Int J Nutr Sci 2026;11(3):1-10

International Journal of Nutrition Sciences

Journal Home Page: ijns.sums.ac.ir

Review Article

The Effect of Ginseng and Ginseng-Containing Supplements on Fatigue: A Systematic Review and Meta-Analysis

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ARTICLE INFO

Keywords:
Panax ginseng
Fatigue
Visual Analog Scale
Herbal medicine

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Email: asady@uma.ac.ir
Received: April 20, 2026
Revised: July 16, 2026
Accepted: July 22, 2026

ABSTRACT

Background: Ginseng is widely used as an adaptogen to reduce fatigue, but evidence for its efficacy, as measured by the Visual Analog Scale (VAS), remains inconsistent. This systematic review and meta-analysis aimed to evaluate the effects of ginseng and ginseng-containing supplements on fatigue severity measured by VAS.

Methods: A comprehensive literature search was conducted in PubMed/Medline, Scopus, Google Scholar, WHO ICTRP, and ClinicalTrials.gov up to July 2025. Randomized controlled trials (RCTs) investigating the effect of Panax ginseng on VAS-measured fatigue were included. Data extraction and risk of bias assessment were performed independently by two reviewers. Statistical analysis was conducted using Stata 15, with a random-effects model to estimate pooled mean differences (MDs) and 95% confidence intervals (CIs). Heterogeneity was assessed using I^2 and Cochran's Q statistics. Subgroup analysis was performed based on intervention duration.

Results: The pooled results showed a significant reduction in VAS fatigue scores in the ginseng group compared to placebo (MD=1.28, 95%CI: 0.69 to 1.87, $p<0.001$) and a substantial heterogeneity was observed ($I^2=89.3\%$, $p<0.001$). Subgroup analysis revealed significant improvements after 2–4 weeks of intervention (MD=1.65–1.80), while longer durations (8–12 weeks) showed no significant effects. Sensitivity analysis confirmed the robustness of the results, and no significant publication bias was detected.

Conclusion: Ginseng supplementation significantly reduced fatigue within short-term interventions (2–4 weeks), supporting its role as a natural adaptogen for fatigue management. However, high heterogeneity among studies highlights the need for further well-designed trials with standardized protocols.

Please cite this article as: Yazdan nasab N, Hormati Oughoulbaig AH, Asadi A, Parandak SZ. The Effect of Ginseng and Ginseng-Containing Supplements on Fatigue: A Systematic Review and Meta-Analysis. Int J Nutr Sci. 2026;11(3):1-10. doi:

Introduction

Fatigue is a common and often debilitating symptom that can seriously affect quality of life, daily functioning, and productivity (1, 2). It impacts a wide range of people, from those living with chronic illnesses or cancer survivors to healthy individuals experiencing intense physical or mental exertion. Because of its prevalence and impact, finding effective and safe ways to reduce fatigue is a priority (3). In recent years, attention has turned to natural adaptogens, and among these, ginseng stands out as one of the most widely recognized and used (4, 5). Panax ginseng, in particular, has been used for centuries in traditional medicine to boost energy, reduce tiredness, and enhance resilience to stress (6), alongside other historically recognized medicinal plants whose genomic and phytochemical profiles are increasingly being mapped to validate traditional therapeutic claims (7).

Despite its long history, the scientific evidence supporting its effect on patient-reported fatigue, often measured using tools like the Visual Analog Scale (VAS) is still mixed. This highlights the need for a comprehensive review and synthesis of available data (8, 9). Panax ginseng has been a primary focus in this research due to its active compounds, ginsenosides, which are thought to influence neuroendocrine function and cellular energy metabolism, offering a plausible biological explanation for its anti-fatigue effects (10, 11). Many clinical trials have explored different forms of Panax ginseng or supplements containing it, making the VAS a particularly useful tool for assessing fatigue in a standardized and sensitive way (12, 13).

