Review Article
Male sexual health and dysfunction

pISSN: 2287-4208 / eISSN: 2287-4690
World J Mens Health Published online Jun 15, 2021
https://doi.org/10.5534/wjmh.210071

The World Journal of MEN's HEALTH

Ginseng for Erectile Dysfunction: A Cochrane Systematic Review

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The objectives of this study were to assess the effects of ginseng on erectile dysfunction. We searched multiple electronic databases from their inceptions to 30 January 2021 without restrictions by language. We included randomized or quasi-randomized controlled trials that evaluated the use of any type of ginseng as a treatment for erectile dysfunction compared to placebo or conventional treatment. The authors independently screened the literature, extracted data, assessed risk of bias, and rated the certainty of evidence (CoE) according to the GRADE approach. We included nine studies, and all compared ginseng to placebo. Ginseng appears to have a trivial effect on erectile dysfunction when compared to placebo based on the Erectile Function Domain of the International Index of Erectile Function (IIEF)-15 instrument (mean difference [MD] 3.52, 95% confidence interval [CI] 1.79 to 5.25; I^2=0%; 3 studies; low CoE). Ginseng may have little to no effect on adverse events compared to placebo (risk ratio [RR] 1.45, 95% CI 0.69 to 3.03; I^2=0%; 7 studies; low CoE). While ginseng may improve men's self-reported ability to have intercourse (RR 2.55, 95% CI 1.76 to 3.69; I^2=23%; 6 studies; low CoE), it may have a trivial effect on men's satisfaction with intercourse based on the Intercourse Satisfaction Domain of the IIEF-15 (MD 1.19, 95% CI 0.41 to 1.97; I^2=0%; 3 studies; low CoE). No study reported quality of life as an outcome.

Keywords: Erectile dysfunction; Ginseng; Meta-analysis; Panax; Systematic review

INTRODUCTION

Dietary supplements with ginseng, or ginseng alone, are widely used for a broad range of conditions, including erectile dysfunction. Compounds containing ginseng are some of the most popular and best-selling herbal medicines in the world [1]. They are used for a broad range of conditions including erectile dysfunction [2,3]. One systematic review presented evidence in support of red ginseng as a treatment for erectile dysfunction

Received: Apr 26, 2021 **Accepted:** May 3, 2021 **Published online** Jun 15, 2021
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This article is based on a Cochrane Review published in the Cochrane Database of Systematic Reviews (CDSR) 2021, Issue 4. Art. No.: CD012654. DOI: 10.1002/14651858.CD012654.pub2 (see www.cochranelibrary.com for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and the CDSR should be consulted for the most recent version of the review.

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[4]. Another systematic review analysis, published in 2013, evaluated all current randomized controlled trials (RCTs) of ginseng in the Korean literature [5] included two additional Korean RCTs related to erectile dysfunction that were not included in the previous review [4], which had demonstrated positive effects of ginseng on erectile dysfunction. Thus, there is a need for a well-organized and up-to-date systematic review to evaluate the efficacy of ginseng for erectile dysfunction. This review critically appraises the current evidence regarding the use of ginseng to treat erectile dysfunction.

MATERIALS AND METHODS

We conducted systematic searches on multiple electronic databases, including CENTRAL, MEDLINE, Embase, CINAHL, AMED, trials registries, and locoregional databases of east Asia, from their inceptions to 30 January 2021 without restrictions on language and publication status using search strategies (for the search strategy, see Supplement Table 1). Hand searches included conference proceedings. We included randomized or quasi-randomized controlled trials that evaluated the use of any type of ginseng as a treatment for erectile dysfunction compared to placebo or conventional treatment. Primary outcomes were erectile function and adverse events. Secondary outcomes were ability to have intercourse reported by participants (or partner), sexual satisfaction, and quality of life. Two authors independently classified studies and three authors independently extracted data and assessed risk of bias in the included studies. We conducted meta-analyses using a random-effects model and 95% confidence intervals [CIs]. We interpreted random-effects meta-analyses with due consideration of the whole distribution of effects. Also, we performed statistical analyses according to the statistical guidelines contained in the Cochrane Handbook [6]. We rated the certainty of evidence according to the GRADE approach.

