



# Efficacy of Ginseng Supplements on Fatigue and Physical Performance: A Meta-analysis

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## INTRODUCTION

Fatigue, which is a lack of energy and motivation, can be a normal and important response to physical activity, emotional stress, boredom, or lack of sleep (1). For the purpose of relieving fatigue, other than conventional medical treatments, approximately 80% of people with chronic fatigue use alternative and complementary therapies such as massage or herbal supplements in the United States (2).

Physical performance relates to the ability to complete certain physical tasks with higher intensity, faster, or with a higher power output (3). In general, the various ginseng supplements currently available in market are claimed to increase energy levels, relieve stress, enhance athletic performance and immune system functions, control blood sugar levels, improve mental functions, and promote general well-being.

According to a review, *Panax ginseng*, the most attractive product of the ginseng markets in South Korea, accounts for approximately 59% in the entire Korean market, and its consumption has continuously risen (4). Extracts of *P. ginseng* C.A. Meyer, more commonly known as Chinese or Korean Ginseng, have a

We conducted a meta-analysis to investigate the efficacy of ginseng supplements on fatigue reduction and physical performance enhancement as reported by randomized controlled trials (RCTs). RCTs that investigated the efficacy of ginseng supplements on fatigue reduction and physical performance enhancement compared with placebos were included. The main outcome measures were fatigue reduction and physical performance enhancement. Out of 155 articles meeting initial criteria, 12 RCTs involving 630 participants (311 participants in the intervention group and 319 participants in the placebo group) were included in the final analysis. In the fixed-effect meta-analysis of four RCTs, there was a statistically significant efficacy of ginseng supplements on fatigue reduction (standardized mean difference, SMD = 0.34; 95% confidence interval [CI] = 0.16 to 0.52). However, ginseng supplements were not associated with physical performance enhancement in the fixed-effect meta-analysis of eight RCTs (SMD = -0.01; 95% CI = -0.29 to 0.27). We found that there was insufficient clinical evidence to support the use of ginseng supplements on reducing fatigue and enhancing physical performance because only few RCTs with a small sample size have been published so far. Further larger RCTs are required to confirm the efficacy of ginseng supplements on fatigue reduction.

**Keywords:** Ginseng Supplements; Fatigue; Physical Performance; Randomized Controlled Trial; Meta-analysis

long history of use in traditional medicine in several Asian countries (5). They also have become readily accepted in many Western countries where people often consume these preparations, expecting that they may offer relief and protection in the fight against stress, disease, and fatigue (5,6). The wide spread use of ginseng had led researchers to assess its efficacy as therapeutic and ergogenic nutritional supplements for combating fatigue and enhancing physical performance (7).

There are two major species of ginseng, Korean ginseng (*P. ginseng*) and American ginseng (*P. quinquefolius*) with various amounts and ingredients. They mainly includes ginsenosides, which are the most important ingredients (8). To date, numerous active compounds (including approximately 40 ginsenosides) have been identified in *P. ginseng* with various pharmacological activities, such as effects on chemical stress, immune modulation in animal studies, antitumor activities, as well as glucose metabolism and enhancement of cognitive performance (9-11). However, those effects are not clinically established.

To date, several randomized controlled trials (RCTs) have reported the efficacy of ginseng supplements on fatigue reduction (12-15) and physical performance enhancement (16-23).

However, those findings remain inconsistent. Also, no meta-analysis has been published on this topic, so far.

This study aimed to investigate the efficacy of ginseng supplements on fatigue relief and physical performance enhancement by using a meta-analysis of RCTs.

## MATERIALS AND METHODS

### Literature search

In October 2015, PubMed, EMBASE, and Cochrane Library were searched by using keywords related ginseng supplements and fatigue or physical performance. Also, we searched the bibliographies of relevant articles in order to locate additional studies. We used the following keywords for the literature search: 'ginseng,' 'red ginseng,' '*P. ginseng*,' 'Korean ginseng,' 'American ginseng,' '*P. quinquefolius*' and 'fatigue,' 'lethargy,' 'exhaustion,' 'tiredness,' 'weariness,' 'physical performance,' and 'exercise performance.'

### Selection criteria

We included RCTs that investigated the efficacy of ginseng supplements on fatigue reduction or physical performance enhancement compared with placebos. There was no restriction on types of populations (e.g., patients with underlying diseases or healthy people) or study periods. The first published or larger study was included in the final analysis, if data were duplicated or shared in more than one study. There was no language restriction.

### Selection of relevant studies

Two of the authors independently evaluated the eligibility of all studies retrieved from the databases based on the pre-determined criteria. Disagreements between evaluators were resolved by discussion. From the trials included in the final analysis, we extracted the following data: study name, journal, species of

ginseng supplements, funding and ginseng supplements source of studies, geographic location, duration of intervention, dose of ginseng supplements, tool name used to measure the efficacy of ginseng supplements, the number of participants, and main results.

