Lepidium meyenii (Maca): A Plant from the Highlands of Peru – from Tradition to Science

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Lepidium meyenii (Maca): A Plant from the Highlands of Peru – from Tradition to Science

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Key Words
Lepidium meyenii · Maca · Experimental studies · Clinical trials

Summary
This review summarizes the current state of knowledge on *Lepidium meyenii* (maca), a cruciferous plant (Brassicaceae family) which is cultivated exclusively at an altitude of 4000–4500 m in the Peruvian Central Andes. Maca is traditionally used for its nutritional and presumed medicinal properties. Over the past 20 years, interest in maca has increased in many parts of the world, and since 2005 maca is considered one of the seven Peruvian flag products. Maca is exported as powder, capsules, pills, flour, liquor, and extracts. There are different types of maca with different colors ranging from white to black. We have studied the pharmacological effects of 3 types; yellow, black, and red maca. Evidence from experimental studies indicates effects of maca on nutrition, fertility, memory, and mood. Black maca has better effects on sperm production than yellow maca which has only moderate effects. Red maca, however, has not effect on sperm production. However, red maca has been shown to reduce prostate size in rats in which prostate hyperplasia had been induced with testosterone enanthate; yellow maca has shown moderate effects here, whereas black maca has not shown any effects. Randomized clinical trials have shown that maca has favorable effects on energy and mood, may decrease anxiety and improve sexual desire. Maca has also been shown to improve sperm production, sperm motility, and semen volume. Serum levels of testosterone, estradiol, LH, FSH, and prolactin were not affected. The exact mechanisms of action are still unclear, but research so far clearly indicates that various bioactive constituents contribute to the clinical effects reported.

Schlüsselwörter
Lepidium meyenii · Maca · Experimentelle Studien · Klinische Studien

Zusammenfassung
Die vorliegende Übersicht fasst den aktuellen Kenntnisstand zu Lepidium meyenii (Maca) zusammen, einem Kreuzblütler (Brassicaceae), der ausschließlich in einer Höhe von 4000–5000 m in den peruanischen Zentralanden wächst. Maca wird traditionell als Nahrungsergänzung und wegen seiner vermuteten medizinischen Eigenschaften verwendet. In den letzten 20 Jahren hat das Interesse an Maca in vielen Teilen der Welt zugenommen, und seit 2005 gilt Maca als eines der sieben peruanischen Vorzeigeprodukte. Maca wird als Puder, Kapsel, Pillen, Mehl, Flüssigkeit oder Extrakt exportiert. Es gibt verschiedene Arten von Maca, die eine unterschiedliche Farbe haben, von weiß bis schwarz. Wir haben die pharmakologischen Wirkungen von gelber, schwarzer und roter Maca untersucht. Experimentelle Studien weisen auf Effekt von Maca auf Ernährungsstatus, Fruchtbarkeit, Gedächtnis und Stimmung hin. Schwarze Maca wirkt sich günstiger auf die Spermaproduktion aus als gelbe Maca, die nur mittlere Effekte hat. Rote Maca hat hingegen keinen Effekt auf die Spermaproduktion. Dafür wurde gezeigt, dass rote Maca eine vergrößerte Prostata bei Ratten reduziert, die zuvor mit Testosteron Enanthat induziert worden war. Bei gelber Maca konnten wiederum mittlere Effekte gezeigt werden, während sich bei schwarzer Maca keine Wirkung auf die Prostategröße nachweisen ließ. Randomisierte klinische Studien zeigten, dass Maca sich günstig auf Energie und Stimmung auswirkt, Angst reduzieren und die sexuelle Appetenz verbessern kann. Darüber hinaus wurde gezeigt, dass Maca die Spermaproduktion, die Spermamotilität und die Spermamenge verbessern kann. Die Konzentrationen von Testosteron, Östradiol, LH, FSH und Prolaktin im Serum blieb unverändert. Die genauen Wirkmechanismen sind noch nicht bekannt, aber die bisherige Forschung weist klar darauf hin, dass verschiedene bioaktive Bestandteile zu den berichteten klinischen Effekten beitragen.

