



Review

Maca (*Lepidium meyenii*) for treatment of menopausal symptoms: A systematic review

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ABSTRACT

Maca (*Lepidium meyenii*), an Andean plant of the brassica (mustard) family has been used for centuries in the Andes as an adaptogenic plant to manage anemia, infertility and female hormone balance. The aim of this review was to assess the evidence for and against the effectiveness of the maca plant as a treatment for menopausal symptoms. We searched 17 databases from their inception up to June 2011 and included all randomized clinical trials (RCTs) that compared any type of maca-based intervention to a placebo for the treatment of menopausal symptoms. All studies were assessed for methodological quality using the Cochrane 'risk of bias' assessment tool. Four RCTs met all inclusion criteria. These RCTs tested the effects of maca on menopausal symptoms in healthy perimenopausal, early postmenopausal, and late postmenopausal women. Using the Kupperman Menopausal Index and the Greene Climacteric Score, all RCTs demonstrated favorable effects of maca. There have been very few rigorous trials of maca for menopausal symptoms. The results of our systematic review provide limited evidence for the effectiveness of maca as a treatment for menopausal symptoms. However, the total number of trials, the total sample size, and the average methodological quality of the primary studies, were too limited to draw firm conclusions. Furthermore, the safety has not been proved yet. Therefore, the efficacy and safety should be tested in larger studies.

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1. Introduction

Hormone replacement therapy (HRT) can effectively alleviate the symptoms of menopause. Long-term HRT, however, increases the risk of several conditions, including breast cancer and coronary heart disease [1]. Thus, many women turn to alternatives such as

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herbal supplements, which, whether correct or incorrect, are often perceived as natural and therefore free of adverse effects.

Maca (*Lepidium meyenii*) is an Andean plant of the brassica (mustard) family that is widely grown in several South American countries [2]. Maca has been traditionally used for centuries in the Andes as an adaptogenic plant to manage anemia, infertility and female hormone balance [2,3]. The introduction of maca in Japan, Europe, and the US has recently occurred [4], and it is increasingly being used in many parts of the world. Although little scientific data support its efficacy, maca is marketed on the internet as a product that benefits sexual function and relieves menopausal symptoms [5].

Maca has been reported to have low toxicity (LD50 for mice is >16.3 g/kg). In both in vivo and in vitro studies, maca administered after being boiled, regardless of extraction method, demonstrated no toxicity [6]. Valentova et al. [7] demonstrated that maca possesses a slight cytoprotective effect in vitro studies. Gonzales et al. [8,9] demonstrated a dose-dependent reduced length of stage I seminiferous tubules and increased length of stage VIII with maca treatment. In a study by Zhang et al. [10], ethanolic extracts of maca reduced ovariectomy-related reduction of lumbar-spine bone mineral density and calcium loss in ovariectomized rats. Maca extracts do not affect the cell morphology and viability of rat primary hepatocytes [7].

Several in vivo experiments suggest that maca has fertility-enhancing properties, likely due to phytoosterols or phytoestrogens [11,12]. The potentially bioactive ingredients include macaridine, macamides, macaene, glucosinolates, maca alkaloid, and maca nutrients [12]. Maca contains several bioactive components including alkaloids, glucosinolates, sterols, fatty acids, minerals, and vitamins [3]. Maca alkaloids have been reported to have anti-sterility activity [13]. Gonzales et al. [14] reported that the glucosinolates of maca could function as antioxidants and free radical scavengers. Additionally, red maca (*L. meyenii*) has been shown to reduce prostate size in rats. However, there have been no clear data presented on biologically active maca components until now.

Some clinical trials have also suggested that maca may have favorable effects on menopausal symptoms in postmenopausal women [15]. Currently, one systematic review of maca for sexual function is published [16]. However, no systematic review of maca on menopausal symptom is available. The objectives of this systematic review were to summarize and critically assess the clinical evidence for and against the effectiveness of maca as a treatment for menopausal symptoms and to offer recommendations for future research.