The VAS allows participants to self-report the intensity of their fatigue along a continuum, capturing the subjective nature of this symptom more directly than many other measures. Its widespread use in fatigue research also enables a more accurate comparison of results across studies (14, 15). Some studies reported meaningful improvements in fatigue, while others show only modest or no effects at all (14-16). These inconsistencies may be due to differences in study design, the types of participants included, such as cancer survivors, patients with chronic illnesses, or healthy individuals, the variety of ginseng preparations and dosages used, and the use of different outcome measures (17, 18).

This variability makes it difficult to draw firm conclusions from individual studies. Consequently, a systematic and comprehensive synthesis of the available data is still needed, with particular attention to standardized measures like the VAS, which allow for more reliable comparisons across trials. The objective of this systematic review and meta-analysis was to evaluate the overall effectiveness of ginseng and ginseng-containing supplements in reducing fatigue severity as measured by VAS, and to determine whether intervention duration influences treatment outcomes. In doing so, the study aimed to provide a more precise pooled estimate of ginseng's short- and long-term anti-fatigue effects and to identify potential sources of variability across trials.

Materials and Methods

A comprehensive and systematic literature search was conducted across multiple electronic databases, including PubMed/Medeline, Scopus, Google Scholar, and trial registries (WHO ICTRP and ClinicalTrials.gov), from inception through July 2025. The search strategy utilized a combination of keywords and Medical Subject Headings (MeSH) related to ginseng interventions and outcomes of interest, including, energy metabolism, anti-fatigue effects, and VAS for fatigue. The full search strategy for PubMed was provided in the supplementary material. All identified records were imported into EndNote X20 for duplicate removal and systematic management of references. After deduplication, titles and abstracts were screened independently by two reviewers to identify potentially eligible studies. Full-text articles of selected records were then assessed for eligibility based on predefined inclusion and exclusion criteria.

Studies were included if they were randomized controlled trials (RCTs) investigating the effect of Panax ginseng, Korean ginseng, red ginseng, or ginseng extract on fatigue measured using the VAS. Non-English publications, studies with incomplete data, and those reporting outcomes only in graphical form without numerical values were excluded. Data were extracted independently by two reviewers using a standardized form. Extracted information included study characteristics (author, year, country), participant demographics, intervention details (type, dose, duration), control group, outcome measures (VAS fatigue scores), and key findings. Any discrepancies were resolved through discussion or consultation with a third reviewer. The methodological quality of included studies was assessed using the Cochrane Risk of Bias Tool (RoB 2.0). Each study was evaluated across five domains of randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Studies were classified as having low risk, some concerns, or high risk of bias.

All statistical analyses were performed using STATA version 15. The effect size for each study

was expressed as the mean difference in VAS fatigue scores between intervention and control groups, along with 95% confidence intervals (CIs). A random-effects model was used to account for anticipated heterogeneity among studies. Heterogeneity was assessed using Cochran's Q test and the I^2 statistic. Subgroup analyses were conducted based on intervention duration to explore potential sources of heterogeneity. Sensitivity analysis was performed using the leave-one-out method to evaluate the robustness of the results. Publication bias was assessed visually using funnel plots and statistically using Egger's test, as the number of included effect sizes reached the commonly recommended threshold for this analysis (Figure 1).

Results

Five randomized controlled trials contributed a total of 10 effect size in comparisons to the quantitative meta-analysis (Table 1, Figure 2). The meta-analysis demonstrated a statistically significant overall positive effect (DL pooled estimate=1.279, 95%CI: 0.688–1.871); while some individual studies showed wide CIs crossing the null, the majority indicated consistent positive effects. Tests of heterogeneity revealed a substantial between-study variation [Cochran's Q=84.15, degree of freedom (df)=9, $p<0.001$; $I^2=89.3\%$, 95%CI: 57.3%–95.3%; H=3.058, 95%CI: 1.530–4.596], suggesting considerable inconsistency across studies. Accordingly, the use of a random-effects model was justified, and the pooled effect size should be interpreted in light of the observed heterogeneity (Table 2, Figure 3).