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Introduction

Lepidium meyenii Walpers (maca) is a Peruvian plant that belongs to the Brassicaceae family (Cruciferae) [1]. Maca mainly grows at an altitude of ≥4,000 m in a habitat of intense cold, extremely intense sunlight and strong winds. Maca has been cultivated in the Peruvian central Andes, in the former Chinchaycocha (Plateau of Bombón); present-day: Carhuamayo, Junin, and Óndores in the Junin Plateau close to Cerro de Pasco [2].

Maca was probably domesticated in San Blas, Junin (present-day: Ondores) some 1,300–2,000 years ago. Maca is used as a food supplement and for its presumed medicinal properties. Peru's native population in the central Andes uses the dry hypocotyls in amounts >20 g/d. There are no reports of adverse reactions after consuming *Lepidium meyenii* in food. Natives from the highlands of Peru recommend that maca be boiled before its consumption because fresh maca may have adverse effects on health [3].

In the present paper, we report on historical aspects and biological properties of maca, gathered from experimental and clinical studies on this species. Data reveal its importance as nutraceutical food, and how maca has adapted to conditions as harsh as observed at high altitude.

Historical Aspects

In 1553, a chronicler of the conquest of Peru noted that in the Peruvian highlands, particularly in the province of Bombón (Chinchaycocha) the natives used certain roots for maintenance [4]. Father Cobo [2] was the first to describe maca and its properties in 1653. He stated that this plant grew in the harshest and coldest areas of the province of Chinchaycocha where no other plant for man's sustenance could be grown. Cobo also referred to the use of maca for fertility. In the 18th century, Hipólito Ruiz referred to the fertility-enhancing properties of maca as well [5]. During the Spanish colonization, the capital of Peru was moved from Jauja (3,410 m) to its current location in Lima (150 m) because – among other reasons – the altitude of Jauja reduced fertility of livestocks [2]. It is described in the chronicles that in 1549, Juan Tello de Sotomayor, a Spaniard named Encomendedero of Chinchaycocha, requested maca from the natives to settle their taxes [6].

Traditionally, after being harvested maca is dried naturally and can thus be stored for many years [3]. The dried hypocotyls are hard as stone. Before dried maca can be eaten, the hypocotyls are boiled in water in order to obtain a soft product which can be consumed as juice [3]. The effect of temperature affects the availability of several secondary metabolites in plants. Quercetine, for example, is sensitive to temperature. Likewise, the constituents of glucosinolates are sensitive to heating [7]. Other metabolites, however, are increased.

Table 1. pH of several aqueous extracts of black, red, and yellow maca

Type of maca	Total weight of hypocotyls of maca (g)	Volume to be boiled (ml)	pH of the aqueous extract after boiling[a]
Black	100	500	5.01
	100	1000	5.04
	100	1500	5.11
Red	100	500	4.94
	100	1000	4.81
	100	1500	4.97
Yellow	100	500	5.04
	100	1000	5.06
	100	1500	5.11

[a]For 2 h.

Heating decreases the activity of epithiospecifier protein and increases formation of sulforaphane, a derivative of isothiocyanates, in broccoli [8]. After 2, 15, and 30 min of heating at 88 °C, the vitamin C content of raw tomato drops significantly. Yet, the content of trans-lycopene per gram of tomato increases [9]. Moreover, antioxidant activity also increases after heating tomatoes [9].

Ecology and Biology

Maca is characterized by an overground and an underground part. The overground part is small and flat in appearance. This seems to be the result of an adaptation process to prevent the impact of strong winds. The principal and the edible part of the plant is a radish-like tuber that constitutes the hypocotyl and the root of the plant. This hypocototyl-root axis is 10–14 cm long and 3–5 cm wide and constitutes the storage organ storing a high content of water. After drying the hypocotyls are dramatically reduced in size to about 2–8 cm in diameter. The average weight of the dried hypocotyls may vary considerably ranging from 7.64 g in hypocotyls from black maca in Yanacancha, Chupaca, to 23.88 g in black maca from Carhuamayo, Junin (both in the Peruvian central Andes).

There are many types of maca that can be characterized by the color of their hypocotyls. In Carhuamayo, Junin, in the Peruvian highlands, 13 colors of maca have been described, ranging from white to black [10]. Recently, it has been demonstrated that different types of maca (according to its color) have different biological properties [11–13].

The soil for maca to grow needs to be rich in organic material and acid. In fact, our studies revealed that aqueous extracts of maca are acidic (table 1).

