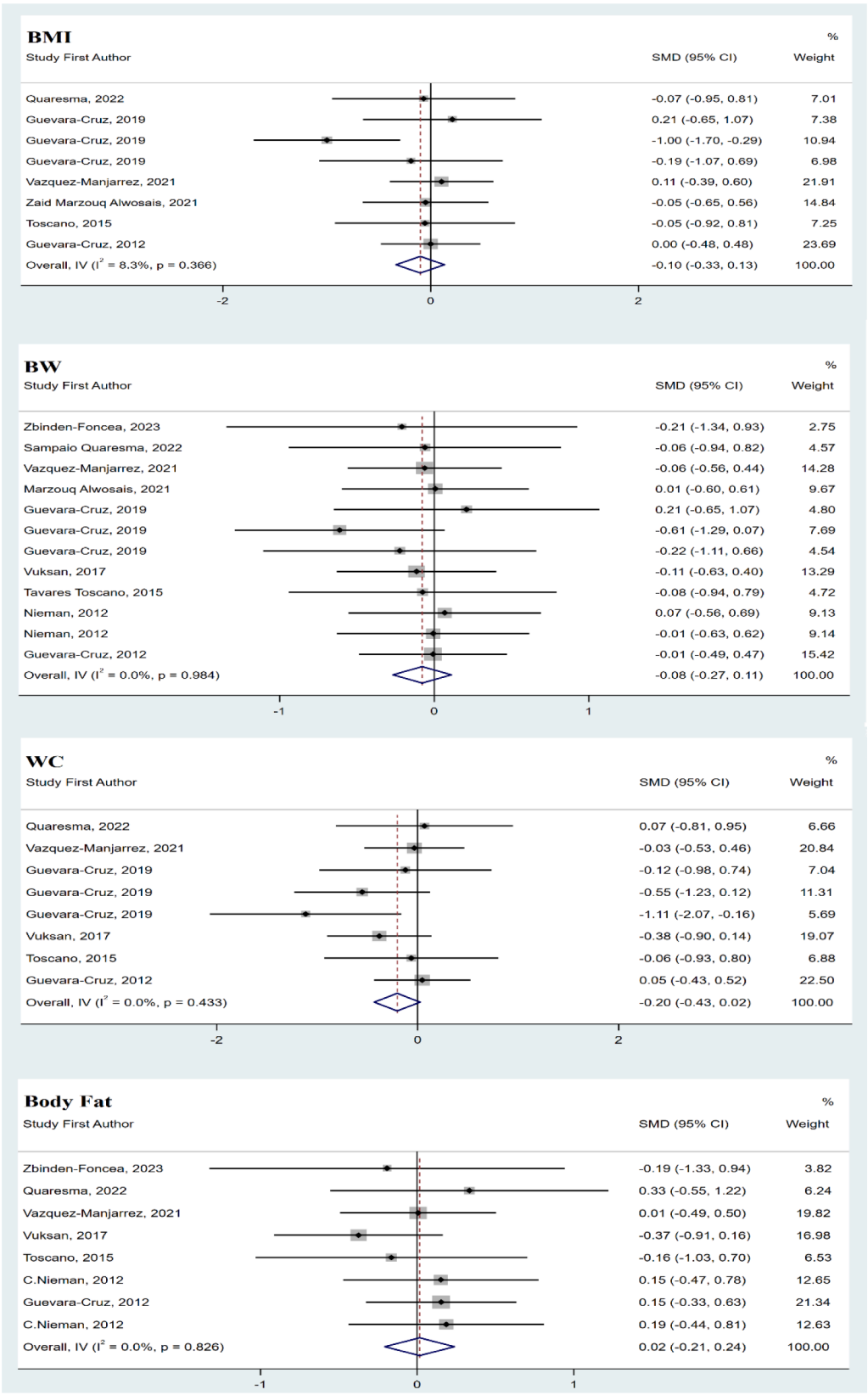

Fig. 2. Forest plot of the effects of chia product supplement on anthropometric measures.

weeks, a supplement dose>25 gr/day, and when chia products were administered alone. Additionally, co-supplementation with chia resulted in a significant reduction in FBG. However, unexpected results were observed in terms of DBP, TC, and LDL-C, where a more favorable influence of chia supplementation was observed in studies with a treatment duration ≤ 10 weeks and a supplement dose ≤ 25 gr/day.

