Phytomedicine Plus 2 (2022) 100326

Contents lists available at ScienceDirect

Phytomedicine Plus

journal homepage: www.sciencedirect.com/journal/phytomedicine-plus

A systematic review of the versatile effects of the Peruvian Maca Root (Lepidium meyenii) on sexual dysfunction, menopausal symptoms and related conditions

Cherie Bower-Cargill, Niousha Yarandi *, Andrea Petróczi

School of Life Sciences, Pharmacy and Chemistry, Kingston University, Kingston upon Thames, Surrey, KT1 2EE, UK

ARTICLE INFO

Keywords:
Maca
Lepidium meyenii
Lepidium peruvianum
Systematic review
Clinical
Pre-clinical

ABSTRACT

Background: The *Lepidium meyenii* plant also known as Peruvian Maca, originates from high altitudes in the Andes, it has a high nutritional content and is extensively used as an herbal supplement for conditions such as sexual dysfunction, semen quality and menopausal symptoms.
Objective: This systematic review was conducted to assess the effects of Maca on variety of conditions and not limited to sexual dysfunction, semen quality and menopausal symptoms.
Methods: An extensive systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2015. Three databases (PubMed, Science Direct and Google Scholar) in addition to patents were searched up to March 2021. The key criteria for inclusion were; (1) in vivo study (2) randomized controlled clinical trial; (3) subjects were given Maca regardless of the type, preparation and/or administration route; and (4) measurable clinical data on a physiological and/or psychological aspect were reported. Studies were categorised into human and animal model studies and were further grouped by the type and preparation of Maca, dose, duration and condition assessed. The studies were also assessed for risk of bias according to the Cochrane Collaborations tool. Studies were compared to ascertain whether a meta-analysis was feasible.
Results: A total of 57 studies, 14 clinical and 43 pre-clinical trials met the pre-defined criteria; although patent applications were searched none met the criteria. Nine different extraction methods of Maca were used with various coloured roots namely black, yellow and red roots or a mixture of all three. Different colour variations showed different effects thought to be due to the presence and/or concentration of secondary metabolites. Maca was reported to have an effect on conditions such as memory impairment, depression, bone structure, UV irradiations amongst others. Placebo and dose-dependant effects were observed in some studies. The overall quality of risk of bias was unclear due to insufficient information being published in addition to a high risk of reporting bias. Doses and durations varied, and an insufficient number of studies had further analysed whether these factors had an effect on the outcome made a meta-analysis unfeasible. Therefore, recommendations for future studies were discussed.
Conclusion: Evidence to date suggests that Maca root could be an effective treatment for a range of conditions with 55 out of 57 studies reporting an effect. Clinical trials with rigorous reporting and methods are warranted.

Introduction

Lepidium meyenii Walp. (Brassicaceae), also known as Peruvian maca is an annual, low growing plant that is found at high altitudes (3800–4400 m) in the Andes; however, maca can be grown outside of its natural habitat (Lim, 2015). Maca has been studied abundantly because of the reported health benefits (such as sexual dysfunction, semen quality and menopausal symptoms), especially species from North America, Europe, Yunnan province in China and the Andean region (Gonzales, 2012)

Maca has two different appearances depending on whether it happens to be in the vegetative or generative state containing both leaves and flowers which progressively get bigger; it also has a fused underground hypocotyl and taproot (Hermann and Heller, 1997). The shape

* Corresponding author at: Biomolecular Sciences, Kingston University, Penrhyn Road, Kingston upon Thames, London KT1 2EE, UK.
E-mail address: n.yarandi@kingston.ac.uk (N. Yarandi).

https://doi.org/10.1016/j.phyplu.2022.100326
Received 21 March 2021; Received in revised form 16 February 2022; Accepted 22 February 2022
Available online 2 August 2022
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and proportions of the root can widely vary and although any root is acceptable, those of about 5 cm long and 3–5 cm wide which are classed as medium sized roots are preferred because the cooking time is shorter with smaller root sizes (Hermann and Heller, 1997).

Although maca comes in different colours, yellow, red-white and black ecotypes are the most predominant and are responsible for 47.8%, 16.5% and 4.2% of the population respectively; Yellow roots are preferred as they are said to be sweeter compared to the other variations and the root of Maca is grown and consumed for a wide variety of health benefits (Hermann and Heller, 1997). The composition of fresh Maca is 80% water whereas dried Maca is similar in nutrition to maize, rice and wheat which includes carbohydrates, proteins, fibre and lipids (approx. 59%, 10.2%, 8.5% and 2.2% respectively) along with other compounds such as essential amino acids, fatty acids, sterols, alkaloids, calcium copper and iron, which is present in higher levels than in white potato (Hermann and Heller, 1997). To date, only the treatment of sexual dysfunction and menopausal symptoms with Maca have been comprehensively studied by a systematic review; therefore, a systematic review and meta-analysis if feasible should be conducted to bridge the gap of knowledge of the full effects of Maca on other conditions such as menopausal discomfort, anti-depressant and UV protection as well as reproductive biology.

Systematic reviews on Maca to date

There are four systematic reviews that cover the treatment of semen quality, sexual function, menopausal symptoms and erectile dysfunction with Maca, the latter including a meta-analysis, in addition there is not a systematic review including animal models to date. All concluded that the evidence was limited due to factors such as sample sizes, the overall methodical quality, number of trials and the safety of Maca leading to the requirement of more rigorous studies (Borrelli et al., 2018; Lee et al., 2011, 2016; Shin et al., 2010). Therefore, no firm conclusions were made for the effect of Maca on these parameters.

Aims

The overall aims of this study were to perform a systematic review and meta-analysis to bridge the gap in knowledge about the versatile effects of Maca in humans and animal models.

Phase 1

This phase was conducted with the aim to perform a comprehensive search to collate all relevant studies where Maca was used as a treatment. The final data-base consisted of 57 studies.

Phase 2

As a continuation of phase one for the purpose of this study the aim was to obtain a subset of studies to ascertain whether a meta-analysis was feasible for human and/or animal studies. To be able to fulfil this aim a systematic review was conducted and if a meta-analysis was unfeasible, the aim was to investigate the reasons why and to also recommend how future studies should be conducted for them to be suitable for a meta-analysis.

Methodology

A systematic review method was used, the main materials used throughout were PRISMA-P 2015, and the Cochrane handbook for systematic reviews of interventions version 5.1.0 (Higgins and Green, 2011; Moher et al., 2015)

Phase 1: Systematic review-database

Identification of the issue

The issue identified was that although Maca is widely used for a variety of different conditions and reasons, only sexual dysfunction, semen quality and menopausal symptoms have been investigated. Therefore, it was decided that a systematic review was warranted to answer the question 'Is Maca able to treat and be applied to other conditions?'

Protocol for literature search

A thorough literature search was done for studies that addressed Maca as a treatment without a limitation on the condition. This was done using a pre-determined set of eligibility criteria and a set of defined keywords. Three databases (PubMed, Science Direct and Google Scholar) in addition to patents were searched up to March 2021.

