# The Effect of Ginseng Supplementation on Cardiovascular Disease Risk Factors: A Comprehensive Systematic Review and Dose-Response Meta-Analysis

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**Short title:** Ginseng Supplementation on Cardiovascular Disease Risk Factors

**Abbreviations:**

**2-h:** 2-hour**, ACE:** Angiotensin-Converting Enzyme**, ALP:** Alkaline Phosphatase**, ALT:** Alanine Aminotransferase**,** , **AST:** Aspartate Aminotransferase**, Bcl-2:** B-cell lymphoma 2**, BF%:** Body Fat Percentage**, BMI:** Body Mass Index**, BUN:** Blood Urea Nitrogen**, CAT:** Catalase**, CENTRAL:** Central Register of Controlled Trials**, CLA:** Conjugated Linoleic Acid**, COX:** Cyclooxygenase**, CRP:** C-Reactive Protein**, CVD:** cardiovascular diseases**, CYP:** Cytochrome P450, **DBP:** Diastolic Blood Pressure**, eNOS:** endothelial Nitric Oxide Synthase**, ERK:** Extracellular Signal-Regulated Kinase**, ESR:** Erythrocyte Sedimentation Rate, **FBS:** Fasting Blood sugar**, GGT:** Gamma-glutamyl Transferase, **GPx:** Glutathione Peroxidase, **GRADE:** Grading of Recommendations, Assessment, Development, and Evaluation, **GSH:** Glutathione, **GSH-Rd:** Glutathione Reductase, **HbA1c:** Hemoglobin A1c**, HDL-C:** High-Density Lipoprotein Cholesterol**, HOMA-B:** Homeostatic Model Assessment of Beta-cell Function**, HOMA-IR:** Homeostatic Model Assessment of Insulin Resistance, **hs-CRP**: high-sensitivity C-reactive protein, **HTN:** Hypertension, **IL-1Ra:** Interleukin-1 Receptor Antagonist, **IL-4**: interleukin-4, **IL-6**: interleukin-6**, IL-8**: interleukin-8**, IL-10**: interleukin-10, **LDL-C:** Low-Density Lipoprotein Cholesterol**, MDA:** Malondialdehyde**, MeSH:** Medical Subject Headings**, MetS,** Metabolic Syndrome**, NAFLD:** Non-Alcoholic Fatty Liver Disease, **NO:** Nitric Oxide**, NF-κB:** Nuclear Factor-kappa B, **PPAR:** Peroxisome Proliferator-Activated Receptors**, PRISMA:** Preferred Reporting Items for Systematic Reviews and Meta-Analyses**, PROSPERO:** Prospective Register of Systematic Reviews**, PUFA:** Polyunsaturated Fatty Acid**, QUICKI:** Quantitative Insulin Sensitivity Check Index**, RAAS:** Renin-Angiotensin-Aldosterone System**, RCT:** Randomized Controlled Trial**, ROS:** Reactive Oxygen Species**, SBP:** Systolic Blood Pressure**, SD:** Standard Deviation, **SE:** Standard Error**, SMD:** Standardized Mean Difference, **SOD:** Superoxide dismutase**, T2DM:** Type 2 Diabetes Mellitus**, TAC:** Total Antioxidant Capacity**, TBARS:** Thiobarbituric Acid Reactive Substances**, TC:** Total Cholesterol**, TG:** Triglycerides**, TNF-α:** Tumor Necrosis Factor-alpha**, WC:** Waist Circumference

## ABSTRACT

Although numerous clinical studies suggest that ginseng supplementation may benefit cardiovascular disease (CVD) risk factors, results remain inconclusive. This systematic review and meta-analysis evaluated the effects of ginseng supplementation on CVD-related risk factors. Relevant studies were identified through electronic searches in Embase, Web of Science, Scopus, PubMed, and CENTRAL up to August 2024. Statistical analyses, including a random-effects model, meta-regression, and non-linear modeling, were used to assess heterogeneity, dose-response relationships, and the overall effects of ginseng supplementation. A total of 70 studies, published between 1998 and 2024 and involving 4,506 participants, were included. Ginseng supplementation significantly affected several biochemical markers, including high-sensitivity C-reactive protein (hs-CRP) (SMD: -0.23; 95% CI: -0.38, -0.08; P = 0.002), gamma-glutamyl transferase (GGT) (SMD: -0.20; 95% CI: -0.36, -0.04; P = 0.015), glutathione reductase (GSH-Rd) (SMD: 0.90; 95% CI: 0.38, 1.42; P = 0.001), reactive oxygen species (ROS) (SMD: -0.94; 95% CI: -1.27, -0.60; P < 0.001), and superoxide dismutase (SOD) (SMD: 0.48; 95% CI: 0.10, 0.87; P = 0.014). Meta-regression analysis showed significant linear associations between ginseng dosage and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) (P = 0.044), and between supplementation duration and malondialdehyde (MDA) (P = 0.007). Dose-response analysis revealed significant associations between ginseng dose and fasting blood glucose (FBG) (P < 0.001), hs-CRP (P = 0.043), Interleukin-6 (IL-6) (P = 0.041), diastolic blood pressure (DBP) (P = 0.022), Interleukin-10 (IL-10) (P = 0.048), fasting insulin (P = 0.012), and total protein (P = 0.010). Supplementation duration was positively associated with MDA levels (P = 0.008). Ginseng supplementation was associated with improvements in inflammatory markers, liver function, and oxidative stress parameters. No significant effects were observed on anthropometric indices, blood pressure, glycemic profile, lipid profile, adipokines, or heart rate.


**Keywords:** Ginseng; inflammatory markers; oxidative stress; liver function; meta-analysis.

## 1. Introduction

Cardiovascular diseases (CVDs), encompassing disorders that affect the heart and blood vessels, represent a major global public health concern due to their high morbidity and mortality rates. CVDs remain the leading cause of death worldwide [(1)]. From 1993 to 2019, the prevalence of CVD nearly doubled, and it is projected to increase further by 2024, underscoring the urgent need for effective public health strategies to address the growing burden of these conditions [(2)]. CVDs affect blood circulation and include coronary artery disease, heart failure, vascular abnormalities, dyslipidemia, and hypertension (HTN). These conditions are prevalent in populations following Western dietary patterns, with contributing risk factors such as oxidative stress, diabetes, high blood pressure (BP), and elevated cholesterol levels [(3)]. Adopting healthy lifestyle practices, including balanced dietary habits, is critical for reducing CVD risk [(4)].

Complementary and alternative therapies, particularly those involving natural products, are gaining attention for their potential roles in the prevention and management of chronic diseases, including cardiovascular and metabolic disorders [(5; 6; 7)]. Natural compounds such as conjugated linoleic acid, Pycnogenol, royal jelly, nuts, and ginseng have demonstrated beneficial effects on inflammation, oxidative stress, lipid metabolism, glycemic control, and vascular function [(8; 9; 10)]. For instance, Pycnogenol has shown anti-inflammatory and antioxidant effects, potentially mitigating vascular dysfunction in chronic disease settings [(11)]. Similarly, royal jelly has demonstrated improvements in glycemic indices and liver enzyme profiles, which are critical in metabolic syndrome (MetS) and CVD development [(10)]. Regular consumption of nuts, particularly walnuts, may promote satiety and help modulate body composition and cardiovascular biomarkers, suggesting a role in dietary strategies for cardiometabolic disease prevention [(9)]. Among these, ginseng has been the focus of increasing scientific inquiry due to its diverse phytochemical composition and its emerging evidence base in supporting cardiovascular health [(12)].

Ginseng, a medicinal plant in the genus *Panax*, is known for its diverse biological activities. Different species of *Panax* contain various bioactive compounds, including ginsenosides, polysaccharides, polyacetylene compounds, and alkaloids, which vary between species, necessitating careful differentiation among them [(13)]. Ginseng and its ginsenosides may confer

cardiovascular benefits through antioxidative effects, reduced platelet adhesion, regulation of vasomotor function, improvement in lipid profiles, and modulation of ion channels [14; 15].

Numerous systematic reviews have investigated the effects of ginseng on cardiovascular risk factors, yielding mixed results that highlight the complexity of its effects. A meta-analysis by Arabi et al., which included 29 randomized controlled trials (RCTs) through January 2024, reported that ginseng supplementation did not significantly alter lipid parameters—such as triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low- density lipoprotein cholesterol (LDL-C)—across various health conditions [16]. Conversely, another systematic review focusing on metabolic parameters, encompassing 23 studies up to 2022, found that ginseng supplementation significantly improved markers of blood glucose, BP, and lipid levels, suggesting potential metabolic benefits [17]. Additionally, a comprehensive review that analyzed 19 meta-analyses up to July 2022 found potential benefits of ginseng in improving fatigue, physical function, and metabolic markers, though the low quality of the included studies limited the reliability of these findings [18]. These mixed results suggest that while ginseng may hold therapeutic promise, more rigorous studies are needed to clarify its efficacy and safety in specific populations.

Given recent literature developments, an updated review of the evidence is warranted. This study aims to address the limitations of earlier systematic reviews by offering comprehensive evidence on ginseng supplementation's impact on cardiovascular disease risk factors. Subgroup analyses were conducted to examine findings across specified outcomes, and the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach was used to evaluate the confidence in the evidence across studies. We believe that a rigorously conducted systematic review and meta-analysis will enhance the knowledge of clinicians, therapists, and patients regarding ginseng's efficacy.

## 2. METHODS

### *2.1 Protocol and Registration*

This study followed a predetermined protocol based on the 2015 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [19]. The systematic review and meta-analysis were registered in Prospective Register of Systematic Reviews (PROSPERO)

under registration number CRD**42023465688**, to ensure transparency. The protocol was also published in BMJ Open [20].

### *2.2 Search Strategy and Study Selection*

A comprehensive search was conducted across the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, Medline (http://www.ncbi.nlm.nih.gov/pubmed), Scopus, and Embase databases to identify articles published up to August 2024. Additionally, prominent journals and reference lists of relevant articles, meta-analyses, and reviews on ginseng were manually reviewed to capture any additional eligible studies. To address publication bias, we expanded our search to include gray literature, such as conference proceedings and trial registries, in addition to published studies, though only RCTs with sufficient data were ultimately included to ensure consistency in quality and analysis. Gray literature was systematically considered to broaden the evidence base and reduce the risk of overlooking relevant findings.

The primary focus was on the effects of ginseng supplementation. Outcomes investigated included changes in body fat percentage (BF%), body mass index (BMI), waist circumference (WC), weight, diastolic BP (DBP), pulse pressure, systolic BP (SBP), 2-hour (2-h) glucose, 2-h insulin, fasting insulin, fasting blood sugar (FBS), hemoglobin A1c (HbA1c), homeostatic model assessment of beta-cell function (HOMA-B), homeostatic model assessment for insulin resistance (HOMA-IR), quantitative insulin sensitivity check index (QUICKI), C- reactive protein (CRP), erythrocyte sedimentation rate (ESR), high-sensitivity C-reactive protein (hs-CRP), interleukin-1 receptor antagonist (IL-1Ra), interleukin-4 (IL-4), interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-10 (IL-10), tumor necrosis factor-alpha (TNF-α), total protein, HDL-C, LDL-C, oxidized LDL-C, TC, TG, albumin, alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), creatinine, gamma-glutamyl transferase (GGT), catalase (CAT), glutathione peroxidase (GPx), glutathione (GSH), glutathione reductase (GSH-Rd), malondialdehyde (MDA), reactive oxygen species (ROS), superoxide dismutase (SOD), total antioxidant capacity (TAC), adiponectin, leptin and heart rate following ginseng supplementation.

The search strategy targeted RCTs involving human subjects and utilized keywords including "ginseng" and "clinical trial." Terms were sourced from Emtree and Medical Subject Headings (MeSH) in PubMed, and search strategies were tailored for each database (PubMed, Web of Science, Embase, Scopus, and Central) using their respective subject headings. Full details of the search methodology are available in **Supplementary Table 1**.

### *2.3 Inclusion/Exclusion Criteria and Data Extraction*

We included trials that investigated the effects of ginseng supplementation on outcomes such as anthropometric measures, blood pressure, glycemic profile, inflammatory markers, lipid profile, liver function, oxidative stress parameters, adipokines, and heart rate. Only studies published in full-text and in English were considered. Observational studies (cohort, case-control, or cross-sectional), letters to the editor, review articles, animal studies, and articles not published in English were excluded.

Two reviewers (F.M and P.B) conducted the initial search and screened studies based on eligibility criteria. Data management was performed using EndNote X7 to merge results and remove duplicates. The selection process followed PRISMA guidelines, and eligible articles were reviewed using a standardized data extraction form created by the primary reviewers (A.J and V.M). Two independent researchers (H.M and K.K) extracted the data, with any unresolved disagreements referred to the project supervisor (A.A) for consensus.

### *2.4 Methodological Quality Assessment and Strength of Evidence Evaluation*

Two reviewers (M.A and B.P) conducted a detailed assessment of the methodological quality of the included trials using the Cochrane criteria. Any disagreements were resolved through discussion or, if necessary, with input from a third reviewer (A.H.F). The criteria used to evaluate each trial included adequacy of sequence generation, allocation concealment, blinding, handling of incomplete outcome data, selective outcome reporting, and identification of other potential biases.

The GRADE framework was applied to assess and summarize the quality of evidence for each outcome included in the meta-analysis. This approach categorizes evidence into four levels: "high," "moderate," "low," or "very low." Evidence quality could be adjusted based on methodological and statistical factors. Two independent reviewers (A.J and A.A) assessed each

outcome for factors such as study design, risk of bias, consistency, precision, directness, effect size, dose-response gradient, and publication bias, with a third reviewer (V.M) serving as an adjudicator if needed.

### *2.5 Statistical Analysis*

Statistical analysis was performed using Stata software, version 17.0 (Stata Corp, College Station, Texas). We extracted pre- and post-treatment means, standard deviations (SDs), and participant counts from both intervention and placebo groups across clinical outcomes, including lipid profile, glycemic control, anthropometric indices, inflammation, BP, oxidative stress, liver function, adipokines, and heart rate. Standardized mean differences (SMDs) between intervention and placebo groups were calculated to assess the impact of ginseng supplementation.

A random effects model using the DerSimonian–Laird method was applied to account for heterogeneity across studies. In cases where SDs for changes were not reported, they were estimated using the Follmann method [(21)], assuming a correlation coefficient (R) of 0.5. When only the standard error (SE) was provided, we calculated SDs using the formula $SD = SE \times \sqrt{n}$, where n is the sample size. The SDs of the change difference were calculated as $SD = \sqrt{[(SD\ pre\text{-}treatment)^2 + (SD\ post\text{-}treatment)^2 - (2R \times SD\ pre\text{-}treatment \times SD\ post\text{-}treatment)]}$, with a correlation coefficient of 0.5.

Meta-regression assessed the potential impact of ginseng dosage (grams per day) and duration on CVD risk factors. For the meta-regression, we used a random-effects model to explore sources of heterogeneity among studies. Heterogeneity was evaluated using the $I^2$ statistic and Cochran's Q test. Meta-regression was conducted using the metareg command in Stata, and covariates with a p-value <0.10 were considered potentially significant modifiers of effect size.

To handle heterogeneity and enhance the generalizability of our results, we performed subgroup analyses based on factors such as study population, study quality, intervention age, gender, ginseng dosage, continent, and duration of intervention allowing us to explore variations in outcomes across different contexts and improve the applicability of our findings. These approaches were complemented by standard sensitivity analyses to assess the robustness of our conclusions, ensuring a comprehensive evaluation of the evidence. Additionally, a non-linear

model was applied to integrate dose-response data from multiple studies, exploring the effects of varying ginseng dosages on CVD risk factors [22]. Sensitivity analysis was performed using a leave-one-out approach, in which the meta-analysis was recalculated after excluding one study at a time to assess the robustness of the results.

## 3 RESULTS

### *1 Study Selection*

The study selection process is illustrated in **Figure 1**. A total of 20,739 studies were identified through database searches: PubMed (n = 2,325), ISI Web of Science (n = 2,841), Scopus (n = 5,362), Embase (n = 8,761), and the Cochrane Library (n = 1,450). After removing 9,796 duplicates, irrelevant studies, and animal studies, 10,943 studies were screened based on titles and abstracts. Of these, 10,802 were excluded, resulting in 141 full-text studies evaluated further. Seventy-four studies were excluded for not reporting the desired outcomes, as detailed in **Supplementary Table 2**. Consequently, 70 studies comprising 4,506 participants were included in the systematic review and meta-analysis.

### *3.2 Study Characteristics*

The characteristics of the included studies are summarized in **Table 1**. **Supplementary Figures 1-9** show the SMDs and 95% CIs for changes in BF%, BMI, WC, weight, DBP, pulse pressure, SBP, 2-hour glucose, 2-hour insulin, fasting insulin, FBS, HbA1c, HOMA-B, HOMA-IR, QUICKI, CRP, ESR, hs-CRP, IL-1Ra, IL-4, IL-6, IL-8, IL-10, TNF-α, total protein, HDL-C, LDL-C, oxidized LDL-C, TC, TG, albumin, ALP, ALT, AST, BUN, creatinine, GGT, CAT, GPx, GSH, GSH-Rd, MDA, ROS, SOD, TAC, adiponectin, leptin, and heart rate.

Studies were published between 1998 and 2024, and were conducted in Brazil [23], Canada [24; 25; 26; 27], China [28; 29; 30; 31], Croatia [32; 33], Iran [34; 35; 36; 37], Iraq [38], Japan [39], South Korea [40; 41; 42; 43; 44; 45; 46; 47; 48; 49; 50; 51; 52; 53; 54; 55; 56; 57; 58; 59; 60; 61; 62; 63; 64; 65; 66; 67; 68; 69; 70; 71; 72; 73; 74; 75; 76; 77; 78; 79; 80; 81; 82; 83; 84; 85; 86], Spain [87], Thailand [88], the UK [89], and the USA [90; 91; 92]. Participant ages in intervention groups ranged from 34.2 to 64 years, with Ginseng doses varying from 50 to 6,000 mg/day over intervention durations of 2 to 35 weeks. Sample sizes ranged from 6 to 195 participants, with studies including only males [23; 46; 55; 62; 71; 84; 87; 88], only females [47; 48; 60; 61; 63; 65; 66; 67; 68; 69; 78; 81; 91], both sexes [24; 25; 26; 27; 28; 30; 31; 32; 33; 35; 36; 37; 38; 39; 40; 41; 42; 43; 44; 45; 49; 50; 51; 52; 53;

54; 56; 57; 58; 59; 64; 70; 72; 73; 74; 75; 76; 77; 79; 80; 82; 83; 85; 86; 89; 90; 92), or not reporting gender (29; 34). Participants had cardiovascular or hypertensive disorders (34; 39; 40; 50; 67; 79; 80), metabolic or glycemic disorders (24; 25; 26; 27; 28; 29; 32; 33; 35; 36; 37; 42; 45; 51; 52; 55; 72; 73; 74; 75; 76; 82; 86), or general health or non-specific conditions (23; 30; 31; 38; 41; 43; 44; 46; 47; 48; 49; 53; 54; 56; 57; 58; 59; 60; 61; 62; 63; 64; 65; 66; 68; 69; 70; 71; 77; 78; 81; 83; 84; 85; 87; 88; 89; 90; 91; 92). The following are the sample sizes for the intervention and control groups across various outcomes: BF%: n = 173 (intervention: 86, control: 87), BMI: n = 784 (intervention: 419, control: 365), WC: n = 272 (intervention: 152, control: 120), Weight: n = 220 (intervention: 111, control: 109), DBP: n = 1537 (intervention: 826, control: 711), Pulse pressure: n = 214 (intervention: 105, control: 109), SBP: n = 1537 (intervention: 826, control: 711), 2-h Glucose: n = 379 (intervention: 204, control: 175), 2-h Insulin: n = 123 (intervention: 61, control: 62), FBS: n = 2515 (intervention: 1354, control: 1161), fasting insulin: n = 1163 (intervention: 630, control: 533), HbA1c: n = 660 (intervention: 376, control: 284), HOMA-B: n = 80 (intervention: 46, control: 126), HOMA-IR: n = 966 (intervention:529 , control: 437), QUICKI: n = 369 (intervention: 200, control: 169), CRP: n = 223 (intervention: 112, control: 111), ESR: n = 169 (intervention: 111, control: 58), hs-CRP: n = 740 (intervention: 428, control: 312), IL-1R: n = 102 (intervention: 54, control: 58), IL-4: n = 306 (intervention: 153, control: 153), IL-6: n = 908 (intervention: 505, control: 403), IL-8: n = 102 (intervention: 54, control: 48), IL-10: n = 205 (intervention: 106, control: 99), TNF-α: n = 933 (intervention: 487, control: 446), Total protein: n = 840 (intervention: 455, control: 385), HDL-C: n = 2196 (intervention: 1192, control: 1004), LDL-C: n = 1873 (intervention:1004 , control: 869), oxidized LDL-C: n = 153 (intervention: 77, control: 76), TC: n = 2740 (intervention: 1490, control: 1250), TG: n = 2403 (intervention: 1318, control: 1085), Albumin: n = 740 (intervention: 405, control: 335), ALP: n = 729 (intervention: 399, control: 330), ALT: n = 1758 (intervention:952 , control: 806), AST: n = 1586 (intervention: 863, control: 723), BUN: n = 786 (intervention: 427, control: 359), creatinine: n = 1507 (intervention: 807, control: 700), GGT: n = 620 (intervention: 351, control: 269), CAT: n = 228 (intervention: 150, control: 78), GPx: n = 241 (intervention: 147, control: 94), GSH: n = 195 (intervention: 124, control: 71), GSH-Rd: n = 170 (intervention: 112, control: 58), MDA: n = 425 (intervention: 242, control: 183), ROS: n = 170 (intervention: 112, control: 58), SOD: n = 331 (intervention: 193, control: 138), TAC: n = 254 (intervention: 170, control: 84), adiponectin: n = 165 (intervention: 99, control: 66), leptin: n = 61 (intervention: 46, control: 15), heart rate: n = 713 (intervention: 383, control: 330).

