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The effect of ginseng supplementation and health outcomes: A GRADE-assessed systematic review and meta-analysis of randomized controlled trials

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ABSTRACT

Ginseng, a widely used herbal remedy, has been proposed to possess cardiometabolic benefits. However, the findings regarding its effects on health outcomes remain inconsistent. This meta-analysis aimed to assess ginseng supplementation's impact on health outcomes. A comprehensive literature search was conducted across multiple databases to identify RCTs evaluating the effect of ginseng supplementation. Forty-four RCTs encompassing 56 intervention arms were included. Ginseng supplementation significantly reduced IL-6 levels (WMD = −2.03 pg/mL; 95 % CI: −3.12 to −0.93; $p < 0.001$). No significant effects were observed on body weight (WMD = −0.52 kg; 95 % CI: −1.47 to 0.44), BMI (WMD = −0.035 kg/m^2; 95 % CI: −0.148 to 0.079), waist circumference, systolic or diastolic blood pressure, or lipid profiles including total cholesterol, triglycerides, HDL-C, and LDL-C. The beneficial effects of ginseng supplementation on SBP and DBP were shown after sensitivity analysis. Ginseng supplementation may improve inflammatory profiles by lowering IL-6 and enhancing adiponectin, but it does not appear to significantly influence anthropometric measures, and lipid profiles. Further well-designed, long-term trials are warranted.

1. Introduction

Cardiovascular diseases (CVDs) and metabolic disorders, including obesity, dyslipidemia, and hypertension, remain the leading causes of morbidity and mortality worldwide (Wu et al., 2023). The global surge in these non-communicable diseases has intensified the focus on complementary and alternative therapies that may help mitigate cardiometabolic risks (Pam et al., 2024; Pam, Asemani, Azizi, & Jamilian, 2024). Among these, *Panax ginseng*, a traditional herbal remedy widely used in East Asia, has gained increasing scientific attention for its purported health-promoting effects (Liu et al., 2022).

Ginseng roots contain numerous bioactive compounds, especially ginsenosides, which are considered the primary pharmacological constituents. These compounds have been shown to exert antioxidant, anti-inflammatory, vasodilatory, immunomodulatory, and metabolic regulatory effects in both experimental and clinical settings (Lü, Yao, & Chen, 2009; Wang et al., 2022). Mechanistically, ginseng may enhance nitric oxide (NO) production and endothelial function, suppress the expression of pro-inflammatory cytokines such as IL-6 and TNF-α, modulate adipokines like leptin and adiponectin, and influence glucose and lipid metabolism via AMPK and PPAR pathways (In-Ho et al., 2018).

Several systematic reviews have examined the impact of ginseng on cardiovascular risk factors, resulting in mixed findings that underscore its complex effects. A meta-analysis by Arabi et al., found that ginseng supplementation did not significantly affect lipid parameters such as triglycerides (TG), total cholesterol, HDL-C, and LDL-C across different health conditions (Arabi et al., 2024). In contrast, a different systematic review concentrated on metabolic parameters revealed that ginseng supplementation significantly improved blood glucose, blood pressure, and lipid markers, indicating possible metabolic advantages (S. K. Park et al., 2021). Several factors could account for this discrepancy, including heterogeneity in dosage, duration of intervention, health status of participants, and outcome measurement methods (He et al., 2018). The varied outcomes indicate that although ginseng shows potential for therapeutic use, further comprehensive research is necessary to determine its effectiveness and safety for particular groups.

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Previous meta-analyses have typically focused on one or two biomarkers or have included a limited number of studies, restricting their generalizability (Arabi et al., 2024; S. K. Park et al., 2021). Moreover, emerging trials in recent years necessitate an updated synthesis of the evidence to determine whether ginseng supplementation offers meaningful benefits in modulating anthropometric and cardiovascular parameters. To address this gap, the present study aimed to systematically review and quantitatively synthesize the available evidence from RCTs investigating the effects of ginseng supplementation on a wide range of anthropometric indicators, lipid profiles, blood pressure, and inflammatory markers. We employed robust meta-analytic techniques, including random-effects modeling, sensitivity analyses, subgroup comparisons, and assessments of publication bias to ensure the reliability and validity of the findings.

2. Method

This study adhered to the guidelines set forth in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Page et al., 2021). The study protocol is officially registered with PROSPERO under the registration code CRD420251043070.

2.1. Search strategy

A thorough search was performed using the Cochrane Central Register of Controlled Trials (Central), Web of Science, Medline (http://www.ncbi.nlm.nih.gov/pubmed), Scopus, and Embase databases to locate articles published up to April 2025. Additionally, key journals and reference lists from pertinent articles, meta-analyses, and reviews on ginseng were manually examined to find any further eligible studies. The details of the search strategy are provided in **Supplementary Table 1**.

2.2. Eligibility criteria

The inclusion and exclusion criteria for selecting studies in this meta-analysis were established a priori based on the PICOS framework (Population, Intervention, Comparator, Outcome, Study design). Studies were included if they met all the following conditions: Inclusion Criteria: Population (P): Adults participants. Intervention (I): Trials in which the intervention consisted of oral supplementation with ginseng. Comparator (C): Studies must include a control group, receiving either placebo or standard care. Outcomes (O): Studies that reported at least one of the following outcomes were eligible: BMI, WC, WHR, SBP, DBP, LDL-C, HDL-C, TC, TG, CRP, IL-6, TNF-α, Adiponectin, or leptin. Only randomized controlled trials (RCTs), including parallel or crossover designs, were included. Observational studies, quasi-experimental studies, and non-randomized trials were excluded.

Exclusion Criteria: Trials not reporting sufficient quantitative data (e.g., means and standard deviations, or change scores) necessary for meta-analysis. Non-English publications, conference abstracts, letters, case reports, and reviews. Studies lacking a placebo or control group. Duplicate publications or multiple reports from the same trial population (in such cases, the most complete and recent dataset was included). Studies conducted on animals or in vitro settings were excluded. Two independent reviewers screened titles, abstracts, and full texts to identify eligible studies. Any discrepancies were resolved through discussion or by consulting a third reviewer.

2.3. Data extraction

The data extraction process was conducted independently by two reviewers (MF and MD), and disagreements were resolved through discussion or, if necessary, by consultation with a third reviewer (XH). If relevant data were missing or unclear, the corresponding authors of the original articles were contacted via email to obtain additional information. From each eligible randomized controlled trial (RCT), the following data were extracted and entered into a standardized form: First author's name, year of publication, country in which the study was conducted. Study design (parallel or crossover), duration of intervention (in weeks), type and form of ginseng used), dose of ginseng supplementation, and details of the control intervention (e.g., placebo). Total sample size in each group (intervention and control), mean age of participants, gender distribution, and health status. All extracted data were double-checked for accuracy and consistency before statistical analysis. If results were presented in different units, appropriate conversions were applied to standardize the outcomes across studies (e.g., mg/dL to mmol/L for lipids when necessary).

2.4. Data synthesis

The primary outcomes of this meta-analysis were assessed by calculating the weighted mean difference (WMD) and 95 % confidence intervals (CIs) for changes in anthropometric, cardiovascular, lipid, and inflammatory markers between participants receiving ginseng supplementation and those in the control (placebo) group. A random-effects model based on the restricted maximum likelihood (REML) method was employed to account for between-study variability and estimate the overall effect size. When the standard deviation (SD) was not directly reported, it was calculated using available data such as standard error of the mean (SEM), confidence intervals, or *p*-values. For instance, SEM was converted to SD using the formula: $SD = SEM \times \sqrt{n}$, where n refers to the sample size of the respective group (Jpt, 2008). Statistical heterogeneity among the studies was evaluated using Cochran's Q test (with a significance threshold of $p < 0.1$) and the I^2 statistic. An I^2 value >50 % combined with $p < 0.1$ was considered indicative of substantial heterogeneity (Higgins & Thompson, 2002). To investigate potential sources of heterogeneity, a priori subgroup analyses were conducted based on: Intervention duration (>10 weeks vs. ≤10 weeks), Participant age (≤50 years vs. >50), Sample size ((≤50 numbers vs. >50), and Ginseng dosage (≤5 g/day vs. >5 g/day). Sensitivity analyses were performed by systematically excluding each individual study to assess its impact on the pooled estimates. When the number of studies for an outcome was ≥10, publication bias was assessed using Begg's rank correlation test and Egger's regression asymmetry test, complemented by visual inspection of funnel plots. All statistical analyses were carried out using STATA software (version 14.0; StataCorp, College Station, TX, USA). A two-sided *p* value of less than 0.05 was considered statistically significant.

2.5. Risk of bias assessment and GRADE approach

Version 2 of the Cochrane risk-of-bias tool (RoB2) was used to assess the quality of the included studies (Sterne et al., 2019). This system comprises seven criteria for assessing the risk of bias, outlined as follows: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases. Individual elements were evaluated for bias (categorized as high, low, or unclear risk), with interpretations of high risk, low risk, and unclear risk, respectively. We employed the GRADE system to determine the certainty of the evidence for each measured outcome (Guyatt et al., 2008).

3. Results

3.1. Study selection and characteristics

A total of 23,276 records were initially identified through database searches and other sources. After removal of duplicates and screening of titles and abstracts, 143 full-text articles were assessed for eligibility. Ultimately, 44 randomized controlled trials (RCTs) comprising 56 intervention arms met the inclusion criteria and were included in the

meta-analysis. Fig. 1 visually illustrates the search process and study selection, adhering to the PRISMA flow diagram.

The trials were published between 1998 and 2024 and conducted in various countries, including South Korea, the United States, Canada, China, Iran, Brazil, Spain, Croatia, and Japan. Sample sizes ranged from 6 to 199 participants per study. The duration of ginseng supplementation varied from 2 to 32 weeks. Most of the included studies followed a parallel-group randomized controlled design, though several used crossover designs. The study populations were diverse and included healthy adults, postmenopausal and premenopausal women, patients with type 2 diabetes mellitus (T2DM), hypertension (HTN), metabolic syndrome (MetS), obesity, non-alcoholic fatty liver disease (NAFLD), erectile dysfunction, glaucoma, hypoimmunity, and other conditions. Sex distribution varied across trials, with some including both male and female participants, while others focused exclusively on one sex. The type, dosage, and form of ginseng supplementation varied notably. Daily ginseng doses ranged from 200 mg to 6000 mg. A detailed description of the characteristics of all included trials is provided in Table 1.

