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Journal of Nutritional Biochemistry 133 (2024) 109718

Journal of Nutritional Biochemistry

RESEARCH PAPER

The effects of nonsoy legumes consumption on serum levels of inflammatory biomarkers and Adiponectin in overweight/obese adults: A systematic review and meta-analysis of randomized controlled trials

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Received 15 March 2024; received in revised form 22 July 2024; accepted 31 July 2024

Abstract

Nonsoy legumes offer many health benefits, including improved arterial function, reduced cholesterol levels, and better management of cardiovascular diseases and type 2 diabetes. This systematic review and meta-analysis aim to clarify the inconclusive findings from randomized controlled trials (RCTs) by comprehensively evaluating the effects of nonsoy legumes consumption on serum levels of inflammatory biomarkers and Adiponectin. The search encompassed databases up to January 2024, including PubMed, EMBASE, MEDLINE, Scopus, Web of Science, and Cochrane CENTRAL to retrieve all RCTs examining the effects of nonsoy legumes on inflammatory biomarkers or Adiponectin. The effect sizes quantified as mean differences (MD) and standard deviations (SD) of outcomes, and an overall effect estimate was derived using a random-effects model. RCTs examining serum levels of C-reactive protein (CRP), Interleukin-6 (IL-6), Tumor Necrosis Factor-alpha (TNF-α), Interleukin-1β (IL-1β), and Adiponectin were included in the final meta-analysis. Results revealed that consumption of nonsoy legumes increased Adiponectin serum levels (P=.0017) and reduced IL-1β serum levels (P<.0001). However, it may not significantly affect CRP (P=.2951), IL-6 (P=.2286), and TNF-α (P=.6661) levels. Subgroup analyses showed that nonsoy legumes consumption significantly decreased TNF-α serum levels in studies involving healthy participants. Additionally, sensitivity analysis using the leave-one-out method suggested a potential significant reduction in serum levels of IL-6. This study indicates that consuming nonsoy legumes can increase levels of Adiponectin and decrease serum levels of IL-1β in overweight or obese adults.

Keywords: Nonsoy legumes; Inflammation; Adiponectin; Diet; Obesity; Overweight.

1. Introduction

Elevated levels of inflammation, a critical risk factor for numerous clinical diseases including cardiovascular disease (CVDs), type 2 diabetes mellitus (T2DM), and various cancers, are often associated with abdominal obesity and increased adipose tissue mass [1,2]. Obesity refers to the abnormal buildup of fat or adipose tissue in the body, which can lead to health issues such as diabetes mellitus, cardiovascular disease, hypertension, and hyperlipidemia [3]. Chronic conditions like obesity are often characterized by a state of low-grade inflammation, which significantly contributes to the progression of these diseases [4,5]. Hence, reducing inflammation in obese patients could serve as a crucial therapeutic strategy to impede the advancement of obesity-related disorders [6]. Various pro-inflammatory and anti-inflammatory markers are linked to obesity, and their levels dictate the

Abbreviations: NAFLD, nonalcoholic fatty liver disease; PCOS, polycystic ovary syndrome; BMI, body mass index; T2DM, type 2 diabetes mellitus; CVDs, Cardiovascular diseases; RCT, randomized controlled trial; Hs-CRP/CRP, High-sensitivity C-reactive protein/C-reactive protein; IL-6, Interleukin-6; IL-1β, Interleukin-1 β; IL-12P40, Interleukin12P40; IL-8, Interleukin-8; IL-1RA, Interleukin-1 receptor antagonist; IL-18, Interleukin-18; IL-4, Interleukin-4; TNF-α, Tumor necrosis factor-α; IFNy, Interferon gamma; MCP-1, Monocyte Chemoattractant Protein 1; LKF-enriched bread, Lupin Kernel flour-enriched bread; LGI diet, Low glycemic index diet; TLC diet, Therapeutic lifestyle changes diet; SD, Standard deviation; SE, Standard error; MD, mean difference.

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https://doi.org/10.1016/j.jnutbio.2024.109718

inflammatory status in obese individuals. For instance, C-reactive protein (CRP) [7], Tumor Necrosis Factor-alpha (TNFα) [8], Interleukin-6 (Il-6) [9], Interleukin-1β (IL-1β) [10] are considered pro-inflammatory biomarkers, whereas Adiponectin, an adipocyte-specific protein, exhibits anti-inflammatory properties [11].

Research has examined how dietary interventions affect not only weight control [12] but also the inflammatory profile in obese patients. Adopting an energy-restricted diet that emphasizes low-glycemic foods, whole-grain products, legumes, vegetables and fruits, nuts, seeds, marine fish, olive oil, green or black tea, as well as various spices and herbs, has been shown to notably enhance the anti-inflammatory properties of a diet [13]. In overweight or obese adults, consuming whole grains instead of refined grains, as indicated by the findings of a randomized crossover trial, has been shown to reduce levels of certain inflammatory markers like IL-6 and CRP [14]. The intake of omega-3 fatty acids and monounsaturated fatty acids (MUFA) has been associated to a lower inflammatory status. Conversely, intake of saturated fats [15] and red meat [16] have been associated with increased levels of inflammatory cytokines.

Nonsoy legumes, comprising various beans, peas, chickpeas, and lentils, are integral components of a balanced diet. They are renowned for their nutritional value, being rich in complex carbohydrates and fiber, boasting a low glycemic index [17], and containing high levels of protein while being low in saturated fat [18]. Among these, lentils are notable for their high protein content compared to other legumes [18,19]. Beans excel in both soluble and insoluble fiber and lead in carbohydrate content, followed by chickpeas [17,19]. Additionally, nonsoy legumes serve as good sources of essential micronutrients such as vitamins, minerals and bioactive compounds [19]. Lentils, compared to other legumes, contain the highest amount of B vitamins such as niacin, pantothenic acid, and riboflavin, while the highest in thiamin and folate are beans and peas respectively. Chickpeas and beans provide higher amounts of calcium and selenium, while lentils are the best source of iron. The primary phenolic compounds in pulses include tannins, phenolic acids, and flavonoids, with lentils having the highest levels of phenolic compounds compared to others [19]. Studies showed a legume-rich diet can elicit major improvements in arterial function and serum cholesterol levels [20,21] and improve disease conditions such as CVDs, T2DM [22], and inflammation [23–27].

Although extensive research has explored the impact of dietary interventions, particularly involving legumes [23–27,28] and soy [29], on inflammation, there is a dearth of studies focusing on nonsoy legumes especially among overweight or obese population. Moreover, the findings from available studies are not unequivocally conclusive. For instance, despite evidence showing the anti-inflammatory effects of certain nonsoy legumes [23,24,25], some studies have failed to find any significant anti-inflammatory benefits from these food components [26,28]. Apart from a systematic review conducted by Amin Salehi-Abargouei in 2015, which demonstrated a reduction in serum levels of CRP associated with nonsoy legumes consumption [28], there is currently no published systematic review comprehensively examining the influence of nonsoy legumes on inflammatory biomarkers beyond CRP or on the overall inflammatory profile. Therefore, the objective of this systematic review is to investigate the effects of nonsoy legumes consumption on serum levels of proinflammatory biomarkers such as CRP, TNFα, IL-6, IL-1β, and Adiponectin as an anti-inflammatory biomarker in overweight or obese populations. The findings of this meta-analysis aim to provide a comprehensive understanding of the impact of nonsoy legumes consumption on inflammatory profiles.

