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SYSTEMATIC REVIEW

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Maca (*L. meyenii*) for erectile dysfunction: a systematic review and meta-analysis

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Abstract

Maca (*Lepidium meyenii*) has been reported to improve erectile function (EF). The purpose of this study was to evaluate the clinical evidence for or against maca as a therapy for erectile dysfunction (ED) in men. We searched 11 databases for randomized controlled trials (RCTs) comparing any type of maca with a placebo in the treatment of ED in men. The primary endpoint was EF, while the secondary endpoints were quality of life and adverse events. Risk of bias (ROB) was assessed using the Cochrane ROB tool 2.0. Study selection, data extraction, and assessment were independently performed by two researchers. RevMan 5.4.1 software (Cochrane Collaboration, 2020) was used for data aggregation, and the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) assessment was used to evaluate the quality of the study outcomes. Only two RCTs met all the inclusion criteria. These RCTs examined the effects of maca on EF in patients with mild ED. One RCT showed a positive effect of maca on EF, whereas the other RCT did not. The results of the meta-analysis indicate that maca has positive effects on EF in men with mild ED (n = 79, MDs 1.13: 0.64 to 1.61, $p = 0.01$; $p < 0.0001$). Our comprehensive review found limited evidence for the benefits of maca in improving EF. Several limitations, including the total number of studies and their sample sizes, were insufficient to draw firm conclusions. Further studies are needed.

Keywords

Lepidium meyenii; Maca; Erectile dysfunction; Systematic review

1. Introduction

One of the most common types of sexual dysfunction in men is erectile dysfunction (ED), which affects half of all men between the ages of 40 and 70 years [1]. ED is currently treated with oral medications (sildenafil, tadalafil, avanafil and vardenafil) [2]. ED therapy can involve the use of numerous other tools, such as intracavernosal or topical vasoactive agents, vacuum devices, extracorporeal shockwave therapy [3], prostheses, and sexual rehabilitation [3–8]. Despite significant advances, the best treatment for ED is still unknown. ED has been treated with a variety of herbal medicines, such as the ginseng and maca (*Lepidium meyenii*) plants [9, 10]. Women and men in the Andes have long relied on maca, a plant that is native to the region, to increase their fertility.

Maca has been shown to have androgen-like effects in rats, thereby increasing sexual activity and daily sperm production [11–13]. Animal studies suggest that maca has spermatogenic and fertility-enhancing effects, probably due to the phytosterols or phytoestrogens present in maca [12]. Several *in vivo* studies have shown that maca can improve sexual behavior and enhance androgen-like effects in rats [14, 15]. Systematic reviews have suggested that maca increases sperm count and motility and improves sexual function in humans [13, 16, 17]. The possible bioactive constituents of maca include macaridin, macamides, macaene, gluosinolates, maca alkaloid, and maca nutrients [12]. A recent study showed that maca significantly increased serum and penile concentrations of NO and penile cGMP, suggesting that sexual enhancement may be regulated by the NO-cGMP pathway [18]. Although maca has shown positive effects on sexual function regardless of sex [17], there have been no comprehensive reviews of its effects on ED in men. The aim of this study was to determine whether maca is an effective treatment for ED in men.

2. Methods

2.1 Registration

The protocol was registered at reviewregistry 1346 [19]. The standard methods of performing systematic reviews were followed for this review. The reporting of this review adheres to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 Checklist [20].

2.2 Inclusion and Exclusion Criteria

2.2.1 Types of Studies

Randomized controlled trials (RCTs) were included in this systematic review. We excluded trials, case studies, case series, qualitative studies and uncontrolled trials. RCTs published in the form of abstracts were included.

2.2.2 Types of Participants

We included studies that involved adult men with ED, irrespective of type and pathologic basis.

2.2.3 Types of Interventions

All maca preparation types were included in the study, regardless of source, age, processing stage, or dosage. One complex herbal drug containing maca was excluded from our study.

2.2.4 Types of Comparisons

Placebo or phosphodiesterase 5 (PDE-5) inhibitors were considered. We excluded studies in which the control groups received other types of herbal medicines and complementary therapies.

2.2.5 Types of Outcome Measures

The primary outcomes were erectile function and adverse events.

The secondary outcomes were sexual satisfaction and quality of life (QoL).

