Review Article

Ethnobiology and Ethnopharmacology of Lepidium meyenii (Maca), a Plant from the Peruvian Highlands

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Lepidium meyenii (maca) is a Peruvian plant of the Brassicaceae family cultivated for more than 2000 years, which grows exclusively in the central Andes between 4000 and 4500 m altitude. Maca is used as a food supplement and also for its medicinal properties described traditionally. Since the 90s of the XX century, an increasing interest in products from maca has been observed in many parts of the world. In the last decade, exportation of maca from Peru has increased from 1,415,000 USD in 2001 to USD 6,170,000 USD in 2010. Experimental scientific evidence showed that maca has nutritional, energizer, and fertility-enhancer properties, and it acts on sexual dysfunctions, osteoporosis, benign prostatic hyperplasia, memory and learning, and protects skin against ultraviolet radiation. Clinical trials showed efficacy of maca on sexual dysfunctions as well as increasing sperm count and motility. Maca is a plant with great potential as an adaptogen and appears to be promising as a nutraceutical in the prevention of several diseases.

1. Introduction

Lepidium meyenii Walpers (maca) is a Peruvian plant growing over 4000 m with high potential for bioprospecting [1]. Maca has been used for centuries in the Andes for nutrition and to enhance fertility in humans and animals [1, 2]. The demand for food particularly with benefits for health is high, but it will increase over the future years. Then, the search of plants with these potentials is of interest.

This plant belongs to the brassica (mustard) family and Lepidium genus [1]. The most relevant plants related to Lepidium meyenii are rapeseed, mustard, turnip, black mustard, cabbage, garden cress, and water cress. Lepidium constitutes one of the largest genera in the Brassicaceae family. The species from North America and Europe has been extensively studied, and the Lepidium meyenii from the Andean region has recently been studied profusely because of the great health benefits [3–5]. Maca grows at a habitat of intense cold, extremely intense sunlight, and strong winds. Maca is used as a food supplement and for its presumed medicinal properties [3].

The Peruvian native population in the central Andes use the hypocotyls after it has been naturally dried and in amounts >20 g/d. There are no reports of adverse reactions after consuming Lepidium meyenii in food [4]. However, natives from the highlands of Peru recommend that maca be boiled before its consumption because fresh maca may have adverse effects on health [5]. The effects of fresh maca on health have not been scientifically assessed yet. Preparations from the maca hypocotyls were reported to be of benefit for health [3–5].

The hypothesis that maca may be effective in improving health status, particularly reproductive function, is supported by several lines of evidence. Historical aspects and biological properties of maca, gathered from experimental and clinical studies on this species, reveal the importance of this plant as nutraceutical food, and that maca was adapted to conditions as harsh as observed at high altitude [2, 3, 5–7]. The aims of this review are to summarize and assess the evidence from experimental and clinical studies for or against the effectiveness of maca in the improvement of different functions.

2. History and Tradition

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.

The first written description about maca (as a root without identification of the botanical or popular name) was published in 1553, in which Cieza de Leon, a chronicler of the Spaniard conquest of Peru noted that in the Peruvian highlands, particularly in the province of Bombón (Chinchaycocha; present day: Junin) the natives used certain roots for maintenance [6]. The roots, he was referring to were maca.

Father Cobo [2] was the first to describe the name of maca and its properties in 1653. He stated that this plant grows 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, Ruiz referred to the fertility-enhancing properties of maca and also its stimulant effect [7]. I believe stimulant effect could be related to energizer effect or an effect on mood or well-being.

Traditionally, after being harvested maca is dried naturally and can thus be stored for many years [5]. The dried hypocotyls are hard as stone (Figure 1). After being naturally dried maca hypocotyls can be eating. Before eaten, the hypocotyls need to be boiled in water to obtain a soft product which can be consumed as juice, the most frequent form of use [4].

The boiling process seems to increase active metabolites. In fact, increased temperature affects the availability of several secondary metabolites in plants sometimes increasing some metabolites and in others a reduction in metabolites is observed. In maca, one of the important constituents is glucosinolates. These compounds are sensitive to heating [8]. Other metabolites, however, are increased after heating. For instance, heating decreases the activity of epithiospecifier protein and increases formation of sulforaphane, a derivative of isothiocyanates and glucosinolates. These compounds are sensitive to heating [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 translycopene per gram of tomato increases [10]. Moreover, antioxidant activity also increases after heating tomatoes [10].

3. Ethnobiology

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 underground part is the hypocotyl-root axis.

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 hypocotyl-root axis is 10–14 cm long and 3–5 cm wide and constitutes the storage organ storing a high content of water. After natural drying, the hypocotyls are dramatically reduced in size to about 2–8 cm in diameter (Figure 1). The average weight of the dried hypocotyls may vary considerably. For instance, in our experience, we found a range of weight between 7.64 and 23.88 g 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 [11]. Recently, it has been demonstrated that different types of maca (according to its color) have different biological properties [16, 20, 35].

4. Chemistry

Primary metabolites correspond to the nutritional component of the hypocotyls, and the secondary metabolites to compound with biological and medicinal properties.

4.1. Primary Metabolites. The dried hypocotyls of maca are approximately 13–16% protein, and are rich in essential amino acids. Fresh hypocotyls contain 80% water and have high amounts of iron and calcium (see [5]). A more complete description of the composition of dry maca shows [12] 10.2% proteins, 59% carbohydrates, 2.2% lipids, and 8.5% of fibre. Free fatty acids are also present in maca, the most abundant being linoleic, palmitic, and oleic acids. Saturated fatty acids represent 40.1% whereas unsaturated fatty acids are present at 52.7%.