2. Methods

2.1. Search strategy

A systematic search across 6 scientific database, PubMed, EMBASE, MEDLINE, Scopus, Web of Science, and Cochrane CENTRAL, as well as a manual search of related articles were conducted by two reviewers (FM and GdS) up to January 30, 2024. The search utilized a variety of keywords encompassing ("Legume/s" OR "pea/s" OR "chickpea/s" OR "bean/s" OR "lentil" OR "lupin" OR "pulses" OR "nonsoy legume" OR "faba" OR "fabaceae") AND ("Inflammation" OR "inflammatory" OR "Tumor necrosis factor" OR "TNF-α" OR "TNF" OR "C-Reactive protein" OR "c reactive protein" OR "high-sensitivity CRP" OR "hs-CRP" OR "CRP" OR "Cytokine" OR "Interleukin" OR "Adiponectin" OR "MCP-1″ OR "IL-1″ OR "IL-6″ OR "IL-8″ OR "IFNγ" OR "Complement C3" OR "Homocysteine" OR "Fibrinogen" OR "IL-4″ OR "IL-10″) AND ("randomized" OR "randomised" OR "controlled trial" OR "clinical trial") without restrictions on language or publication date. Retrieved articles were imported into EndNote software 21.2 for citation management, duplicate removal, and to streamline the review process. This systematic review and meta-analysis adhere to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [30] and the study protocol is registered in the International Prospective Register of Systematic Reviews website (PROSPERO) (https://www.crd.york.ac.uk/PROSPERO/; registration no: CRD42024512136).

2.2. Inclusion criteria

This study includes only parallel or crossover RCTs which assessed the serum level of at least one of the inflammatory biomarkers or Adiponectin after consumption of any type of nonsoy legumes, legume-based diet or a functional food derived from nonsoy legumes as an intervention and consumption of any type of legume-free diet or legume-free alternative as the control in overweight or obese adults (aged $\geq$18 and BMI $\geq$25) with or without metabolic disorders. Out of 37 potentially related studies, 20 studies met the eligibility criteria for inclusion in this systematic review and meta-analysis [23–27,31–45].

2.3. Exclusion criteria

The studies did not employ randomization, lacked a well-defined control group as the comparator, or were conducted on population aged less than 18 years were excluded, in addition to the trials involving participants with cancer and trials with duration of less than one week. Furthermore, studies in which the levels of biomarkers before and after intervention were not clearly specified in both experimental and control groups were inevitably excluded from the final meta-analysis. If a trial assessed the serum level of only one inflammatory biomarker and no other studies were available to evaluate that specific biomarker, the study was excluded from final meta-analysis due to limited data availability.

2.4. Data extraction

The last name of the first author, the country of origin, publication date, number of participants in both intervention and control groups, gender, mean age with standard deviation (SD) [23,24,26,27,33,34,37–40,42,43] or standard error (SE) [25,31,32,35,36,41,44,45], study design (parallel [23,26,27,31,33,35,36,38–40,42,43,45] or crossover [24,25,32,34,37,41,44]), details of dietary intervention in both experimental

and control groups, study duration and the mean value with SD [27,38,42,43], SE [24,25,31,32,35–37,41,44,45], or 95 % CIs [23,26,33,34,39,42] of biomarkers before and after intervention in both groups were extracted by single author (FM). In one study, the serum levels of Adiponectin [31], and in another one, the serum levels of inflammatory biomarkers [45] were available only as graphical representations. Additionally, in two other studies, the unit of measurement for serum levels of CRP were not understandable [26,35]. Therefore, the authors were contacted to seek clarification or obtain missing data.

2.5. Quality assessment and risk of bias

The study quality was assessed using version 2 of the Cochrane risk of bias tool for RCTs (RoB2.0) [46]. The following methodological domains were considered: Risk of bias arising from the randomization process, Risk of bias arising from period and carryover effects (crossover RCTs), Risk of bias due to deviations from the intended interventions, risk of bias due to missing outcome data, Risk of bias in measurement of the outcome, Risk of bias in selection of the reported result. Each item was scored as a low, some concerns or high regarding risk of bias. Two authors (FM and GdS) independently assessed the studies. The final evaluations were determined through agreement between authors.

2.6. Statistical analysis

A meta-analysis was performed for each biomarker outcome (Adiponectin, CRP, IL-6, TNFα and IL-1β) when data from at least two studies were available, using the dplyr, meta, and metafor packages in RStudio version 2023.03.1+ 446. The effect size was reported as mean difference (MD) and 95% CIs. Data were collected as mean change and SD. If mean changes in both intervention and control groups were not reported for each study, the mean change was determined by subtracting the postintervention mean from the baseline mean. The SD for this calculated mean was determined according to the method specified in the Cochrane guideline [47]. When only SDs were unavailable, they were derived from the 95% confidence intervals (CIs) and standard errors (SEs) [47]. In order to consider heterogeneity in study methodology, random-effects models were employed to calculate the pooled effect size. One study [41], due to its design with two intervention groups evaluating two different legumes, was treated as two separate trials in the meta-analysis. Crossover trials were included in the meta-analysis alongside parallel trials, by comparing measurements from the intervention periods with those from the control periods. While this method may introduce a unit-of-analysis error, it is deemed a conservative approach [47]. Furthermore, sensitivity analyses were performed by conducting paired analyses of crossover trials, incorporating various correlation coefficients (0.25, 0.5, and 0.75), to investigate potential underweighting of crossover studies.

Sensitivity and subgroup analyses were employed to investigate sources of heterogeneity. Sensitivity analyses, using the leave-one-out method, were conducted to assess the impact of each individual study on the overall pooled effect by systematically excluding one study at a time and recalculating the summary estimates. Subgroup analyses were conducted for study duration ($<12/\geq 12$ weeks), study design (parallel/crossover), health status of participants (Healthy/Unhealthy with any type of metabolic diseases). The between-study heterogeneity was evaluated using the I^2 statistic, categorized according to Cochrane guidelines: low heterogeneity (I^2=0% to 40%); moderate heterogeneity (I^2=30% to 60%); substantial heterogeneity (I^2=50% to 90%); and considerable heterogeneity (I^2=75% to 100%) [47]. Publication bias was examined through formal testing using Egger's test and visual inspection of funnel plots [48]. A significance level of P-value <0.05 was established through the study.

3. Results

3.1. Study selection

Figure 1 depicts the PRISMA diagram of the comprehensive systematic search and literature selection process. Out of the initially identified 1302 records from databases and manual searches, 224 duplicates were eliminated. Among the 1078 records subjected to title and abstract screening, 1041 were deemed ineligible based on the inclusion and exclusion criteria. A thorough examination of the full text was performed on 37 records, leading to the exclusion of an additional 17 studies that did not meet the eligibility criteria. Ultimately, 20 studies met the criteria and were included in the systematic review and meta-analysis.

3.2. Study characteristics

Table 1 illustrates the detailed characteristics of included trial. Twenty studies included in this systematic review and meta-analysis were conducted within eleven distinct countries, including Iran (25%) [24,25,27,36,37], Canada (20%) [34,35,40,43], The U.S. (10%) [32,41], Australia (10%) [33,42], Sweden (5%) [44], Spain (5%) [23], South Korea (5%) [31], China (5%) [26], Greece (5%) [38], Mexico (5%) [39], and Germany (5%) [45]. These studies were published between 2007 and 2022. Among these trials, seven studies utilized a crossover design [24,25,32,34,37,41,44], while the other trials used a parallel design [23,26,27,31,33,35,36,38–40,42,43,45]. Six studies implemented some level of blinding, with four employing single-blind design [31,34,38,43] and two studies employing double-blind design [35,42]. The study duration varied from 4 weeks to 52 weeks. All of the studies assessed the serum levels of at least one inflammatory biomarker or Adiponectin. Six studies evaluated the serum levels of Adiponectin, eighteen studies assessed the CRP levels, seven studies evaluated the IL-6 and TNF-α levels, and two studies evaluated the serum levels of IL-1β. Moreover, the serum levels of Complement C3 and Homocysteine in one study [23], Interleukin-12 subunit p40 (IL-12P40), Interleukin-8 (IL-8), Interferon gamma (IFNγ), and Monocyte chemoattractant protein-1 (MCP-1) levels in one other study [35], and the serum levels of Fibrinogen in another study [40] have been evaluated. However, due to the limited number of studies on these biomarkers, they were not included in the meta-analysis.