3.2. Risk of bias and quality of evidence

The risk of bias assessment for the included randomized controlled trials was conducted using the Cochrane Collaboration's Risk of Bias 2.0 (RoB 2) tool and is presented in Table 1. Most studies were judged to have a low or some concerns risk of bias, particularly in domains related to the randomization process and deviations from intended interventions. A few studies had high risk of bias due to incomplete outcome data or selective reporting. The overall certainty of the evidence was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework and is summarized in Table 2. According to GRADE, the certainty of evidence for most outcomes ranged from low to moderate, mainly due to imprecision and heterogeneity among studies. However, outcomes such as the effect of ginseng on WC, leptin, adiponectin, TC, LDL, and HDL were graded as having moderate certainty, reflecting more consistent and precise findings across studies.

3.3. Effects of ginseng supplementation on obesity-related indices

3.3.1. Weight

Data on body weight changes were extracted from seven intervention arms (Hernández-García et al., 2024; Hosseini, Alipour, Ghadiry, & Zakerkish, 2016; D. H. Kwon et al., 2012; Reeds et al., 2011; Seong et al., 2021; Vuksan et al., 2019). The pooled analysis showed that ginseng supplementation resulted in a non-significant reduction in body weight compared with placebo (Weighted Mean Difference [WMD] = 0.08 kg; 95 % Confidence Interval [CI]: −0.56 to 0.72; $p = 0.813$). Heterogeneity among studies was moderate ($I^2 = 0.0$ %, $p = 0.998$) (**Supplementary Fig. 1**).

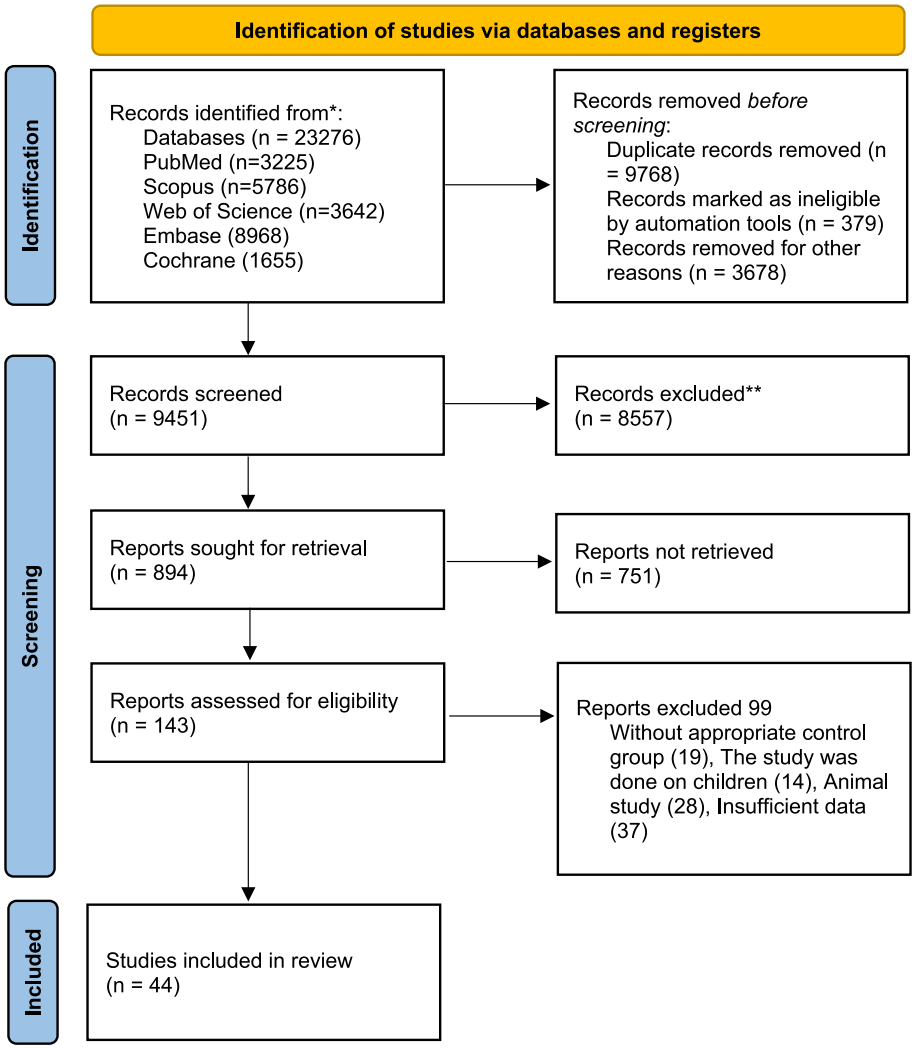

Fig. 1. Study Selection Flow Diagram.

Table 1
Characteristic of included studies in the meta analysis.

Author name	country	Study design	gender	Int. mean age	Con. mean age	N (Int)	N (Con)	Health condition	Intervention type (Inv)	Dose (mg/day)	Intervention type (Con)	Duration (week)	Quality
Ahn et al., 2011	Korea	Parallel, R, PC, SB	M/F (50)	61.4 ± 12.4	59.5 ± 11.8	25	25	Patients with first ST-segment elevation AMI requiring stent implantation	Red ginseng	3000	Placebo (75 mL of distilled water with ginseng fragrance)	32	High Risk
Reeds et al., 2011	US	Parallel, R, PC, DB	M/F (10)	46 ± 3	46 ± 3	5	5	Overweight and obese subjects with impaired glucose tolerance or newly diagnosed T2DM	Korean red ginseng extract (Spectrum Laboratories, Gardena, CA)	5500	placebo	4	Low Risk
Yoon et al., 2012 (a)	Korea	Parallel, R, PC, DB	M/F (30)	52.7 ± 11	54.8 ± 10	15	15	Type 2 diabetic	Vinegar extract from *Panax ginseng*	1500	placebo	8	Low Risk
Yoon et al., 2012 (b)	Korea	Parallel, R, PC, DB	M/F (29)	52.7 ± 11	54.8 ± 10	14	15	Type 2 diabetic	Vinegar extract from *Panax ginseng*	2000	placebo	8	Low Risk
Yoon et al., 2012 (c)	Korea	Parallel, R, PC, DB	M/F (32)	52.7 ± 11	54.8 ± 10	17	15	Type 2 diabetic	Vinegar extract from *Panax ginseng*	3000	placebo	8	Low Risk
Hong et al., 2016	Korea	Parallel, R, PC, SB	M/F (66)	47.8 ± 14.9	47.8 ± 14.9	35	31	Patients with NAFLD	Korean Red Ginseng (KRG) + *Silybum marianum* (450 mg/day), recommendation: regular aerobic exercise for >30 min/day	3000	placebo	3	High Risk
Hernández-García et al., 2024 (a)	Spain	Parallel, R, PC, TB	M (39)	34.3	37.8	15	24	Male recreational athletes	dry extract of *Panax ginseng* (capsule)	500	placebo	2	Some Concerns
Hernández-García et al., 2024 (b)	Spain	Parallel, R, PC, TB	M (36)	34.3	37.8	12	24	Male recreational athletes	Aerobic Exercise (10 Km race) & dry extract of *Panax ginseng*	500	placebo	2	Some Concerns
Xu et al., 2017	China	R, PC	M/F (177)	59.2 ± 8.5	58.4 ± 7.8	91	86	Patients with early chronic kidney disease	Ginsenoside Rb1 (GS-Rb1)	500	placebo	24	Some Concerns
Kim et al., 2012 (a)	Korea	Parallel, R, PC, DB	M/F (38)	36.4 ± 7.54	37.0 ± 9.76	19	19	Healthy participants	Korean red ginseng	3000	Placebo (KRG-flavored capsule containing corn starch)	8	High Risk
Kim et al., 2012 (b)	Korea	Parallel, R, PC, DB	M/F (38)	36.4 ± 7.54	37.0 ± 9.76	19	19	Healthy participants	Korean red ginseng	6000	Placebo (KRG-flavored capsule containing corn starch)	8	High Risk
Kwon et al., 2012	Korea	Parallel, R, PC, DB	F (45)	40.91 ± 9.65	46.48 ± 9.79	22	23	Obese women	Korean red ginseng	6000	Placebo (KRG-flavored capsule containing corn starch)	8	Some Concerns
Mucalo et al., 2013	Croatia	Parallel, R, PC, DB	M/F (64)	62.1 ± 8.80	63.9 ± 10.93	30	34	Subjects with type-2 diabetes and concomitant hypertension	American Ginseng (AG) root + usual antihypertensive and hypoglycemic medications	3000	Placeco (corn starch)	12	High Risk
Delui et al., 2013	Iran	Parallel, R, PC, DB	NR (36)	>20 years	>20 years	18	18	Hyperlipidemic patients	*Panax Ginseng*	500	Placeco	8	High Risk
Oh et al., 2014	Korea	Parallel, R, PC, DB	M/F (42)	53.2 ± 8.24	53.5 ± 8.70	21	21	Type 2 Diabetic Patients	Fermented Red Ginseng	2700	Placeco	4	High Risk
Park et al., 2012	Korea	Parallel, R, PC, DB	M/F (45)	43.1 ± 10.6	46.2 ± 11.0	23	22	Metabolic Syndrome	Korean Red Ginseng	4500	Placeco	12	Low Risk
Cho et al., 2013 (a)	Korea	Parallel, R, PC, DB	M/F (74)	42.6 ± 9.1	43.1 ± 8.9	34	34	Non-diabetic healthy overweight and obese adults	Korean red ginseng	6000	Placebo	12	Some Concerns
Cho et al., 2013 (b)	Korea	Parallel, R, PC, DB	M (118)	57.49 ± 7.94	57.32 ± 8.41	59	59	Men with mild-to-moderate ED	Korean red ginseng	1400	Placebo	8	Some Concerns
Bang et al., 2014	Korea	Parallel, R, PC, DB	M/F (41)	58.81 ± 7.88	56.10 ± 9.74	21	20	Subjects with IFG, IGT or newly diagnosed T2DM	Red ginseng	5000	Placebo	12	High Risk