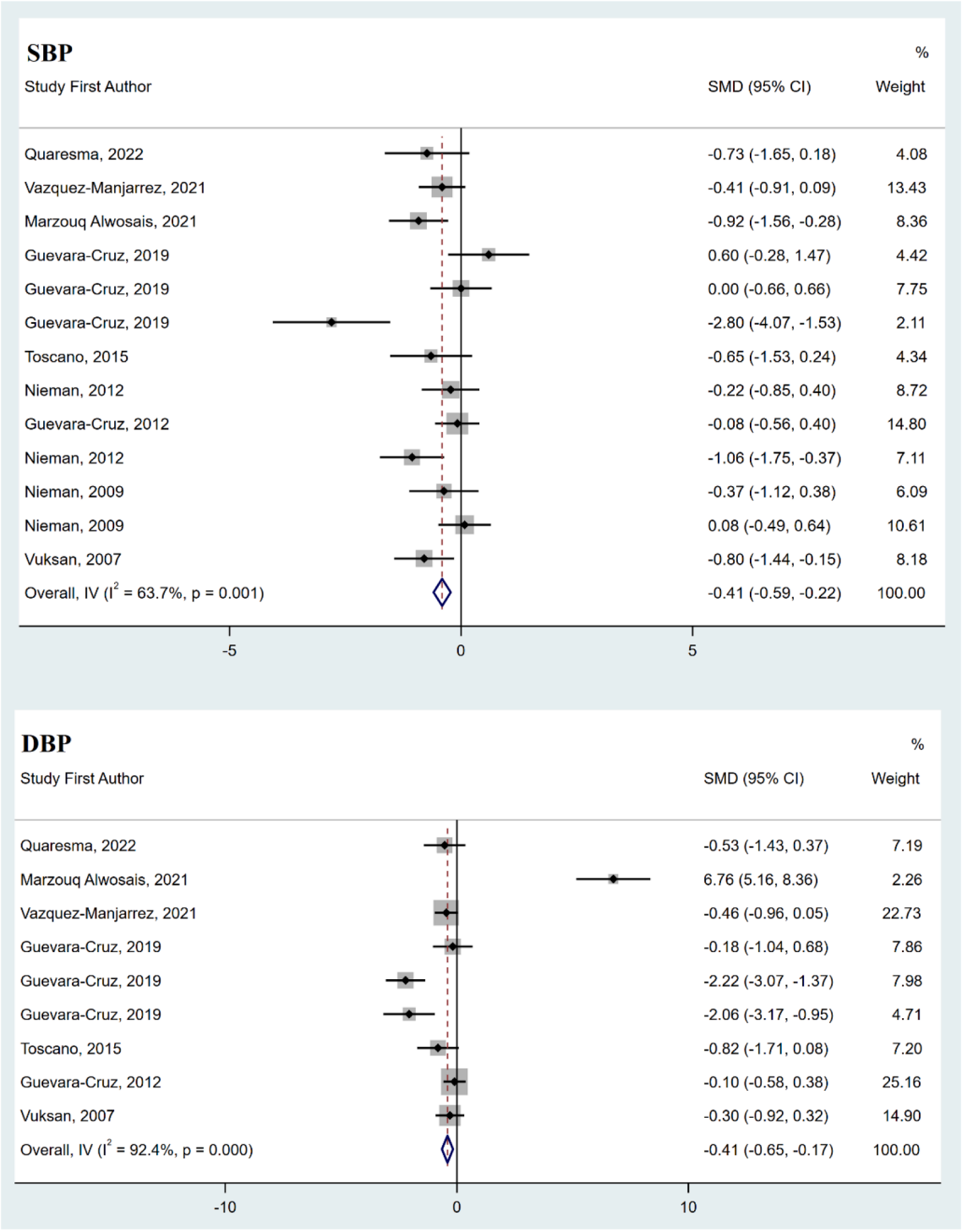

Fig. 3. Forest plot of the effects of chia product supplement on blood pressure.

4. Discussion

The present systematic review and *meta*-analysis of 14 RCTs, involving 729 subjects, investigated the available evidence on the effects of chia products on anthropometric measures, blood pressure, glycemic-related parameters, lipid profile, and inflammatory indicators. The results obtained from the pooled analysis suggested that chia product supplementation, in comparison with placebo/control, led to a significant reduction in SBP and DBP, TC, LDL-C, HDL-C and TG. However, our results suggested that chia product supplementation did not have a significant impact on anthropometric measures, glycemic-related parameters, and inflammatory factors. The results of subgroup analysis indicated that a more favorable effect of chia supplementation on SBP was observed in studies with a duration of treatment > 10 weeks, studies with a dose of supplement > 25 mg/day, and studies that administered chia products alone. With regards to these results, it seems that chia products may require more time and higher doses to exert their full effects on SBP. In fact, over an extended period, the cumulative effects of the bioactive compounds, such as omega-3 fatty acids and fiber in chia products might become more pronounced. We also observed a