### Assessment of methodological quality

We assessed the methodological quality of the included studies using a validated scale for RCTs developed by Jadad and colleagues (24). This 5-point quality scale allocates points for randomization (1 point if study is described as randomized, additional 1 point if table of random numbers or computer-generated randomized was used), double-blind (1 point if described as double-blind, additional 1 point if masking such as identical placebo was used), and follow-up (1 point if the numbers and reasons of withdrawal are described for each group) in the report of an RCT. Trials having scores of 2 or less were considered as low-quality and scores of 3 to 5 as high-quality (24).

### Main and subgroup analyses

We investigated the overall efficacy of ginseng supplements on relieving fatigue and enhancing physical performance. Also, we conducted subgroup analyses by funding source, ginseng supplements source, species of ginseng supplements, duration of ginseng supplements, geographic location of studies, and dose of intervention.

### Statistical analyses

We investigated the efficacy of ginseng supplements on relieving fatigue and enhancing physical performance before and after intervention compared with placebo. Because of the different scales for fatigue reduction or physical performance enhancement across the studies, we used standardized mean difference (SMD) as a main effect size to calculate those differences

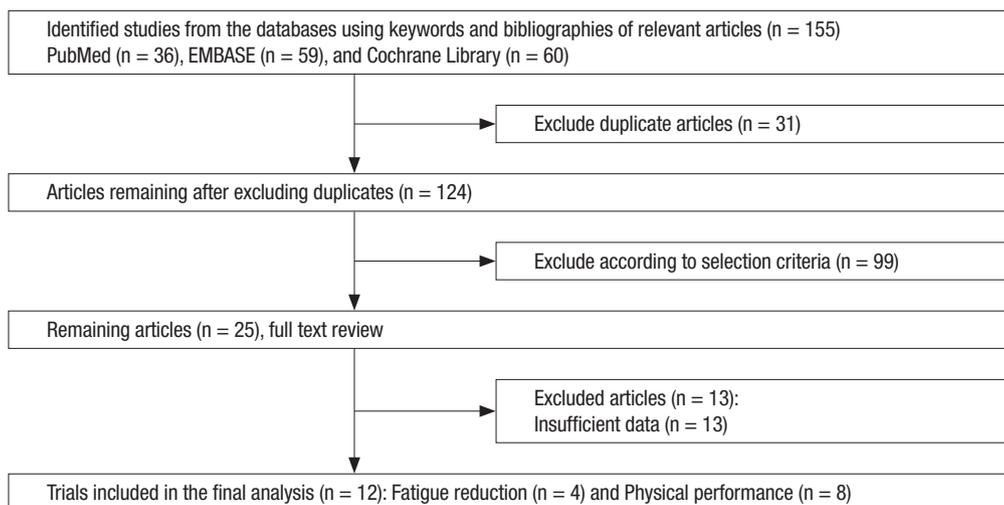


Fig. 1. Flow diagram for identification of relevant clinical trials.

between the intervention and control groups. SMD is a difference in means between the two groups divided by standard deviation (SD). SMD was calculated as follows:

$$\text{SMD} = (M_1 - M_2) / \text{pooled SD}$$

Where  $M_1$  is a mean of fatigue reduction in the intervention group,  $M_2$  is a mean of fatigue reduction in the control group, and pooled SD is a pooled intervention specific standard deviation (25). If the intervention group has a higher fatigue relief than the control group, SMD will have a positive value. In order to estimate heterogeneity across studies, we used Higgins  $I^2$ , which measures the percentage of total variation across studies. Negative values of  $I^2$  are set at zero;  $I^2$  ranges between 0% (no observed heterogeneity) and 100% (maximal heterogeneity). An  $I^2$  value greater than 50% is considered as having substantial heterogeneity (26). The SMD with 95% confidence intervals (CI) was

calculated on the basis of either the fixed- or random-effects models. When substantial heterogeneity was not observed, the SMD calculated based on the fixed-effects model was reported. When substantial heterogeneity was observed, the SMD based on the random-effects model was reported. Stata SE version 12.1 software package (StataCorp, College Station, TX, USA) was used for statistical analysis.

## RESULTS

### Selection of trials

A total of 155 articles were retrieved after searching three databases and relevant bibliographies (Fig. 1). After excluding duplicated articles and reviewing articles based on those title and abstracts, we reviewed 25 articles with full texts and then includ-