The key criteria for inclusion were; (1) in vivo study (2) randomized controlled clinical trial; (3) subjects were given Maca regardless of the type, preparation and/or administration route; and (4) measurable clinical data on a physiological and/or psychological aspect were reported. In vivo studies that met the inclusion criteria were included regardless of duration, dosage, and gender/species.

Studies were excluded if (1) Maca root was given in conjunction with any other supplement as the outcome cannot be associated with the effects of Maca alone (2) the method in which the study was carried out was not clear and (3) outcome(s) measured were not reported. The search terms used in the search were: *Lepidium meyenii* "or" Maca "or" *Lepidium Peruvianum* "and" method and the limitations of the search were articles published in English and in vivo trials. The collection of studies was conducted according to the PRISMA-P 2015 guidelines and any reasons for excluding a study were noted.

Phase 2- Systematic review and meta-analysis

Data extraction

The main characteristics of each individual study were extracted in duplicate. The lead author, sample, age, duration, placebo and treatment regimen, condition assessed, key outcomes, other outcomes and the type of Maca used were all tabulated (Tables B.1 and C.1: Systematic review-appendix B and C).

Quality assessment

The risk of bias for each study was assessed according to the Cochrane Collaborations tool. For the animal studies, attrition, reporting and two types of selection bias were assessed (Table 3), for the human studies performance and detection bias were assessed in addition to those mentioned for animal studies (Table 4)

Qualitative and quantitative analysis discussion

The data was qualitatively combined, and overviews of the findings were discussed.

To establish if studies were similar enough to combine for meta-analysis, subsets of human and animal studies were obtained and comparisons were made on; the outcome(s) measured, sample size, duration, dose, type of Maca, colour of roots used, subgroups, when the outcome (s) were measured and how the data were expressed (Tables 1 and 2-Meta-analysis) The reasons why a meta-analysis was not feasible and recommendations to make future studies suitable were discussed.

Results

Phase 2- Data extraction-human subset for meta-analysis
Phase 2- Data extraction-animal subset for meta-analysis
Risk of bias assessment

Table 1-
Aspects from human candidate studies compared for meta-analysis *.

Study	Outcomes quantitatively measured	Sample size and duration	Type and dose of Maca	Subgroups	Measurements taken after admission
(Brooks et al., 2008)	Body weight, estradiol, follicle-stimulating hormone, luteinizing hormone, sex hormone binding globulin	$n = 14$, 12 weeks	3.5 g/day Aqueous extract dry powder, to be taken food/beverage Colour(s) not stated	MP PM	6 and 12 weeks
(Dording et al., 2015)	Massachusetts General Hospital Sexual Function Questionnaire, Arizona Sexual Experience Scale	$n = 42$, 12 weeks	3.0 g/day Preparation and type not specified Colour(s) not stated	P M	Biweekly
(El-Kilani et al., 2019)	osteoporotic postmenopausal in women. Gingival index, pocket depth and clinical attachment level	$n = 15$, 6 months	1 g/tid finely powdered dried seeds of Lepidium sativum	M	Every 3 months
(Gonzales-Arimborgo et al., 2016)	Fasting glycaemia, systolic blood pressure, diastolic blood pressure, haemoglobin	$n = 175$, 12 weeks	3.0 g/day Hydro-ethanol Red and black	2 x control 2 x treatment	Monthly
(Jurcău et al., 2020)	anxiety, glycemia and salivary pH in healthy men	$n = 24$, 12 and 21 days	*Lepidium meyenii* (Maca) root powder (0.5 g) 3 tablets/day Preparation and type not specified Colour(s) not stated	1 x C 2 x M	before treatment, 15 min before exercise, 30 min after exercise, 4 h after exercise
(Meissner et al., 2005)	Luteinizing hormone, follicle-stimulating hormone, oestrogen, progesterone, genitourinary syndrome of menopause	$n = 12$, 3 months $n = 8$, 9 months	2 g/day gelatinized powder-hard gel capsules, twice daily Colour(s) not stated	PM	After 1 month (placebo) and post treatment
(Meissner et al., 2006b)	Follicle-stimulating hormone, oestrogen, progesterone, luteinizing hormone, cholesterol, triglycerides, Kupperman Menopause Index, genitourinary syndrome of menopause	$n = 88$, 3 months $n = 38$, 4 months	2 g/day gelatinized powder-hard gel capsules, twice daily Black, yellow and red mix	APMM AMMP APMMP APPM AMMPP AMMPM	Monthly
(Meissner et al., 2006e)	BMI, systolic blood pressure, diastolic blood pressure, follicle-stimulating hormone, oestrogen, progesterone, luteinizing hormone, cortisol, adrenocorticotropic Hormone, thyroid hormones, triglycerides, cholesterol, calcium, phosphorous, iron, forearm bone density, kupperman menopause index, genitourinary syndrome of menopause	$n = 31$, 4 months	2 g/day gelatinized powder-hard gel capsules, twice daily Black, yellow and red mix	APPMM AMMPP	Monthly
(Meissner et al., 2006f)	Cortisol, adrenocorticotropic hormone, thyroid hormones, calcium, phosphorous, iron, triglycerides, total cholesterol, body weight, systolic blood pressure, diastolic blood pressure, kupperman menopause index	$n = 18$, 4 months	2.0 g/day, hard gel capsules, twice daily Black, yellow and red mix	PPMM MMPP	Monthly
(Melnikovova et al., 2015)	Luteinizing hormone, follicle-stimulating hormone, thyroid hormones, estradiol, testosterone, normal sperm morphology, sperm, count, concentration, progressive motility, semen volume, mobile sperm count	$n = 18$, 12 weeks	1.75 g/day gelatin enterosolvent capsules, five times daily Yellow	P M	Post treatment
(Valentová et al., 2008)	BMI, creatinine, uric acid, glucose, cholesterol, triglycerides, apolipoprotein A-I, apolipoprotein B-100, alanine and aspartate amino transferase, creatine kinase, systolic blood pressure, diastolic blood pressure, Magnesium, urea, albumin, C-reactive protein	$n = 53$, 90 days	0.6 g/day Dehydrated powder- tablets Colour(s) not stated	P M	Post treatment
(Zenico et al., 2009)	follicle-stimulating hormone, luteinizing hormone, Prolactin, total and free testosterone, satisfaction Profile	$n = 50$, 12 weeks	2.4 g/day, tablets, twice daily Dry pulverised tablets Colour(s) not stated	P M	Post treatment

* Length of the study including treatment, control and any washout periods. M-Maca, P-Placebo.