### *3.3 Qualitative Data Assessment*

Using the Cochrane Risk of Bias Assessment tool (ROB2), nine studies were rated as good quality [28; 59; 63; 64; 65; 71; 73; 85; 92], twenty two as fair [23; 25; 26; 30; 31; 33; 47; 48; 51; 53; 60; 66; 68; 74; 75; 78; 83; 84; 86; 87; 88; 90], and the remaining studies as poor [24; 27; 29; 32; 34; 35; 36; 37; 38; 39; 40; 41; 42; 43; 44; 45; 46; 49; 50; 52; 54; 55; 56; 57; 58; 61; 62; 67; 69; 70; 72; 76; 77; 79; 80; 81; 82; 89; 91] (**Table 2**).

### *3.4 Effects of Ginseng Supplementation on Anthropometric Indices*

Ginseng supplementation did not show significant effects on BF%, BMI, WC, or weight (**Supplementary Figure 1**). Egger's test did not indicate significant publication bias for BF% (p = 0.798), BMI (p = 0.652), WC (p = 0.909), or weight (p = 0.511). Sensitivity analyses, excluding individual studies, revealed no changes in these results.

### *3.5 Effects of Ginseng Supplementation on Blood Pressure*

Ginseng supplementation did not demonstrate significant effects on DBP **(Supplementary Figure 2)**, pulse pressure, or SBP. Egger's test indicated no significant publication bias for DBP (p = 0.552), pulse pressure (p = 0.905), or SBP (p = 0.966). Sensitivity analysis, excluding studies by En-Yuan et al. [49] (SMD: -0.29; 95% CI: -0.57, -0.02), Hwang et al. [53] (SMD: -0.28; 95% CI: -0.57, 0.00), and Dickman et al. [91] (SMD: -0.30; 95% CI: -0.57, -0.02) resulted in changes to the overall effect estimates for DBP. Excluding studies by En-Yuan et al. [49] (SMD: -0.26; 95% CI: -0.51, -0.01) altered the overall results on SBP.

### *3.6 Effects of Ginseng Supplementation on Glycemic Profile*

Our meta-analysis did not show any significant changes in 2h-glucose **(Supplementary Figure 3)**, 2h-insulin, fasting insulin, FBS, HbA1c, HOMA-B, HOMA-IR, and QUICKI.

Unlike other parameters in this subgroup, significant publication bias was observed in 2h-glucose (Egger's P = 0.010), and QUICKI (Egger's P = 0.004). Sensitivity analysis showed no alteration in this group's parameters.

### *3.7 Effects of Ginseng Supplementation on Inflammatory Markers*

Studies indicated a significant reduction in hs-CRP upon ginseng administration (SMD= -0.23, 95% CI: -0.38, -0.08; P= 0.002; $I^2$=0.0, P= 0.463) **(Supplementary Figure 4)**. However, no

significant results were found on CRP, ESR, IL-1Ra, IL-4, IL-6, IL-8, IL-10, TNF-α, and total protein.

No publication bias was suggested among the parameters in this group. Sensitivity analysis showed significant changes in IL-4 results upon excluding Yang et al. [31] (SMD: -0.36, 95% CI: -0.64, -0.08).

### *3.8 Effects of Ginseng Supplementation on Lipid Profile*

According to our results, ginseng supplementation is not beneficial on HDL-C **(Supplementary Figure 5)**, LDL-C, oxidized LDL-C, TC, and TG.

Sensitivity analysis shows the exclusion of Beak et al. [41] leads to changes in overall results in LDL-C levels and TC levels. Egger's test indicated no evidence of publication bias in lipid profile parameters.

### *3.9 Effects of Ginseng Supplementation on Liver Function*

Ginseng supplementation demonstrated a beneficial effect on GGT levels (SMD= -0.20, 95% CI: -0.37, -0.04; P= 0.015; $I^2$=0.0, P= 0.619) **(Supplementary Figure 6)**. However, no changes were seen in albumin, ALP, ALT, AST, BUN, and creatinine.

No publication bias was suggested among the parameters in this group. Unlike other parameters in this group, sensitivity analysis showed that removing the study by Shen et al. [84] (SMD: -0.16, 95% CI: -0.34, 0.02) affected the overall results on GGT.

### *3.10 Effects of Ginseng Supplementation Oxidative Stress Parameters*

Trials revealed a significant impact on GSH-Rd (SMD= 0.90, 95% CI: 0.38, 1.42; P= 0.001; $I^2$=58.5, P= 0.065) **(Supplementary Figure 7)**, ROS (SMD= -0.94, 95% CI: -1.27, -0.60; P= <0.001; $I^2$=0.0, P= 0.824) and SOD (SMD= 0.49, 95% CI: 0.10, 0.87; P= 0.014; $I^2$=65.2, P= 0.008). However, no changes were seen on CAT, GPx, GSH, MDA, and TAC.

A considerable publication bias was observed for CAT (Egger's P = 0.013), whereas no publication bias was detected for the other oxidative stress parameters.

Sensitivity analysis showed that the exclusion of the study by Kim et al. [58] altered the results for CAT (SMD: 0.34; 95% CI: 0.00, 0.69). The exclusion of the study by Kim et al. [59] changed the

overall effect on GSH (SMD: 0.58; 95% CI: 0.11, 1.05). The study by Dickman et al. [91] showed changes in sensitivity analysis on MDA (SMD: -0.73; 95% CI: -1.36, -0.10) Additionally, the exclusion of the study by Kim et al. [60] affected the results for SOD (SMD = 0.43, 95% CI: -0.01, 0.87.

### *3.11 Effects of Ginseng Supplementation on Adipokines*

No significant changes were observed in adiponectin or leptin levels following ginseng supplementation (**Supplementary Figure 8**).

Sensitivity analysis revealed no significant alterations upon exclusion of any of the included studies. No publication bias was detected for either adiponectin or leptin.

### *3.12 Effects of Ginseng Supplementation on Heart Rate*

The pooled results from studies examining the effects of ginseng on heart rate showed no significant decrease **(Supplementary Figure 9)**.

Sensitivity analysis indicated no significant changes in the overall results after the exclusion of any of the studies. There was no publication bias detected for heart rate, as indicated by Egger's test.

### *3.13 Subgroup Analysis*

In the subgroup analysis **(Table 3)** of ginseng interventions, participants were categorized by health conditions, geographical region, dosage, duration of intervention, gender, age, and study quality. The health conditions were divided into cardiovascular or hypertensive disorders, metabolic or glycemic disorders, and general or non-specific conditions. These included patients with coronary artery disease, type 2 diabetes mellitus (T2DM), HTN, chronic fatigue, and more.

The health conditions were organized into three distinct, non-overlapping categories for analysis: (1) cardiovascular or hypertensive disorders, (2) metabolic or glycemic disorders, and (3) general health or non-specific conditions. The cardiovascular or hypertensive disorders category included patients with heart-related conditions such as coronary artery disease or heart failure, as well as those with BP disorders like HTN or prehypertension, and individuals with elevated cholesterol levels. The metabolic or glycemic disorders category comprised participants with

conditions affecting blood sugar regulation, such as type 2 diabetes (T2D), MetS, or impaired glucose tolerance, alongside related issues like non-alcoholic fatty liver disease (NAFLD). The general health or non-specific conditions category encompassed a diverse group, including healthy adults, smokers, physically active individuals, postmenopausal women, and individual with fatigue, among others. Although these categories were designed to be mutually exclusive for analytical clarity, we recognize that some participants may have concurrent conditions (e.g., a patient with both diabetes and HTN). In such instances, participants were assigned to the category corresponding to their primary diagnosis or the condition most relevant to the study's focus, as reported by the original study authors, ensuring a consistent and interpretable subgroup analysis.

Participants came from Asia, Europe, and Canada/USA, with ginseng dosages split into those receiving less than 3000 mg/day, more than 3000 mg/day, or unspecified doses. The duration of interventions was categorized as either 8 weeks or less, or longer than 8 weeks. Gender groups included male, female, both, or not specified, while age was categorized as 48 years or younger, or older than 48 years. Finally, the study quality was assessed as poor, fair, or good to evaluate the reliability of the outcomes. This structured subgrouping allows for a detailed exploration of ginseng's effects across various demographics and conditions.

In our subgroup analysis, ginseng supplementation showed significant effects in patients with cardiovascular or hypertensive disorders on DBP, TNF-α, LDL-C, and TC. In those with metabolic or glycemic complications, significant changes were seen in FBS, total protein, albumin, and AST. For the general population, ginseng improved HOMA-IR, GGT, and hs-CRP. Positive results for SBP were consistent across all health conditions.

Based on continent, ginseng supplementation showed improvements in hs-CRP, IL-6, GGT, and MDA among Asian participants. For MDA, studies conducted in Canada or the USA reported significant findings, while for SBP, only one study from Croatia reported promising outcomes [32].

In the gender subgroup analysis, ginseng supplementation showed significant improvements in both males and females for hs-CRP, IL-6, GGT, and MDA. In females, significant changes were

observed in total protein and albumin, whereas in males, improvements were noted in DBP, SBP, albumin, and GGT.

In the dose subgroup analysis, ginseng supplementation at doses lower than 3000 mg showed significant improvements in hs-CRP, while doses higher than 3000 mg resulted in significant changes in MDA, based on one study [60].

In the duration subgroup analysis, ginseng supplementation for less than eight weeks showed significant improvements in DBP and total protein, while interventions lasting more than eight weeks resulted in significant changes in hs-CRP, LDL-C, and TC.

In the age subgroup analysis, ginseng supplementation in participants younger than 48 years showed significant improvements in DBP, hs-CRP, ALT, and MDA. In contrast, those older than 48 years exhibited significant changes in HOMA-IR, LDL-C, and TC. Ginseng supplementation showed an increase in fasting insulin in participants younger than 48 years.

Based on the quality of the included studies, significant improvements in DBP, hs-CRP, LDL-C, and albumin were observed in studies rated as poor. In studies with fair quality, notable changes were seen in GGT and MDA. Additionally, studies classified as good quality demonstrated significant effects on MDA and total protein.

### *3.14 Meta-regression and Non-linear Dose-Response Analysis*

A non-linear dose-response regression model was used to examine the relationship between ginseng dosage and cardiovascular outcomes. The meta-regression analysis revealed a significant association between ginseng dosage and HOMA-IR ($P = 0.044$), suggesting that higher doses may improve insulin resistance. Additionally, a significant association was found between intervention duration and MDA ($P = 0.007$), indicating that prolonged supplementation could increase MDA levels, which may be undesirable **(Supplementary Figures 10-11)**.

The dose-response analysis also demonstrated significant associations between ginseng dose and several markers, including FBS ($P < 0.001$), hs-CRP ($P = 0.043$), IL-6 ($P = 0.041$), DBP ($P = 0.022$), IL-10 ($P = 0.048$), fasting insulin ($P = 0.012$), and total protein ($P = 0.010$), suggesting that higher doses reduce these markers. Conversely, a positive association was found between

MDA (P = 0.008) and duration of supplementation, indicating that prolonged use may elevate MDA levels **(Supplementary Figures 12-13).**

### *3.15 GRADE Assessment*

The GRADE profile of ginseng supplementation, indicating the certainty of outcomes is presented in **Table 4**. Quality of evidence for FBS, total protein, oxidized LDL-C, ALT, AST, BUN, GGT, and heart rate were moderate. ROS, creatinine, albumin, ALP, TC, TG, TNF-α, IL-6, HOMA-B, weight, and BMI were graded as low and the rest of the outcomes were very low in quality (**Figure 2)**.

## 4. DISCUSSION

### *4.1 Summary of Findings*

This systematic review and meta-analysis synthesized data from 70 RCTs (4,506 participants) to assess ginseng's effects on various health outcomes, particularly highlighting its potential for metabolic and cardiovascular health. Key findings indicated significant reductions in hs-CRP and ROS, along with increases in antioxidant markers (SOD, GSH-Rd), which suggest ginseng's anti-inflammatory and antioxidant properties. However, other oxidative stress (catalase [CAT], GSH, GPx, MDA, and TAC) and inflammatory biomarkers (TNF-α, ILs, and ESR) were not altered significantly following ginseng supplementation. Linear and non-linear associations between these biomarkers and the dose suggested that the differences in the administered dosage can be one of the possible reasons for this controversy in these findings. Dose-response analysis revealed that lower doses were associated with more decrease in FBS (300 mg/day), hs-CRP (300 mg/day), IL-6 (300 mg/day), DBP (100 mg/day), and insulin (50 mg/day). Ginsenosides, the primary active compounds in ginseng, interact with specific receptors, including nuclear receptors like peroxisome proliferator-activated receptors (PPARs), which play a role in anti-inflammatory and antioxidant activities. Excessive doses may cause receptor downregulation or desensitization, diminishing the response [(93)]. The recommended dose of ginseng is 200 to 600 milligrams of extract [(94)]. High doses of ginseng can lead to mild adverse effects, including slight elevations in BP or gastrointestinal disturbances, which may reduce its net therapeutic benefit [(95)]. Lower doses are associated with fewer side effects, allowing the beneficial effects of ginseng to predominate.

According to the results of subgroup analysis, ginseng supplementation was associated with reductions in SBP, DBP, TNF-α, LDL-C, and TC in participants with cardiovascular or hypertensive disorders. Additionally, in the metabolic or glycemic disorders subgroup, ginseng supplementation resulted in significant decrease in FBS. These findings indicated that high baseline values are one of the factors that can influence the effectiveness of ginseng on cardiometabolic risk factors. Moreover, the observed changes in GGT levels, highlighted ginseng's potential role in liver health. However, without a significant effect on other liver biomarkers, this finding must be interpreted with caution.

### *4.2 Comparison with Previous Studies*

Although hs-CRP was significantly reduced in our study, previous findings have been mixed, with some studies, such as those in acute myocardial infarction [(40)] and menopausal populations [(65)], reporting no significant changes in hs-CRP with ginseng supplementation for 8 and 3 months, respectively. However, Hosseini et al. conducted a study on T2D patients that demonstrated a significant decrease in hs-CRP levels after eight weeks of using a standardized extract of ginseng [(96)]. Our subgroup analysis demonstrated variability by geography, suggesting population-specific responses to ginseng. Similarly, a pooled analysis of six trials involving 308 participants showed no significant change in hs-CRP overall; however, significant reductions were observed in studies conducted in Iran, indicating possible geographical variability in ginseng's effectiveness [(97)].

While a meta-analysis of 10 studies reported reductions in TC and LDL-C in MetS patients [(98)], our findings highlighted these reductions specifically in the cardiovascular group, indicating potential differences based on underlying health conditions.

Similarly, we observed significant antioxidant effects, consistent with reports that ginsenosides enhance GSH levels and antioxidant enzymes such as GPx, SOD, and CAT [(99; 100)]. Ginsenosides have been linked to increased SOD and CAT activities in various studies, which parallels our findings on reduced ROS and increased SOD, highlighting ginseng’s role in oxidative stress mitigation [(101)]. However, while previous studies focus on general oxidative markers, our analysis suggests specific effects on ROS, adding a targeted dimension to ginseng’s antioxidant profile.

### *4.3 Mechanisms of Action*

Ginseng's health benefits are attributed to a range of bioactive compounds, primarily ginsenosides, which have been shown to exert anti-inflammatory, antioxidant, and metabolic regulatory effects at the molecular level. Ginseng, especially through its active ginsenosides, regulates inflammatory responses by inhibiting key signaling pathways like nuclear factor-kappa B (NF-κB) and mitogen-activated protein kinases (MAPKs) [102; 103]. The NF-κB pathway, crucial in the transcription of pro-inflammatory cytokines, is suppressed by ginsenosides, which reduce NF-κB activation and the phosphorylation of its inhibitor, IκBα. This inhibition leads to decreased production of pro-inflammatory cytokines, such as TNF-α, thereby reducing systemic inflammation. Ginseng also inhibits the MAPK pathway, specifically the Extracellular signal-regulated kinase (ERK)1/2, c-Jun N-terminal kinase (JNK), and p38 branches, which further suppresses pro-inflammatory cytokine synthesis and cellular stress responses [104]. This anti-inflammatory effect is coupled with a reduced production of inflammatory mediators such as prostaglandin E2 while also suppressing the expression of enzymes like cyclooxygenase-2 (COX-2). These molecular pathways play a crucial role in reducing oxidative stress and inflammation, further supporting the increase in antioxidant enzymes like SOD, CAT, and GPx [105].

Moreover, ginseng regulates the expression of pro-apoptotic and anti-apoptotic proteins, such as by decreasing caspase-3 activity and increasing B-cell lymphoma 2 (Bcl-2) levels, enhancing cell survival and stability in liver tissue [106; 107]. This broadened biochemical response could explain the significant change in GGT levels, reflecting potentially increased enzymatic activity in hepatocytes and highlighting ginseng's multifaceted contribution to liver health.

Ginseng has shown potential as a complementary treatment for managing BP in individuals with HTN. Ginsenosides, particularly Rg1, Rb1, and Rg3, have been found to stimulate nitric oxide (NO) production in endothelial cells by activating endothelial nitric oxide synthase (eNOS). NO is a key molecule in promoting vasodilation, leading to a reduction in vascular resistance and BP [108]. Some ginsenosides, such as Rg3, have been shown to block calcium channels in vascular smooth muscle cells, leading to muscle relaxation and a decrease in vascular tone [109]. Ginsenosides may influence the renin-angiotensin-aldosterone system (RAAS), which plays a central role in BP regulation by controlling fluid balance and vasoconstriction. Studies suggest

that ginseng inhibits angiotensin-converting enzyme (ACE), leading to decreased levels of angiotensin II, a potent vasoconstrictor. Reduced angiotensin II activity can lower BP by preventing blood vessel narrowing and promoting sodium excretion [110].

Additionally, our results indicate that ginseng supplementation leads to a significant reduction in TC and LDL-C, among individuals with cardiovascular or hypertensive disease. Ginsenosides also play a role in lipid regulation, which may contribute to their cardiovascular benefits. Studies have shown that ginsenosides influence lipid synthesis and transport by modulating enzymes involved in cholesterol metabolism, such as 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase [111]. This modulation leads to reduced levels of TC and LDL-C.

In our meta-analysis, we did not observe a significant effect of ginseng supplementation on FBS, which aligns with the findings of several previous studies that also reported no significant impact on glycemic control [112]. Despite these consistent results, some research suggests that ginseng may have a potential role in managing blood glucose levels [113], indicating that further investigation is warranted to explore the conditions and mechanisms under which ginseng might demonstrate beneficial effects on glucose regulation. Subgroup analysis showed that in the metabolic or glycemic disorders subgroup, ginseng supplementation resulted in significant decrease in FBS. The mechanisms by which ginseng exerts its hypoglycemic effects are not entirely understood, but several hypotheses have been proposed. Several studies suggest that ginseng exerts its hypoglycemic effects through multiple mechanisms, including the stimulation of insulin secretion and improved glucose uptake [114]. Ginsenosides have been shown to promote glucose-stimulated insulin release from pancreatic β-cells, enhance insulin sensitivity, and activate AMP-activated protein kinase, a key regulator of glucose and lipid metabolism [114; 115].

The observed improvements in oxidative stress and inflammatory markers (e.g., hs-CRP, ROS, SOD) align with the broader evidence on natural compounds modulating cardio-metabolic pathways. For instance, conjugated linoleic acids (CLAs) have demonstrated anti-inflammatory and antioxidant properties, though their effects on lipid metabolism and body composition remain inconsistent, mirroring the variability seen in ginseng's impact on lipid profiles [8]. Similarly, Pycnogenol, a pine bark extract, reduces inflammation via NF-Kb inhibition and enhances antioxidant defenses—mechanisms analogous to those of ginsenosides—but its efficacy in chronic diseases depends on dosing and population characteristics [11]. The null

effects of ginseng on glycemic indices in our analysis parallel findings from studies on royal jelly, where significant reductions in fasting blood glucose were only observed in specific subgroups (e.g., longer interventions or unhealthy populations) [10]. This underscores the importance of tailoring supplementation protocols to patient subgroups, as seen in walnut studies, where satiety and lipid benefits were linked to their polyunsaturated fatty acid (PUFA) and fiber content rather than direct metabolic modulation [9]. Notably, Zhang et al. [12] reported significant reductions in SBP and LDL-C with ginseng, conflicting with our findings, potentially due to differences in study populations (e.g., baseline health status) or ginseng isomer specificity. Collectively, these comparisons highlight that natural products like ginseng exert context-dependent effects, influenced by bioactive compound composition, intervention duration, and target populations, necessitating precision in clinical applications.

The observed heterogeneity in ginseng's efficacy across different population subgroups, particularly the more pronounced cardiovascular benefits in Asian cohorts, might be attributed to several factors. Genetic polymorphisms in drug-metabolizing enzymes, especially cytochrome P450 (CYP) variants like CYP3A4 and CYP2C9, which are known to differ in frequency between Asian and non-Asian populations, may influence the pharmacokinetics of ginsenosides [116]. These genetic variations can affect the biotransformation of ginsenosides to their active metabolites, potentially explaining the enhanced responsiveness observed in Asian populations [117]. Additionally, dietary patterns characteristic of Asian populations, which typically include higher consumption of plant-based foods rich in complementary phytochemicals, may synergistically enhance ginseng's pharmacological effects through modulation of gut microbiota composition [118]. The gut microbiome plays a crucial role in ginsenoside metabolism, converting primary ginsenosides to more bioavailable and pharmacologically active secondary forms through intestinal bacterial deglycosylation [119]. Differences in intestinal microbiota profiles between ethnic groups may therefore contribute to varying levels of ginsenoside bioactivation and subsequent therapeutic efficacy.