2.3 Search Method for Identifying Studies

The data sources used were PubMed, the Allied and Complementary Medicine Database (AMED), EMBASE, the Cochrane Central Register of Controlled Trials, six Korean medical databases (Korean Studies Information, DBPIA, Korea Institute of Science and Technology Information, KERIS, KoreaMed, and the Korean National Assembly Library), and one Chinese medical database (China National Knowledge Infrastructure (CNKI); https://www.cnki.net). We searched these DBs from their inception to May 2022. There were no language or chronological restrictions. The terms "(*Lepidium meyenii* OR maca) and (sexual dysfunction or erectile dysfunction or aphrodisiac or sexual performance or impotence)" were used for the search. All references in the articles we found were carefully checked for other publications on similar topics.

2.4 Data Extraction and Risk of Bias Assessment

Data were extracted from all publications by two independent reviewers according to prespecified criteria. We identified the authors, year of publication, country, sample size, age of participants, type of maca, dose, treatment duration, main outcomes, and adverse events. For analysis, the extracted data are presented in tables. The review authors (HWL and KJK) based their assessment on the Risk of Bias Assessment Tool (RoB 2.0) developed by the Cochrane Collaboration [21]. The following five aspects were examined: randomization, deviations from planned interventions, missing outcome data, the measurement of outcomes, and the selection of reported outcomes. Risk of bias was graded as "low risk of bias", "some concern", or "high risk of bias" for each area of each study. Disagreements were resolved by involving a third reviewer (MSL) when necessary.

2.5 Grades of Recommendation, Assessment, Development and Evaluation (GRADE) System

We used the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) system to evaluate the level of evidence [22]. The quality of evidence was categorized as high, moderate, low or very low quality.

2.6 Data Synthesis

The Cochrane Collaboration Review Manager (v.5.4.1) software for Windows (Cochrane Collaboration, 2020) was used to perform statistical analyses. To examine clinical effectiveness, categorical data were analyzed in terms of risk ratios. In addition, the mean difference (MD) was used to evaluate continuous data. Both continuous and categorical variables are reported as efficacy values with 95% confidence intervals. In cases where the scales of the outcome variables varied, the standardized MD was preferred over the weighted MD. If heterogeneity ($p < 0.1$ *via* the chi-square test and Higgins $I^2 \geq 50\%$) was detected, we performed subgroup analyses to determine the reason for the clinical heterogeneity. Publication bias was assessed using the Egger regression method and funnel plots.

3. Results

3.1 Study Description

The literature review identified 137 papers, 135 of which were excluded (Fig. 1). Two RCTs met our inclusion criteria [23, 24]. Table 1 (Ref. [23, 24]) summarizes the main results of these studies. One RCT was conducted in Italy [24], while the other was conducted in Japan [23]. Both RCTs used a two-arm parallel group design and included 79 participants. Daily maca doses were 1.2 g [23] or 2.4 g [24] over 8 to 12 weeks, respectively. As outcome measures, these studies used the International Index of Erectile Dysfunction (IIEF)-5 [24] and the IIEF-15 [23]. One RCT examined commercial products [23], while the other examined biologically dried maca [24].

3.2 Risk of Bias

Two studies were assessed using the RoB 2.0 tool (Fig. 2). For the randomization process, one study [23] reported a simple randomization method (using random numbers), and the other study [24] only provided a statement that randomization was conducted. Only one study [23] reported that randomization allocation was concealed. For deviations from the intended interventions, both studies [23, 24] provided a statement that the trial was double-blinded and did not describe the blinding methods in detail. Intention-to-treat analysis was used to estimate the effect of the interventions, and there were no dropouts reported in either study [23, 24]. The trial protocols/registrations were also not available for either study [23, 24]. Overall, the risk of bias of the two included studies