Subgroup analysis showed that interventions of 2 weeks (DL=1.649, 95%CI: 1.091–2.206) and 4 weeks (DL=1.796, 95%CI: 0.663–2.930) revealing their positive pooled effects, whereas the 8-, 10-, and 12-week subgroups did not demonstrate any significant benefits. The overall pooled effect remained significant (DL=1.279, 95%CI: 0.688–1.871). Heterogeneity was high across studies (Q=84.15, $p<0.001$, $I^2=89.3\%$), with significant variation between subgroups (Q=19.86, $p=0.001$), suggesting that intervention duration contributed to the observed inconsistency (Figure 4).

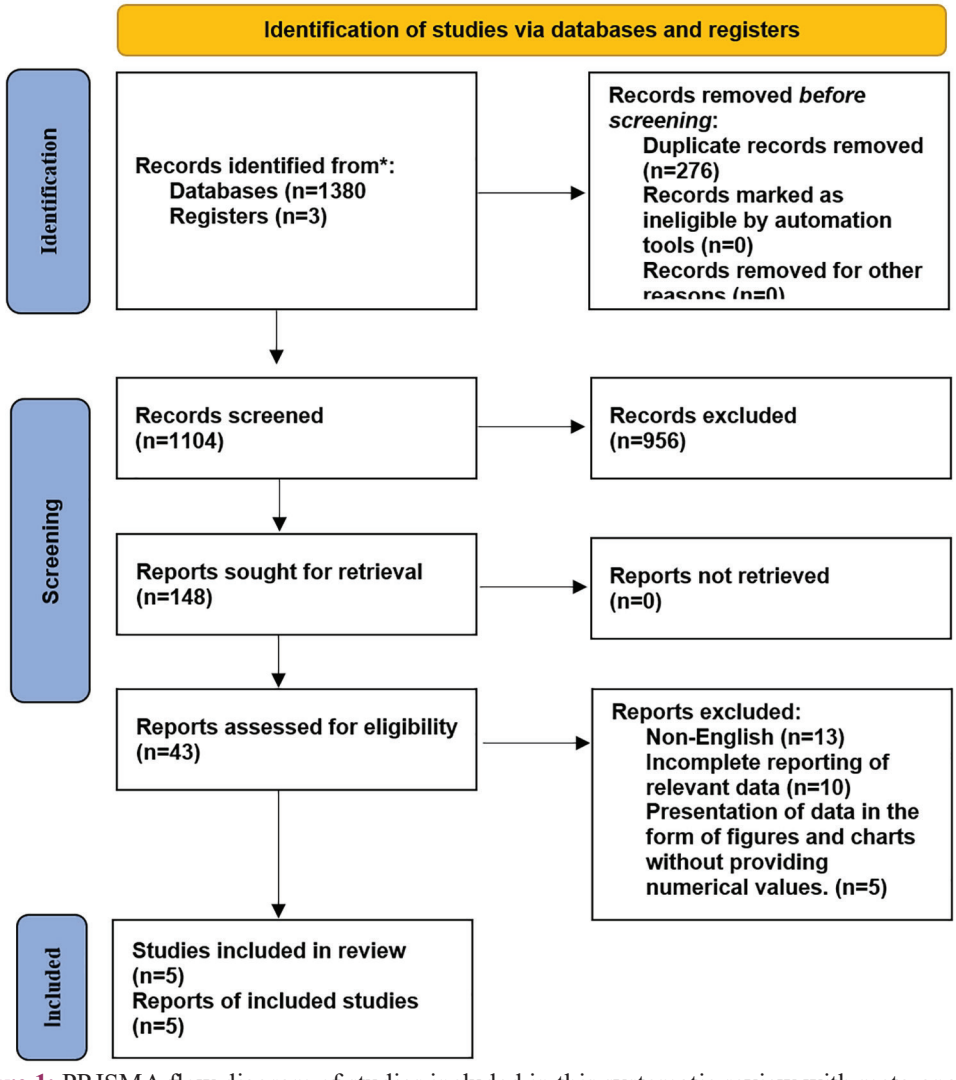

Figure 1: PRISMA flow diagram of studies included in this systematic review with meta-analysis.