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Table 1 (*continued*)

Author name	country	Study design	gender	Int. mean age	Con. mean age	N (Int)	N (Con)	Health condition	Intervention type (Inv)	Dose (mg/day)	Intervention type (Con)	Duration (week)	Quality
Rhee et al., 2014 (a)	Korea	Parallel, R, DB	M/F (60)	56.5 ± 12.1	52 ± 12.9	30	30	Non-diabetic healthy overweight and obese adults	Ginseol K-g1	100	NR	12	High Risk
Rhee et al., 2014 (b)	Korea	Parallel, R, DB	M/F (60)	56.5 ± 12.1	52 ± 12.9	30	30	Men with mild-to-moderate ED	Ginseol K-g1	300	NR	8	High Risk
Jung et al., 2020 (a)	Korea	Parallel, R, DB	M/F (54)	42.83 ± 11.03	42.67 ± 10.85	28	26	Participants with elevated alanine aminotransferase levels	Fermented ginseng powder 125	1400	Placebo	12	High Risk
Jung et al., 2020 (b)	Korea	Parallel, R, DB	M/F (56)	42.83 ± 11.03	42.67 ± 10.85	30	26	Participants with elevated alanine aminotransferase levels	Fermented ginseng powder 125	1400	Placebo	8	High Risk
Rhee et al., 2011	Korea	Parallel, R, DB	M/F (64)	55 ± 9	58 ± 6	30	34	Subjects with HTN	Korean red ginseng	3000	Placebo	12	Low Risk
Cha et al., 2016	Japan	Parallel, R, DB	M/F (62)	42.7 ± 12.6	41.4 ± 10.7	31	31	Prehypertensive subjects	Korean red ginseng	5000	Placebo	12	High Risk
Shen et al., 2020	Korea	Parallel, R, DB	M/F (60)	42.60 ± 11.74	41.73 ± 7.15	30	30	Patients with hepatic dysfunction	*Panax ginseng* extract	3000	Placebo	12	Some Concerns
Hosseini et al., 2016	Iran	Parallel, R, DB	M/F (40)	47.9 ± 4.7	47.3 ± 6.4	20	20	T2DM	Ginseng extract	3000	Placebo	8	High Risk
Chung et al., 2021	Korea	Parallel, R, DB	F (63)	58.7 ± 4.2	59.7 ± 4.2	33	30	Postmenopausal women	Korean Red Ginseng	2000	Placebo	8	Some Concerns
Park et al., 2020 (a)	Korea	Parallel, R, PC, DB	M/F (59)	61.2 ± 8.45	60.9 ± 7.23	28	31	T2DM	Korean Red Ginseng (KRG) extract + oral antidiabetic agents	3000	Placebo (corn starch and cellulose)	24	Some Concerns
Park et al., 2020 (b)	Korea	Parallel, R, PC, DB	M/F (61)	59.3 ± 8.79	59.7 ± 7.22	30	31	T2DM	Korean Red Ginseng (KRG) extract	3000	Placebo (corn starch and cellulose)	24	Some Concerns
Kim et al., 2010	Korea	Crossover, R, PC, DB	M/F (18)	59.03 ± 12.47	59.03 ± 12.47	9	9	Patients with Glaucoma	Korean red ginseng	4500	Placebo	12	Low Risk
Seong et al., 2021	Korea	Parallel, R, DB	M/F (50)	53.60 ± 8.45	49.84 ± 10.56	25	25	Patients with metabolic syndrome	Korean Red Ginseng	6000	Placebo	8	High Risk
Vuksan et al., 2019	Canada	Crossover, R, DB	M/F (48)	64 ± 7	64 ± 7	24	24	Individuals with type 2 diabetes	American Ginseng	3000	Placebo	8	High Risk
Kwon et al., 2020	Korea	Parallel, R, PC, DB	F (68)	55.9 ± 5.9	58.1 ± 4.7	36	32	Postmenopausal women with hypercholesterolemia	Korean red ginseng	2000	Placebo	4	High Risk
Chung et al., 2021	Korea	Parallel, R, DB	F (55)	49.42 ± 4.91	48.58 ± 5.04	29	26	Premenopausal women diagnosed with gynecologic cancer	Korean Red Ginseng	3000	Placebo	12	High Risk
Yang et al., 2024	China	Parallel, R, PC, DB	F (104)	54.37	54.33	52	52	People with hypoimmunity	Red ginseng	NR	Placebo	25	High Risk
Baek et al., 2019	Korea	Crossover, R, DB	M/F (63)	39.59 ± 12.36	41.29 ± 11.73	32	31	Nurses and fire fighters (members of two high stress occupations)	Korean Red Ginseng	2000	Placebo	6	High Risk
De Andrade et al., 2007	Brazil	Parallel, R, DB	M (60)	52.6	54.3	30	30	Patients with mild or moderate erectile dysfunction	Korean Red Ginseng	1000	Placebo	12	Some Concerns
Caron et al., 2002	US	Parallel, R, DB	M/F (30)	21.6 ± 2.7	21.6 ± 2.7	15	15	Healthy Adults	American ginseng (*Panax quinquefolius*)	200	Placebo	4	Some Concerns
Cha et al., 2016	Japan	Parallel, R, DB	M/F (62)	42.7 ± 12.6	41.4 ± 10.7	31	31	Prehypertensive subjects)	Korean Red Ginseng	5000	Placebo	12	Some Concerns
Lee et al., 2012 (a)	Korea	Parallel, R, DB	M/F (98)	39.8 ± 9.3	40.8 ± 11.3	41	57	Healthy volunteers	20 % ethanol extract of 4-year-old *Panax Ginseng* root	1000	Placebo	4	Low Risk
Lee et al., 2012 (b)	Korea	Parallel, R, DB	M/F (99)	39.8 ± 9.3	40.8 ± 11.3	42	57	Healthy volunteers	20 % ethanol extract of 4-year-old *Panax Ginseng* root	2000	Placebo	4	Low Risk

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Table 1 (*continued*)

Author name	country	Study design	gender	Int. mean age	Con. mean age	N (Int)	N (Con)	Health condition	Intervention type (Inv)	Dose (mg/day)	Intervention type (Con)	Duration (week)	Quality
Lee et al., 2012 (c)	Korea	Parallel, R, DB	M/F (71)	39.8 ± 9.3	40.8 ± 11.3	14	57	Healthy volunteers	20 % ethanol extract of 4-year-old *Panax Ginseng* root	1000	Placebo	4	Low Risk
Lee et al., 2012 (d)	Korea	Parallel, R, DB	M/F (71)	39.8 ± 9.3	40.8 ± 11.3	14	57	Healthy volunteers	20 % ethanol extract of 4-year-old *Panax Ginseng* root	2000	Placebo	4	Low Risk
(Dickman et al., 2009a, 2009b)	US	Parallel, R, DB	F (25)	62.3 ± 1.7	61.7 ± 1.8	12	13	Postmenopausal women	Dry whole-root American ginseng	1000	Placebo	16	High Risk
(Gao et al., 2024)	China	Crossover, R, PC, DB	M/F (199)	53	53.1	97	98	Prediabetics	Zhenyuan Capsule (Chinese patented medicine consisting of ginseng berry saponins extracted from the mature berry of *Panax Ginseng*) + lifestyle intervention	50	Lifestyle intervention and placebo	4	Low Risk
En-Yuan et al., 2002	US	Parallel, R, DB	M/F (75)	58.7 ± 5.1	57.4 ± 5.0	50	25	Healthy Elders	Korean Red Ginseng	3000	Placebo	4	High Risk
(Seo et al., 2014a, 2014b)	Korea	Crossover, R, PC, DB	F (71)	53.86 ± 3.21	54.33 ± 2.52	35	36	Postmenopausal women	Korean Red Ginseng	1000	Lifestyle intervention and placebo	15	Low Risk
Han et al., 1998	Korea	PC	M/F (8)	58.8 ± 8.8	58.8 ± 8.8	4	4	White Coat Hypertension	Red ginseng	4500	Placebo	8	High Risk
Hwang et al., 2020 (a)	Korea	R, PC, DB	M/F (30)	55.00 ± 2.95	53.00 ± 3.66	15	15	Healthy people	GINST & GS-3 K8, root, rootlets	3000	placebo	12	Some Concerns
Hwang et al., 2020 (b)	Korea	R, PC, DB	M/F (29)	55.00 ± 2.95	53.00 ± 3.66	14	15	Healthy people	GINST & GS-3 K8, root, rootlets	3000	placebo	12	Some Concerns
(Kim & Lee, 2001)	Korea	Parallel, R, PC, DB	M (6)	23.8 ± 2.9	22.2 ± 1.9	3	3	Smokers	Red ginseng (*Panax ginseng* C. A. Meyer)	1800	Placebo	4	High Risk
Jovanovski et al., 2021	Canada	R, PC, DB	M/F (80)	59.44 ± 7.4	60.58 ± 6.9	43	37	Patients with type 2 diabetes and HTN	Rg3-Korean red ginseng (KRG) + American Ginseng (AG)	2250	placebo	12	Some Concerns
Jovanovski et al., 2021	Canada	R, PC, DB	M/F (79)	59.44 ± 7.4	60.58 ± 6.9	43	36	Individuals with hypertension and type 2 diabetes	Rg3-Korean red ginseng (KRG) + American Ginseng (AG)	2250	placebo	12	Some Concerns
Jung et al., 2016	Korea	Parallel, R, DB	M (62)	48.2 ± 10.9	45.2 ± 9.7	32	30	Participants with metabolic syndrome	Red Ginseng	3000	Placebo	4	High Risk
Hyun et al., 2021	Korea	Parallel, R, DB	M.F (100)	50.12 ± 6.43	50.38 ± 5.97	50	50	Healthy adults	Korean Red Ginseng	2000	Placebo	8	High Risk

Footprint: B, Both Sex; BMI, Body Mass Index; CON, Control Group; DB, Double-Blinded; DBP, Diastolic Blood Pressure; F, Female.