Maca contains amino acids (mg/g protein) like leucine (91.0 mg), arginine (99.4 mg), phenylalanine (55.3 mg), lysine (54.3 mg), glycine (68.30 mg), alanine (63.1 mg), valine (79.3 mg), isoleucine (47.4 mg), glutamic acid (156.5 mg), serine (50.4 mg), and aspartic acid (91.7 mg). Other amino acids present but in less proportion are histidine (21.9 mg), threonine (33.1 mg), tyrosine (30.6 mg), methionine (28.0 mg), hydroxyproline (26 mg), proline (0.5 mg), and sarcosine (0.70 mg). Minerals reportedly found in maca were iron (16.6 mg/100 g dry matter), calcium (150 mg/100 g dry matter), copper (5.9 mg/100 g dry matter), zinc (3.8 mg/100 g
4.2. Secondary Metabolites. Maca contains several secondary metabolites [5]. The secondary metabolites macaridine, macaene, macamides, and maca alkaloids are only found in this plant [13]. Macaenes are unsaturated fatty acids [13]. Other compounds include sterols as beta-sitosterol, campesterol, and stigmasterol.

Different glucosinolates as the aromatic glucosinolate glucotropaeolin have been described within maca. Benzyl glucosinolate has been suggested as chemical marker for maca biological activity. However, this has been discarded since glucosinolates may easily metabolize to isothiocyanates and these in other smaller metabolites [14].

Benzyl glucosinolate is also present in another Peruvian plant named mashua (*Tropaeolum tuberosum*). This plant, however, has opposed effects to maca since administration to male rats reduced sperm count [15] in contrast with the known effect of maca increasing sperm count [16].

It has been observed that maca batches from different producers significantly vary in the amount of macaene, macamides, sterols, and glucosinolates [17–19]. In 2005 appeared the first publication indicating that different maca color types have different properties [20]. More recently, it has been found that maca colors associate with variations in concentrations of distinct bioactive metabolites [19, 21]. These compounds individually or acting in synergy may be acting favoring the reported biological properties from maca.

The differences in proportion of secondary metabolites between maca colors may explain different biological properties described for maca.

5. Ethnopharmacology of Maca

5.1. Experimental Studies. Since 2000 to this date, several studies have been reported on biological or pharmacological effect of maca on experimental animals. The results have been consolidated in Table 1.

| Species | Property | Source |
|---------|----------|--------|
| Mice    | Increase male sexual behavior | [13]   |
|         | Increase embryo survival | [33]   |
|         | Prevent testosterone-induced prostatic hyperplasia | [34]   |
|         | Increase number of offsprings | [33]   |
|         | Improve memory and learning | [35–37] |
| Guinea pigs | Increase number of offsprings | [38]   |
| Fish    | Nutritional | [39, 40] |
|         | Increase embryo survival | [39]   |
| Bulls   | Improve sperm quantity and quality | [41]   |
|         | Unaffected mating behavior |        |

6. Experimental Studies on Reproduction

6.1. Male Reproduction

6.1.1. Sexual Function. Treatments of experimental animals 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 [22, 24]. The first study found increased sexual behavior of males at treatment days 1 and 15 [22] whereas the second study did not find changes in male sexual behavior at treatment days 1 or 21 [24]. Macaenes and macamides have been reported as novel compounds in maca [13] and probably responsible to improve sexual behavior [13], although this needs to be further demonstrated.

6.1.2. Sperm Function. Maca has been found to increase sperm count in normal rats and in pathological conditions produced by exposure to high altitude [42], lead acetate injections [43], and malathion [44]. Maca also increases sperm motility [16]. Black maca and in minor proportion yellow maca are the varieties responsible to increase sperm count and sperm motility whereas red maca had no effect [16].
6.1.3. Prostate Function. Testosterone enanthate (TE) administered to mice [34] and rats [14, 20, 45] induced prostatic hyperplasia. Red maca administered with TE for 21 and 42 days to male rats or mice prevented the prostatic hyperplasia. Yellow maca had intermediate effects and black had not effect on prostate size. In fact, red maca reduced prostate weight in a dose-response manner without any changes in testosterone levels and seminal vesicle weight [14, 45]. Regarding the secondary metabolites involved in the effect of red maca on prostate size, when different doses of benzylglucosinolates in red maca extracts were assessed, a dose-dependent reduction in prostate weight was observed, suggesting that these compounds may be responsible for the biological effect of red maca [14]. However, other secondary metabolites presented in red maca could be also responsible for the effect on prostate size. In fact, other authors found that polyphenols could inhibit prostate size [46, 47]. Recently, it was suggested that polyphenols in red maca may be related to the reduction in prostate size [34].

Prostate zinc levels were increased by TE administration, an experimental model to induce prostatic hyperplasia. Red maca was able to reduce zinc levels in TE-treated rats. Although red maca was able to reverse the effect of TE administration in prostate weight and zinc levels, no effect was observed in seminal vesicle weight, another androgen-dependent organ [20]. Finasteride, the standard pharmacological treatment for prostatic benign hyperplasia, which inhibits the activity of the enzyme 5 alpha reductase which in turn blocks the conversion of testosterone to dihydrotestosterone, was able to reduce both prostate and seminal vesicle weights but did not completely reduce zinc levels in prostate (unpublished data). Our results may possibly suggest that red maca and finasteride could have different mechanisms of action. In fact, previous studies showed that red maca specifically affects prostate size without altering testosterone or estradiol levels either in mice or in rats with prostatic hyperplasia induced by TE [14, 20, 45]. Also, it has been published that maca has no effect on androgen receptor [48, 49]. The latter supports the hypothesis that red maca effect is at a postandrogen receptor action level [14] or that RM exerts an inhibitory effect at a level postdihydrotestosterone conversion [45].