Discussion

Human studies-systematic review

Study parameters

Critical analysis of eleven human studies showed that Maca is a potential candidate for conditions associated with; bone structure, hormone levels, physical activity and depression. The minimum and maximum sample sizes used were $n = 8$ (Stone et al., 2009) and $n = 175$ (Meissner et al., 2006e) respectively with ages ranging from 21 to 65 years old, one study (Higgins and Deeks, 2011) failed to state this parameter. Doses varied from 0.6 g/day to 3.5 g/day and were taken between one to six times per day; five studies specified certain timings (Gonzales et al., 2003a; Jurcău et al., 2020; Meissner et al., 2005, 2006e, 2006f) such as before food and/or in the morning or evening, the remaining studies did not enforce these stipulations. Most of studies opted for 12 weeks, the shortest duration was 12 days, the longest being 9 months, and all studies included a control regime. A mixture of males and females was used (Higgins and Deeks, 2011; Meissner et al., 2006e), but due to the nature of the outcomes being assessed, seven (El-Kilani et al., 2019; Hermann and Heller, 1997; Lim, 2015; Meissner et al., 2006e, 2006f; Turner et al., 2013; Zenico et al., 2009) and five (Chen et al., 2017; Gonzales et al., 2003a; Gonzales, 2012; Jurcău et al., 2020; Meissner et al., 2005) studies used only females and males respectively.

Table 2
Aspects from animal model studies compared for meta-analysis*.

Study	Outcomes quantitatively measured	Sample size, duration and animal model	Extract and dose of Maca	Subgroups	Measurements taken after admission
(Ai et al., 2014)	Movement distance, rearing times, serotonin, noradrenaline, dopamine	$n = 72$, 6 weeks Kunming mice	Petroleum ether 125, 250 or 500 mg/kg Colour(s) not stated	3x P 3x M	Post treatment
(Bustos-Obregón et al., 2005)	Seminiferous epithelium stage lengths I, II–III, IV–VI, VII, VIII, IX, X–XI and X	$n = 48$, 7,14,21 days Asnell mice	Aqueous 66.6 mg/day Colour(s) not stated	1x P 2x M	Days 8, 15 and post treatment
(Chain et al., 2014)	Liver superoxide dismutase activity, liver and RBC catalase activity	$n = 110$, 60 days Wistar rats	Ethanol partitioned with petroleum ether 100 mg/kg/day Black, yellow and purple	2x P 9x M	Post treatment
(Choi et al., 2012)	Glucose, free fatty acids, lactate, lactate dehydrogenase, liver and skeletal muscle glycogen, thiobarbituric acid reactive substances, glutathione, superoxide dismutase and catalase	$n = 60$, 3 weeks Sprague Dawley rats	Lipid-soluble 30 or 100 mg/10 ml/kg Yellow	1x P 2x M	Post treatment
(Cicero et al., 2001)	Mount and intromission frequencies, ejaculation inactivity, intercopulatory interval and copulatory efficacy	$n = 60$, 15 days Sprague-Dawley rats	Saline 15 or 75 mg/kg Colour(s) not stated	1x P 2x M	Post treatment
(Gasco et al., 2007a)	Body, testes, epididymis, seminal vesicles, ventral prostate, spleen and liver weights. Daily sperm production, Epididymal sperm count and Vas deferens sperm count	$n = 32$, 84 days Holtzman rats	Aqueous 1 g/kg Black, yellow and red	1x P 3x M	Post treatment
(Gasco et al., 2007b)	Initial and final body weight, reproductive, no reproductive organs, daily sperm production, epididymal sperm count and vas deferens sperm count	$n = 24$, 21 days Holtzman rats	Aqueous 2 g/kg Red	2x P 2x M	Post treatment
(Gonzales et al., 2003a)	Testicular and epididymal weight, seminiferous tubules lengths and frequencies II, II-III, IV-V, IX-XI, XII and XIII-XIV	$n = 20$, 14 days Holtzman rats	Aqueous 133.4 mg/day Colour(s) not stated	P M	Post treatment
(Gonzales et al., 2003b)	Seminiferous tubular lengths I, II-III, IV-V, VI, VII, VIII, IX-XI, XII and XIII-XIV, sperm count (epididymis), testosterone	$n = 54$, 7,14 and 21 days Holtzman rats	Ethanol 48 mg/day and 96 mg/day Colour(s) not stated	P 2x M	Days 7,14 and post treatment
(Gonzales et al., 2004)	Body weight, sperm count, testosterone	$n = 72$, 7, 14 and 21 days Holtzman rats	Aqueous 666.6 mg/day Colour(s) not stated	2x P 2x M	7,14 and post treatment
(Gonzales et al., 2005)	Ventral prostate weight	$n = 71$, 7 days Holtzman rats	Aqueous 2 g/kg/day Black, yellow and red	1x P 3x M	Post treatment
(Gonzales et al., 2006a)	Prostate and seminal vesicles weights, sperm transit rate, testosterone, Estradiol	$n = 48$, 7 and 42 days Holtzman rats	Aqueous 1.66 g/kg Black, yellow and red	1x P 3x M	Post treatment
(Gonzales et al., 2007)	Prostate weight	$n = 10$, 14 days Holtzman rats	Aqueous and hydroalcoholic 0.1 mg of benzylglucosin-olate Red	3x P 3x M	Post treatment
(Gonzales et al., 2008)	Prostate weight, prostatic acinar and stromal areas, testosterone, Estradiol	$n = 36$, 7,14 and 21 days Mice- Strain not stated	Aqueous ethanol 140 mg/kg Red	2x P 4x M	Days 7,14 and post treatment
(Gonzales et al., 2010)	Epithelial height in epididymis, testosterone, epididymal tubules area	$n = 60$, 12 days Holtzman rats	Aqueous 2 g/kg Black	1x P 1x M	Days 1, 3, 5, 7 and post treatment
(Gonzales et al., 2012)	Prostate, preputial and seminal vesicle weights	$n = 12$, 7 and 14 days Holtzman rats	Aqueous 2 g/kg Red	3x P 4x M	Post treatment
(Gonzales-Castañeda et al., 2011)	Solar cell damage (MS = 3) Leukocyte infiltration (MS = 4) D-E activity (MS = 3) Atypical keratinocytes (MS = 3) Severity of atypia (MS = 4) Solar cell damage, Leukocyte infiltration Epidermal-dermal layer activity, keratinocytes, structural cell abnormalities	$n = 36$, 5 days Swiss mice	Hydro-ethanol 200 µl of 1 mg pyrogalol/ml Black, yellow and red	3x P 3x M	Post treatment
(López-Fando et al., 2004)	Glucose, immobility time	$n = 28$, 7 days Swiss mice		2x P 2x M	Post treatment

(continued on next page)

Table 2 (*continued*)