2. Methods

2.1. Data sources

We searched records from the following electronic databases up to June 2011: Medline, AMED, CINAHL, EMBASE, PsycInfo, the Cochrane Central Register of Controlled Trials, The Cochrane Database of Systematic Reviews, DARE, the Psychology and Behavioral Sciences Collection, six Korean Medical Databases (Korean Studies Information, DBPIA, Korea Institute of Science and Technology Information, KERIS, KoreaMed, and Korean National Assembly Library), the Chinese Medical Database (CNKI; www.cnki.net) and the Japan Science and Technology Information Aggregator,

Electronic. The search terms used were “(maca OR *Lepidium*) AND (menopause\$ OR climate OR perimenopause OR peri menopause OR post menopause\$ OR post menopause OR hot flash\$ OR hot-flash\$ OR hot flush\$ OR hot-flush\$)”. To include multiple possible terms, we used the wild character ‘\$’ for each search term. We also manually searched our departmental files and relevant journals [FACT (Focus on Alternative and Complementary Therapies) and Forschende Komplementärmedizin (Research in Complementary Medicine)] through June 2011. The references in all located articles were searched manually for further relevant articles. In addition, dissertations and abstracts were included.

2.2. Study selection

We included all articles reporting a randomized clinical trial (RCT) in which peri- or postmenopausal women were treated with any type of maca (*Lepidium*) preparation, regardless of the maca's origin. Trials were included if they employed maca as the sole treatment or as an adjunct to conventional treatments compared to a placebo control. Trials comparing two different extracts or doses of maca and those with no clinical data or with insufficient data were excluded. No language restrictions were imposed.

2.3. Extraction of data and assessment of risk of bias

All of the included articles were read in full. Three independent reviewers (MSL and BCS) extracted the data according to predetermined criteria (Table 1). The Cochrane classification (i.e., sequence generation, blinding, incomplete outcome measures and allocation concealment) was applied for evaluation of the risk of bias [17]. Differences in opinion between the reviewers were settled through discussion.

2.4. Data analysis

We originally intended to conduct a formal meta-analysis; however, the absence of data needed for possible pooling prevented us from doing so. Thus, the findings of the review are presented as a descriptive synthesis. The method that gave the best evidence for synthesis [18] was used to formulate the conclusions on the effectiveness of maca. This method consists of four levels of evidence and takes the methodological quality and outcomes of the studies into account [19]. These levels of evidence are:

- Level 1: strong evidence – provided by generally consistent findings in multiple, relevant, high-quality RCTs.
- Level 2: moderate evidence – provided by generally consistent findings in one relevant, high-quality RCT and one or more relevant, low-quality RCTs.
- Level 3: limited evidence – provided by generally consistent findings in multiple relevant, low-quality RCTs.
- Level 4: inconclusive evidence – provided by only one relevant, low-quality RCT, no relevant RCTs or RCTs with conflicting results.

Effect size (ES) and 95% confidence interval (CI) were calculated for menopausal symptoms using Cochrane Collaboration's software [Review Manager (RevMan) Version 5.0 for Windows. Copenhagen: The Nordic Cochrane Centre]. We used the generic inverse variance method in RevMan to analyze the difference in means between the

Table 1
Summary of double-blind, randomized clinical crossover trials with maca for menopausal women.