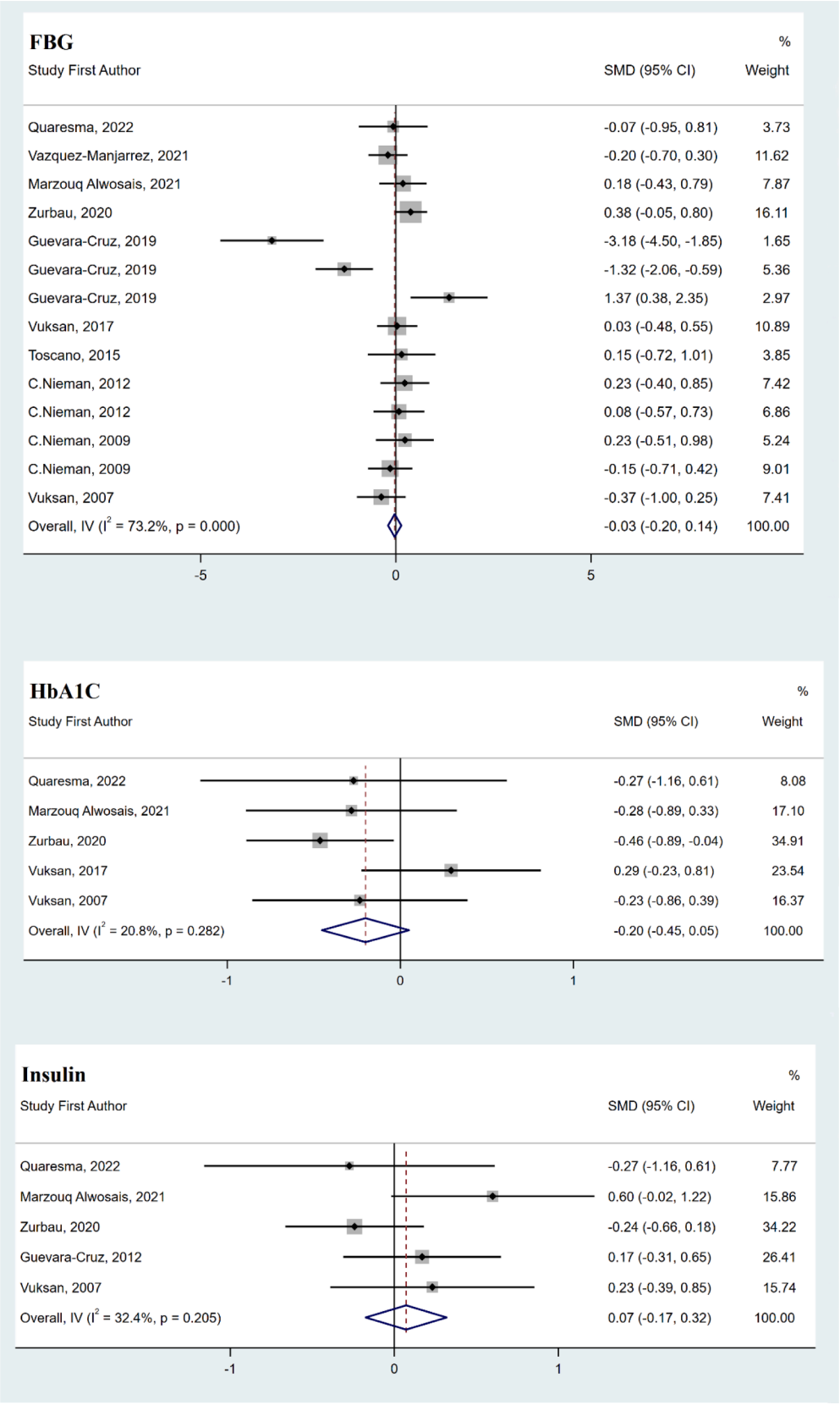

Fig. 4. Forest plot of the effects of chia product supplement on glycemic indices.

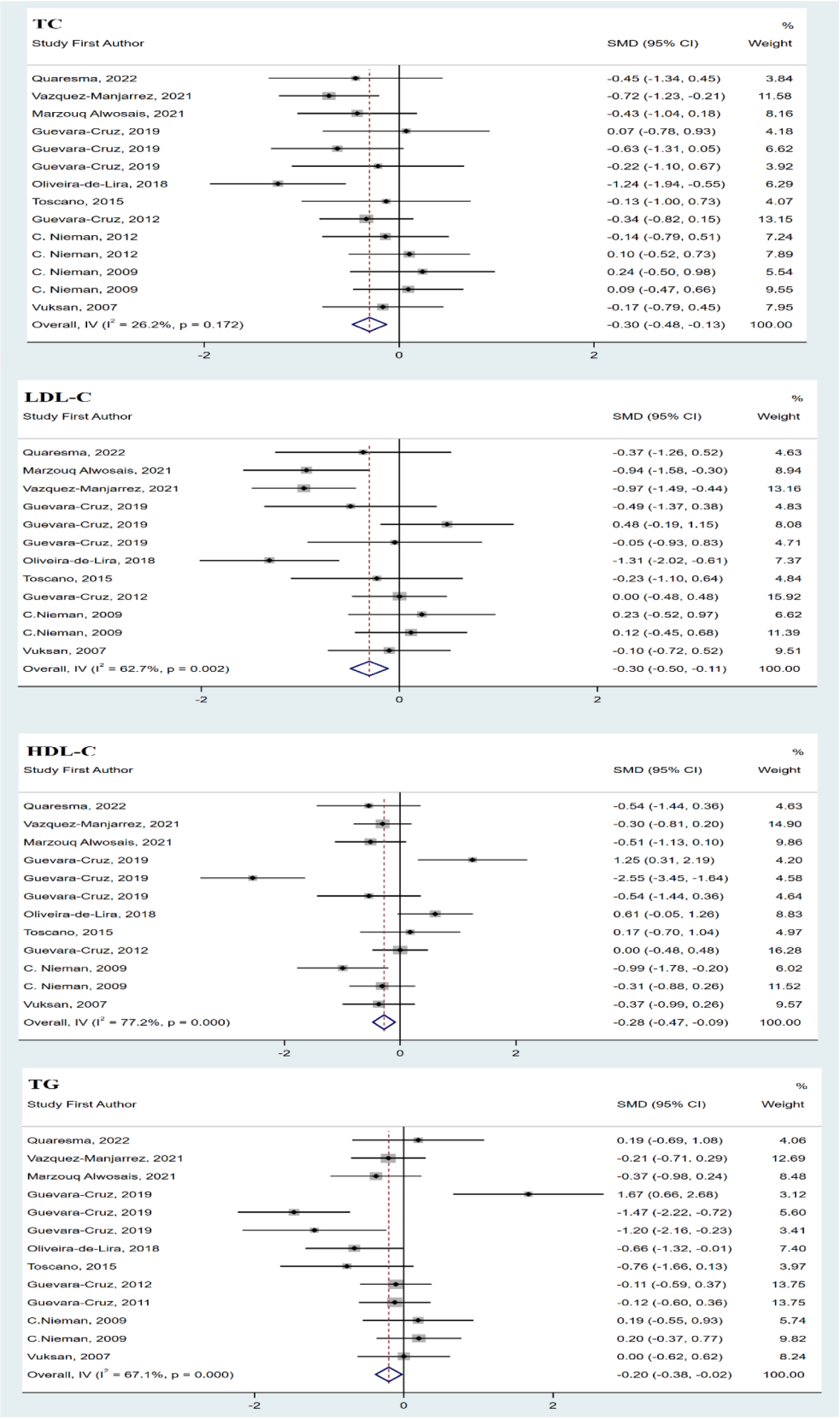

Fig. 5. Forest plot of the effects of chia product supplement on lipid profile.