3.2.1. Participant characteristics

The twenty studies included in the analysis enrolled a total of 1436 participants, including 1012 women (70%) and 424 men (30%) aged from 18 to 78 years and randomly assigned. Most studies included both male and female participants, while five studies exclusively recruited only females [36,39,40,43,44]. The sample size of each study ranged from 16 [41] to 383 [31] participants. Alongside meeting the inclusion criterion of being overweight or obese, participant health status encompassed T2DM [24,26,27,37], T2DM and NAFLD [45], hypercholesterolemia [32], hypertriglyceridemia [39], and polycystic ovary syndrome (PCOS) [43].

3.2.2. Dietary intervention

Six of the included studies in this meta-analysis (35%) implemented a pulse-based or legume-based diet as an intervention,

Table 1
Study characteristics of the included RCTs.

First author (year, country)	Participants	sex	Mean of age (year)	Study design	Intervention	Control (comparator)	Duration (week)	Biomarkers with presented data in IG and CG	Note about participants
Han et al. [31], South Korea	IG: 160, CG: 223	CG: 93 M/130 F IG: 68 M/92 F	CG: 48·5±0·85 IG:49·4±1·12	Parallel	Legume-enriched diet (LD): replacing one-third of refined rice consumption with legumes three times per day as a carbohydrate source	Usual diet (UD)	12	hs-CRP (mg/dl)	Obese (BMI (kg/m^2): IG: 27.6±0.21and CG: 27.4±0.16)
Winham et al. [32], The U.S.	IG: 23, CG: 23	10 M/13 F	45.9±2.2	Crossover	Daily 1/2 cup serving of vegetarian baked beans with normal diet	Daily 1/2 cup serving of canned carrot with normal diet	8	hs-CRP (mg/L)*	Overweight or obese and hypercholesterolemic (BMI (kg/m^2): 27.4±0.9)
Hodgson et al. [33], Australia	IG: 37, CG: 37	26 M/48 F	IG: 59.0±7.4 CG: 56.8±8.5	Parallel	LKF-enriched bread: replacing 15–20% of usual daily energy intake with LKF-enriched bread in an ad libitum diet	White bread: replacing 15–20% of usual daily energy intake with white bread in an ad libitum diet	16	Adiponectin (mg/l) hs-CRP (mg/L)	Overweight and obese (BMI (kg/m^2): IG: 30.6±3.6 and CG: 30.5±3.4)
Hermsdorff et al. [23], Spain	IG: 15, CG: 15	17 M/13 F	36±8	Parallel	Calorie restricted legume-based diet: 4 weekly different cooked-servings (160–235 g) of lentils, chick peas, peas or beans	Calorie restricted legume-free diet:	8	CRP (mg/l) ComplementC3, (g/l) IL-6 (pg/ml) TNF-α (pg/ml) Homocysteine (μmol/l)	Obese (BMI (kg/m^2): 32.5±4.5)
Abeysekara et al. [34], Canada	IG: 87, CG: 87	30 M/57 F	59·7±6·3	Crossover	Pulse-based diet (two servings daily of beans, chickpeas, peas or lentils; about 150g/d dry weight)	Regular diet	8	CRP (nmol/l)	Overweight or obese (BMI (kg/m^2): 27·5±4·5)
Lambert et al. [35], Canada	IG: 22, CG: 22	9 M/41 F	44±15	Parallel	PF: 15 g/d pea fiber (3 serving/d wafers containing 5 g/serving of yellow pea fiber)	PL: isocaloric dose of control wafers with no pea fiber	12	CRP (mg/L) IFNy (pg/ml) IL-12P40 (pg/ml) IL-1β (pg/ml) IL-6 (pg/ml) IL-8 (pg/ml) MCP1 (pg/ml) TNF-α (pg/ml)	Overweight or obese (BMI (kg/m^2): IG: 33.1±1.3 and CG: 33.3±1.3)

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Table 1 (*continued*)

First author (year, country)	Participants	sex	Mean of age (year)	Study design	Intervention	Control (comparator)	Duration (week)	Biomarkers with presented data in IG and CG	Note about participants
Hosseinpour-Niazi et al. [24], Iran	IG: 31, CG: 31	7 M/ 24 F	58·1± 6.0	Crossover	Nonsoya legume-based TLC diet (replacing two servings of red meat by different types of cooked legumes such as lentils, chickpeas, peas and beans for 3d per week in TLC diet)	Legume-free TLC diet (50–60% of energy from carbohydrate, 15% of energy from protein and 25 to 35% of energy from fat as well as intake of,200mg cholesterol and 25–30g fiber)	8	hs-CRP (mg/l) IL-6(pg/ml) TNF-α (pg/ml)	Overweight or obese and T2DM (BMI=25-30 kg/m^2)
Safaeiyan et al. [36], Iran	IG: 17, CG: 17	34 F	IG: 35.5±8.6, CG: 36.8±7.8	Parallel	Hypocaloric diet enriched with legumes (HDEL) comprised two servings or 1 cup per day of cooked nonsoy legumes including red, white and wax beans; cowpea, chickpeas, split peas; and lentil instead of meat)	Hypocaloric diet without legumes (HDWL)	8	hs-CRP (mg/l)	Central obesity (BMI >25 kg/m^2)
Saraf-Bank et al. [25], Iran	IG: 26, CG: 26	12 M / 14 F	50± 1.29	Crossover	Habitual diet enriched with legumes	Habitual diet	6	hs-CRP (mg/L) IL-6 (pg/ml) TNF-α (pg/ml) Adiponectin (μg/mL)	Overweight or obese with family history of diabetes (BMI (kg/m^2: 28.92± 0.85)
Liu et al. [26], China	IG: 51, CG: 51	CG: 24 M/27 F IG: 23 M/28 F	IG: 57.6±8.8 CG: 57.4±8.8	Parallel	Daily consumption of extruded adzuki bean convenient food (EABCF) (2 bags of EABCF instant powder before each of the three meals and chew the EABCF hard candies, two at a time, three times a day)	Traditional diabetic low glycemic index diet	4	hs-CRP (pg/ml) IL-6 (pg/ml) TNF-α (pg/ml)	Overweight or obese and T2DM (BMI (kg/m^2): IG: 27.07 (26.23-27.90) CG: 26.11 (25.21- 27.01)
Mirmiran et al. [37], Iran	IG: 31, CG: 31	7 M/24 F	58.1 ±6.0	Crossover	Nonsoya legume-based TLC diet (replacing two servings of red meat by different types of cooked legumes such as lentils, chickpeas, peas and beans for 3d per week in TLC diet)	Legume-free TLC diet (50–60% of energy from carbohydrate, 15% of energy from protein and 25 to 35% of energy from fat as well as intake of,200mg cholesterol and 25–30g fiber)		Adiponectin (mg/l)	Overweight or obese and T2DM (BMI=25-30 kg/m^2
Binou et al. [38], Greece	IG: 35, CG: 35	CG: 14 M/21 F, IG: 12 M/23 F	IG: 42.9 ±14.7, CG: 46.0± 9.1	Parallel	Daily 70 g of an isocaloric amount of wheat biscuits enriched with plant proteins (PB) originating from legumes and seeds, respectively	Daily 70 g of conventional wheat biscuits	12	hs-CRP (mg/L) IL-6 (pg/ml) TNF-α (pg/ml) Adiponectin (mg/L) IL-1β (pg/mL)	Overweight or obese (BMI (kg/m^2): IG: 30.6 ±4.2 and CG: 30.9 ±3.7)

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Table 1 (*continued*)