Table 2
Quality of evidence using the GRADE approach.

	Number of patients (RCT)	WMD (95 % CI)	Risk of bias[1]	Inconsistency[2]	Indirectness[3]	Imprecision[4]	Publication bias[5]	Quality of evidence[6]
Weight (kg)	220 (7)	0.08 (−0.56, 0.72)	Serious	Not Serious	Not Serious	Serious	Not Serious	Downgraded
BMI (kg/m^2)	784 (18)	−0.03 (−0.15, 0.08)	Serious	Not Serious	Not Serious	Serious	Not Serious	Downgraded
WC (Cm)	272 (7)	0.08 (−0.82, 0.99)	Serious	Not Serious	Not Serious	Not Serious	Not Serious	Moderate
Leptinn (ng/mL)	61 (3)	−0.69 (−2.15, 0.78)	Serious	Not Serious	Not Serious	Not Serious	Not Serious	Moderate
Adiponectin (μg/mL)	165 (5)	0.00 (0.00, 0.00)	Not Serious	Serious	Not Serious	Serious	Not Serious	Moderate
TC (mg/dL)	2740 (49)	−0.37 (−0.90, 0.15)	Not Serious	Not Serious	Not Serious	Serious	Not Serious	Moderate
LDL-c (mg/dL)	1873 (31)	−0.19 (−0.55, 0.18)	Not Serious	Not Serious	Not Serious	Serious	Not Serious	Moderate
HDL-c (mg/dL)	2196 (38)	0.06 (−0.15, 0.26)	Not Serious	Not Serious	Not Serious	Serious	Not Serious	Moderate
TG (mg/dL)	2403 (44)	−0.36 (−1.06, 0.33)	Serious	Not Serious	Not Serious	Serious	Not Serious	Downgraded
CRP (mg/L)	223 (4)	0.07 (−0.09, 0.23)	Serious	Serious	Not Serious	Serious	Not Serious	Downgraded
h-CRP (mg/L)	740 (15)	−0.04 (−0.11, 0.03)	Not Serious	Serious	Not Serious	Serious	Not Serious	Downgraded
SBP (mmHg)	1537 (34)	−1.22 (−2.60, 0.16)	Serious	Serious	Not Serious	Not Serious	Not Serious	Downgraded
DBP (mmHg)	1537 (34)	−0.66 (−1.68, 0.35)	Serious	Serious	Not Serious	Not Serious	Not Serious	Downgraded

3.3.2. BMI

Eighteen intervention arms assessed BMI changes. The overall result showed no significant change (WMD = −0.03 kg/m^2; 95 % CI: −0.15 to 0.08; $p = 0.550$), and heterogeneity was negligible ($I^2 = 0$ %, $p = 0.999$) (**Supplementary Fig. 2**) (Bang, Kwak, Ahn, Shin, & Lee, 2014; Cha, Kim, Kim, Chae, & Lee, 2016; Y. H. Cho et al., 2013; Chung, Kim, Seol, Kim, & Lee, 2021; Delui et al., 2013; Hosseini et al., 2016; D. H. Jung et al., 2016; J. Y. Kim, Park, Kang, Kim, & Lee, 2012; D. H. Kwon et al., 2012; Y. J. Kwon, Jang, Liu, & Jung, 2020; K. Park, Ahn, Kim, & Nam, 2020; Reeds et al., 2011; Seong et al., 2021; Yoon et al., 2012). Subgroup analyses based on intervention duration, ginseng dosage, sample size and age did not identify any significant sources of heterogeneity (Table 3).

3.3.3. WC

Seven studies reported data on waist circumference. The pooled estimate showed a non-significant reduction (WMD = 0.08 cm; 95 % CI: −0.82 to 0.99; $p = 0.856$), with low heterogeneity ($I^2 = 0.0$ %, $p = 0.706$) (**Supplementary Fig. 3**) (D. H. Kwon et al., 2012; Y. J. Kwon et al., 2020; B. J. Park et al., 2012; Seong et al., 2021; Yoon et al., 2012).

3.4. Effects on cardiovascular indices

3.4.1. SBP

From 34 intervention arms, ginseng led to a modest but non-significant reduction in SBP (WMD = −1.22 mmHg; 95 % CI: −2.60 to 0.16; $p = 0.082$), with high heterogeneity ($I^2 = 85.7$ %, $p < 0.0001$) (**Supplementary Fig. 4**) (Bang et al., 2014; Caron et al., 2002; Cha et al., 2016; Chung et al., 2021; Dickman, Koenig, & Ji, 2009a; En-Yuan et al., 2002; Han et al., 1998; Hwang et al., 2020; Hyun et al., 2021; Jovanovski et al., 2020; Jovanovski et al., 2021; D. H. Jung et al., 2016; J. Y. Kim et al., 2012; N.-R. Kim, Kim, & Kim, 2010; D. H. Kwon et al., 2012; Y. J. Kwon et al., 2020; Mucalo et al., 2013; B. J. Park et al., 2012; K. Park et al., 2020; Rhee et al., 2014; Rhee et al., 2011; Seong et al., 2021; Vuksan et al., 2008; Vuksan et al., 2019; Yang et al., 2024; Yoon et al., 2012).

3.4.2. DBP

Similarly, ginseng did not significantly affect DBP (WMD = −0.66 mmHg; 95 % CI: −1.68 to 0.35; $p = 0.201$), and heterogeneity was substantial ($I^2 = 84.6$ %, $p < 0.001$) (**Supplementary Fig. 5**) (Bang et al., 2014; Caron et al., 2002; Cha et al., 2016; Chung et al., 2021; Dickman, Koenig, & Ji, 2009b; En-Yuan et al., 2002; Han et al., 1998; Hwang et al., 2020; Hyun et al., 2021; Jovanovski et al., 2020; Jovanovski et al., 2021; D. H. Jung et al., 2016; J. Y. Kim et al., 2012; N.-R. Kim et al., 2010; D. H. Kwon et al., 2012; Y. J. Kwon et al., 2020; Mucalo et al., 2013; B. J. Park et al., 2012; K. Park et al., 2020; Rhee et al., 2014; Rhee et al., 2011; Seong et al., 2021; Vuksan et al., 2008; Vuksan et al., 2019; Yang et al., 2024; Yoon et al., 2012).

3.5. Effects on inflammatory markers

3.5.1. h-CRP

Fifteen intervention arms assessed the effect of ginseng supplementation on hs-CRP levels. The pooled analysis showed no significant effect (WMD = −0.04 mg/L; 95 % CI: −0.11 to 0.03; $p = 0.233$), and moderate heterogeneity was observed ($I^2 = 39.4$ %, $p = 0.059$) (**Supplementary Fig. 6**) (Cha et al., 2016; Delui et al., 2013; S. J. Jung et al., 2020; J. Y. Kim et al., 2012; K. Park et al., 2020; S. I. Park, Lee, Lee, Yim, & Kim, 2022; Shen et al., 2020; Yoon et al., 2012). Subgroup analysis indicated duration of intervention is source of heterogeneity (Table 3).

3.5.2. CRP

Four study arms reported data on standard CRP levels. The meta-analysis found no significant change in CRP following ginseng supplementation (WMD = 0.07 mg/L; 95 % CI: −0.09 to 0.23; $p = 0.398$). Heterogeneity was moderate ($I^2 = 64.6$ %, $p = 0.037$) (**Supplementary Fig. 7**) (Baek et al., 2019; D. H. Jung et al., 2016; B. J. Park et al., 2012; Seong et al., 2021).

3.5.3. IL-6

Seventeen arms assessed TNF-α. The pooled estimate showed significant effect (WMD = −2.03 pg/mL; 95 % CI: −3.12 to −0.93; $p < 0.001$), with high heterogeneity ($I^2 = 98.6$ %, $p < 0.001$) (**Supplementary Fig. 8**) (Ahn et al., 2011; Baek et al., 2019; Hernández-García

Table 3
Pooled estimate effects of ginseng treatment different subgroups.