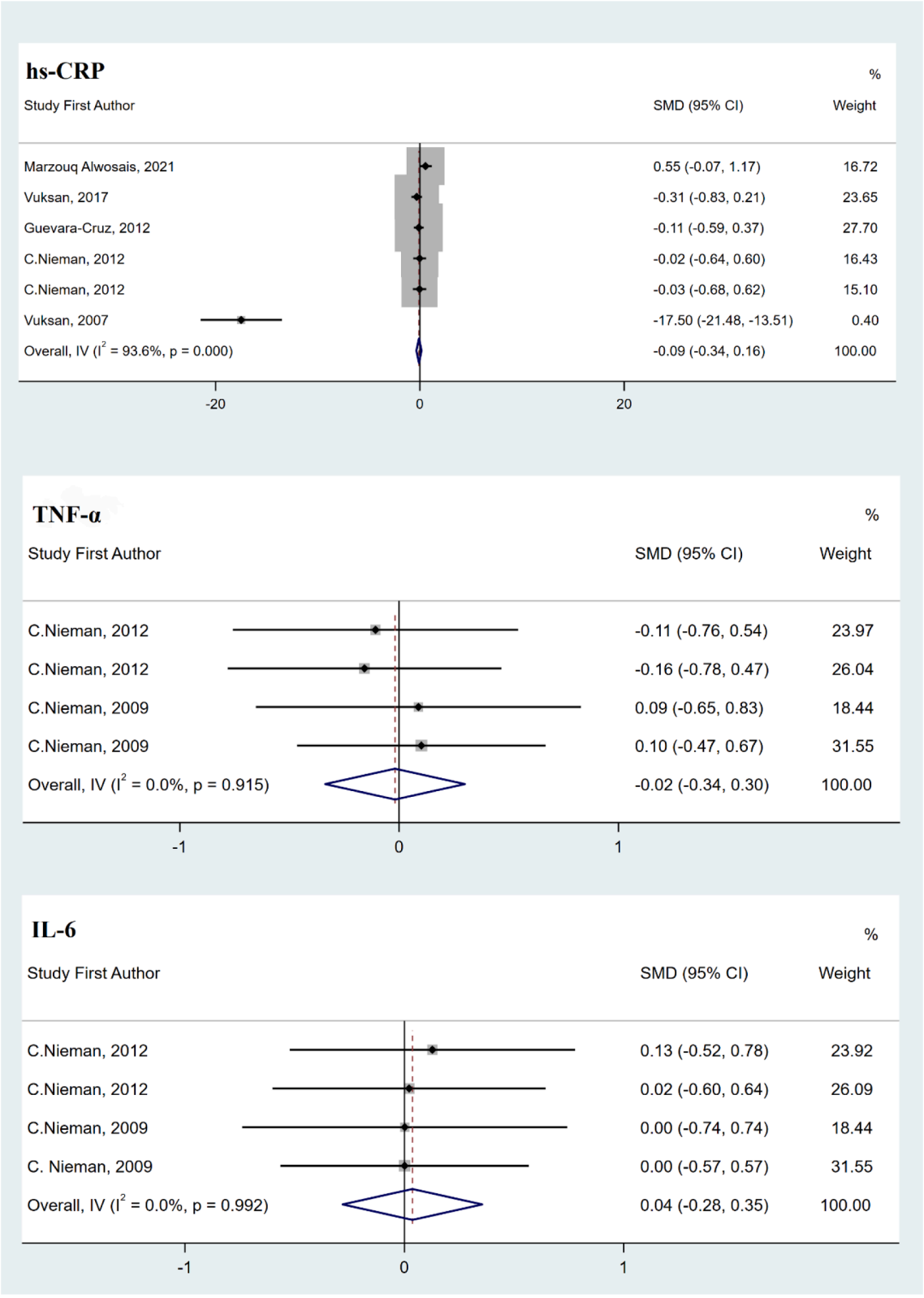

Fig. 6. Forest plot of the effects of chia product supplement on inflammatory factors.

significant reduction in FBG when chia was administered as co-supplementation. To our surprise, a more favorable influence of chia supplementation in terms of DBP, TC, and LDL-C was observed in studies with a treatment duration $\leq$ 10 weeks and a dose of supplement $\leq$ 25 mg/day. These findings may be attributed to variations in study design and quality of evidence included in these subgroups. Further, chia products might have more immediate and pronounced effects on these variables when administered at lower doses and for shorter durations. Also, there could be a possibility of a threshold effect, where even lower doses of chia provide sufficient bioactive compounds to influence DBP,

Table 3
Subgroup analysis of chia product supplementation.