Please see review published in Cochrane Library for further details on the methods [7].

No ethical approval was required for this manuscript as this study did not involve human subjects or laboratory animals.

RESULTS

We included nine studies [8-16] with 587 men with mild to moderate erectile dysfunction, aged from 20 to 70 years old (Supplement Fig. 1). The studies all compared ginseng to placebo. We found only short-term follow-up data (up to 12 weeks). Supplement Tables 2 and 3 summarized the characteristics the included studies. The assessments of risk of bias were shown in Supplement Fig. 2. Supplement Table 4 list the excluded studies and their details reasons.

Primary outcomes: Ginseng appears to have a trivial effect on erectile dysfunction when compared to placebo based on the Erectile Function Domain of the International Index of Erectile Function (IIEF)-15 instrument (scale: 1 to 30, higher scores imply better function; mean difference [MD] 3.52, 95% CI 1.79 to 5.25; I^2=0%; 3 studies; low certainty evidence) assuming a minimal clinically important difference (MCID) of 4 (Table 1) [13,14,16,17]. Ginseng probably also has a trivial effect on erectile function when compared to placebo based on the IIEF-5 instrument (scale: 1 to 25, higher scores imply better function; MD 2.39, 95% CI 0.89 to 3.88; I^2=0%; 3 studies; moderate certainty evidence) assuming a MCID of 5 [12,14,16]. Ginseng may have little to no effect on adverse events compared to placebo (risk ratio [RR] 1.45, 95% CI 0.69 to 3.03; I^2=0%; 7 studies; low certainty evidence) [8-14]. Based on 86 adverse events per 1,000 men in the placebo group, this would correspond to 39 more adverse events per 1,000 (95% CI 27 fewer to 174 more).

Secondary outcomes: Ginseng may improve men's self-reported ability to have intercourse (RR 2.55, 95% CI 1.76 to 3.69; I^2=23%; 6 studies; low certainty evidence) [8-12,14]. Based on 207 per 1,000 men self-reporting the ability to have intercourse in the placebo group, this would correspond to 321 more men (95% CI 158 more to 558 more) per 1,000 self-reporting the ability to have intercourse. Ginseng may have a trivial effect on men's satisfaction with intercourse based on the Intercourse Satisfaction Domain of the IIEF-15 (scale: 0 to 15, higher scores imply greater satisfaction; MD 1.19, 95% CI 0.41 to 1.97; I^2=0%; 3 studies; low certainty evidence) based on a MCID of 25% improvement from baseline [13,14,16]. It may also have a trivial effect on men's satisfaction with intercourse based on item 5 of the IIEF-5 (scale: 0 to 5, higher scores imply more satisfaction; MD 0.60, 95% CI 0.02 to 1.18; 1 study; low certainty evidence)

Table 1. GRADE summary of findings for ginseng for erectile dysfunction compared to placebo