Furthermore, methodological variations and baseline health status differences across studies might explain the discrepancies observed between population groups and health conditions. The significant improvements in lipid profiles (LDL-C, TC) and BP (DBP) among participants with pre-existing cardiovascular or hypertensive disorders suggest that ginseng's effects may be more

pronounced in individuals with dysregulated cardiometabolic parameters at baseline. This therapeutic threshold effect is consistent with findings for other natural compounds, where clinical benefits are often more evident in populations with established pathophysiological conditions rather than healthy individuals [120]. The duration-dependent effects noted in our subgroup analysis, with certain parameters like hs-CRP, LDL-C, and TC showing significant improvements only after eight weeks of supplementation, indicate that ginseng's cardiovascular benefits may require sustained administration to achieve meaningful physiological changes [12]. This time-dependent response likely reflects the gradual accumulation of bioactive metabolites and the progressive modulation of cellular signaling pathways, particularly those involved in inflammatory cascades and lipid metabolism [121]. Additionally, age-related differences in treatment response, evidenced by distinct parameter improvements in younger versus older participants, may be attributed to age-associated variations in pharmacokinetics, receptor sensitivity, and baseline inflammatory status [122].

### *4.4 Strengths and Limitations*

While our analysis provides valuable insights, it is important to recognize that we did not observe significant effects of ginseng supplementation on several health outcomes. This lack of significant findings may stem from variations in dosing regimens, participant characteristics, and underlying health conditions among the studies included in our meta-analysis. However, when we conducted subgroup analyses, we found meaningful associations for certain outcomes, such as SBP and DBP in individuals with CVD. These insights underscore the need for further studies to explore the impact of ginseng supplementation across diverse populations and health conditions. Future investigations should focus on standardizing dosing protocols and examining the mechanisms underlying ginseng's beneficial effects. Long-term studies are also necessary to evaluate the sustained impact of ginseng supplementation on various health outcomes. A key limitation of this meta-analysis was the inability to conduct subgroup analyses based on ginseng species. While this dimension is clinically relevant due to interspecies variability in ginsenoside composition and pharmacological activity, our effort was hindered by insufficient and inconsistent reporting in the primary studies. Notably, approximately half of the included trials did not specify the ginseng species used, and among those that did, variation in extraction methods and lack of standardized ginsenoside profiling further complicated classification. This

lack of consistent botanical specification limited the statistical power and interpretability of species-specific comparisons, precluding robust subgroup analysis along this axis. Therefore, although the therapeutic potential of different ginseng species may differ, the current body of evidence does not yet allow for reliable interspecies meta-analytic evaluation.

Despite these limitations, our meta-analysis highlights the promising health benefits of ginseng, advocating for its consideration as a complementary approach in managing diverse health conditions, while emphasizing the need for additional research to strengthen the evidence base.

### *4.5 Future Research Directions*

As ginseng supplementation continues to demonstrate potential health benefits, future research should focus on several key areas to enhance our understanding and application of this natural remedy. First, standardization of dosage and formulations is essential; research should prioritize the establishment of standardized dosages to address variability in dosing across studies, ensuring optimal doses for various health outcomes. Longitudinal studies are also needed to assess the sustained effects of ginseng supplementation on health outcomes, helping to elucidate the duration necessary for ginseng to exert its beneficial effects and identify any potential long-term impacts on health. Additionally, investigating the specific molecular mechanisms through which ginseng exerts its anti-inflammatory and antioxidant effects is crucial, as understanding these pathways could lead to the development of targeted therapies for metabolic and CVD. Future research should also include diverse populations to evaluate the effectiveness of ginseng across different demographic groups, identifying variations in response to supplementation based on genetic, environmental, and lifestyle factors.

Exploring the synergistic effects of ginseng with other herbal supplements or conventional medications may provide valuable insights into its therapeutic potential; thus, research should investigate whether combining ginseng with other agents enhances its health benefits or mitigates any adverse effects. Investigating ginseng's role in specific clinical populations, such as those with chronic diseases or elderly patients, could further support its use as a complementary therapy, while identifying health conditions that may benefit most from supplementation will enhance its applicability in clinical settings.

To enable future evidence syntheses that assess species-specific effects of ginseng on cardiovascular outcomes, researchers should prioritize rigorous reporting of intervention details. Future RCTs should systematically document the botanical species used, provide standardized ginsenoside content, and describe extraction and preparation methods in line with established guidelines. Clear and consistent taxonomic reporting will not only enhance reproducibility and transparency but also facilitate more granular meta-analyses, including dose-response and network meta-analyses across ginseng types. Such improvements in methodological reporting are essential to optimize the clinical utility and mechanistic understanding of ginseng supplementation in cardiovascular health.

Lastly, understanding how dietary factors and lifestyle choices interact with ginseng supplementation could shed light on its effectiveness, informing comprehensive health strategies that incorporate ginseng within a broader context of lifestyle management. By addressing these research directions, future studies can build on the current body of evidence, ultimately supporting the integration of ginseng as a beneficial supplement in health management and disease prevention.

## 5 CONCLUSIONS

In conclusion, this meta-analysis suggests that ginseng supplementation may have potential benefits some inflammatory liver function, and oxidative stress parameters. However, results on some studied biomarkers do not support this finding. In addition, the certainty of evidence for all biomarkers is very low-to-moderate. Therefore, our results must be interpreted with caution. Moreover, observed effect sizes are not clinically significant. Consequently, ginseng can only be considered as a complementary approach in managing various health conditions. Further high-quality research is warranted to confirm these findings and to provide more robust evidence regarding the therapeutic applications of ginseng.

## Declaration of Competing Interest

The authors whose names are listed in this article certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements),

or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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**Availability of data and materials**

All relevant data are provided within the manuscript and supplementary file. Additionally, data analyzed for this study are available upon request from the corresponding author.

**Human ethics and consent to participate**

As a systematic review and meta-analysis, our manuscript did not necessitate any referral for review to our institutional clinical ethics committee.

**Consent to participate**

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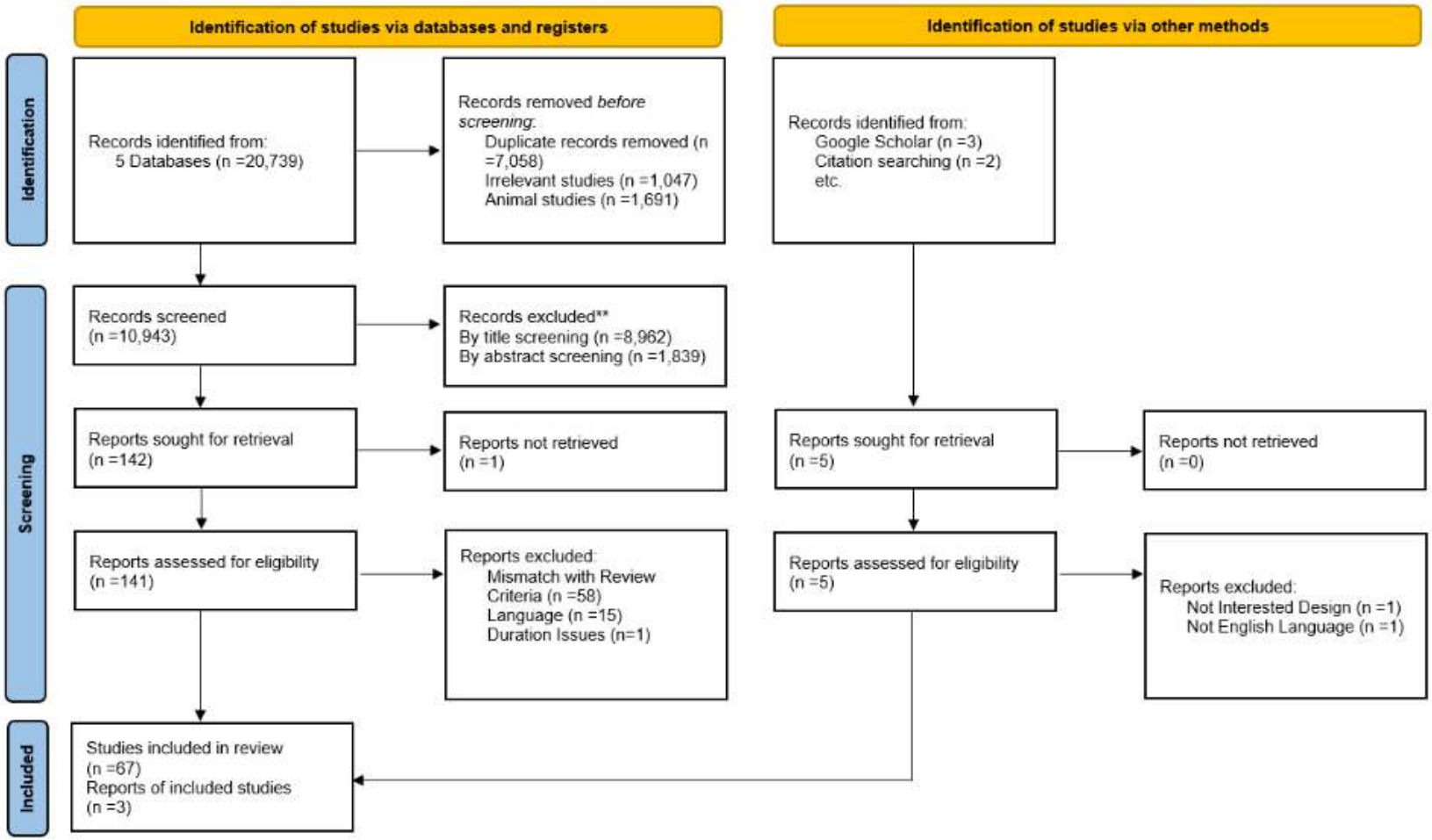