**Table 1.** General characteristics of studies in the final analysis (n = 12)

No.	Source (project name)	Country location	Participants (follow-up period)	Intervention vs. Control	Type of ginseng	Main outcome measures used	Measurement tools	Mean $\pm$ SD (baseline/follow-up)	
								Intervention	Placebo
1	Engels 1996	USA	19 healthy adult females (8 wk)	1,000 mg/day (n = 10) vs. placebo (n = 9)	<i>Panax ginseng</i>	Recovery oxygen uptake ( $VO_2$ )	Incremental Bicycle Ergometer Exercise	4 $\pm$ 0.2/3.9 $\pm$ 0.3 (mL/kg per min)	4.1 $\pm$ 0.3/4 $\pm$ 0.2 (mL/kg per min)
2	Engels 1997	USA	31 healthy adult males (8 wk)	2,000 mg/day (n = 10) vs. 1,000 mg/day (n = 11) vs. Placebo (n = 10)	<i>Panax ginseng</i>	Maximal oxygen uptake ( $VO_2$ max)	Incremental Bicycle Ergometer Exercise	42.3 $\pm$ 1.6/41.4 $\pm$ 1.5 (mL/kg per min)	42.3 $\pm$ 3.1/42.9 $\pm$ 2.9 (mL/kg per min)
3	Ziembra 1999	Poland	15 healthy people (6 wk)	350 mg/day (n = 7) vs. placebo (n = 8)	<i>Panax ginseng</i>	Maximal oxygen uptake ( $VO_2$ max)	Incremental Bicycle Ergometer Exercise	3.9 $\pm$ 0.09/3.8 $\pm$ 0.14 (L/min)	3.8 $\pm$ 0.15/3.8 $\pm$ 0.15 (L/min)
4	Engels 2001	USA	20 healthy women (8 wk)	2,000 mg/day (n = 12) vs. placebo (n = 12)	<i>Panax ginseng</i>	Rate of fatigue	Wingate test	47.89 $\pm$ 6.73/45.5 $\pm$ 8.4	47.68 $\pm$ 8.18/48.04 $\pm$ 6.31
5	Engels 2003	USA	27 healthy students (8 wk)	2,000 mg/day (n = 15) vs. placebo (n = 12)	<i>Panax ginseng</i>	Mean power output	Wingate test	-0.13 $\pm$ 0.07 W/kg (Change score between before and after intervention)	-0.08 $\pm$ 0.08 W/kg (Change score between before and after intervention)
6	Liang 2005	USA	29 healthy people (4 wk)	1,350 mg/day (n = 13) vs. placebo (n = 16)	<i>Panax notoginseng</i>	Exercise time to exhaustion ( $T_{max}$ )	Incremental Bicycle Ergometer Exercise	30.5 $\pm$ 12.8/37.6 $\pm$ 10.2 (min)	30 $\pm$ 12.6/33.6 $\pm$ 10.5 (min)
7	Kulaputana 2007	Thailand	57 health males (8 wk)	500 mg/day (n = 28) vs. placebo (n = 29)	<i>Panax ginseng</i>	Total exercise time	Incremental Bicycle Ergometer Exercise	18.6 $\pm$ 2.8/19.7 $\pm$ 2.6 (min)	17.2 $\pm$ 2.6/18.3 $\pm$ 2 (min)
8	Yoon 2008	Korea	14 healthy students (8 wk)	3,000 mg/day (n = 10) vs. placebo (n = 10)	<i>Panax ginseng</i>	Oxygen uptake ( $VO_2$ )/Maximal oxygen uptake ( $VO_2$ max)	Wingate test	48.6 $\pm$ 2.3/50.1 $\pm$ 2.6 (%)	48.5 $\pm$ 1.8/49.9 $\pm$ 2.7 (%)
9	Kim 2011	USA	47 health participants (6 wk)	100 mg/day in the 1st week, 200 mg/day in the 2nd week, 400 mg/day in the following 4 weeks for intervention group vs. placebo (Crossover study)	<i>Panax quinquefolius</i>	Fatigue score	Modified Fatigue Impact Scale	47 $\pm$ 15/42.7 $\pm$ 15.7	47 $\pm$ 15/43.7 $\pm$ 16.7
10	Barton 2013	USA	271 men and women with cancer-related fatigue defined as a score of 4 or more (8 wk)	2,000 mg of American ginseng/day (n = 183) vs. Placebo (n = 181)	<i>Panax quinquefolius</i>	The subjective experience of fatigue	The Multidimensional Fatigue Symptom Inventory-Short Form.	20 $\pm$ 27 (Change score between before and after intervention)	10.3 $\pm$ 26.1 (Change score between before and after intervention)
11	Etemadifar 2013	Iran	52 female multiple sclerosis patients (12 wk)	500 mg of Korean ginseng/day (n = 26) vs. Placebo (n = 26)	<i>Panax ginseng</i>	Fatigue score	Modified Fatigue Impact Scale	31.69 $\pm$ 14.9/23.65 $\pm$ 12.8	22.23 $\pm$ 13.21/23.69 $\pm$ 12.94
12	Kim 2013	Korea	88 participants with idiopathic chronic fatigue (ICF) (4 wk)	2,000 mg/day (n = 29) vs. 1,000 mg/day (n = 29) vs. Placebo (n = 30)	<i>Panax ginseng</i>	Fatigue severity	Numerical Rating Scale	60.8 $\pm$ 10.3/41.8 $\pm$ 13.2	59.3 $\pm$ 10.6/48.8 $\pm$ 7.3

ed 12 trials in the final analysis. We excluded 13 articles because of insufficient data (n = 13).