Patient or population: erectile dysfunction, Setting: randomized controlled trial, Intervention: Ginseng, Comparison: placebo.						
Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		What happens?
				Risk with placebo	Risk difference with ginseng	
Erectile function Assessed with: EF domain of IIEF-15 Scale from: 1 (worst: severe ED) to 30 (best: no ED) Follow-up: 8 weeks MCID: 4	245 (3 RCTs)	⨁⨁◯◯ LOW[a,b]	-		MD 3.52 higher (1.79 higher to 5.25 higher)	Ginseng may have a trivial (clinically unimportant) effect on EF when assessed using the IIEF-15
Erectile function Assessed with: IIEF-5 scale from: 1 (worst: severe ED) to 25 (best: no ED) Follow-up: range 8 weeks to 12 weeks MCID: 5	236 (3 RCTs)	⨁⨁⨁◯ MODERATE[a]	-		MD 2.39 higher (0.89 higher to 3.88 higher)	Ginseng probably has a trivial (clinically unimportant) effect on EF when assessed using the IIEF-5
Adverse events Follow-up: range 4 weeks to 12 weeks MCID: absolute risk reduction/increase of 5%	418 (7 RCTs)	⨁⨁◯◯ LOW[a,b]	RR 1.45 (0.69–3.03)	Study population 86 per 1,000 Assumed baseline risk[c] 19 per 1,000	39 more per 1,000 (27 fewer to 174 more) 9 more per 1,000 (6 fewer to 39 more)	Ginseng may have little to no effect on adverse events
Participant's ability to have intercourse Reported by participant (or partner) Follow-up: range 4 weeks to 12 weeks MCID: absolute risk reduction/increase of 5%	349 (6 RCTs)	⨁⨁◯◯ LOW[a,d]	RR 2.55 (1.76–3.69)	Study population 183 per 1,000	284 more per 1,000 (139 more to 492 more)	Ginseng may improve participant's ability to have intercourse as self-reported by participant (or partner)
Sexual satisfaction Assessed with: IIEF-intercourse satisfaction domain Scale from: 0 (worst: no attempt) to 15 (best: very satisfied) Follow-up: range 8 weeks to 12 weeks MCID: 1.5	245 (3 RCTs)	⨁⨁◯◯ LOW[a,b,e]	-		MD 1.19 higher (0.41 higher to 1.97 higher)	Ginseng may have a trivial (clinically unimportant) effect on sexual satisfaction based on the IIEF intercourse satisfaction domain
Sexual satisfaction Assessed with: IIEF-5 question 5 Scale from: 0 (worst: no attempt) to 5 (best: very satisfied) Follow-up: 12 weeks MCID: 0.75	60 (1 RCT)	⨁⨁◯◯ LOW[a,b,f]			MD 0.60 higher (0.02 higher to 1.18 higher)	Ginseng may have a trivial (clinically unimportant) effect on sexual satisfaction based on the IIEF-5 intercourse satisfaction domain

Table 1. Continued

Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		What happens?
				Risk with placebo	Risk difference with ginseng	
Quality of life-not measured	-	-	-	-	-	We found no studies and therefore do not know

The risk in the intervention group (and its 95% confidence interval [CI]) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
MD: mean difference, RR: risk ratio, EF: erectile function, ED: erectile dysfunction, IIEF: International Index of Erectile Function, MCID: minimal clinically important difference, RCTs: randomized controlled trials.
GRADE Working Group grades of evidence. High certainty: We are very confident that the true effect lies close to that of the estimate of the effect. Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.
[a]Downgraded by one level for study limitations: unclear or high risk in half of domains in included studies. [b]Downgraded by one level for imprecision: confidence interval crossed assumed threshold of minimal clinically important difference or effect size. [c]Estimates for control event rates for cardiovascular adverse events come from Rosenzweig et al [17]. [d]Downgraded by one level for indirectness: different definitions for measuring the outcome among included studies. [e]Minimal clinically important difference: 25% improvement (greater than 1.5 points) from the baseline (overall: 5.7). [f]Minimal clinically important difference: 25% improvement (greater than 0.75 points) from the baseline (ginseng: 2.7; placebo: 3.0).

based on a MCID of 25% improvement from baseline [12]. No study reported quality of life as an outcome. We found no trial evidence to inform comparisons to other treatments for erectile dysfunction, such as phosphodiesterase-5 inhibitors. We were unable to conduct any predefined subgroup analyses.

DISCUSSION

Most of the included studies were conducted in South Korea. Currently, it is not known if growing regions (*i.e.,* differences in soil and the environment) affect the therapeutic effects of ginseng by impacting the chemical formulation. It is unclear how applicable the findings of this Cochrane Review may be to other forms of ginseng (*i.e.,* American or Chinese ginseng) that are grown in other areas.