The finding that maca reduces benign prostatic hyperplasia (BPH) is a contribution of science since no traditional description refer to this effect. This is comprehensible since BPH occurs since 50 years of age, and before century XX, expectancy of life was below 50 years.

6.1.4. Serum Hormone. 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. However, the mechanism is not yet known [48]. Thus, further chemical and molecular research is required to identify which of the many components of maca accounts for the effects observed.

6.2. Female Reproduction. Serum estradiol levels were not affected in different studies which used mice [50], rats [16, 45], or humans [51]. Moreover, with an 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].

Maca extract has been demonstrated to improve the number of offsprings in mice [33]. This effect seems to be due to an effect favoring survival of embryos. This has also been suggested in rainbow trouts [39, 40]. Recently, in our laboratory it has been demonstrated that extract of red maca is more effective to improve quality of embryos in mice (unpublished data).

Extracts of red and black maca have protective effects on bone architecture in ovariectomized rats without showing estrogenic effects on uterine weight [28]. This finding may suggest the possibility to study effect of extracts of maca for treatment of women with osteoporosis.

7. Memory and Learning

Although no traditional descriptions have been found about effect of maca on learning and memory, actually natives in the central Peruvian Andes ascribe to the use of maca in children improves school performance. They do not exactly know which variety of maca has better effect on memory and learning. Experimental studies have shown that black variety of maca has beneficial effects on learning and memory in experimental animal models. Black maca improved learning and memory in ovariectomized mice [35, 37] and in scopolamine-induced memory impairment in mice [36].

Three varieties have been studied (black, red, and yellow maca) and black maca was the only one showing significant biological effects [35]. Studies have been performed using hydroalcoholic extracts of maca or boiled aqueous extract of maca. Both were similarly effective in improving memory and learning [35–37]. Black maca (0.5 and 2.0 g/kg) decreased brain malondialdehyde (MDA) levels marker of oxidative stress and acetylcholinesterase (Ache) levels in ovariectomized mice whereas no differences were observed in monoamine oxidase (MAO) levels [37]. Black maca seems to improve experimental memory impairment induced by ovariectomy, orchidectomy, scopolamine, and alcohol due in part to its antioxidant and Ache inhibitory activities.

In summary, different evidences suggest that maca, particularly black maca, improves learning and memory.

8. Studies in Humans

Interest in maca has in increased worldwide during the last 10 years. This increased interest in maca has also been accompanied by some concern about safety. Piacente et al. (2002) [52] described the presence of (1R,3S)-1-methyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid (MTCA) in maca hypocotyls. On this finding, the authors made some generalizations about the action of MTCA suggesting that it can be toxic. These affirmations have motivated the French Agency for Sanitary Security (AFFSFA) issued an opinion about the risk for the health of the consumer using the pulverized roots of maca [53]. However, MTCA also occurs on
fruits like oranges and grapefruit and fruit juices [54], which are frequently used because of their favorable properties on health. MTCA has been described on the fermented garlic extract [55, 56], and its concentration increases with time, in turn increasing its antioxidant activity. Moreover, MTCA is detected in several foods, and in some, in concentrations relatively high (greater than the ones found by Piacente in maca) suggesting that claims are overestimated.

In a recent paper, several arguments indicate that MTCA in maca is safe [57]. In addition, maca is not mutagenic but it contains several beneficial compounds, some of which have anticarcinogenic properties [5, 58]. The consumption of maca must not generate concern, taking in account that, as mentioned in the French alert [53], it has not been reported any toxicity in the case of maca traditional consumption that requires a boiling process. MTCA is a natural constituent of several plants and on consumption of such plants there is no toxicity found. This suggests that as a multicomponent it may lose its adversity as drug action.

Furthermore, a recent study was designed to investigate health status in a population from the Peruvian central Andes (Carhuamayo, 4100 m) which traditionally consumes maca and compared it with a population from the same place which does not consume maca. The study, based on a survey, assessed maca consumption, sociodemographic aspects, health status, and fractures in men and women aged 35–75 years old. In a subsample were assessed the hepatic and kidney functions and hemoglobin values. From the sample studied, 80% of the population consumed maca. 85% of them consume maca for a nutritional purpose.

Maca is used since childhood and mainly after hypocotyls it is naturally dried. The consumption is mainly as juices, and the variety that they consume is a mixture of different colors of the hypocotyls. Maca consumption is associated with higher score in health status (Figure 2), lower rate of fractures, and lower scores of signs and symptoms of chronic mountain sickness. In addition, maca consumption is associated with low body mass index and low systolic blood pressure.

Hepatic and kidney function, lipidic profile, and glycemia were normal in the population consuming maca. In summary, this study demonstrated in a population traditionally using maca that consumption of this food is safe [4].

9. Maca and Sexual Function

Sexual dysfunctions are highly prevalent in our society worldwide, and the occurrence of sexual dysfunctions increases directly with age for both men and women [59]. They occur in 20–30% of men and 40–45% of women according to 18 descriptive epidemiological studies from around the world [60].