Group	No. of comparisons	WMD (95 % CI)	P-value	I^2 (%)	P-heterogeneity
BMI (kg/m^2)					
Age of participants					
<50	9	−0.05 (−0.23, 0.14)	0.626	0.0	0.998
≥50	9	−0.03 (−0.17, 0.12)	0.706	0.0	0.914
Dose of ginseng					
< 5 (g/day)	11	−0.03 (−0.16, 0.09)	0.607	0.0	0.977
≥ 5 (g/day)	7	−0.04 (−0.29, 0.21)	0.758	0.0	0.979
Duration of treatment (weeks)					
<10	13	−0.04 (−0.16, 0.07)	0.467	0.0	0.997
≥10	5	0.10 (−0.36, 0.56)	0.666	0.0	0.875
Sample size					
<50	10	−0.01 (−0.19, 0.17)	0.902	0.0	0.998
≥50	8	−0.05 (−0.20, 0.10)	0.500	0.0	0.999
TC (mg/dL)					
Age of participants					
<50	24	2.07 (−0.67, 4.81)	0.138	0.0	0.528
≥50	25	−0.46 (−1.00, 0.07)	0.090	77.5	<0.001
Dose of ginseng					
< 5 (g/day)	43	−0.37 (−0.91, 0.16)	0.170	67.0	<0.001
≥ 5 (g/day)	6	−0.55 (−5.87, 4.77)	0.839	0.0	0.547
Duration of treatment (weeks)					
<10	31	−0.09 (−0.44, 0.26)	0.621	34.8	0.031
≥10	18	−3.69 (−15.59, 1.65)	0.113	71.4	0.004
Sample size					
<50	2	−14.83 (−23.17, −6.5)	<0.001	0	0.437
≥50	3	−1.35 (−6.04, −1.33)	**0.002**	79.2	<0.001
LDL-c (mg/dL)					
Age of participants					
<50	12	−1.77 (−6.98, 3.45)	0.507	64.2	0.001
≥50	19	−0.14 (−0.44, 0.16)	0.350	60.7	<0.001
Dose of ginseng					
< 5 (g/day)	26	−0.16 (−0.51, 0.20)	0.386	63.2	<0.001
≥ 5 (g/day)	5	−5.70 (−11.94, 0.54)	0.073	21.4	0.279
Duration of treatment (weeks)					
<10	16	−0.03 (−0.40, 0.34)	0.871	65.1	<0.001
≥10	15	−1.38 (−2.72, −0.03)	**0.045**	57.3	0.003
Sample size					
<50	13	−0.08 (−0.54, 0.38)	0.729	64.7	0.001
≥50	18	−0.66 (−1.74, 0.43)	0.235	60.8	<0.001
HDL-c (mg/dL)					
Age of participants					
<50	19	−0.01 (−0.97, 0.95)	0.987	0.0	0.566
≥50	19	0.06 (−0.15, 0.27)	0.581	88.9	<0.001
Dose of ginseng					
< 5 (g/day)	32	0.07 (−0.14, 0.28)	0.526	82.4	<0.001
≥ 5 (g/day)	6	−0.74 (−2.53, 1.04)	0.415	0	0.873
Duration of treatment (weeks)					
<10	22	0.04 (−0.10, 0.18)	0.570	57.4	<0.001
≥10	16	0.43 (−0.43, 1.29)	0.322	87.3	<0.001
Sample size					
<50	17	−0.03 (−0.10, 0.03)	0.364	0.0	0.606
≥50	21	0.47 (−0.25, 1.19)	0.199	83.2	<0.001
TG (mg/dL)					
Age of participants					
<50	23	2.39 (−3.75, 8.53)	0.446	31.3	0.077
≥50	21	−0.40 (−1.08, 0.28)	0.245	84.8	<0.001
Dose of ginseng					
< 5 (g/day)	38	−0.41 (−1.10, 0.28)	0.242	76.2	<0.001
≥ 5 (g/day)	6	15.02 (2.87, 27.17)	**0.015**	0.0	0.864
Duration of treatment (weeks)					
<10	27	0.17 (−0.41, 0.74)	0.573	57.8	<0.001
≥10	17	−1.57 (−3.49, 0.35)	0.109	75.2	<0.001
Sample size					
<50	22	0.14 (−0.07, 0.34)	0.196	0.0	0.613
≥50	22	−0.81 (−3.09, 1.47)	0.486	83.4	<0.001
IL-6 (pg/mL)					
Age of participants					
<50	9	−0.57 (−1.50, 0.36)	0.277	96.0	<0.001
≥50	8	−1.44 (−7.53, 4.64)	0.643	99.2	<0.001
Duration of treatment (weeks)					
<10	12	−0.45 (−1.37, 0.48)	0.344	94.6	<0.001
≥10	5	−4.62 (−11.82, 2.58)	0.208	99.5	<0.001
Sample size					
<50	9	−1.04 (−1.87, −0.21)	**0.014**	4.9	0.395
≥50	8	−2.85 (−4.18, −1.53)	**<0.001**	99.4	<0.001
h-CRP (mg/L)					
Age of participants					
<50	8	−0.19 (−0.40, 0.02)	0.082	49.2	0.055
≥50	7	0.00 (−0.05, 0.04)	0.901	0.1	0.422
Duration of treatment (weeks)					
<10	7	−0.03 (−0.12, 0.06)	0.493	60.8	0.018
≥10	8	−0.08 (−0.16, 0.01)	0.079	0.0	0.591
Sample size					
<50	8	−0.05 (−0.18, 0.09)	0.480	60.9	0.012
≥50	7	−0.07 (−0.13, 0.00)	0.052	0.0	0.907
TNF-α (pg/mL)					
Age of participants					
<50	7	−4.58 (−11.98, 2.83)	0.226	97.4	<0.001
≥50	10	0.48 (−1.64, 2.59)	0.654	97.4	<0.001

(*continued on next page*)

Table 3 (*continued*)

Group	No. of comparisons	WMD (95 % CI)	P-value	I^2 (%)	P-heterogeneity
Duration of treatment (weeks)					
<10	11	−2.02 (−6.33, 2.28)	0.357	95.7	<0.001
≥10	6	−0.83 (−3.64, 1.97)	0.561	98.5	<0.001
Sample size					
<50	9	−0.78 (−3.36, 1.79)	0.550	83.4	<0.001
≥50	8	−2.14 (−5.17, 0.89)	0.167	99	<0.001

et al., 2024; M. Hong et al., 2016; Hosseini et al., 2016; K. Park et al., 2020; S. I. Park et al., 2022; Seok Kyo Seo et al., 2014; Xu, Lu, Wu, Li, & Sun, 2017; Yoon et al., 2012). Significant reductions in IL-6 were observed in studies with larger sample sizes (≥50 participants: WMD = −2.85; 95 % CI: −4.18 to −1.53; p < 0.001) and smaller sample sizes (WMD = −1.04; $p = 0.014$). However, when stratified by age or duration, the effects were not significant, although greater numerical reductions were seen in longer trials and among older participants (**Table 3**).

3.5.4. TNF-α

Seventeen intervention arms evaluated the effect of ginseng supplementation on TNF-α levels. The pooled analysis demonstrated no significant effect of ginseng on TNF-α concentrations compared to placebo (WMD = −1.41 pg/mL; 95 % CI: −3.32 to 0.51; $p = 0.150$) (**Supplementary Fig. 9**). There was substantial heterogeneity among studies ($I^2 = 97.8$ %, p < 0.001) (Ahn et al., 2011; Baek et al., 2019; Y. J. Cho, Son, & Kim, 2014; Hernández-García et al., 2024; M. Hong et al., 2016; Hosseini et al., 2016; Hyun et al., 2021; K. Park et al., 2020; Xu et al., 2017; Yang et al., 2024; Yoon et al., 2012). Although numerical decreases in TNF-α were observed, especially among younger participants and in shorter trials, these findings were not statistically significant across any subgroup (**Table 3**).

3.6. Effects on lipid profile

3.6.1. TC

Data from 49 arms revealed a non-significant reduction in total cholesterol (WMD = −0.37 mg/dl; 95 % CI: −0.90 to 0.15; $p = 0.166$), with considerable heterogeneity ($I^2 = 63$ %, $p < 0.001$) (Fig. 2) (Ahn et al., 2011; Baek et al., 2019; Bang et al., 2014; Cha et al., 2016; Y. H. Cho et al., 2013; H. S. Choi et al., 2018; Y. D. Choi et al., 2013; Chung et al., 2021; De Andrade et al., 2007; Delui et al., 2013; En-Yuan et al., 2002; Hernández-García et al., 2024; J. T. Hong et al., 2021; M. Hong et al., 2016; Hosseini, Ehsanpour, Asgari, & Malihi, 2013; Hwang et al., 2020; Hyun et al., 2021; Jovanovski et al., 2021; D. H. Jung et al., 2016; S. J. Jung et al., 2020; J. Y. Kim et al., 2012; D. H. Kwon et al., 2012; Y. J. Kwon et al., 2020; Lee et al., 2012; Oh et al., 2014; B. J. Park et al., 2012; K. Park et al., 2020; S. I. Park et al., 2022; S. Y. Park et al., 2016; Reeds et al., 2011; Rhee et al., 2011; Seong et al., 2021; Shen et al., 2020; Vuksan et al., 2019; Xu et al., 2017; Yoon et al., 2012). Subgroup analysis based on sample size, showed that a significant reduction in TC in studies with fewer than 50 participants (WMD = −14.83 mg/dL; 95 % CI: −23.17 to −6.50; $p < 0.001$; $I^2 = 0$ %) (**Table 3**).

3.6.2. TG

Forty-four arms assessed TG, and ginseng showed no significant effect (WMD = −0.36 mg/dl; 95 % CI: −1.06 to 0.33; $p = 0.305$), with high heterogeneity (($I^2 = 73.7$ %, p < 0.001) (Fig. 3) (Baek et al., 2019; Bang et al., 2014; Cha et al., 2016; Y. J. Cho et al., 2014; H. S. Choi et al., 2018; Chung et al., 2021; Delui et al., 2013; En-Yuan et al., 2002; Hernández-García et al., 2024; J. T. Hong et al., 2021; Hosseini et al., 2013; Hwang et al., 2020; Hyun et al., 2021; Jovanovski et al., 2021; D. H. Jung et al., 2016; S. J. Jung et al., 2020; J. Y. Kim et al., 2012; D. H. Kwon et al., 2012; Lee et al., 2012; Oh et al., 2014; B. J. Park et al., 2012; K. Park et al., 2020; S. I. Park et al., 2022; S. Y. Park et al., 2016; Reeds et al., 2011; Rhee et al., 2011; Seong et al., 2021; Shen et al., 2020; Xu et al., 2017; Yoon et al., 2012). A significant increase in TG was observed only in the high-dose subgroup (≥5 g/day: WMD = 15.02 mg/dL; 95 % CI: 2.87 to 27.17; $p = 0.015$), whereas no significant changes were seen in subgroups based on age, duration, or sample size (**Table 3**).