### General characteristics of the included trials

Table 1 illustrates general characteristics of the 12 articles included in the final analysis. The included trials involved a total of 659 participants. The intervention periods ranged from 4 weeks to 12 weeks. They were published from 1996 through 2013 and conducted in America (n = 7), Korea (n = 2), Iran (n = 1), Thailand (n = 1), and Poland (n = 1). They used Korean ginseng (14-20, 22, 23), *P. notoginseng* (21), and American Ginseng (12, 13). Six different measurement tools were used in the studies. The questionnaires used for the assessment of fatigue were the Multidimensional Fatigue Symptom Inventory-Short Form (MFSI-SF), Modified Fatigue Impact Scale (MFIS), Numerical Rating Scale (NRS), and the Short Form 36 Health Survey Version 2 (SF-36v2). The tests used for the assessment of physical performance were the Incremental Bicycle Ergometer Exercise and Wingate test.

### Methodological quality of trials

Table 2 illustrates the methodological quality of all 12 RCTs included in the final analysis based on the Jadad scale. All of them have 3, 4, and 5 points, which implies that all trials have a low risk of bias.

### Efficacy of ginseng supplements on fatigue reduction and physical performance enhancement

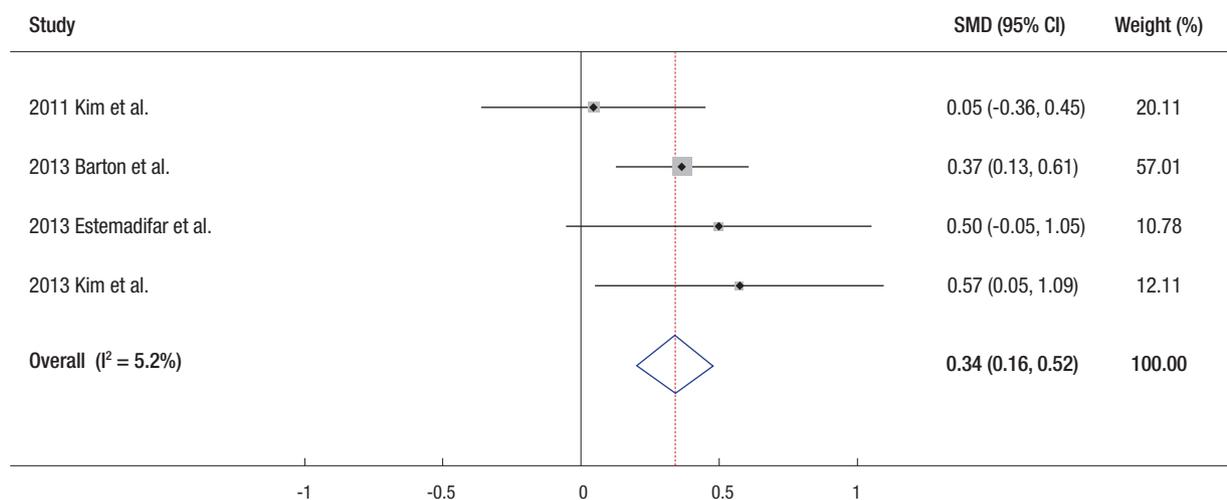
In the fixed-effects meta-analysis, ginseng supplements showed a statistically significant efficacy on fatigue reduction (SMD = 0.34; 95% CI = 0.16 to 0.52, n = 4) (Fig. 2). However, there was no significant association between ginseng supplements and physical performance enhancement (SMD = -0.01; 95% CI = -0.29 to 0.27, n = 8) (Fig. 3).

### Subgroup meta-analysis by various factors

Table 3 shows the findings from the subgroup meta-analysis by various factors for both fatigue reduction and physical performance enhancement. Overall, subgroup meta-analysis by vari-

**Table 2.** Methodological quality of trials based on the Jadad scale (n = 12)

No.	Study	Randomization	Description of randomization methods	Double-blind	Using identical placebo	Follow-up reporting	Total score
1	Engels et al. 1996	1	0	1	1	1	4
2	Engels et al. 1997	1	1	1	1	1	5
3	Ziemba et al. 1999	1	0	1	1	1	4
4	Engels et al. 2001	1	0	1	1	1	4
5	Engels et al. 2003	1	0	1	1	1	4
6	Liang et al. 2005	1	1	1	1	1	5
7	Kulaputana et al. 2007	1	0	1	1	1	4
8	Yoon et al. 2008	0	0	1	1	1	3
9	Kim et al. 2011	1	1	1	1	1	5
10	Barton et al. 2013	1	1	1	1	1	5
11	Etemadifar et al. 2013	1	1	1	1	1	5
12	Kim et al. 2013	1	1	1	0	1	4



**Fig. 2.** Efficacy of ginseng supplements on fatigue reduction in the meta-analysis of RCTs (n = 4)\*.

SMD = standardized mean difference, CI = confidence interval.