Most of the included studies used a ginseng dose of 3,000 mg or less, which is less than the dose typically recommended by manufacturers. While there are no clear guidelines on the appropriate dosing of ginseng for erectile dysfunction, the small effects observed with ginseng in this review (which are less than the MCID), may be due to suboptimal doses for erectile dysfunction.

We consistently downgraded the certainty of the evidence for study limitations. The most common reasons were lack of information on random sequence generation and allocation concealment, which are known to result in an overestimation of the effect size [18,19]. We further downgraded the certainty of the evidence for indirectness (different definitions in the questionnaires measuring the outcome) and imprecision (threshold of clinically important effect size or MCID and a wide CI). Lastly, we downgraded for imprecision in light of wide confidence intervals that crossed predefined thresholds of clinical importance.

CONCLUSIONS

Based on mostly low certainty evidence, ginseng may only have trivial effects on erectile function or satisfaction with intercourse compared to placebo when assessed using validated instruments. Ginseng may improve men's self-reported ability to have intercourse. It may have little to no effect on adverse events. We found no trial evidence comparing ginseng to other agents with a more established role in treating erectile

dysfunction, such as phosphodiesterase-5 inhibitors.

ACKNOWLEDGEMENTS

We are grateful to the editors of the Cochrane Urology Group and the Korean Satellite of the Cochrane Urology Group for providing helpful comments and support for the review. We also thank Ji Hee Jun and Lin Ang who helped to search Chinese databases and to screen the results of those database searches. We also thank external reviewers, including Professor Maoling Wei, Professor Jiaping Liu, Professor Junhua Zhang and Dr Joshua A Bodie, for their constructive comments.

HWL and MSL were supported by Korea Institute of Oriental Medicine (K18043 and KSN2013210), Korea. Funder made no fluence on this work.

Conflict of Interest

Prof. Myeong Soo Lee is one of editorial board of Journal of Ginseng Research, but it made no influence on this work in relation with topic. CZ: serves as President of the Chinese Medicine Council of New South Wales (Australia) and receives payment from the organization for his role; serves as Member of the Accreditation Committee of the Chinese Medicine Board of Australia and receives payment from the organization for his role; received consultancy support paid to his institution by the Korea Institute of Oriental Medicine to fund a research assistant to work on a research project relating to post sequelae of stroke; his institution (University of Technology Sydney, Australia) received payment from the Korea Institute of Oriental Medicine for consultancy research not related to this review; and received support from the Korea Institute of Oriental Medicine for conference attendance at the Korea Institute of Oriental Medicine Other authors have no potential conflicts of interest to disclose.

Author Contribution

Conception of the review: HWL and MSL. Design of the review: HWL, MSL, and THK. Co-ordination of the review: MSL. The protocol was drafted by HWL, MSL, THK, TA, CZ, JWK, and DGM. The search strategy was developed and run by MSL and THK. Copies of studies were obtained by HWL and THK. Selection of the studies for inclusion was done by HWL and THK; MSL acted as an arbiter in the study selection stage. Extraction of data from studies was performed by HWL, MSL, and THK; TA acted as an arbiter in the data extraction stage. Entering data into RevMan was performed by HWL and CZ. Assessment of the risk of bias in the included studies: HWL, MSL, THK, and TA. Assessment of the certainty in the body of evidence: MSL and THK. The analysis was carried out by HWL, MSL, THK, TA, CZ, JWK, and DGM. Interpretation of the analysis was done by HWL, MSL, THK, TA, CZ, JWK, and DGM. The final review was drafted by HWL, MSL, THK, TA, CZ, JWK, and DGM. The review will be updated by HWL, MSL, THK, TA, CZ, JWK, and DGM.

Supplementary Materials

Supplementary materials can be found *via* https://doi.org/10.5534/wjmh.210071.

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