3.6.3. HDL-C

HDL-C was assessed in 38 intervention arms (Ahn et al., 2011; Baek et al., 2019; Bang et al., 2014; Cha et al., 2016; Y. H. Cho et al., 2013; H. S. Choi et al., 2018; Y. D. Choi et al., 2013; Chung et al., 2021; De Andrade et al., 2007; Delui et al., 2013; Hosseini et al., 2013; Jovanovski et al., 2021; D. H. Jung et al., 2016; S. J. Jung et al., 2020; J. Y. Kim et al., 2012; D. H. Kwon et al., 2012; Lee et al., 2012; Oh et al., 2014; B. J. Park et al., 2012; K. Park et al., 2020; S. I. Park et al., 2022; S. Y. Park et al., 2016; Reeds et al., 2011; Rhee et al., 2011; Seong et al., 2021; Shen et al., 2020; Vuksan et al., 2019; Xu et al., 2017; Yoon et al., 2012). The meta-analysis indicated no significant effect of ginseng supplementation on HDL-C levels (WMD = 0.06 mg/dl; 95 % CI: −0.15 to 0.26; $p = 0.593$) (Fig. 4). Heterogeneity was moderate ($I^2 = 79.3$ %, p < 0.001). No subgroup demonstrated significant improvement in HDL-C. Slight increases were seen in older adults (≥50 years: WMD = 0.06; $p = 0.581$) and longer trials (≥10 weeks: WMD = 0.43; $p = 0.322$), but the differences were not statistically meaningful. Interestingly, lower doses (<5 g/day) and shorter durations (<10 weeks) were associated with more stable effects and less heterogeneity (**Table 3**).

3.6.4. LDL-C

Thirty-one intervention arms evaluated LDL-C (Ahn et al., 2011; Baek et al., 2019; Bang et al., 2014; Cha et al., 2016; Y. H. Cho et al., 2013; H. S. Choi et al., 2018; Y. D. Choi et al., 2013; De Andrade et al., 2007; Delui et al., 2013; Hosseini et al., 2013; Jovanovski et al., 2021; S. J. Jung et al., 2020; J. Y. Kim et al., 2012; Oh et al., 2014; K. Park et al., 2020; S. I. Park et al., 2022; Reeds et al., 2011; Rhee et al., 2011; Seong et al., 2021; Shen et al., 2020; Vuksan et al., 2019; Xu et al., 2017; Yoon et al., 2012). The pooled effect showed no significant change in LDL-C following ginseng supplementation (WMD = −0.19 mg/dl; 95 % CI: −0.55 to 0.18; $p = 0.315$), with substantial heterogeneity ($I^2 = 61.3$ %, p < 0.001) (Fig. 5). The reduction in LDL-C was significant only in trials with longer duration (≥10 weeks: WMD = −1.38 mg/dL; 95 % CI: −2.72 to −0.03; $p = 0.045$). No significant effects were seen in subgroups by age, dose, or sample size, although a trend toward greater LDL-C reduction was noted in the high-dose subgroup (≥5 g/day: WMD = −5.70; $p = 0.073$) (**Table 3**).

3.7. Effects on Adipokines

3.7.1. Adiponectin

Five arms reported on adiponectin, and the pooled analysis showed a marginal significant (WMD = 0.0 μg/mL; 95 % CI: 0.00 to 0.00; p < 0.001), with minimal heterogeneity ($I^2 = 0.0$ %, $p = 0.969$) (**Supplementary Fig. 10**) (Ahn et al., 2011; M. Hong et al., 2016; Yoon et al., 2012).

Leptin. Leptin was reported in only three arms, and ginseng had no significant effect (WMD = −0.69 ng/mL; 95 % CI: −2.15 to 0.78; $p = 0.359$) (**Supplementary Fig. 11**) (Yoon et al., 2012). Due to limited data, subgroup analysis was not feasible.

3.8. Sensitivity and publication bias analyses

Sensitivity analyses indicated that the pooled effect sizes for most outcomes were stable, suggesting that no single study had a disproportionate influence on the overall results. Specifically, no evidence of

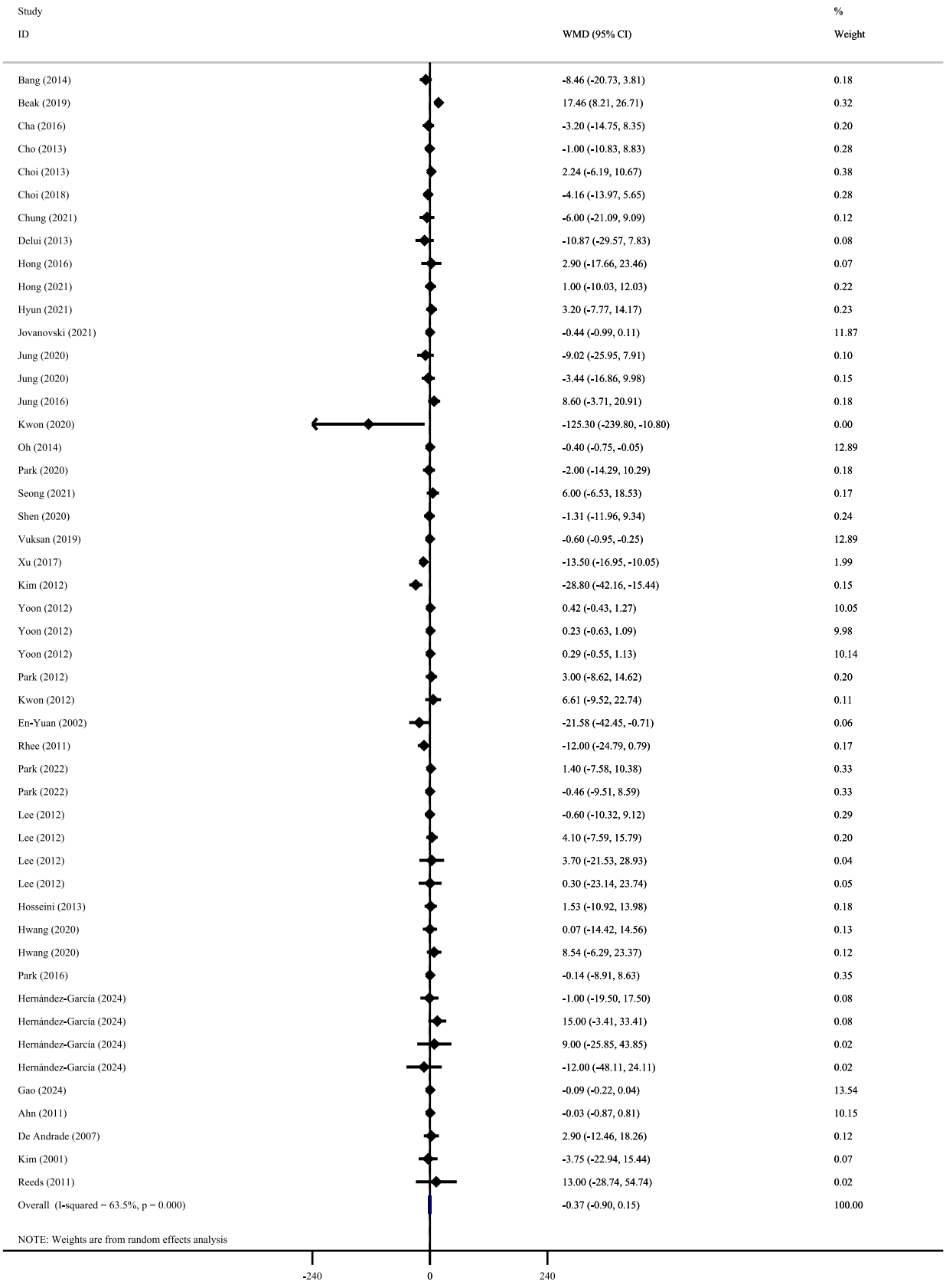

Fig. 2. Forest Plot Detailing Mean Difference and 95 % Confidence Intervals (CIs) of the Effects of Ginseng Supplementation on TC Levels.

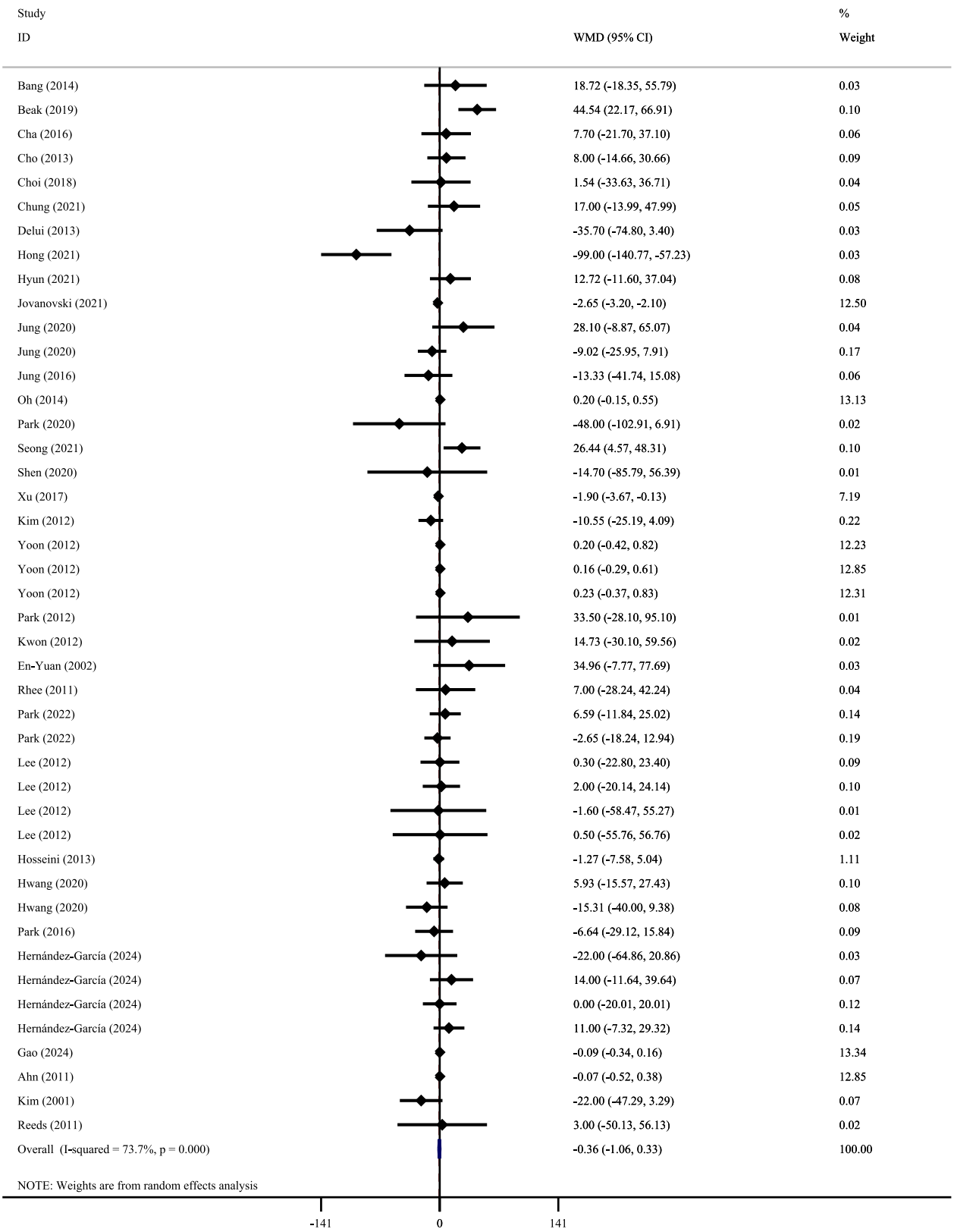

Fig. 3. Forest Plot Detailing Mean Difference and 95 % Confidence Intervals (CIs) of the Effects of Ginseng Supplementation on TG Levels.