First author (year, country)	Participants	sex	Mean of age (year)	Study design	Intervention	Control (comparator)	Duration (week)	Biomarkers with presented data in IG and CG	Note about participants
Ramírez-Jiménez et al. [39], Mexico	IG: 14, CG: 12	26 F	IG: 38.00± 7.39, CG: 33.00 ±8.30	Parallel	Daily consumption of a bean and oats snack bar (BOSB) (50 g (25 g two times) per day	No intake of BOSB	8	hs-CRP (μg/ml)	Overweight or obese and hypertriglyceridemia (BMI (kg/m^2): IG: 30.59 ±4.84 and CG: 29.93 ±6.19)
Gravel et al. [40], Canada	IG: 68, CG: 66	134F	IG: 52.5±7.5, CG: 50.0±9.6	Parallel	750 ml of pulses weekly	No pulse intake	16	Fibrinogen (g/l) CRP (mg/l) IL-6 (pg/ml) TNF-α (pg/ml)	Overweight or obese (BMI (kg/m^2): IG: 29.6±4.5 and CG: 30.1±5.7)
Winham et al. [41], The U.S.	IG: 16, CG: 16	7 M/9 F	43±3	Crossover	Two intervention groups: 1-daily intake of 1/2 cup pinto beans, 2- daily intake of 1/2 cup black-eyed peas	Daily intake of 1/2 cup carrots	8	hs-CRP (mg/L)	Overweight or obese (BMI (kg/m^2): 27.8±0.9
Belski et al. [42], Australia	IG: 68, CG: 63	CG: 29 M/34 F, IG: 34 M/34 F	IG: 46.5±10.1, CG: 46.7±9.4	Parallel	Lupin-enriched foods (contain of Lupin flour instead of wheat flour	Matching high-carbohydrate control foods	52	hs-CRP (mg/L)	Overweight or obese (BMI (kg/m^2): IG: 31.3±2.7 and CG: 31.4±2.8)
Kazemi et al. [43], Canada	IG: 47, CG: 48	95 F	IG: 27.0 ±4.6, CG: 26.9 ±4.4	Parallel	The pulse-based diet included soups, salads, and main course meals prepared with yellow split peas, green lentils, red split lentils, chickpeas, and pinto, black, and kidney beans. (two meals /d of prepared meals that each meal contained approximately 90 g of split peas or 225 g of chickpeas or beans or 150 g of lentils)	TLC diet (consume low-fat cuts of meat, poultry, and low fat or skim dairy as the main sources of protein and limit their pulse consumption)	16	hs-CRP (mg/L)	Overweight or obese and PCOS (BMI (kg/m^2): IG: 32.5±8.4 and CG: 33.3±9.0)
Hematdar et al. [27], Iran	IG: 20, CG: 23	CG: 4 M/19 F IG: 7 M/13 F	IG: 59±5.9 CG: 56±7.3	Parallel	Consumption of a cup of cooked nonsoy legumes three days a week	Consumption of two servings of red meat three days a week	8	CRP (μg/ml)	Overweight or obese and T2DM (BMI (kg/m^2): IG: 27.2±3.4 and CG: 26.7±2.9)
Tovar et al. [44], Sweden	IG: 46, CG: 46	46 F	61·6±0·8	Crossover	Functional diet (diet rich in kernel-based barley products, brown beans and chickpeas)	Control diet (similar macronutrients but lacking legumes and barley)	4	CRP (mg/l)	Overweight or obese (BMI (kg/m^2): 28·8±1·2
Markova et al. [45], Germany	IG: 19, CG: 18	24 M/13 F	IG: 63.7±1.5, CG: 65.0±1.4	Parallel	Diet high in plant protein (PP); consisted mainly of legume protein	Diet high in animal protein (AP)	6	Adiponectin (ng/ml)	Overweight or obese and T2DM and NAFLD (BMI (kg/m^2): IG: 29.4±1.0 and CG: 31.0±0.8)

BMI, body mass index; CRP, C-reactive protein; CG, control group; F, female; IL, interleukin; hs, high-sensitivity; IFNy, Interferon y; IL, Interleukin; IG, Intervention group; LKF-enriched, Lupin kernel flour enriched; MCP-1, M, male; Monocyte Chemoattractant Protein-1; NAFLD, Nonalcoholic Fatty Liver Disease; PCOS, Polycystic Ovary Syndrome; T2DM, Type 2 Diabetes Mellitus; TNF-α, Tumor Necrosis Factor; TLC diet, therapeutic lifestyle change diet.

* Serum level of hs-CRP is available for 22 participants.

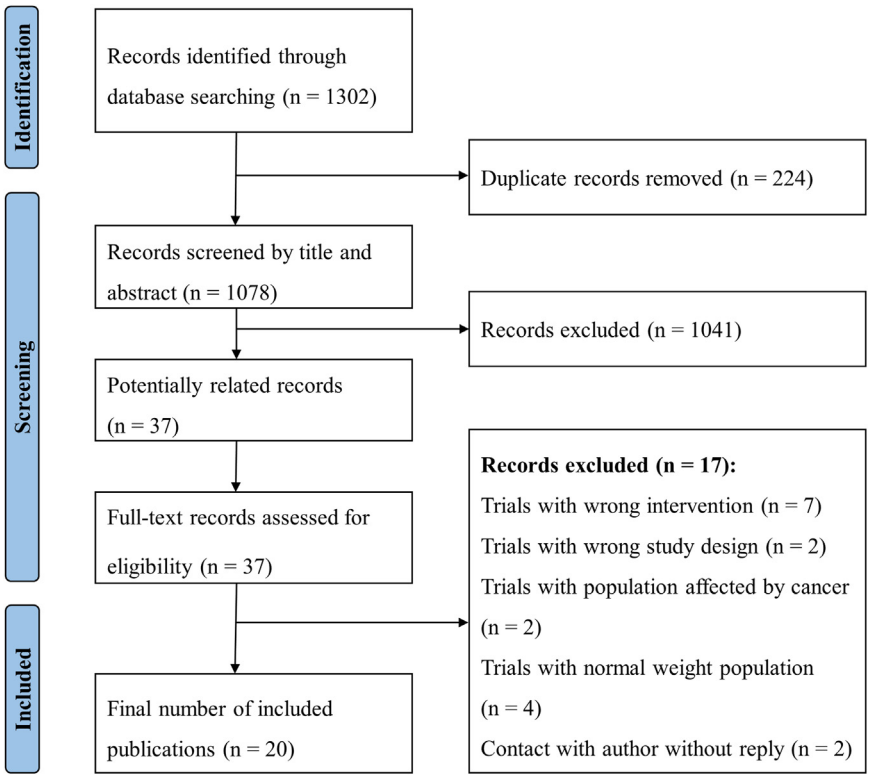

Fig. 1. Flow diagram of literature search and study selection process.

comparing it with another diet lacking legumes [23,25,34,36,43–45]. Five trials (25%) involved the consumption of specific legume-enriched food compared to an isocaloric legume-free alternative or placebo. For instance, pea fiber wafers [35], wheat biscuits enriched with plant proteins sourced from legumes and seeds [38], lupin-enriched food [43], extruded adzuki bean convenient food (EABCF) [26], and bean and oats snack bar [39]. Four of the included studies (20%) employed food substitution as the dietary intervention; two of them substituted red meat with legumes in Therapeutic Lifestyle Changes (TLC) diet [24,37]. Other trials replaced one-third of refined rice consumption with legumes in a usual diet [31] and incorporated 15–20% of usual daily energy intake in an ad libitum diet with LKF-enriched bread (bread enriched with Lupin kernel flour) [33]. The remaining studies (20%) compared the consumption of a certain amounts of legumes as an intervention with the nonconsumption of legumes or consumption of a nonlegume alternative [27,32,40,41]. Notably, four studies included nonsoy legumes as part of an energy-restricted diet [23,36,38,42], and one study incorporated nonsoy legumes as part of a low-glycemic index (LGI) diet [26].

3.2.3. Quality assessment and risk of bias

The Cochrane RoB2.0 tool was used to assess the quality and risk of bias in the eligible trials. Results are presented in Table 2 and supplementary table 1. Overall, the risk of bias ranged from “low” to “some concerns” across all included studies. Thirteen studies exhibited a low risk of bias [24–27,33–38,42–44], whereas seven studies had some concerns [23,31,39,40]. All included trials employed random allocation of participants [23–27,31–45]. Allocation concealment was clearly reported in six trials [25,31,34,35,37,42], whereas other studies had an unclear risk of bias regarding allocation concealment. Only six trials had a well-defined level of blinding [31,34,37,38,42,43].