Sub-grouped by	No. of trials	SMD (95%CI)	P-value	P for heterogeneity	I^2 (%)	P for between subgroup heterogeneity
BMI						
Total	8	−0.1 (−0.33, 0.13)	0.401	0.366	8.3	
Duration of treatment						
≤10 week						
>10 week	5	−0.05 (−0.49, 0.38)	0.805	0.109	47.2	0.807
Dose of supplement	3	−0.12 (−0.40, 0.16)	0.402	0.999	0	
≤25 mg						
>25 mg						
Type of intervention	5	−0.12 (−0.40, 0.16)	0.402	0.109	47.2	0.807
Chia	3	−0.05 (−0.49, 0.38)	0.805	0.999	0	
Co−supplementation						
	3	0.03 (−0.32, 0.38)	0.881	0.91	0	0.345
	5	−0.20 (−0.51, 0.11)	0.21	0.162	38.9	
Weight						
Total	12	−0.08 (−0.27, 0.11)	0.416	0.984	0	
Duration of treatment						
≤10 week						
>10 week	8	−0.08 (−0.31, 0.14)	0.469	0.856	0	0.922
Dose of supplement	4	−0.06 (−0.40, 0.27)	0.703	0.993	0	
≤25 mg						
>25 mg						
Type of intervention	7	−0.08 (−0.31, 0.15)	0.506	0.997	0	0.987
Chia	5	−0.08 (−0.39, 0.24)	0.64	0.776	0	
Co−supplementation						
	7	−0.04 (−0.28, 0.19)	0.723	0.999	0	0.633
	5	−0.14 (−0.45, 0.17)	0.382	0.584	0	
WC						
Total	8	−0.20 (−0.43, 0.02)	0.079	0.433	0	
Duration of treatment						
≤10 week						
>10 week	5	−0.19 (−0.47, 0.08)	0.168	0.196	33.8	0.91
Dose of supplement	3	−0.22 (−0.62, 0.18)	0.273	0.636	0	
≤25 mg						
>25 mg						
Type of intervention	5	−0.19 (−0.47, 0.08)	0.168	0.196	33.8	0.91
Chia	3	−0.22 (−0.62,0.18)	0.273	0.636	0	
Co−supplementation						
	3		0.289	0.613	0	0.845
	5		0.157	0.203	32.7	
		−0.18(−0.51, 0.15)				
		−0.23 (−0.54, 0.09)				
Body fat						
Total	8	0.02 (−0.21, 0.24)	0.888	0.826	0	
Duration of treatment						
≤10 week						
>10 week	4	0.13(−0.18, 0.45)	0.397	0.95	0	0.289
Dose of supplement	4	−0.11 (−0.42, 0.21)	0.513	0.55	0	
≤25 mg						
>25 mg						
Type of intervention	4	0.12 (−0.16, 0.39)	0.406	0.966	0	0.216
Chia	4	−0.18 (−0.56, 0.20)	0.354	0.617	0	
Co−supplementation						
	6	−0.05 (−0.31, 0.21)	0.696	0.773	0	0.331
	2	0.19 (−0.23, 0.62)	0.367	0.726	0	
SBP						
Total	13	−0.41 (−0.59, −0.22)	< 0.0001	0.001	63.7	
Duration of treatment						
≤10 week						
>10 week	7	−0.33 (−0.57, −0.09)	0.007	0	76.2	0.342
Dose of supplement	6	−0.51 (−0.80, −0.23)	0	0.227	27.7	
≤25 mg						
>25 mg						

(*continued on next page*)

Table 3 (*continued*)

Sub-grouped by	No. of trials	SMD (95%CI)	P-value	P for heterogeneity	I^2 (%)	P for between subgroup heterogeneity
Type of intervention	7	−0.33 (−0.57, −0.09)	0.007	0	76.2	0.342
Chia	6	−0.51 (−0.80, −0.23)	0	0.227	27.7	
Co−supplementation						
	8	−0.50(−0.73, −0.27)	0	0.186	30.3	0.168
	5	−0.22 (−0.55, 0.10)	0.169	0	81.1	
DBP						
Total	9	−0.41 (−0.65, −0.17)	0.001	0	92.4	
Duration of treatment						
≤10 week						
>10 week	5	−0.61 (−0.90, −0.32)	0	0	84.5	0.014
Dose of supplement	4	0.04 (−0.39, 0.47)	0.866	0	95.9	
≤25 mg						
>25 mg						
Type of intervention	5	−0.61 (−0.90, −0.32)	0	0	84.5	0.014
Chia	4	0.04 (−0.39, 0.47)	0.866	0	95.9	
Co−supplementation						
	4	−0.11 (−0.47, 0.24)	0.522	0	96	0.025
	5	−0.67 (−1.0, −0.33)	0	0	84.3	
FBG						
Total	14	−0.03 (−0.2, 0.14)	0.723	0	73.2	
Duration of treatment						
≤10 week						
>10 week	6	−0.23 (−0.52, 0.05)	0.106	0	87.6	0.08
Dose of supplement	8	0.08 (−0.13, 0.30)	0.444	0.665	0	
≤25 mg						
>25 mg						
Type of intervention	6	−0.23 (−0.52, 0.05)	0.106	0	87.6	0.08
Chia	8	0.08 (−0.13, 0.30)	0.444	0.665	0	
Co−supplementation						
	9	0.1 (−0.09, 0.3)	0.287	0.836	0	0.003
	5	−0.53 (−0.90, −0.16)	0.005	0	88.7	
HbA1c						
Total	5	−0.20 (−0.45, 0.05)	0.117	0.282	29.8	
Duration of treatment						
≤12 week						
>12 week	3	−0.26 (−0.65, 0.13)	0.19	0.949	0	0.496
	2	−0.16 (−0.49, 0.17)	0.344	0.027	79.5	
Insulin						
Total	5	0.07 (−0.17, 0.32)	0.568	0.205	32.4	
Duration of treatment						
≤10 week						
>10 week	2	0.20 (−0.23, 0.63)	0.348	0.78	0	0.842
Dose of supplement	3	0.15 (−0.16, 0.45)	0.366	0.176	42.5	
≤30 mg						
>30 mg						
Type of intervention	2	0.07 (−0.35, 0.49)	0.751	0.388	0	0.948
Chia	3	0.07 (−0.23, 0.48)	0.635	0.075	61.3	
Co−supplementation						
	3	0.28 (−0.11, 0.67)	0.163	0.279	21.6	0.183
	2	−0.06 (−0.38, 0.25)	0.696	0.207	37.3	
TC						
Total	14	−0.30 (−0.48, −0.13)	0.001	0.172	26.2	
Duration of treatment						
≤10 week						
>10 week	8	−0.42 (−0.64, −0.20)	0	0.099	42	0.107
Dose of supplement	6	−0.12 (−0.40, 0.16)	0.382	0.705	0	
≤25 mg						
>25 mg						
Type of intervention	9	−0.39 (−0.60, −0.18)	0	0.125	36.6	0.093
Chia	5	−0.11 (−0.43, 0.20)	0.476	0.567	0	
Co−supplementation						
	9	−0.20 (−0.42, 0.01)	0.064	0.432	1.5	0.118
	5	−0.50 (−0.80, −0.20)	0.001	0.122	43.4	
LDL−C						
Total	12	−0.30 (−0.50, −0.11)	0.002	0.002	62.7	
Duration of treatment						
≤10 week						
>10 week	6	−0.39 (−0.65, −0.13)	0.003	0.001	75.9	0.34
Dose of supplement	6	−0.20 (−0.49, 0.08)	0.157	0.167	36	