sensitivity was detected for body weight, WC, BMI, adiponectin, leptin, CRP, hs-CRP, TNF-α, HDL-C, LDL-C, TC, and TG. For SBP, and DBP, sensitivity analysis revealed that excluding individual studies such as En-Yuan (2002) (En-Yuan et al., 2002), Caron (2002) (Caron et al., 2002), and Dickman et al., 2009b) led to a more pronounced reduction in SBP, and DBP.

Regarding publication bias, Begg's and Egger's tests showed no significant evidence of bias for most outcomes, including body weight (Begg's test $P = 0.548$), WC (Begg's test $P = 0.547$), BMI (Begg's test $P = 0.881$, and Egger's $P = 0.077$), adiponectin (Begg's test $P = 0.525$),

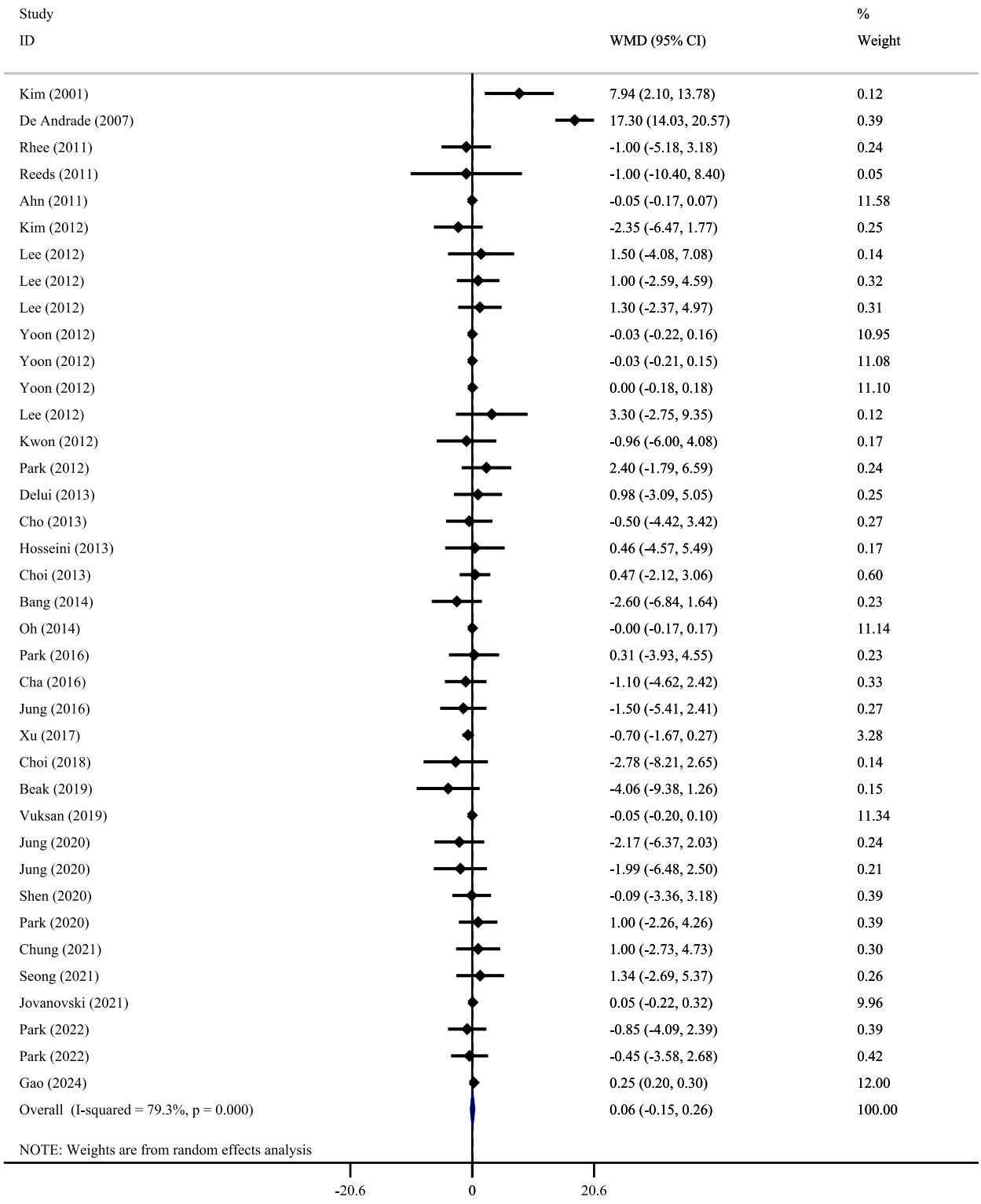

Fig. 4. Forest Plot Detailing Mean Difference and 95 % Confidence Intervals (CIs) of the Effects of Ginseng Supplementation on HDL-C Levels.

leptin (Begg's test $P = 0.256$), CRP (Begg's test $P = 0.652$), hs-CRP (Begg's test $P = 0.092$, and Egger's $P = 0.195$), TNF-α (Begg's test $P = 0.773$, and Egger's $P = 0.467$), HDL-C (Begg's test P = 0.881, and Egger's P = 0.077), LDL-C (Begg's test $P = 0.415$, and Egger's $P = 0.453$), TC (Begg's test $P = 0.423$, and Egger's $P = 0.155$), TG (Begg's test $P = 0.307$, and Egger's $P = 0.327$), SBP (Begg's test $P = 0.678$, unlike Egger's $P = 0.022$), and DBP (Begg's test $P = 0.790$, unlike Egger's $P > 0.001$). However, for interleukin-6 (IL-6), Begg's test ($P > 0.023$) unlike Egger's test ($p = 0.212$) indicated possible publication bias. The trim and fill test was performed because an uneven distribution of studies was recorded for all outcomes after performing the funnel plot assessment's visual inspection. Therefore, alterations were made to the results' significance after performing trim and fill analysis for SBP (eight imputed studies, WMD = −3.12 mmHg; 95 % CI: −4.02 to −1.73; p<0.05) (**Supplementary Fig. 12**), and TNF-α (Five imputed studies, WMD = −2.89 pg/mL; 95 % CI: −5.04 to −0.74; p<0.05)

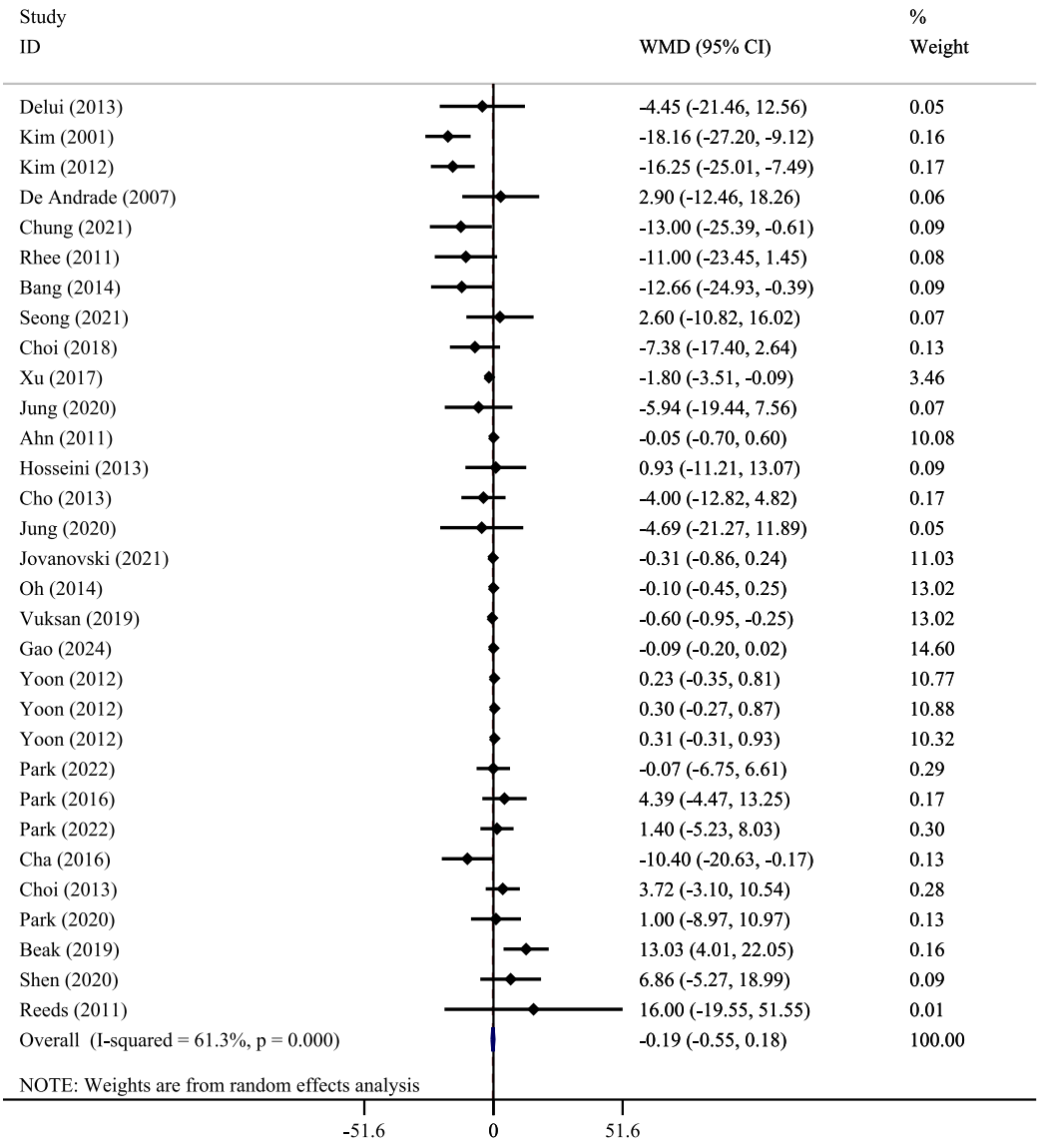

Fig. 5. Forest Plot Detailing Mean Difference and 95 % Confidence Intervals (CIs) of the Effects of Ginseng Supplementation on LDL-C Levels.