3.3. Meta-analysis results

3.3.1. Effect of nonsoy legumes consumption on serum level of Adiponectin

The meta-analysis of the six studies examining the serum levels of Adiponectin (339 observation; 170 intervention and 169 control subjects) indicated that relative to the comparator diet or comparator food, nonsoy legumes consumption can significantly elevate the serum level of Adiponectin (MD=0.7405 mg/l; 95% CI: 0.2777, 1.2033, P=.0017) with nonsignificant between-study heterogeneity (I^2=40.2%, P=.14) (Fig. 2).

Subgroup analysis by trial duration modified the heterogeneity in studies <12 weeks (I^2=0.0%, P=.38), while among studies with the trial duration of ≥12 weeks, heterogeneity was still moderate (I^2=43.7%, P=.17). Subgroup analysis by study design reduced heterogeneity among both crossover (I^2=0.0%, P=.45) and parallel (I^2=0.0%, P=.27) trials. Moreover, subgroup analysis by health status of participants could also reduce heterogeneity among studies with healthy (I^2=35.1%, P=.20) and unhealthy participants (I^2=21.3%, P=.26). The reduction in serum levels of Adiponectin following consumption of nonsoy legumes was statistically significant across all subgroups (Table 3).

3.3.2. Effect of nonsoy legumes consumption on serum level of CRP

The comprehensive meta-analysis of eighteen studies (1654 observation; 800 intervention and 854 control subjects) revealed nonsoy legumes consumption may not change the serum levels of CRP significantly (MD=−0.0895 mg/l; 95% CI: −0.2570, 0.0780, P=.2951), exhibiting low heterogeneity between studies (I^2=22.7%, P=.18) (Fig. 3). Table 3 presents the subgroup analysis outcomes for CRP serum levels. The decrease in serum levels of CRP did not attain statistical significance in any of the subgroups.

Table 2
Summary risk of bias assessment of selected RCTs (RoB 2.0 domains).

Study references	Randomization process	period and carryover effects (crossover design)	deviations from the intended interventions	Missing outcome data	measurement of the outcome	selection of the reported result	Overall Quality Score	Reasons for concern
Han et al. [31]	Low	-	Some concerns	Some concerns	Low	High	Some concerns	Missing data likely to be associated with outcomes, ambiguity in reporting the results
Hodgson et al. [33]	Low	-	Some concerns	Low	Low	Low	Low	No concerns
Hermsdorff et al. [23]	Some concerns	-	Some concerns	Low	Low	Some concerns	Some concerns	No complete information on randomisation
Lambert et al. [35]	Low	-	Low	Low	Low	Low	Low	No concerns
Safaeiyan et al. [36]	Low	-	Some concerns	Low	Low	Some concerns	Low	No concerns
Liu et al. [26]	Low	-	Low	Low	Low	Some concerns	Low	No concerns
Binou et al. [38]	Low	-	Some concerns	Low	Low	Some concerns	Low	No concerns
Ramírez-Jiménez et al. [39]	Some concerns	-	Some concerns	Low	Low	Some concerns	Some concerns	Little information on randomisation and concealment
Gravel et al. [40]	Some concerns	-	Some concerns	Low	Low	Some concerns	Some concerns	No clear information on concealment, the risk because of the effect of assignment to intervention
Belski et al. [42]	Low	-	Low	Low	Low	Some concerns	Low	No concerns
Kazemi et al. [43]	Some concerns	-	Low	Low	Low	Some concerns	Low	No concerns
Hematdar et al. [27]	Low	-	Low	Low	Low	Low	Low	No concerns
Markova et al. [45]	Some concerns	-	Low	Low	Some concerns	Some concerns	Some concerns	Ambiguity in reporting the results
Winham et al. [32]	Some concerns	Low	Low	Some concerns	Low	Some concerns	Some concerns	Little information on concealment
Abeysekara et al. [34]	Low	Low	Low	Some concerns	Low	Low	Low	No concerns
Hosseinpour-Niazi et al. [24]	Some concerns	Low	Low	Low	Low	Some concerns	Low	No concerns
Saraf-Bank et al. [25]	Low	Low	Some concerns	Low	Low	Some concerns	Low	No concerns
Mirmiran et al. [37]	Low	Low	Some concerns	Low	Low	Some concerns	Low	No concerns
Winham et al. [41]	Some concerns	Low	Low	Some concerns	Low	Some concerns	Some concerns	Little information on concealment
Tovar et al. [44]	Low	Low	Low	Low	Low	Low	Low	No concerns

3.3.3. Effect of nonsoy legumes consumption on serum level of IL-6

The overall outcome of the meta-analysis comprising seven different studies (498 observations; 252 interventions and 246 control subjects) showed that nonsoy legumes consumption cannot significantly decrease the serum level of IL-6 (MD=−0.3200 pg/ml; 95% CI: −0.8411, 0.2010, *P*=.2286) compared to control diets with a substantial between-study heterogeneity (I^2=62.1%, *P*=.01) (Fig. 4). Subgroup analyses eliminated between-study heterogeneity among studies with the trial duration <12 weeks (I^2=0.0%, *P*=.70), employing crossover design (I^2=0.0%, *P*=.34), and unhealthy partic-

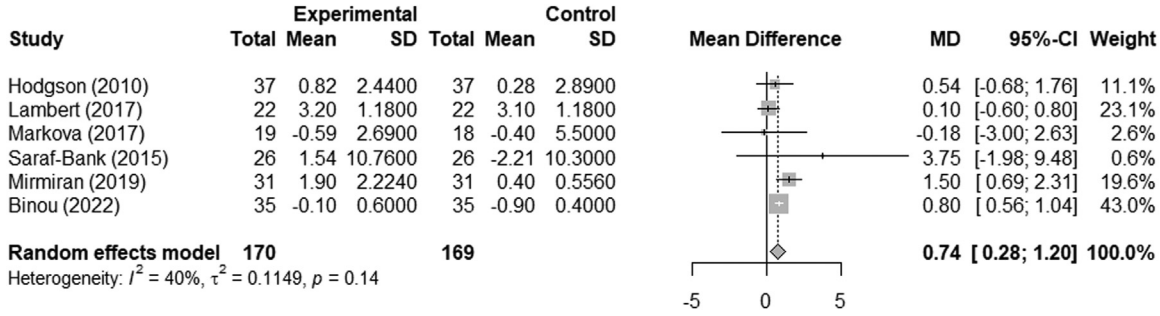

Fig. 2. Forest plot demonstrating the mean differences (MDs) corresponding with 95% CI of the effect of nonsoy legumes consumption on serum level of Adiponectin.

Table 3
The results of subgroup analyses for serum levels of Adiponectin, CRP, IL-6, and TNFα.