(*continued on next page*)

Table 3 (*continued*)

Sub-grouped by	No. of trials	SMD (95%CI)	P-value	P for heterogeneity	I^2 (%)	P for between subgroup heterogeneity
≤25 mg						
>25 mg						
Type of intervention	6	−0.39 (−0.65, −0.13)	0.003	0.001	75.9	0.34
Chia	6	−0.20 (−0.49, 0.08)	0.157	0.167	36	
Co−supplementation						
	7	−0.49 (−0.73, −0.24)	0	0.003	70.1	0.018
	5	−0.01 (−0.32, 0.3)	0.944	0.426	0	
HDL−C						
Total	12	−0.28 (−0.47, −0.09)	0.005	0	77.2	
Duration of treatment						
≤10 week						
>10 week	6	−0.15 (−0.42, 0.11)	0.261	0	88.1	0.167
Dose of supplement	6	−0.43 (−0.71, −0.14)	0.003	0.529	0	
≤25 mg						
>25 mg						
Type of intervention	6	−0.15 (−0.42, 0.11)	0.261	0	88.1	0.167
Chia	6	−0.43 (−0.71, −0.14)	0.003	0.529	0	
Co−supplementation						
	7	−0.25 (−0.49, −0.01)	0.039	0.065	49.4	0.692
	5	−0.33 (−0.66, −0.001)	0.048	0	88.9	
TG						
Total	13	−0.20 (−0.38, −0.02)	0.027	0	67.1	
Duration of treatment						
≤10 week						
>10 week	7	−0.30 (−0.53, −0.07)	0.011	0	79.9	0.194
Dose of supplement	6	−0.06 (−0.34, 0.22)	0.687	0. 418	0	
≤25 mg						
>25 mg						
Type of intervention	7	−0.30 (−0.53, −0.07)	0.011	0	79.9	0.194
Chia	6	−0.06 (−0.34, 0.22)	0.687	0. 418	0	
Co−supplementation						
	7	−0.19 (−0.43, 0.05)	0.119	0.309	15.8	0.878
	6	−0.22 (−0.49, 0.05)	0.114	0	83	
hs−CRP						
Total	6	−0.09 (−0.34, 0.16)	0.495	0	93.6	
Duration of treatment						
≤10 week						
>10 week	3	−0.06 (−0.39, 0.26)	0.706	0.971	0	0.812
Dose of supplement	3	−0.13 (−0.52, 0.27)	0.534	0	97.4	
≤25 mg						
>25 mg						
	2	−0.36 (−0.83, 0.12)	0.144	0	98.6	0.91
	4	0.02 (−0.28, 0.31)	0.918	0.219	32.2	
TNF−α						
Total	4	0.00 (−0.34, 0.30)	0.994	0.999	0	
Duration of treatment						
≤10 week						
>10 week	2	−0.13 (−0.58, 0.32)	0.56	0.913	0	0.915
Dose of supplement	2	0.10 (−0.35,0.55)	0.674	0.978	0	
≤25mg						
>25mg						
	2	−0.13 (−0.58, 0.32)	0.56	0.913	0	0.915
	2	0.10 (−0.35,0.55)	0.674	0.978	0	
IL−6						
Total	4	0.04 (−0.28, 0.35)	0.028	0.992	0	
Duration of treatment						
≤10 week						
>10 week	2	0.07 (−0.38, 0.52)	0.753	0.989	0	0.827
Dose of supplement	2	0.00 (−0.45, 0.45)	0.995	0.999	0	
≤25 mg						
>25 mg						
	2	0.07 (−0.38, 0.52)	0.753	0.989	0	0.827
	2	0.00 (−0.45, 0.45)	0.995	0.999	0	

TC, and LDL-C within a relatively short time frame. Beyond this threshold, higher doses may not lead to significantly greater benefits. The compliance and tolerance of the study participant are also among the factors needed to be considered. Participants in studies with shorter durations and lower doses may have better compliance and tolerance for supplementation of chia products, which could result in consistent usage and more reliable results.