\*Fixed-Effect Model.

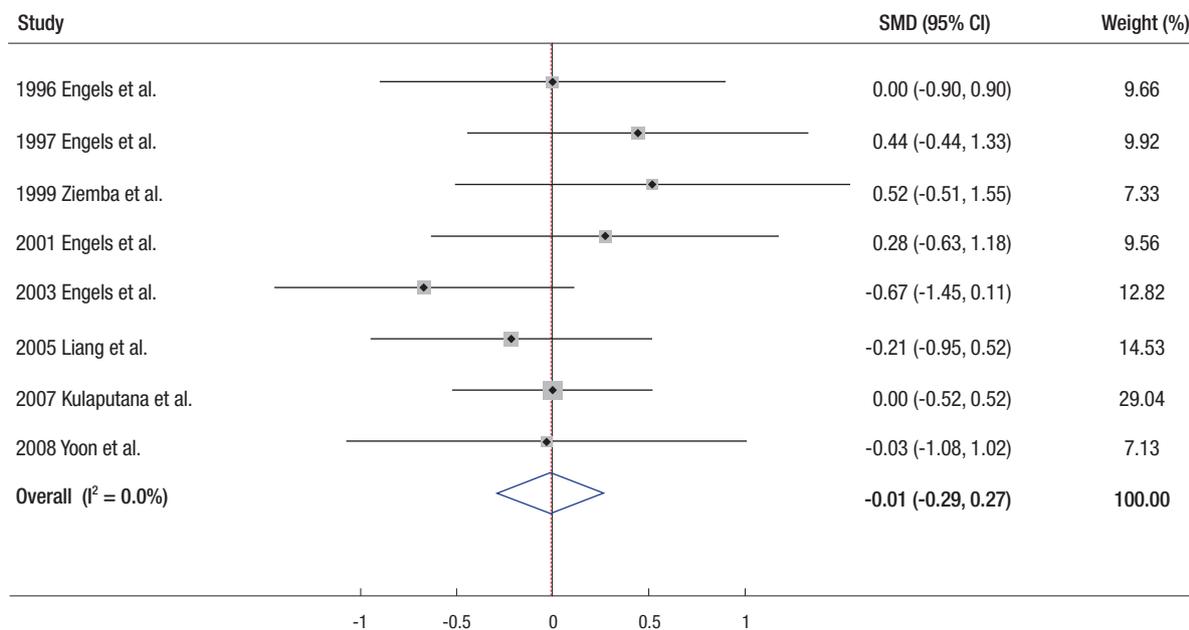


Fig. 3. Efficacy of ginseng supplements on physical performance enhancement in the meta-analysis of RCTs (n = 8)\*.

SMD = standardized mean difference, CI = confidence interval.

\*Fixed-Effect Model.

ous factors showed that ginseng supplements had an efficacy on fatigue reduction. However, the use of ginseng supplements with short duration (< 6 weeks) and lower dose (< 1,000 mg/day) showed no significant efficacy. Regarding physical performance enhancement, overall there was no efficacy of ginseng supplements.

## DISCUSSION

In this meta-analysis of RCTs, we found that the use of ginseng supplements had the efficacy on fatigue reduction, but not physical performance enhancement. Specifically, the effect size on the efficacy of ginseng supplements on fatigue reduction (SMD = 0.34) was between the small (SMD = 0.20) and medium levels (SMD = 0.50) based on Cohen's rule of thumb (27). However, we found that only four relevant RCTs have been published regarding fatigue reduction, and the total number of the study participants included in those trials was only 429. Thus, there was no sufficient clinical evidence to support the use of ginseng supplements on reducing fatigue and enhancing physical performance.

There are some possible biological mechanisms for the efficacy of ginseng supplements on mental and physical fatigue reduction and physical performance enhancement. Regarding mental fatigue, although a human study indicated that ginseng increases cognitive performance (28), its mechanisms remain not known, but may be related to the ginseng's glycemic properties (29,30). Ginseng affects brain activity, specifically by increasing cortical levels of dopamine, noradrenalin, serotonin,

and cyclic adenosine monophosphate (cAMP) (31). An in vitro study suggested that ginseng increases energy produced aerobically in the brain (32). Ginseng saponins showed moderate depressant actions on the electroencephalogram and the behavior in cats (33). As for physical fatigue and physical performance, ergogenic aids are believed to increase performance by some of the following mechanisms: renewing or increasing energy stores in the body, facilitating the biochemical reactions that yield energy, reducing or neutralizing performance-inhibiting metabolic by products, and facilitating recovery (34,35). Although the mechanism on the ergogenicity of ginseng on physical performance has not been fully identified, theories include stimulation of the hypothalamic-pituitary-adrenal cortex axis and increased resistance to the stress of exercise, enhanced myocardial metabolism, increased hemoglobin levels, vasodilatation, increased oxygen extraction by muscles, and improved mitochondrial metabolism in the muscle, all of which theoretically could enhance physical performance (36-39). A clinical experimental study reported that the use of ginseng supplements before exhaustive aerobic exercise can reduce creatine kinase leakage during exercise, possibly due to ginseng's ability to reduce cellular and muscle damage (40).