Most sexual problems relate to sexual desire (interest in sex) in both females and males and male erectile dysfunction (ED) [60]. Interest in medicinal plants to treat sexual dysfunctions has increased in the last 20 years [61].

Maca has been described to improve sexual behavior in experimental animals [13, 22, 23], although conflictive results may be observed [24]. Traditionally maca has been referred to as a plant to improve fertility [2] and as an energizer [3]. In a randomized study we were unable to demonstrate effect of maca on penile erection in apparently healthy adult men after 12 weeks of treatment with gelatinized maca compared with results using placebo [Gonzales, unpublished data].

Recently, a systematic review has been performed on effect of maca on sexual function in humans [62]. In this review, according to the authors only four randomized clinical trials (RCT) met all the inclusion criteria [49, 63–65].

According to the review, two RCTs suggested a significant positive effect of maca on sexual dysfunction or sexual desire in healthy menopausal women [49] or healthy adult men [63], respectively, while the other RCT according to the reviewers failed to show any effects in healthy cyclists. However, analyzing results from such study, authors showed that maca extract significantly improved the self-rated sexual desire score compared to the baseline test (P = 0.01), and compared to the placebo trial after supplementation (P = 0.03) [64]. The effect in this study was as early as 14 days of treatment which is significantly shorter that that showed with gelatinized maca in which effects were observed after 8 weeks of treatment.

A further RCT assessed the effects of maca in patients with mild erectile dysfunction using the International Index of Erectile Dysfunction-5 and showed significant effects on subjective perception of general and sexual well-being [65].

A study was not included in the systematic review because no placebo effect was assessed [66]. In such study, maca was administered in two doses (1.5 g/day and 3–0 g/day) to patients with selective-serotonin reuptake inhibitor-(SSRI-)induced sexual dysfunction. The Arizona Sexual Experience Scale (ASEX) and the Massachusetts General Hospital Sexual Function Questionnaire (MGH-SFQ) were used to measure sexual dysfunction.

Subjects on 3.0 g/day maca had a significant improvement in ASEX (from 22.8 ± 3.8 to 16.9 ± 6.2; z = −2.20,
showed that gelatinized maca reduced systolic and diastolic blood pressure after 12 weeks of treatment [3]. Moreover, maca significantly inhibited the hypertension relevant angiotensin I-converting enzyme (ACE) in vitro [69].

In a population traditionally consuming maca, systolic blood pressure was lower than in those not consuming maca [4]. Similarly, AST levels were similar in those consuming and those not consuming maca [4].

Maca contains high amounts of potassium [5]. Potassium is an important nutrient to reduce risk of hypertension [70] and as a primary metabolite may be useful in patients with hypertension. In addition other secondary metabolites may also be active to reduce blood pressure [69].

13. Maca and Osteoarthritis

In a randomized double-blind study on 95 patients with osteoarthritis, a combination of Uncaria guianensis (cat’s claw; 300 mg) and maca (1,500 mg) was administered twice a day for 8 weeks and compared with a treatment with glucosamine sulfate. Both treatments substantially improved pain, stiffness, and functioning in the patients [71]. However, as the study did not include a placebo control group, glucosamine effects remain unclear.

14. 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 [5]. Previous review data on in vivo and in vitro studies with maca indicate that its use is safe [5]. Further evidence shows that aqueous and methanolic extracts of maca do not display in vitro hepatotoxicity [72]. Moreover, freeze-dried aqueous extract of maca (1 g/kg BW) in mice did not reveal any toxic effect on the normal development of preimplanted mouse embryos [73].

Results in rats show that different types of maca (black, red, and yellow) have no acute toxicity at ≤17 g of dried hypocotyls/kg BW. Rats treated chronically for 84 days with 1 g/Kg BW showed no side effects and a histological picture of liver similar to that observed in controls [74]. 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, as referred above in a study in 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 [68]. This has not been confirmed in other studies [3, 4]. Data on population of 600 subjects in the Peruvian central Andes showed that maca consumption was safety and that health status was improved [4].

15. Final Comments

Consumption of Maca worldwide has significantly increased during the last 10 years. This is depicted in Figure 3 which presents data on maca export from Peru, the only country producing maca. During 2010, Peru exported maca for
entities. However, the active principles behind each 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 and appears to be promising as a nutraceutical in the prevention of several diseases. Scientific evidence showed effects on sexual behavior, fertility, mood, memory, osteoporosis, metabolism, and the treatment of some tumor entities. However, the active principles behind each effect are still unknown. Macamides have been described as novel compounds of maca that have not been found in any other plant species so far [13]. It is suggested that this lipid fraction of maca may be responsible for the increase in sexual behavior [13, 23]. Studies on testicular function, spermatogenesis, fertility, mood, memory, and prostatic hyperplasia [16, 35, 42, 75] were performed with aqueous extracts that contain only trace amounts of macamides [17]. This suggests that compounds other than macamides are responsible for these activities.

| Table 2: Semen variables before and 4 month after maca treatment. |
|---------------------------------------------------------------|
| Semen variable | Before maca N = 9 | After maca N = 9 | P value |
|------ |-----------------|-----------------|---------|
| Volume (mL) | 2.23 ± 0.28 | 2.91 ± 0.28 | <0.05 |
| pH | 7.47 ± 0.09 | 7.44 ± 0.07 | NS |
| Sperm count (10⁶/mL) | 67.06 ± 18.61 | 90.33 ± 20.46 | NS |
| Total sperm count (10⁶/mL) | 140.95 ± 31.05 | 259.29 ± 68.17 | <0.05 |
| Motile sperm count (10⁶/mL) | 87.72 ± 19.87 | 183.16 ± 47.84 | <0.05 |
| Sperm motility grade a (%) | 29.00 ± 5.44 | 33.65 ± 3.05 | NS |
| Sperm motility grade a + b (%) | 62.11 ± 3.64 | 71.02 ± 2.86 | <0.05 |
| Normal sperm morphology (%) | 75.50 ± 2.02 | 76.90 ± 1.23 | NS |

Data are mean ± standard error of the mean. N = number of subjects, NS: not significant, source: [67].