First author (year) location	Sample size/condition age (years)	Intervention (regimen)	Control intervention (regimen)	Measurement of menopausal symptoms	Intergroup differences	Risk of bias [†] comment
Brooks (2008) [15] Australia	14 Healthy postmenopausal women who were not receiving hormone therapy either currently or within the previous 6 months 53.5 (±10.8)	Maca (dried powder taken in their breakfast cereal, soup or a milk shake, 3.5 g, once daily for 6 weeks, n = 14) <i>Lepidium meyenii</i>	Placebo power (refined white rice flour taken in their breakfast cereal, soup or a milk shake, 3.5 g/day, daily for 6 weeks, n = 14)	GCS (1) Total score (2) Psychological scale (3) Somatic (4) Vasomotor (5) Sexual dysfunction	(1) 17.3% more reduction than placebo, $P < 0.05$ (values not reported) (2) Total, ES, $-2.80 [-3.65, -1.95]$, $P < 0.001$; anxiety, ES, $-1.53 [-1.19, -1.08]$, $P < 0.001$; depression, ES, $-1.26 [-1.73, -0.79]$, $P < 0.001$ (3) ES, $0.27 [-0.03, 0.57]$, $P = 0.08$ (4) ES, $0.04 [-0.33, 0.41]$, $P = 0.83$ (5) ES, $-0.70 [-0.85, -0.55]$, $P < 0.001$	(U, U, L, U) No placebo run-in period, crossover design
Meissner (2006) [23] [*] Australia	102 Caucasian early postmenopausal women 30 ml U/mL \leq FSH 49–58	Maca [hard gel encapsulated with pre-gelatinized dried and pulverized hypocotyls of maca, total 2 g daily (500 mg \times 2 capsules \times 2 times/day) for 2 months, n = 102] <i>Lepidium peruvianum Chacon</i>	Placebo power (hard gel encapsulated with sorbitol and cellulose, 500 mg \times 4 capsules/day for 1 month, n = 102)	(1) KMI (2) GCS	(1) APMM (n = 55), MD, $-11.87 [-14.14, -9.60]$, $P < 0.001$; AMMP (n = 33), MD, $-7.8 [-10.35, -5.33]$, $P < 0.001$ (2) APMM (n = 55), MD, $-7.45 [-9.19, -5.71]$, $P < 0.001$; AMMP (n = 33), MD, $-2.85 [-4.69, -1.01]$, $P = 0.02$	(L, L, L, L) One month placebo and 2 months Maca use
Meissner (2006) [23] [*] Australia	66 Caucasian early postmenopausal women 49–58	Maca [hard gel encapsulated with pre-gelatinized dried and pulverized hypocotyls of maca, total 2 g daily (500 mg \times 2 capsules \times 2 times/day) for 1–3 months, n = 66] <i>Lepidium peruvianum Chacon</i>	Placebo power (hard gel encapsulated with sorbitol and cellulose, 500 mg \times 4 capsules/day for 1–2 months, n = 66)	(1) KMI (2) GCS	(1) APMMP, MD, $-7.33 [-10.03, -4.63]$, $P < 0.001$ APPMM, MD, $-9.95 [-12.52, -7.38]$, $P < 0.001$ AMMPP, MD, $-5.94 [-8.49, -3.39]$, $P < 0.001$ AMMPM, MD, $-5.92 [-8.37, -3.47]$ (2) APMMP, MD, $-2.23 [-5.21, 0.75]$, $P = 0.14$ APPMM, MD, $-3.65 [-6.47, -0.83]$, $P = 0.01$ AMMPP, MD, $1.59 [-1.10, -4.28]$, $P < 0.001$ AMMPM, MD, $-0.60 [-3.70, -2.50]$, $P < 0.001$	(L, L, L, L)
Meissner (2006) [24] Australia	20 Caucasian women in perimenopausal stage 41–50	Maca [hard gel encapsulated with pre-gelatinized dried and pulverized hypocotyls of maca, total 2 g daily (500 mg \times 2 capsules \times 2 times/day) for 2 months, n = 20] <i>Lepidium peruvianum Chacon</i>	Placebo power (hard gel encapsulated with sorbitol and cellulose, 500 mg \times 4 capsules/day for 2 months, n = 20)	KMI	Maca treatment alleviated postmenopausal symptoms; $P < 0.05$	(L, L, L, U) No placebo run-in period, crossover design

DB: double blind; MCT: multi-centre trial; GCS: Greene's Climacteric Score; FSH: follicle stimulation hormone; KMI: Kupperman's Menopausal Index; A: admission; M: maca session; P: placebo session; ES: effect size; MD: mean difference.

[†] Risk of bias: (Sequence generation, incomplete outcome measures, blinding, allocation concealment); L: low risk of bias; H: high risk of bias; U: uncertain risk of bias.

^{*} Two trials reported in the same paper.

two groups because most of the included trials reported only mean differences and standard errors.

3. Results

3.1. Study description

The literature searches revealed 17 articles, of which 14 studies had to be excluded (Fig. 1). Among these, three RCTs [20–22] were duplicate publications with other included trials [23]. Four RCTs [one article [23] contained two trials] met our inclusion criteria, and their key data are summarized in Table 1 [15,23,24]. All RCTs were conducted in Australia and adopted a double-blind, placebo-controlled crossover design. The four trials included a total of 202 subjects. Three RCTs employed pre-gelatinized maca [23,24], and dried maca was administered in the fourth RCT [15]. The doses were 2.0–3.5 g of maca daily for 1.5–2 months. The outcome measures in these trials were Green Climacteric Scores (GCSs) [15,23] and the Kupperman Menopausal Index (KMI) [23,24]. All four RCTs used commercial products.

3.2. Risk of bias

Three RCTs reported their methods of sequence generation [23,24]. All of the included trials employed a double-blind design. Three trials reported completion of outcome measures [23,24]. Two RCTs in one publication employed allocation concealment [23].