Table 1: Meta-analysis summary of effect sizes and Visual Analog Scale (VAS) confidence intervals (CIs).

Authors (Reference)	Effect	CI Lower	CI Upper	% Weight
(19)	-0.500	-3.237	2.237	3.37
(1, 20)	1.500	1.062	1.938	11.36
(2)	2.100	1.674	2.526	11.40
(3)	2.200	1.691	2.709	11.12
(4)	2.700	2.212	3.188	11.19
(21)	1.200	0.572	1.828	10.66
(22)	1.400	0.413	2.387	9.06
(1, 23)	0.550	-0.039	1.139	10.82
(2)	0.160	-0.496	0.816	10.54
(3)	0.080	-0.591	0.751	10.48
Overall (DL)	1.279	0.688	1.871	100.00

Positive mean differences in VAS scores indicate greater fatigue improvement in the ginseng group compared with the control group, whereas negative values indicate less improvement or worsening of fatigue symptoms.

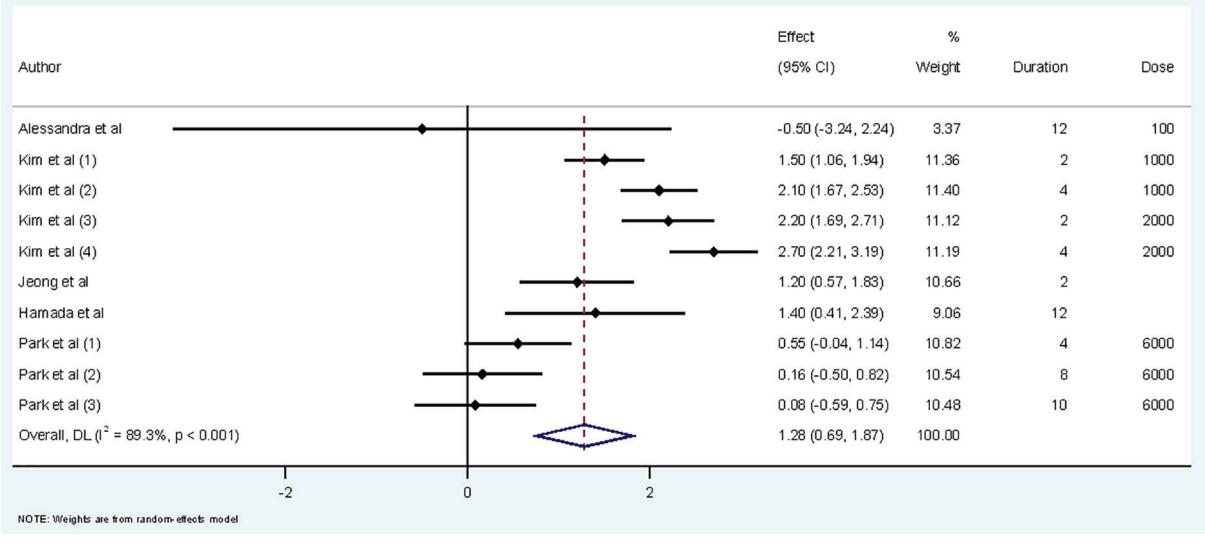

Figure 2: Forest Plot of Visual Analog Scale (VAS).

Table 2: Subgroup analysis by intervention duration (in weeks) on Visual Analog Scale (VAS) outcomes.

Duration (weeks)	(Reference)	Effect	95%CI (Lower–Upper)	% Weight
2	(1)	1.500	1.062–1.938	11.36
	(3)	2.200	1.691–2.709	11.12
	(21)	1.200	0.572 – 1.828	10.66
Subgroup (DL)		1.649	1.091–2.206	33.14
4	(2)	2.100	1.674–2.526	11.40
	(4)	2.700	2.212–3.188	11.19
	(1)	0.550	-0.039–1.139	10.82
Subgroup (DL)		1.796	0.663–2.930	33.41
8	(2)	0.160	-0.496–0.816	10.54
Subgroup (DL)		0.160	-0.496–0.816	10.54
10	(3)	0.080	-0.591–0.751	10.48
Subgroup (DL)		0.080	-0.591–0.751	10.48
12	(19)	-0.500	-3.237–2.237	3.37
	(22)	1.400	0.413–2.387	9.06
Subgroup (DL)		0.896	-0.747–2.540	12.43
Overall (DL)		1.279	0.688–1.871	100.00