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References

[1] C. Quiroz and R. Aliaga, "Maca (Lepidium meyenii Walp.)," in Andean Roots and Tubers: Ahipa, Arracacha, Maca and Yacon. Promoting the Conservation and Use of Underutilized Neglected Crops, M. Hermann and J. Hellers, Eds., vol. 21, pp. 173–197, International Plant Genetic Resources Institute, Rome, Italy, 1997.
[2] B. Cobo, History of the New World, Biblioteca de Autores Españoles, Madrid, Spain, 1956.
[3] G. F. Gonzales, "Biological effects of Lepidium meyenii, maca, a plant from the highlands of Peru," in Natural Products, VK Singh, R Bhardwaj, JN Govil, and RK Sharma, Eds., vol. 15 of Recent Progress in Medicinal Plants, pp. 209–234, Studium Press, Houston, Tex, USA, 2006.
[4] G. F. Gonzales, “MACA: Del alimento perdido de los Incas al milagro de los Andes: Estudio de seguridad alimentaria y nutricional,” Seguранza Alimentar e Nutricional, Campinas, vol. 16-17, no. 1, pp. 16–36, 2010.
[5] L. G. Valerio and G. F. Gonzales, “Toxicological aspects of the South American herbs cat’s claw (Uncaria tomentosa) and maca (Lepidium meyenii): a critical synopsis,” Toxicological Reviews, vol. 24, no. 1, pp. 11–35, 2005.
[6] P. Cieza de León, Chronicle of Peru. First Part, Hakluyt Society, London, UK, 1553.
[7] H. Ruiz, Relaci´on hist´orica del viaje a los reinos del Per´u y Chile, 1777-1778, Academia de Ciencias Exactas, Físicas y Naturales, Madrid, Spain, 1952.
[8] K. Oerlemans, D. M. Barrett, C. B. Suades, R. Verkerk, and M. Dekker, "Thermal degradation of glucosinolates in red cabbage," Food Chemistry, vol. 95, no. 1, pp. 19–29, 2006.
[9] N. V. Matusheski, J. A. Juvik, and E. H. Jeffery, "Heating decreases epithiospecifier protein activity and increases sulforaphane formation in broccoli," Phytochemistry, vol. 65, no. 9, pp. 1273–1281, 2004.
[10] V. Dewanto, X. Wu, K. K. Adom, and R. H. Liu, “Thermal processing enhances the nutritional value of tomatoes by...
increasing total antioxidant activity,” *Journal of Agricultural and Food Chemistry*, vol. 50, no. 10, pp. 3010–3014, 2002.

[11] J. Tello, M. Hermann, and A. Calderón, “La maca (Lepidium meyenii Walp.) cultivo alimenticio potencial para las zonas altoandinas,” *BoL Lima*, vol. 14, pp. 59–66, 1992.

[12] A. Dini, G. Migliuolo, L. Rastrelli, P. Saturnino, and O. Schettino, “Chemical composition of Lepidium meyenii,” *Food Chemistry*, vol. 49, no. 4, pp. 347–349, 1994.

[13] B. L. Zheng, K. He, C. H. Kim et al., “Effect of a lipidic extract from Lepidium meyenii on sexual behavior in mice and rats,” *Urology*, vol. 55, no. 4, pp. 598–602, 2000.

[14] G. F. Gonzales, V. Vasquez, D. Rodriguez et al., “Effect of two different extracts of red maca in male rats with testosterone-induced prostatic hyperplasia,” *Asian Journal of Andrology*, vol. 9, no. 2, pp. 245–251, 2007.

[15] I. Cárdenas-Valencia, J. Nieto, M. Gasco et al., “Tropeolum tuberosum (Mashua) reduces testicular function: effect of different treatment times,” *Andrologia*, vol. 40, no. 6, pp. 352–357, 2008.

[16] C. Gonzales, J. Rubio, M. Gasco, J. Nieto, S. Yucra, and G. F. Gonzales, “Effect of short-term and long-term treatments with three ecotypes of Lepidium meyenii (MACA) on spermatogenesis in rats,” *Journal of Ethnopharmacology*, vol. 103, no. 3, pp. 448–454, 2006.

[17] M. M. McCollom, J. R. Villinski, K. L. McPhail, L. E. Craker, and S. Gafner, “Analysis of macamides in samples of Maca (Lepidium meyenii) by HPLC-UV-MS/MS,” *Phytochemical Analysis*, vol. 16, no. 6, pp. 463–469, 2005.

[18] M. Gonzera, J. Zhao, I. Muhammad, and I. A. Khan, “Chemical profiling and standardization of Lepidium meyenii (Maca) by reversed phase high performance liquid chromatography,” *Chemical and Pharmaceutical Bulletin*, vol. 50, no. 7, pp. 988–991, 2002.