Study	Outcomes quantitatively measured	Sample size, duration and animal model	Extract and dose of Maca	Subgroups	Measurements taken after admission
			Methanol 125 mg/kg and 250 mg/kg Colour(s) not stated		
(Meissner et al., 2006a)	Body weight, white blood cells, red blood cells, haemoglobin, haematocrit, platelets and lymphocyte counts, glucose, cholesterol, triglycerides, sodium, potassium, iron, cortisol, Adrenocorticotropic hormone, thyroid hormones, prostate specific antigen, progesterone, Estradiol , luteinizing hormone, follicle-stimulating hormone, prolactin, Dry matter, ash, crude protein, total fat, calcium and phosphorus from muscles and bones	$n = 30$, 28 days $n = 60$, 90 days Sprague-Dowley rats	Pre-gelatinized 0.75 g/kg and 7.5 g/kg Black, yellow and red mix	1x P 2x M	Post treatment
(Meissner et al., 2006b)	Estradiol, progesterone, cortisol, ATCH, thyroid hormones, red blood cells, white blood cells, lymphocytes, monocytes, granulocytes; platelets, haemoglobin; haematocrit, erythrocytes, iron, cholesterol, entries and duration in darkened and lit areas, distance travelled	$n = 72$, 28 days Wistar rats	Pre-gelatinized 500 mg/kg/day Black, yellow and red mix	2x P 2x M	Post treatment
(Rubio et al., 2006a)	Body and uterine weight, immobility time	$n = 80$, 21 days Swiss mice	Aqueous 1 g/kg Black, yellow and red	1x P 3x M	Post treatment
(Rubio et al., 2006b)	Left testis, left epididymis, seminal vesicle and ventral prostate weights Caput/corpus and cauda sperm count, sperm motility, daily sperm production, sperm transit	$n = 49$, 35 days Holtzman strain	Aqueous 2.2 g/kg Colour(s) not stated	4x P 3x M	Post treatment
(Rubio et al., 2007)	Acetylcholesterolinesterase, monoamine oxidase, number of errors and step-down latency	$n = 60$, 35 days Kunming mice	Aqueous and aqueous ethanol (0.50 and 2.00 g/kg) and (0.25 and 1.00 g/kg) respectively Black	2x P 4x M	Post treatment
(Rubio et al., 2011a)	Number of errors, step-down latency, malonalehyde acetylcholesterolinesterase and monoamine oxidase activity	$n = 50$, 35 days Kunming mice	Aqueous 0.5 and 2.0 g/kg Black	3x P 2x M	Post treatment
(Rubio et al., 2011b)	Body weight	$n = 66$, 28 days Swiss mice	Aqueous ethanol 0.125, 0.25, 0.50 or 1.00 g/kg Black	3x P 4x M	Post treatment
(Uchiyama et al., 2014)	luteinizing hormone, follicle-stimulating hormone, growth hormone, thyroid hormones, prolactin, adrenocorticotropic hormone, body, pituitary, hypothalamus, right and left ovary, and uterus weights	$n = 60$, 7 weeks Sprague-Dawley rats	Petroleum ether 3.0, 15, or 30 g/kg Colour(s) not stated	1x P 3x M	Post treatment
(Ybañez-Julca et al., 2021)	Antidepressant activity and Spatial memory	$n = 30$, 28days Male Sprague-Dawley rats	500 g of dried Red Maca, added to 1.5 L of aqueous, and the mixture was subjected to reflux for 2 h. The extraction process was repeated two times with another 1.5 L of aqueous finally lyophilized and freeze-dried	1x P 2x M	Post treatment
(Yucra et al., 2008)	Left testis and epididymis, seminal vesicle and ventral prostate weights. Epididymal sperm count and Vas deferens sperm count	$n = 4$, 7 days Holtzman rats	Petroleum ether, chloroform, ethyl acetate, n-butanol, and water partitioned from aqueous ethanol Black	1x P 6x M	Post treatment
(Zhang et al., 2006)	Body and uterine weight, femur length, diameter, volume and wet and dry weight Midshaft femur bone mineral density, Lumbar spine bone mineral density, Ash weight, Max-load, stress, stroke, and strain, Elastic, Energy Alkaline phosphatase, calcium, phosphorous	40, 28 weeks Sprague-Dawley rats	Ethanol 0.5 or 1.25 g/kg Colour(s) not stated	2x P 2x M	Post treatment
(Zhang et al., 2014)	Body and uterine weight, oestradiol, testosterone, follicle-stimulating hormone	$n = 50$, 28 weeks Sprague-Dawley rats	Ethanol 0.096 or 0.24 g/kg Colour(s) not stated	3x P 2x M	12 weeks and post treatment
(Zhang et al., 2017)	Body and liver weight, liver index	$n = 60$, 4 weeks Institute of Cancer Research mice	Ethanol 200 mg/kg, 600 mg/kg or 1800 mg/kg Colour(s) not stated	3x P 3x M	Post treatment
(Zheng et al., 2000)	Sperm-positive females, Latent period of erection, complete intromissions	$n = 135$, 22 days Shenyang mice $n = 120$, 1 day Beijing mice $n = 20$, 20 days Wistar rats	Ethanol 40 mg/g, 4 g/kg and 45, 180, or 1800 mg/kg Colour(s) not stated	P 2x M	Post treatment

* Length of the study including treatment, control and any washout periods. M-Maca, P-Placebo.

Table 3
Risk of bias for individual animal studies.

study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Incomplete data outcome (attrition bias)	Selective reporting (reporting bias)
(Ai et al., 2014)	U	U	U	H
(Bilal et al., 2016)	U	U	U	U
(Bramara et al., 2017)	U	U	H	H
(Bustos-Obregón et al., 2005)	U	U	U	U
(Choi et al., 2012)	U	U	U	H
(Cicero et al., 2001)	U	U	U	H
(Clément et al., 2010b)	U	U	U	H
(Gasco et al., 2007a)	U	U	U	H
(Gasco et al., 2007b)	U	U	U	H
(Gonzales et al., 2001)	U	U	U	H
(Gonzales et al., 2003b)	U	U	L	U
(Gonzales et al., 2004)	U	U	U	H
(Gonzales et al., 2005)	U	U	U	H
(Gonzales et al., 2006a)	U	U	L	H
(Gonzales et al., 2006b)	U	U	U	H
(Gonzales et al., 2007)	U	U	L	U
(Gonzales et al., 2008)	U	U	L	H
(Gonzales et al., 2010)	U	U	U	H
(Gonzales et al., 2012)	U	U	U	H
(Gonzales-Castañeda and Gonzales, 2008)	U	U	U	H
(Gonzales-Castañeda et al., 2011)	U	U	U	H
(Lee et al., 2004)	U	U	U	U
(Lee et al., 2005)	U	U	U	H
(Li et al., 2017a)	U	U	U	H
(Li et al., 2017b)	U	U	U	H
(Li et al., 2018)	U	U	U	H
(López-Fando et al., 2004)	U	U	L	H
(Meissner et al., 2006a)	U	U	L	U
(Meissner et al., 2006b)	U	U	U	H
(Qiu et al., 2016)	U	U	U	H
(Rubio et al., 2006a)	U	U	L	H
(Rubio et al., 2006b)	U	U	U	H
(Rubio et al., 2007)	U	U	U	H
(Rubio et al., 2011a)	U	U	U	H
(Rubio et al., 2011b)	U	U	U	H
(Uchiyama et al., 2014)	U	U	U	H
(Wan et al., 2018)	U	U	U	H
(Ybañez-Julca et al., 2021)	U	U	U	U
(Yucra et al., 2008)	U	U	U	H
(Zhang et al., 2006)	U	U	L	H
(Zhang et al., 2014)	U	U	L	U
(Zhang et al., 2017)	U	U	U	H
(Zheng et al., 2000)	U	U	U	U

Key = *L* = low bias *H* = high bias *U* = unclear.