Chronic diseases are a major global health concern, affecting individuals of all ages, genders, and ethnicities, and accounting for over two-thirds of deaths worldwide (38 million) in 2014, according to the World Health Organization (Alwan, 2010; Anderson & Durstine, 2019). Poor nutrition is a significant risk factor for chronic diseases,

highlighting the importance of dietary interventions in their prevention and treatment (Bergman & Brighenti, 2020).

The results of our analysis suggested that chia supplementation could decrease SBP, DBP, TC, LDL-C, TG, and HDL-C significantly. However, no significant effect was observed in terms of anthropometric measures, glycemic-related parameters, and inflammatory factors. In line with our result, Silva et al. in a systematic review and *meta*-analysis study in 2021 suggested that chia supplementation led to a significant decrease in TC, LDL-C and TG. Besides, in contrast to our findings, the results of their analysis suggested that chia supplementation could increase HDL-C (Silva et al., 2021). In addition, in a *meta*-analysis by Teoh et al. in 2018, the pooling of results suggested that favorable effects of chia supplementation on postprandial blood glucose, HDL-C, and blood pressure were observed at higher doses of chia seed (Teoh et al., 2018). Our analysis yielded null findings in some variables, which may be attributed to several factors. First, although our *meta*-analysis included a larger number of studies, which may have provided a more comprehensive representation of the diverse range of results observed in different research contexts, but it should be mentioned which limited number of studies for various variables may have hindered our ability to detect statistically significant results due to the small sample size. Second, the high heterogeneity observed between studies which may be related to study populations, methodologies, and treatment protocols could account for some of the discrepancies. Third, the metabolic effects of chia supplementation can be influenced by various factors, including the baseline health status of participants, the specific dosage and duration of chia supplementation, dietary patterns, and genetic factors. These variables can introduce variability in how individuals respond to chia supplementation, potentially leading to differing outcomes across studies. Fourth, the quality of evidence in many of the included studies was rated low, suggesting that errors in study design may have influenced the non-significant results. In terms of glycemic-related parameters, our insignificant findings could be explained by the possibility that the individuals included in our analysis already had optimal baseline glycemic control.

Various mechanisms have been proposed to explain the potential positive effects of chia on the health status of patients with chronic disease. The dietary fiber found in chia seeds is 95% insoluble, possessing a water-holding capacity that promotes satiety (Alfredo, Gabriel, Luis, & David, 2009). Additionally, the soluble and viscous fibers present in chia seed mucilage have been shown to exert a hypocholesterolemic effect by modulating hepatic metabolism (Gregorio, Areas, & Reyes, 2001). This is achieved through increased loss of bile acid, reduced absorption of cholesterol and circulating lipids, and inhibition of hepatic synthesis of free fatty acids (FFAs) (Ullah et al., 2016). Furthermore, chia contains functional proteins and bioactive peptides obtained through enzymatic treatments that have been demonstrated to inhibit 3-hydroxy-3-methylglutaryl coenzyme reductase (HMG-CoA), a key marker of cholesterol synthesis. Ultimately, this leads to a reduction in cholesterol synthesis (Coelho, Soares-Freitas, Arêas, Gandra, & Salas-Mellado, 2018).

The PUFA composition of chia also affects lipid metabolism. Literature suggests that chia reduces serum TG levels by inhibiting the synthesis and reduction of hepatic secretion of VLDL, LDL, and other chylomicrons (Adkins & Kelley, 2010; Kelley, Siegel, Vemuri, Chung, & Mackey, 2008). Other mechanisms, including a decline in lipogenesis, an increase in beta-oxidation, and a decrease in FFAs in the liver, have also been linked to the lower availability of substrates for TG biosynthesis (Mozaffarian & Wu, 2011). In studies where PUFA replaced SFA, plasma TC and LDL levels decreased, while HDL levels increased (Hammad, Pu, & Jones, 2016; Lunn & Theobald, 2006; Siri-Tarino, Sun, Hu, & Krauss, 2010). The precise mechanism behind the elevation of high-density lipoprotein (HDL) levels remains uncertain; nevertheless, recent investigations have demonstrated that ω-3 fatty acids exhibit a propensity to enhance the levels of the HDL subtype that possesses more anti-atherogenic properties (Jain, Aggarwal, & Zhang, 2015). Regarding the omega-3 in chia seeds, it plays a role in regulating nuclear receptors that participate in the transport and oxidation of fatty acids. This includes the activation of peroxisome proliferator-activated receptors (PPAR)-α and -γ, as well as the down-regulation of transcription factors. These actions are crucial in the process of liver lipogenesis. The combined impact of these actions can lead to a decrease in lipoprotein levels and an enhancement in bile acid production, hence positively influencing the metabolic profile (Creus, Benmelej, Villafañe, & Lombardo, 2017; Fernández-Martínez et al., 2019). Additionally, the consumption of chia seeds has been found to inhibit the translocation of fatty acid translocase (FAT/CD36), so reducing the input of FFAs and saturated fatty acids (SFAs), ultimately leading to a decrease in lipogenesis (Grancieri, Martino, & Gonzalez de Mejia, 2019).