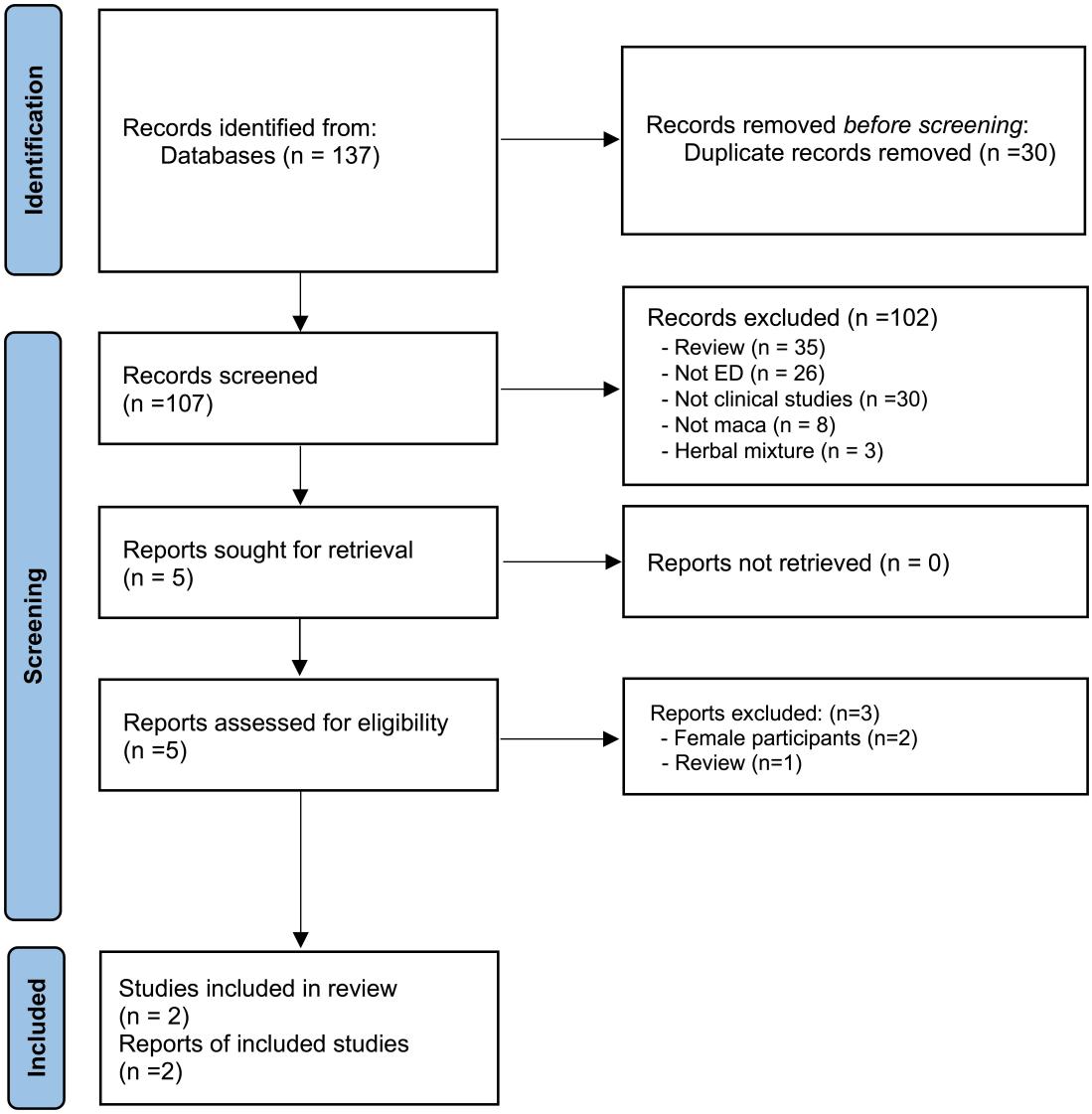

FIGURE 1. Study selection process. ED: erectile dysfunction.

TABLE 1. Summary of randomized clinical trials with maca for men with erectile dysfunction.

First author (year) [ref] Country	Sample size/Condition Age (years)/Duration of disease	Intervention (regimen) Control (regimen)	Main outcome measures	Results	Adverse events
Zenico (2009) [24] Italy	50/Mild ED (17≤ IIEF-5 ≤21) 36/n. r.	(A) Maca (pulverised dehydrated maca roots directly imported from Peruvian Andes, tablets, 2400 mg daily for 12 weeks, n = 25), no follow-up (B) Placebo tablets (n = 25)	EF (IIEF-5)	MD, 1.10 (0.61, 1.59), $p < 0.001$	n. r.
Ito (2020) [23] Japan	32/Mild to moderate ED (17≤ EF domain of IIEF-15 ≤25) 36 (45-65)/n. r.	(A) Maca (company commercial product, gelatinised maca, 1200 mg daily for 8 weeks, n = 14), no follow-up (B) Placebo tablets (n = 15)	EF (IIEF-15)	MD, 2.80 (−2.34, 7.94), $p = 0.29$	None

ED, erectile dysfunction; EF, erectile function; IIEF, International Index of Erectile Dysfunction; MD, mean difference; n. r.: not reported. Both studies did not report the study period.