Outcome	Number of trials	MD (95% CI)	*P*	Heterogeneity (I^2)
Serum Adiponectin level				
Overall	6	0.7405 (0.2777, 1.2033)	.0017	40.2%, *P*=.14
Trial duration				
<12 weeks	3	1.4149 (0.6462, 2.1836)	.0003	0.0%, *P*=.38
≥12 weeks	3	0.5725 (0.0986, 1.0464)	.0179	43.7%, *P*=.17
Study design				
Parallel	4	0.5915 (0.1939, 0.9892)	.0036	0.0%, *P*=.27
Crossover	2	1.5438 (0.7447, 2.3429)	.0002	0.0%, *P*=.45
Participants Health status				
Healthy	4	0.5922 (0.1146, 1.0698)	.0151	35.1%, *P*=.20
Unhealthy	2	1.2202 (−0.0080, 2.4485)	.0515	21.3%, *P*=.26
Serum CRP level				
Overall	18	−0.3200 (−0.8411, 0.2010)	.2286	62.1%, *P*=.01
Trial duration				
<12 weeks	11	−0.4058 (−1.0613, 0.2497)	.225	25.2% *P*=.22
≥12 weeks	7	−0.0282 (−0.2346, 0.1783)	.7891	18.8 %, *P*=.29
Study design				
Parallel	12	−0.0608 (−0.1862, 0.0646)	.3421	11.8 %, *P*=.33
crossover	6	−0.4269 (−1.3128, 0.4591)	.345	42.1 %, *P*=.11
Participants Health status				
Healthy	12	−0.1652 (−0.4806, 0.1503)	.3047	43 %, *P*=.05
Unhealthy	6	−0.0983 (−0.2258, 0.0291)	.1304	0.0 %, *P*=.91
Serum IL-6 level				
Overall	7	−0.3200 (−0.8411, 0.2010)	.2286	62.1 %, *P*=.01
Trial duration				
<12 weeks	4	−0.6998 (−1.5242, 0.1246)	.0962	0.0 %, *P*=.70
≥12 weeks	3	−0.1552 (−0.8987, 0.5884)	.6826	86.1 %, *P*<.01
Study design				
Parallel	5	−0.2819 (−0.8351, 0.2713)	.3179	72.8 %, *P*<.01
Crossover	2	−1.1488 (−3.6205, 1.3229)	.3623	0.0 %, *P*=.34
Participants Health status				
Healthy	5	−0.2320 (−0.8747, 0.4106)	.4791	74.4 %, *P*<.01
Unhealthy	2	−0.7852 (−1.8108, 0.2405)	.1335	0.0 %, *P*=.78
Serum TNFα level				
Overall	7	−0.0922 (−0.5109, 0.3265)	.6661	22.8% %, *P*=.82
Trial duration				
<12 weeks	4	−0.6697 (−2.9072, 1.5678)	.5574	42.3 %, *P*=.16
≥12 weeks	3	−0.1242 (−0.4160, 0.1675)	.4039	22.2 %, *P*=.28
Study design				
Parallel	5	−0.0803 (−0.6495, 0.4889)	.7822	47.8 %, *P*=.1
crossover	2	−0.2169 (−2.8134, 2.3796)	.8699	0.0 %, *P*=.73
Participants Health status				
Healthy	5	−0.1984 (−0.2320, −0.1648)	< .0001	0.0 %, *P*=.53
Unhealthy	2	−2.7964 (−8.1042, 2.5114)	.3018	67.4 %, *P*=.08

Abbreviation, CI, confidence interval; CRP, c-reactive protein; IL-6, interleukin 6; MD, mean difference; TNF-α, tumor necrosis factor-α.

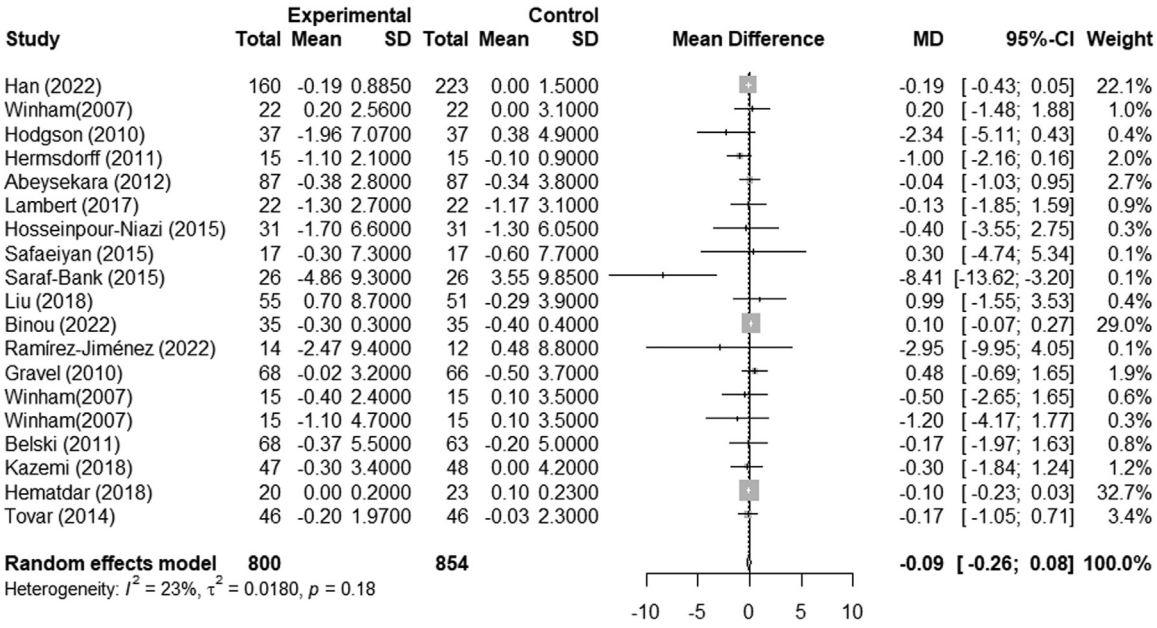

Fig. 3. Forest plot demonstrating the mean differences (MDs) corresponding with 95% CI of the effect of nonsoy legumes consumption on serum level of CRP.

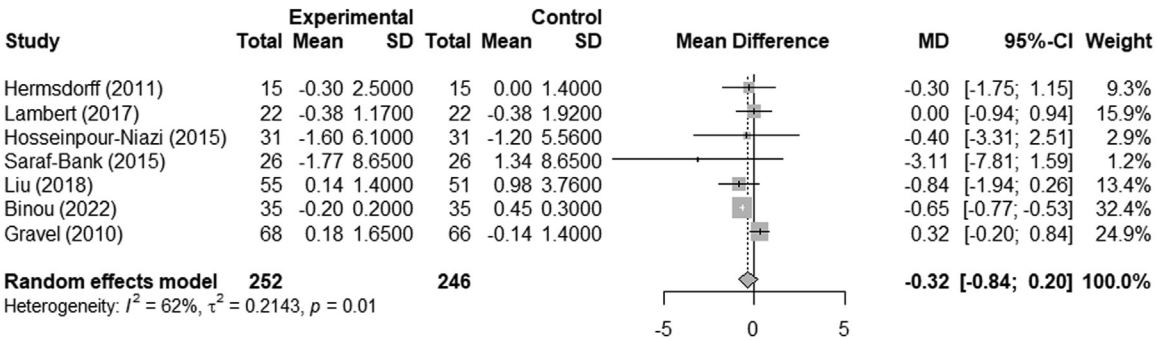

Fig. 4. Forest plot demonstrating the mean differences (MDs) corresponding with 95% CI of the effect of nonsoy legumes consumption on serum level of IL-6.

ipants (I^2=0.0%, P=.78) (Table 3). Serum levels of IL-6 did not change significantly with nonsoy legumes consumption in any of the subgroups.

3.3.4. Effect of nonsoy legumes consumption on serum level of TNFα

The result of meta-analysis of seven studies (498 observations; 252 interventions and 246 control subjects) showed that nonsoy legumes consumption may not significantly reduce the serum level of TNFα (MD=−0.0922 pg/ml; 95% CI: −0.5109; 0.3265, P=.6661) compared to control diets with a low between-study heterogeneity (I^2=22.8%, P=.26) (Fig. 5). The results of subgroup analysis are shown in table 3. Subgroup analysis based on study design adjusted the between-study heterogeneity in studies with crossover design (I^2=0.0%, P=.73), while the change in serum level of TNFα did not reach statistical significance. On the other hand, subgroup analysis by health status of participants showed that nonsoy legumes consumption can significantly reduce the serum levels of TNFα among studies with healthy participants (MD=−0.1984 pg/ml; 95% CI: −0.2320, −0.1648, P<.0001) with no between-study heterogeneity (I^2=0.0%, P=.53). Subgroup analysis based on trial duration did not alter heterogeneity, and the changes in serum TNFα level did not reach statistical significance (Table 3).

3.3.5. Effect of nonsoy legumes consumption on serum level of IL-1β

The result of meta-analysis of two studies (114 observation; 57 intervention and 57 control subjects) assessing the serum levels IL-1β indicated a significant decrease in serum level of IL-1β (MD=−0.3013 pg/ml; 95% CI: −0.3748, −0.2274, P<.0001) with no between-study heterogeneity (I^2=0.0%, P=.78) (Fig. 6) following nonsoy legumes consumption compared to control diets.