Table 4
Risk of bias for individual human studies.

study	**Random sequence generation (selection bias)**	**Allocation concealment (selection bias)**	**Incomplete data outcome (attrition bias)**	**Selective reporting (reporting bias)**	**Blinding of participants and personnel (performance bias)**	**Blinding of outcome assessment (detection bias)**
(Brooks et al., 2008)	U	U	L	H	U	U
(Dording et al., 2015)	U	U	L	U	U	U
(El-Kilani et al., 2019)	L	L	L	U	U	U
(Gonzales et al., 2003a)	U	U	U	H	U	U
(Gonzales-Arimborgo et al., 2016)	U	L	L	H	L	U
(Jurcău et al., 2020)	U	U	U	U	U	U
(Meissner et al., 2005)	U	U	L	U	U	U
(Meissner et al., 2006c)	U	U	L	H	L	U
(Meissner et al., 2006e)	U	U	L	H	L	U
(Meissner et al., 2006f)	U	L	L	U	L	U
(Melnikovova et al., 2015)	L	L	L	U	U	U
(Stone et al., 2009)	U	U	L	U	U	U
(Valentová et al., 2008)	U	U	U	U	U	U
(Zenico et al., 2009)	U	U	L	H	U	U

Key = *L* = low bias *H* = high bias *U* = unclear.

Questionnaires such as Massachusetts General Hospital Sexual Function Questionnaire (MGHSFQ), Kupperman's Menopause Index (KMI), Greene's Menopause Score (GMS), Arizona Sexual Experience Scale (ASEX), Clinical Global Impression-Improvement (CGI-I), Clinical Global Impression-Severity (CGI-S) and Satisfaction Profile (SAT-P) were used in some cases (G. Gonzales et al., 2003; Hermann and Heller, 1997; Meissner et al., 2006e; Turner et al., 2013; Zenico et al., 2009).

Type and preparation of Maca

Two preparation methods (pre-gelatinisation or dehydration) were used to produce a powder for oral solid dose units (capsules or tablets), one study did not state any of these factors (Meissner et al., 2006e) and two stated the preparation method but not the formulation type (Meissner et al., 2006e, 2006f). Pre- gelatinised capsules (Hermann and Heller, 1997; Lim, 2015; Turner et al., 2013; Zenico et al., 2009) and tablets (Gonzales, 2012) as well as dehydrated capsules (Chen et al., 2017; Meissner et al., 2005) and tablets (Gonzales et al., 2003a) were used. One study investigated the difference between dehydrated tablets and capsules (Higgins and Deeks, 2011), no differences were seen, and the data were pooled (Valentová et al., 2008). The process to produce gelatinised Maca consists of the removal of starch via boiling and pressurising (Bennett, 2016). This can make Maca easier to digest and avoid potential minor side effects such as bloating, indigestion and gas (Bennett, 2016). However, this process could potentially destroy, inactivate or alter secondary metabolites that are bioactive in Maca due to the high temperatures used (Bennett, 2016). The type of Maca is distinguished by the colour of the root which, can be identified only by the outer layer of the hypocotyls as the inside is white, with the exception of yellow Maca which is yellow (Clément et al., 2010a). Some studies used a variety of colours with the composition being 16%, 48%, 9% and 27% of black, yellow, red and other varieties respectively (Hermann and Heller, 1997; Turner et al., 2013; Zenico et al., 2009), red and black Maca were compared for their effects on humans at high and low altitudes (Meissner et al., 2006e) and yellow Maca only was used to treat semen parameters and hormone levels (Chen et al., 2017). The remaining studies did not specify the type of Maca used.

The colour(s) of the Maca roots could potentially have an effect on the outcomes observed; evidence has shown that the nutrient content and the concentration and presence of secondary metabolites differ between the colour variations of Maca. This is particularly the case for glucosinolates, macamides and macaenes with the exception of β-sitosterol and campesterol (Clément et al., 2010a). These compounds amongst others are of interest as they are thought to be bioactive ingredients, however, it is not fully understood which compounds are responsible or are active for different conditions and their mechanisms of action. A range of glucosinolates were found in higher concentrations in red and violet coloured Maca compared to yellow (Clément et al., 2010a). Macaenes were found in higher concentrations in yellow Maca, and *n*- benzyl palmitamide and n-benzyl-5-oxo-6E, 8E-octadecadienamide were high in violet Maca (Clément et al., 2010a). A correlation was not deduced between metabolites from the spectrum of pink and violet to black Maca (Clément et al., 2010a). It is important to note that he macamide and macaene content depends on the drying method and the initial glucosinolate content; a recent research has focused on developing drying processes under controlled conditions so that the biochemistry of glucosinolate hydrolysis is modulated and the content of bioactive compounds in the root flour optimised (Esparza et al., 2020).

Reported outcomes

Of the fourteen studies included, ten reported that Maca was effective on the condition studied. Serum hormone levels, in particular oestradiol (ES),follicle-stimulating hormone (FSH), luteinizing hormone (LH) and testosterone (T) were observed to be unaffected by three studies (Chen et al., 2017; Gonzales, 2012; Meissner et al., 2006f) despite hormones being a common measurement in human studies. Therefore, when comparing the results to another study (Lim, 2015) it was seen that Maca capsules reported a positive outcome in serum hormone levels; a possible explanation for the difference could be associated with the fact that tablets were used (Gonzales, 2012). Tablets are less expensive to make however, they are sometimes able to pass through the GI tract without breaking down thus reducing the dose given (Challem, 2003). Sublingual tablets could be used as an alternative to capsules as they dissolve under the tongue increasing absorption through the vast network of blood vessels present, unfortunately, this could increase costs (Challem, 2003). Maca was also administered as a powder to be added to beverages or food (Meissner et al., 2006f), the outcome of this method could be related to the exact dose not being taken due to spillage or unfinished meals or drinks, compliance could also be an issue as Maca has a malty taste which could deter individuals from taking it (Challem, 2003; Dash et al., 2000). The colour of Maca root that was chosen could have affected the results obtained (Chen et al., 2017) as it is possible that the bioactive compound(s) were not present and/or the concentrations were too low in yellow Maca to have an effect on the parameter studied such as serum hormone levels. However, this cannot be concluded as the remaining studies did not report what variations were used.

Two studies looked at the safety parameters of using Maca. In candidates with metabolic syndrome (Valentová et al., 2008) results showed that Maca increased aspartate aminotransferase and diastolic blood pressure (DBP) levels in both sexes in addition to systolic blood pressure (SBP) in females. In a study that investigated the effects of red and black Maca in humans at different altitudes, blood pressure was not affected and a higher dose by 2.4 g/day was used. Maca has shown to inhibit Angiotensin I-converting enzyme in vitro which means it has a high potential to act as an anti-hypertensive compound and is therefore more likely to lower blood pressure (Ranilla et al., 2010).