In 1982, the International Board for the Protection of Genetic Resources declared maca in danger of extinction as a domesticated plant [14]. Over the last 10 years, due to the interest of the European, North American, and Japanes markets, the production of maca has been markedly increased, though.

Table 2. Properties of maca after in vivo administration in different species

Property	Reference
Rats	
Increase sperm count	Gonzales et al., 2004; Chung et al., 2005
Increase male sexual behavior	Zheng et al., 2000; Cicero et al., 2001, 2002
Nutritional	Canales et al., 2000
Anti-stress	Tapia et al., 2000; Lopez-Fando et al., 2004
Prevent testosterone-induced prostatic hyperplasia	Gonzales et al., 2005
Against osteoporosis	Zhang et al., 2006
Learning and memory	Rubio et al., 2006
Mice	
Increase male sexual behavior	Zheng et al., 2000
Increase embryo survival	Ruiz-Luna et al., 2005
Guinea pigs	
Increase number of offsprings	Alvarez, 1993
Fish	
Nutritional	Lee et al., 2004, 2005
Increase embryo survival	Lee et al., 2004

Experimental Studies

A summary of biological properties is presented in table 2.

Nutritional Properties

The nutritional properties of maca as described traditionally [2] have been proven scientifically in studies on rats [15] and fish [16, 17]. The nutritional components of maca have been described early [18].

Male Reproduction

The effects of maca on fertility were described as early as 1653 [2]. At an international level, the first description that maca improves sexual behavior in rodents, was published in 2000 [19]. In 2001, maca was reported to increase sperm count in men [20].

Sperm Count: Scientific studies have shown that maca may increase daily sperm production (DSP), epididymal sperm count or vas deferens sperm count in both healthy rats [20, 21] or when spermatogenesis was disturbed by different experimentally-induced abnormal conditions such as exposure to high altitude [22], injection of malathion [23], or administration of lead acetate [24].

One of the effects of maca administered for 7 days of treatment was that it increased the lengths of stages VIII (spermiation) in a dose-response fashion [22]. This allows an increased number of sperm in the epididymis. Also, an increase in the frequency of stages IX–XI of mitosis was observed after 7, 14, or 21 days of treatment with maca [20, 25].

More recently, it has been described that black maca has a better effect on sperm count than yellow maca, whereas red maca was without any effect. Effects on increased epididymal sperm motility were observed only with black maca after 42 days of treatment. As compared to the control group, red Maca neither affected testicular and epididymal weight nor epididymal sperm motility and sperm count [12].

In studies with varying treatment periods between 1–84 days, the first action of black maca could be observed at the epididymal level in terms of an increased sperm count after 1 day of treatment; whereas an increase in sperm count in the vas deferens was only observed at day 3 of the treatment. Finally, an increase in DSP was observed after 7 days of treatment. Testicular testosterone was not affected even after 7 days of treatment with black maca [26]. Treatment for 84 days with yellow or black maca increased epididymal sperm count without affecting DSP. Maca seems to modulate sperm count at the reproductive tract level [27].

Aqueous extract of maca is only effective after boiling pulverized maca hypocotyls in water. The greatest effect on spermatogenesis was observed with the ethyl acetate fraction of the hydroalcoholic extract of black maca [28].

Prostatic Hyperplasia: Prostate growth is mainly regulated by androgens, especially by dihydrotestosterone (DHT) [29]. However, estrogens also play an important role in this process, as 3-β-diol is responsible for tissue apoptosis through its union with estrogen receptors [30]. An alteration to the balance of testosterone and estrogen might contribute to the formation of benign prostatic hyperplasia (BPH) [31].

Prostate pathologies in adult men occur frequently, caused by an abnormal prostate growth which can be malignant. BPH is associated with a series of symptoms of the lower urinary tract [32]. The incidence of BPH increases proportionally with age, starting at about 50 years of age [33].