The funnel plot showed the distribution of included studies according to effect size and standard error. Most studies were symmetrically distributed around the pooled effect estimate, with larger studies (smaller standard error) concentrated near the top and smaller studies (larger standard error) spread at the bottom. There was no obvious asymmetry, suggesting minimal evidence of publication bias.

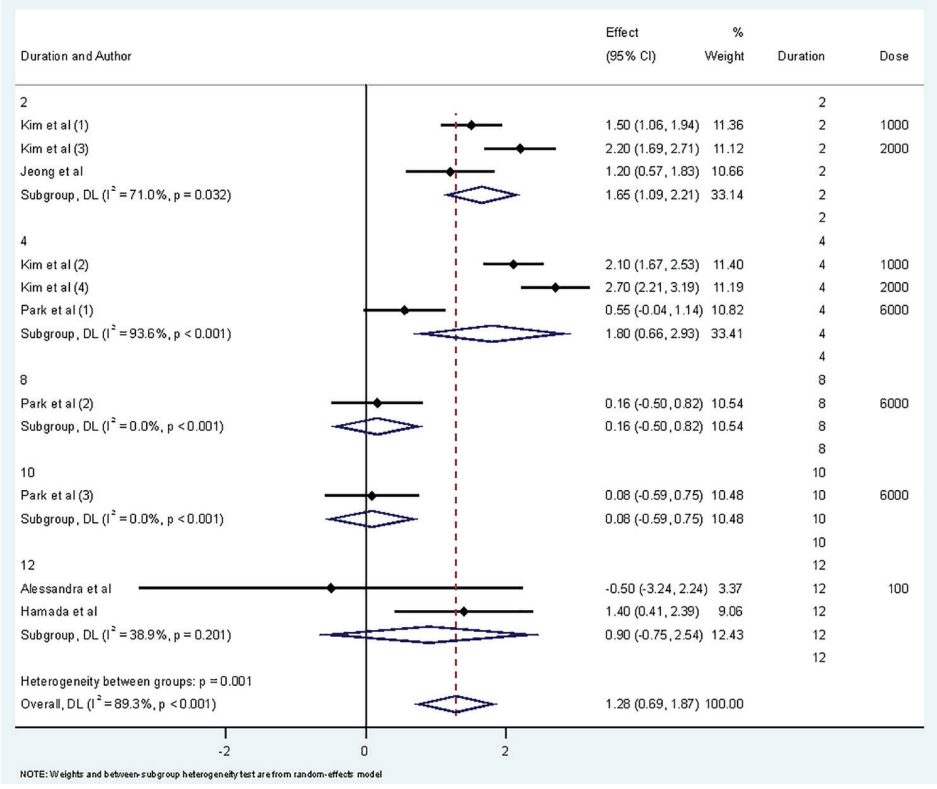

Figure 3: Forest Plot of Subgroup analysis by intervention duration (in weeks) on VAS. VAS: Visual Analog Scale.