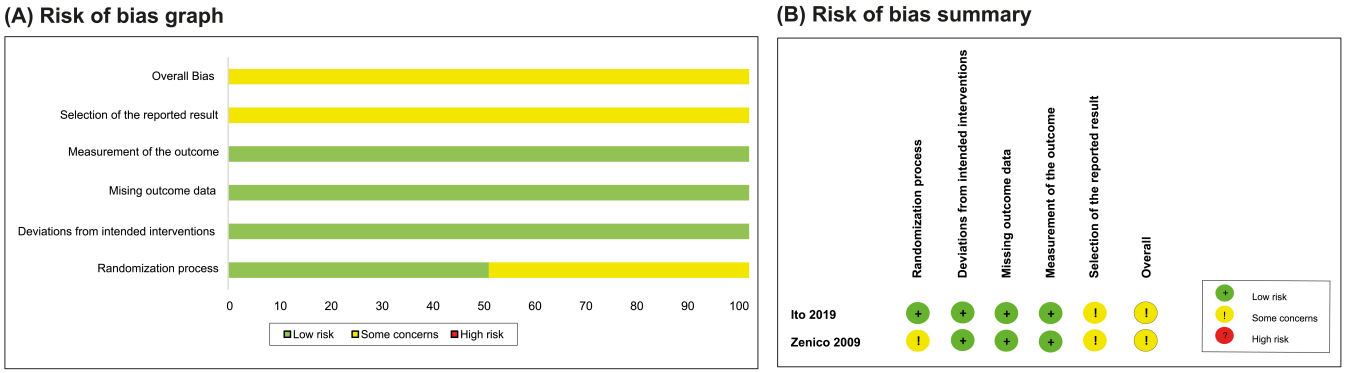

FIGURE 2. Risk of bias. (A) Risk-of-bias graph and (B) risk-of-bias summary.

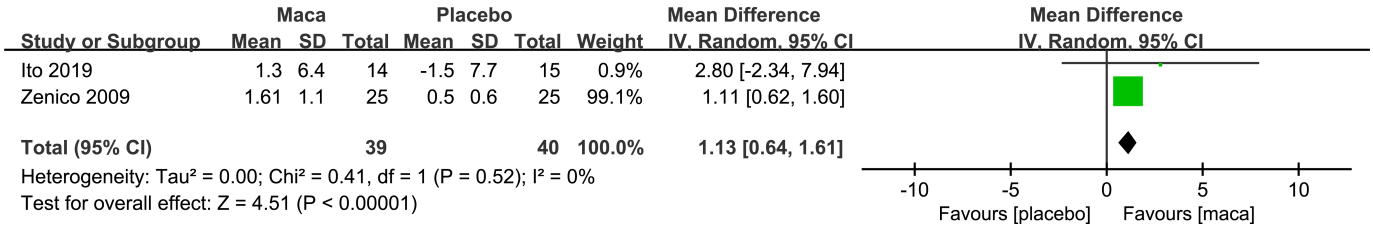

FIGURE 3. Forest plot of the effect of maca on erectile function.

was judged to be concerning.

3.3 Outcomes

Zenico *et al.* [24] assessed the effects of maca in patients with mild ED. Participants were randomized into the following groups: the maca (n = 25) and placebo (n = 25) groups. At the end of the treatment period, there were significant differences in EF (IIEF-5) between the two groups ($p < 0.001$).

Ito *et al.* [23] investigated the effects of maca in patients with mild ED. Thirty-two patients were randomly allocated to the maca group (n = 16) or to the placebo group (n = 16). After eight weeks of treatment sessions, there were no significant differences in EF (IIEF-15) between the two groups ($p = 0.29$).