**Figure 1.** Flowchart of study selection for inclusion trials in systematic review.

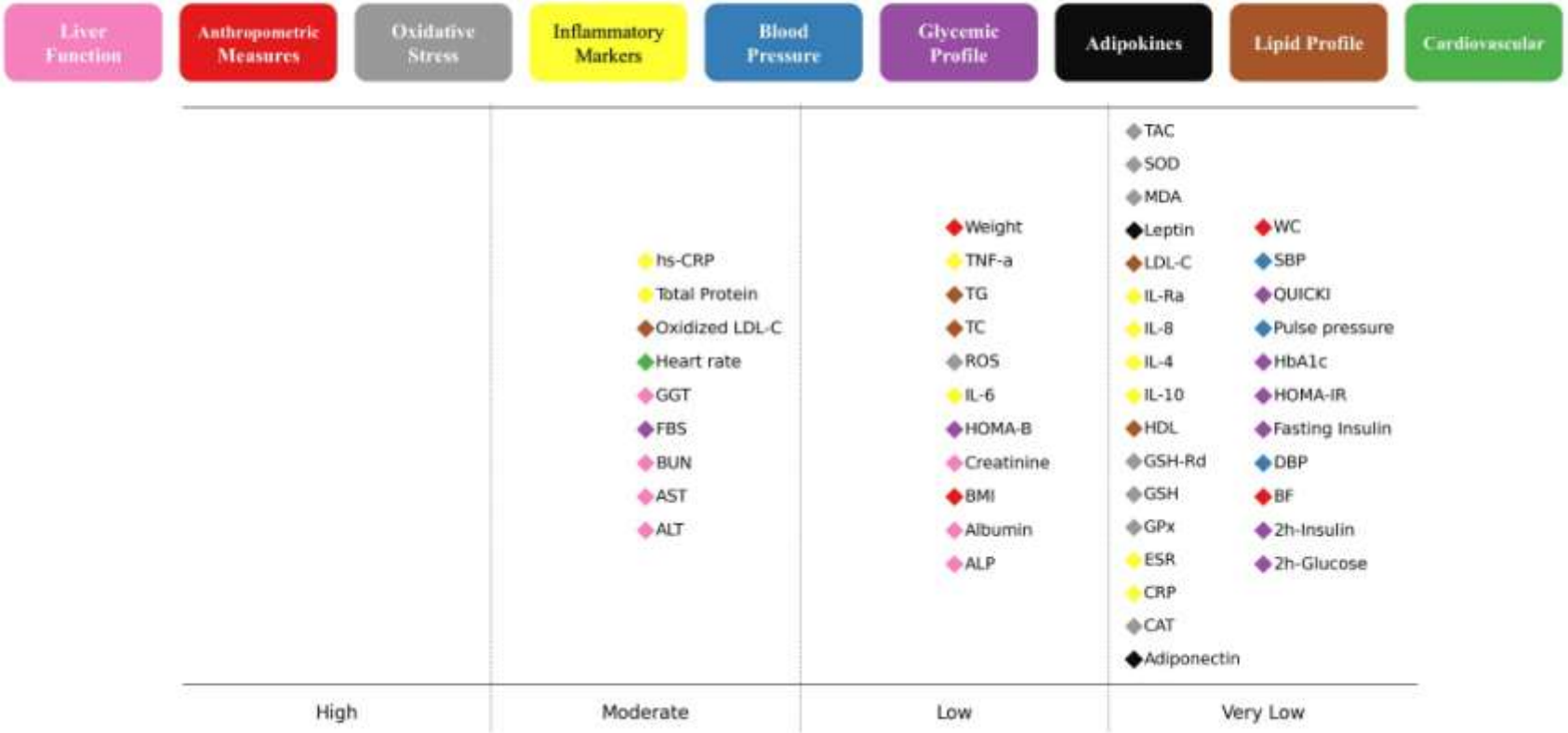


**Figure 2.** Credibility assessment for included outcomes

**Table 1.** Characteristic of included studies in the meta-analysis

| Studies. Year (Ref.) | Country | Study Design | Health Condition | Sample Size (Sex) | Sample Size (INT/CON) | Trial Duration (*Week*) | Means Age (INT/CON) | Dose of Supplement *(mg/d)* | Type of Supplement (INT/CON) | Outcomes |
|---|---|---|---|---|---|---|---|---|---|---|
| Han, 1998 (50) | Korea | PC | White Coat HTN | 8 (B) | 4 / 4 | 8 | 58.8 ± 8.8 | 4500 | Red ginseng (Ginseng Radix Rubra, obtained from Korean Tobacco & Ginseng Corporation, Taejeon, Korea) / Placebo | SBP, DBP, HR |
| Kim, 2001 | Korea | R, DB, | Smokers | 6 (M) | 3/3 | 4 | 23.8 ± 2.9 / | 1800 | red ginseng | TC, HDL-C, |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| (62) | | PC | | | | | 22.2 ± 1.9 | | (Panax ginseng C. A. Meyer) / placebo | LDL-C, TG, MDA |
| Caron, 2002 (90) | United States | R, DB, PC | Healthy | 30 (B) | 15 / 15 | 4 | 21.6 ± 2.7 | 200 | American ginseng (Panax quinquefolius) capsule is 100 mg of ginseng extract / Placebo (lactose monohydrate, Hemco, Texarkana, TX) | SBP, DBP |
| En-Yuan, 2002 (49) | Korea | PC, DB | Healthy | 75 (B) | 50 / 25 | 4 | 58.7 ± 5.1 / 57.4 ± 5.0 | 3000 | Korean Red Ginseng (KRG) / Placebo (NR) | SBP, DBP, TC, TG, Glucose, HR |
| de Andrade, 2007 (23) | Brazil | R, DB, PC, | Mild or moderate ED | 60 (M) | 30 / 30 | 12 | 52.6 / 54.3 | 1000 | KRG / placebo (capsules containing starch with KRG flavor) | HDL-C, LDL-C, Cholesterol |
| Kennedy, | United | R, DB, | Healthy | 16 (B) | 8 / 8 | 8 | 38.31 ± 10.3 | 200 | Korean panax | Insulin, HbA1c |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 2007 [89] | Kingdom | PC, Crossover | | | | | | | ginseng extract / Placebo | |
| Kulaputana, 2007 [88] | Thailand | R, DB, PC | Healthy | 60 (M) | 30 / 30 | 8 | 19.6 ± 0.8 / 19.1 ± 0.9 | 3000 | Korean ginseng powder capsules/ Placebo (lactose powder) | AST, ALT, BUN, Creatinine |
| Ma, 2008 [29] | China | Crossover, R, PC, DB | T2D | 20 (NR) | 10 / 10 | 4 | 51.5 ± 8.4970583144992 | 2214 | American ginseng (Panax quinquefolius L/) and Asian ginseng (Panax ginseng C/A Meyer) / Placebo (corn starch) | FG, 2-h OGTT Glucose, Fasting Insulin, 2-h OGTT Insulin, HOMA-IR, MDA |
| Vuksan, 2008 [26] | Canada | Crossover, R, PC, DB | T2D | 19 (B) | 10 / 9 | 12 | 64 ± 2 | 6000 | Korean red ginseng (Panax ginseng) – rootles / Placebo (NR) | FPG, FPI, HOMA-IS, HbaA1c, AST, ALT, Serum Creatinine, SBP, |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | DBP |
| Dickman, 2009 [91] | US | R, DB, PC | Postmenopausal women | 25 (F) | 12 / 13 | 16 | 62.3 ± 1.7 / 61.7 ± 1.8 | 1000 | Dry whole-root American ginseng powder / Placebo (rice poweder) | HR, SBP, DBP, glucose, plasma GSH, MDA, MDA Hemoglobin |
| Kim, 2010 [64] | Korea | R, PC, DB, Crossover | Patients with Glaucoma | 18 (B) | 9 / 9 | 12 | 59.03 ± 12.47 | 4500 | KRG (Jeong Kwan Jang; 300 mg/capsule, total powder capsule, made by steaming and drying 100% 6-year-old red ginseng roots) / Placebo (identical capsules filled with corn starch 95/25%, red ginseng fragrance 4/0%, natural | DBP, SBP, Heart rate |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | food color 0/15%, and caramel food color 0/6%) | |
| Ahn, 2011 (40) | Korea | R, SB | Patients with first ST-segment elevation AMI requiring stent implantation | 50 (B) | 25 / 25 | 32 | 61.4 ± 12.4 / 59.5 ± 11.8 | 3000 | Red ginseng / Placebo (75 mL of distilled water with ginseng fragrance) | IL-6, hs-CRP, TNF-α, HR, Adiponectin, HDL-C, LDL-C, TC, TG |
| Kim, 2011 (59) | South Korea | R, PC, DB | Healthy | 81 (B) | 27+27 / 27 | 4 | 40.4 / 40.4 | 1000 & 2000 | 20% ethanol extract of P/ ginseng (high dose group) & Mixture of 50% P/ ginseng and 50% placebo (low dose group) / Placebo made by mixing 99/36% cornstarch (Daesang Co/, Republic of Korea), 0/3% P/ ginseng | ROS, SOD, MDA, TAC, CAT, GSH, GSH Peroxidase, GSH Reductase |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | flavoring (Hanbit Flavor & Fragrance Co/, Republic of Korea), and 0/02% caramel coloring (Nam Young Food Co/, Republic of Korea) P/ ginseng flavoring (Hanbit Flavor & Fragrance Co/, Republic of Korea), and 0/02% caramel coloring (Nam Young Food | |
| Rhee, 2011 (80) | Korea | R, PC, DB | Subjects with HTN | 64 (B) | 30 / 34 | 12 | 55 ± 9 / 58 ± 6 | 3000 | KRG+ antihypertensive medication / Placebo (NR) | Fasting Glucose, TC, LDL-C, TG, HDL-C, SBP, DBP, |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | MAP, HR |
| Reeds, 2011 [92] | US | R, DB, PC | Overweight and obese subjects with impaired glucose tolerance or newly diagnosed T2DM | 10 (B) | 5 / 5 | 4 | 46 ± 3 | 5500 | Korean red ginseng extract (Spectrum Laboratories, Gardena, CA) / Placebo | BW, BMI, FM, glucose, insulin, HbA1c, TC, TG, HDL-C, LDL-C |
| Kim, 2012 [63] | Korea | R, PC, DB | Healthy | 57 (B) | 19+19 / 19 | 8 | 36.4 ± 7.54 / 37.0 ± 9.76 | 3000 & 6000 | Korean red ginseng (KRG) / Placebo (KRG-flavored capsule containing corn starch) | BMI, SBP, DBP, CAT, 8-epi-PGF 2α |
| Kim, 2012 [65] | Korea | R, PC, DB | Postmenopausal women | 63 (F) | 31 / 32 | 12 | 52.98 ± 3.04 / 55.01 ± 3.67 | 3000 | Korean red ginseng (KRG) / Placebo (95/25% cornstarch, 4% ginseng aromatic powder, 0/15% natural dye, and 0/6% caramel dye) | TC, LDL-C, HDL-C, TG, hs-CRP |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Kwon, 2012 [66] | Korea | R, PC, DB | Obese women | 45 (F) | 22 / 23 | 8 | 40.91 ± 9.65 / 46.48 ± 9.79 | 6000 | Korean Red Ginseng (KRG) / Placebo (NR) | BW, BMI, WC, WHR, BF, BFM, TG, HDL-C, TC, SBP, DBP |
| Lee, 2012 [68] | Korea | R, DB, PC | Healthy volunteers | 98 (B) | 49 / 49 | 12 | 45.5 ± 8.1 / 46.3 ± 9.8 | 3000 | KRG (concentrated red ginseng) / Placebo (contained 30% hop extracts and 45% soybean oil) | ALP, AST, ALT, Glucose, γ-GT, Total protein, Albumin, BUN, Creatinine |
| Lee, 2012 [71] | Korea | R, DB, PC | Healthy volunteers | 168 (B) | 41+42+14+ 14 / 57 | 4 | 39.8±9.3/ 40.8 ± 11.3, | 1000 & 2000 | 20% ethanol extract of 4-year-old Panax Ginseng root / Placebo | ESR, AST, ALT, ALP, Cholesterol, TG, HDL-C, Glucose, Total protein, Albumin, Creatinine, BUN |
| Park, 2012 [73] | Korea | R, PC, DB | MetS | 45 (B) | 23 / 25 | 12 | 43.1 ± 10.6 / 46.2 ± 11.0 | 4500 | Korean Red Ginseng (KRG) / Placebo (with | WC, SBP, DBP, TC, HDL-C, TG, Insulin, |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | ginseng flavor) | HOMA-IR, CRP, FPG, Oxidized LDL-C |
| Yoon, 2012 [86] | Korea | R, PC, DB | T2D | 61 (B) | 15+14+17 / 15 | 8 | 52.7 ± 11 / 54.8 ± 10 | 1500, 2000 & 3000 | Vinegar extract from Panax ginseng / Placebo (NR) | Adiponectin, BMI, SBP, DBP, WC, Fasting glucose, HbA1c, Insulin, TC, TG, HDL-C, LDL-C, AST, ALT, Creatinine, HOMA-IR, TNF-α, IL-6, QUICKI, Leptin, 2-h PG, GGT, HOMA-B, hs-CRP |
| Cho, 2013 [44] | South Korea | R, PC, DB | Non-diabetic healthy overweight and obese adults | 74 (B) | 34 / 34 | 12 | 42.6 ± 9.1 / 43.1 ± 8.9 | 6000 | Korean Red Ginseng (KRG) rootlets / Placebo (NR) | Fasting Glucose, %BF, SAD, BMI, Fasting Insulin, HOMA-IR, QUICKI, TC, LDL-C, HDL- |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | C, Triglyceride, Creatinine, ALT |
| Choi, 2013 (46) | South Korea | multicenter, R, DB, PC | Men with mild-to-moderate ED | 118 (M) | 59 / 59 | 8 | 57.49 ± 7.94 / 57.32 ± 8.41 | 1400 | Korean ginseng berry (SKGB) / Placebo (NR) | TC, HDL-C, LDL-C |
| Delui, 2013 (34) | Iran | R, DB, PC | Hyperlipidemic | 36 (NR) | 18 / 18 | 8 | >20 years | 500 | Panax Ginseng / Placebo (Granular powder included Lactose, starch and Magnesium stearate) | BMI, Creatinine, FBS, TC, TG, LDL-C, HDL-C, PAB, hs-CRP |
| Hosseini, 2013 (36) | Iran | R, PC, DB | T2DM | 30 (B) | 15 / 15 | 8 | 48.1 ± 5.7 / 46 ± 4.5 | 300 | Ginseng extract (G115) + hypoglycemic medicine (metformin, glibenclamide) / Placebo (flour) | FBS, TG, Cholesterol, LDL-C, HDL-C, HbA1c |
| Kim, 2013 (58) | Korea | R, DB, PC | Adults who had experienced chronic fatigue | 88 (B) | 29+29 / 30 | 4 | 40.25 ± 7.84 / 40.75 ± 8.82 | 1000 & 2000 | P/ginseng extract / Placebo (corn | ROS, MDA, TAC, SOD, CAT, GSH |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | for longer than 6 months | | | | | | starch, P/ginseng and caramel colouring) | contents, GSH-Px, GSH-Rd |
| Mucalo, 2013 [32] | Croatia | R, DB, PC | T2D & concomitant HTN | 64 (B) | 30 / 34 | 12 | 62.1 ± 8.80 / 63.9 ± 10.93 | 3000 | American Ginseng (AG) root + usual antihypertensive and hypoglycemic medications / Placeco (corn starch) | SBP, DBP, Pulse pressure, HR |
| Bang, 2014 [42] | Korea | R, PC, DB | IFG, IGT or newly diagnosed T2DM | 41 (B) | 21 / 20 | 12 | 58.81 ± 7.88 / 56.10 ± 9.74 | 5000 | Red ginseng / Placebo (corn starch) | HOMA-IR, HbA1c, BMI, SBP, DBP, TG, TC, HDL-C, LDL-C |
| Cho, 2014 [43] | South Korea | Single-center, R, PC, DB | Good general health volunteers | 60 (B) | 29 / 31 | 14 | 57.42 ± 4.09 / 58.69 ± 4.34 | 6000 | Ginseng polysaccharide (Y-75) / Placebo (caramel syrup & starch) | TNF-α |
| Lee, 2014 [69] | Korea | R, DB, PC | Postmenopausal women | 93 (F) | 49 / 44 | 2 | 58.5 ± 5.5 / 58.6 ± 5.8 | 2100 | Fermented Red Ginseng (FRG) | Insulin, Glucose |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | / Placebo (Starch) | |
| Mucalo, 2014 [33] | Croatia | R, DB, PC | T2D | 74 (B) | 35 / 39 | 12 | 61.9 ± 8.59 / 63.7 ± 10.28 | 3000 | American Ginseng (AG) root + usual antihypertensive & hypoglycaemic medications / Placebo (corn starch) | AST, ALT, Creatinine |
| Oh, 2014 [72] | Korea | R, DB, PC | T2D | 42 (B) | 21 / 21 | 4 | 53.2 ± 8.24 / 53.5 ± 8.70 | 2700 | Fermented Red Ginseng (FRG) / Placebo (composed primarily of dried yeast, and the flavor) | FPG<br>Fasting Plasma insulin<br>Postprandial plasma glucose 2h<br>Postprandial plasma insulin 2h<br>TC<br>HDL-C<br>LDL-C<br>TG |
| Park, 2014 | Korea | R, DB, | Impaired fasting | 20 (B) | 11 / 9 | 8 | 50.45 ± 12.36 / | 960 | Hydrolyzed | HOMA-IR, |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| (76) | | PC | glucose | | | | 44.56 ± 10.48 | | ginseng extract (HGE) / Placebo (composed primarily of powdered rice and pumpkin seed oil) | HOMA-β, Insulin, Glucose |
| Rhee, 2014 (79) | Korea | multi-center, R, DB, PC | Prehypertensive or stage I hypertensive | 90 (B) | 30+30 / 30 | 8 | 56.5 ± 12.1 / 52 ± 12.9 | 100 & 300 | Low dose Ginseol K-g1 (150 mg) & High dose Ginseol K-g1 (300 mg) / NR | SBP, DBP |
| Seo, 2014 (81) | Korea | Single center, R, DB, PC | Postmenopausal women | 71 (F) | 35 / 36 | 15 | 53.86 ± 3.21 / 54.33 ± 2.52 | 1000 | Korean Red Ginseng (KRG) / Placebo (containing corn starch, ginseng aromatic powder, natural dye and caramel dye) | SOD, glutathione peroxidase (GPx), MDA, 8-OHdG, IL-6, AST, ALT, GGT |
| Cha, 2016 | Japan | R, PC, | Prehypertensive | 62 (B) | 31 / 31 | 12 | 42.7 ± 12.6 / | 5000 | Korean Red | TC, HDL-C, |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| [39] | | DB | | | | | 41.4 ± 10.7 | | Ginseng (KRG) / Placebo (red ginseng-flavored capsules containing corn starch) | Total NO, Oxidized LDL-C, SBP, DBP, Lp-PLA2 activity, BMI, LDL-C, TG, hs-CRP, Glucose, Insulin |
| Hong, 2016 [52] | Korea | R, SB, PC | NAFLD | 66 (B) | 35 / 31 | 3 | 47.8 ± 14.9 | 3000 | Korean Red Ginseng (KRG) + Silybum marianum (450 mg/day), recommendation: regular aerobic exercise for >30 min/day / Placebo (NR) | ALT, GGT, LDH, Cholesterol, ALP, Albumin, Total protein, Glucose, IL-6, TNF-α, Adiponectin, AST |
| Hosseini, 2016 [35] | Iran | R, PC, DB | T2DM | 40 (B) | 20 / 20 | 8 | 47.9 ± 4.7 / 47.3 ± 6.4 | 300 | Ginseng extract (G115) / Placebo (NR) | Weight, BMI, WHR, FBS, HbA1c, IL-6, TNF-α, hs-CRP |
| Jung, 2016 | Korea | Single | MetS | 62 | 32 / 30 | 4 | 48.2 ± 10.9 / | 3000 | Red Ginseng / | BMI, SBP, |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| (55) | | center, R, DB, PC | | (M) | | | 45.2 ± 9.7 | | Placebo (containing over 90% corn starch) | DBP, FPG, TC, TG, HDL-C, HOMA-IR, AST, ALT, CRP, Insulin |
| Lee, 2016 (70) | South Korea | R, PC, DB | Healthy | 52 (B) | 26 / 26 | 4 | 62.1 ± 5.18 / 60.1 ± 4.44 | 2000 | Enzyme-modified ginseng extract (EMGE) / Placebo (starch, artificial ginseng flavoring and caramel color) | AST, ALT, BUN, Creatinine |
| Park, 2016 (78) | Korea | R, DB, PC | Healthy skin | 78 (F) | 39 / 39 | 24 | 51.16 ± 7.07 / 51.15 ± 3.83 | 750 | Enzyme-treated red ginseng powder complex (BG11001) / Placebo (excipients of lactose powder, microcrystalline cellulose, and powder maltitol syrup) | ALP, AST, ALT, γ-GT, Total protein, Albumin, Creatinine, Glucose, TC, HDL-C, LDL-C, TG |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Al-Kuraishy, 2017 [38] | Iraq | R, PC, SB | Healthy volunteers | 75 (B) | 35 / 30 | 4 | 22.61 ± 3.63 | 500 | Panax Ginseng / Placebo (Starch) | MDA |
| Hosseini, 2017 [37] | Iran | DB, R, PC | T2D | 45 (B) | 23 / 22 | 6 | 47.9 ± 4.7 / 47.3 ± 6.4 | 300 | Ginseng Extract (G115) / Placebo (Containing Starch) | FBS, HOMA-IR, HOMA β, HOMA-S, QUICKI |
| Kim, 2017 [61] | Korea | R, DB, PC | Epithelial ovarian cancer | 30 (F) | 15 / 15 | 12 | 55.9 ± 12.1 / 52.9 ± 10.1 | 3000 | Red Ginseng / Placebo (NR) | AST, ALT, ALP, BUN, Creatinine |
| Xu, 2017 [30] | China | R, PC | Early chronic kidney disease | 177 (B) | 91 / 86 | 24 | 59.2 ± 8.5 / 58.4 ± 7.8 | 500 | Ginsenoside Rb1 (GS-Rb1) / Placebo (NR) | Creatinine, TNF-α, IL-6, TC, HDL-C, LDL-C, TG, 8-OHdG |
| Choi, 2018 [45] | South Korea | Single-center, R, DB, PC | Participants with FBG within a range of 100-140 mg/dL | 63 (B) | 34 / 29 | 12 | 52.76 ± 10.24 / 51.89 ± 9.46 | 1000 | Ginseng berry / Placebo (NR) | HOMA-β cell, LDL-C, HbA1c, HOMA-IR, TC, TG, HDL-C |
| Beak, 2019 [41] | Korea | R, PC, DB | Nurses and fire fighters (members of two high stress occupations) | 63 (B) | 32 / 31 | 6 | 39.59 ± 12.36 / 41.29 ± 11.73 | 2000 | Korean Red Ginseng (KRG) / NR | HDL-C, LDL-C, TG, TC, IL-1β, IL-4, IL-6, IL-10, IFN-α, TNF-α, CRP, |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | Fasting blood sugar, HbA1c |
| Vuksan, 2019 [27] | Canada | Single center,R, DB, cross-over, PC | T2D | 48 (B) | 24 / 24 | 8 | 64 ± 7 | 3000 | American Ginseng (AG) extract / Placebo (cornstarch) | HbA1c, Fasting Glucose, Fasting insulin, SBP, DBP, TC, LDL-C, HDL-C, Body weight, Creatinine, ALT, Nitric Oxide |
| Hwang, 2020 [53] | Korea | R, PC, DB | Healthy | 44 (B) | 15+14 / 15 | 12 | 55.00±2.95/ 53.00 ± 3.66 | 3000 | GINST & GS-3K8, root, rootlets / Placebo (maltodextrin, soybean oil, palm oil, lecithin, rice branwax, cacao color, and annatto extract) | ALP, GGT, AST, ALT, Total protein, Albumin, BUN, Creatinine, TC, TG, Glucose, SBP, DBP, Heart Rate |
| Jovanovski, 2020 [24] | Canada | two-center, R, PC | HTN & T2D | 79 (B) | 43 / 36 | 12 | 59.44 ± 7.4 / 60.58 ± 6.9 | 2250 | Rg3-Korean red ginseng (KRG) + | Central DBP, HR, Central SBP |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | American Ginseng (AG) / Placebo (wheat-bran) | |
| Jung, 2020 (57) | Korea | R, DB, PC | Participants with elevated ALT levels | 84 (B) | 28+30 / 26 | 12 | 42.83 ± 11.03 / 42.67 ± 10.85 | 1400 | Fermented ginseng powder 125 (GBCK25) & Fermented ginseng powder 500 (GBCK25) / Placebo (containing refined glucose, cellulose, ginseng flavor, caramel coloring, paprika color, magnesium stearate, silicon dioxide, coating materials) | ALT, GGT, AST, TC, TG, HDL-C, LDL-C, TAC, hs-CRP |
| Kwon, | Korea | R, DB, | Postmenopausal | 68 (F) | 36 / 32 | 4 | 55.9 ± 5.9 / | 2000 | Korean Red | BMI, SBP, |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 2020 [67] | | PC | women with hypercholesterolemia | | | | 58.1 ± 4.7 | | Ginseng (KRG) / Placebo (containing over 90% corn starch) | DBP, AST, ALT Heart Rate, WC, cholesterol |
| Park, 2020 [74] | Korea | Single center, R, DB, PC | T2D | 59 (B) | 28 / 31 | 24 | 61.2 ± 8.45 / 60.9 ± 7.23 | 3000 | Korean Red Ginseng (KRG) extract + oral antidiabetic agents / Placebo (corn starch and cellulose) | BMI, SBP, DBP, HbA1c, FPG, Insulin, HOMA-IR, hs-CRP, IL-6, TNF-α |
| Park, 2020 [75] | Korea | Single center, R, DB, PC | T2D | 61 (B) | 30 / 31 | 24 | 59.3 ± 8.79 / 59.7 ± 7.22 | 3000 | Korean Red Ginseng (KRG) extract / Placebo (corn starch and cellulose) | BMI, SBP, DBP, HbA1c, FPG, Insulin, TC, TG, HDL-C, LDL-C, Apo A1, Apo B, hs-CRP, IL-6, TNF-α, 2h GLC, 2h insulin, |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | HOMA-IR |
| Shen, 2020 (83) | Korea | multicenter, R, DB, PC | Hepatic dysfunction | 60 (B) | 30 / 30 | 12 | 42.60 ± 11.74 / 41.73 ± 7.15 | 3000 | Panax ginseng extract (GS-KG9) / Placebo (consisted of crystalline cellulose, ginseng flavor powder, caramel coloring, magnesium stearate, and silicon dioxide) | ALT, GGT, AST, ALP, Total protein, Albumin, BUN, Creatinine, Glucose, TC, TG, HDL-C, LDL-C, hs-CRP |
| Sung, 2020 (85) | South Korea | R, DB, PC | Chronic Fatigue | 47 (B) | 24 / 23 | 6 | 49 ± 8.351 / 47.087 ± 10.795 | 3000 | KRG powder Capsules containing the ginsenosides Rb1, Rc, Rb2, Rg3(S), Rf, Rg3(R), Rg1, Re, Rh, Rg2(S), and Rd/ Placebo (corn starch and cellulose) | SOD, TBARS |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Chung, 2021 [48] | Korea | R, DB, PC | Postmenopausal women | 63 (F) | 33 / 30 | 8 | 58.7 ± 4.2 / 59.7 ± 4.2 | 2000 | Korean Red Ginseng (KRG) / Placebo (contains cornstarch and cellulose) | BMI, SBP, DBP, Fasting Plasma Glucose, TC, HDL-C, Triglyceride, LDL-C, AST, ALT, GGT |
| Chung, 2021 [47] | Korea | R, DB, PC | Premenopausal women diagnosed with gynecologic cancer | 55 (F) | 29 / 26 | 12 | 49.42 ± 4.91 / 48.58 ± 5.04 | 3000 | Korean Red Ginseng (KRG) (Panax ginseng C/A/ Meyer) / Placebo (contains Corn starch, ginseng aromatic powder, natural dye and caramel dye) | AST, ALT, BUN, Creatinine |
| Hong, 2021 [51] | Korea | multicenter, R, PC | NAFLD | 90 (B) | 44 / 46 | 4 | 50.0 ± 13.3 / 49.7 ± 13.2 | 2000 | Korean Red Ginseng (KRG) + milk-thistle dried extract powder (450 mg/day), recommendatio | AST, GGT, Cholesterol, Triglyceride, Fasting Glucose, CK18, ALT |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | n: regular aerobic exercise for >30 min/day / Placebo (cellulose) | |
| Hyun, 2021 [54] | Korea | DB, R, PC | Healthy | 100 (B) | 50 / 50 | 8 | 50.12 ± 6.43 / 50.38 ± 5.97 | 2000 | Korean Red Ginseng (KRG) / Placebo (cellulose) | TNF-α, INF-ϒ, IL-4, AST, TC, Glucose, BUN, TG, Creatinine, ALP, r-glutamyl transferase, SBP, DBP, T-protein, Pulse, ALT |
| Jovanovski, 2021 [25] | Canada | multicenter, R, PC | T2D & HTN | 80 (B) | 43 / 37 | 12 | 59.44 ± 7.4 / 60.58 ± 6.9 | 2250 | Rg3-Korean red ginseng (KRG) + American Ginseng (AG) / Placebo (wheat-bran) | Office SBP, Office DBP, Heart Rate, Fasting Glucose, Fasting Insulin, TC, LDL-C, HDL-C, TG, Creatinine, ALT |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Jung, 2021 (56) | Korea | R, DB, PC | Allergic rhinitis | 40 (B) | 20 / 20 | 4 | 33.7 ± 42.93 / 35.5 ± 46.95 | 3 mg/kg/day | Korean Red Ginseng (KRG) / Placebo (NR) | IL-4, IL-10 |
| Kim, 2021 (60) | South Korea | Single-center, R, DB, PC | Postmenopausal women with hand osteoarthritis | 43 (F) | 23 / 20 | 12 | 60.17 ± 9.49 / 60.55 ± 7.86 | 3000 | Red Ginseng / Placebo (cornstarch, ginseng aromatic powder, natural dye, and caramel dye) | SOD, Oxidative LDL-C, MDA |
| Seong, 2021 (82) | Korea | Single center, R, DB, PC | MetS | 50 (B) | 25 / 25 | 8 | 53.60 ± 8.45 / 49.84 ± 10.56 | 6000 | Korean Red Ginseng (KRG) / Placebo (containing crystalline cellulose, maltodextrin, magnesium stearate, silicon dioxide, food color) | HOMA-IR, Insulin, Glucose, TG, TC, HDL-C, LDL-C, Body weight, BMI, WC, Fat mass, Fat percentage, SBP, DBP, Pulse rate, CRP |
| Park, 2022 (77) | Korea | R, PC, DB | Healthy volunteers | 172 (B) | 58+57 / 57 | 6 | 38.2 ± 12.3 / 37.5 ± 12.8 | 1500 | KGR-BG1 & Red ginseng / | hs-CRP, IL-6, Insulin, |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | Placebo (maltodextrin) | Glucose, HOMA-IR, HbA1c, TC, TG, HDL-C, LDL-C |
| Shen, 2022 (84) | Korea | R, DB, PC | Hepatic dysfunction | 120 (M) | 60 / 60 | 12 | 39.98 ± 9.61 / 38.30 ± 9.42 | 800 | SGL 121(ginsenoside F2-enhanced mixture) / Placebo (crystalline cellulose) | ALT, GGT, AST, ALP, Albumin, Total protein, LDH, Glucose, BUN, Creatinine, CK |
| Gao, 2024 (28) | China | R, DB, PC, Crossover trial | Prediabetics | 195 (B) | 97 / 98 | 4 | 53 / 53.1 | 50 | Zhenyuan Capsule (Chinese patented medicine consisting of ginseng berry saponins extracted from the mature berry of Panax Ginseng) + lifestyle intervention / Lifestyle | FPG, 2-h PG, Fasting insulin, HOMA-IR, QUICKI, TG, TC, HDL-C, LDL-C |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | intervention and placebo | |
| Hernández-Garcí, 2024 [87] | Spain | R, DB, PC, Trial | Recreational athletes | 51 (M) | 15+12 / 24 | 2 | 34.3 / 37.8 | 500 | dry extract of Panax ginseng (capsule) + Aerobic Exercise (10 Km race) & dry extract of Panax ginseng (capsule) + Aerobic Exercise (Sub-maximal performance test) / placebo (miocrystalline cellulose) | Weight, Total lipids, Phospholipids, TC, Triacylglycerides, Non-esterified, IL-1Ra, IL-6, IL-8, IL-10, TNF-α, Heart Rate |
| Yang, 2024 [31] | China | R, DB, PC | Hypoimmunity | 104 (B) | 52 / 52 | 25 | 54.37 / 54.33 | NR | JungKwanJang Red ginseng (capsule) / Placebo (capsules containing lactose, microcrystalline cellulose, | SBP, DBP, Heart rate, Total protein, Albumin, ALT, AST, Urea, Creatinine, FPG, TNF-α, INF-y, IL-2, |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | silica, magnesium stearate,tartrazine, allura red, brilliant blue, food flavoring essence) | IL-4 |

**Footprint*:*** ALP, Alkaline Phosphatase; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; B, Both Sex; BF, Body Fat; BFM, Body Fat Mass; BMI, Body Mass Index; CON, Control Group; DB, Double-Blinded; DBP, Diastolic Blood Pressure; ED, Erectile Dysfunction; F, Female; FBG, Fasting Blood Glucose; FBS, Fasting Blood Sugar; FPG, Fasting Plasma Glucose, HbA1c, Hemoglobin A1C; HDL-C, High-Density Lipoprotein; HC, Hip Circumference; HOMA-IR, Homeostatic Model Assessment of Insulin Resistance; hs-CRP, High-Sensitivity C-Reactive Protein; HTN, Hypertension; INT, Intervention Group; LDH, Lactate Dehydrogenase; LDL-C, Low-Density Lipoprotein Cholesterol; MDA, Malondialdehyde; MetS, Metabolic Syndrome; NAFLD, Non-Alcoholic Fatty Liver Disease; NR, Not Reported; PCOS, Polycystic Ovary Syndrome; QUICKI, Quantitative Insulin Sensitivity Check Index; RCT, Randomized Controlled Trial; SBP, Systolic Blood Pressure; T2D, Type 2 Diabetes; T2DM, Type 2 Diabetes Mellitus; TB, Triple-Blinded; TC, Total Cholesterol; TG, Triglycerides; TNF- α, Tumor Necrosis Factor-alpha; WC, Waist Circumference; WHR, Waist-to-Hip Ratio.