However, the ingestion of chia seeds also results in an increase in LA levels (Silva et al., 2021). LA and ALA exhibit distinct metabolic signaling properties and engage in enzymatic competition for 6 desaturase, a crucial enzyme involved in their respective metabolic pathways (Dias, Wood, & Garg, 2016; Jump, Depner, & Tripathy, 2012). Although alpha- linolenic acid (ALA) exhibits cardioprotective and antioxidant properties, the converse is observed with LA, as it plays a pro-inflammatory function by signaling vasoconstriction, platelet aggregation, and thrombotic activities (Saini & Keum, 2018). As a result, only a diet high in omega-3 fatty acids can deliver them to the body, and a healthy balance of both is required (Zare, Rupasinghe, Boughton, & Roessner, 2019).

Salba was employed as a source of chia in two investigations (V Vuksan et al., 2017; Vladimir Vuksan et al., 2007). Salba is a white-colored variety of the species, but the potent impacts that could be noticed after its ingestion suggest that its composition is very similar (Silva et al., 2021). Both of these experiments also examined the effects of including chia into bread preparations that were subjected to heat exposure. Presently, the existing body of literature elucidates that the chemical makeup of chia seeds can be influenced by several factors such as geographical location, post-harvest practices, cultivation methods, and predominantly, thermal processing (Kulczyński et al., 2019; Segura-Campos, Ciau-Solís, Rosado-Rubio, Chel-Guerrero, & Betancur-Ancona, 2014). The protein, fatty acid (FA), and polyunsaturated fatty acid (PUFA) that are found in chia oil and seeds are diminished with the utilization of heat (Knez Hrnčič, Ivanovski, Cör, & Knez, 2019). Additionally, it induces oxidation and the production of volatile chemicals that impart undesirable odors and tastes, so affecting the overall composition (Bordón, Meriles, Ribotta, & Martinez, 2019). The utilization of low temperatures is associated with reduced detrimental effects on the bioactive compounds and the quality of the FAs (Musa Özcan, Al-Juhaimi, Mohamed Ahmed, Osman, & Gassem, 2019).

The present *meta*-analysis exhibited considerable strengths. To the best of our knowledge, this study represents the most thorough and recent systematic review and *meta*-analysis conducted to examine the impact of chia products on anthropometric parameters, blood pressure, glycemic-related parameters, lipid profile, and inflammatory markers. This analysis exclusively used findings derived from randomized, double-blinded clinical trials, which are often regarded as the most rigorous form of clinical evidence. Furthermore, our investigation yielded no indications of publication bias that may have influenced the outcomes of the *meta*-analysis. In addition, we endeavored to mitigate any biases in the review process by performing a thorough literature search and following the PRISMA standards for conducting and reporting the review. Furthermore, we conducted an evaluation of the methodological quality of the studies included in our analysis by employing the Cochrane Collaboration tool system for each specific outcome. Also, subgroup analyses were performed in order to investigate the effects within different subgroups and ascertain potential factors contributing to the observed heterogeneity. Notwithstanding the merits outlined, it is imperative to acknowledge the limitations inherent in our study. Initially, despite our successful integration of data from many studies in our *meta*-analysis, the collective sample size remained rather limited,

hence leading to diminished statistical power. Furthermore, there are apprehensions regarding the heterogeneity of the included research with respect to the study population, dose, and length, potentially influencing the effectiveness of the findings. Furthermore, a significant proportion of the research included in the analysis were done over a very short duration, specifically less than six months. So, our study was unable to examine the long-term effects of chia products on the study variables. Besides, it is worth noting that the impact of physical activity and calorie intake on anthropometric and glycemic-related parameters is significant. However, it is important to mention that none of the research included in this analysis accounted for potential changes in these parameters when interpreting their findings. Hence, the net impact of chia product supplementation could not be determined. In addition, due to the limited number of studies, we were unable to assess the dose–response associations between chia products supplementation and studied variables. Finally, several of the included studies did not account for potential confounders in their analyses, therefore their impacts were not considered.

Implications for practice

The evidence from our study indicates that the administration of chia products results in a significant reduction in SBP and DBP, TC, LDL-C, HDL-C, and TG. However, no significant impacts were observed in terms of anthropometric measures, glycemic-related parameters, and inflammatory factors.

Implications for research

Future clinical trials should be conducted on a larger scale and with higher quality to minimize the risk of bias and adhere to current reporting standards. To accurately interpret the results, it is necessary to consider the influence of various confounding factors, including medication type, lifestyle, dietary compliance, and the genetic background of participants. Furthermore, RCTs should be conducted in diverse clinical settings to strengthen the evidence base in this area.

5. Conclusion

In conclusion, chia product supplementation leads to a significant reduction in SBP and DBP, TC, LDL-C, HDL-C, and TG. However, no significant effect was observed in terms of anthropometric measures, glycemic-related parameters, and inflammatory factors. Further RCTs that incorporate larger sample sizes and longer durations are necessary to validate and improve the accuracy of our results.

Ethics statement

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval for the study was obtained from the Ethics Committee of Golestan University of Medical Sciences (IR.GOUMS.REC.1401.494).

CRediT authorship contribution statement

Omid Nikpayam: Writing – review & editing, Writing – original draft, Software, Methodology, Formal analysis, Conceptualization. **Ali Jafari:** Writing – original draft, Software, Methodology, Formal analysis, Conceptualization. **Ehsan Safaei:** Writing – original draft, Validation, Investigation, Data curation. **Niayesh Naghshi:** Writing – original draft, Validation, Investigation, Data curation. **Marziyeh Najafi:** Writing – original draft, Methodology, Investigation, Data curation. **Golbon Sohrab:** Writing – review & editing, Supervision, Software, Project administration, Investigation, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jff.2023.105867.

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