In a meta-analysis of the two RCTs, maca was shown to have a positive effect on EF (n = 79, MD 1.13: 0.64 to 1.61, $p = 0.01$; $I^2 = 0\%$, $p < 0.0001$)(Fig. 3).

3.4 Certainty of Evidence

According to the GRADE system, the EF outcome was ranked as having low-quality evidence. There was some concern regarding the risk of bias across studies. This study was judged to have methodological limitations. There were significant benefits because the total number of patients enrolled in both studies was small. We determined that the evidence had bounded inaccuracies. The details of the evidence quality assessment are shown in Table 2.

4. Discussion

The effects of maca on ED have been studied in only a few RCTs. Although maca appears to improve EF, few studies with limited sample sizes have investigated this topic, which calls into question the validity of the research (Low CoE).

Although both the RCTs included placebo controls, neither study reported its blinding procedure. Both RCTs had small sample sizes, and the studies may not have been adequately powered. One study failed to describe its methods, and its overall ROB was uncertain [24]. The recommended dosage of maca is unclear. Single-dose studies have used concentrations of 1.2 g/day for 8 weeks [23] and 2.4 g/day for 12 weeks [24]. One RCT, in which a low dose was administered over a short treatment duration [23], failed to demonstrate any beneficial effects of maca, while the other RCT, in which a higher dose was administered over a longer treatment duration [24], reported positive results. The lack of effectiveness found in the former study may have been due to the use of an insufficiently high dose.

In addition, the data from the two studies could be combined. The most common reasons for using meta-analyses are to strengthen the impacts of studies, refine their results, clarify ambiguities due to conflicting results, and develop new hypotheses [25]. Although several experiments can be combined for a meta-analysis, such statistical analyses do not guarantee the validity of the conclusions that are drawn. Moreover, the findings of a meta-analysis based on only two RCTs must be interpreted with caution.

We excluded studies with nonrandomization from our study. While we believe that nonrandomization increases the likelihood of biased selection, we believe that the results are irreversible. Such studies, in our opinion, would not be able to provide objective clinical data. In these studies, there was no conclusive evidence for the efficacy of the use of maca for improving EF. Therefore, we believe that it was correct to exclude studies of this type.

This study has several limitations. First, because of the small amount of data and low CoE, it is likely that the evidence considered is insufficient. Second, the two RCTs have not

TABLE 2. Summary of findings.

Outcomes	No of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with placebo	Risk difference with Maca
Erectile function (EF) assessed with: IIEF	79 (2 RCTs) No follow-up	⨁⨁◯◯[a,b]LOW	-		MD 1.13 higher (0.64 higher to 1.61 higher)

**The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). CI, confidence interval; MD, mean difference. [a]: Downgraded by one level: unclear or high risk of bias; [b]:Downgraded by one level: small sample size. GRADE Working Group grades of evidence. Low certainty: our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.*

been independently replicated because of a lack of reporting details. Third, publication biases and regional biases can affect systematic reviews and meta-analyses.

To date, there is no clear evidence in research that maca benefits people suffering from ED, nor of the potential magnitude of the benefit. More solid results are certainly desirable to determine the best ED patients for treatment with maca and the possibility of using maca in combination with other medications. Nevertheless, our results suggest that maca may be one of the treatment options for ED. However, this conclusion, based on the studies included in this review, should be considered with caution, given the limitations mentioned above.

Future research on the effects of maca should include a study design that is appropriate to the subject. Double-blind, placebo-controlled trials with a randomization scheme that conceals participant allocation are preferable, as are studies that use appropriate sample size calculations and determine the optimal treatment dose. Moreover, studies that use validated outcome measures and provide detailed descriptions of the interventions studied are needed.

5. Conclusions

We found limited evidence to support the claim that maca can improve EF in men with mild ED. However, the number of studies, their sample sizes, and the quality of the primary research were insufficient to draw firm conclusions from the data. More thorough research is needed.

ABBREVIATIONS

ED, erectile dysfunction; EF, erectile function; MD, mean difference; RCT, randomized controlled trial; ROB, risk of bias.

AVAILABILITY OF DATA AND MATERIALS

All data generated or analyzed during this study are included in this published article.

AUTHOR CONTRIBUTIONS

HWL and MSL—designed and performed the research. HWL, MSL and KJK—analyzed the data and wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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