The treatment of choice for prostatic hyperplasie is an inhibitor of 5-alpha-reductase II (5AR-II), an enzyme that specifically inhibits the conversion from testosterone to DHT in the reproductive tract. Red maca has been shown to effectively reduce prostate size in rats and mice in which hyperplasia had been induced with testosterone enanthate [11, 34]. When red maca treatment was compared to the 5AR-II inhibitor, it was observed that red maca reversed the effect of testosterone enanthate even more efficiently than the conventional treatment [27]. Moreover, only maca reversed the effect of testosterone enanthate on the intraprostatic concentration of zinc [personal data]. Histological analyses revealed that BPH increased the acinar and stromal areas [34]. Both treatments reduced the acinar area, but only maca also reduced the stromal area [34]. The 5AR-II inhibitor acts on the androgenic pathway, regulating the prostatic growth, but this organ is regulated by androgens and estrogens. These results combined with the fact that red maca does not exert its action on another androgen-dependent organ, such as the seminal vesicle, suggests that maca acts on the estrogen pathway.

The effect of maca on BPH seems to be related to the content of benzyl glucosinolate. Both, aqueous and hydroalcoholic extract of red maca, to a similar extent, reduced the prostate weight in rats with prostatic hyperplasia induced by TE [35]. The study mentioned demonstrated that boiling resulted in a lower amount of benzyl glucosinolate per 100 g of dry hypocotyls of maca than contained in the hydroalcoholic extract. A possible explanation for this is that heating transforms benzyl glucosinolate to a more potent compound. For instance, sulforaphane, an isothiocyanate from broccoli, is one of the most potent food-derived anticarcinogens. This substance, however, is not present in the intact vegetable but formed from its glucosinolate precursor, glucoraphanin, by the action of myrosinase. However, several studies have demonstrated that sulforaphane yield from glucoraphanin is low, and that a non-bioactive nitrile analog, sulforaphane nitrile, is the primary product of hydrolysis when plant tissue is crushed at room temperature. Heating fresh broccoli florets or broccoli sprouts to 60 °C increased the formation of sulforaphane and decreased the formation of sulforaphane nitrile [8]. It is still unknown if any specific compound is produced by heating red maca, but this possibility cannot be ruled out.

Sexual Behavior

The use of medicinal plants for the treatment of sexual disorders is currently under investigation. Treatments with pulverized maca hypocotyls in doses of 15, 25, 75, and 100 mg/kg and the assessment of sexual behavior at 1, 7, 15, and 21 days of treatment yielded different results [36, 37]. The one study found increased sexual behavior of males at treatment days 1 and 15 [37], whereas the other study did not find changes in male sexual behavior at treatment days 1 or 21 [36]. Also, two studies, which used lipidic extracts of maca, found an increase in male sexual behavior in rats and mice [19, 37, 38]. Further studies are required to clarify these discrepancies.

Testosterone controls sexual desire and spermatogenesis. However, the effect of maca on these physiological processes does not seem to be regulated by changes in serum testosterone or intratesticular testosterone levels. An alternative explanation would be that maca affects the androgen receptor. However, in another study maca did not modulate androgen receptors [39]. Thus, further chemical and molecular research is required to identify which of the many components of maca [3] accounts for the effects observed.

Female Fertility

Fertility-enhancing properties of maca in females have been described for different species including sheep, guinea pigs, rats, mice, and fish [16, 40, 41]. Several studies in mice and rats did not find an increase in the number of ova released or embryos implanted [27, 41, 42]. Instead, a 28-day treatment with yellow maca increased litter size in pregnant female mice [41]. More recently, however, we have demonstrated that treatment with black maca did increase litter size in pregnant mice [unpublished data]. This effect seemed to be due to a reduction in embryo resorption. Supplementation of maca in diets also improved growth rates and survival of rainbow trout *Oncorhynchus mykiss* (Walbaum) alevins and juveniles [16].

Treatments with yellow [41] or black maca [Gonzales et al, unpublished data] neither affected the sex ratio nor the time of vaginal opening, a sign of sexual maturation in mice. In fish, the period of sex differentiation is highly sensitive to a possible action of phytochemicals with steroid activity. However, sex ratios between a maca-treated group of rainbow trouts and controls did not differ significantly [16]. These results suggest that maca has no estrogen-like effect.

It has been suggested that the improvement of embryo survival could be a progesterone-like effect of maca [41]. An increase in the concentration of serum progesterone in female mice treated with maca has been reported [42].