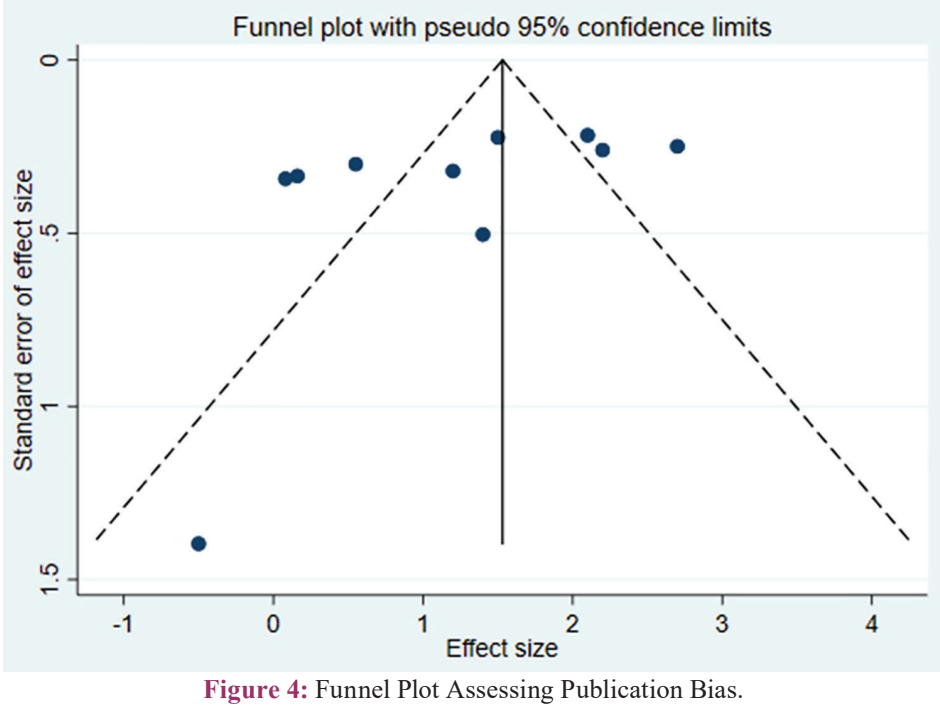

Figure 4: Funnel Plot Assessing Publication Bias.

One small study with a negative effect appeared slightly outside the funnel, but this did not substantially affect the overall symmetry. These findings indicate that the meta-analysis results are unlikely to be significantly influenced by selective reporting (Table 3, Figure 5).

The leave-one-out sensitivity analysis was performed to assess the robustness of the pooled effect size (mean difference). The analysis revealed that the overall estimate remained stable and was not disproportionately influenced by any single study. As illustrated in Figure 5, the sequential omission of each study yielded recalculated pooled estimates (indicated by the diamond markers) whose confidence intervals all overlapped with the original meta-analysis estimate of 1.279 (95%CI: 0.688 to 1.871). This consistency indicates that the findings are robust and not dependent on the results of any one particular study included in the meta-analysis (Table 3, Figure 5).

Table 3: Risk of bias assessment for included studies using the Cochrane RoB 2.0 tool.

(Reference)	D1: Randomization process	D2: Deviations from intended interventions	D3: Missing outcome data	D4: Measurement of the outcome	D5: Selection of the reported result	Overall risk of bias
(19)	◯ Some concerns	◯ Some concerns	Low	Low	Low	◯ Some concerns
(20)	Low	Low	Low	Low	Low	Low
(21)	◯ Some concerns	Low	Low	Low	Low	◯ Some concerns
(22)	Low	Low	Low	Low	Low	Low
(23)	Low	Low	Low	Low	Low	Low

Legend: Low risk, ◯ Some concerns, High risk.