3.3. Details of included trials

Brooks et al. [15] conducted a double-blind, placebo-controlled RCT to assess the effects of maca (details were not reported) for menopausal symptoms in postmenopausal women. Fourteen healthy postmenopausal women were divided randomly into two crossover groups. They received 3.5 g/day of either powdered maca for 6 weeks or a matching placebo for 6 weeks over a 12-week period. The outcome measures were reported as GCSs. Significant improvements in the total GCS score ($P < 0.05$), sexual function ($P < 0.001$) and psychological symptoms ($P < 0.001$) such as anxiety ($P < 0.001$) and depression ($P < 0.001$) after maca consumption compared to placebo were reported.

Meissner et al. [23] tested the effects of maca (*Lepidium peruvianum*) on menopausal symptoms with GCSs and KMI in early postmenopausal women. Patients ($n = 102$) were randomized into two experimental protocols. One group ($n = 62$) was given a placebo for 1 month and maca for 2 months (commercial Maca-GO, 2 g/day), whereas the other group ($n = 40$) was given maca for 2 months and placebo for 1 month. The overall menopausal symptoms with both the GCS ($P < 0.001$) and KMI ($P < 0.001$) were improved during maca intake compared to placebo.

The same group [23] also carried out an RCT to assess the effects of maca compared to placebo on GCS and KMI in 66 early postmenopausal women randomly divided into six different treatment groups. In this study, however, the authors only reported the results of four of the groups. Their conclusion was that maca significantly improved the symptoms of GCS ($P < 0.001$) and KMI ($P < 0.001$) compared to placebo.

Meissner et al. [24] performed a pilot RCT evaluating the effect of maca (*L. peruvianum*) compared to placebo. Twenty perimenopausal women were randomized into two groups treated with maca ($n = 10$) or placebo ($n = 10$). The primary outcome (measured as KMI) was improved following maca treatment compared to placebo ($P < 0.05$).

3.4. Level of evidence

Three RCTs, which had a low risk of bias, reported positive effects of maca (*L. peruvianum*) on menopausal symptoms [23,24]. The designs of these RCTs, however, were limited, making it difficult to identify the effectiveness of maca. One RCT, which had a high risk of bias, also showed positive effects of maca powder on menopausal symptoms [15]. Therefore, the evidence was limited (level 3) but suggested that maca was more effective than placebo treatment.

4. Discussion

Perhaps the most important finding of this systematic review is that there have been very few rigorous trials examining the effects of maca on menopausal symptoms. This lack is surprising given that maca has been marketed as effective for the treatment of menopausal symptoms. Three of the four studies concerning menopausal symptom treatment originated from a single research group, and most of the studies reviewed herein were burdened with methodological flaws. Although the results of these studies suggest that maca is more effective than a placebo in improving menopausal symptoms, the small number of trials and small total sample size limit the utility of these studies. Furthermore, none of the included studies assessed the safety of maca.

Although all included RCTs used placebo controls and were double-blind designs, none reported the success of their blinding methods. Moreover, none of the studies included a power calculation. The same group authored three of the four RCTs, therefore warranting independent replications of these studies. The study design of all four RCTs had several caveats, making it difficult to resolve the positive effects of maca on menopausal symptoms. None of the RCTs included washout periods between crossovers; thus, the possibility of carryover effects must be considered. In two of the studies, participants were given placebo or maca for unequal amounts of time (2 months vs. 1 month or vice versa) [23]. Furthermore, none of the included trials had placebo run-in periods. Considering that menopausal symptoms have been shown to be vulnerable to placebo [25], a placebo run-in period is warranted. None of the included trials reported parameter information relevant to menopausal symptoms such as the time since menopause, body mass index, prevalence of smoking, and medical history including thyroid diseases. The participant ages were also not provided for either the maca or the placebo groups. Future studies should include the relevant parameter information related to menopause symptoms to allow for a clear interpretation of the trial results.

The RCTs were clinically heterogeneous, and some of the trials provided insufficient data. Statistical pooling was thus impossible and would not have been informative. Trials were disparate with regard to the type of maca, dosage, study design and treatment duration. Therefore, we performed a qualitative review and opted for a synthesis of the best evidence. In such analyses, sound evidence should be drawn only from studies of higher quality, which are less likely to be biased. Although three of the reported trials are of higher quality, their study designs were not good enough to clarify the effectiveness of maca. This factor turns the moderate evidence level into limited evidence that suggests that maca is effective for relieving menopausal symptoms.

The extent to which the therapeutic effects of maca depend on the type of maca used and the amounts of various constituents in the preparation is unclear. The optimum dose of maca is unknown. Three RCTs [23,24] employed 2.0 g/day and one RCT [15] used 3.5 g/day. There are no established criteria for dosing levels of maca for medicinal use. The information for half-life is also not available.