Others suggest that some properties of maca may be explained by an estrogen-like effect, because maca extracts exhibited estrogenic activity comparable to the effect of silymarin in MCF-7 cells using MTT viability test [43]. However, these data are not supported by other data in the existing literature. For instance, serum estradiol levels were not affected in different studies which used mice [42], rats [12, 27], or humans [44]. Moreover, with a different in vitro assay in our laboratory, we could not show that maca has a proliferative effect on MCF-7 cells [Vaisberg and Gonzales, unpublished observations]. Studies in female mice demonstrated that aqueous extract of maca did not modify uterine weight and increased embryo survival [16, 41]. It is suggested that this activity may result from a progestin-like effect. In mice and rats, progesterone is much more important than estrogen to maintain pregnancy [45].

Osteoporosis

Osteoporosis is a systemic disease of the skeleton characterized by a reduction in bone mass and an alteration in the micro-architecture of the bone tissue with a consequent increase in bone fragility and susceptibility to fracture [46]. This could either be due to an increased osteoclastic activity or to a decreased osteoblastic activity [47, 48]. During post-menopause, the decline of estrogen would be the key for osteoporosis leading to an increase in osteoclastic activity [49].

Hormone replacement therapy (HRT) has been demonstrated to effectively prevent loss of bone mass and reduce the fracture index in postmenopausal women [50]. However, the risk of breast and endometrial cancer seems to be increased [51].

Recent studies have shown that red maca may reduce prostate size [27]. The fact that red maca exhibits a protective effect on an organ the development of which is regulated by a balance between steroid hormones, where estrogen activity is of great importance, suggests that red maca plays an important role in the homeostatic balance of other functions regulated by steroid hormones which also applies for bone metabolism.

In another study, ovariectomized (OVX) rats were treated with orally administered ethanol extract of maca at either 0.096 or 0.24 g/kg for 28 weeks. The findings regarding bone mineral density, biomechanical, biochemical and histiopathological parameters indicated that higher doses of ethanol extract of maca effectively prevented bone loss due to estrogen deficiency. The type of maca administered in this study was not given [52].

Recently, we evaluated the effects of red, black, and yellow maca on bone structure in OVX rats. Both red and black maca revealed a good effect on this parameter, but no effect was observed with yellow maca [unpublished data]. The results obtained are similar to those obtained with estradiol treatment, and in some of the cases the effect was even better with maca. On the other hand, red maca has been demonstrated to have a better effect on the ash weight of femur and the percentage of trabecular bone of the lumbar vertebra. This suggests that red maca is involved in the regulation not only of bone resorption but also in the formation of new bone. This could be due to an action on the estrogenic pathway, similarly as in the study on the effects of red maca on prostate [35].

In the same study, the uterus weight increased when estrogens were administered, but was not affected when any type of maca was administered. This suggests that the estrogenic role of maca may be specific, as it does not affect the uterus weight as estrogens do. According to the literature, there are selective estrogen receptor modulators such as raloxifen, which specifically act on the bone but not on the uterus or the breast. This may have a beneficial effect, because it avoids an increase of estradiol concentrations in several tissues, which could be associated with uterus and breast cancer [51]. This differential effect of red maca has also been described in male rats and mice, where prostate size was reduced in BPH without affecting the size of the seminal vesicles, contrary to treatment with 5AR-II inhibitors [11, 27].

Learning and Memory

According to the natives of the highlands, maca is given to children to improve performance in school examinations. This property of maca was not described by the chroniclers. Several experimental studies were performed in our laboratory to determine the effects of maca on learning and memory [13, 53, 54]. In addition, experiments to assess antidepressant and antistress effects were done in our and others' laboratories [13, 55, 56].

Two models of impaired memory and learning were assessed, (1) after ovariectomy, (2) after administration of scopolamine. Similarities between memory impairments of Alzheimer patients and scopolamine-treated animals have been reported, and it has been proposed that scopolamine, a muscarinic cholinergic receptor antagonist, could serve as pharmacological tool to produce a partial model of the disorder [57].

Black maca yielded the best responses in a water-finding task, particularly in trained OVX mice. However, all three types of maca effectively reduced finding latency in non-trained and trained OVX mice ($p < 0.05$). In conclusion, black maca appeared to have better effects on latent learning in OVX mice [13]. Another study was performed to determine if maca revealed antioxidant activity and anti-cholinesterase activity in the brain. Black maca (0.5 and 2.0 g/kg) improved memory as compared to OVX control mice, and decreased MDA and acetylcholinesterase (AChE) levels in OVX mice; however, no changes in monoamine oxidase activity (MAO) were observed. Therefore, it is suggested that black maca improves experimental memory impairment induced by ovariectomy, partly for its antioxidant and AChE-inhibiting activities [54].