However, although there are some possible biological mechanisms on the efficacy of ginseng supplements on physical performance enhancement in in vivo animal or in vitro laboratory studies, our meta-analysis of eight randomized controlled trials found that there was no sufficient evidence on the efficacy. Several explanations could be considered for this inconsistency. First, preclinical studies, including in vivo laboratory studies

**Table 3.** Efficacy of ginseng supplements on fatigue reduction and physical performance enhancement in the subgroup meta-analysis of RCTs by various factors

Factors	No. of trials	SMD (95% CI)	Heterogeneity I <sup>2</sup> (%)	Model used
<b>Fatigue</b>				
Funding sources				
From companies	-	-	-	
From non-companies*	4	0.34 (0.16-0.52)	5.2	Fixed-effects
Ginseng supplement sources				
From companies*	2	0.28 (0.08-0.49)	43.7	Fixed-effects
From non-companies*	2	0.54 (0.16-0.92)	0	Fixed-effects
Species of ginseng				
Korean ginseng*	2	0.54 (0.16-0.92)	0	Fixed-effects
Non-Korean ginseng*	2	0.28 (0.08-0.49)	43.7	Fixed-effects
Duration of intervention				
1-6 wk	2	0.28 (-0.23-0.80)	59.3	Random-effects
> 6 wk*	2	0.39 (0.17-0.61)	0	Fixed-effects
Geographic location of studies				
Asian countries*	2	0.54 (0.16-0.92)	0	Fixed-effects
Western countries*	2	0.28 (0.08-0.49)	43.7	Fixed-effects
Dose of intervention				
< 1,000 mg/day	2	0.20 (-0.12-0.53)	40.5	Fixed-effects
≥ 1,000 mg/day*	2	0.40 (0.18-0.62)	0	Fixed-effects
<b>Physical performance</b>				
Funding resources				
From companies	1	-0.03 (-1.08-0.28)	-	Fixed-effects
From non-company	7	-0.01 (-0.30-0.28)	0	Fixed-effects
Ginseng supplement sources				
From companies	3	-0.08 (-0.29-0.31)	0	Fixed-effects
From non-companies	5	0.06 (-0.34-0.47)	0	Fixed-effects
Species of ginseng				
Korean ginseng	7	0.02 (-0.28-0.33)	0	Fixed-effects
Non-Korean ginseng	1	-0.21 (-0.95-0.52)	-	Fixed-effects
Duration of intervention				
1-6 wk	2	0.03 (-0.57-0.63)	22.1	Fixed-effects
> 6 wk	6	-0.02 (-0.34-0.29)	0	Fixed-effects
Geographic location of studies				
Asian countries	2	-0.01 (-0.47-0.46)	0	Fixed-effects
Western countries	6	-0.01 (-0.36-0.34)	8	Fixed-effects
Dose of intervention				
< 1,000 mg/day	2	0.11 (-0.36-0.57)	0	Fixed-effects
≥ 1,000 mg/day	6	-0.08 (-0.43-0.27)	0	Fixed-effects

SMD = standardized mean difference, CI = confidence interval.

\*Statistically significant association.

and animal studies might not represent the biological mechanism in the human body. Therefore, although preclinical studies showed an efficacy of ginseng supplements on physical performance enhancement, clinical circumstances could report no benefit of ginseng supplements. Second, the sample size of the final meta-analysis is a limitation to evaluate the efficacy. We only included eight RCTs with 212 participants due to a paucity of data. Third, there was heterogeneity in the participants in each trial. While two American studies including 39 participants were conducted in healthy adult females (16,19), American (17) and Thailand (22) studies including 88 participants were conducted in health adult males. Finally, the dose and duration of the intervention in each trial varied from 350 mg/day/person to 3,000 mg/day/person and 4 weeks to 8 weeks among included studies.

We have limitations in the current meta-analysis. Although

we found that there was a significant efficacy of ginseng supplements on fatigue reduction, no sufficient RCTs were published in order to confirm this finding. The number of the study participants was not enough to draw conclusions. Specifically, out of a total of 429 study participants from all four RCTs, 271 participants were from Barton's study (13), which indicated a significant efficacy. Also, many RCTs were excluded from the final analysis because of insufficient data.

To the best of our knowledge, this meta-analysis is thought to be the first meta-analysis of RCTs about this issue. Although there is no sufficient clinical evidence about the efficacy of ginseng supplements for health, in some countries, especially Korea, some sellers promote the sale of ginseng supplements as if these are clinically approved effective against fatigue or some diseases, and also many people have consumed ginseng supplements in the belief that these prevent diseases and improve their health.