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

| Study, Year (Ref.) | Random sequence generation | Allocation concealment | Blinding of participants & personnel | Blinding of outcome assessment | Incomplete outcome data | Selective outcome reporting | Other sources of bias | Overall quality |
|---|---|---|---|---|---|---|---|---|
| Han, 1998 [50] | H | H | U | U | H | U | L | Poor |
| Kim, 2001 [123] | U | U | L | U | L | L | L | Poor |
| Caron, 2002 [90] | L | U | L | U | L | L | L | Fair |
| En-Yuan, 2002 [49] | U | H | U | H | L | L | L | Poor |
| de Andrade, 2007[124] | L | U | L | U | L | L | L | Fair |
| Kennedy, 2007 [89] | L | U | L | U | H | H | L | Poor |
| Kulaputana, 2007 [125] | L | U | L | U | L | L | L | Fair |
| Ma, 2008 [29] | U | U | L | U | L | L | L | Poor |
| Vuksan, 2008 [26] | L | L | L | U | H | L | L | Fair |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Dickman, 2009 [91] | U | U | L | U | L | L | L | Poor |
| Kim, 2010 [64] | L | L | L | L | L | L | L | Good |
| Ahn, 2011[126] | L | H | H | H | H | L | L | Poor |
| Kim, 2011 [59] | L | L | L | U | L | L | L | Goog |
| Rhee, 2011 [80] | U | H | L | H | H | L | L | Poor |
| Reeds, 2011[92] | L | L | L | U | L | L | L | Good |
| Kim, 2012 [63] | U | U | L | U | L | L | L | Poor |
| Kim, 2012 [65] | L | L | L | L | L | L | L | Good |
| Kwon, 2012 [66] | L | L | L | U | H | L | L | Fair |
| Lee, 2012 [68] | L | H | L | L | L | L | L | Fair |
| Lee, 2012 [71] | L | L | L | L | L | L | L | Good |
| Park, 2012 [73] | L | L | L | U | L | L | L | Good |
| Yoon, 2012 [86] | L | L | L | U | L | L | L | Good |
| Cho, 2013 [44] | U | H | U | H | L | L | L | Poor |
| Choi, 2013 [46] | L | H | L | L | L | L | L | Fair |
| Delui, 2013 [34] | U | H | U | H | L | L | L | Poor |
| Hosseini, 2013 [36] | U | H | U | H | L | L | L | Poor |
| Kim, 2013 [58] | L | H | U | H | L | L | L | Poor |
| Mucalo, 2013 [32] | L | H | L | L | H | L | L | Poor |
| Bang, 2014 [42] | U | H | U | H | H | L | L | Poor |
| Cho, 2014 [43] | L | L | L | L | H | L | L | Fair |
| Lee, 2014 [69] | L | H | U | H | H | L | L | Poor |
| Mucalo, 2014 [33] | L | H | L | L | L | L | L | Fair |
| Oh, 2014 [72] | L | H | L | H | L | L | L | Poor |
| Park, 2014 [76] | L | H | L | H | H | L | L | Poor |
| Rhee, 2014 [79] | U | H | L | H | L | L | L | Poor |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Seo, 2014 [81] | L | H | L | H | H | L | L | Poor |
| Cha, 2016 [39] | L | H | U | H | H | L | L | Poor |
| Hong, 2016 [52] | L | H | L | H | H | L | L | Poor |
| Hosseini, 2016 [35] | U | H | L | H | L | L | L | Poor |
| Jung, 2016 [55] | L | H | L | H | H | L | L | Poor |
| Lee, 2016 [70] | L | H | L | H | H | L | L | Poor |
| Park, 2016 [78] | L | L | L | H | L | L | L | Fair |
| Al-Kuraishy, 2017 [38] | U | H | H | H | L | L | L | Poor |
| Hosseini, 2017 [37] | U | H | L | H | L | L | L | Poor |
| Kim, 2017 [61] | U | H | U | H | H | L | L | Poor |
| Xu, 2017 [30] | L | L | U | H | L | L | L | Fair |
| Choi, 2018 [45] | L | H | L | L | H | L | L | Poor |
| Beak, 2019 [41] | L | H | L | H | H | L | L | Poor |
| Vuksan, 2019 [27] | L | H | L | L | H | L | L | Poor |
| Hwang, 2020 [53] | L | U | L | H | L | L | L | Fair |
| Jovanovski, 2020 [24] | U | H | H | H | L | L | L | Poor |
| Jung, 2020 [57] | L | H | L | H | L | L | L | Poor |
| Kwon, 2020 [67] | L | H | L | H | H | L | L | Poor |
| Park, 2020 [74] | L | L | L | L | H | L | L | Fair |
| Park, 2020 [75] | U | H | L | L | H | L | L | Poor |
| Shen, 2020 [83] | L | L | L | H | L | L | L | Fair |
| sung, 2020[127] | L | L | L | L | L | L | L | Good |
| Chung, 2021 [48] | L | L | L | H | L | L | L | Fair |
| Chung, 2021 [47] | L | H | L | H | L | L | L | Poor |
| Hong, 2021 [51] | L | H | U | U | L | L | L | Fair |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Hyun, 2021 [54] | L | H | U | H | L | L | L | Poor |
| Jovanovski, 2021 [25] | U | H | L | L | L | L | L | Fair |
| Jung, 2021 [56] | U | H | U | U | U | L | L | Poor |
| Kim, 2021 [60] | L | L | L | H | L | L | L | Fair |
| Seong, 2021 [82] | L | U | L | H | H | L | L | Poor |
| Park, 2022 [77] | U | H | L | H | L | L | L | Poor |
| Shen, 2022 [84] | L | L | L | H | L | L | L | Fair |
| Gao, 2024 [28] | L | L | L | L | L | L | L | Good |
| HernándezGarcí, 2024 [87] | L | L | L | U | H | L | L | Fair |
| Yang, 2024 [31] | L | L | L | U | H | L | L | Fair |

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

**Table 3.** Description of the analysis and subgroup results of Ginseng supplementation

| | **Studies N** | **Participant N** | **SMD (95%CI)** | ***P*-value** | **Heterogeneity** | | |
|---|---|---|---|---|---|---|---|
| | | | | | *P* heterogeneity | $I^2$ | *P* between sub-groups |
| **Analysis and subgroup results of Ginseng supplementation on BF%** | | | | | | | |
| **Overall effect** | 4 | 173 | 0.03 (-0.27, 0.33) | 0.852 | 0.501 | 0.0 | |
| **Analysis and subgroup results of Ginseng supplementation on BMI** | | | | | | | |
| **Overall effect** | 18 | 784 | 0.00 (-0.14, 0.14) | 0.971 | 0.997 | 0.0 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | 3 | 166 | 0.06 (-0.24, 0.37) | 0.692 | 0.938 | 0.0 | 0.439 |
| Metabolic or Glycemic Disorders | 9 | 374 | 0.07 (-0.14, 0.27) | 0.526 | 0.968 | 0.0 | |
| General Health or Non-specific Conditions | 6 | 244 | -0.14 (-0.39, 0.12) | 0.297 | 0.963 | 0.0 | |
| **Continent** | | | | | | | |
| Asia | 17 | 774 | 0.01 (-0.14, 0.15) | 0.926 | 0.996 | 0.0 | 0.615 |
| Europe | - | - | - | - | - | - | |
| Canada/USA | 1 | 10 | 0.00 (-0.14, 0.14) | 0.620 | 0.997 | 0.0 | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 6 | 246 | -0.01 (-0.26, 0.25) | 0.944 | 0.824 | 0.0 | 0.914 |
| ≥ 3000 | 12 | 538 | 0.01 (-0.16, 0.18) | 0.928 | 0.992 | 0.0 | |
| Not given | - | - | - | - | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 13 | 493 | -0.01 (-0.2, 0.26) | 0.886 | 0.988 | 0.0 | 0.781 |
| 8 < weeks | 5 | 291 | 0.03 (-0.20, 0.26) | 0.810 | 0.854 | 0.0 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Gender** | | | | | | | |
| Male & female | 13 | 510 | 0.03 (-0.15, 0.20) | 0.763 | 0.992 | 0.0 | 0.950 |
| Female | 3 | 176 | -0.04 (-0.33, 0.26) | 0.811 | 0.502 | 0.0 | |
| Male | 1 | 30 | -0.11 (-0.61, 0.39) | 0.668 | - | - | |
| Not given | 1 | 18 | 0.05 (-0.60, 0.70) | 0.884 | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 9 | 381 | -0.06 (-0.26, 0.14) | 0.565 | 0.999 | 0.0 | 0.399 |
| >48 | 9 | 403 | 0.63 (-0.14, 0.26) | 0.536 | 0.894 | 0.0 | |
| **Study quality** | | | | | | | |
| Poor | 12 | 609 | -0.04 (-0.20, 0.14) | 0.514 | 0.998 | 0.0 | 0.661 |
| Fair | 5 | 165 | 0.06 (-0.14, 0.26) | 0.536 | 0.894 | 0.0 | |
| Good | 1 | 10 | 0.05 (-0.60, 0.14) | 0.884 | - | - | |
| **Analysis and subgroup results of Ginseng supplementation WC** | | | | | | | |
| **Overall effect** | 7 | 272 | 0.05 (-0.19, 0.30) | 0.662 | 0.761 | 0.0 | |
| **Analysis and subgroup results of Ginseng supplementation on Weight** | | | | | | | |
| **Overall effect** | 7 | 220 | 0.04 (-0.22, 0.31) | 0.737 | 0.999 | 0.0 | |
| **Analysis and subgroup results of Ginseng supplementation on DBP** | | | | | | | |
| **Overall effect** | 34 | 1537 | -0.23 (-0.51, 0.05) | 0.107 | < 0.001 | 85.0 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | 7 | 309 | -1.43 (-2.49, -0.37) | **0.008** | < 0.001 | 93.5 | 0.007 |
| Metabolic or Glycemic Disorders | 14 | 647 | -0.17 (-0.48, 0.13) | 0.262 | < 0.001 | 70.0 | |
| General Health or Non-specific Conditions | 13 | 581 | 0.24 (-0.09, 0.58) | 0.157 | < 0.001 | 71.4 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Continent** | | | | | | | |
| Asia | 27 | 1217 | -0.22 (-0.56, 0.11) | 0.185 | < 0.001 | 86.2 | 0.932 |
| Europe | 1 | 64 | -0.14 (-0.64, 0.35) | 0.562 | - | - | |
| Canada/USA | 6 | 256 | -0.29 (-0.93, 0.34) | 0.364 | < 0.001 | 81.8 | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 12 | 639 | -0.18 (-0.66, 0.31) | 0.475 | < 0.001 | 87.4 | 0.727 |
| ≥ 3000 | 21 | 794 | -0.28 (-0.67, 0.11) | 0.160 | < 0.001 | 84.9 | |
| Not given | 1 | 104 | -0.06 (-0.44, 0.33) | 0.770 | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 18 | 571 | -0.34 (-0.67, -0.00) | **0.048** | < 0.001 | 77.4 | 0.463 |
| 8 < weeks | 16 | 786 | -0.12 (-0.59, 0.35) | 0.617 | < 0.001 | 89.5 | |
| **Gender** | | | | | | | |
| Male & female | 29 | 1274 | -0.27 (-0.59, 0.05) | 0.097 | < 0.001 | 85.8 | 0.021 |
| Female | 4 | 201 | 0.18 (-0.44, 0.80) | 0.576 | 0.004 | 77.6 | |
| Male | 1 | 62 | -0.93 (-1.46, -0.41) | **< 0.001** | - | - | |
| Not given | - | - | - | - | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 7 | 305 | -0.97 ( -1.92, -0.02) | **0.045** | < 0.001 | 92.8 | 0.070 |
| >48 | 27 | 1232 | -0.06 (-0.32, 0.20) | 0.656 | < 0.001 | 78.7 | |
| **Study Quality** | | | | | | | |
| Poor | 20 | 1010 | -0.53 ( -0.95, -0.10) | **0.015** | < 0.001 | 89.8 | 0.027 |
| Fair | 11 | 443 | 0.13 (-0.16, 0.43) | 0.373 | 0.029 | 50.0 | |
| Good | 3 | 84 | 0.15 (-0.28, 0.58) | 0.483 | 0.451 | 0.0 | |