Both extracts of black maca significantly ameliorated scopolamine-induced memory impairment in both the Morris water maze and the step-down avoidance tests [53]. Black maca extracts inhibited AChE activity but did not affect MAO activity.

All three types of maca assessed (red, black, yellow) showed antidepressant activity [13].

Protection against UV Exposure

Ultraviolet radiation (UVR) has three different bands, UV-A, UV-B, and UV-C. UV-A and UV-B reach the earth's surface, but UV-C is blocked by the ozone layer [58]. UVR intensity increases with altitude [59], and it has been proposed that some organisms like plants have developed adaptation mechanisms against this increased radiation [60]. Maca grows in places characterized by high UVR [3]. If maca can grow in such environments it is likely that it has developed mechanisms to protect against UVR. Recently, it has been reported that an aqueous extract of yellow maca hypocotyls can prevent the epidermal hyperplasia induced by UV-A, UV-B, and UV-C radiation in rats if applied topically minutes before exposition to UVR [61].

Maca is traditionally prepared by boiling it for several hours. The UV absorption spectrum was assessed for the traditional aqueous extract (boiled) and for an aqueous pulverized extract (non-boiled). Although both extracts showed UV absorption, the traditional aqueous extract had a greater effect. Polyphenols and glucosinolates were found in both (boiled and non-boiled) extracts, yet to a greater content in the boiled extract. Heating isomerizes polyphenols [62], so this could indicate that boiling may be necessary to improve the activity of these compounds.

UVR is absorbed by the epidermis and the dermis and can generate erythema, melanine pigmentation, solar keratosis, photoaging, and finally skin cancer [63]. Microscopically, UVR increases the height of the epidermis [64] and the content of keratin in the stratum corneus, indicating an alteration in the physical properties of the skin [65]. Maca aqueous extract prevents UV-induced epidermal damages as it prevents an increase of the epidermal height in a dose-dependent way [61].

Clinical Studies

Several clinical trials have assessed the efficacy and safety of maca consumption. Two of them included healthy men [44, 66, 67], and four trials included participants with pathological conditions [68–72]. The majority of these studies focused on the effects of maca on sexual behavior and sperm count (table 3).

In one clinical trial performed in healthy men, using a double-blind placebo-controlled, randomized, parallel-group design, treatment with three different schedules of gelatinized maca (45 men in total; 30 men were administered 1,500 mg/day maca, 15 men were administered 3,000 mg/day maca) was compared with placebo (15 men). Treatment with maca as compared to placebo increased sexual desire [44, 67] after 8 weeks of treatment; improved mood and anxiety, and increased activity [73]. No difference was observed between groups taking 1,500 or 3,000 mg/day of maca. A second study in 9 men who had received maca for 4 months showed an increase in sperm count and sperm motility [66]. Serum hormone levels were not affected by treatment with maca [66].

In three other studies on patients with sexual dysfunction, treatment with maca improved libido and sexual well-being. In fact, maca at a dose of 2,400 mg improved the perception of general and sexual being in men with mild erectile dysfunction after 12 weeks of treatment [72]. Similarly, a double-blind, randomized, parallel-group study was performed in women with sexual dysfunction due selective serotonin reuptake inhibitors (SSRIs), in order to determine the effect of maca on sexual dysfunction. Patients were administered either 1.5 or 3.0 g/day of maca. Improvements in sexual dysfunctions were observed at a dose 3 g/day [70]. In postmenopausal women, treatment with 3.5 g/day of maca for 6 weeks reduced psychological symptoms including anxiety and depression and reduced measures of sexual dysfunction [69].

As maca may increase sexual behavior in rodents [19, 37, 38] and men [67, 69, 70, 72], it is assumed that these effects are due to an increase in testosterone concentrations or to a testosterone-like action. However, only one study has demonstrated an increase in serum testosterone levels in mice [42]; in other studies, serum testosterone levels were not affected by administration of maca to rats [26] or men [44, 66, 67]. In recent studies, maca powder and maca extract were unable to activate androgen receptor-mediated transcription in prostate cancer cell lines [39] or in a yeast-based hormone-dependent reporter assay [69].