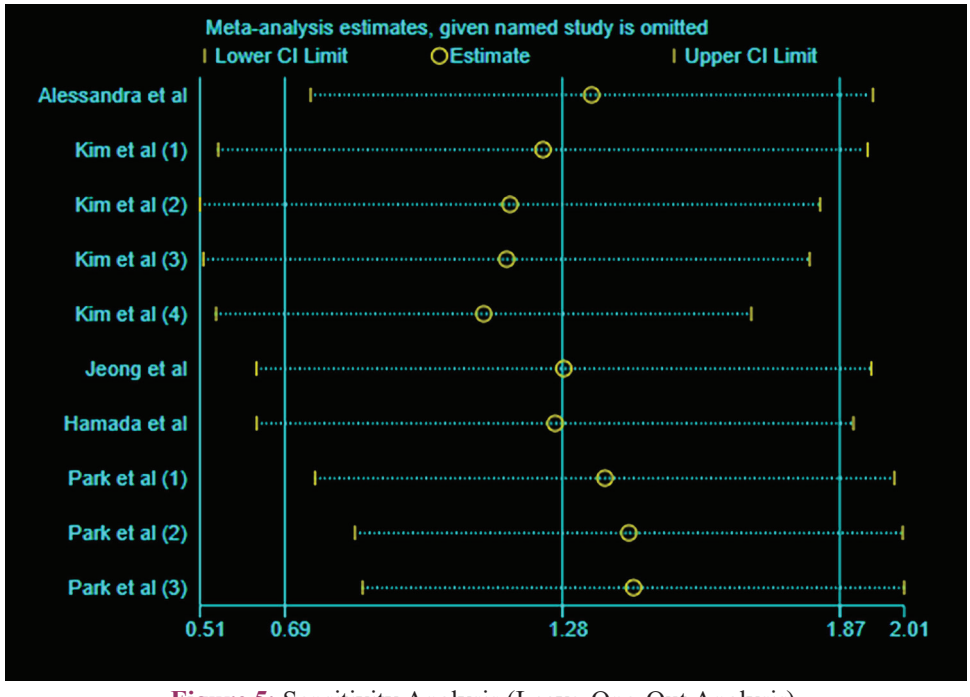

Figure 5: Sensitivity Analysis (Leave-One-Out Analysis).

Discussion

This meta-analysis of 10 randomized controlled trials demonstrated that ginseng supplementation significantly reduced fatigue severity measured by VAS (pooled effect size: 1.279, 95%CI: 0.688–1.871). Subgroup analysis revealed the most substantial benefits occurred after 2–4 weeks of intervention, while longer durations (8–12 weeks) showed diminished effects. The notable anti-fatigue effect of ginseng observed in our analysis (pooled estimate: 1.279) aligns well with findings from several previous systematic reviews. For example, Arring *et al.* (2018) reported that Panax ginseng significantly improved fatigue scores compared to placebo, particularly in individuals with chronic illnesses—results that are consistent with what we found (24).

On the other hand, our findings differ somewhat from the comprehensive review by Wee *et al.*, which suggested that while ginseng has biological activities potentially relevant to reducing fatigue, the clinical evidence across studies was inconsistent. This difference likely stems from methodological variations. Wee *et al.*'s review included diverse outcome measures and populations, whereas our analysis focused specifically on fatigue assessed via the VAS, allowing for a more uniform evaluation. They also highlighted that factors such as the type of ginseng preparation, dosage, and duration of treatment can significantly affect outcomes (25).

Our subgroup analysis supports this, showing that the anti-fatigue effects of ginseng tended to be smaller in longer intervention periods. Another contrasting example comes from the RCT by Kim *et al.*, which found no significant benefit of red ginseng on fatigue in healthy physicians working night shifts (20). This null result may reflect population-specific factors of acute severe fatigue caused by sleep

deprivation that may involve different physiological mechanisms in comparison to the chronic or general fatigue examined in other trials. The anti-fatigue effects of ginseng observed in this meta-analysis may be attributed to the bioactive properties of its key compounds, particularly ginsenosides. The time-dependent efficacy observed in our subgroup analysis, particularly the stronger effects during shorter interventions (2–4 weeks), is biologically plausible and may reflect an initial adaptive physiological response to ginseng supplementation. Experimental studies have suggested that ginsenosides may rapidly modulate mitochondrial energy metabolism, oxidative stress pathways, and neuroendocrine signaling during early treatment phases, which may intersect with the regulation of neuronal membrane excitability and ionic homeostasis governed by nervous system ion and chloride channels (26).

This is consistent with evidence indicating that cellular redox-sensing adaptors, such as tightly bridge oxidative stress, inflammatory pathways, and neuro-functional recovery (27). Over longer intervention periods, however, receptor desensitization or compensatory physiological adaptations may attenuate these responses, potentially explaining the diminished effects observed in longer-duration studies (20). These compounds are hypothesized to modulate the hypothalamic-pituitary-adrenal (HPA) axis, potentially reducing cortisol secretion in response to stress and enhancing the body's resilience to fatigue (28).