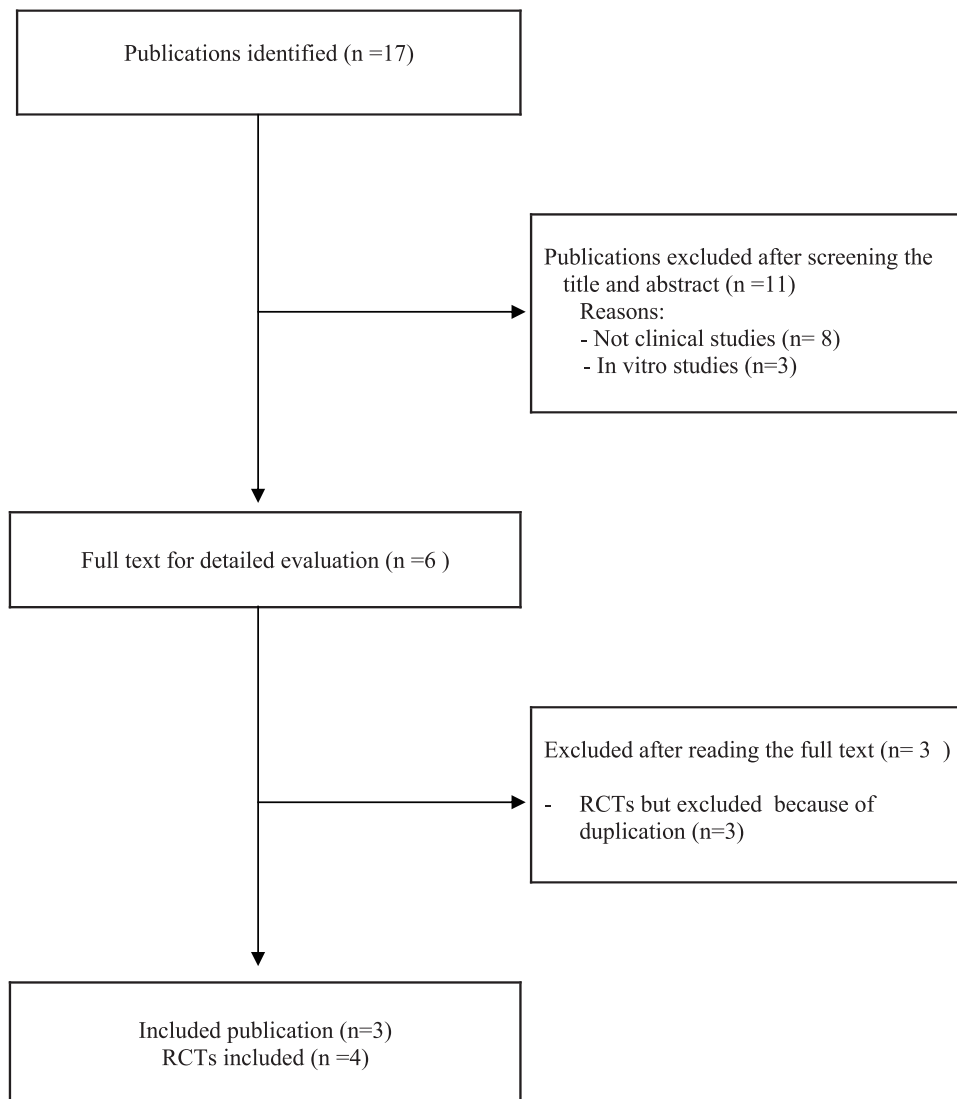


Fig. 1. Flowchart for selection of inclusion trials. RCT: randomized clinical trial.

Therefore, dose determination studies are required to identify the optimum dose.

The origin of maca is also a concern. The therapeutic effects of maca may vary according to the regions in which it is cultivated. Most studies have been performed with cultivated maca from Peru (*L. peruvianum*), which has been claimed to be unique compared to other maca species. Of all the studies included in our review, three RCTs [23,24] applied commercially developed gelatinized, dried and pulverized hypocotyls of *L. peruvianum*. One study used commercially developed dried maca (the origin was not reported) [15]. The difference of ES may come from the type of maca, extraction methods, and/or doses.