3.4. Sensitivity analysis

To assess whether the results were potentially underweighted in the crossover trial, paired analysis of crossover RCTs with correlation coefficients of 0.25, 0.5, and 0.75 were conducted (supplementary table 2). The incorporation of correlation coefficients demonstrated that for serum levels of Adiponectin, CRP, and TNFα, overall results were largely consistent with the primary analyses. On the contrary, the observed decrease in the serum levels of IL-6 may be inconsistent with primary analyses and achieve statistical significance (supplementary table 2). In addition, sensitivity analyses using the leave-one-out method were performed to identify studies that may have exaggerated effect sizes. Although in the initial meta-analysis, the alteration in serum IL-6 levels did not achieve statistical significance, upon the exclusion

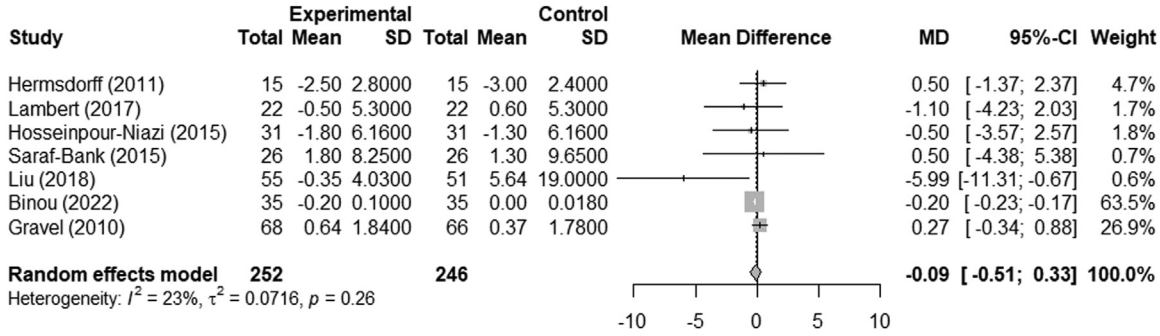

Fig. 5. Forest plot demonstrating the mean differences (MDs) corresponding with 95% CI of the effect of nonsoy legumes consumption on serum level of TNF-α.

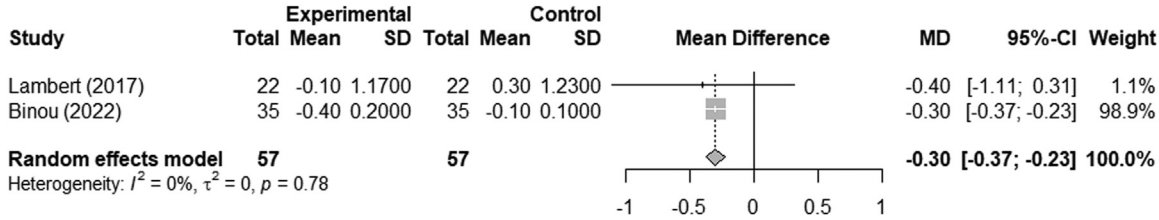

Fig. 6. Forest plot demonstrating the mean differences (MDs) corresponding with 95% CI of the effect of nonsoy legumes consumption on serum level of IL-1 β.

of one study [40], there was a significant reduction in the levels of this biomarker (MD=−0.6409 pg/ml; 95% CI: −0.7582; −0.5236, P<.0001) with no between-study heterogeneity (I^2=0.0%, P=.66). No other sensitivity analysis revealed any significant findings using this method (data not shown). The subgroup analyses were conducted in order to evaluate trial duration, study design, and health status of study participants. The outcomes of subgroup analysis are shown in Table 3.

3.5. Publication bias

Upon visual inspection of funnel plots and the results of Egger's test, there was no evidence of publication bias for studies investigating the effect of nonsoy legumes consumption on serum levels of Adiponectin (bias estimate: 0.0114, SE=0.4327, P=.9803) (Fig. 7 A), CRP (bias estimate: −0.1781, SE=0.1860, P=.3517) (Fig. 7 B) and IL-6 (Bias estimate: 0.3229, SE=0.7966, P=.7020) (Fig. 7 C) and TNF-α (Bias estimate: −0.1040, SE=0.5047, P=.8448) (Fig. 7 D). However, Egger's test could not be applied to assess small study effects for serum levels of IL-1β, because of the limited number of studies.

4. Discussion

Current study demonstrates that consumption of nonsoy legumes can have anti-inflammatory effects. This systematic review is the first comprehensive assessment examining the impact of consuming nonsoy legumes on the serum levels of four significant pro-inflammatory biomarkers: CRP, IL-6, TNF-α, IL-1β, and Adiponectin. All available clinical trials published between 2007 and 2022 with the trial duration of 4–52 weeks have been investigated. Results revealed that consumption of nonsoy legumes can have a beneficial effect on the inflammatory profile in overweight or obese adults. In particular, incorporating nonsoy legumes into the diet or using them as a supplementary food significantly lower serum levels IL-1β and increase Adiponectin, potentially providing beneficial effects against inflammation and insulin resistance [11]. Regarding the serum levels of IL-6, overall analysis showed that nonsoy legumes consumption may not change levels of this pro-inflammatory cytokine. However, the sensitivity analysis by the leave-one-out method indicated a potential of nonsoy legumes in reducing IL-6 levels when excluding one study [40]. In contrast, no statistically significant changes were observed in CRP and TNF-α serum levels. Of note, the subgroup analysis showed that serum level of TNF-α significantly decreased in studies involving healthy participants. However, in other instances, despite mitigating between-study heterogeneity, the subgroup analysis did not achieve statistical significance. This could be attributed to the limited number of studies available. While there are various biomarkers associated with inflammation beyond CRP, such as IL-6, TNF-α, IL-1β, and Adiponectin, which have been explored in clinical trials involving the intake of nonsoy legumes, a meta-analysis was feasible only for these specific biomarkers. This limitation arose from an exhaustive literature review revealing that additional biomarkers were only assessed in a single trial that met the inclusion criteria. For instance, only one study [23] evaluated the serum levels of Complement C3 and Homocysteine, another study [35] looked at the serum levels of IL-12P40, IL-8, IFNγ, and MCP-1, and a different study [40] investigated the serum levels of Fibrinogen. In a clinical trial by Lambert et al., a significant reduction in serum IL-8 levels was measured in both the experimental group, which consumed wafers with 5 g/serving of yellow pea fiber, and the control group, which consumed isocaloric wafers without pea fiber. However, the changes in serum levels of IL-12P40, IFNγ, and MCP-1 observed in the trial did not reach statistical significance [35]. In RCT carried out by Hermsdorff et al., following a legume-enriched, calorie-restricted diet, there was a significant decrease in serum Complement C3 levels (P=.039) compared to control group, whereas the levels of Homocysteine remained unchanged in a statistically significant manner [23]. Furthermore, Gravel et al. noted a significant reduction in plasma Fibrinogen concentration (P=.0169) after participants consumed 750 ml of pulses weekly for 16 weeks [40]. Despite the disparity in findings across clinical trials, such as the favorable impact of nonsoy legumes consumption on inflammation [23–26,37,38,49] versus instances where no effects were observed [40,50], this systematic review demonstrates that nonsoy legumes consumption may indeed have a beneficial effect on inflammation.