Furthermore, cellular studies suggest that ginsenosides can enhance mitochondrial function and promote adenosine triphosphate (ATP) production, leading to improved cellular energy metabolism (29). In line with other plant-derived bioactive metabolites, such as flavonoids (e.g., rutin) that trigger energy balance and metabolic activation (30), preserving mitochondrial membrane stability and counteracting phospholipid or cardiolipin peroxidation are critical molecular mechanisms underlying fatigue mitigation and energy homeostasis The time-dependent efficacy observed in our subgroup analysis, where shorter interventions (2–4 weeks) showed stronger effects, may reflect an adaptive physiological response. Initially, ginseng may rapidly influence neuroendocrine and metabolic pathways, while prolonged administration could lead to receptor desensitization or compensatory mechanisms that diminish its effect over time (31-33).

These findings highlight ginseng's potential role as a short-term adaptogen for fatigue management, particularly in populations experiencing stress-related or chronic fatigue (34, 35), potentially acting upon regulatory enzymes and pathways that maintain whole-body energy balance and metabolic stability (36). However, the high heterogeneity (I^2=89.3%) underscores the need for personalized approaches, considering factors such as ginseng dosage, formulation, and individual physiological profiles to optimize therapeutic outcomes (37-39).

Despite our subgroup analyses point to underlying differences that remained unexplained. These likely stem from the diversity in ginseng preparations, such as variations in extraction methods, ginsenoside concentrations, and dosage regimens, as well as differences in the demographic and clinical characteristics of the study populations. Furthermore, by restricting our analysis solely to studies that used the VAS, we have ensured internal consistency in fatigue measurement, but this choice may also narrow the applicability of our conclusions to clinical or research settings that employ different assessment tools.

The interpretation of results for certain intervention durations, particularly the 8- and 10-week subgroups, is also constrained by the limited number of available studies, which reduced confidence in these specific findings. A notable constraint of this review was the absence of individual-level participant data, which precluded more granular analyses and limited a deeper exploration of factors contributing to the observed heterogeneity, which prevented a more nuanced exploration of how factors like age, gender, or initial fatigue severity might influence an individual's response to ginseng supplementation. Looking ahead, there is a clear need for more standardized and comprehensive research. Future trials would benefit greatly from employing larger sample sizes and utilizing rigorously standardized ginseng products with well-characterized active compound profiles. This would help to minimize heterogeneity and allow for more definitive conclusions.

A critical question emerging from our analysis is the apparent reduction in effect size with longer administration periods; this warrants specific investigation to determine the optimal duration for treatment cycles. Research should also strive to identify which populations are most responsive to ginseng, potentially by examining the interplay between supplementation and variables such as specific health conditions, genetic makeup, and lifestyle factors. Finally, to move beyond correlation and understand causation, future studies should integrate subjective fatigue reporting with objective biochemical measurements, including biomarkers of mitochondrial turnover, autophagy, and cellular lipid metabolism (40). Assessing changes in stress hormones, cellular energy markers, and inflammatory

profiles could illuminate the precise physiological mechanisms through which ginseng alleviates fatigue, bridging the gap between traditional use and modern evidence-based practice.

Conclusion

This systematic review and meta-analysis confirmed that ginseng and ginseng-containing supplements can effectively reduce fatigue, particularly when used for shorter durations. The findings highlight ginseng's potential as a natural adaptogen for managing fatigue, likely due to its bioactive compounds influencing energy metabolism and stress response. However, variability in study designs and populations suggests the need for more standardized research to optimize its use.

Acknowledgement

The authors gratefully acknowledge the support and contributions of all those who assisted in the completion of this study.

Funding

This research was financially supported by the University of Mohaghegh Ardabili.

Authors' Contribution

All authors contributed to the conception and design of the study, data collection and analysis, interpretation of the results, and preparation and revision of the manuscript. All authors read and approved the final version of the manuscript.

AI Use Disclosure

The authors used generative AI tools only for linguistic refinement and to improve the manuscript's grammatical flow.

Conflict of Interest

The authors declare that they have no conflict of interest.

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