Animal studies-systematic review

Study parameters

Animal studies investigated a wider variety of conditions compared to human studies, a total of thirty-eight showed that Maca had positive effects on spermatogenesis, homoeostasis, prostatic hyperplasia, UV irradiations and memory impairment to name but a few. Some conditions were induced by the removal of ovaries from female models or by the administration of TE, ethanol, streptozotocin, scopolamine or lead acetate. With the exception of five studies (Choi et al., 2012; Meissner et al., 2006b; Rubio et al., 2006b, 2007, 2011a) where the models were racehorses, fish, hamsters or bulls; rat or mice models were employed. The strains of mice used were Shenyang, Beijing, Swiss, Kunming and Asnell, and the strains of rats used were Wistar, Holtzman and Sprague-Dowley.

Sample sizes varied from $n = 20$ (Melnikovova et al., 2015) to $n = 960$ (Choi et al., 2012), the large difference is due to the range of animal models used with the largest sample size entailing fish. When only taking rats and mice models into account, the largest sample size was $n = 135$ (Stone et al., 2009). The age range was two to sixteen weeks old with the exception of two studies (Rubio et al., 2007, 2011a) in which 55–84 weeks old bulls and 6.5 ± 1.17 years old racehorses were used respectively. Doses were either reported *per* kg, mg/day or mg/l and the ranges were 20 mg/kg to 7500 mg/kg, 48 mg/day to 96 mg/day and 0.13 mg/ml to 1.3 mg/ml respectively. Some studies standardised the content of certain compounds present e.g. a polysaccharide (Gasco et al., 2007b), or isolated and purified different polysaccharides (Bustos-Obregón et al., 2005; Zhang et al., 2006). Overall animal studies were carried out for shorter periods of time compared to human studies, the minimum and maximum durations were 1 and 28 weeks respectively, and all studies included a control regime.

Type and preparation of Maca

Dermal administration was carried out for three studies due to the nature of the outcomes being measured (Ley, 2003; Richens, 2001;

Rubio et al., 2011b). Seven studies (Choi et al., 2012; Meissner et al., 2006b; Rubio et al., 2011a, 2007, 2006b; Wang and Bakhai, 2006; Ybañez-Julca et al., 2021) incorporated Maca into the animals normal feed however this can reduce the precision and accuracy of dosing (Turner et al., 2011). For the remaining studies a liquid dose unit administered orally or nasally by gavage was used, this usually involves restraining the animal which can cause adverse effects due to stress especially if the volume of liquid is large (Turner et al., 2011). Administration by intra-peritoneal injection was also used (Valentová et al., 2008), the route of administration determines the pharmacokinetics of a substance including absorption, distribution, metabolism and excretion (Turner et al., 2011). The bioavailability is the amount of substance in the systemic circulation, for parenteral routes bioavailability is higher since first pass metabolism in the liver is avoided; The pharmacokinetics of intra-peritoneal administration closely resembles oral administration compared to parenteral despite being classed as the latter, this is because the compound can pass through the liver by the absorption into vessels that join the portal vein, however this is mainly practiced in animal models making the results from this study harder to generalise as it does not match the intended administration route of Maca for humans (Turner et al., 2011). Some studies conducted freeze or spray drying methods in the preparation of Maca, low and high temperatures are used respectively therefore the latter technique can cause a loss of or degradation of thermal sensitive compounds, spray drying can also cause decreased activity (Turner et al., 2011). This could have an effect on the presence and/or concentration of certain secondary metabolites in Maca and therefore the outcomes of certain conditions.

In total, nine different extracts of Maca were used; a large proportion of studies used an aqueous extract and referred to the process as the 'traditional method' which in general comprises of placing dried hypocotyls in water, boiling and filtering (Gonzales et al., 2001; Rubio et al., 2011a). Very few studies used a mixture of the varieties of Maca (Challem, 2003; Dash et al., 2000; Ybañez-Julca et al., 2021), whilst some employed methods that allowed different groups to be used to compare the different effects of black, yellow and red or purple Maca on the same outcome (Brooks et al., 2008; Gasco et al., 2007a; Gonzales et al., 2003b; Moher et al., 2015; Richens, 2001; Rubio et al., 2006a, 2011a; Uchiyama et al., 2014). The remaining studies either used an individual colour or did not specify this factor.

Reported outcomes

DSP, reproductive organ weights, DNA levels (Moher et al., 2015) and seminal vesicle weights specifically of TE treated rats (Gonzales-Castañeda et al., 2011) showed Maca had no effect in two studies by the same author. However, evidence from other studies (Bennett, 2016; Brooks et al., 2008; Cicero et al., 2001; Gasco et al., 2007a; Gonzales et al., 2005; Meissner et al., 2006a; Melnikovova et al., 2015; Zheng et al., 2000) show that Maca has an effect on seminal vesicle, testicular, epididymal and prostate weights. When assessing the reasons why such differences were reported it was noticed that in some cases the same preparation and type of Maca was used and therefore it was unlikely that these factors affected the outcome, however, the dose used was approximately 33–633 mg/day higher. In regards to DSP, one study (Lee et al., 2016) measured the same outcome and three measured ESP (Dording et al., 2015; Gonzales et al., 2005, 2006a; again a higher dose by approximately 15–633 mg/day was used. Therefore, a higher dose may be needed for Maca to increase sperm production and reduce reproductive organ weights. Evidence on effects of Maca on DNA levels is scarce as only one study investigated this; therefore, it was not possible to assess the results obtained.

Risk of bias assessment

Risk of bias for human studies

One study (Chen et al., 2017) successfully reduced selection bias, the remaining studies all reported the use of randomised sequence but failed to present sufficient evidence for the methods used to accomplish this aspect. Allocation concealment which is another form of selection bias was unclear for the majority of studies and low for four studies (Chen et al., 2017; El-Kilani et al., 2019; Hermann and Heller, 1997; Meissner et al., 2006e). With the exception of two studies (Gonzales, 2012; Higgins and Deeks, 2011) that were classified as unclear for attrition bias as they did not address this issue, either no outcome data was missing or the reason(s) for missing the data were acceptable and therefore risk of bias was low. Reporting bias was an issue as 50% of studies were high risk as they either did not report outcomes that were specified, or data was reported incompletely so that it could not be inputted into a meta-analysis. The remaining half was classified as unclear because the study protocol was not accessible to determine whether pre-specified data were reported. There could be differences between publications and protocols and although these should be specified it has been shown that 150 studies from samples (Chan et al., 2004) did not, therefore the reporting bias cannot be assumed (Higgins and Green, 2011). Four studies (Hermann and Heller, 1997; Meissner et al., 2006e; Turner et al., 2013; Zenico et al., 2009) had low performance bias by implementing blinding of the participants and the researchers with the rest being unclear due to insufficient evidence. The blinding of outcome assessors was not reported and therefore the risk of detection bias was unclear for all studies.

Risk of bias for animal studies

Although all studies stated that random assignment of animals to groups was conducted, none of them reported the methods for the randomisation or allocation concealment of the animals, therefore all were classified as unclear for both types of selection bias. Approximately three quarters of studies were classified as having an unclear risk of attrition bias due to insufficient evidence. One study (Rubio et al., 2011b), was classified as a high risk due to some results stating that sample sizes were $n = 8$ irrespective of stating animal grouping was $n = 6$. The remaining studies had a low risk linked to the same reasons mentioned for the human studies. Reporting bias was high for the majority of studies with eight of them (Bennett, 2016; Challem, 2003; Dording et al., 2015; Meissner et al., 2006b; Rubio et al., 2007; Shin et al., 2010; Stone et al., 2009; Yucra et al., 2008) publishing the primary outcomes which reduced the risk but study protocols were unavailable and so were classified as unclear.