In summary, we found that there was insufficient clinical evidence to support the use of ginseng supplements on reducing fatigue and enhancing physical performance because only a few RCTs with a small sample size were published so far. Further larger RCTs are needed to confirm the efficacy of ginseng supplements for fatigue reduction and physical performance enhancement.

## DISCLOSURE

The authors have no potential conflicts of interest to disclose.

## AUTHOR CONTRIBUTION

Study design: Myung SK, Kim J. Database search and study selection: Bach HV, Cho YA. Data management and Statistical analysis: Myung SK, Bach HV. Interpretation of the findings: Myung SK, Kim J. Drafting of the manuscript: Myung SK, Bach HV. Revision of manuscript: Myung SK, Bach HV, Kim J. Final approval: all authors.

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## REFERENCES

1. U.S. National Library of Medicine. MedlinePlus: fatigue [Internet]. Available at <https://www.nlm.nih.gov/medlineplus/ency/article/003088.htm> [accessed on 9 November 2015].
2. Jones JF, Maloney EM, Boneva RS, Jones AB, Reeves WC. Complementary and alternative medical therapy utilization by people with chronic fatiguing illnesses in the United States. *BMC Complement Altern Med* 2007; 7: 12.
3. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). Scientific opinion on the substantiation of a health claim related to beta-alanine and increase in physical performance during short-duration, high-intensity exercise pursuant to Article 13(5) of Regulation (EC) No 1924/2006. *EFSA J* 2014; 12: 3755.
4. Baeg IH, So SH. The world ginseng market and the ginseng (Korea). *J Ginseng Res* 2013; 37: 1-7.
5. Sticher O. Biochemical, pharmaceutical, and medical perspectives of ginseng. In: Lawson LD, Bauer R, editors. *Phytomedicines of Europe: Chemistry and Biological Activity*. Washington, D.C.: American Chemical Society, 1998, p221-40.
6. Blumenthal M, Busse WR. *The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines*. Austin, TX: American Botanical Council, 1998.
7. Vuksan V, Sievenpiper JL, Xu Z, Wong EY, Jenkins AL, Beljan-Zdravkovic U, Leiter LA, Josse RG, Stavro MP. Konjac-Mannan and American ginseng: emerging alternative therapies for type 2 diabetes mellitus. *J Am Coll Nutr* 2001; 20: 370S-380S.
8. Allergy Research Group. Natural standard monographs: *Panax ginseng*. Available at <http://www.allergyresearchgroup.com/monographs> [accessed on 10 November 2015].
9. Lee NH, Son CG. Systematic review of randomized controlled trials evaluating the efficacy and safety of ginseng. *J Acupunct Meridian Stud* 2011; 4: 85-97.
10. Shim JY, Kim MH, Kim HD, Ahn JY, Yun YS, Song JY. Protective action of the immunomodulator ginsan against carbon tetrachloride-induced liver injury via control of oxidative stress and the inflammatory response. *Toxicol Appl Pharmacol* 2010; 242: 318-25.
11. Suh SO, Kroh M, Kim NR, Joh YG, Cho MY. Effects of red ginseng upon postoperative immunity and survival in patients with stage III gastric cancer. *Am J Chin Med* 2002; 30: 483-94.
12. Kim E, Cameron M, Lovera J, Schaben L, Bourdette D, Whitham R. American ginseng does not improve fatigue in multiple sclerosis: a single center randomized double-blind placebo-controlled crossover pilot study. *Mult Scler* 2011; 17: 1523-6.
13. Barton DL, Liu H, Dakhil SR, Linquist B, Sloan JA, Nichols CR, McGinn TW, Stella PJ, Seeger GR, Sood A, et al. Wisconsin Ginseng (*Panax quinquefolius*) to improve cancer-related fatigue: a randomized, double-blind trial, N07C2. *J Natl Cancer Inst* 2013; 105: 1230-8.
14. Etemadifar M, Sayahi F, Abtahi SH, Shemshaki H, Doroooshi GA, Goodarzi M, Akbari M, Fereidan-Esfahani M. Ginseng in the treatment of fatigue in multiple sclerosis: a randomized, placebo-controlled, double-blind pilot study. *Int J Neurosci* 2013; 123: 480-6.
15. Kim HG, Cho JH, Yoo SR, Lee JS, Han JM, Lee NH, Ahn YC, Son CG. Anti-fatigue effects of *Panax ginseng* C.A. Meyer: a randomised, double-blind, placebo-controlled trial. *PLoS One* 2013; 8: e61271.
16. Engels H, Said JM, Wirth JC. Failure of chronic ginseng supplementation to affect work performance and energy metabolism in healthy adult females. *Nutr Res* 1996; 16: 1295-305.
17. Engels HJ, Wirth JC. No ergogenic effects of ginseng (*Panax ginseng* C.A. Meyer) during graded maximal aerobic exercise. *J Am Diet Assoc* 1997; 97: 1110-5.
18. Ziemba AW, Chmura J, Kaciuba-Uscilko H, Nazar K, Wisnik P, Gawronski W. Ginseng treatment improves psychomotor performance at rest and during graded exercise in young athletes. *Int J Sport Nutr* 1999; 9: 371-7.
19. Engels HJ, Kolokouri I, Cieslak TJ 2nd, Wirth JC. Effects of ginseng supplementation on supramaximal exercise performance and short-term recovery. *J Strength Cond Res* 2001; 15: 290-5.
20. Engels HJ, Fahlman MM, Wirth JC. Effects of ginseng on secretory IgA, performance, and recovery from interval exercise. *Med Sci Sports Exerc* 2003; 35: 690-6.
21. Liang MT, Podolka TD, Chuang WJ. *Panax notoginseng* supplementation enhances physical performance during endurance exercise. *J Strength Cond Res* 2005; 19: 108-14.
22. Kulaputana O, Thanakomsirichot S, Anomasiri W. Ginseng supplementation does not change lactate threshold and physical performances in physically active Thai men. *J Med Assoc Thai* 2007; 90: 1172-9.
23. Yoon SJ, Kim KH, Kim CJ, Park HC, Kang KH, Kim MJ, Kang SM, Kwak UH, Kim HJ. Effects of red ginseng supplementation on aerobic · anaerobic performance, central and peripheral fatigue. *J Ginseng Res* 2008; 32: 210-9.

24. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, McQuay HJ. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials* 1996; 17: 1-12.
25. Higgins JP, Green S. Cochrane handbook for systematic reviews of interventions: version 5.1.0. Available at <http://handbook.cochrane.org/> [updated March 2011; accessed on 9 November 2015].
26. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002; 21: 1539-58.
27. Cohen J. A power primer. *Psychol Bull* 1992; 112: 155-9.
28. Scholey AB, Kennedy DO. Acute, dose-dependent cognitive effects of Ginkgo biloba, *Panax ginseng* and their combination in healthy young volunteers: differential interactions with cognitive demand. *Hum Psychopharmacol* 2002; 17: 35-44.
29. Reay JL, Kennedy DO, Scholey AB. Single doses of *Panax ginseng* (G115) reduce blood glucose levels and improve cognitive performance during sustained mental activity. *J Psychopharmacol* 2005; 19: 357-65.
30. Reay JL, Kennedy DO, Scholey AB. Effects of *Panax ginseng*, consumed with and without glucose, on blood glucose levels and cognitive performance during sustained 'mentally demanding' tasks. *J Psychopharmacol* 2006; 20: 771-81.
31. Itoh T, Zang YF, Murai S, Saito H. Effects of *Panax ginseng* root on the vertical and horizontal motor activities and on brain monoamine-related substances in mice. *Planta Med* 1989; 55: 429-33.
32. Samira MM, Attia MA, Allam M, Elwan O. Effect of the standardized Ginseng Extract G115 on the metabolism and electrical activity of the rabbit's brain. *J Int Med Res* 1985; 13: 342-8.
33. Kaku T, Miyata T, Uruno T, Sako I, Kinoshita A. Chemico-pharmacological studies on saponins of *Panax ginseng* C. A. Meyer. II. Pharmacological part. *Arzneimittelforschung* 1975; 25: 539-47.
34. Lawrence ME, Kirby DF. Nutrition and sports supplements: fact or fiction. *J Clin Gastroenterol* 2002; 35: 299-306.
35. Maughan RJ, King DS, Lea T. Dietary supplements. *J Sports Sci* 2004; 22: 95-113.
36. Kim DH, Moon YS, Jung JS, Min SK, Son BK, Suh HW, Song DK. Effects of ginseng saponin administered intraperitoneally on the hypothalamo-pituitary-adrenal axis in mice. *Neurosci Lett* 2003; 343: 62-6.
37. Zhang HG, Li XH, Yang ZC. Effects of *Panax notoginseng* saponins on myocardial G $\alpha$  mRNA expression and ATPase activity after severe scald in rats. *Burns* 2003; 29: 541-6.
38. Bae JW, Lee MH. Effect and putative mechanism of action of ginseng on the formation of glycated hemoglobin in vitro. *J Ethnopharmacol* 2004; 91: 137-40.
39. Li Z, Chen X, Niwa Y, Sakamoto S, Nakaya Y. Involvement of Ca<sup>2+</sup>-activated K<sup>+</sup> channels in ginsenosides-induced aortic relaxation in rats. *J Cardiovasc Pharmacol* 2001; 37: 41-7.
40. Hsu CC, Ho MC, Lin LC, Su B, Hsu MC. American ginseng supplementation attenuates creatine kinase level induced by submaximal exercise in human beings. *World J Gastroenterol* 2005; 11: 5327-31.