[19] C. Clément, D. Díaz, I. Manrique et al., “Secondary metabolites in maca as affected by hypocotyl color, cultivation history, and site,” *Agronomy Journal*, vol. 102, no. 2, pp. 431–439, 2010.

[20] G. F. Gonzales, S. Miranda, J. Nieto et al., “Red maca (Lepidium meyenii) reduced prostate size in rats,” *Reproductive Biology and Endocrinology*, vol. 3, article 5, 2005.

[21] C. Clément, D. A. Díaz Grados, B. Avula et al., “Influence of colour type and previous cultivation on secondary metabolites in hypocotyls and leaves of maca (Lepidium meyenii Walpers),” *Journal of the Science of Food and Agriculture*, vol. 90, no. 5, pp. 861–869, 2010.

[22] A. F. G. Cicero, E. Bandieri, and R. Arlettii, “Lepidium meyenii Walp. improves sexual behaviour in male rats independently from its action on spontaneous locomotor activity,” *Journal of Ethnopharmacology*, vol. 75, no. 2–3, pp. 225–229, 2001.

[23] A. F. G. Cicero, S. Placente, A. Plaza, E. Sala, R. Arlettii, and C. Pizza, “Hexanic Maca extract improves rat sexual performance more effectively than methanolic and chloroformic Maca extracts,” *Andrologia*, vol. 34, no. 3, pp. 177–179, 2002.

[24] A. Lentz, K. Gravitt, C. C. Carson, L. Marson, and F. Giuliano, “Acute and chronic dosing of Lepidium meyenii (Maca) on male rat sexual behavior,” *Journal of Sexual Medicine*, vol. 4, no. 2, pp. 332–340, 2007.

[25] M. Canales, J. Aguilar, A. Prada, A. Marcelo, C. Huamán, and L. Carbajal, “Nutritional evaluation of Lepidium meyenii (maca) in albino mice and their descendants,” *Archivos Latinoamericanos de Nutricion*, vol. 50, no. 2, pp. 126–133, 2000 (Spanish).

[26] A. López-Fando, M. P. Gómez-Serranillos, I. Iglesias, O. Lock, U. P. Upamayta, and M. E. Carretero, “Lepidium peruvianum chacon restores homeostasis impaired by restraint stress,” *Phytotherapy Research*, vol. 18, no. 6, pp. 471–474, 2004.

[27] A. Tapia, C. López, A. Marcelo, and J. L. Aguilar, “The Maca (Lepidium meyenii) and their effect antistress in an animal model in mice,” *Acta Andina*, vol. 8, pp. 45–56, 2000 (Spanish).

[28] C. Gonzales, I. Cárdenas-Valencia, J. Leiva-Revilla, C. Anza-Ramírez, J. Rubio, and G. F. Gonzales, “Effects of different varieties of Maca (Lepidium meyenii) on bone structure in ovariecetomized rats,” *Forschende Komplementarmedizin*, vol. 17, no. 3, pp. 137–143, 2010.

[29] Y. Zhang, L. Yu, M. Ao, and W. Jin, “Effect of ethanol extract of Lepidium meyenii Walp. on osteoporosis in ovariecetomized rat,” *Journal of Ethnopharmacology*, vol. 105, no. 1–2, pp. 274–279, 2006.

[30] A. Pino-Figueroa, D. Nguyen, and T. J. Maher, “Neuroprotective effects of Lepidium meyenii (Maca),” *Annals of the New York Academy of Sciences*, vol. 1199, pp. 77–85, 2010.

[31] C. Gonzales-Castañeda and G. F. Gonzales, “Hypocotyls of Lepidium meyenii (maca), a plant of the Peruvian highlands, prevent ultraviolet A-, B-, and C-induced skin damage in rats,” *Photodermatology Photoimmunology and Photomedicine*, vol. 24, no. 1, pp. 24–31, 2008.

[32] R. Véchea, J. Orolin, N. Škotovtov et al., “The influence of maca (Lepidium meyenii) on antioxidant status, lipid and glucose metabolism in rat,” *Plant Foods for Human Nutrition*, vol. 62, no. 2, pp. 59–63, 2007.

[33] A. C. Ruiz-Luna, S. Salazar, N. J. Aspajo, J. Rubio, M. Gasco, and G. F. Gonzales, “Lepidium meyenii (Maca) increases litter size in normal adult female mice,” *Reproductive Biology and Endocrinology*, vol. 3, article no. 16, 2005.

[34] G. F. Gonzales, M. Gasco, A. Malheiros-Pereira, and C. Gonzales-Castañeda, “Antagonistic effect of Lepidium meyenii (red maca) on prostatic hyperplasia in adult mice,” *Andrologia*, vol. 40, no. 3, pp. 179–185, 2008.

[35] J. Rubio, M. Caldas, S. Dávila, M. Gasco, and G. F. Gonzales, “Effect of three different cultivars of Lepidium meyenii (Maca) on learning and depression in ovariecetomized mice,” *BMC Complementary and Alternative Medicine*, vol. 6, article no. 23, 2006.

[36] J. Rubio, H. Dang, M. Gong, X. Liu, S. L. Chen, and G. F. Gonzales, “Aqueous and hydroalcoholic extracts of Black Maca (Lepidium meyenii) improve scopolamine-induced memory impairment in mice,” *Food and Chemical Toxicology*, vol. 45, no. 10, pp. 1882–1890, 2007.

[37] X. Liu, J. Rubio, W. Qiong et al., “Aqueous extract of black maca (Lepidium meyenii) on memory impairment induced by ovariectomy in mice,” *Evidence-Based Complementary and Alternative Medicine*, vol. 2011, Article ID 253958, 7 pages, 2011.