Meta-analysis

A meta-analysis was not feasible for both human and animal studies as there was no consensus for the process of choosing studies to combine for a meta-analysis, therefore this part of the method is subjective, and was taken into account when interpreting the results as it had an effect on the conclusions drawn.

Dosage

Maca is a food and there is no set dose to be administered daily, however it has been recommended that two to ten grams divided between two to three doses a day is optimum (Ley, 2003). Maca root is sold as a powder and capsules by stores such as Holland & Barrett whose capsules contain 500 mg each with stated dose of one capsule three times a day, this totals 1.5 g/day and the guidelines express that this should not be exceeded ("Holland and Barrett Maca Capsules 500 mg," 2017). A different brand (health spark) capsules contain 250 mg each, however the directions state to take one daily with food ("Health Spark Maca Root Capsules" 2017). The recommended dose for Maca powder is 10–15 g/day and although the doses between different brands vary, the dose for powdered Maca is significantly higher in comparison. This demonstrates that an indicative dosage has not been set, furthermore guidelines do not state minimum or maximum durations for the use of Maca ("Naturya Organic Maca Powder Maca" 2022). Human and animal studies used a variety of doses and a response(s) were observed in most

cases. Most studies state that the reason the dose was chosen was due to the response obtained in previous studies using a similar strength however, some human studies used multiple groups to test different doses and some animal studies carried out dose response trials before the main outcomes were measured. Therefore, after careful consideration it was decided that studies differing in durations and doses would not be combined. There were also an insufficient number of studies to further analyse whether the differences of these parameters had an effect on the outcomes measured.

Human studies

Reporting. Ten studies were included in the subset for meta-analysis. Reporting issues was a major reason studies were not suitable to combine. Although quantitative outcomes were measured, the data were presented visually as bar and scatter graphs plotted as means with error bars without exact values being stated (Gonzales et al., 2003a; Gonzales, 2012; Hermann and Heller, 1997; Meissner et al., 2006f, 2005). This issue also relates to a high risk of selective reporting bias. Other issues included reporting the results as a two way analysis and a multiple regression to show the correlation between different groups (Gonzales, 2012) and using p values by stating whether the result was significant or not (Gonzales, 2012; Turner et al., 2013; Zenico et al., 2009). The most common reporting method of data is Standard deviation (SD) or Standard error of mean (SEM) but three studies reported Standard error of difference (SED) (Chen et al., 2017; Turner et al., 2013; Zenico et al., 2009), unlike standard error of mean it cannot be converted to standard deviation as it is associated with the difference between the groups rather than the mean and therefore depending on the meta-analysis software, it may not be suitable to use (Higgins and Green, 2011). One study (Higgins and Deeks, 2011) did not state what the data were expressed as, and therefore this could not be assumed. All of the factors mentioned made the studies incompatible with the meta-analysis program as statistical values are required. Lastly, it was not possible to combine certain studies due to them being the only single study to measure certain outcomes. Sexual dysfunction in females induced by antidepressants (Meissner et al., 2006e) and physical activity (Meissner et al., 2005) are very scarce, the latter is surprising since Maca is described as a supplement ideal for enhancing performance levels, stamina and energy levels("Holland and Barrett Maca Capsules 500 mg," 2017).

Methodology. The methodology of the studies also proved problematic when making comparisons, in particular the different group designs used. In general, a parallel design (non-crossover) was the most popular choice nevertheless crossover designs were also used (Hermann and Heller, 1997; Lim, 2015; Turner et al., 2013; Zenico et al., 2009). For a crossover design to be efficient, the condition being measured should be stable, this is important as the baseline measurements should return to normal after a treatment is ceased so that the next treatment is carried out under the same conditions (Richens, 2001). A possible issue with this design could be the carryover effect, regardless of a washout period the results can be affected by the order of administration (Wang and Bakhai, 2006). Although applying the random effects model when carrying out a meta-analysis can compensate for such heterogeneity, the additional problem of parallel studies employing more treatment groups due to different subjects partaking made the studies unsuitable to combine for a meta-analysis.

Animal studies

Models. The subset for animal models consisted of twenty-eight studies, five studies (Choi et al., 2012; Meissner et al., 2006b; Rubio et al., 2011a, 2007, 2006b) using bovine bulls, hamsters, rainbow trout fish or racehorses were excluded as the remaining studies used rats and mice making them incompatible to combine. When considering the animal models used in general pre-clinical trials, mice are the most predominant (Home Office, 2009). The model must be chosen carefully when carrying out a study, if not the risk of a drug/compound failing in clinical trials increases due to issues related to reduced safety and effectiveness when translated to humans (Akhtar, 2015). The Food and Drug Administration (FDA) estimated that in 2004 92% of drugs failed to be brought to the market irrespective of passing preclinical trials which is mainly due to interspecies differences related to genetics and physiology however, differences can also exist within different strains of the same species and even those of the same strain but acquired from different providers can affect test results (Akhtar, 2015).

Maca extracts. The principal issue when comparing studies to combine for meta-analysis was the diversity of extracts used. Extracting Maca using various solvents can have an effect on the concentration and presence of some secondary metabolites. It has been shown that fresh Maca contains low levels of free fatty acids, benzyl amine and amides but high levels of benzyl glucosinolate, the latter is sensitive to high temperatures however some metabolites increase after heating e.g. boiling (Esparza et al., 2015; Gonzales, 2012). Although none of the studies used fresh Maca they did carry out extractions on dried Maca roots, hypocotyls or powder grown in different regions from different suppliers. The native environment of Maca exposes it to low pressures, extreme cycles of temperature, strong lighting and it remains in these conditions for two months (Esparza et al., 2015). Maca dried using these conditions has been analysed and amides, amines and free fatty acids were present in very high concentrations (Esparza et al., 2015). There is also evidence to support a difference in secondary metabolites depending on the cultivation area of Maca as soil quality; climate and other environmental factors can have an effect (Chen et al., 2017). Ethanol extractions have been used to obtain polysaccharides in Maca e.g. rhamnose and arabinose and these have shown to be active as an antioxidant, the concentration has the highest stimulus on the yield and purity obtained (Table A.1) (Zha et al., 2014). Other parameters that have an effect on the extraction process in order of importance are; liquid: solid ratio, time and temperature (Campos et al., 2013). Twelve macamides have been extracted from Maca using hexane, whilst petroleum ether has been used to extract a macaridine, macaene and alkamides (Chain et al., 2014; Muhammad et al., 2002).