**Analysis and subgroup results of Ginseng supplementation Pulse Pressure**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Overall effect** | 3 | 214 | -0.08 (-0.57, 0.41) | 0.741 | 0.045 | 67.7 | |
| **Analysis and subgroup results of Ginseng supplementation on SBP** | | | | | | | |
| **Overall effect** | 34 | 1537 | -0.18 (-0.45, 0.08) | 0.164 | < 0.001 | 82.7 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | 7 | 309 | -0.71 (-1.40, -0.01) | **0.046** | < 0.001 | 87.0 | 0.001 |
| Metabolic or Glycemic Disorders | 14 | 647 | -0.43 (-0.82, -0.04) | **0.032** | < 0.001 | 81.4 | |
| General Health or Non-specific Conditions | 13 | 581 | 0.33 (0.05, 0.60) | **0.020** | 0.005 | 58.8 | |
| **Continent** | | | | | | | |
| Asia | 27 | 1217 | -0.12 (-0.37, 0.14) | 0.361 | < 0.001 | 78.5 | < 0.001 |
| Europe | 1 | 64 | -1.99 (-2.60, -1.39) | **< 0.001** | - | - | |
| Canada/USA | 6 | 256 | -0.14 (-0.83, 0.55) | 0.694 | < 0.001 | 82.7 | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 12 | 639 | 0.05 ( -0.33, 0.43) | 0.783 | < 0.001 | 80.3 | 0.348 |
| ≥ 3000 | 21 | 794 | -0.34 ( -0.72, 0.04) | 0.082 | < 0.001 | 84.3 | |
| Not given | 1 | 104 | -0.08 (-0.46, 0.31) | 0.692 | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 18 | 571 | -0.16 (-0.48, -0.15) | 0.310 | < 0.001 | 74.9 | 0.892 |
| 8 < weeks | 16 | 786 | -0.20 (-0.63, 0.23) | 0.365 | < 0.001 | 87.7 | |
| **Gender** | | | | | | | |
| Male & female | 29 | 1274 | -0.19 (-0.47, 0.10) | 0.203 | < 0.001 | 82.6 | < 0.001 |
| Female | 4 | 201 | 0.18 (-0.44, 0.80) | 0.680 | 0.029 | 66.6 | |
| Male | 1 | 62 | -1.45 (-201, -0.88) | **< 0.001** | - | - | |
| Not given | - | - | - | - | - | - | |
| **Intervention Age (year)** | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ≤ 48 | 7 | 305 | -0.47 ( -1.31, 0.38) | 0.278 | < 0.001 | 91.4 | 0.427 |
| > 48 | 27 | 1232 | -0.11 ( -0.36, 0.14) | 0.398 | < 0.001 | 76.9 | |
| **Study Quality** | | | | | | | |
| Poor | 20 | 1010 | -0.40 ( -0.80, 0.00) | 0.050 | < 0.001 | 88.6 | 0.125 |
| Fair | 11 | 443 | 0.06 ( -0.14, 0.26) | 0.563 | 0.394 | 5.1 | |
| Good | 3 | 84 | 0.05 (-0.41, 0.51) | 0.824 | 0.337 | 8.0 | |
| **Analysis and subgroup results of Ginseng supplementation 2-h Glucose** | | | | | | | |
| **Overall effect** | 7 | 379 | -0.15 (-0.73, 0.42) | 0.600 | < 0.001 | 81.1 | |
| **Analysis and subgroup results of Ginseng supplementation 2-h Insulin** | | | | | | | |
| **Overall effect** | 3 | 123 | 0.21 (-0.55, 0.96) | 0.591 | 0.021 | 74.2 | |
| **Analysis and subgroup results of Ginseng supplementation on FBS** | | | | | | | |
| **Overall effect** | 44 | 2515 | -0.85 (-0.19, 0.02) | 0.109 | 0.014 | 34.8 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | 3 | 162 | 0.07 (-0.24, 0.38) | 0.644 | 0.575 | 0.0 | 0.135 |
| Metabolic or Glycemic Disorders | 20 | 1009 | -0.23 (-0.45, -0.02) | **0.030** | < 0.001 | 58.9 | |
| General Health or Non-specific Conditions | 21 | 1344 | -0.01 (-0.12, 0.10) | 0.844 | 0.819 | 0.0 | |
| **Continent** | | | | | | | |
| Asia | 39 | 2357 | -0.07 (-0.18, 0.03) | 0.170 | 0.017 | 35.3 | 0.555 |
| Europe | - | - | - | - | - | - | |
| Canada/USA | 5 | 158 | -0.22 (-0.67, 0.24) | 0.354 | 0.151 | 40.6 | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 26 | 1593 | -0.13 (-0.28, 0.02) | 0.091 | 0.002 | 50.7 | 0.530 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ≥ 3000 | 17 | 818 | -0.02 (-0.16, 0.12) | 0.759 | 0.577 | 0.0 | |
| Not given | 1 | 104 | 0.01 (-0.37, 0.40) | 0.942 | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 28 | 1524 | -0.15 (-0.30, 0.00) | 0.056 | 0.002 | 48.7 | 0.177 |
| 8 < weeks | 16 | 991 | -0.01 (-0.14, 0.11) | 0.827 | 0.675 | 0.0 | |
| **Gender** | | | | | | | |
| Male & female | 32 | 1849 | -0.09 (-0.22, 0.04) | 0.194 | 0.002 | 46.3 | 0.289 |
| Female | 6 | 386 | 0.04 (-0.16, 0.24) | 0.716 | 0.931 | 0.0 | |
| Male | 4 | 224 | -0.21 (-0.48, 0.05) | 0.118 | 0.928 | 0.0 | |
| Not given | 2 | 56 | -0.56 (-1.32, 0.21) | 0.152 | 0.174 | 46.0 | |
| **Intervention Age (year)** | | | | | | | |
| ≤ 48 | 20 | 1150 | -0.14 (-0.32, 0.03) | 0.115 | 0.003 | 52.7 | 0.308 |
| > 48 | 24 | 1365 | -0.03 (-0.15, 0.08) | 0.566 | 0.363 | 7.1 | |
| **Study Quality** | | | | | | | |
| Poor | 23 | 1282 | -0.15 (-0.33, 0.02) | 0.089 | < 0.001 | 57.6 | 0.644 |
| Fair | 14 | 811 | -0.06 (-0.20, 0.08) | 0.417 | 0.457 | 0.0 | |
| Good | 7 | 422 | -0.04 (-0.24, 0.15) | 0.648 | 0.981 | 0.0 | |
| **Analysis and subgroup results of Ginseng supplementation on HbA1c** | | | | | | | |
| **Overall effect** | 16 | 660 | 0.07 (-0.24, 0.38) | 0.641 | < 0.001 | 70.0 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | - | - | - | - | - | - | 0.203 |
| Metabolic or Glycemic Disorders | 11 | 398 | -0.06 (-0.50, 0.37) | 0.772 | < 0.001 | 75.2 | |
| General Health or Non-specific | 5 | 262 | 0.28 (-0.02, 0.57) | 0.065 | 0.298 | 18.3 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Conditions | | | | | | | |
| **Continent** | | | | | | | |
| Asia | 12 | 591 | -0.02 (-0.37, 0.33) | 0.904 | < 0.001 | 74.5 | 0.202 |
| Europe | 1 | 16 | 0.93 (-0.11, 1.96) | 0.081 | - | - | |
| Canada/USA | 3 | 53 | 0.31 ( -0.41, 1.02) | 0.401 | 0.205 | 36.9 | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 9 | 424 | 0.06 ( -0.41, 0.54) | 0.796 | < 0.001 | 79.3 | 0.927 |
| ≥ 3000 | 7 | 236 | 0.03 ( -0.34, 0.41) | 0.856 | 0.098 | 43.9 | |
| Not given | - | - | - | - | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 11 | 417 | 0.12 ( -0.33, 0.58) | 0.591 | < 0.001 | 76.3 | 0.570 |
| 8 < weeks | 5 | 243 | -0.04 (-0.38, 0.30) | 0.819 | 0.145 | 41.4 | |
| **Gender** | | | | | | | |
| Male & female | 16 | 660 | 0.07 (-0.24, 0.38) | 0.641 | < 0.001 | 70.0 | |
| Female | - | - | - | - | - | - | |
| Male | - | - | - | - | - | - | |
| Not given | - | - | - | - | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 7 | 332 | -0.07 ( -0.66, 0.53) | 0.829 | < 0.001 | 83.0 | 0.574 |
| >48 | 9 | 328 | 0.13 ( -0.19, 0.45) | 0.434 | 0.062 | 46.1 | |
| **Study Quality** | | | | | | | |
| Poor | 10 | 511 | -0.11 ( -0.49, 0.27) | 0.563 | < 0.001 | 75.7 | 0.157 |
| Fair | 5 | 139 | 0.46 (-0.17, 1.09) | 0.154 | 0.037 | 60.9 | |
| Good | 1 | 10 | 0.85 (-0.45, 2.16) | 0.201 | - | - | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Analysis and subgroup results of Ginseng supplementation HOMA-B** | | | | | | | |
| **Overall effect** | 5 | 126 | -0.31 (-0.69, 0.07) | 0.105 | 0.755 | 0.0 | |
| **Analysis and subgroup results of Ginseng supplementation on HOMA-IR** | | | | | | | |
| **Overall effect** | 17 | 966 | -0.10 ( -0.35, 0.15) | 0.442 | < 0.001 | 70.6 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | - | - | - | - | - | - | 0.002 |
| Metabolic or Glycemic Disorders | 14 | 725 | -0.23 (-0.49, 0.04) | 0.096 | 0.001 | 62.9 | |
| General Health or Non-specific Conditions | 3 | 241 | 0.36 (0.10, 0.15) | **0.007** | 0.776 | 0.0 | |
| **Continent** | | | | | | | |
| Asia | 17 | 966 | -0.10 ( -0.35, 0.15) | 0.442 | < 0.001 | 70.6 | |
| Europe | - | - | - | - | - | - | |
| Canada/USA | - | - | - | - | - | - | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 9 | 555 | -0.29 (-0.69, 0.12) | 0.162 | < 0.001 | 76.9 | 0.077 |
| ≥ 3000 | 8 | 411 | 0.12 (-0.08, 0.32) | 0.242 | 0.414 | 2.0 | |
| Not given | - | - | - | - | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 11 | 626 | -0.20 (-0.57, 0.18) | 0.303 | < 0.001 | 76.7 | 0.279 |
| 8 < weeks | 6 | 340 | 0.05 (-0.19, 0.29) | 0.690 | 0.280 | 20.3 | |
| **Gender** | | | | | | | |
| Male & female | 15 | 884 | -0.12 (-0.39, 0.15) | 0.400 | < 0.001 | 71.2 | 0.095 |
| Female | - | - | - | - | - | - | |
| Male | 1 | 62 | 0.41 (-0.09, 0.91) | 0.109 | - | - | |
| Not given | 1 | 20 | -0.56 (-1.46, 0.33) | 0.217 | - | - | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 6 | 396 | 0.24 ( -0.01, 0.50) | 0.065 | 0.156 | 37.6 | 0.003 |
| >48 | 11 | 570 | -0.33 (-0.60, -0.06) | **0.018** | 0.024 | 51.6 | |
| **Study Quality** | | | | | | | |
| Poor | 11 | 603 | -0.02 ( -0.27, 0.22) | 0.860 | 0.018 | 53.3 | 0.864 |
| Fair | 4 | 120 | -0.07 (-0.45, 0.32) | 0.725 | 0.886 | 0.0 | |
| Good | 2 | 243 | -0.34 (-1.49, 0.82) | 0.568 | < 0.001 | 92.3 | |
| **Analysis and subgroup results of Ginseng supplementation on Fasting Insulin** | | | | | | | |
| **Overall effect** | 22 | 1163 | 0.00 (-0.22, 0.22) | 0.981 | < 0.001 | 67.5 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | 1 | 62 | -0.13 (-0.63, 0.36) | 0.598 | - | - | 0.270 |
| Metabolic or Glycemic Disorders | 15 | 741 | -0.07 (-0.37, 024) | 0.671 | < 0.001 | 72.6 | |
| General Health or Non-specific Conditions | 6 | 360 | 0.19 (-0.02, 0.40) | 0.080 | 0.456 | 0.0 | |
| **Continent** | | | | | | | |
| Asia | 17 | 1014 | -0.01 (-0.26, 0.25) | 0.957 | < 0.001 | 71.6 | 0.973 |
| Europe | 1 | 16 | 0.10 (-0.88, 1.08) | 0.834 | - | - | |
| Canada/USA | 4 | 133 | 0.03 (-0.60, 0.67) | 0.921 | 0.062 | 59.1 | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 11 | 678 | -0.04 (-0.41, 0.33) | 0.816 | < 0.001 | 78.4 | 0.604 |
| ≥ 3000 | 11 | 485 | 0.07 (-0.15, 0.29) | 0.527 | 0.198 | 25.8 | |
| Not given | - | - | - | - | - | - | |
| **Duration of intervention** | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 8 ≥ weeks | 15 | 766 | 0.01 (-0.30, 0.33) | 0.925 | < 0.001 | 73.8 | 0.976 |
| 8 < weeks | 7 | 397 | 0.02 (-0.23, 0.27) | 0.865 | 0.170 | 33.8 | |
| **Gender** | | | | | | | |
| Male & female | 19 | 988 | 0.02 (-0.24, 0.28) | 0.881 | < 0.001 | 70.7 | 0.380 |
| Female | 1 | 93 | -0.15 (-0.56, 0.25) | 0.458 | - | - | |
| Male | 1 | 62 | 0.27 (-0,23, 0.77) | 0.291 | - | - | |
| Not given | 1 | 20 | -0.54 (-1.43, 0.35) | 0.238 | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 8 | 439 | 0.24 (0.05, 0.43) | **0.015** | 0.838 | 0.0 | 0.043 |
| >48 | 14 | 724 | -0.13 (-0.44, 0.17) | 0.395 | < 0.001 | 70.7 | |
| **Study Quality** | | | | | | | |
| Poor | 13 | 691 | 0.14 (-0.04, 0.32) | 0.127 | 0.174 | 26.8 | 0.295 |
| Fair | 6 | 219 | -0.10 (-0.37, 0.18) | 0.494 | 0.568 | 0.0 | |
| Good | 3 | 253 | -0.27 (-1.25, 0.71) | 0.589 | < 0.001 | 87.4 | |
| **Analysis and subgroup results of Ginseng supplementation on QUICKI** | | | | | | | |
| **Overall effect** | 6 | 369 | 0.24 ( -0.24, 0.72) | 0.323 | 0.004 | 71.0 | |
| **Analysis and subgroup results of Ginseng supplementation on CRP** | | | | | | | |
| **Overall effect** | 4 | 223 | 0.13 (-0.30, 0.55) | 0.559 | 0.055 | 60.5 | |
| **Analysis and subgroup results of Ginseng supplementation on ESR** | | | | | | | |
| **Overall effect** | 4 | 169 | 0.10 (-0.28, 0.47) | 0.617 | 0.272 | 23.2 | |
| **Analysis and subgroup results of Ginseng supplementation on hs-CRP** | | | | | | | |
| **Overall effect** | 15 | 740 | -0.23 (-0.38, -0.08) | **0.002** | 0.463 | 0.0 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive | 3 | 139 | -0.24 (-0.60, 0.12) | 0.186 | 0..321 | 12.0 | 0.995 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Disorders | | | | | | | |
| Metabolic or Glycemic Disorders | 6 | 221 | -0.22 (-0.56, 0.12) | 0.200 | 0.232 | 27.1 | |
| General Health or Non-specific Conditions | 6 | 380 | -0.22 (-0.43, -0.10) | **0.040** | 0.457 | 0.0 | |
| **Continent** | | | | | | | |
| Asia | 15 | 740 | -0.23 (-0.38, -0.08) | **0.002** | 0.463 | 0.0 | |
| Europe | - | - | - | - | - | - | |
| Canada/USA | - | - | - | - | - | - | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 8 | 372 | -0.35 (-0.60, -0.10) | **0.007** | 0.276 | 19.4 | |
| ≥ 3000 | 7 | 368 | -0.13 (-0.34, 0.07) | 0.205 | 0.769 | 0.0 | 0.201 |
| Not given | - | - | - | - | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 7 | 310 | -0.27 (-0.57, 0.02) | 0.072 | 0.210 | 28.6 | |
| 8 < weeks | 8 | 430 | -0.20 (-0.39, -0.01) | **0.042** | 0.642 | 0.0 | 0.680 |
| **Gender** | | | | | | | |
| Male & female | 13 | 641 | -0.19 (-0.35, -0.03) | **0.019** | 0.461 | 0.0 | |
| Female | 1 | 63 | -0.37 (-0.87, 0.13) | 0.147 | - | - | |
| Male | - | - | - | - | - | - | 0.367 |
| Not given | 1 | 36 | -0.65 (-1.32, 0.02) | 0.057 | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 8 | 455 | -0.31 (-0.54, -0.08) | **0.008** | 0.214 | 26.9 | |
| >48 | 7 | 285 | -0.14 (-0.38, 0.10) | 0.284 | 0.764 | 0.0 | 0.321 |
| **Study Quality** | | | | | | | |
| Poor | 9 | 497 | -0.32 (-0.51, -0.14) | **0.001** | 0.543 | 0.0 | 0.621 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Fair | 5 | 180 | 0.07 (-0.23, 0.38) | 0.637 | 0.766 | 0.0 | |
| Good | 1 | 63 | -0.37 ( -0.87, 0.13) | 0.147 | - | - | |
| **Analysis and subgroup results of Ginseng supplementation on IL-1Ra** | | | | | | | |
| **Overall effect** | 4 | 102 | -0.03 ( -0.42, 0.36) | 0.885 | 0.692 | 0.0 | |
| **Analysis and subgroup results of Ginseng supplementation on IL-4** | | | | | | | |
| **Overall effect** | 4 | 306 | -0.18 (-0.58, 0.22) | 0.380 | 0.032 | 66.1 | |
| **Analysis and subgroup results of Ginseng supplementation on IL-6** | | | | | | | |
| **Overall effect** | 17 | 908 | -0.32 (-1.04, 0.40) | 0.390 | < 0.001 | 95.4 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | 1 | 41 | -0.54 (-1.16, 0.08) | 0.090 | - | - | |
| Metabolic or Glycemic Disorders | 7 | 287 | -0.41 (-1.20, 0.37) | 0.303 | < 0.001 | 88.5 | 0.900 |
| General Health or Non-specific Conditions | 9 | 580 | -0.23 (-1.45, 0.99) | 0.712 | < 0.001 | 97.3 | |
| **Continent** | | | | | | | |
| Asia | 13 | 806 | -0.42 (-1.31, 0.46) | **0.348** | < 0.001 | 96.5 | |
| Europe | 4 | 102 | -0.08 (-0.31, 0.48) | 0.682 | 0.541 | 0.0 | 0.306 |
| Canada/USA | - | - | - | - | - | - | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 12 | 659 | -0.17 (-1.15, 0.82) | 0.739 | < 0.001 | 96.4 | |
| ≥ 3000 | 5 | 249 | -0.67 (-1.04, 0.23) | 0.147 | < 0.001 | 90.4 | 0.462 |
| Not given | - | - | - | - | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 12 | 499 | 0.05 (-0.66, 0.75) | 0.899 | < 0.001 | 91.7 | 0.170 |
| 8 < weeks | 5 | 409 | -1.16 (-2.73, 0.41) | 0.148 | < 0.001 | 97.7 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Gender** | | | | | | | |
| Male & female | 13 | 806 | -0.43 (-1.42, 0.55) | **0.390** | < 0.001 | 96.8 | 0.370 |
| Female | 1 | 31 | -0.30 (-0.77, 0.16) | 0.203 | - | - | |
| Male | 3 | 71 | 0.08 (-0.31, 0.48) | 0.682 | 0.541 | 0.0 | |
| Not given | - | - | - | - | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 9 | 438 | -0.09 (-0.95, 0.78) | 0.845 | < 0.001 | 93.8 | 0.521 |
| >48 | 8 | 470 | -0.57 (-1.77, 0.63) | 0.352 | < 0.001 | 96.5 | |
| **Study Quality** | | | | | | | |
| Poor | 8 | 509 | -0.25 (-1.08, 0.57) | 0.544 | < 0.001 | 94.5 | 0.891 |
| Fair | 7 | 399 | -0.36 (-1.66, 0.94) | 0.586 | < 0.001 | 96.2 | |
| Good | - | - | - | - | - | - | |
| **Analysis and subgroup results of Ginseng supplementation on IL-8** | | | | | | | |
| **Overall effect** | 4 | 102 | -0.04 ( -0.47, 0.38) | 0.840 | 0.323 | 13.9 | |
| **Analysis and subgroup results of Ginseng supplementation on IL-10** | | | | | | | |
| **Overall effect** | 10 | 205 | 0.35 (-0.49, 1.20) | 0.413 | < 0.001 | 87.5 | |
| **Analysis and subgroup results of Ginseng supplementation on TNF-α** | | | | | | | |
| **Overall effect** | 17 | 933 | -0.15 (-0.86, 0.57) | 0.683 | < 0.001 | 95.6 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | 1 | 41 | -1.26 (-1.93, -0.59) | **< 0.001** | - | - | 0.059 |
| Metabolic or Glycemic Disorders | 7 | 287 | 0.00 (-0.95, 0.95) | 1.00 | < 0.001 | 92.0 | |
| General Health or Non-specific Conditions | 9 | 605 | -0.15 (-1.28, 0.97) | 0.793 | < 0.001 | 97.1 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Continent** | | | | | | | |
| Asia | 13 | 831 | -0.01 (-1.61, 0.52) | 0.976 | < 0.001 | 96.5 | 0.446 |
| Europe | 4 | 102 | -0.55 (-1.61, 0.52) | 0.316 | < 0.001 | 83.8 | |
| Canada/USA | - | - | - | - | - | - | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 10 | 520 | -0.06 (-1.23, 1.10) | 0.914 | < 0.001 | 96.6 | 0.747 |
| ≥ 3000 | 6 | 309 | -0.33 (-1.41, 0.75) | 0.545 | < 0.001 | 94.6 | |
| Not given | 1 | 104 | 0.10 (-0.28, 0.48) | 0.610 | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 11 | 431 | 0.03 (-0.86, 0.93) | 0.946 | < 0.001 | 93.7 | 0.528 |
| 8 < weeks | 6 | 502 | -0.46 (-1.70, 0.78) | 0.466 | < 0.001 | 97.4 | |
| **Gender** | | | | | | | |
| Male & female | 13 | 831 | -0.03 (-0.87, 0.84) | 0.976 | < 0.001 | 96.5 | 0.446 |
| Female | - | - | - | - | - | - | |
| Male | 4 | 102 | -0.55 (-1.61, 0.52) | 0.316 | < 0.001 | 83.8 | |
| Not given | - | - | - | - | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 7 | 271 | -0.33 (-1.77, 1.11) | 0.650 | < 0.001 | 96.0 | 0.728 |
| >48 | 10 | 662 | -0.04 (-0.89, 0.82) | 0.933 | < 0.001 | 95.8 | |
| **Study Quality** | | | | | | | |
| Poor | 6 | 370 | -0.11 (-1.38, 1.16) | 0.863 | < 0.001 | 96.6 | 0.942 |
| Fair | 11 | 563 | -0.17 (-1.09, 0.75) | 0.716 | < 0.001 | 95.3 | |
| Good | - | - | - | - | - | - | |