Maca has been shown to reduce scores in depression and anxiety inventories, act as an energizer, and increase sexual desire and sperm count [66, 67, 69], leaving unaffected serum levels of luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactin, testosterone, and estradiol [44, 66, 69, 73].

Finally, in a randomized double-blind study on 95 patients with osteoarthritis, a combination of *Uncaria gianensis* (300 mg) and maca (1,500 mg) was administered twice a day for 8 weeks and compared with a treatment with glucosamine sulfate.

Table 3. Properties of maca observed in clinical trials on humans

Property	Reference
Increase sperm count and sperm motility	Gonzales et al., 2001
Increase sexual desire	Gonzales et al., 2002; Zenico et al., 2009; Dording et al., 2008; Brooks et al., 2008
Anti-stress	Gonzales et al. (unpublished data)
Decrease score for anxiety and depression	Gonzales, 2006
Energizer	Gonzales, 2006
Improves pain, stiffness and function in osteoarthritis	Mehta et al., 2007

Both treatments substantially improved pain, stiffness, and functioning in the patients [68]. However, as the study did not include a placebo control group, glucosamine effects remain unclear.

A summary of the significant results yielded in clinical trials is presented in table 3.

Modes of Action

According to the results obtained in different studies, maca may act as an antioxidant [74] or as an immunomodulator [16, 75] depending on its biological properties. The maca constituent with antioxidant capacity has high polarity and can be extracted by methanol [17]. However, it has been shown that neither aqueous nor methanolic extracts of maca prevent oxidative damage in hepatocytes intoxicated by t-butyl hydroperoxide [43].

It has also been suggested that some effects of maca act through paracrine control affecting activity of IGF-1 [75]. In fact, maca enhanced basal IGF-1 mRNA levels in human chondrocytes by 2.7. Interleukine-1 beta (IL-1 beta) has several deleterious effects on chondrocytes. Maca may prevent most of these effects. The authors suggest that maca may act on fertility and fetal development also by activating IGF-1 production in target tissues [75].

Toxicity

Maca has been used for centuries in the Central Andes of Peru and, no toxic effects have been reported if it was consumed after boiling [3]. Previous review data on in vivo and in vitro studies with maca indicate that its use is safe [3]. Further evidence shows that aqueous and methanolic extracts of maca do not display in vitro hepatotoxicity [43]. Moreover, freeze-dried aqueous extract of maca (1 g/kg BW) in mice did not reveal any toxic effect on the normal development of pre-implanted mouse embryos [76].

Results in rats show that different types of maca (black, red, yellow) have no acute toxicity ≤17g of dried hypocotyls/kg BW. As usual doses in rats are 1–2 g/Kg BW, it is suggested that maca is safe. Human consumption of ≤1 g/kg per day is considered safe, as well. However, in a recent study with patients with metabolic syndrome the administration of maca at a dose of 0.6 g/day for 90 days resulted in a moderate elevation of AST and diastolic arterial pressure [71]. Previously, no changes in arterial blood pressure were found in healthy men who took gelatinized maca at doses of 1.5 of 3.0 g/d for 90 days [73]. Further data on safety, derived from larger data sets, are required to adequately assess safety of maca.

Final Comments

Maca is increasingly used in many parts of the world. Clearly, further research is required to address the mechanisms of actions and the active principles of this medicinal plant, however, available data suggest that maca has several important biological properties, and scientific evidence of these properties could be important for farmers, dealers, and consumers. Furthermore, it is necessary to demonstrate the biological effects of specific secondary metabolites of maca and their actions when added as a mixture.

Maca is a plant with great potential as an adaptogen. Scientific evidence showed effects on sexual behavior, fertility, mood, memory, and the treatment of several tumor entities. However, the active principles behind each effect is still unknown. Macamides have been described as novel compounds of maca that have not been found in any other plant species so far [19]. It is suggested that this lipidic fraction of maca may be responsible for the increase in sexual behavior [19, 38]. Studies on testicular function, spermatogenesis, fertility, mood, memory, and prostatic hyperplasia [12, 13, 21, 22] were performed with aqueous extracts that contain only trace amounts of macamides [77]. This suggests that compounds other than macamides are responsible for these activities.

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Conflict of Interests

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