[38] C. J. Alvarez, *Utilización de diferentes niveles de Maca en la fertilidad de cobayos*, Bachelor thesis, Faculty of Agriculture and Cattle Sciences, Universidad Nacional Daniel Alcides Carrión, Pasco, Peru, 1993.

[39] K. J. Lee, K. Dabrowski, J. Rinchard, C. Gomez, L. Guz, and C. Vilchez, “Supplementation of maca (Lepidium meyenii) tuber meal in diets improves growth rate and survival of rainbow trout Oncorhynchus mykiss (Walbaum) alevins and juveniles,” *Aquaculture Research*, vol. 35, no. 3, pp. 215–223, 2004.

[40] K. J. Lee, K. Dabrowski, M. Sandoval, and M. J. S. Miller, “Activity-guided fractionation of phytochemicals of maca meal, their antioxidant activities and effects on growth, feed utilization, and survival in rainbow trout (Oncorhynchus mykiss) juveniles,” *Aquaculture*, vol. 244, no. 1–4, pp. 293–301, 2005.
Evidence-Based Complementary and Alternative Medicine

[41] C. Clément, J. Kneubühl, A. Urwyler, U. Witschi, and M. Kreuzer, “Effect of maca supplementation on bovine sperm quantity and quality followed over two spermatogenic cycles,” 

[42] G. F. Gonzales, M. Gasco, A. Córdova, A. Chung, J. Rubio, and L. Villegas, “Effect of Lepidium meyenii (Maca) on spermatogenesis in male rats acutely exposed to high altitude (4340 m),” 

[43] J. Rubio, M. I. Riquerros, M. Gasco, S. Yucra, S. Miranda, and G. F. Gonzales, “Lepidium meyenii (Maca) reversed the lead acetate induced-Damage on reproductive function in male rats,” 

[44] E. Bustos-Obregón, S. Yucra, and G. F. Gonzales, “Lepidium meyenii (Maca) reduces spermatogenic damage induced by a single dose of malathion in mice,” 

[45] M. Gasco, L. Villegas, S. Yucra, J. Rubio, and G. F. Gonzales, “Dose-response effect of Red Maca (Lepidium meyenii) on benign prostatic hyperplasia induced by testosterone enantate,” 

[46] Q. Chen, S. Ganapathy, K. P. Singh, S. Shankar, and R. K. Srivastava, “Resveratrol induces growth arrest and apoptosis through activation of FOXO transcription factors in prostate cancer cells,” 

[47] I. A. Siddiqui, M. Asim, B. B. Hafeez, V. M. Adhami, R. S. Tarapore, and H. Mukhtar, “Green tea polyphenol EGCG blunts androgen receptor function in prostate cancer,” 

[48] P. Bogani, F. Simonini, M. Iriti et al., “Lepidium meyenii (Maca) does not exert direct androgenic activities, ” 

[49] N. A. Brooks, G. Wilcox, K. Z. Walker, J. F. Ashton, M. B. Cox, and L. Stojanovska, “Beneficial effects of Lepidium meyenii (Maca) on psychological symptoms and measures of sexual dysfunction in postmenopausal women are not related to estrogen or androgen content,” 

[50] M. Oshima, Y. Gu, and S. Tsukada, “Effects of Lepidium meyenii Walp and Jatropha macrantha on blood levels of estradiol-17β, progesterone, testosterone and the rate of embryo implantation in mice,” 

[51] G. F. Gonzalez, A. Córdova, K. Vega, A. Chung, A. Villena, and C. Gómez, “Effect of Lepidium meyenii (Maca), a root with aphrodisiac and fertility-enhancing properties, on serum reproductive hormone levels in adult healthy men,” 

[52] S. Piacente, V. Carbone, A. Plaza, A. Zampelli, and C. Pizza, “Investigation of the tuber constituents of maca (Lepidium meyenii Walp),” 

[53] APSSA, “From the French Agency of Sanitary Security on foods relative to the risk assessment for health by consuming pulverized maca roots or as alimentary supplement,” 

[54] T. Herraz and J. Galisteo, “Tetrahydro-β-carboline alkaloids occur in fruits and fruit juices. Activity as antioxidants and radical scavengers,” 

[55] E. Sato, M. Kohno, and Y. Niwano, “Increased level of tetrahydro-β-carboline derivatives in short-term fermented garlic,” 

[56] M. Ichikawa, J. Yoshida, N. Ide, T. Sasaoka, H. Yamaguchi, and K. Ono, “Tetrahydro-β-carboline derivatives in aged garlic extract show antioxidant properties,” 

[57] G. F. Gonzales and C. Gonzales-Castañeda, “The methyltetrahydro-β-carbolines in Maca (Lepidium meyenii),” 

[58] G. F. Gonzales and L. G. Valerio, “Medicinal plants from Peru: a review of plants as potential agents against cancer,” 

[59] L. R. Derogatis and A. L. Burnett, “The epidemiology of sexual dysfunctions,” 

[60] R. W. Lewis, K. S. Fugl-Meyer, G. Corona et al., “Definitions/epidemiology/risk factors for sexual dysfunction,” 

[61] D. MacKay, “Nutrients and botanicals for erectile dysfunction: examining the evidence,” 

[62] B. C. Shin, M. S. Lee, E. J. Yang, H. S. Lim, and E. Ernst, “Maca (L. meyenii) for improving sexual function: a systematic review,” 