**Analysis and subgroup results of Ginseng supplementation on Total Protein**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Overall effect** | 13 | 840 | 0.17 (-0.04, 0.37) | 0.110 | 0.020 | 50.0 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | - | - | - | - | - | - | 0.090 |
| Metabolic or Glycemic Disorders | 1 | 66 | 0.59 (0.09, 1.08) | **0.019** | - | - | |
| General Health or Non-specific Conditions | 12 | 774 | 0.13 (-0.08, 0.33) | 0.233 | 0.040 | 46.1 | |
| **Continent** | | | | | | | |
| Asia | 13 | 840 | 0.17 (-0.04, 0.37) | 0.110 | 0.020 | 50.0 | |
| Europe | - | - | - | - | - | - | |
| Canada/USA | - | - | - | - | - | - | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 7 | 467 | 0.25 (-0.06, 0.55) | 0.109 | 0.028 | 57.5 | 0.768 |
| ≥ 3000 | 5 | 269 | 0.07 (-0.34, 0.47) | 0.746 | 0.049 | 58.1 | |
| Not given | 1 | 104 | 0.14 (-0.24, 0.53) | 0.465 | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 6 | 335 | 0.37 (0.15, 0.59) | **0.001** | 0.493 | 0.0 | 0.029 |
| 8 < weeks | 7 | 505 | -0.01 (-0.28, 0.25) | 0.920 | 0.058 | 50.8 | |
| **Gender** | | | | | | | |
| Male & female | 7 | 473 | 0.08 (-0.16, 0.32) | 0.496 | 0.140 | 37.8 | 0.175 |
| Female | 3 | 205 | 0.44 (0.15, 0.72) | **0.003** | 0.987 | 0.0 | |
| Male | 3 | 162 | 0.22 (-0.58, 1.02) | 0.583 | 0.027 | 72.2 | |
| Not given | - | - | - | - | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 8 | 513 | 0.19 (-0.11, 0.50) | 0.222 | 0.009 | 62.6 | 0.915 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| >48 | 5 | 327 | 0.17 (-0.09, 0.43) | 0.197 | 0.281 | 20.9 | |
| **Study Quality** | | | | | | | |
| Poor | 2 | 166 | 0.30 (-0.21, 0.82) | 0.246 | 0.102 | 62.5 | 0.058 |
| Fair | 7 | 505 | -0.01 (-0.28, 0.25) | 0.920 | 0.058 | 50.8 | |
| Good | 4 | 169 | 0.49 (0.16, 0.81) | **0.003** | 0.853 | 0.0 | |
| **Analysis and subgroup results of Ginseng supplementation on HDL-C** | | | | | | | |
| **Overall effect** | 38 | 2196 | 0.08 (-0.10, 0.27) | 0.389 | < 0.001 | 76.8 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | 4 | 203 | -0.11 (-0.38, 0.17) | 0.449 | 0.833 | 0.0 | 0.511 |
| Metabolic or Glycemic Disorders | 14 | 757 | 0.09 (-0.29, 0.47) | 0.633 | < 0.001 | 82.9 | |
| General Health or Non-specific Conditions | 20 | 1236 | 0.10 (-0.14, 0.33) | 0.424 | < 0.001 | 72.9 | |
| **Continent** | | | | | | | |
| Asia | 34 | 2022 | 0.02 (-0.14, 0.19) | 0.777 | < 0.001 | 68.9 | 0.415 |
| Europe | - | - | - | - | - | - | |
| Canada/USA | 4 | 174 | 0.61 (-0.79, 2.01) | 0.393 | < 0.001 | 93.3 | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 23 | 1476 | 0.20 (-0.10, 0.49) | 0.180 | < 0.001 | 84.8 | 0.096 |
| ≥ 3000 | 15 | 720 | -0.08 (-0.22, 0.07) | 0.302 | 0.965 | 0.0 | |
| Not given | - | - | - | - | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 22 | 1146 | 0.12 (-0.14, 0.38) | 0.361 | < 0.001 | 75.4 | 0.646 |
| 8 < weeks | 16 | 1050 | 0.03 (-0.23, 0.30) | 0.799 | < 0.001 | 77.3 | |
| **Gender** | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Male & female | 25 | 1497 | -0.02 (-0.24, 0.20) | 0.850 | < 0.001 | 75.7 | 0.383 |
| Female | 6 | 375 | 0.02 (-0.19, 0.23) | 0.846 | 0.787 | 0.0 | |
| Male | 6 | 288 | 0.80 (-0.12, 1.71) | 0.088 | < 0.001 | 90.3 | |
| Not given | 1 | 36 | 0.16 (-0.50, 0.81) | 0.637 | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 19 | 915 | -0.3 (-0.17, 0.10) | 0.611 | 0.797 | 0.0 | 0.305 |
| >48 | 19 | 1281 | 0.15 (-0.18, 0.48) | 0.368 | < 0.001 | 87.1 | |
| **Study Quality** | | | | | | | |
| Poor | 20 | 1033 | -0.10 (-0.22, 0.02) | 0.115 | 0.900 | 0.0 | 0.140 |
| Fair | 10 | 678 | 0.21 (-0.22, 0.64) | 0.335 | < 0.001 | 84.3 | |
| Good | 8 | 485 | 0.35 ( -0.22, 0.91) | 0.227 | < 0.001 | 86.6 | |
| **Analysis and subgroup results of Ginseng supplementation on LDL-C** | | | | | | | |
| **Overall effect** | 31 | 1873 | -0.12 (-0.26, 0.02) | 0.083 | 0.001 | 51.0 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | 4 | 203 | -0.33 (-0.61, -0.05) | **0.020** | 0.640 | 0.0 | 0.327 |
| Metabolic or Glycemic Disorders | 12 | 647 | -0.16 (-0.38, 0.06) | 0.154 | 0.089 | 37.8 | |
| General Health or Non-specific Conditions | 15 | 1023 | -0.06 (-0.28, 0.16) | 0.604 | < 0.001 | 63.4 | |
| **Continent** | | | | | | | |
| Asia | 27 | 1699 | -0.11 (-0.26, 0.03) | 0.136 | 0.002 | 49.7 | 0.632 |
| Europe | - | - | - | - | - | - | |
| Canada/USA | 4 | 174 | -0.26 (-0.87, 0.34) | 0.394 | 0.026 | 67.7 | |
| **Ginseng dosage (mg/day)** | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| < 3000 | 19 | 1307 | -0.05 (-0.21, 0.10) | 0.507 | 0.024 | 43.3 | 0.211 |
| ≥ 3000 | 12 | 566 | -0.25 (-0.52, 0.02) | 0.066 | 0.006 | 58.4 | |
| Not given | - | - | - | - | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 16 | 871 | 0.00 (-0.24, 0.23) | 0.984 | 0.003 | 56.9 | 0.125 |
| 8 < weeks | 15 | 1002 | -0.22 (-0.38, -0.06) | **0.006** | 0.086 | 35.3 | |
| **Gender** | | | | | | | |
| Male & female | 24 | 1449 | -0.11 (-0.26, 0.04) | 0.141 | 0.20 | 41.0 | 0.858 |
| Female | 3 | 204 | -0.39 (-1.06, 0.27) | 0.248 | 0.004 | 82.2 | |
| Male | 3 | 184 | -0.03 (-0.68, 0.63) | 0.938 | 0.053 | 65.9 | |
| Not given | 1 | 36 | -0.17 (-0.82, 0.48) | 0.609 | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 12 | 592 | -0.01 (-0.25, 0.23) | 0.917 | 0.036 | 47.0 | 0.252 |
| >48 | 19 | 1281 | -0.19 (-0.36, -0.01) | **0.033** | 0.005 | 51.4 | |
| **Study Quality** | | | | | | | |
| Poor | 19 | 971 | -0.19 (-0.38, -0.01) | **0.041** | 0.010 | 48.3 | 0.123 |
| Fair | 9 | 634 | 0.07 (-0.14, 0.28) | 0.504 | 0.145 | 34.1 | |
| Good | 3 | 268 | -0.36 (-0.98, 0.26) | 0.254 | 0.029 | 71.8 | |
| **Analysis and subgroup results of Ginseng supplementation on Oxidized LDL-C** | | | | | | | |
| **Overall effect** | 3 | 513 | -0.22 (-0.53, 0.10) | 0.182 | 0.874 | 0.0 | |
| **Analysis and subgroup results of Ginseng supplementation on TC** | | | | | | | |
| **Overall effect** | 49 | 2740 | -0.10 (-0.22, 0.03) | 0.137 | < 0.001 | 58.8 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive | 5 | 271 | -0.32 (-0.56, -0.08) | **0.009** | 0.663 | 0.0 | 0.194 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Disorders | | | | | | | |
| Metabolic or Glycemic Disorders | 16 | 910 | -0.08 (-0.26, 0.09) | 0.347 | 0.071 | 36.6 | |
| General Health or Non-specific Conditions | 28 | 1559 | -0.05 (-0.25, 0.14) | 0.599 | < 0.001 | 69.3 | |
| **Continent** | | | | | | | |
| Asia | 41 | 2464 | -0.09 (-0.23, 0.04) | 0.173 | < 0.001 | 60.9 | 0.380 |
| Europe | 4 | 102 | 0.15 (-0.25, 0.54) | 0.466 | 0.437 | 0.0 | |
| Canada/USA | 4 | 174 | -0.32 (-0.91, 0.27) | 0.292 | 0.029 | 66.6 | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 31 | 1908 | -0.10 (-0.26, 0.07) | 0.246 | < 0.001 | 63.5 | 0.974 |
| ≥ 3000 | 18 | 832 | -0.09 (-0.29, 0.11) | 0.373 | 0.008 | 50.2 | |
| Not given | - | - | - | - | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 31 | 1645 | 0.00 (-0.13, 0.14) | 0.963 | 0.010 | 41.0 | 0.059 |
| 8 < weeks | 18 | 1095 | -0.24 (-0.46, -0.03) | **0.027** | < 0.001 | 66.1 | |
| **Gender** | | | | | | | |
| Male & female | 31 | 1870 | -0.11 (-0.28, 0.05) | 0.181 | < 0.001 | 65.5 | 0.118 |
| Female | 7 | 444 | -0.20 (-0.53, 0.12) | 0.215 | 0.009 | 65.0 | |
| Male | 10 | 390 | 0.14 (-0.06, 0.34) | 0.170 | 0.922 | 0.0 | |
| Not given | 1 | 36 | -0.38 (-1.04, 0.28) | 0.259 | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 24 | 1084 | 0.08 (-0.04, 0.20) | 0.188 | 0.616 | 0.0 | 0.005 |
| >48 | 26 | 1656 | -0.24 (-0.42, -0.05) | **0.012** | < 0.001 | 68.7 | |
| **Study Quality** | | | | | | | |
| Poor | 24 | 1342 | -0.13 (-0.29, 0.03) | 0.109 | 0.003 | 49.5 | 0.689 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Fair | 17 | 913 | 0.00 (-0.26, 0.27) | 0.975 | < 0.001 | 71.1 | |
| Good | 8 | 485 | -0.13 (-0.43, 0.18) | 0.423 | 0.031 | 54.6 | |
| **Analysis and subgroup results of Ginseng supplementation on TG** | | | | | | | |
| **Overall effect** | 44 | 2403 | -0.03 (-0.17, 0.12) | 0.723 | < 0.001 | 66.1 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | 4 | 203 | -0.06 (-0.36, 0.24) | 0.699 | 0.331 | 12.4 | 0.503 |
| Metabolic or Glycemic Disorders | 14 | 820 | -0.14 (-0.52, 0.23) | 0.450 | < 0.001 | 83.7 | |
| General Health or Non-specific Conditions | 26 | 1380 | 0.06 (-0.07, 0.20) | 0.372 | 0.078 | 29.8 | |
| **Continent** | | | | | | | |
| Asia | 37 | 2211 | 0.01 (-0.11, 0.14) | 0.811 | 0.001 | 46.6 | 0.550 |
| Europe | 4 | 102 | -1.09 (-3.20, 1.03) | 0.635 | 0.419 | 0.0 | |
| Canada/USA | 2 | 90 | -1.09 (-3.20, 1.03) | 0.314 | 0.002 | 89.8 | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 28 | 1662 | -0.06 (-0.27, 0.15) | 0.564 | < 0.001 | 75.3 | 0.495 |
| ≥ 3000 | 16 | 741 | 0.03 (-0.12, 0.18) | 0.714 | 0.382 | 6.3 | |
| Not given | - | - | - | - | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 27 | 1368 | 0.07 (-0.10, 0.24) | 0.410 | 0.001 | 53.4 | 0.135 |
| 8 < weeks | 17 | 1035 | -0.16 (-0.42, 0.09) | 0.212 | < 0.001 | 74.8 | |
| **Gender** | | | | | | | |
| Male & female | 29 | 1780 | -0.01 (-0.21, 0.20) | 0.937 | < 0.001 | 75.6 | 0.417 |
| Female | 6 | 375 | -0.01 (-0.22, 0.19) | 0.912 | 0.577 | 0.0 | |
| Male | 8 | 212 | -0.06 (-0.33, 0.22) | 0.688 | 0.555 | 0.0 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Not given | 1 | 36 | -0.60 (-0.32, 0.21) | 0.080 | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 23 | 1017 | 0.07 (-0.08, 0.21) | 0.363 | 0.238 | 16.4 | 0.262 |
| >48 | 22 | 1403 | -0.10 (-0.35, 0.15) | 0.440 | < 0.001 | 78.9 | |
| **Study Quality** | | | | | | | |
| Poor | 21 | 1184 | 0.12 (-0.04, 0.27) | 0.147 | 0.020 | 42.9 | 0.154 |
| Fair | 15 | 734 | -0.21 (-0.57, 0.14) | 0.232 | < 0.001 | 78.6 | |
| Good | 8 | 485 | -0.05 (-0.23, 0.13) | 0.578 | 0.859 | 0.0 | |
| **Analysis and subgroup results of Ginseng supplementation on Albumin** | | | | | | | |
| **Overall effect** | 12 | 740 | -0.09 (-0.43, 0.24) | 0.575 | < 0.001 | 77.9 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | - | - | - | - | - | - | 0.014 |
| Metabolic or Glycemic Disorders | 1 | 66 | 0.59 (0.09, 1.08) | **0.020** | - | - | |
| General Health or Non-specific Conditions | 11 | 674 | -0.16 (-0.50, 0.17) | 0.344 | < 0.001 | 76.0 | |
| **Continent** | | | | | | | |
| Asia | 12 | 740 | -0.09 (-0.43, 0.24) | 0.575 | < 0.001 | 77.9 | |
| Europe | - | - | - | - | - | - | |
| Canada/USA | - | - | - | - | - | - | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 6 | 367 | 0.05 (-0.44, 0.55) | 0.831 | < 0.001 | 79.2 | 0.628 |
| ≥ 3000 | 6 | 269 | -0.26 (-0.89, 0.37) | 0.417 | < 0.001 | 82.4 | |
| Not given | 1 | 104 | -0.23 (-0.62, 0.15) | 0.241 | - | - | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 5 | 235 | 0.23 (-0.23, 0.69) | 0.325 | 0.033 | 61.7 | 0.091 |
| 8 < weeks | 7 | 505 | -0.29 (-0.68, 0.10) | 0.147 | < 0.001 | 76.8 | |
| **Gender** | | | | | | | |
| Male & female | 6 | 373 | -0.24 (-0.72, 0.23) | 0.307 | < 0.001 | 78.0 | 0.004 |
| Female | 3 | 205 | 0.45 (0.01, 0.89) | **0.046** | 0.098 | 57.0 | |
| Male | 3 | 162 | -0.48 (-0.80, -0.16) | **0.003** | 0.519 | 0.0 | |
| Not given | - | - | - | - | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 8 | 513 | -0.07 (-0.50, 0.35) | 0.728 | < 0.001 | 80.4 | 0.850 |
| >48 | 4 | 227 | -0.15 (-0.78, 0.49) | 0.646 | 0.004 | 77.9 | |
| **Study Quality** | | | | | | | |
| Poor | 1 | 66 | 0.59 (0.09, 1.08) | **0.020** | - | - | 0.024 |
| Fair | 7 | 505 | -0.29 (-0.68, 0.10) | 0.147 | < 0.001 | 76.8 | |
| Good | 4 | 169 | 0.10 (-0.49, 0.69) | 0.740 | 0.031 | 66.2 | |
| **Analysis and subgroup results of Ginseng supplementation on ALP** | | | | | | | |
| **Overall effect** | 13 | 729 | -0.01 (-0.15, 0.14) | 0.932 | 0.996 | 0.0 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | - | - | - | - | - | - | 0.417 |
| Metabolic or Glycemic Disorders | 1 | 66 | -0.20 (-0.68, 0.29) | 0.424 | - | - | |
| General Health or Non-specific Conditions | 12 | 663 | 0.01 (-0.14, 0.17) | 0.868 | 0.997 | 0.0 | |
| **Continent** | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Asia | 13 | 729 | -0.01 (-0.15, 0.14) | 0.932 | 0.996 | 0.0 | |
| Europe | - | - | - | - | - | - | |
| Canada/USA | - | - | - | - | - | - | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 7 | 439 | 0.02 (-0.17, 0.21) | 0.816 | 0.996 | 0.0 | 0.638 |
| ≥ 3000 | 6 | 290 | -0.05 (0.28, 0.18) | 0.677 | 0.836 | 0.0 | |
| Not given | - | - | - | - | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 6 | 335 | -0.02 (0.24, 0.20) | 0.875 | 0.936 | 0.0 | 0.892 |
| 8 < weeks | 7 | 394 | 0.00 (-0.20, 0.20) | 0.978 | 0.950 | 0.0 | |
| **Gender** | | | | | | | |
| Male & female | 6 | 360 | -0.01 (-0.21, 0.20) | 0.957 | 0.754 | 0.0 | 0.991 |
| Female | 4 | 235 | 0.00 (-0.26, 0.27) | 0.976 | 0.999 | 0.0 | |
| Male | 3 | 134 | -0.03 (-0.37, 0.32) | 0.882 | 0.909 | 0.0 | |
| Not given | - | - | - | - | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 8 | 476 | -0.05 (-0.23, 0.14) | 0.617 | 0.983 | 0.0 | 0.467 |
| >48 | 5 | 253 | 0.07 (-0.18, 0.32) | 0.593 | 0.920 | 0.0 | |
| **Study Quality** | | | | | | | |
| Poor | 3 | 196 | 0.01 (-0.27, 0.29) | 0.937 | 0.572 | 0.0 | 0.969 |
| Fair | 6 | 364 | 0.00 (-0.21, 0.20) | 0.990 | 0.899 | 0.0 | |
| Good | 4 | 169 | -0.04 (-0.36, 0.28) | 0.799 | 0.986 | 0.0 | |
| **Analysis and subgroup results of Ginseng supplementation on ALT** | | | | | | | |
| **Overall effect** | 32 | 1758 | -0.10 (-0.23, 0.04) | 0.158 | 0.003 | 45.8 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | 1 | 68 | 0.04 (-0.43, 0.52) | 0.862 | - | - | 0.742 |
| Metabolic or Glycemic Disorders | 10 | 473 | -0.16 (-0.44, 0.11) | 0.247 | 0.045 | 47.9 | |
| General Health or Non-specific Conditions | 21 | 1217 | -0.07 (-0.24, 0.09) | 0.371 | 0.010 | 46.7 | |
| **Continent** | | | | | | | |
| Asia | 28 | 1561 | -0.11 (-0.26, 0.03) | 0.120 | 0.004 | 46.2 | 0.601 |
| Europe | 1 | 74 | -0.13 (-0.67, 0.24) | 0.353 | - | - | |
| Canada/USA | 3 | 123 | 0.20 (-0.48, 0.88) | 0.563 | 0.070 | 62.4 | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 17 | 983 | -0.11 (-0.27, 0.05) | 0.165 | 0.127 | 28.9 | 0.935 |
| ≥ 3000 | 14 | 671 | -0.06 (-0.32, 0.21) | 0.668 | 0.001 | 62.4 | |
| Not given | 1 | 104 | -0.07 (-0.45, 0.32) | 0.725 | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 16 | 809 | -0.13 (-0.35, 0.08) | 0.221 | 0.011 | 50.6 | 0.614 |
| 8 < weeks | 16 | 949 | -0.06 (-0.24, 0.11) | 0.491 | 0.040 | 42.0 | |
| **Gender** | | | | | | | |
| Male & female | 19 | 1013 | -0.16 (-0.35, 0.04) | 0.112 | 0.004 | 52.5 | 0.374 |
| Female | 8 | 492 | 0.04 (-0.16, 0.23) | 0.709 | 0.301 | 16.4 | |
| Male | 5 | 253 | -0.11 (-0.45, 0.24) | 0.550 | 0.144 | 41.6 | |
| Not given | - | - | - | - | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 13 | 747 | -0.23 (-0.41, -0.05) | **0.010** | 0.156 | 28.7 | 0.073 |
| >48 | 19 | 1011 | 0.00 (-0.18, 0.19) | 0.976 | 0.008 | 49.6 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Study Quality** | | | | | | | |
| Poor | 12 | 688 | -0.07 (-0.30, 0.16) | 0.565 | 0.010 | 55.4 | 0.894 |
| Fair | 16 | 901 | -0.11 (-0.31, 0.10) | 0.307 | 0.009 | 51.7 | |
| Good | 4 | 169 | -0.16 (-0.48, 0.15) | 0.314 | 0.768 | 0.0 | |
| **Analysis and subgroup results of Ginseng supplementation on AST** | | | | | | | |
| **Overall effect** | 29 | 1586 | -0.60 (-0.20, 0.08) | 0.396 | 0.009 | 42.7 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | 1 | 68 | 0.05 (-0.43, 0.52) | 0.849 | - | - | 0.306 |
| Metabolic or Glycemic Disorders | 8 | 369 | -0.22 (-0.43, -0.01) | **0.041** | 0.435 | 0.0 | |
| General Health or Non-specific Conditions | 20 | 1149 | -0.02 (-0.20, 0.16) | 0.826 | 0.009 | 51.5 | |
| **Continent** | | | | | | | |
| Asia | 27 | 1493 | -0.04 (-0.19, 0.10) | 0.578 | 0.007 | 44.9 | 0.441 |
| Europe | 1 | 74 | -0.25 (-0.71, 0.21) | 0.287 | - | - | |
| Canada/USA | 1 | 19 | -0.51 (-1.43, 0.40) | 0.271 | - | - | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 16 | 903 | -0.08 (-0.25, 0.09) | 0.362 | 0.100 | 32.8 | 0.302 |
| ≥ 3000 | 12 | 579 | -0.07 (-0.32, 0.19) | 0.612 | 0.014 | 53.6 | |
| Not given | 1 | 104 | 0.25 (-0.14, 0.63) | 0.206 | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 15 | 785 | -0.11 (-0.32, 0.10) | 0.305 | 0.016 | 49.4 | 0.449 |
| 8 < weeks | 14 | 801 | 0.00 (-0.18, 0.18) | 0.966 | 0.104 | 33.8 | |
| **Gender** | | | | | | | |
| Male & female | 16 | 841 | -0.12 (-0.31, 0.08) | 0.238 | 0.038 | 42.3 | 0.666 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Female | 8 | 492 | -0.03 (-0.26, 0.21) | 0.830 | 0.115 | 39.6 | |
| Male | 5 | 253 | 0.08 (-0.35, 0.51) | 0.720 | 0.038 | 60.7 | |
| Not given | 1 | 30 | 0.58 (-0.15, 1.31) | 0.122 | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 12 | 679 | -0.12 (-0.31, 0.07) | 0.219 | 0.136 | 31.8 | 0.462 |
| >48 | 17 | 907 | -0.02 (-0.21, 0.18) | 0.862 | 0.012 | 49.1 | |
| **Study Quality** | | | | | | | |
| Poor | 10 | 596 | -0.15 (-0.39, 0.09) | 0.232 | 0.024 | 52.9 | 0.616 |
| Fair | 15 | 821 | 0.01 (-0.19, 0.20) | 0.949 | 0.041 | 42.6 | |
| Good | 4 | 169 | -0.08 (-0.44, 0.27) | 0.642 | 0.319 | 14.7 | |
| **Analysis and subgroup results of Ginseng supplementation on BUN** | | | | | | | |
| **Overall effect** | 14 | 786 | -0.05 (-0.24, 0.14) | 0.610 | 0.076 | 37.6 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | - | - | - | - | - | - | |
| Metabolic or Glycemic Disorders | - | - | - | - | - | - | |
| General Health or Non-specific Conditions | 14 | 786 | -0.05 (-0.24, 0.14) | 0.610 | 0.076 | 37.6 | |
| **Continent** | | | | | | | |
| Asia | 14 | 786 | -0.05 (-0.24, 0.14) | 0.610 | 0.076 | 37.6 | |
| Europe | - | - | - | - | - | - | |
| Canada/USA | - | - | - | - | - | - | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 7 | 441 | 0.03 (-0.23, 0.29) | 0.808 | 0.122 | 40.3 | 0.370 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ≥ 3000 | 7 | 345 | -0.14 (-0.43, 0.14) | 0.320 | 0.134 | 38.7 | |
| Not given | - | - | - | - | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 7 | 378 | -0.04 (-0.26, 0.18) | 0.714 | 0.359 | 9.2 | 0.762 |
| 8 < weeks | 7 | 408 | -0.10 (-0.42, 0.22) | 0.539 | 0.028 | 57.6 | |
| **Gender** | | | | | | | |
| Male & female | 6 | 355 | -0.02 (-0.23, 0.19) | 0.825 | 0.488 | 0.0 | 0.047 |
| Female | 4 | 212 | -0.33 (-0.76, 0.09) | 0.119 | 0.087 | 54.4 | |
| Male | 4 | 219 | 0.27 (0.00, 0.54) | 0.052 | 0.910 | 0.0 | |
| Not given | - | - | - | - | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 8 | 504 | 0.08 (-0.13, 0.30) | 0.451 | 0.224 | 25.7 | 0.068 |
| >48 | 6 | 282 | -0.24 (-0.52, 0.03) | 0.048 | 0.271 | 21.7 | |
| **Study Quality** | | | | | | | |
| Poor | 3 | 182 | -0.07 (-0.36, 0.22) | 0.639 | 0.480 | 0.0 | 0.998 |
| Fair | 7 | 435 | -0.06 (-0.37, 0.25) | 0.709 | 0.028 | 57.7 | |
| Good | 4 | 169 | -0.08 (-0.49, 0.34) | 0.717 | 0.205 | 34.5 | |
| **Analysis and subgroup results of Ginseng supplementation on Creatinine** | | | | | | | |
| **Overall effect** | 26 | 1507 | -0.26 (-0.60, 0.08) | 0.137 | < 0.001 | 89.3 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | 1 | 36 | 0.61 (-0.60, 1.28) | 0.074 | - | - | 0.060 |
| Metabolic or Glycemic Disorders | 7 | 258 | -0.07 (-0.52, 0.37) | 0.750 | 0.024 | 58.9 | |
| General Health or Non-specific | 18 | 1213 | -0.35 (-0.78, 0.08) | 0.108 | < 0.001 | 91.8 | |

| Conditions | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Continent** | | | | | | | |
| Asia | 22 | 1310 | -0.30 (-0.70, 0.09) | 0.131 | < 0.001 | 90.8 | 0.421 |
| Europe | 1 | 74 | 0.05 (-0.40, 0.51) | 0.816 | - | - | |
| Canada/USA | 3 | 123 | -0.01 (-0.36, 0.35) | 0.974 | 0.894 | 0.0 | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 13 | 851 | -0.56 (-1.19, 0.07) | 0.083 | < 0.001 | 94.1 | 0195 |
| ≥ 3000 | 12 | 552 | 0.04 (-0.13, 0.21) | 0.646 | 0.953 | 0.0 | |
| Not given | 1 | 104 | 0.05 (-0.13, 0.21) | 0.810 | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 12 | 499 | -0.18 (-0.50, 0.14) | 0.280 | 0.002 | 61.8 | 0.727 |
| 8 < weeks | 14 | 1008 | -0.29 (-0.82, 0.24) | 0.290 | < 0.001 | 93.6 | |
| **Gender** | | | | | | | |
| Male & female | 16 | 962 | -0.34 (-0.88, 0.19) | 0.203 | < 0.001 | 92.9 | 0.122 |
| Female | 5 | 290 | -0.07 (-0.35, 0.21) | 0.617 | 0.230 | 28.8 | |
| Male | 4 | 219 | -0.28 (-0.73, 0.17) | 0.218 | 0.105 | 51.1 | |
| Not given | 1 | 36 | 0.61 (-0.06, 1.28) | 0.074 | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 10 | 608 | -0.01 (-0.20, 0.17) | 0.904 | 0.256 | 20.3 | 0.224 |
| >48 | 16 | 899 | -0.37 (-0.92, 0.18) | 0.185 | < 0.001 | 92.8 | |
| **Study Quality** | | | | | | | |
| Poor | 6 | 310 | -0.08 (-0.39, 0.23) | 0.618 | 0.117 | 43.2 | 0.630 |
| Fair | 16 | 1028 | -0.31 (-0.82, 0.21) | 0.247 | < 0.001 | 93.1 | |
| Good | 4 | 169 | -0.31 (-0.78, 0.16) | 0.199 | 0.129 | 47.1 | |