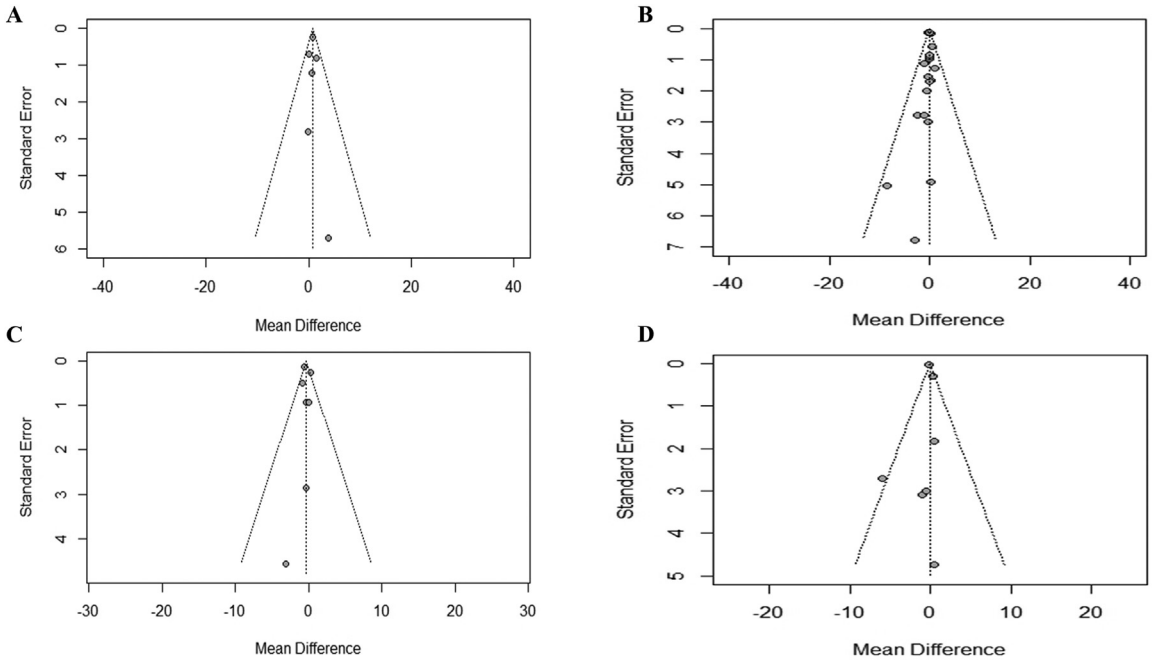

Fig. 7. Funnel plot for the mean differences (MDs) versus their SEs (standard errors) for studies that assessed the serum level of Adiponectin (A), CRP (B), IL-6 (C), and TNFα (D).

Certain constituents within nonsoy legumes could account for their favorable effects on inflammatory biomarkers. For instance, a thorough review conducted by Hutchins et al. in 2012 revealed that consuming beans, due to their fiber content, their protein fraction enabling a starch-protein interaction thus reducing starch digestibility, along with the presence of phytic acid, may lead to reduced blood glucose and insulin response following food intake [17], which can have an improving effect on inflammation [51]. Evidence indicates that consuming beans may lead to weight loss, potentially improving inflammatory cytokines [52], irrespective of energy restriction or other dietary factors. [53,54]. Moreover, nonsoy legumes serve as a rich source of bioactive compounds and antioxidants, including phenolic compounds and saponins, which possess promising anti-inflammatory properties [55]. Another beneficial effect of nonsoy legumes, largely attributed to their high fiber and bioactive compound content, may be their ability to improve gut microbiota, thereby preventing intestinal inflammation. [56,57,58,59]. Also, anti-inflammatory properties of legumes could stem from alterations in the methylation pattern of certain genes associated with the inflammatory process, leading to reduce inflammatory biomarkers [60]. However, certain studies have associated this effect with bioactive compounds found in legumes, such as Bowman-Birk protease inhibitors (BBI), which are bioactive compounds found in the albumin fraction of legumes and can exert anti-inflammatory effects [61,62,63]. Additionally, legumes are commonly recognized for their richness in essential vitamins and minerals, including magnesium, iron, zinc, copper, thiamine (vitamin B1), and folates [64]. Among these, evidence clearly underscores the crucial role of magnesium in supporting optimal immune function and regulating inflammation [65], as well as the anti-inflammatory effects of thiamine [66] and zinc [67]. In a review by Janiszewska et al., it is suggested that incorporating nonsoy legumes into a healthy, plant-based diet could positively influence Adiponectin levels. This potential benefit is attributed to the legumes' low caloric density and high fiber content [68]. Furthermore, the observed elevation in Adiponectin levels linked to nonsoy legumes consumption might be attributed to their abundance in polyphenols and antioxidants. This assertion is bolstered by studies indicating that Adiponectin demonstrates an enhanced response to diets rich in antioxidants [68,69,70]. The reduction in serum levels of IL-1β associated with consuming nonsoy legumes can be primarily attributed to their high fiber content and low levels of fat and sugar [71,72]. Nevertheless, a comprehensive characterization of the mechanism underlying the anti-inflammatory effects of nonsoy legumes is still undergoing exploration, with only partial findings reported in a limited body of research [73]. Studies have indicated that the anti-inflammatory effects of legumes are associated to their bioactive compounds, which can inhibit the Toll-like receptors (TLR) signaling pathway, decrease the mRNA expression of Inducible nitric oxide synthase (iNOS), IL-1β, IL-6, and TNF-α, reducing the production of inflammatory molecules such as IL-1β, IL-6, and TNF-α [73,55], and increasing the production of anti-inflammatory adipokines such as Adiponectin. Additionally, it has been verified that unsaturated fats, present in good amounts in nonsoy legumes [74], can boost the expression of the Adiponectin gene [75].

One notable strength of this meta-analysis lies in its pioneering nature, as it represents one of the first studies to comprehensively assess multiple biomarkers associated with inflammation, providing a comprehensive overview of the impact of nonsoy legumes consumption on inflammatory profiles. Additionally, the utilization of Egger's test revealed the absence of publication bias in studies examining the effects of nonsoy legumes consumption on inflammatory markers, further enhancing the reliability and robustness of the findings. A major limitation of this systematic review and meta-analysis could be the scant evidence available for certain biomarkers under evaluation. This challenge emerged from not only a scarcity of clinical trials investigating the impact of nonsoy legumes consumption on inflammatory biomarkers, but also from the exclusion of some reported serum biomarker levels from the meta-analysis due to ambiguous result reporting in certain studies. For example, in one study [45], the serum levels of seven in-

flammatory biomarkers including TNFα, Interleukin-1 receptor antagonist (IL-1RA), MCP-1, Interleukin-18 (IL-18), IL-8, Interleukin-4 (IL-4), IL-6 were presented as figures, and in another study [31], serum levels of Adiponectin were also displayed graphically, without providing specific numerical values. Additionally, only six of the studies incorporated into this meta-analysis explicitly defined their levels of blinding [31,34,37,38,42,43]. Additionally, some RCTs included nonsoy legumes as part of an energy-restricted diet [23,36,38,42] and one study incorporated nonsoy legumes within a low-glycemic index diet [26]. Since these types of diet have demonstrated potential anti-inflammatory effects [13,76], the observed anti-inflammatory effects in these studies might be influenced by the confounding effects of the specific diet used. Another significant limitation to consider is the wide range of nonsoy legumes consumed, encompassing various types and dosages. This variability introduces a potential source of bias within this systematic review and meta-analysis, as the diverse consumption patterns may influence the observed effects on inflammatory biomarkers. It is imperative to acknowledge and address this variability in order to accurately interpret the findings and draw meaningful conclusions regarding the impact of nonsoy legumes consumption on inflammatory markers.

In conclusion, the results of the current meta-analysis of all published RCTs between 2007 and 2022 showed a notable increase in serum levels of Adiponectin and a considerable reduction in serum levels of IL-1β following nonsoy legumes consumption. However, the intake of nonsoy legumes may not alter CRP, IL-6, and TNF-α serum levels significantly. While the findings of the present systematic review and meta-analysis suggest the possibility of a beneficial effect of consuming nonsoy legumes on inflammation, further clinical trials with larger sample sizes and a broader spectrum of inflammatory biomarkers are warranted to substantiate these observations.

Declaration of competing interest

The authors declare that there are no conflicts of interest.

CRediT authorship contribution statement

Fatemeh Mansouri: Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Gaia de Simone:** Investigation, Data curation. **Laura Bordoni:** Writing – review & editing, Supervision, Investigation, Conceptualization. **Rosita Gabbianelli:** Writing – review & editing, Supervision, Resources.

Funding

This work supported by doctoral grant of "AGRIBIOSERV_PNC_MISURA B4" and the University of Camerino.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jnutbio.2024.109718.

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