(**Supplementary Fig. 13**). However, the results for TC (One imputed study), TG (Four imputed studies), BMI (Three imputed studies), and IL-6 (Seven imputed studies) 7did not alter after trim and fill analysis (**Supplementary Fig. 14–17**).

4. Discussion

The present systematic review and meta-analysis aimed to comprehensively evaluate the effects of ginseng supplementation on anthropometric, cardiovascular, lipid, and inflammatory markers across randomized controlled trials. In total, 44 studies comprising 56 intervention arms were analyzed, providing a broad assessment of ginseng's potential health benefits. While the overall results revealed modest improvements in certain inflammatory biomarkers, particularly IL-6 and adiponectin, the effects on anthropometric indices, lipid profiles, and blood pressure were largely non-significant. However, sensitivity analysis revealed that omitting three studies led to a significant result, in which ginseng supplementation could decrease SBP and DBP levels. Based on the Cochrane assessment of included studies (Caron et al., 2002; Dickman et al., 2009a; En-Yuan et al., 2002), the random allocation of research was inappropriate, which can be a potential source of bias and affect the final result.

Our findings regarding anthropometric and lipid parameters align with those of Arabi et al. (2024), who concluded that ginseng supplementation had minimal effects on lipid profiles in a dose-response meta-analysis (Arabi et al., 2024). Similarly, a systematic review by Park et al. (2022) found that while ginseng showed antioxidant activities, its effects on lipid metabolism were inconsistent (Park, Lee, et al., 2022). However, other studies have reported beneficial effects on blood pressure and lipid parameters, possibly due to differences in populations studied (e.g., patients with hypertension or diabetes), dosage forms (e.g., fermented versus raw ginseng), and duration of interventions (Abdelazim et al., 2019; Szymańska, Nowak, Lipert, & Kochan, 2024).

The significant reduction in IL-6 levels observed in our meta-analysis is consistent with findings from animal and human studies suggesting that ginseng can suppress pro-inflammatory cytokine expression. Studies such as those by Seo et al. (2014a) and Hong et al. (2016) have previously demonstrated that ginseng supplementation leads to reductions in IL-6 and other inflammatory markers (M. Hong et al., 2016; Seo et al., 2014b). Moreover, the observed increase in adiponectin, an anti-inflammatory adipokine with cardioprotective effects, reinforces the notion that ginseng's primary benefits may be mediated through modulation of inflammatory pathways rather than through traditional anthropometric or lipid profile improvements.

The observed reduction in IL-6 levels by −2.03 pg/mL in this meta-analysis may hold clinical relevance, considering established role of IL-6 as a predictor of cardiovascular events and mortality (Gager et al., 2020). Elevated IL-6 levels have been associated with increased cardiovascular risk, with studies indicating that levels above 3.3 pg/mL significantly predict long-term cardiovascular mortality. Furthermore, each standard deviation increase in IL-6 correlates with a 25 % higher risk of coronary heart disease events (Mehta, deGoma, & Shapiro, 2024). While there is no universally defined minimal clinically important difference (MCID) for IL-6, the reduction observed in this study suggests a potential shift from higher to lower risk categories.

The subgroup analyses from your meta-analysis highlight that the effects of ginseng on cardiovascular risk markers vary based on study parameters. Specifically, reductions in TC were significant in studies with sample sizes over 50 participants, suggesting that larger cohorts may better detect lipid-lowering effects. Similarly, a significant decrease in LDL-C was observed in studies with durations exceeding 10 weeks, indicating that prolonged supplementation may be necessary for lipid modulation. TG levels showed significant reduction only at doses above 5 g per day, pointing to a potential dose-response relationship. Interestingly, IL-6 levels decreased significantly in studies with smaller sample sizes (<50), which might reflect a more homogeneous participant group or other study-specific factors. These findings underscore the importance of considering study design elements, such as sample size, duration, and dosage, when evaluating the clinical efficacy of ginseng on cardiovascular risk factors.

Several mechanisms may explain the observed effects. Ginsenosides, the major active components of ginseng, are known to enhance nitric oxide production, improve endothelial function, and suppress the expression of pro-inflammatory mediators such as IL-6 and TNF-α. Activation of AMP-activated protein kinase (AMPK) and peroxisome proliferator-activated receptor gamma (PPAR-γ) pathways has been implicated in the anti-inflammatory and metabolic regulatory effects of ginseng (Im, 2020; Smith, Williamson, Putnam, Farrimond, & Whalley, 2014). Furthermore, ginseng may promote the secretion of adiponectin and inhibit the secretion of leptin and TNF-α, thus shifting the adipokine profile toward an anti-inflammatory state (Angeloni et al., 2024).

Despite these promising mechanistic pathways, the absence of significant effects on clinical indices like BMI, WC, and lipid parameters may suggest that the intensity or duration of ginseng supplementation in available RCTs was insufficient to translate molecular changes into measurable clinical outcomes. Alternatively, the baseline health status of participants, many of whom were healthy or only mildly at risk, could have attenuated the observable effects.

The heterogeneity observed in several outcomes may be attributed to differences in ginseng species (e.g., *Panax ginseng* vs. *Panax quinquefolius*), forms (e.g., powder, extract, fermented), dosages (ranging from 200 mg to 6000 mg/day), duration of intervention (2 to 32 weeks), and characteristics of study populations (healthy individuals vs. patients with T2DM, MetS, or HTN). Studies utilizing higher doses (>5 g/day) or longer durations (>10 weeks) tended to report more favorable outcomes, although these differences were not always statistically significant.

Additionally, the variability in outcome measurements, such as fasting vs. non-fasting lipid profiles and different methods of blood pressure measurement, might have contributed to inconsistencies. Furthermore, some smaller trials with fewer participants tended to report larger effect sizes, raising the possibility of small-study effects or publication bias, particularly for inflammatory markers like IL-6.

4.1. Strengths of the study

This meta-analysis possesses several notable strengths. First, it is among the most comprehensive evaluations of ginseng's effects on a broad range of cardiometabolic outcomes to date, encompassing 44 RCTs and over 56 intervention arms. Second, robust meta-analytic methods were applied, including sensitivity analyses, subgroup comparisons, and publication bias assessments to ensure the reliability and validity of the findings. Third, the study design adhered to rigorous PRISMA guidelines and employed a pre-registered protocol on PROSPERO, enhancing transparency and reproducibility.

Moreover, subgroup analyses provided valuable insights into potential effect modifiers such as participant age, sample size, intervention duration, and dosage, which can guide future research and clinical applications.

4.2. Limitations of the study

Several limitations should be acknowledged. First, substantial heterogeneity was observed for several outcomes, particularly IL-6 and SBP, despite subgroup and sensitivity analyses. Although a random-effects model was used to account for this variability, residual heterogeneity may have influenced the pooled estimates. Second, the overall quality of evidence as assessed by GRADE ranged from low to moderate, reflecting issues such as imprecision, publication bias, and risk of bias in the original studies. Third, many included studies were of short duration (≤12 weeks), which may not be sufficient to observe significant changes in slow-evolving clinical parameters like lipid profiles or anthropometric measures. Fourth, while Begg's and Egger's tests did not indicate significant publication bias for most outcomes, possible small-study effects were detected for IL-6, suggesting that selective publication of positive findings cannot be completely ruled out. Finally, variation in the type and preparation of ginseng products used across studies (e.g., red vs. white ginseng, extract vs. capsule) may limit the generalizability of the results.

5. Conclusions

In conclusion, ginseng supplementation appears to exert modest but significant anti-inflammatory effects, as evidenced by reductions in IL-6 and increases in adiponectin levels. The beneficial effects of ginseng supplementation on SBP and DBP were shown after sensitivity analysis. However, its impact on anthropometric indices, lipid profiles, and blood pressure remains limited. These findings suggest that ginseng may serve as a complementary strategy for modulating inflammation rather than as a primary intervention for cardiometabolic risk factors. Future RCTs should aim for longer intervention durations, larger sample sizes, and standardized ginseng preparations to confirm and extend these findings. Moreover, mechanistic studies elucidating the molecular pathways through which ginseng exerts its effects will be essential to better target clinical applications.

CRediT authorship contribution statement

Xu Huang: Conceptualization, Formal analysis, Funding acquisition, Investigation, Project administration, Supervision, Writing – original draft, Writing – review & editing. **Mahdi Daneshi:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Formal analysis. **Maryam Falahatzadeh:** Writing – review & editing, Writing – original draft, Project administration, Formal analysis, Data curation, Conceptualization. **Mahsa Rounagh:** Writing – original draft, Visualization, Supervision, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Ethical consideration

The following study was carried out and reported based on PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) with attention to its main guiding principles.

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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.

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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.2025.106879.

Data availability

Data will be made available on request.

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