| Analysis and subgroup results of Ginseng supplementation on GGT | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Overall effect** | 13 | 620 | -0.20 (-0.36, -0.40) | **0.015** | 0.619 | 0.0 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | - | - | - | - | - | - | |
| Metabolic or Glycemic Disorders | 5 | 214 | -0.13 (-0.41, 0.15) | 0.368 | 0.716 | 0.0 | |
| General Health or Non-specific Conditions | 8 | 406 | -0.24 (-0.45, -0.03) | **0.023** | 0.384 | 5.9 | |
| **Continent** | | | | | | | |
| Asia | 13 | 620 | -0.20 (-0.36, -0.40) | **0.015** | 0.619 | 0.0 | |
| Europe | - | - | - | - | - | - | |
| Canada/USA | - | - | - | - | - | - | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 8 | 436 | -0.18 (-0.40, 0.04) | 0.114 | 0.267 | 20.5 | |
| ≥ 3000 | 5 | 184 | -0.24 (-0.54, 0.06) | 0.121 | 0.895 | 0.0 | 0.771 |
| Not given | - | - | - | - | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 6 | 277 | -0.18 (-0.42, 0.06) | 0.147 | 0.751 | 0.0 | 0.822 |
| 8 < weeks | 7 | 434 | -0.22 (-0.47, 0.02) | 0.079 | 0.299 | 17.1 | |
| **Gender** | | | | | | | |
| Male & female | 10 | 394 | -0.21 (-0.42, -0.01) | **0.042** | 0.889 | 0.0 | |
| Female | 2 | 134 | -0.03 (-0.46, 0.59) | 0.932 | 0.072 | 69.1 | 0.505 |
| Male | 1 | 92 | -0.43 (-0.85, -0.021) | **0.040** | - | - | |
| Not given | - | - | - | - | - | - | |
| **Intervention Age (year)** | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ≤48 | 5 | 293 | -0.37 (-0.60, -0.13) | 0.002 | 0.906 | 0.0 | 0.061 |
| >48 | 8 | 327 | -0.05 (-0.28, 0.17) | 0.632 | 0.609 | 0.0 | |
| **Study Quality** | | | | | | | |
| Poor | 5 | 284 | -0.16 (-0.44, 0.11) | 0.240 | 0.274 | 22.1 | 0.650 |
| Fair | 8 | 336 | -0.24 (-0.47, -0.02) | **0.030** | 0.718 | 0.0 | |
| Good | - | - | - | - | - | - | |
| **Analysis and subgroup results of Ginseng supplementation on CAT** | | | | | | | |
| **Overall effect** | 6 | 228 | 0.24 (-0.12, 0.59) | 0.191 | 0.151 | 38.3 | |
| **Analysis and subgroup results of Ginseng supplementation on GPx** | | | | | | | |
| **Overall effect** | 5 | 241 | -0.09 (-0.37, 0.20) | 0.551 | 0.322 | 14.5 | |
| **Analysis and subgroup results of Ginseng supplementation on GSH** | | | | | | | |
| **Overall effect** | 5 | 195 | 0.43 (-0.03, 0.90) | 0.066 | 0.053 | 57.2 | |
| **Analysis and subgroup results of Ginseng supplementation on GSH-Rd** | | | | | | | |
| **Overall effect** | 4 | 170 | 0.90 (0.38, 1.42) | **0.001** | 0.065 | 58.5 | |
| **Analysis and subgroup results of Ginseng supplementation on MDA** | | | | | | | |
| **Overall effect** | 11 | 425 | -0.39 (-1.14, 0.36) | 0.306 | < 0.001 | 91.0 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | - | - | - | - | - | - | 0.106 |
| Metabolic or Glycemic Disorders | 1 | 20 | 0.50 (-0.39, 1.39) | 0.272 | - | - | |
| General Health or Non-specific Conditions | 10 | 405 | -0.48 (-1.26, 0.30) | 0.231 | < 0.001 | 91.3 | |
| **Continent** | | | | | | | |
| Asia | 9 | 375 | -1.02 (-1.51, -0.54) | **< 0.001** | < 0.001 | 76.3 | < 0.001 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Europe | - | - | - | - | - | - | |
| Canada/USA | 2 | 50 | 2.54 (1.12, 3.96) | **< 0.001** | - | - | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 10 | 382 | -0.35 (-1.20, 0.49) | 0.411 | < 0.001 | 91.9 | 0.592 |
| ≥ 3000 | 1 | 43 | -0.64 (-1.26, -0.03) | **0.041** | - | - | |
| Not given | - | - | - | - | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 3 | 67 | -1.13 (-1.76, -0.50) | < 0.001 | < 0.001 | 78.4 | 0.021 |
| 8 < weeks | 4 | 358 | 0.87 (-0.71, 2.46) | 0.278 | < 0.001 | 94.5 | |
| **Gender** | | | | | | | |
| Male & female | 5 | 235 | -1.50 (-1.96, -1.04) | **< 0.001** | 0.060 | 55.8 | < 0.001 |
| Female | 4 | 164 | 0.87 (-0.71, 2.46) | 0.278 | < 0.001 | 94.5 | |
| Male | 1 | 6 | -0.40 (-2.02, 1.23) | 0.632 | - | - | |
| Not given | 1 | 20 | 0.50 (-0.39, 1.39) | 0.272 | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 6 | 241 | -1.43 (-1.88, -0.97) | **< 0.001** | 0.056 | 53.7 | 0.001 |
| >48 | 5 | 184 | 0.78 (-0.49, 2.06) | 0.227 | < 0.001 | 92.9 | |
| **Study Quality** | | | | | | | |
| Poor | 8 | 300 | -0.06 (-1.12, 0.99) | 0.906 | < 0.001 | 93.3 | 0.033 |
| Fair | 1 | 43 | -0.64 (-1.26, -0.03) | **0.041** | - | - | |
| Good | 2 | 82 | -1.41 (-1.92, -0.90) | **< 0.001** | 0.944 | 0.0 | |
| **Analysis and subgroup results of Ginseng supplementation on ROS** | | | | | | | |
| **Overall effect** | 4 | 170 | -0.94 (-1.27, -0.60) | **< 0.001** | 0.824 | 0.0 | |
| **Analysis and subgroup results of Ginseng supplementation on SOD** | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Overall effect** | 7 | 331 | 0.49 (0.10, 0.87) | **0.014** | 0.008 | 65.2 | |
| **Analysis and subgroup results of Ginseng supplementation on TAC** | | | | | | | |
| **Overall effect** | 6 | 254 | 0.08 (-0.18, 0.34) | 0.546 | 0.585 | 0.0 | |
| **Analysis and subgroup results of Ginseng supplementation on Adiponectin** | | | | | | | |
| **Overall effect** | 5 | 165 | 0.39 (-0.57, 1.35) | 0.427 | < 0.001 | 85.9 | |
| **Analysis and subgroup results of Ginseng supplementation on Leptin** | | | | | | | |
| **Overall effect** | 3 | 61 | -0.29 (-0.87, 0.30) | 0.336 | 0.816 | 0.0 | |
| **Analysis and subgroup results of Ginseng supplementation on Heart Rate** | | | | | | | |
| **Overall effect** | 16 | 713 | -0.02 (-0.22, 0.18) | 0.842 | 0.073 | 36.4 | |
| **Health condition** | | | | | | | |
| Cardiovascular or Hypertensive Disorders | 4 | 166 | -0.02 (-0.60, 0.56) | 0.935 | 0.037 | 64.7 | 0.405 |
| Metabolic or Glycemic Disorders | 3 | 222 | 0.11 (-0.18, 0.40) | 0.447 | 0.308 | 15.2 | |
| General Health or Non-specific Conditions | 9 | 325 | -0.15 (-0.41, 0.10) | 0.243 | 0.310 | 14.8 | |
| **Continent** | | | | | | | |
| Asia | 10 | 426 | -0.13 (-0.43, 0.16) | 0.384 | 0.037 | 49.3 | 0.418 |
| Europe | 3 | 104 | 0.05 (-0.33, 0.44) | 0.782 | 0.886 | 0.0 | |
| Canada/USA | 3 | 183 | 0.19 (-0.20, 0.57) | 0.340 | 0.202 | 37.5 | |
| **Ginseng dosage (mg/day)** | | | | | | | |
| < 3000 | 7 | 366 | -0.03 (-0.36, 0.31) | 0.881 | 0.033 | 56.3 | 0.944 |
| ≥ 3000 | 8 | 243 | 0.01 (-0.30, 0.32) | 0.934 | 0.230 | 25.0 | |
| Not given | 1 | 104 | -0.07 (-0.46, 0.31) | 0.712 | - | - | |
| **Duration of intervention** | | | | | | | |
| 8 ≥ weeks | 6 | 217 | -0.33 (-0.70, 0.04) | 0.082 | 0.166 | 36.2 | 0.032 |
| 8 < weeks | 10 | 496 | 0.12 (-0.06, 0.30) | 0.181 | 0.476 | 0.0 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Gender** | | | | | | | |
| Male & female | 12 | 580 | -0.07 (-0.32, 0.18) | 0.585 | 0.020 | 48.9 | 0.552 |
| Female | 2 | 93 | 0.19 (-0.21, 0.60) | 0.349 | 0.362 | 0.0 | |
| Male | 2 | 40 | -0.04 (-0.70, 0.60) | 0.911 | 0.735 | 0.0 | |
| Not given | - | - | - | - | - | - | |
| **Intervention Age (year)** | | | | | | | |
| ≤48 | 2 | 40 | -0.04 (-0.70, 0.60) | 0.911 | 0.735 | 0.0 | 0.965 |
| >48 | 14 | 673 | -0.02 (-0.24, 0.20) | 0.849 | 0.037 | 44.6 | |
| **Study Quality** | | | | | | | |
| Poor | 8 | 408 | 0.00 (-0.37, 0.38) | 0.978 | 0.002 | 68.7 | 0.921 |
| Fair | 6 | 269 | -0.09 (-0.33, 0.15) | 0.478 | 0.999 | 0.0 | |
| Good | 2 | 36 | -0.06 (-0.71, 0.59) | 0.857 | 0.593 | 0.0 | |

**Footnote:** ALP; Alkaline Phosphatase, ALT; Alanine Aminotransferase, AST; Aspartate Aminotransferase, BF%; Body Fat Percentage, BMI; Body Mass Index, BUN; Blood Urea Nitrogen, CAT; Catalase, CI; Confidence Interval, CRP; C-Reactive Protein, DBP; Diastolic Blood Pressure, ESR; Erythrocyte Sedimentation Rate, FBS; Fasting Blood Sugar, GPx; Glutathione Peroxidase, GSH; Glutathione, GSH-RD; Glutathione Reductase, GGT; Gamma-Glutamyltransferase, HbA1c; Glycated Hemoglobin, HC; Hip Circumference, HDL-C; High-Density Lipoprotein Cholesterol, HOMA-B; Homeostatic Model Assessment of Beta Cell Function, HOMA-IR; Homeostatic Model Assessment of Insulin Resistance, hs-CRP; High-Sensitivity C-Reactive Protein, IL-1R; Interleukin-1 Receptor, IL-6; Interleukin-6, IL-8; Interleukin-8, IL-10; Interleukin-10, LDL-C; Low-Density Lipoprotein Cholesterol, MDA; Malondialdehyde, Oxidized LDL-C; Oxidized Low-Density Lipoprotein Cholesterol, QUICKI; Quantitative Insulin Sensitivity Check Index, ROS; Reactive Oxygen Species, SMD**;** Standardized Mean Difference, SBP; Systolic Blood Pressure, SOD; Superoxide Dismutase, TAC; Total Antioxidant Capacity, TC; Total Cholesterol, TG; Triglycerides, TNF-α; Tumor Necrosis Factor-alpha, WC; Waist Circumference.

**Table 4.** GRADE profile of Ginseng supplementation on CVD outcomes.

| Outcomes | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication Bias | Number (INT/CON) | SMD (95%CI) | Quality of evidence |
|---|---|---|---|---|---|---|---|---|
| BF | serious[a] | not serious | not serious | very serious[b,c] | none | 86 / 87 | 0.03 (-0.27, 0.33) | ⊕◯◯◯ Very low |
| BMI | serious[a] | not serious | not serious | serious[c] | none | 419 / 365 | 0.00 (-0.14, 0.14) | ⊕⊕◯◯ Low |
| WC | not serious | not serious | serious[d] | very serious[b,c] | none | 152 / 120 | 0.05 (-0.19, 0.30) | ⊕◯◯◯ Very low |
| Weight | not serious | not serious | not serious | very serious[b,c] | none | 111 / 109 | 0.04 (-0.22, 0.31) | ⊕⊕◯◯ Low |
| DBP | serious[a] | serious[e] | not serious | serious[c] | none | 826 / 711 | -0.23 (-0.51, 0.05) | ⊕◯◯◯ Very low |
| Pulse pressure | serious[a] | serious[e] | not serious | very serious[b,c] | none | 105 / 109 | -0.08 (-0.57, 0.41) | ⊕◯◯◯ Very low |

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|---|---|---|---|---|---|---|---|---|
| SBP | serious[a] | serious[e,f] | not serious | very serious[b,c] | none | 826 / 711 | -0.18 (-0.45, 0.08) | ⊕◯◯◯ Very low |
| 2h-Glucose | not serious | serious[e] | not serious | very serious[b,c] | publication bias strongly suspected[f] | 204 / 175 | -0.15 (-0.73, 0.42) | ⊕◯◯◯ Very low |
| 2h-Insulin | serious[a] | serious[e] | not serious | very serious[b,c] | none | 61 / 62 | 0.21 (-0.55, 0.96) | ⊕◯◯◯ Very low |
| Fasting Insulin | serious[a] | serious[e] | not serious | serious[c] | none | 630 / 533 | 0.00 (-0.22, 0.22) | ⊕◯◯◯ Very low |
| FBS | serious[a] | not serious | not serious | Serious[C] | none | 1354 / 1161 | -0.85 (-0.19, 0.02) | ⊕⊕⊕◯ Moderate |
| HbA1c | serious[a] | serious[e] | not serious | serious[c] | none | 376 / 284 | 0.07 (-0.24, 0.38) | ⊕◯◯◯ Very low |
| HOMA-B | not serious | not serious | not serious | very serious[b,c] | none | 80 / 46 | -0.31 (-0.69, 0.07) | ⊕⊕◯◯ Low |
| HOMA-IR | serious[a] | serious[e] | not serious | serious[c] | none | 529 / 437 | -0.10 ( -0.35, 0.15) | ⊕◯◯◯ Very low |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| QUICKI | not serious | serious[e] | not serious | very serious[b,c] | publication bias strongly suspected[f] | 200 / 169 | 0.24 ( -0.24, 0.72) | ⊕◯◯◯ Very low |
| CRP | serious[a] | serious[e] | serious[d] | very serious[b,c] | none | 1112 / 111 | 0.13 (-0.30, 0.55) | ⊕◯◯◯ Very low |
| ESR | serious[a] | not serious | not serious | not serious | none | 111 / 58 | 0.10 (-0.28, 0.47) | ⊕◯◯◯ Very low |
| hs-CRP | serious[a] | not serious | not serious | not serious | none | 428 / 312 | -0.23 (-0.38, -0.08) | ⊕⊕⊕◯ Moderate |
| IL-Ra | not serious | not serious | serious[d] | very serious[b,c] | none | 54 / 58 | -0.03 ( -0.42, 0.36) | ⊕◯◯◯ Very low |
| IL-4 | not serious | serious[e] | not serious | very serious[b,c] | none | 153 / 153 | -0.18 (-0.58, 0.22) | ⊕◯◯◯ Very low |
| IL-6 | not serious | serious[e] | not serious | serious[c] | none | 505 / 403 | -0.32 (-1.04, 0.40) | ⊕⊕◯◯ Low |
| IL-8 | not serious | not serious | serious[d] | very serious[b,c] | none | 54 / 48 | -0.04 ( -0.47, 0.38) | ⊕◯◯◯ Very low |

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|---|---|---|---|---|---|---|---|---|
| IL-10 | not serious | serious[e] | not serious | very serious[b, c] | none | 106 / 99 | 0.35 (-0.49, 1.20) | ⊕◯◯◯ Very low |
| TNF-α | not serious | serious[e] | not serious | serious[c] | none | 487 / 446 | -0.15 (-0.86, 0.57) | ⊕⊕◯◯ Low |
| Total Protein | not serious | not serious | not serious | serious[c] | none | 455 / 358 | 0.17 (-0.04, 0.37) | ⊕⊕⊕◯ Moderate |
| HDL-C | serious[a] | serious[e] | not serious | serious[c] | none | 1192 / 1004 | 0.08 (-0.10, 0.27) | ⊕◯◯◯ Very low |
| LDL-C | serious[a] | serious[e] | not serious | serious[c] | none | 1004 / 869 | -0.12 (-0.26, 0.02) | ⊕◯◯◯ Very low |
| Oxidized LDL-C | not serious | not serious | not serious | serious[c] | none | 77 / 76 | -0.22 (-0.53, 0.10) | ⊕⊕⊕◯ Moderate |
| TC | not serious | serious[e] | not serious | serious[c] | none | 1490 / 1250 | -0.10 (-0.22, 0.03) | ⊕⊕◯◯ Low |
| TG | not serious | serious[e] | not serious | serious[c] | none | 1318 / 1085 | -0.03 (-0.17, 0.12) | ⊕⊕◯◯ Low |

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|---|---|---|---|---|---|---|---|---|
| Albumin | not serious | serious[e] | not serious | serious[c] | none | 405 / 335 | -0.09 (-0.43, 0.24) | ⊕⊕◯◯ Low |
| ALP | not serious | not serious | serious[d] | serious[c] | none | 399 / 330 | -0.01 (-0.15, 0.14) | ⊕⊕◯◯ Low |
| ALT | not serious | not serious | not serious | serious[c] | none | 952 / 806 | -0.10 (-0.23, 0.04) | ⊕⊕⊕◯ Moderate |
| AST | not serious | not serious | not serious | serious[c] | none | 863 / 723 | -0.60 (-0.20, 0.08) | ⊕⊕⊕◯ Moderate |
| BUN | not serious | not serious | not serious | serious[c] | none | 427 / 359 | -0.05 (-0.24, 0.14) | ⊕⊕⊕◯ Moderate |
| Creatinine | not serious | serious[e] | not serious | serious[c] | none | 807 / 700 | -0.26 (-0.60, 0.08) | ⊕⊕◯◯ Low |
| GGT | not serious | not serious | serious[d] | not serious | none | 351 / 269 | -0.20 (-0.36, -0.40) | ⊕⊕⊕◯ Moderate |
| CAT | serious[a] | not serious | serious[d] | very serious[b, c] | publication bias strongly suspected[f] | 150 / 78 | 0.24 (-0.12, 0.59) | ⊕◯◯◯ Very low |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| GPx | not serious | not serious | serious[d] | very serious[b,c] | none | 147 / 94 | -0.09 (-0.37, 0.20) | ⊕◯◯◯ Very low |
| GSH | serious[a] | serious[e] | not serious | very serious[b,c] | none | 124 / 71 | 0.43 (-0.03, 0.90) | ⊕◯◯◯ Very low |
| GSH-Rd | not serious | serious[e] | serious[d] | serious[b] | none | 112 / 58 | 0.90 (0.38, 1.42) | ⊕◯◯◯ Very low |
| MDA | erious[a] | serious[e] | not serious | serious[c] | none | 242 / 183 | -0.39 (-1.14, 0.36) | ⊕◯◯◯ Very low |
| ROS | not serious | not serious | serious[a] | serious[b] | none | 112 / 58 | -0.94 (-1.27, -0.60) | ⊕⊕◯◯ Low |
| SOD | not serious | serious[e] | serious[d] | serious[b] | none | 193 / 138 | 0.49 (0.10, 0.87) | ⊕◯◯◯ Very low |
| TAC | serious[a] | not serious | serious[d] | very serious[b,c] | none | 170 / 84 | 0.08 (-0.18, 0.34) | ⊕◯◯◯ Very low |
| Adiponectin | not serious | serious[e] | serious[d] | very serious[b,c] | none | 99 / 66 | 0.39 (-0.57, 1.35) | ⊕◯◯◯ Very low |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Leptin | not serious | not serious | serious[d] | very serious[b, c] | none | 46 / 15 | -0.29 (-0.87, 0.30) | ⊕◯◯◯ Very low |
| Heart rate | not serious | not serious | not serious | serious[c] | none | 383 / 330 | -0.02 (-0.22, 0.18) | ⊕⊕⊕◯ Moderate |

**Footnote:** ALP; Alkaline Phosphatase, ALT; Alanine Aminotransferase, AST; Aspartate Aminotransferase, BF; Body Fat, BMI; Body Mass Index, BUN; Blood Urea Nitrogen, CAT; Catalase, CI; Confidence Interval, CRP; C-Reactive Protein, DBP; Diastolic Blood Pressure, ESR; Erythrocyte Sedimentation Rate, FBS; Fasting Blood Sugar, GPx; Glutathione Peroxidase, GSH; Glutathione, GSH-RD; Glutathione Reductase, GGT; Gamma-Glutamyltransferase, HbA1c; Glycated Hemoglobin, HC; Hip Circumference, HDL-C; High-Density Lipoprotein Cholesterol, HOMA-B; Homeostatic Model Assessment of Beta Cell Function, HOMA-IR; Homeostatic Model Assessment of Insulin Resistance, hs-CRP; High-Sensitivity C-Reactive Protein, IL-1R; Interleukin-1 Receptor, IL-6; Interleukin-6, IL-8; Interleukin-8, IL-10; Interleukin-10, LDL-C; Low-Density Lipoprotein Cholesterol, MDA; Malondialdehyde, Oxidized LDL-C; Oxidized Low-Density Lipoprotein Cholesterol, QUICKI; Quantitative Insulin Sensitivity Check Index, ROS; Reactive Oxygen Species, SBP; Systolic Blood Pressure, SMD; Standardized Mean Difference, SOD; Superoxide Dismutase, TAC; Total Antioxidant Capacity, TC; Total Cholesterol, TG; Triglycerides, TNF-α; Tumor Necrosis Factor-alpha, WC; Waist Circumference.

**Explanations**

a. Downgraded since more than 50% of the participants were from high-risk bias studies.

b. Downgraded since the participants included were less than 400 people.

c. Downgraded since the 95% CI crosses the threshold of interest.

d. Downgraded for indirectness in the country.

e. Publication Bias was detected through Egger and Begg's test. (p-value < 0.05)

f. The $I^2$ value was >50% (or Heterogeneity among the studies was high).