The possible mechanisms that may be involved in maca for menopausal symptoms are hypothetical. One possible mechanism may be the estrogenic activities previously associated with female fertility [3,26]. One study has proposed that maca may stimulate the production of estrogens that optimize ovarian function and suppress Follicle-stimulating hormone [23], while the other studies failed to do so [9,15]. Therefore, further investigations are needed to clarify these results. Another possible mechanism is the stimulation of hormonal reserves via fortification of the body's ability to regain and maintain hormonal homeostasis in the face of stressors [2,21]. None of these theories, however, have been fully established.

One argument for using maca for the management of menopausal symptoms might be that it causes fewer adverse effects than conventional drug treatments. None of the four RCTs assessed adverse events among maca users. It has been claimed that there are no reports of adverse events after consuming maca in food. However, natives in Peru recommendation for usage is maca be boiled before its consumption because of adverse events of fresh maca. Five cases of adverse events were noted in the Australian Adverse Drug Reactions database [13]. They included Budd-Chiari syndrome, attention disturbances, weight loss, agitation, abdominal pain, epistaxis, gingival bleeding, headache, nausea, vomiting, and abnormal liver function. It is possible that maca was directly responsible for the adverse events. However, in the Budd-Chiari syndrome case, the 40 year-old female patient was concomitantly using other medicine. The other potential adverse events of maca may relate to its estrogen-like functions. The result could be possible adverse events related to estrogen-sensitive diseases such as endometriosis and breast cancer. Therefore, adverse events should be tested in future studies or post-marketing surveillance.

The value of conducting a systematic review of a limited number of studies with low methodological quality may be considered controversial. The conclusion is often trivial for many practically and traditionally used medicines. However, systematic reviews can

increase power, improve precision, answer questions not asked by individual studies, settle controversies arising from conflicting results, improve the quality of future primary studies, and generate new hypotheses [27–29]. Moreover, systematic reviews can avoid biases and draw conclusions in a manner that is as objective as possible [28]. Finally, systematic reviews that fail to find primary studies to include can be valuable in that they may indicate important gaps in our knowledge. Nonetheless, systematic reviews are retrospective and strongly depend on the quality of the primary studies included [28], and they may lead to contradictory overall conclusions [28]. The use of statistics does not guarantee that the results are valid. In our case, given that the conclusions are from only four RCTs, the conclusions must remain tentative.

Our review has a number of other limitations. Although strong efforts were made to retrieve all RCTs on the subject, we cannot be absolutely certain that our searches located all relevant RCTs. Moreover, selective publishing and reporting are major causes of bias that have to be considered. It is conceivable that several negative RCTs remain unpublished and thus distort the overall picture [30,31]. It is noteworthy that a number of studies were supported by manufacturers of maca products, a factor that may have introduced a degree of bias. Most trials sponsored by the industry had positive outcomes. In this review, three included RCTs [23,24] received the maca powder for trials from a company associated with maca product (NatureCorp Pty, Ltd.). Another possible bias is that all of the included trials were carried out in Australia. There is the possibility that the effects are crucially dependent on cultural context; however, more research would be required to systematically address this interesting point. Further limitations include the paucity and the often suboptimal methodological quality of the primary data. Some of the RCTs included in the present review were not successful in minimizing bias. These factors limit the conclusiveness of this systematic review.

Future trials testing the effects of maca should adhere to rigorous trial designs that are adequately suited to the research question being asked. Such trials should preferably be randomized, double-blinded, and be controlled for placebo effects. Moreover, they should have adequate allocation concealment, optimal treatment dosages and sample sizes based on proper sample size calculations, use validated outcome measures and include a full description of the actual interventions being tested. According to the results of our analysis, future studies should include a placebo run-in phase and at least two consecutive phases of maca use to clarify its effectiveness. Furthermore, the use of standardized maca is essential to control the bias from the differences of maca formulation. Importantly, future studies should be reported adequately, preferably according to CONSORT guidelines [32].

In conclusion, the results of our systematic review provide only limited evidence for the effectiveness of maca in improving menopausal symptoms. The total number of trials, total sample size and average methodological quality of the primary studies are too low to draw firm conclusions. Moreover, our current knowledge of the risks of maca intake is insufficient. Therefore, more rigorous studies appear to be warranted.

Contributors

Myeong Soo Lee and Byung-Cheul Shin designed the review, performed searches, appraised and selected trials, extracted data, contacted authors for additional data, carried out analysis and interpretation of the data, and drafted this report.

Eun Jin Yang, Hyun-Ja Lim and Edzard Ernst reviewed and critiqued on the review protocol and this report, assisted in designing of the review

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