Reporting. The same reporting issues associated with visual representation of quantitative data and not reporting exact values seen in human studies was also very evident in animal studies. Six studies (Bustos-Obregón et al., 2005; Gonzales et al., 2003b, 2006a; Ley, 2003; Rubio et al., 2011b; Zhang et al., 2006) were excluded because although they measured quantitative data not a single outcome was reported as numerical data and therefore could not be included in a meta-analysis. In addition, due to the wide variation of conditions investigated; the outcomes measured varied significantly in some cases and the number of studies for certain conditions were limited therefore making a meta-analysis unpractical.

Recommendations for future human and animal studies

For future studies using Maca as a treatment, a number of factors should be considered:

1. Measure standardised outcomes for certain conditions:

When reproductive hormone levels were studied, most measured FSH, P, T and E making them compatible the outcomes measured. If different outcomes are measured for the same condition, then they are still unsuitable for meta-analysis.

2. Conduct more clinical trials:

For those conditions limited in the number of studies, more should be conducted, namely for physical activity. In addition, more conditions

were studied using animal models therefore studies should be replicated using human participants to allow the findings to be generalised to the wider population.

3. Report exact numerical data

Future studies must report all data using the exact values to both enable data to be inputted into the meta-analysis program but to also reduce bias. This is especially the case for p values and the uses of visual representations e.g. bar and scatter graphs.

4. Report the effect size:

Studies with small sample sizes can be included in meta-analyses, however some individuals choose to exclude them since they are likely carrying a higher risk of bias, in addition when applying the random effects model in meta-analysis, small and large studies are weighted equally (Turner et al., 2013). It has been found that the heterogeneity between studies can decrease when underpowered studies were excluded from meta-analyses (Turner et al., 2013). However, if a study is carried out with a small sample size but reports a large effect size then the findings could be just as well justified as those from a study with a large sample size and therefore should be acknowledged regardless. In the particular case of animal studies, the use of large sample sizes goes against the three R's, replace, refine and reduce that have been put in place for animal welfare.

5. Reduce the risk of bias:

Studies should publish exactly what was carried out in order to

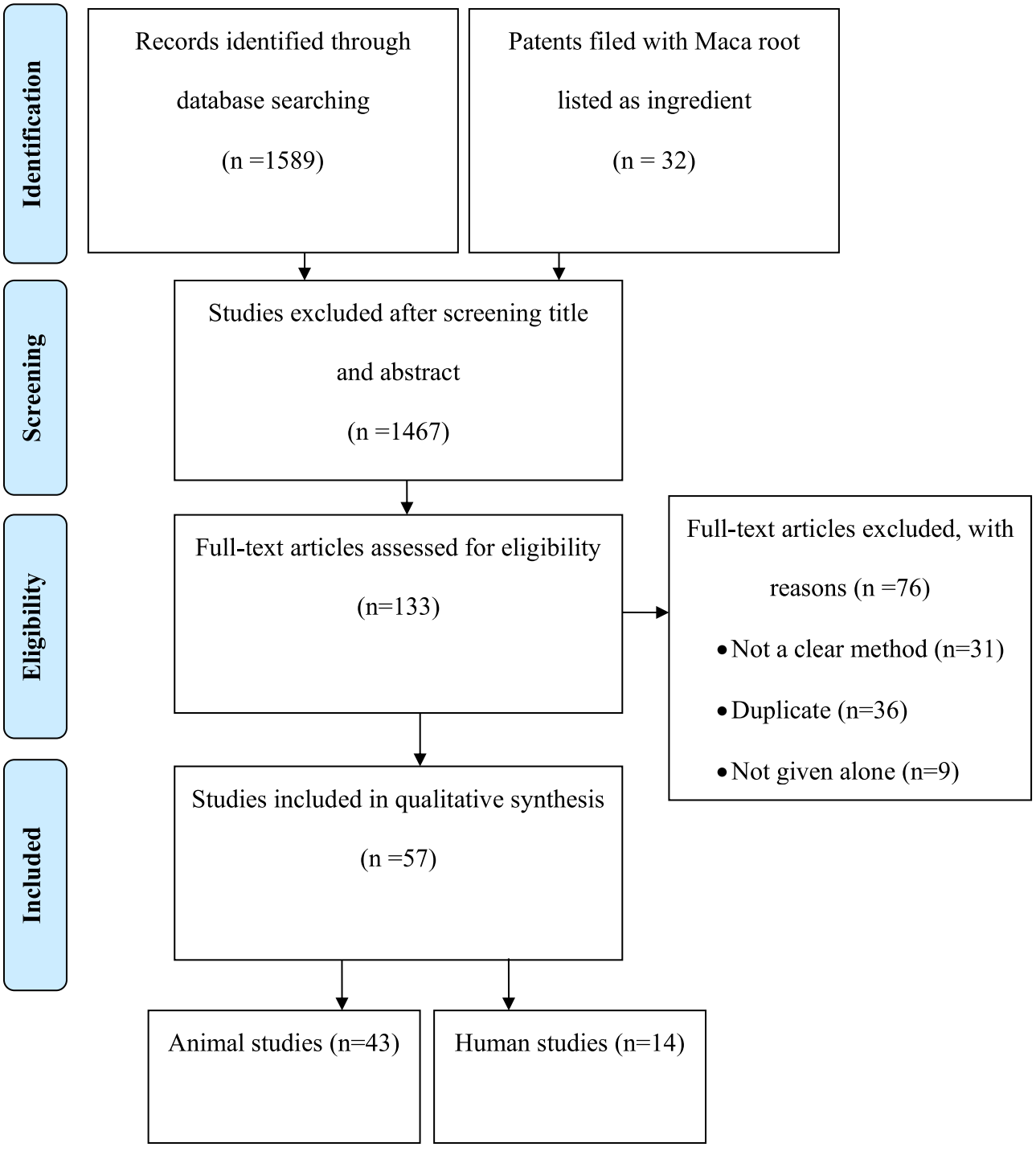

Fig. 1. PRISMA diagram of the selection process.

reduce the risk of biases. Generic statements such as 'participants/animals were randomly assigned to groups' should be avoided as this is not sufficient evidence to prove this was carried out. The technique used should be described.

In regards to meta-analyses in general, there is a need for more guidelines with respect to doses and durations e.g. if a range was included in the meta-analysis a minimum number of studies large enough to prove the differences have no effect on the outcome(s) should be assessed unless it has already been proved so. This is highly unlikely in the case of Maca since a number of studies have shown dose dependant responses.

Conclusion

On the basis of the studies included in this review, Maca appears to be effective at treating a range of conditions other than sexual dysfunction and menopausal symptoms. While people could benefit from the use of Maca, studies with more rigorous methods and reporting are warranted to improve the reliability and precision of the results. Standardised doses, durations and extraction methods should be established to facilitate a meta-analysis and further research into the safety and potential side effects of Maca should be conducted. Fig. 1

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors contributions

A.P. and C.B. conceived and designed the experiments; C.B and N.Y analysed the data; C.B. and N.Y. wrote the paper with contributions from A.P.

Availability of data and materials

All data generated of analysed in this study are included in this publishes article.

Declaration of Competing Interest

The authors declare no conflict of interest.

Acknowledgments

The authors thank Dirk Folkerts for his contribution.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.phyplu.2022.100326.

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