[63] G. F. Gonzales, A. Córdova, K. Vega et al., “Effect of Lepidium meyenii (MACA) on sexual desire and its absent relationship with serum testosterone levels in adult healthy men,” 

[64] M. Stone, A. Ibarra, M. Roller, A. Zangara, and E. Stevenson, “A pilot investigation into the effect of maca supplementation on physical activity and sexual desire in sportsmen,” 

[65] T. Zienico, A. E. G. Cicero, L. Valmorri, M. Mercuriali, and E. Bercovich, “Subjective effects of Lepidium meyenii (Maca) extract on well-being and sexual performances in patients with mild erectile dysfunction: a randomised, double-blind clinical trial,” 

[66] C. M. Dording, L. Fisher, G. Papakostas et al., “A double-blind, randomized, pilot dose-finding study of maca root (L. meyenii) for the management of SSRI-induced sexual dysfunction,” 

[67] G. F. Gonzales, A. Córdova, C. Gonzales, A. Chung, K. Vega, and A. Villena, “Improved sperm count after administration of Lepidium meyenii (maca) in adult men,” 

[68] K. Valentonová, D. Stejskal, J. Bartek et al., “Maca (Lepidium meyenii) and yacon (Smallanthus sonchifolius) in combination with silymarin as food supplements: in vivo safety assessment,” 

[69] L. G. Ranilla, Y. I. Kwon, E. Apostolidis, and K. Shetty, “Phenolic compounds, antioxidant activity and in vitro inhibitory potential against key enzymes relevant for hyperglycemia and hypertension of commonly used medicinal plants, herbs and spices in Latin America,” 

[70] J.--S. Lee, J. Park, and J. Kim, “Dietary factors related to hypertension risk in korean adults-data from the Korean national health and nutrition examination survey III,” 

[71] R. W. Lewis, K. S. Fugl-Meyer, G. Corona et al., “Definitions/epidemiology/risk factors for sexual dysfunction,” 

[72] D. MacKay, “Nutrients and botanicals for erectile dysfunction: examining the evidence,” 

[73] B. C. Shin, M. S. Lee, E. J. Yang, H. S. Lim, and E. Ernst, “Maca (L. meyenii) for improving sexual function: a systematic review,” 

[74] G. F. Gonzales, A. Córdova, K. Vega et al., “Effect of Lepidium meyenii (MACA) on sexual desire and its absent relationship with serum testosterone levels in adult healthy men,” 

[75] M. Stone, A. Ibarra, M. Roller, A. Zangara, and E. Stevenson, “A pilot investigation into the effect of maca supplementation on physical activity and sexual desire in sportsmen,” 

[76] T. Zienico, A. E. G. Cicero, L. Valmorri, M. Mercuriali, and E. Bercovich, “Subjective effects of Lepidium meyenii (Maca) extract on well-being and sexual performances in patients with mild erectile dysfunction: a randomised, double-blind clinical trial,” 

[77] C. M. Dording, L. Fisher, G. Papakostas et al., “A double-blind, randomized, pilot dose-finding study of maca root (L. meyenii) for the management of SSRI-induced sexual dysfunction,” 

[78] G. F. Gonzales, A. Córdova, C. Gonzales, A. Chung, K. Vega, and A. Villena, “Improved sperm count after administration of Lepidium meyenii (maca) in adult men,” 

[79] K. Valentonová, D. Stejskal, J. Bartek et al., “Maca (Lepidium meyenii) and yacon (Smallanthus sonchifolius) in combination with silymarin as food supplements: in vivo safety assessment,” 

[80] L. G. Ranilla, Y. I. Kwon, E. Apostolidis, and K. Shetty, “Phenolic compounds, antioxidant activity and in vitro inhibitory potential against key enzymes relevant for hyperglycemia and hypertension of commonly used medicinal plants, herbs and spices in Latin America,” 

[81] J.--S. Lee, J. Park, and J. Kim, “Dietary factors related to hypertension risk in korean adults-data from the Korean national health and nutrition examination survey III,”
[71] K. Mehta, J. Gala, S. Bhasale et al., “Comparison of glucosamine sulfate and a polyherbal supplement for the relief of osteoarthritis of the knee: a randomized controlled trial [ISRCTN25438351],” *BMC Complementary and Alternative Medicine*, vol. 7, article no. 34, 2007.

[72] K. Valentová, D. Buckiová, V. Křen, J. Pěknicová, J. Ulrichová, and V. Šimánek, “The in vitro biological activity of *Lepidium meyenii* extracts,” *Cell Biology and Toxicology*, vol. 22, no. 2, pp. 91–99, 2006.

[73] G. D’Arrigo, V. Benavides, and J. Pino, “Preliminary evaluation effect of *Lepidium meyenii* Walp on the embryo development of mouse,” *Revista Peruana de Biología*, vol. 11, pp. 103–106, 2004.

[74] M. Gasco, J. Aguilar, and G. F. Gonzales, “Effect of chronic treatment with three varieties of *Lepidium meyenii* (Maca) on reproductive parameters and DNA quantification in adult male rats,” *Andrologia*, vol. 39, no. 4, pp. 151–158, 2007.

[75] F. Chung, J. Rubio, C. Gonzales, M. Gasco, and G. F. Gonzales, “Dose-response effects of *Lepidium meyenii* (Maca) aqueous extract on testicular function and weight of different organs in adult rats,” *Journal of Ethnopharmacology*, vol. 98, no. 1-2, pp. 143–147, 2005.